SUBSTITUTED 7-AZABICYCLES AND THEIR USE AS OREXIN RECEPTOR MODULATORS

CROSS REFERENCE TO RELATED APPLICATIONS

This application claims the benefit of U.S. Provisional Application No. 61/780,428, filed March 13, 2013, which is incorporated herein by reference in its entirety.

TECHNICAL FIELD

The present invention is directed to substituted 7-azabicyclic compounds, pharmaceutical compositions comprising them, methods of making them, and methods of using them for the modulation of the orexin receptor for the treatment of disease states, disorders, and conditions mediated by orexin receptor activity.

BACKGROUND

Orexin/hypocretin signaling is mediated by two receptors and two peptide agonists. The peptides (orexin-A and orexin-B) are cleavage products of the same gene, pre-pro orexin. In the central nervous system, neurons producing pre-pro orexin are found solely in the perifornical nucleus, the dorsal hypothalamus, and the lateral hypothalamus (Peyron et al., 1998, *J. Neurosci.* 18: 9996-10015). Orexigenic cells in these regions project to many areas of the brain, extending rostrally to the olfactory bulbs and caudally to the spinal cord (Van den Pol, 1999, *J. Neurosci.* 19: 3171-3182).

The orexins bind to two high affinity receptors, referred to as orexin-1 and orexin-2 receptors. Orexin-1 and orexin-2 receptors are G-protein-coupled, seven transmembrane receptors that share over 64% amino acid sequence identity with one another. Both receptors are generally excitatory, the common cellular response to orexin-induced receptor activation being increases in intracellular calcium. Homology between the species orthologs is high and there are no known pharmacological differences. Orexin-A and -B are usually considered equal ligands for orexin-2 receptor but orexin-B is thought to be 5- to 100-fold weaker ligand than orexin-A at the orexin-1 receptor (Sakurai et al., 1998, *Cell* 92: 573-585; Ammoun et al., 2003, *J. Pharmacol. Exp. Ther.* 305: 507-514).

Many regions of the brain have fairly selective expression of the orexin-1 or orexin-2 receptors (Marcus et al., 2001, *J. Comp Neurology* 435, 6-25; Trivedi et al., 1998, *FEBS Letters*, 438, 71-75). Orexin-1 receptors are selective for the limbic system (bed nucleus of the stria terminalis and amygdala), cingulate cortex and noradrenergic neurons in the locus coeruleus.

Conversely, the orexin-2 receptor is almost the exclusive orexin receptor in the histaminergic neurons in the tuberomammilary nucleus which play a critical role in wake promotion; in paraventricular neurons and the parabrachial nucleus. In other brain regions like the dorsal raphe, the ventral tegmental area or the prefontal cortex both receptors are coexpressed.

The broad CNS distribution of cells producing orexin, as well as cells expressing the orexin receptors, suggests involvement of orexin in a number of physiological functions, including feeding and metabolism, regulation of wakefulness and sleep, sympathetic activation and stress response (de Lecea, 2012, *Progress in Brain Research*, 198, 15-24; Kukkonen, 2013, *Am J. Physiol. Cell Physiol.*, 304, C2-C32). Orexin also plays a key role regulating motivation and reward associated with food intake and with drugs of abuse (Mahler et al., 2012, *Progress in Brain Research*, 198, 79-121).

Several lines of evidence indicate that the orexin system is an important modulator of arousal. Rodents administered orexin intracerebroventricularly spend more time awake (Piper et al., 2000, *J. Neurosci.* 12: 726-730. Orexin-mediated effects on arousal have been linked to orexin neuronal projections to histaminergic neurons in the tuberomammillary nucleus (Yamanaka et al., 2002, *Biochem. Biophys. Res. Comm.* 290: 1237-1245). Rodents whose pre-pro orexin gene has been knocked out, or whose orexigenic neurons have been killed, display altered sleep/wake cycles similar to narcolepsy (Chemelli et al., 1999, *Cell* 98: 437-451; Hara et al., 2001, *Neuron* 30: 345-354). Dog models of narcolepsy have been shown to have mutant or non-functional orexin-2 receptors (Lin et al., 1999, *Cell* 98: 365-376). Orexin signaling as a target for sleep-promoting therapies was further validated clinically by findings of attenuated orexin levels and loss of orexinergic neurons in human narcoleptic patients (Mignot et al., 2001, *Am. J. Hum. Genet.* 68: 686-699; Minot & Thorsby, 2001, *New England J. Med.* 344: 692) or, in rare cases, to mutations in the orexin-2 gene (Peyron et al., 2000, *Nature Med.* 6: 991-997). Disorders of the sleep-wake cycle are therefore likely targets for orexin-2 receptor modulator activity. Examples of sleep-wake disorders that may be treated by agonists or other modulators that up-regulate orexin-2 receptor-mediated processes include narcolepsy, jet lag (sleepiness) and sleep disorders secondary to neurological disorders such as depression. Examples of disorders that may be treated by antagonists or other modulators that down-regulate orexin-2 receptor-mediated processes include insomnia, restless leg syndrome, jet lag (wakefulness) and sleep disorders secondary to neurological disorders such as mania, schizophrenia, pain syndromes and the like.

Evidence has accumulated to demonstrate a clear involvement of orexin signaling in reward pathways associated with drug dependence (Mahler et al., 2012, *Progress in Brain*

Research, 198, 79-121). Orexinergic neurons send projections to the ventral tegmental area and other brain regions involved in reward processing. Orexin ligands mediate reward behavior, and antagonizing these effects with a selective orexin-1 receptor antagonist in various preclinical model of addiction has suggested that these actions are mediated through orexin-1 receptor. Specifically, a selective orexin-1 antagonist attenuates morphine conditioned place preference and reinstatement (Harris et al., 2005, *Nature*, 437, 556-5599; Narita et al., 2006, *J Neurosci.*,26, 398-405; Harris et al., 2007, *Behav Brain Res*, 183, 43-51), stress-induced cocaine reinstatement, cocaine-induced behavioral and synaptic plasticity (Borgland et al., 2006, *Neuron*, 49, 589-601), and intake and cue and stress-induced reinstatement of ethanol (Lawrence et al., 2006, *Br J Pharmacol*, 148, 752-759), in addition to attenuating precipitated morphine withdrawal (Sharf et al., 2008, *Biol Psychiatry*, 64, 175-183) and nicotine self-administration (Hollander et al., 2008, *Proc Natl Acad Sci U S A.*, 105, 19480-19485). Another recent study has also suggested a role for OX2R (Shoblock et al., 2011, *Psychopharmacology*, 215, 191-203).

Orexin's role in more complex emotional behavior is also emerging (Johnson et al., 2012, *Progress in Brain Research*, 198, 133-161). Changes in orexin levels in patients with panic and posttraumatic stress disorders have been noted as have changes in the prevalence of anxiety behaviors in narcoleptic patients (Johnson et al., 2010, *Nature Medicine*, 16, 111-115; Fortuyn et al., 2010, *General Hospital Psychiatry*, 32, 49–56; Strawn et al., 2010, *Psychoneuroendocrinology*, 35, 1001–1007). Lactate infusion or acute hypercapnia , which causes panic in humans, and are used as an animal model of panic, activates orexin neurons in the perifornical hypothalamus. This activation correlates with anxiety in the social interaction test or open field test. Blocking orexin signaling with either siRNA or selective orexin-1 receptor antagonists attenuates panic-like responses to lactate (Johnson et al., 2010, *Nature Medicine*, 16, 111-115; Johnson et al., 2012, *Neuropsychopharmacology*, 37, 1911, 1922).

Cerebral spinal fluid (CSF) levels of orexin are lower in depressed or suicidal patients, and the level of orexin inversely correlates with illness severity (Brundin et al., 2007, *European Neuropsychopharmacology*, 17, 573-579; Salomon et al., 2003, *Biol Psychiatry*,54, 96-104). A positive correlation between orexin-1 receptor mRNA in the amygdala and depressive behavior in the forced swim test in mice has been reported (Arendt, 2013, *Behavioral Neuroscience*, 127, 86-94).

The orexin system also interacts with brain dopamine systems. Intracerebroventricular injections of orexin in mice increase locomotor activity, grooming and stereotypy; these behavioral effects are reversed by administration of D2 dopamine receptor antagonists (Nakamura et al., 2000, *Brain Res.* 873: 181-187). Therefore, orexin receptor modulators may

be useful to treat various neurological disorders; e.g., agonists or up-regulators to treat catatonia, antagonists or down-regulators to treat Parkinson's disease, Tourette's syndrome, anxiety, delerium and dementias.

Orexins and their receptors have been found in both the myenteric and submucosal plexus of the enteric nervous system, where orexins have been shown to increase motility *in vitro* (Kirchgessner & Liu, 1999, *Neuron* 24: 941-951) and to stimulate gastric acid secretion *in vitro* (Takahashi et al., 1999, *Biochem. Biophys. Res. Comm.* 254: 623-627). Orexin effects on the gut may be driven by a projection via the vagus nerve (van den Pol, 1999, *supra*), as vagotomy or atropine prevent the effect of an intracerebroventricular injection of orexin on gastric acid secretion (Takahashi et al., 1999, *supra*). Orexin receptor antagonists or other down-regulators of orexin receptor-mediated systems are therefore potential treatments for ulcers, irritable bowel syndrome, diarrhea and gastroesophageal reflux.

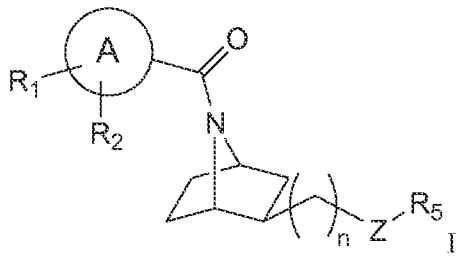
Body weight may also be affected by orexin-mediated regulation of appetite and metabolism. Some effects of orexin on metabolism and appetite may be mediated in the gut, where, as mentioned, orexins alter gastric motility and gastric acid secretion. Orexin antagonists therefore are likely to be useful in treatment of overweight or obesity and conditions related to overweight or obesity, such as insulin resistance/type II diabetes, hyperlipidemia, gallstones, angina, hypertension, breathlessness, tachycardia, infertility, sleep apnea, back and joint pain, varicose veins and osteoarthritis. Conversely, orexin agonists are likely to be useful in treatment of underweight and related conditions such as hypotension, bradycardia, ammenorrhea and related infertility, and eating disorders such as anorexia and bulimia.

Intracerebroventricularly administered orexins have been shown to increase mean arterial pressure and heart rate in freely moving (awake) animals (Samson et al., 1999, *Brain Res.* 831: 248-253; Shirasaka et al., 1999, *Am. J. Physiol.* 277: R1780-R1785) and in urethane-anesthetized animals (Chen et al., 2000, *Am. J. Physiol.* 278: R692-R697), with similar results. Orexin receptor agonists may therefore be candidates for treatment of hypotension, bradycardia and heart failure related thereto, while orexin receptor antagonists may be useful for treatment of hypertension, tachycardia and other arrhythmias, angina pectoris and acute heart failure.

From the foregoing discussion, it can be seen that the identification of orexin receptor modulators, will be of great advantage in the development of therapeutic agents for the treatment of a wide variety of disorders that are mediated through these receptor systems.

SUMMARY

The present invention is directed to compounds of Formula I:



wherein ring A is phenyl, naphthalenyl, pyridyl, quinolinyl, isoquinolinyl, imidazopyridyl, furanyl, thiazolyl, isoxazolyl, pyrazolyl, imidazothiazolyl, benzimidazolyl, or indazolyl; R_1 is H, alkyl, alkoxy, hydroxyalkylene, OH, halo, phenyl, triazolyl, oxazolyl, isoxazolyl, pyridyl, pyrimidinyl, pyrazinyl, pyridazinyl, piperazinyl, pyrazolyl, oxadiazolyl, pyrrolidinyl, thiophenyl, morpholinyl, or dialkylamino, wherein phenyl, triazolyl, oxazolyl, isoxazolyl, pyridyl, pyrimidinyl, pyrazinyl, pyridazinyl, piperazinyl, pyrazolyl, oxadiazolyl, pyrrolidinyl, thiophenyl, or morpholinyl is optionally substituted with up to two substituents selected from halo and alkyl; R_2 is H, alkyl, alkoxy, hydroxyalkylene, or halo; Z is NH, N-alkyl, or O; R_5 is pyridyl, pyrimidinyl, pyrazinyl, pyridazinyl, quinazolinyl, quinoxalinyl, pyrazolyl, thiazolyl, thiadiazolyl, benzoxazolyl, imidazopyrazinyl, triazolopyrazinyl, optionally substituted with one or two substituents independently selected from the group consisting of alkyl, cyano, alkyl carboxylate, alkoxy, and halo; and n is 0 or 1. Enantiomers and diastereomers of the compounds of Formula I are also described, as well as the pharmaceutically acceptable salts.

Methods of making the compounds of Formula I are also described. The invention also relates to pharmaceutical compositions comprising therapeutically effective amounts of compounds of Formula I. Methods of using the compounds of the invention are also within the scope of the invention.

BRIEF DESCRIPTION OF DRAWINGS

Figure 1 depicts a Powder X-Ray Diffraction (PXRD) pattern for one embodiment of the invention, Example 238, Form 1.

Figure 2 depicts a Powder X-Ray Diffraction (PXRD) pattern for one embodiment of the invention, Example 238, Form 2.

DETAILED DESCRIPTION OF ILLUSTRATIVE EMBODIMENTS

The invention may be more fully appreciated by reference to the following description, including the following glossary of terms and the concluding examples.

The term "alkyl" refers to a straight- or branched-chain alkyl group having from 1 to 12 carbon atoms in the chain. In some embodiments, an alkyl group is a C_1-C_6 alkyl group. In some

embodiments, an alkyl group is a C_1-C_4 alkyl group. Examples of alkyl groups include methyl (Me) ethyl (Et), n-propyl, isopropyl, butyl, isobutyl, sec-butyl, tert-butyl (tBu), pentyl, isopentyl, tert-pentyl, hexyl, isohexyl, and groups that in light of the ordinary skill in the art and the teachings provided herein would be considered equivalent to any one of the foregoing examples. Alkyl groups of the invention can be optionally substituted with, for example, one or more halogen atoms. One exemplary substitutent is fluoro. Certain substituted alkyl groups of the invention include trihalogenated alkyl groups such as trifluoromethyl groups.

Alkyl groups of the invention can also refer to "cycloalkyl" moieties. Cycloalkyl refers to monocyclic, non-aromatic hydrocarbon groups having from 3 to 7 carbon atoms. Examples of cycloalkyl groups include, for example, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, 1-methylcyclopropyl, 2-methylcyclopentyl, and the like.

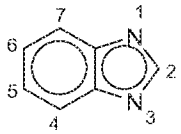
The term "alkoxy" includes a straight chain or branched alkyl group with a terminal oxygen linking the alkyl group to the rest of the molecule. In some embodiments, an alkoxy group is a C_1-C_6 alkoxy group. In some embodiments, an alkoxy group is a C_1-C_4 alkoxy group. Alkoxy includes methoxy, ethoxy, propoxy, isopropoxy, butoxy, t-butoxy, pentoxy and so on. Alkoxy groups of the inventions can be optionally substituted with, for example, one or more halogen atoms (haloalkoxy). One exemplary substitutent is fluoro. Preferred substituted alkoxy groups of the invention are substituted with one, two, or three halogen atoms, for example, –$OCHCF_2$.

The term "alkyl carboxylate" refers to the group –(C=O)O-alkyl, where alkyl is as defined above.

The term "amino" represents NH_2. The term "dialkylamino" represents the moiety wherein each H of the amino group is replaced by an alkyl group. These alkyl groups ca be the same or different. Preferred alkyl groups are the C_{1-6}alkyl groups. Examples of dialkyl amino groups include dimethylamino, diethylamino, diisopropylamino, and the like. Other examples include methylethylamino, methylisopropylamino, and the like.

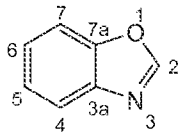
The term "aryl ring" represents" a mono- or bi-cyclic aromatic, hydrocarbon ring structure. Aryl rings can have 6 or 10 carbon atoms in the ring.

The term "benzimidazolyl" represents the following moiety:



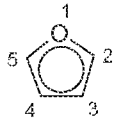
The benzimidazolyl moiety can be attached through any one of the 1-, 2-, 3-, 4-, 5-, 6-, or 7-position atoms and is optionally substituted with alkyl or halo or alkoxy groups.

The term "benzoxazolyl" represents the following moiety:



The benoxazolyl moiety can be attached through any one of the 2-, 4-, 5-, 6-, or 7-position carbon atoms and is optionally substituted with alkyl or halo or alkoxy groups.

The term "furanyl" represents the following moiety:



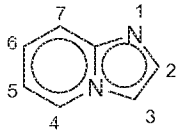
The furanyl moiety can be attached through any one of the 2-, 3-, 4-, or 5-position carbon atoms.

The term "halogen" represents chlorine, fluorine, bromine, or iodine. The term "halo" represents chloro, fluoro, bromo, or iodo.

The term "heteroaryl ring" represents a mono-or bicyclic aromoatic ring structure including carbon atoms as well as up to four heteroatoms selected from nitrogen, oxygen, and sulfur. Heteroaryl rings can include a total of 5, 6, 9, or 10 ring atoms.

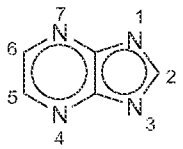
The term "hydroxyalkylene" represents an alkyl group, terminally substituted with OH. Examples of hydroxyalkylene moieties include $-CH_2$-OH, -CH_2CH_2-OH, -$CH_2CH_2CH_2$-OH, and the like.

The term "imidazopyridyl" represents the following moiety:



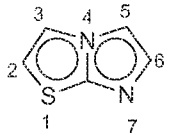
The imidazopyridyl moiety can be attached through any one of the 2-, 3-, 4-, 5-, 6-, or 7-position carbon atoms and is optionally substituted with alkyl or halo or alkoxy groups.

The term "imidazopyrazinyl" represents the following moiety:



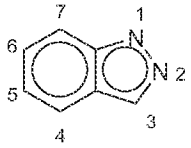
The imidazopyrazinyl moiety can be attached through any one of the 2-, 5-, or 6-position carbon atoms.

The term "imidazothiazolyl" represents the following moiety:



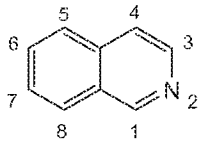
The imidazothiazolyl moiety can be attached through any one of the 2-, 3-, 5-, or 6-position carbon atoms.

The term "indazolyl" represents the following moiety:



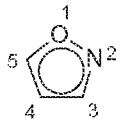
The indazolyl moiety can be attached through any one of the 1-, 3-, 4-, 5-, 6-, or 7-position atoms and is optionally substituted with alkyl or halo or alkoxy groups.

The term "isoquinolinyl" represents the following moiety:



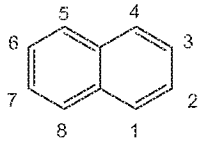
The isoquinolinyl moiety can be attached through any one of the 1-, 3-, 4-, 5-, 6-, 7-, or 8-position carbon atoms and is optionally substituted with alkyl or halo or alkoxy groups.

The term "isoxazolyl" represents the following moiety:



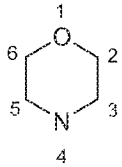
The isoxazolyl moiety can be attached through any one of the 3-, 4-, or 5-position carbon atoms. Isoxazolyl groups of the invention can be optionally substituted with, for example, one or two alkyl groups, for example, one or two methyl groups.

The term "naphthalenyl" represents the following moiety:



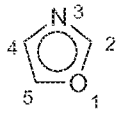
The naphthalenyl moiety can be attached through any one of the 1-, 2-, 3-, 4-, 5-, 6-, 7-, or 8-position carbon atoms and is optionally substituted with alkyl or halo or alkoxy groups.

The term "morpholinyl" represents the following moiety:



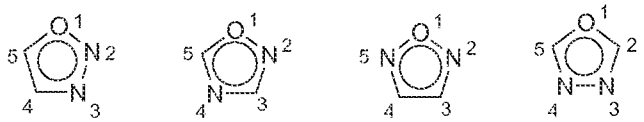
The 4-position nitrogen atom may be substituted with H or alkyl, for example methyl. The 4-position nitrogen can also be protected with a nitrogen protecting group such as a butyl-oxycarbonyl (-Boc). The morpholinyl moiety can be attached through any one of the 2-, 3-, 4-, 5-, or 6-position atoms. The morpholinyl ring is optionally substituted with halo or alkyl groups.

The term "oxazolyl" represents the following moiety:



The oxazolyl moiety can be attached through any one of the carbon atoms. Oxazolyl groups of the invention can be optionally substituted with, for example, one or two alkyl groups, for example, one or two methyl groups.

The term "oxadiazolyl" represents a 1,2,3-oxadiazole, 1,2,4-oxadiazole, 1,2,5-oxadiazole, or 1,3,4-oxadiazole moiety:



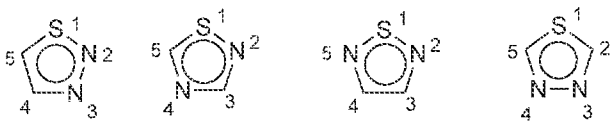
The oxadiazolyl moieties can be attached through any one of the carbon or nitrogen atoms. Within the scope of the invention, "oxadiazolyl" groups can be substituted with an alkyl group, preferably a methyl group.

The term "thiazolyl" represents the following moiety:



The thiazolyl moiety can be attached through any one of the carbon atoms. Thiazolyl groups of the invention can be optionally substituted with, for example, one or two alkyl groups, for example, one or two methyl groups.

The term "thiadiazolyl" represents a 1,2,3-thiadiazole, 1,2,4-thiadiazole, 1,2,5-thiadiazole, or 1,3,4-thiadiazole moiety:



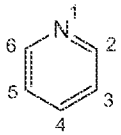
The thiadiazolyl moieties can be attached through any one of the carbon or nitrogen atoms. Within the scope of the invention, "thiadiazolyl" groups can be substituted with an alkyl group, preferably a methyl group.

The term "phenyl" represents the following moiety:



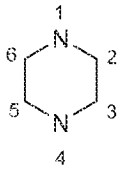
Phenyl groups of the inventions can be optionally substituted with, for example, one or more halogen atoms (halo-phenyl) or alkyl or alkoxy groups. Exemplary substitutents are fluoro, bromo, and chloro. Preferred substituted phenyl groups of the invention are substituted with one, two, or three halogen atoms.

The term "pyridyl" represents the following moiety:



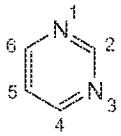
The pyridyl moiety can be attached through any one of the 2-, 3-, 4-, 5-, or 6-position carbon atoms. Pyridyl groups of the invention can be optionally substituted with, for example, one or more halo or alkyl groups, for example, one or two methyl groups.

The term "piperazinyl" represents the following moiety:



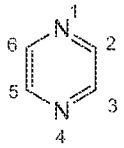
The piperazinyl moiety can be attached through any one of the 1-, 2-, 3-, 4-, 5-, or 6-position atoms. Any one of the nitrogen atoms of the piperazinyl moiety can be substituted with H or alkyl, for example, methyl.

The term "pyrimidinyl" represents the following moiety:



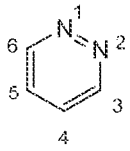
The pyrimidinyl moiety can be attached through any one of the 2-, 4-, 5-, or 6-position carbon atoms. Within the scope of the invention, "pyrimidinyl" groups of the invention can be substituted with halogen or alkyl, for example fluoro or methyl or trifluoromethyl.

The term "pyrazinyl" represents the following moiety:



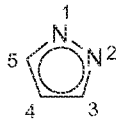
The pyrazinyl moiety can be attached through any one of the 2-, 3-, 5-, or 6-position carbon atoms and may be optionally substituted with alkyl, alkoxy or halo.

The term "pyridazinyl" represents the following moiety:



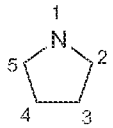
The pyridazinyl moiety can be attached through any one of the 3-, 4-, 5-, or 6-position carbon atoms and may be substituted with alkyl, alkoxy or halo groups.

The term "pyrazolyl" represents the following moiety:



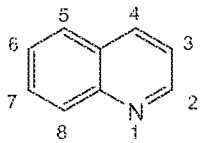
The pyrazolyl moiety can be attached through any one of the 1-, 2-, 3-, 4-, or 5-position carbon atoms. Pyrazolyl groups of the invention can be optionally substituted with, for example, one or two alkyl groups, for example, one or two methyl groups.

The term "pyrrolidinyl" represents the following moiety:



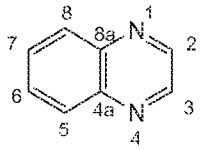
The pyrrolidinyl moiety can be attached through any one of the 1-, 2-, 3-, 4-, or 5-position atoms. When the pyrrolidinyl moiety is not attached through the 1-position nitrogen, the nitrogen can be substituted with H or alkyl, for example methyl.

The term "quinolinyl" represents the following moiety:



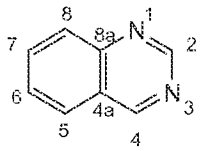
The quinolinyl moiety can be attached through any one of the 2-, 3-, 4-, 5-, 6-, 7-, or 8-position carbon atoms and may be optionally substituted with alkyl, halo or alkoxy groups.

The term "quinoxalinyl" represents the following moiety:



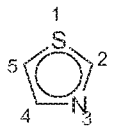
The quinoxalinyl moiety can be attached through any one of the 2-, 3-, 5-, 6-, 7-, or 8-position carbon atoms and may be optionally substituted with alkyl, halo or alkoxy groups.

The term "quinazolinyl" represents the following moiety:



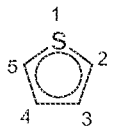
The quinoxalinyl moiety can be attached through any one of the 2-, 4-, 5-, 6-, 7-, or 8-position carbon atoms and may be optionally substituted with alkyl, halo or alkoxy groups.

The term "thiazolyl" represents the following moiety:



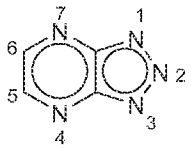
The thiazolyl moiety can be attached through any one of the 2-, 4-, or 5-position carbon atoms.

The term "thiophenyl" represents the following moiety:



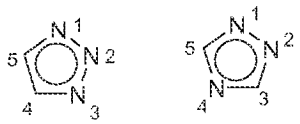
The thiophenyl moiety can be attached through any one of the 2-, 3-, 4-, or 5-position carbon atoms.

The term "triazolopyrazinyl" represents the following moiety:



The triazolopyrazinyl moiety can be attached through any one of the 1-, 3-, 4-, 5-, 6-, or 7-position atoms.

The term "triazolyl" represents a 1,2,3-triazole or a 1,2,4-triazole moiety:



The triazolyl moieties can be attached through any one of their atoms.

"Pharmaceutically acceptable" means approved or approvable by a regulatory agency of the Federal or a state government or the corresponding agency in countries other than the United States, or that is listed in the U.S. Pharmacopoeia or other generally recognized pharmacopoeia for use in animals, and more particularly, in humans.

"Pharmaceutically acceptable salt" refers to a salt of a compound of the invention that is pharmaceutically acceptable and that possesses the desired pharmacological activity of the parent compound. In particular, such salts are non-toxic may be inorganic or organic acid addition salts and base addition salts. Specifically, such salts include: (1) acid addition salts, formed with inorganic acids such as hydrochloric acid, hydrobromic acid, sulfuric acid, nitric acid, phosphoric acid, and the like; or formed with organic acids such as acetic acid, propionic acid, hexanoic acid, cyclopentanepropionic acid, glycolic acid, pyruvic acid, lactic acid, malonic acid, succinic acid, malic acid, maleic acid, fumaric acid, tartaric acid, citric acid, benzoic acid, 3-(4-hydroxybenzoyl)benzoic acid, cinnamic acid, mandelic acid, methanesulfonic acid, ethanesulfonic acid, 1,2-ethane-disulfonic acid, 2-hydroxyethanesulfonic acid, benzenesulfonic acid, 4-chlorobenzenesulfonic acid, 2-naphthalenesulfonic acid, 4-toluenesulfonic acid, camphorsulfonic acid, 4-methylbicyclo[2.2.2]-oct-2-ene-1-carboxylic acid, glucoheptonic acid, 3-phenylpropionic acid, trimethylacetic acid, tertiary butylacetic acid, lauryl sulfuric acid, gluconic acid, glutamic acid, hydroxynaphthoic acid, salicylic acid, stearic acid, muconic acid, and the like; or (2) salts formed when an acidic proton present in the parent compound either is replaced by a metal ion, e.g., an alkali metal ion, an alkaline earth ion, or an aluminum ion; or coordinates with an organic base such as ethanolamine, diethanolamine, triethanolamine, N-methylglucamine and the like. Salts further include, by way of example only, sodium, potassium, calcium, magnesium, ammonium, tetraalkylammonium, and the like; and when the compound contains a basic functionality, salts of non toxic organic or inorganic acids, such as hydrochloride, hydrobromide, tartrate, mesylate, acetate, maleate, oxalate and the like.

"Pharmaceutically acceptable vehicle" refers to a diluent, adjuvant, excipient or carrier with which a compound of the invention is administered. A "pharmaceutically acceptable excipient" refers to a substance that is non-toxic, biologically tolerable, and otherwise biologically suitable for administration to a subject, such as an inert substance, added to a pharmacological composition or otherwise used as a vehicle, carrier, or diluent to facilitate administration of a agent and that is compatible therewith. Examples of excipients include calcium carbonate, calcium phosphate, various sugars and types of starch, cellulose derivatives, gelatin, vegetable oils, and polyethylene glycols.

"Subject" includes humans. The terms "human," "patient," and "subject" are used interchangeably herein.

"Treating" or "treatment" of any disease or disorder refers, in one embodiment, to ameliorating the disease or disorder (i.e., arresting or reducing the development of the disease or at least one of the clinical symptoms thereof). In another embodiment "treating" or "treatment" refers to ameliorating at least one physical parameter, which may not be discernible by the subject. In yet another embodiment, "treating" or "treatment" refers to modulating the disease or disorder, either physically, (e.g., stabilization of a discernible symptom), physiologically, (e.g., stabilization of a physical parameter), or both. In yet another embodiment, "treating" or "treatment" refers to delaying the onset of the disease or disorder.

In treatment methods according to the invention, a therapeutically effective amountof a pharmaceutical agent according to the invention is administered to a subject suffering from or diagnosed as having such a disease, disorder, or condition. A "therapeutically effective amount" means an amount or dose sufficient to generally bring about the desired therapeutic or prophylactic benefit in patients in need of such treatment for the designated disease, disorder, or condition. Effective amounts or doses of the compounds of the present invention may be ascertained by routine methods such as modeling, dose escalation studies or clinical trials, and by taking into consideration routine factors, e.g., the mode or route of administration or drug delivery, the pharmacokinetics of the compound, the severity and course of the disease, disorder, or condition, the subject's previous or ongoing therapy, the subject's health status and response to drugs, and the judgment of the treating physician. An example of a dose is in the range of from about 0.001 to about 200 mg of compound per kg of subject's body weight per day, preferably about 0.05 to 100 mg/kg/day, or about 1 to 35 mg/kg/day, in single or divided dosage units (e.g., BID, TID, QID). For a 70-kg human, an illustrative range for a suitable dosage amount is from about 0.05 to about 7 g/day, or about 0.2 to about 2.5 g/day. "Compounds of the present invention," and equivalent expressions, are meant to embrace compounds of the Formula (I) as described herein, which expression includes the pharmaceutically acceptable salts, and the solvates, e.g., hydrates, where the context so permits. Similarly, reference to intermediates, whether or not they themselves are claimed, is meant to embrace their salts, and solvates, where the context so permits.

As used herein, the term "isotopic variant" refers to a compound that contains unnatural proportions of isotopes at one or more of the atoms that constitute such compound. For example, an "isotopic variant" of a compound can be radiolabeled, that is, contain one or more non-radioactive or radioactive isotopes, such as for example, deuterium (^{2}H or D), carbon-13 (^{13}C),

nitrogen-15 (^{15}N), or the like. It will be understood that, in a compound where such isotopic substitution is made, the following atoms, where present, may vary, so that for example, any hydrogen may be $^{2}H/D$, any carbon may be ^{13}C, or any nitrogen may be ^{15}N, and that the presence and placement of such atoms may be determined within the skill of the art. Likewise, the invention may include the preparation of isotopic variants with radioisotopes, in the instance for example, where the resulting compounds may be used for drug and/or substrate tissue distribution studies. Radiolabeled compounds of the invention can be used in diagnostic methods such as Single-photon emission computed tomography (SPECT). The radioactive isotopes tritium, *i.e.* ^{3}H, and carbon-14, *i.e.* ^{14}C, are particularly useful for their ease of incorporation and ready means of detection. Further, compounds may be prepared that are substituted with positron emitting isotopes, such as ^{11}C, ^{18}F, ^{15}O and ^{13}N, and would be useful in Positron Emission Topography (PET) studies for examining substrate receptor occupancy.

All isotopic variants of the compounds of the invention, radioactive or not, are intended to be encompassed within the scope of the invention. In one aspect, provided herein are deuterated analogs of compounds of Formula I as described in the Examples section. In one embodiment, deuterated analogs of compounds of Formula I comprise deuterium atoms attached to one or more positions on the 7-azabicyclic ring, such as bridgehead carbons, or non-bridgehead carbons of the 7-azabicyclic ring, and preferably comprise one or more deuterium atoms attached to non-bridgehead carbons of the 7-azabicyclic ring. Also contemplated within the scope of embodiments described herein are compounds in which a single proton in compounds of Formula I is replaced with a deuterium, or 2 protons in compounds of Formula I are replaced with deuterium, or more than 2 protons in compounds of Formula I are replaced with deuterium. Deuteration of a compound of Formula I may also be effected on one or more substituents (such as e.g., ring A, R^1, R^2, or R^5) present on the 7-azabicyclic ring. Deuterated analogs of compounds of Formula IA are also contemplated within the scope of embodiments provided herein.

It is also to be understood that compounds that have the same molecular formula but differ in the nature or sequence of bonding of their atoms or the arrangement of their atoms in space are termed "isomers." Isomers that differ in the arrangement of their atoms in space are termed "stereoisomers."

Stereoisomers that are not mirror images of one another are termed "diastereomers" and those that are non-superimposable mirror images of each other are termed "enantiomers." When a compound has an asymmetric center, for example, it is bonded to four different groups, a pair of enantiomers is possible. An enantiomer can be characterized by the absolute configuration of

its asymmetric center and is described by the R-and *S*-sequencing rules of Cahn and Prelog, or by the manner in which the molecule rotates the plane of polarized light and designated as dextrorotatory or levorotatory (*i.e.*, as (+) or (-)-isomers respectively). A chiral compound can exist as either individual enantiomer or as a mixture thereof. A mixture containing equal proportions of the enantiomers is called a "racemic mixture."

"Tautomers" refer to compounds that are interchangeable forms of a particular compound structure, and that vary in the displacement of hydrogen atoms and electrons. Thus, two structures may be in equilibrium through the movement of π electrons and an atom (usually H). For example, enols and ketones are tautomers because they are rapidly interconverted by treatment with either acid or base. Another example of tautomerism is the aci-and nitro-forms of phenyl nitromethane, that are likewise formed by treatment with acid or base.

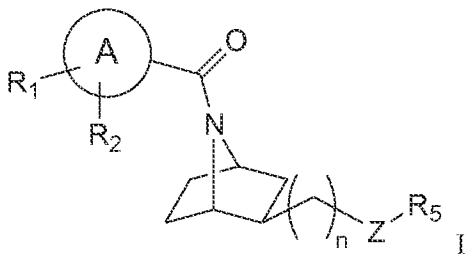
Tautomeric forms may be relevant to the attainment of the optimal chemical reactivity and biological activity of a compound of interest.

Compounds of the invention may also exist as "rotamers," that is, conformational isomers that occur when the rotation leading to different conformations is hindered, resulting a rotational energy barrier to be overcome to convert from one conformational isomer to another.

The compounds of this invention may possess one or more asymmetric centers; such compounds can therefore be produced as individual (*R*)-or (*S*)-stereoisomers or as mixtures thereof.

Unless indicated otherwise, the description or naming of a particular compound in the specification and claims is intended to include both individual enantiomers and mixtures, racemic or otherwise, thereof. The methods for the determination of stereochemistry and the separation of stereoisomers are well-known in the art.

The present invention is directed to compounds of Formula I:



I

wherein

ring A is phenyl, naphthalenyl, pyridyl, quinolinyl, isoquinolinyl, imidazopyridyl, furanyl, thiazolyl, isoxazolyl, pyrazolyl, imidazothiazolyl, benzimidazolyl, or indazolyl;

R_1 is H, alkyl, alkoxy, hydroxyalkylene, OH, halo, phenyl, triazolyl, oxazolyl, isoxazolyl, pyridyl, pyrimidinyl, pyrazinyl, pyridazinyl, piperazinyl, pyrazolyl, oxadiazolyl, pyrrolidinyl, thiophenyl, morpholinyl, or dialkylamino, wherein phenyl, triazolyl, oxazolyl, isoxazolyl, pyridyl, pyrimidinyl, pyrazinyl, pyridazinyl, piperazinyl, pyrazolyl, oxadiazolyl, pyrrolidinyl, thiophenyl, or morpholinyl is optionally substituted with up to two substituents selected from halo and alkyl;

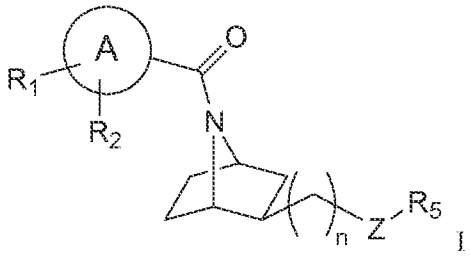
R_2 is H, alkyl, alkoxy, hydroxyalkylene, or halo;

Z is NH, N-alkyl, or O;

R_5 is pyridyl, pyrimidinyl, pyrazinyl, pyridazinyl, quinazolinyl, quinoxalinyl, pyrazolyl, thiazolyl, thiadiazolyl, benzoxazolyl, imidazopyrazinyl, or triazolopyrazinyl, optionally substituted with one or two substituents independently selected from the group consisting of alkyl, cyano, alkyl carboxylate, alkoxy, and halo; and

n is 0 or 1.

In one aspect the invention is directed to compounds of Formula I:



I

wherein

ring A is phenyl, naphthalenyl, pyridyl, quinolinyl, isoquinolinyl, imidazopyridyl, furanyl, thiazolyl, isoxazolyl, pyrazolyl, imidazothiazolyl, benzimidazolyl, or indazolyl;

R_1 is H, alkyl, alkoxy, hydroxyalkylene, OH, halo, phenyl, triazolyl, oxazolyl, isoxazolyl, pyridyl, pyrimidinyl, pyrazinyl, pyridazinyl, piperazinyl, pyrazolyl, oxadiazolyl, pyrrolidinyl, thiophenyl, morpholinyl, or dialkylamino;

R_2 is H, alkyl, alkoxy, hydroxyalkylene, or halo;

Z is NH, N-alkyl, or O;

R_5 is pyridyl, pyrimidinyl, pyrazinyl, pyridazinyl, quinazolinyl, quinoxalinyl, pyrazolyl, benzoxazolyl, imidazopyrazinyl, or triazolopyrazinyl, optionally substituted with

a one or two substituents independently selected from the group consisting of alkyl, alkoxy, or halo; and

n is 0 or 1.

Enantiomers and diastereomers of the compounds of Formula I are also within the scope of the invention. Also within the scope of the invention are the pharmaceutically acceptable salts of the compounds of Formula I, as well as the pharmaceutically acceptable salts of the enantiomers and diastereomers of the compounds of Formula I. Also contemplated within the scope of the embodiments provided herein are isotopic variants of compounds of Formula I, such as, by way of example, deuterated compounds of Formula I.

In preferred embodiments of the invention, Z is NH. In other embodiments, Z is N-alkyl, preferably N-C_{1-6}alkyl, preferably N-CH_3.

In alternative embodiments, Z is O.

In preferred embodiments of the invention, ring A is a heteroaryl ring. Preferably, ring A is furanyl, which can be attached to the compounds of Formula I through any available atom, preferably the 2-position carbon atom. In other embodiments, ring A is thiazolyl, which can be attached to the compounds of Formula I through any available atom, preferably the 4-position carbon atom.

In still other embodiments, ring A is isoxazolyl, which can be attached to the compounds of Formula I through any available atom, preferably the 4-position carbon atom.

In yet other embodiments, ring A is pyrazolyl, which can be attached to the compounds of Formula I through any through any available atom, preferably the 3- or 4-position carbon atoms.

Also preferred are embodiments wherein ring A is imidazothiazolyl, which can be attached to the compounds of Formula I through any available atom, preferably the 5-position carbon atom.

In certain embodiments of the invention, ring A is benzimidazolyl, which can be attached to the compounds of Formula I through any available atom, preferably the 2-position carbon atom.

In other embodiments of the invention, ring A is indazolyl, which can be attached to the compounds of Formula I through any available atom, preferably the 3-position carbon atom.

In yet other embodiments, ring A is imidazopyridyl, which can be attached to the compounds of Formula I through any available atom, preferably the 4-, or 7-position carbon atom

In still other embodiments, ring A is quinolinyl, which can be attached to the compounds of Formula I through any available carbon atom, preferably the 5- or 8-position carbon atom.

In other embodiments, ring A is isoquinolinyl, which can be attached to the compounds of Formula I through any available carbon atom, preferably the 4-position carbon atom.

In certain embodiments, ring A is pyridyl, which can be attached to the compounds of Formula I through any available carbon atom, preferably the 2-, 3-, or 4-position carbon atom.

In some preferred embodiments, ring A can be an aryl ring. In certain embodiments, ring A is phenyl. In other embodiments, ring A is naphthalenyl, which can be attached to the compounds of Formula I through any available carbon atom, preferably the 1-position carbon atom.

In preferred embodiments of the invention, R_1 is H. In other embodiments, R_1 is alkyl, preferably a C_{1-6}alkyl, for example, methyl.

In still other embodiments, R_1 is alkoxy, preferably a C_{1-6}alkoxy such as methoxy or ethoxy. Alternatively, R_1 is a substituted alkoxy, preferably substituted with one or more halo such as F, Cl, or Br. One preferred haloalkoxy is difluoromethoxy.

In other embodiments, R_1 is hydroxyalkylene, for example, hydroxyC_{1-6}alkylene such as $-CH_2$-OH or $-CH_2CH_2$-OH. In yet other embodiments, R_1 is OH.

In other preferred embodiments, R_1 is halo, that is, any one of F, Cl, Br, or I, with F, Cl, or Br being particularly preferred.

In still other embodiments, R_1 is phenyl. In some embodiments, R_1 is phenyl optionally substituted with up to two substituents selected from halo and alkyl. In some embodiments, the phenyl can be substituted with at least one halo, for example, phenyl substituted with at least one of F, Cl, or Br.

In certain embodiments, R_1 is triazolyl, with 1,2,3-triazolyl being preferred. The triazolyl can be attached through any available atom. In preferred embodiments, the 1,2,3-triazolyl is attached through the 2-position nitrogen atom. In other embodiments, the 1,2,3-triazolyl is attached through the 1-position nitrogen atom. In some embodiments, R_1 is triazolyl optionally substituted with up to two substituents selected from halo and alkyl.

In yet other embodiments, R_1 is oxazolyl, which can be attached through any available atom, preferably attached through the 2-position carbon. In some embodiments, R_1 is oxazolyl optionally substituted with up to two substituents selected from halo and alkyl. In some embdoiments, the oxazolyl can be substituted with alkyl, for example, a C_{1-6}alkyl such as methyl.

In other embodiments, R_1 is isoxazolyl, which can be attached through any available atom. In some embodiments, R_1 is isoxazolyl optionally substituted with up to two substituents

selected from halo and alkyl. In some embodiments, the isoxazolyl can be substituted with alkyl, for example, a C_{1-6}alkyl such as methyl.

In still other embodiments, R_1 is pyridyl, which can be attached through any available carbon atom. In some embodiments, R_1 is pyridyl optionally substituted with up to two substituents selected from halo and alkyl. In some embodiments, the pyridyl can be substituted with withat least one alkyl, for example, C_{1-6}alkyl such as methyl.

In certain embodiments, R_1 is pyrimidinyl, which can be attached through any available carbon atom. In other embodiments, R_1 is pyrazinyl, which can be attached through any available carbon atom. In yet other embodiments, R_1 is pyridazinyl, which can be attached through any available carbon atom. In some of such embodiments, R_1 is pyrimidinyl, or pyrazinyl, or pyridazinyl, each optionally substituted with up to two substituents selected from halo and alkyl.

In other embodiments, R_1 is piperazinyl which can be attached through any available atom. In some embodiments, R_1 is piperazinyl optionally substituted with up to two substituents selected from halo and alkyl. In some embodiments, one or both nitrogen atoms of the piperazinyl may be substituted with H or alkyl, for example, C_{1-6}alkyl such as methyl.

In still other embodiments, R_1 is morpholinyl, which can be attached through any available atom. In some embodiments, R_1 is morpholinyl optionally substituted with up to two substituents selected from halo and alkyl. In some embodiments, the nitrogen of the morpholinyl may be substituted with H or alkyl, for example, C_{1-6}alkyl such as methyl.

In yet other embodiments, R_1 is pyrrolidinyl, which can be attached through any available atom. In some embodiments, R_1 is pyrrolidinyl optionally substituted with up to two substituents selected from halo and alkyl. In some embodiments, the nitrogen of the pyrrolidinyl may be substituted with H or alkyl, for example, C_{1-6}alkyl such as methyl.

In other embodiments, R_1 is dialkylamino, for example, dimethylamino, diethylamino, or methylethylamino.

In other embodiments, R_1 is pyrazolyl, which can be attached through any available atom. In some embodiments, R_1 is pyrazolyl optionally substituted with up to two substituents selected from halo and alkyl. In some embodiments, the pyrazolyl can be substituted with with one or two alkyl, for example, C_{1-6}alkyl such as methyl.

In yet other embodiments, R_1 is oxadiazolyl, which can be a 1,2,3-oxadiazolyl, 1,2,4-oxadiazolyl, 1,2,5-oxadiazolyl, or 1,3,4-oxadiazolyl. Preferably, the oxadiazolyl is 1,2,4-oxadiazolyl. The oxadiazolyl can be attached through any available atom. In some embodiments, R_1 is oxadiazolyl optionally substituted with up to two substituents selected from

halo and alkyl. In some embodiments, the oxadiazolyl can be substituted with with alkyl, for example, C_{1-6}alkyl such as methyl.

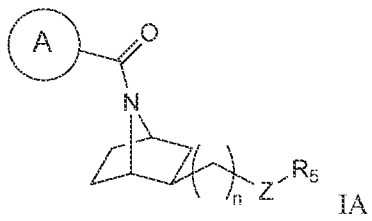
In still other embodiments, R_1 is thiophenyl, which can be attached through any available carbon atom. In some embodiments, R_1 is thiophenyl optionally substituted with up to two substituents selected from halo and alkyl.

In preferred embodiments of the invention, R_2 is H. In other embodiments, R_2 is alkyl, for example, C_{1-6}alkyl such as methyl or ethyl. In yet other embodiments, R_2 is alkoxy, for example, C_{1-6}alkoxy such as methoxy or ethoxy. In other embodiments, R_2 is hydroxylalkene, for example, -CH_2-OH or CH_2CH_2-OH. In still other embodiments, R_2 is halo, preferably, any one of F, Cl, or Br.

In some embodiments of Formula I, ring A is aryl, preferably phenyl, R_1 is a ring selected from phenyl, triazolyl, oxazolyl, isoxazolyl, pyridyl, pyrimidinyl, pyrazinyl, pyridazinyl, piperazinyl, pyrazolyl, oxadiazolyl, pyrrolidinyl, thiophenyl, and morpholinyl; preferably triazolyl, pyridyl or pyrimidinyl; R_2 is H, alkyl, alkoxy, hydroxyalkylene, or halo; preferably halo; Z is NH or O, preferably NH, R_5 is a heteroaryl, preferably pyridyl or pyrazinyl; and n is 0. In some of such embodiments, R_1 is a ring at the ortho position on ring A relative to the carbonyl group in Formula I, and R_2 is at the ortho, meta or para position on ring A relative to the carbonyl group in Formula I, preferably R_2 is at the meta position adjacent to R_1. In some other such embodiments, R_1 is a ring at the ortho position on ring A relative to the carbonyl group in Formula I, and R_2 is at the ortho, meta or para position on ring A relative to the carbonyl group in Formula I, preferably R_2 is at the meta position not adjacent to R_1. R_1 and R_5 may be optionally substituted as described above.

In some embodiments of Formula I, ring A is heteroaryl, preferably pyridinyl, R_1 is a ring selected from phenyl, triazolyl, oxazolyl, isoxazolyl, pyridyl, pyrimidinyl, pyrazinyl, pyridazinyl, piperazinyl, pyrazolyl, oxadiazolyl, pyrrolidinyl, thiophenyl, and morpholinyl; preferably triazolyl, pyridyl or pyrimidinyl; R_2 is H, alkyl, alkoxy, hydroxyalkylene, or halo; preferably halo; Z is NH or O, preferably NH, R_5 is a heteroaryl, preferably pyridyl or pyrazinyl; and n is 0. In some of such embodiments, R_1 is a ring at the ortho position on ring A relative to the carbonyl group in Formula I, and R_2 is at the ortho, meta or para position on ring A relative to the carbonyl group in Formula I, preferably R_2 is at the meta position adjacent to R_1. In some other such embodiments, R_1 is a ring at the ortho position on ring A relative to the carbonyl group in Formula I, and R_2 is at the ortho, meta or para position on ring A relative to the carbonyl group in Formula I, preferably R_2 is at the meta position not adjacent to R_1. R_1 and R_5 may be optionally substituted as described above.

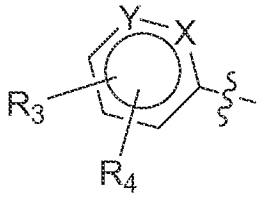
In one aspect, the invention is directed to compounds of Formula IA:



IA

wherein

ring A is



wherein

X is CR_6, N, or NR_6;

Y is CR_7, N, or NR_7;

R_6 is H, alkyl, alkoxy, OH, halo, triazolyl, oxazolyl, oxadiazolyl, pyridyl, pyrimidinyl, pyrazinyl, pyridazinyl, pyrazolyl, or thiophenyl, wherein triazolyl, oxazolyl, oxadiazolyl, pyridyl, pyrimidinyl, pyrazinyl, pyridazinyl, pyrazolyl, or thiophenyl is optionally substituted with up to two substituents selected from halo and alkyl;

R_7 is H, alkyl, alkoxy, or halo;

R_3 is H, alkyl, alkoxy, hydroxyalkylene, OH, halo, phenyl, triazolyl, oxazolyl, isoxazolyl, pyridyl, pyrimidinyl, pyrazinyl, pyridazinyl, piperazinyl, pyrazolyl, oxadiazolyl, pyrrolidinyl, thiophenyl, morpholinyl, or dialkylamino, wherein phenyl, triazolyl, oxazolyl, isoxazolyl, pyridyl, pyrimidinyl, pyrazinyl, pyridazinyl, piperazinyl, pyrazolyl, oxadiazolyl, pyrrolidinyl, thiophenyl, or morpholinyl is optionally substituted with up to two substituents selected from halo and alkyl;

R_4 is H, alkyl, alkoxy, or halo;

or

R_6 and R_7, together with the atoms to which they are attached, form a 5- or 6-membered heteroaryl ring optionally substituted with alkyl; or

R_3 and R_4, together with the atoms to which they are attached, form a 6-membered aryl or 6-membered heteroaryl ring; or

R_7 and R_4, together with the atoms to which they are attached, form a 6-membered aryl or 6-membered heteroaryl ring;

Z is NH, N-alkyl, or O;

R_5 is pyridyl, pyrimidinyl, pyrazinyl, pyridazinyl, quinazolinyl, quinoxalinyl, pyrazolyl, thiazolyl, thiadiazolyl, benzoxazolyl, imidazopyrazinyl, or triazolopyrazinyl, optionally substituted with a one or two substituents independently selected from the group consisting of alkyl, cyano, alkyl carboxylate, alkoxy, or halo; and

n is 0 or 1.

Enantiomers and diastereomers of the compounds of Formula IA are also within the scope of the invention. Also within the scope of the invention are the pharmaceutically acceptable salts of the compounds of Formula IA, as well as the pharmaceutically acceptable salts of the enantiomers and diastereomers of the compounds of Formula IA. Also contemplated within the scope of the embodiments provided herein are isotopic variants of compounds of Formula IA, such as, by way of example, deuterated compounds of Formula IA.

In certain of these embodiments, X is CR_6 and Y is CR_7.

In other of these embodiments, X is CR_6 and Y is N.

In still other of these embodiments, X is N and Y is CR_7.

In those embodiments wherein X is CR_6, for example those embodiments wherein X is CR_6 and Y is CR_7 or X is CR_6 and Y is N, R_6 is H. Alternatively, R_6 is alkyl, for example, C_{1-6}alkyl such as methyl or ethyl.

In other of these embodiments, R_6 is alkoxy, for example, C_{1-6}alkoxy such as methoxy or ethoxy.

In still other of these embodiments, R_6 is OH.

In yet other of these embodiments, R_6 is halo, preferably, any one of F, Cl, or Br.

In those embodiments wherein X is CR_6, for example those embodiments wherein X is CR_6 and Y is CR_7 or X is CR_6 and Y is N, R_6 is triazolyl with 1,2,3-triazolyl being preferred. The triazolyl can be attached through any available atom. In preferred embodiments, the 1,2,3-triazolyl is attached through the 2-position nitrogen atom. In other embodiments, the 1,2,3-triazolyl is attached through the 1-position nitrogen atom.

In those embodiments wherein X is CR_6, for example those embodiments wherein X is CR_6 and Y is CR_7 or X is CR_6 and Y is N, R_6 is oxazolyl, which can be attached through any available atom. In some embodiments, the oxazolyl can be substituted with with alkyl, for example, C_{1-6}alkyl such as methyl.

In those embodiments wherein X is CR_6, for example those embodiments wherein X is CR_6 and Y is CR_7 or X is CR_6 and Y is N, R_6 is oxadiazolyl, which can be a 1,2,3-oxadiazolyl,

1,2,4-oxadiazolyl, 1,2,5-oxadiazolyl, or 1,3,4-oxadiazolyl. Preferably, the oxadiazolyl is 1,2,4-oxadiazolyl. The oxadiazolyl can be attached through any available atom. In some embodiments, the oxadiazolyl can be substituted with with alkyl, for example, C_{1-6}alkyl such as methyl.

In those embodiments wherein X is CR_6, for example those embodiments wherein X is CR_6 and Y is CR_7 or X is CR_6 and Y is N, R_6 is pyrazolyl, which can be attached through any available atom. In some embodiments, the pyrazolyl can be substituted with one or two alkyl, for example, C_{1-6}alkyl such as methyl.

In those embodiments wherein X is CR_6, for example those embodiments wherein X is CR_6 and Y is CR_7 or X is CR_6 and Y is N, R_6 is thiophenyl, which can be attached through any available atom.

In those embodiments wherein X is CR_6, for example those embodiments wherein X is CR_6 and Y is CR_7 or X is CR_6 and Y is N, R_6 is pyridyl, which can be attached through any available atom. In some embodiments, the pyridyl can be substituted with one or more alkyl, for example, C_{1-6}alkyl such as methyl. One exemplary substituted pyridyl is methyl-pyridyl.

In those embodiments wherein X is CR_6, for example those embodiments wherein X is CR_6 and Y is CR_7 or X is CR_6 and Y is N, R_6 is pyrimidinyl, which can be attached through any available atom. In other embodiments, R_6 is pyrazinyl, which can be attached through any available atom. In still other embodiments, R_6 is pyridazinyl, which can be attached through any available atom.

In preferred embodiments wherein Y is CR_7, for example, those embodiments wherein X is CR_6 and Y is CR_7 or X is N and Y is CR_7, R_7 is H. In other embodiments, R_7 is alkyl, for example, C_{1-6}alkyl such as methyl or ethyl.

In those embodiments wherein Y is CR_7, for example, those embodiments wherein X is CR_6 and Y is CR_7 or X is N and Y is CR_7, R_7 is alkoxy, for example, C_{1-6}alkoxy such as methoxy or ethoxy. In other embodiments, the alkoxy is substituted with, for example, one or more halo. One preferred substituted alkoxy is difluoromethoxy.

In those embodiments wherein Y is CR_7, for example, those embodiments wherein X is CR_6 and Y is CR_7 or X is N and Y is CR_7, R_7 is halo, preferably one of F, Cl, or Br.

In some embodiments, X is NR_6 and Y is CR_7.

In other embodiments, X is CR_6 and Y is NR_7.

In other embodiments, X is CR_6 and Y is CR_7.

In those embodiments wherein X is NR_6 and Y is CR_7 or X is CR_6 and Y is NR_7, R_6 and R_7, together with the atoms to which they are attached, form a 5-membered heteroaryl ring.

These 5-membered rings can optionally substituted with alkyl, for example C_{1-6}alkyl such as methyl.

In those embodiments wherein X is NR_6 and Y is CR_7 or X is CR_6 and Y is NR_7, R_6 and R_7, together with the atoms to which they are attached, form a 6-membered heteroaryl ring. These 5-membered rings can optionally substituted with alkyl, for example C_{1-6}alkyl such as methyl.

In those embodiments wherein Y is CR_7 or NR_7, R_7 and R_4, together with the atoms to which they are attached, form a 6-membered aryl ring. Alternatively, R_7 and R_4, together with the atoms to which they are attached, form a 6-membered heteroaryl ring.

In preferred embodiments, R_3 is H. In other embodiments, R_3 is alkyl, for example, C_{1-6}alkyl such as methyl or ethyl.

In other embodiments, R_3 is alkoxy, for example, C_{1-6}alkoxy such as methoxy or ethoxy. In some embodiments, the alkoxy is substituted with, for example, one or more halo. One preferred substituted alkoxy is difluoromethoxy.

In some embodiments, R_3 is hydroxyalkylene, for example, hydroxyC_{1-6}alkylenesuch as $-CH_2$-OH and $-CH_2CH_2$-OH. In yet other embodiments, R_3 is OH.

In other preferred embodiments, R_3 is halo, preferably any one of F, Cl, or Br.

In still other embodiments, R_3 is phenyl. In some embodiments, the phenyl can be substituted with one or more halo, for example, phenyl substituted with at least one of F, Cl, or Br.

In certain embodiments, R_3 is triazolyl, with 1,2,3-triazolyl being preferred. The triazolyl can be attached through any available atom. In preferred embodiments, the 1,2,3-triazolyl is attached through the 2-position nitrogen atom. In other embodiments, the 1,2,3-triazolyl is attached through the 1-position nitrogen atom.

In yet other embodiments, R_3 is oxazolyl, which can be attached through any available atom, preferably attached through the 2-position carbon. In some embdoiments, the oxazolyl can be substituted with alkyl, for example, a C_{1-6}alkyl such as methyl.

In other embodiments, R_3 is isoxazolyl, which can be attached through any available atom. In some embodiments, the isoxazolyl can be substituted with alkyl, for example, a C_{1-6}alkyl such as methyl.

In other embodiments, R_3 is oxadiazolyl, which can be a 1,2,3-oxadiazolyl, 1,2,4- oxadiazolyl, 1,2,5- oxadiazolyl, or 1,3,4- oxadiazolyl. Preferably, the oxadiazolyl is 1,2,4-oxadiazolyl. The oxadiazolyl can be attached through any available atom. In some

embodiments, the oxadiazolyl can be substituted with with alkyl, for example, C_{1-6}alkyl such as methyl.

In still other embodiments, R_3 is pyridyl, which can be attached through any available carbon atom. In some embodiments, the pyridyl can be substituted with with one or more alkyl, for example, C_{1-6}alkyl such as methyl.

In other embodiments, R_3 is pyrazolyl, which can be attached through any available atom. In some embodiments, the pyrazolyl can be substituted with with one or two alkyl, for example, C_{1-6}alkyl such as methyl.

In certain embodiments, R_3 is pyrimidinyl, which can be attached through any available carbon atom. In other embodiments, R_3 is pyrazinyl, which can be attached through any available carbon atom. In yet other embodiments, R_3 is pyridazinyl, which can be attached through any available carbon atom.

In other embodiments, R_3 is piperazinyl which can be attached through any available atom. In some embodiments, one or both nitrogen atoms of the piperazinyl may be substituted with H or alkyl, for example, C_{1-6}alkyl such as methyl.

In still other embodiments, R_3 is morpholinyl, which can be attached through any available atom. In some embodiments, the nitrogen atom of the morpholinyl may be substituted with H or alkyl, for example, C_{1-6}alkyl such as methyl.

In yet other embodiments, R_3 is pyrrolidinyl, which can be attached through any available atom. In some embodiments, the nitrogen atom of the pyrrolidinyl may be substituted with H or alkyl, for example, C_{1-6}alkyl such as methyl.

In other embodiments, R_3 is dialkylamino, for example, dimethylamino, diethylamino, or methylethylamino.

In other embodiments, R_3 is pyrazolyl, which can be attached through any available atom. In some embodiments, the pyrazolyl can be substituted with with one or two alkyl, for example, C_{1-6}alkyl such as methyl.

In still other embodiments, R_3 is thiophenyl, which can be attached through any available carbon atom.

In preferred embodiments of the invention, R_4 is H. In other embodments, R_4 is alkyl, for example, C_{1-6}alkyl such as methyl or ethyl. In still other embodiments, R_4 is alkoxy, for example, C_{1-6}alkoxy such as methoxy or ethoxy. In yet other embodiments, R_4 is halo, preferably, any one of F, Cl, or Br.

In some embodiments, R_3 and R_4, together with the atoms to which they are attached, form a 6-membered aryl ring.

In other embodiments, R_3 and R_4, together with the atoms to which they are attached, form a 6-membered heteroarylaryl ring.

In preferred embodiments of the invention, R_5 is a heteroaryl ring. In some of such embodiments, R_5 is a heteroaryl optionally substituted with a one or two substituents independently selected from the group consisting of alkyl, cyano, alkyl carboxylate, alkoxy, and halo. According to some embodiments of the invention, R_5 is pyridyl, which can be attached through any available atom, optionally substituted with a one or two substituents independently selected from the group consisting of alkyl, alkoxy, or halo. In some embodiments, alkyl is trihaloalkyl, for example trifluoromethyl.

According to some embodiments of the invention, R_5 is pyrimidinyl, which can be attached through any available atom, optionally substituted with a one or two substituents independently selected from the group consisting of alkyl, alkoxy, or halo. In some embodiments, alkyl is trihaloalkyl, for example trifluoromethyl. In other embodiments, alkyl is dihaloalkyl, e.g., difluoromethyl or monohaloalkyl, e.g., monofluoromethyl.

According to some embodiments of the invention, R_5 is pyrazinyl, which can be attached through any available atom, optionally substituted with a one or two substituents independently selected from the group consisting of alkyl, alkoxy, or halo. In some embodiments, alkyl is trihaloalkyl, for example trifluoromethyl. In other embodiments, alkyl is dihaloalkyl, e.g., difluoromethyl or monohaloalkyl, e.g., monofluoromethyl.

According to some embodiments of the invention, R_5 is pyridazinyl, which can be attached through any available atom, optionally substituted with a one or two substituents independently selected from the group consisting of alkyl, alkoxy, or halo. In some embodiments, alkyl is trihaloalkyl, for example trifluoromethyl. In other embodiments, alkyl is dihaloalkyl, e.g., difluoromethyl or monohaloalkyl, e.g., monofluoromethyl.

According to some embodiments of the invention, R_5 is quinazolinyl, which can be attached through any available atom, optionally substituted with a one or two substituents independently selected from the group consisting of alkyl, alkoxy, or halo. In some embodiments, alkyl is trihaloalkyl, for example trifluoromethyl. In other embodiments, alkyl is dihaloalkyl, e.g., difluoromethyl or monohaloalkyl, e.g., monofluoromethyl.

According to some embodiments of the invention, R_5 is quinoxalinyl, which can be attached through any available atom, optionally substituted with a one or two substituents independently selected from the group consisting of alkyl, alkoxy, or halo. In some

embodiments, alkyl is trihaloalkyl, for example trifluoromethyl. In other embodiments, alkyl is dihaloalkyl, e.g., difluoromethyl or monohaloalkyl, e.g., monofluoromethyl.

According to some embodiments of the invention, R_5 is pyrazolyl, which can be attached through any available atom, optionally substituted with a one or two substituents independently selected from the group consisting of alkyl, alkoxy, or halo. In some embodiments, alkyl is trihaloalkyl, for example trifluoromethyl. In some embodiments, the pyrazolyl is methyl-pyrazolyl substituted with trifluoromethyl. In other embodiments, alkyl is dihaloalkyl, e.g., difluoromethyl or monohaloalkyl, e.g., monofluoromethyl.

According to some embodiments of the invention, R_5 is benzoxazolyl, which can be attached through any available atom, optionally substituted with a one or two substituents independently selected from the group consisting of alkyl, alkoxy, or halo. In some embodiments, alkyl is trihaloalkyl, for example trifluoromethyl. In other embodiments, alkyl is dihaloalkyl, e.g., difluoromethyl or monohaloalkyl, e.g., monofluoromethyl.

According to some embodiments of the invention, R_5 is imidazopyrazinyl, which can be attached through any available atom, optionally substituted with a one or two substituents independently selected from the group consisting of alkyl, alkoxy, or halo. In some embodiments, alkyl is trihaloalkyl, for example trifluoromethyl. In other embodiments, alkyl is dihaloalkyl, e.g., difluoromethyl or monohaloalkyl, e.g., monofluoromethyl.

According to some embodiments of the invention, R_5 is triazolopyrazinyl, which can be attached through any available atom, optionally substituted with a one or two substituents independently selected from the group consisting of alkyl, alkoxy, or halo. In some embodiments, alkyl is trihaloalkyl, for example trifluoromethyl. In other embodiments, alkyl is dihaloalkyl, e.g., difluoromethyl or monohaloalkyl, e.g., monofluoromethyl.

According to some embodiments of the invention, R_5 is thiazolyl which can be attached through any available atom, optionally substituted with a one or two substituents independently selected from the group consisting of alkyl, alkoxy, or halo. In some embodiments, alkyl is trihaloalkyl, for example trifluoromethyl. In other embodiments, alkyl is dihaloalkyl, e.g., difluoromethyl or monohaloalkyl, e.g., monofluoromethyl.

According to some embodiments of the invention, R_5 is thiadiazolyl which can be attached through any available atom, optionally substituted with a one or two substituents independently selected from the group consisting of alkyl, alkoxy, or halo. In some embodiments, alkyl is trihaloalkyl, for example trifluoromethyl. In other embodiments, alkyl is dihaloalkyl, e.g., difluoromethyl or monohaloalkyl, e.g., monofluoromethyl.

In some embodiments of the invention n is 0. In other embodiments, n is 1.

The invention relates to methods of using the compounds described herein to treat subjects diagnosed with or suffering from a disease, disorder, or condition mediated by orexin receptor activity. These methods are accomplished by administering to the subject a compound of the invention. In some embodiments, the compounds described herein are selective for orexin-1 receptor activity. In some embodiments, the compounds described herein are selective for orexin-1 receptor activity over orexin-2 receptor activity.

Diseases, disorders, and conditions mediated by orexin receptor activity include disorders of the sleep-wake cycle, insomnia, restless legs syndrome, jet-lag, disturbed sleep, sleep disorders secondary to neurological disorders, mania, depression, manic depression, schizophrenia, pain syndromes, fibromyalgia, neuropathic pain, catatonia, Parkinson's disease, Tourette's syndrome, anxiety, delirium, dementia, overweight, obesity, or conditions related to overweight or obesity, insulin resistance, type II diabetes, hyperlipidemia, gallstones, angina, hypertension, breathlessness, tachycardia, infertility, sleep apnea, back and joint pain, varicose veins, osteoarthritis, hypertension, tachycardia, arrhythmias, angina pectoris, acute heart failure, ulcers, irritable bowel syndrome, diarrhea gastroesophageal reflux, mood disorders, post-traumatic stress disorder, panic disorders, attention deficit disorders, cognitive deficiencies, or substance abuse.

Compounds of the invention are particularly suited for the treatment of mood disorders, post-traumatic stress disorder, panic disorders, attention deficit disorders, cognitive deficiencies, or substance abuse.

In one aspect, compounds of the invention are particularly suited for the treatment of mood disorders. Non-limiting examples of mood disorders include anxiety-related mood disorders, depression, panic-related mood disorders, stress related mood disorders and the like. In another aspect, compounds of the invention are suitable for the treatment of post-traumatic stress disorder, panic disorders, attention deficit disorders, cognitive deficiencies, or substance abuse (e.g., morphine abuse, cocaine abuse, alcohol abuse and the like). It will be understood that certain disorders such as, for example, depression and/or schizophrenia and/or substance abuse and/or cognitive impairments also have elements of anxiety and/or panic and/or stress associated with them and the treatment of such conditions and/or combinations of conditions are also contemplated within the scope of embodiments presented herein. In some embodiments, advantageously, compounds of the invention treat a mood disorder (e.g., anxiety) with reduced concomitant sedation and/or with reduced effect on sleep (e.g. attenuated arousal effects). In one embodiment, compounds of the invention are particularly suited for the treatment of anxious

depression. In another embodiment, compounds of the invention are particularly suited for the treatment of panic, schizophrenia, and substance abuse.

Sleep disorders include, but are not limited to, sleep-wake transition disorders, insomnia, restless legs syndrome, jet-lag, disturbed sleep, and sleep disorders secondary to neurological disorders (e.g., manias, depressions, manic depression, schizophrenia, and pain syndromes (e.g., fibromyalgia, neuropathic).

Metabolic disorders include, but are not limited to, overweight or obesity and conditions related to overweight or obesity, such as insulin resistance, type II diabetes, hyperlipidemia, gallstones, angina, hypertension, breathlessness, tachycardia, infertility, sleep apnea, back and joint pain, varicose veins and osteoarthritis.

Neurological disorders include, but are not limited to, Parkinson's disease, Alzheimer's disease, Tourette's Syndrome, catatonia, anxiety, delirium and dementias.

In treatment methods according to the invention, a therapeutically effective amount of a pharmaceutical agent according to the invention is administered to a subject suffering from or diagnosed as having such a disease, disorder, or condition. A "therapeutically effective amount" means an amount or dose sufficient to generally bring about the desired therapeutic or prophylactic benefit in patients in need of such treatment for the designated disease, disorder, or condition. Effective amounts or doses of the compounds of the present invention may be ascertained by routine methods such as modeling, dose escalation studies or clinical trials, and by taking into consideration routine factors, e.g., the mode or route of administration or drug delivery, the pharmacokinetics of the compound, the severity and course of the disease, disorder, or condition, the subject's previous or ongoing therapy, the subject's health status and response to drugs, and the judgment of the treating physician. An example of a dose is in the range of from about 0.001 to about 200 mg of compound per kg of subject's body weight per day, preferably about 0.05 to 100 mg/kg/day, or about 1 to 35 mg/kg/day, in single or divided dosage units (e.g., BID, TID, QID). For a 70-kg human, an illustrative range for a suitable dosage amount is from about 0.05 to about 7 g/day, or about 0.2 to about 2.5 g/day.

Once improvement of the patient's disease, disorder, or condition has occurred, the dose may be adjusted for preventative or maintenance treatment. For example, the dosage or the frequency of administration, or both, may be reduced as a function of the symptoms, to a level at which the desired therapeutic or prophylactic effect is maintained. Of course, if symptoms have been alleviated to an appropriate level, treatment may cease. Patients may, however, require intermittent treatment on a long-term basis upon any recurrence of symptoms.

In addition, the compounds of the invention may be used in combination with additional active ingredients in the treatment of the above conditions. The additional active ingredients may be coadministered separately with a compound of the invention or included with such an agent in a pharmaceutical composition according to the invention. In an exemplary embodiment, additional active ingredients are those that are known or discovered to be effective in the treatment of conditions, disorders, or diseases mediated by orexin activity, such as another orexin modulator or a compound active against another target associated with the particular condition, disorder, or disease. The combination may serve to increase efficacy (e.g., by including in the combination a compound potentiating the potency or effectiveness of an active agent according to the invention), decrease one or more side effects, or decrease the required dose of the active agent according to the invention.

The compounds of the invention are used, alone or in combination with one or more additional active ingredients, to formulate pharmaceutical compositions of the invention. A pharmaceutical composition of the invention comprises: (a) an effective amount of at least one compound in accordance with the invention; and (b) a pharmaceutically acceptable excipient.

Delivery forms of the pharmaceutical compositions containing one or more dosage units of the active agents may be prepared using suitable pharmaceutical excipients and compounding techniques known or that become available to those skilled in the art. The compositions may be administered in the inventive methods by a suitable route of delivery, e.g., oral, parenteral, rectal, topical, or ocular routes, or by inhalation.

The preparation may be in the form of tablets, capsules, sachets, dragees, powders, granules, lozenges, powders for reconstitution, liquid preparations, or suppositories. Preferably, the compositions are formulated for intravenous infusion, topical administration, or oral administration.

For oral administration, the compounds of the invention can be provided in the form of tablets or capsules, or as a solution, emulsion, or suspension. To prepare the oral compositions, the compounds may be formulated to yield a dosage of, e.g., from about 0.05 to about 100 mg/kg daily, or from about 0.05 to about 35 mg/kg daily, or from about 0.1 to about 10 mg/kg daily. For example, a total daily dosage of about 5 mg to 5 g daily may be accomplished by dosing once, twice, three, or four times per day.

Oral tablets may include a compound according to the invention mixed with pharmaceutically acceptable excipients such as inert diluents, disintegrating agents, binding agents, lubricating agents, sweetening agents, flavoring agents, coloring agents and preservative agents. Suitable inert fillers include sodium and calcium carbonate, sodium and calcium

phosphate, lactose, starch, sugar, glucose, methyl cellulose, magnesium stearate, mannitol, sorbitol, and the like. Exemplary liquid oral excipients include ethanol, glycerol, water, and the like. Starch, polyvinyl-pyrrolidone (PVP), sodium starch glycolate, microcrystalline cellulose, and alginic acid are suitable disintegrating agents. Binding agents may include starch and gelatin. The lubricating agent, if present, may be magnesium stearate, stearic acid or talc. If desired, the tablets may be coated with a material such as glyceryl monostearate or glyceryl distearate to delay absorption in the gastrointestinal tract, or may be coated with an enteric coating.

Capsules for oral administration include hard and soft gelatin capsules. To prepare hard gelatin capsules, compounds of the invention may be mixed with a solid, semi-solid, or liquid diluent. Soft gelatin capsules may be prepared by mixing the compound of the invention with water, an oil such as peanut oil or olive oil, liquid paraffin, a mixture of mono and di-glycerides of short chain fatty acids, polyethylene glycol 400, or propylene glycol.

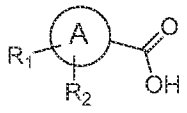
Liquids for oral administration may be in the form of suspensions, solutions, emulsions or syrups or may be lyophilized or presented as a dry product for reconstitution with water or other suitable vehicle before use. Such liquid compositions may optionally contain: pharmaceutically-acceptable excipients such as suspending agents (for example, sorbitol, methyl cellulose, sodium alginate, gelatin, hydroxyethylcellulose, carboxymethylcellulose, aluminum stearate gel and the like); non-aqueous vehicles, e.g., oil (for example, almond oil or fractionated coconut oil), propylene glycol, ethyl alcohol, or water; preservatives (for example, methyl or propyl p-hydroxybenzoate or sorbic acid); wetting agents such as lecithin; and, if desired, flavoring or coloring agents.

The active agents of this invention may also be administered by non-oral routes. For example, the compositions may be formulated for rectal administration as a suppository. For parenteral use, including intravenous, intramuscular, intraperitoneal, or subcutaneous routes, the compounds of the invention may be provided in sterile aqueous solutions or suspensions, buffered to an appropriate pH and isotonicity or in parenterally acceptable oil. Suitable aqueous vehicles include Ringer's solution and isotonic sodium chloride. Such forms will be presented in unit-dose form such as ampules or disposable injection devices, in multi-dose forms such as vials from which the appropriate dose may be withdrawn, or in a solid form or pre-concentrate that can be used to prepare an injectable formulation. Illustrative infusion doses may range from about 1 to 1000 .mu.g/kg/minute of compound, admixed with a pharmaceutical carrier over a period ranging from several minutes to several days.

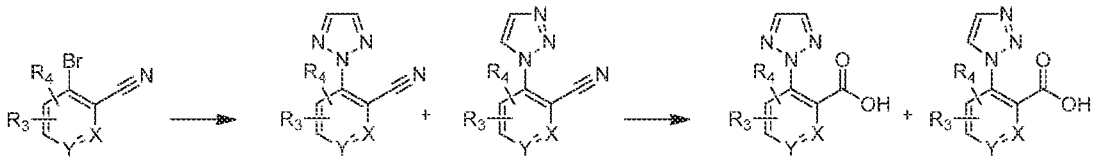
For topical administration, the compounds may be mixed with a pharmaceutical carrier at a concentration of about 0.1% to about 10% of drug to vehicle. Another mode of administering the compounds of the invention may utilize a patch formulation to affect transdermal delivery.

Compounds of the invention may alternatively be administered in methods of this invention by inhalation, via the nasal or oral routes, e.g., in a spray formulation also containing a suitable carrier.

Exemplary compounds useful in methods of the invention will now be described by reference to the illustrative synthetic schemes for their general preparation below and the specific examples that follow. Artisans will recognize that, to obtain the various compounds herein, starting materials may be suitably selected so that the ultimately desired substituents will be carried through the reaction scheme with or without protection as appropriate to yield the desired product. Alternatively, it may be necessary or desirable to employ, in the place of the ultimately desired substituent, a suitable group that may be carried through the reaction scheme and replaced as appropriate with the desired substituent. Unless otherwise specified, the variables are as defined above in reference to Formula (I). Reactions may be performed between the melting point and the reflux temperature of the solvent, and preferably between 0 °C and the reflux temperature of the solvent. Reactions may be heated employing conventional heating or microwave heating. Reactions may also be conducted in sealed pressure vessels above the normal reflux temperature of the solvent.

The synthesis of exemplary intermediates of structure  , i.e., formula $(R^1R^2A)CO_2H$, is shown in Schemes 1-6 below, and also in the Examples section below (Intermediates A-1 to A-71).

Scheme 1

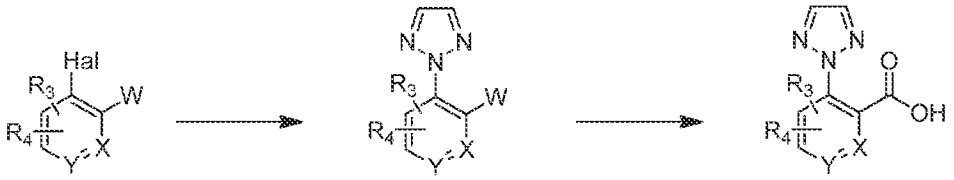


(A) (IIa) (IIb) (IIIa) (IIIb)

Intermediate compounds of formula (IIIa) and (IIIb) can be prepared as outlined in Scheme 1 from commercially available or synthetically accessible compounds of formula (A) where R_3, R_4, are defined in formula (IA) as above, or R_3 is H, R_4 is analogous to R_2 in Formula I as above, and X and Y are independently selected from C and N. Compounds of formula (IIa)

and (IIb), are obtained by reacting a compound of formula (A), with commercially available 1,2,3-triazole, in the presence K_2CO_3 in DMF or dioxane, at temperatures ranging from about 60 °C to about 100 °C. Compounds of formula (IIIa) and (IIIb) are obtained by reacting compounds of formula (II) in the presence of a base such as NaOH in a solvent such as EtOH at temperatures ranging from 80 °C to 100 °C. One skilled in the art will recognize that 1,2,3-triazole can exist in two tautomeric forms defined as 2H-[1,2,3]triazole and 1H-[1,2,3]triazole thus accounting for the formation of (IIIa) and (IIIb).

Scheme 2



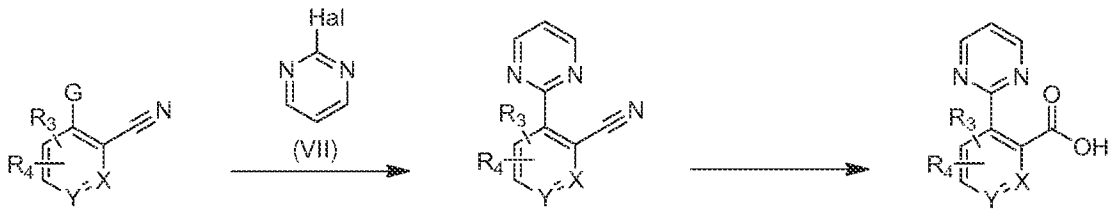
(IVa) W is CN
(IVb) W is CO_2Alkyl
(IVc) W is CO_2H

(Va) W is CN
(Vb) W is CO_2Alkyl
(III) W is CO_2H

(III)

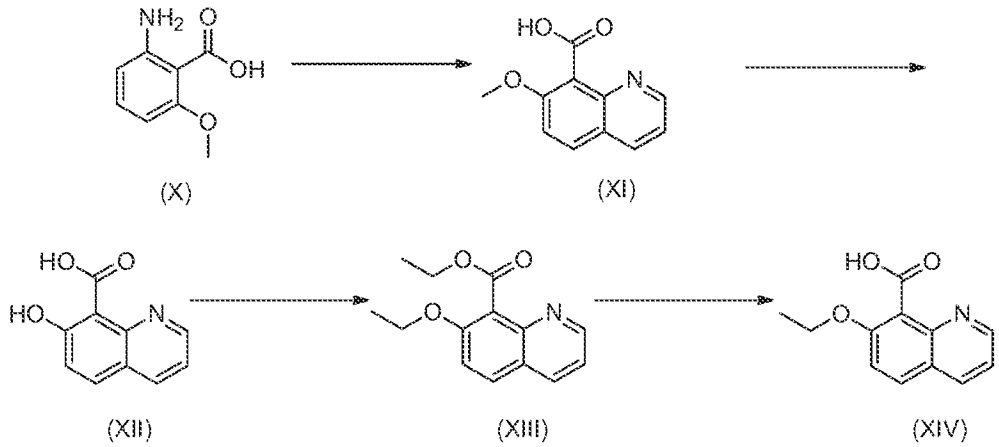
Intermediate compounds of formula (III) can be prepared as outlined in Scheme 2 from commercially available or synthetically accessible compounds of formula (IV_{a-c}). Compounds of formula (III), (Va) and (Vb) are obtained by reacting compounds of formula (IVa), (IVb) and (IVc) where Hal is –Br, or –I; W is CO_2H, CO_2Alkyl, or CN and R_3 and R_4 are -H, halo, -C_{1-4}alkyl, -C_{1-4}alkoxy and R_3 and R_4 together with the atoms to which they are attached form a 6- membered aryl or 6 membered heteroaryl ring, or R_3 is H, R_4 is analogous to R_2 in Formula I as above, and X and Y are independently selected from C and N, with commercially available 1,2,3-triazole, in the presence of, for example, copper(I)iodide, Cs_2CO_3 and trans-N,N'-dimethyl-1,2-cyclohexanediamine in, for example, DMF or dioxane, at temperatures ranging from about 60 °C to about 120 °C. Compounds of formula (IVc) can be converted to the corresponding esters (Vb) by treatment with, for example, alkyl iodide in the presence of a base such as K_2CO_3 in a solvent such as DMF. Compounds of formula (III) are obtained by reacting a compound of formula (Va) and (Vb) in the presence of a base such as NaOH in a solvent such as EtOH at temperatures ranging from about 80 °C to about 100 °C. One skilled in the art will recognize that 1,2,3-triazole can exist in two tautomeric forms defined as 2H-[1,2,3]triazole and 1H-[1,2,3]triazole thus compounds of formula (Va), (Vb), and (III) can also exist as the N1 linked variant (structure not shown). It will be understood that the heterocycle in (Va) and (Vb) is not limited to triazole and may be any other suitable heterocycle.

Scheme 3



Intermediate compounds of formula (IX) are prepared as outlined in Scheme 3 from commercially available or synthetically accessible compounds of formula (VI) where R_3, R_4, are defined as in formula IA above, or R_3 is H, R_4 is analogous to R_2 in Formula I as above, and X and Y are independently selected from C and N, G is $SnBu_3$ or 4,4,5,5 tetramethyl-1,dioxaboralane and Hal is Cl, or Br, preferably Br in this case. Compounds of formula (VIII) are obtained by reacting a compound of formula (VI) with commercially available (VII) in the presence of a catalyst such as 1,1'-Bis(di-tert-butylphosphino)ferrocene palladium dichloride and a base such as Na_2CO_3 in a solvent such as 2-MeTHF or THF at temperatures ranging from about 60°C to about 90°C. Compounds of formula (IX) are obtained by reacting a compound of formula (VIII) in the presence of a base such as NaOH in a solvent such as MeOH at temperatures ranging from about 80°C to about 100°C or acids such as H_2SO_4 in solvents such as H_2O at temparatures ranging from about 80 to about 100 °C. It will be understood that the heterocycle in (VII) is not limited to pyrimidine and may be any other suitable heterocycle.

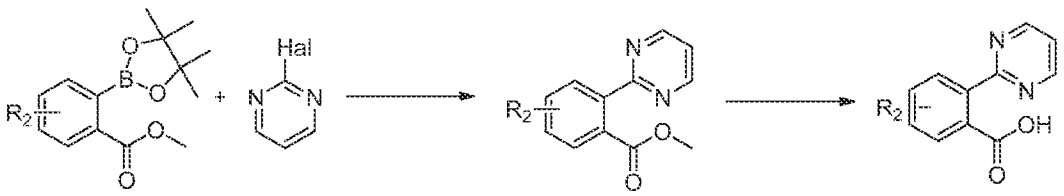
Scheme 4



Intermediate compound (XIV) is prepared as outlined in Scheme 4 from commercially available compound (X). Compounds (XI) is obtained by reacting compound (X) with commercially available acrolein in a solvent such as 1,4 dioxane at temperatures of about 200°C

in a microwave reactor. Compound (XII) can be prepared from compound (XI) by treatment with an acid such as HBr in a solvent such as toluene at a temperature of about 90°C. Compound (XIII) can be obtained by treatment of compound (XII) with commercially available iodoethane and a base such as K_2CO_3 in a solvent such as DMF at temperatures ranging from about 45°C to about 65°C. Compound (XIV) is obtained by treating compound (XIII) with a base such as NaOH in a solvent such as MeOH at temperatures ranging from about 80°C to about 100°C.

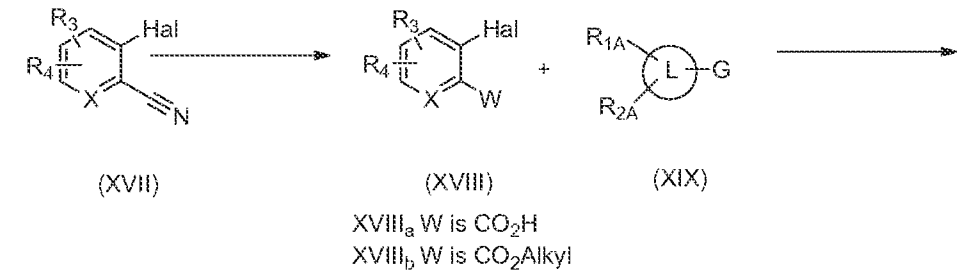
Scheme 5



(XIV) (VII) (XV) (XVI)

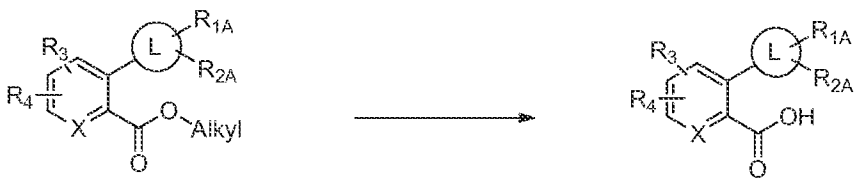
Intermediate compounds of formula (XVI) are prepared as outlined in Scheme 5 from ommercially available or synthetically accessible compounds of formula (XIV) where R_2 is -H, -C_{1-4}alkyl,or -C_{1-4}alkoxy; or R_2 is -H, halo, -C_{1-4}alkyl,or -C_{1-4}alkoxy. Compounds of formula (XV) are obtained by reacting a compound of formula (XIV) with commercially available (VII) in the presence of a catalyst such as $Pd(dppf)Cl_2$ and a base such as Na_2CO_3 in a solvent such as 2-MeTHF at temperatures ranging from 75°C to 150°C. Compounds of formula (XVI) are obtained by reacting a compound of formula (XV) in the presence of a base such as NaOH in a solvent such as MeOH at temperatures ranging from about 80°C to about 100°C.

Scheme 6



(XVII) (XVIII) (XIX)

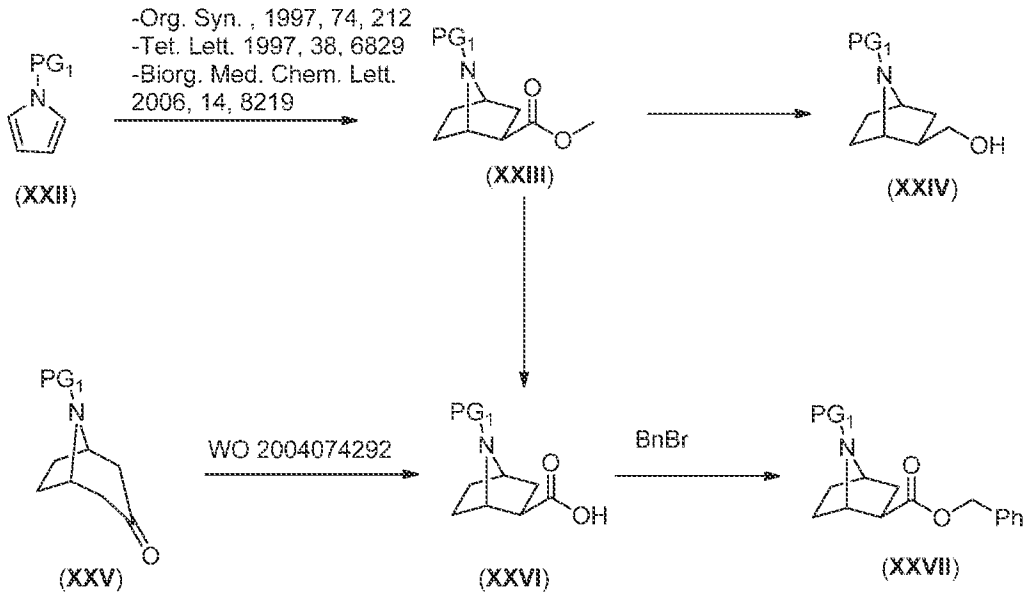
XVIII_a W is CO_2H
XVIII_b W is CO_2Alkyl



(XX) (XXI)

Intermediate compounds of formula (XXI) can be prepared as outlined in Scheme 6 from commercially available or synthetically accessible compounds of formula (XVII) where Hal is Br or I; and where R_3 is H, R_4 is analogous to R_2 in Formula I as above, and X and Y are independently selected from C and N. Compounds of formula (XVIIIa) can be converted to the corresponding ester (XVIIIb) by treatment with thionyl chloride in a solvent such as MeOH. Compounds of the formula (XX) are obtained by reacting compounds of formula (XVIIIb) with commercially available compounds of the formula XIX where L is a heterocyle such as pyrazole, pyridyl, or oxazole; G is $SnBu_3$ or 4,4,5,5 tetramethyl-1,dioxaboralane and R_{1A} and R_{2A} are -H, -alkyl,or –alkoxy; or R_{1A} and R_{2A} are -H, halo, -C_{1-4}alkyl,or -C_{1-4}alkoxy, in the presence of a catalyst such as $Pd(Ph_3P)_4$ and a base such as Na_2CO_3 in a mixture of solvents such as DME and H_2O at temperatures ranging from 100°C to 150°C. Compounds of formula (XXI) are obtained by reacting a compound of formula (XX) in the presence of a base such as NaOH in a solvent such as MeOH at temperatures ranging from about 80°C to about 100°C.

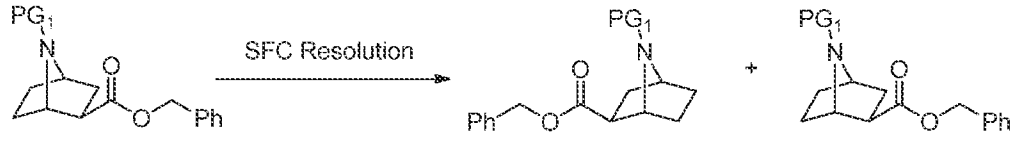
Scheme 7



Intermediate compounds of formula (XXIV) and (XXVII) are readily prepared as outlined in Scheme 7 from commercially available or synthetically accessible compounds of formula (XXII) or (XXV). Compounds of formula (XXIII) can be obtained from compounds of formula (XXII) as described in the references listed in Scheme 7. Compounds of formula

(XXIV) can be obtained from compounds of formula (XXIII) by treatment with reducing agents such as Dibal-H, $LiAlH_4$ or $LiBH_4$ in solvents such as THF or diethyl ether at temperatures ranging from about 0 °C to about 70 °C. Compounds of formula (XXVI) can be obtained from compounds of formula (XXIII) by treatment with bases such as aqueous sodium hydroxide, potassium hydroxide and lithium hydroxide in solvents such as water, methanol or THF. Compounds of formula (XXVI) can also be obtained from compounds of formula (XXV) using procedures described in WO 2004074292.

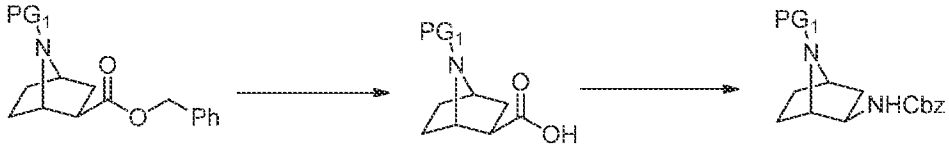
Scheme 8



(±)-(**XXVII**) (-)-(**XXVII**) (+)-(**XXVII**)

Referring to Scheme 8, where PG_1 is a Boc protecting group, compounds of formula (±)-(XXVII) were resolved into individual enantiomers of formula (+)-(XXVII) and (-)-(XXVII) using SFC chromatography on a chiral SFC (CHIRALPAK IC 5 μM 250 X 20mm) column using 80% CO_2/20% *i*PrOH as the mobile phase.

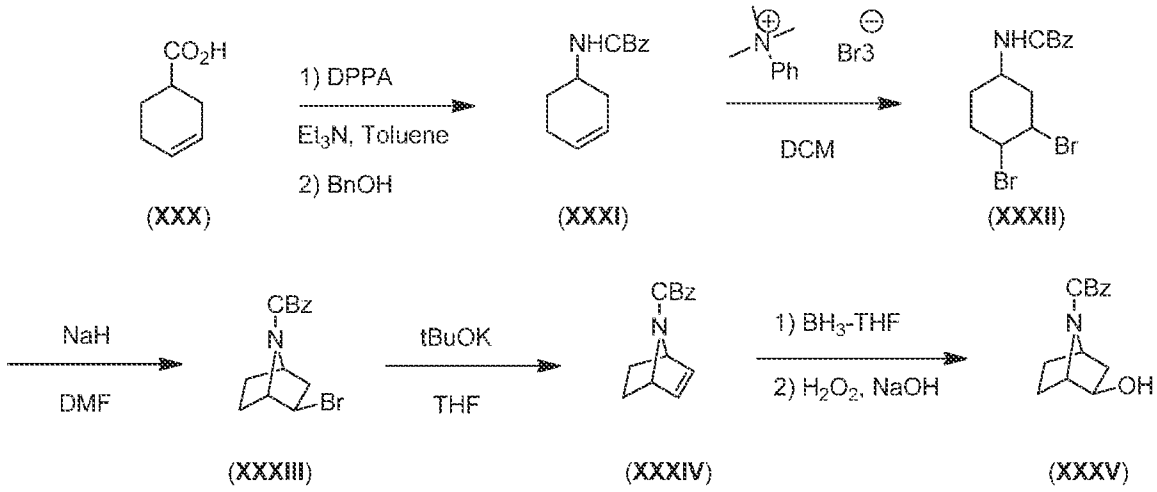
Scheme 9



(+)-(**XXVII**) (**XXVIII**) (**XXIX**)

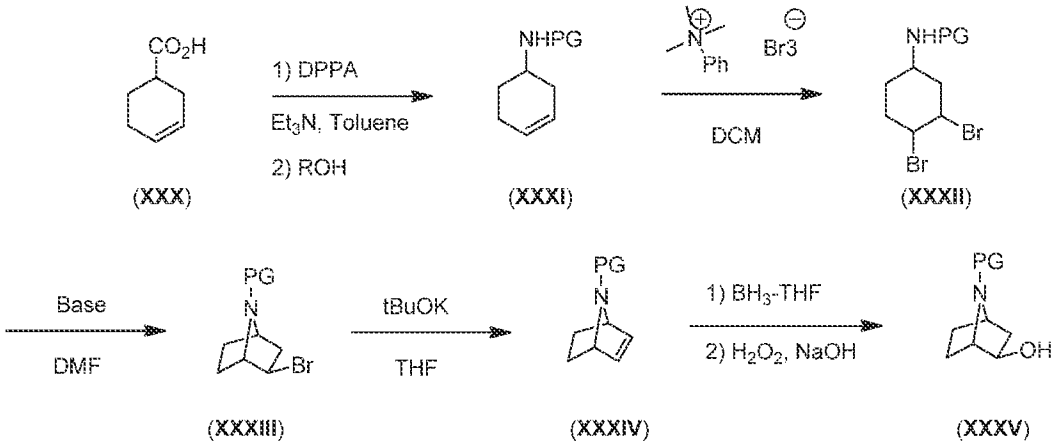
Referring to Scheme 9, where PG_1 is a Boc protecting group, compounds of formula (XXVIII) are prepared compounds of formula (+)-(XXIX). Compounds of formula (XXVIII) are readily prepared from compounds of formula (+)-(XXVII) by treatment with metal catalyst such as PtO_2, Pd/C, or $Pd(OH)_2$ in solvents such as AcOH, MeOH or EtOH under an atmosphere of hydrogen. Compounds of formula (XXIX) are readily prepared from compounds of formula (XXVIII) by reaction with DPPA and TEA in a solvent such as toluene at temperatures ranging from about 0 °C to about 100 °C, preferably about 65 °C for a period of about 1 to 8 hours. BnOH is then added to afford a compound of formula (XXIX).

Scheme 10



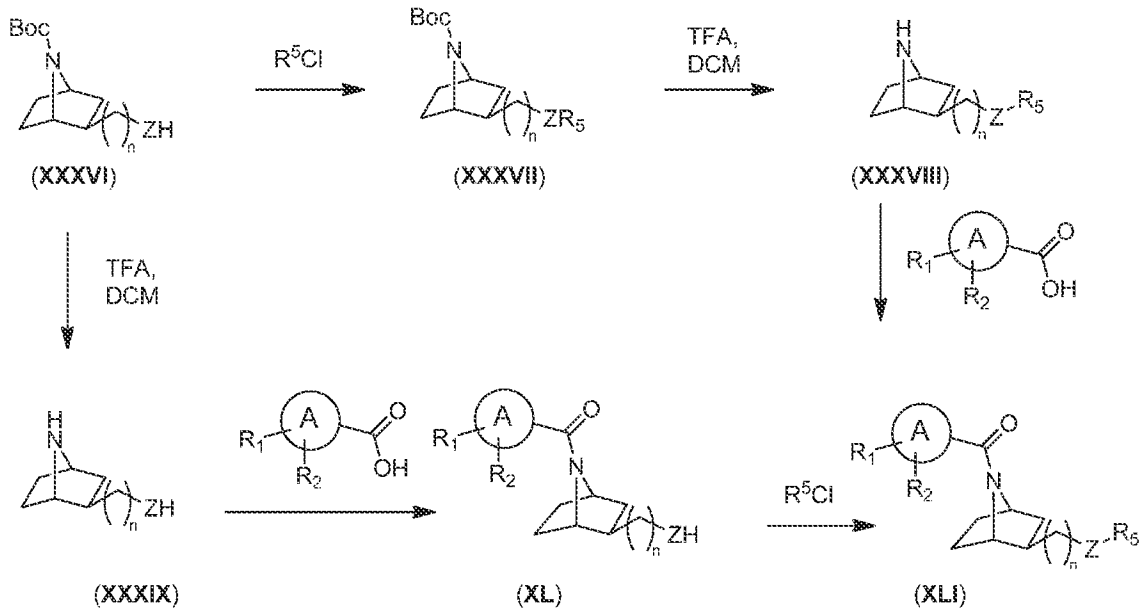
According to Scheme 10, compound (XXXI) is obtained by reaction of compound (XXX) with, for example, DPPA and TEA in a solvent such as toluene at temperatures ranging from about 0 °C to about 100 °C, preferably about 65 °C for a period of about 1 to 8 hours, preferably about 4 h. Benzyl alcohol (BnOH) is then added to afford a compound of formula (XXXI). Compound (XXXII) is obtained from compound (XXXI) by reaction with trimethylphenyl ammonium tribromide at temperatures ranging from about 0 °C to about 23 °C, preferably about 0 °C for a period of from 2 to 6 hours, preferably about 4 hours. Compound (XXIII) is obtained from compound (XXXII) by treatment with a base, preferably NaH in a solvent such as DMF. Compound (XXXIV) is obtained from compound (XXXIII) by elimination of HBr with tBuOK in a solvent such as THF for a period ranging from 2 to 24 hours. Compound (XXXV) is obtained from compound (XXXIV) by hydroboration oxidation by treating the compound (XXXIV) with borane in a solvent such as THF at temperatures ranging from about 0 °C to about 23 °C, preferably at about 23 °C, for 2 to 12 hours, preferably about 2 hours followed by reaction with, for example, hydrogen peroxide in the presence of a base such as sodium hydroxide. Also contemplated within the scope of embodiments presented here are other nitrogen protecting groups which are known to one skilled in the art.

Scheme 10-A



Certain variations of Scheme 10 are described in Scheme 10-A above. It will be understood that the protecting group in compound (XXXI) may be varied as shown in Scheme 10-A, for example, by adding any other suitable alcohol. An alcohol such as BnOH or preferably tBuOH is added to afford a compound of formula (XXXI). Additionally, the protecting group in a compound of formula (XXXI) can be exchanged utilizing standard methods, for example, from BOC to TFA. It will be further understood that the base utilized for the conversion of compound (XXXII) to (XXXIII) may be varied as shown in Scheme 10-A. Compound (XXIII) is obtained from compound (XXXII) by treatment with a base, such as NaH or preferably K_2CO_3 is a solvent such as DMF or preferably toluene at temperatures ranging from about 0 °C to about 100 °C with or without a protecting group present. Further, the choice of the protecting group and/or base and/or solvents and/or reaction temperatures will vary depending on the reaction substrate and all such variations are contemplated within the scope of embodiments provided herein.

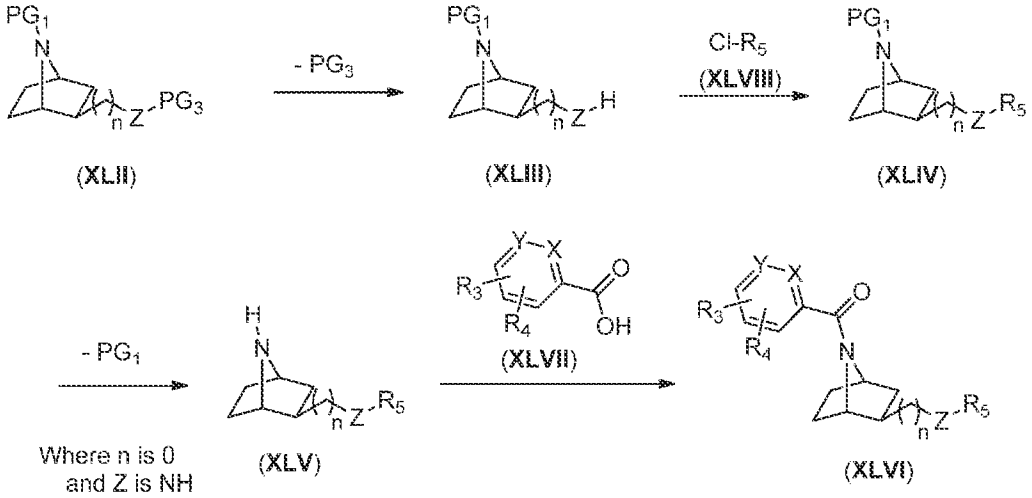
Scheme 11



Referring to Scheme 11, one skilled in the art would recognize that compounds of formula (XLI) may be obtained from compounds of formula (XXXVI) by converging pathways. In one sequence, a compound of formula (XXXVII) is obtained by treating a compound of formula (XXXVI) with R^5Cl, where R^5 is optionally substituted pyridyl, pyrimidyl, pyrazinyl, pyridazinyl, quinazolinyl, quinoxalinyl, pyrazolyl, benzoxazolyl, imidazopyrazinyl, triazolopyrazinyl. Commercially available or synthetically accessible suitably substituted heteroaryl compounds of formula R^5Cl are reacted with compounds of formula (XXXVI), in the presence of a suitably selected tertiary organic or inorganic base such as NaH, Cs_2CO_3, K_2CO_3, TEA, iPr_2NEt and the like; in a solvent such as DMF, dichloromethane, THF, and the like; at a temperature between room temperature and the reflux temperature of the solvent. In a preferred embodiment the base is NaH and the solvent is DMF. Removal of the *tert*-butylcarbamate (Boc) in compounds of formula (XXXVII) is accomplished by using methods known to one skilled in the art, such as, HCl, TFA, or *p*-toluenesulfonic acid, in a solvent such as CH_3OH, dioxane, or CH_2Cl_2. In a preferred embodiment, a compound of formula (XXXVII) is treated with TFA in DCM or HCl to afford a compound of formula (XXXVIII). A compound of formula (XLI) is obtained by treating a compound of formula (XXXVIII) with $(R^1R^2A)CO_2H$, where R^1 is H, alkyl, alkoxy, hydroxyalkylene, OH, halo, phenyl, triazolyl, oxazolyl, isoxazolyl, pyridyl, pyrimidyl, pyrazinyl, pyridazinyl, piperazinyl, pyrazolyl, oxadiazolyl, pyrrolidinyl, thiophenyl, morpholinyl, or dialkylamino and R_2 is H, alkyl, alkoxy, or halo. Commercially available or synthetically accessible suitably substituted carboxcylic acid compounds of formula

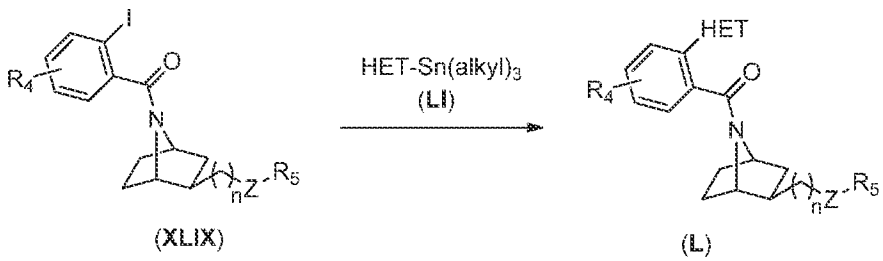
$(R^1R^2A)CO_2H$ are combined with compounds of formula (XXXVIII) using under amide coupling methods known to one skilled in the art, such as, CDI, EDCI, HATU, or T3P in a solvent such as THF, DCM, or DMF In a preferred embodiment, a compound of formula (XXXVIII) and $(R^1R^2A)CO_2H$ are treated with EDCI in the presence of HOBT in DMF at ambient temperature to afford a compound of formula (XLI). One skilled in the art would recognize that compounds of formula (XLI) may also be obtained from compounds of formula (XL). Removal of the *tert*-butylcarbamate (Boc) in compounds of formula (XXXVI) is accomplished by using methods known to one skilled in the art, such as, HCl, TFA, or *p*-toluenesulfonic acid, in a solvent such as CH_3OH, dioxane, or CH_2Cl_2. In a preferred embodiment, a compound of formula (XXXVI) is treated with TFA in DCM or HCl to afford a compound of formula (XXXIX). A compound of formula (XL) is obtained by treating a compound of formula (XXXIX) with $(R^1R^2A)CO_2H$. Commercially available or synthetically accessible suitably substituted carboxcylic acid compounds of formula $(R^1R^2A)CO_2H$ are combined with compounds of formula (XXXIX) under amide coupling methods known to one skilled in the art, such as, CDI, EDCI, HATU, or T3P in a solvent such as THF, DCM, or DMF In a preferred embodiment, a compound of formula (XXXIX) and $(R^1R^2A)CO_2H$ are treated with EDCI in the presence of HOBT in DMF at ambient temperature to afford a compound of formula (XL). A compound of formula (XLI) is obtained by treating a compound of formula (XL) with R^5Cl. Commercially available or synthetically accessible suitably substituted heteroaryl compounds of formula R^5Cl are reacted with compounds of formula (XL), in the presence of a suitably selected tertiary organic or inorganic base such as NaH, Cs_2CO_3, K_2CO_3, TEA, iPr_2NEt and the like; in a solvent such as DMF, dichloromethane, THF, and the like; at a temperature between room temperature and the reflux temperature of the solvent. In a preferred embodiment the base is NaH and the solvent is DMF to provide compounds of formula (XLI).

Scheme 12



Referring to Scheme 12, compounds of formula (XLVI) were synthesized from compounds of formula (XLII) where PG_1 is Boc, PG_3 is Cbz, Z is O or NH and n is 0 or 1. PG_3 was removed when compound of formula (XLII) was treated with, for example, a Pd catalyst such as 10 wt% Pd/C wet Degussa under an atmosphere of H_2 in a solvent such as EtOH to give compound of formula (XLIII). Compounds of formula (XLIV) were obtained from compounds of formula (XLIII) using compounds of formula (XLVIII) in a suitable solvent such as DMSO or DMF in the presence of a base such as K_2CO_3 at a temperature of about 70 °C. Compounds of formula (XLIV) could also be obtained when compounds of formula (XLIII) and (XLVIII) were treated with a Pd catalyst such as $Pd(OAc)_2$, a ligand such as racemic BINAP, a base such as sodium tert-butoxide in a solvent such as toluene at a temperature of about 70 °C. Compound of formula (XLV) were obtained from compounds of formula (XLIV) when treated with an acid such as HCl in a suitable solvent such as EtOAc or DCM at room temperature. Compound of formula (XLVI) were obtained from compounds of formula (XLV) using compounds of formula (XLVII) in a suitable solvent such as DMF or DCM in the presence of a peptide coupling reagent such as HATU or T3P, a base such as DIPEA at a temperature ranging from room temperature to about 45 °C.

Scheme 13



Referring to Scheme 13, compounds of formula (**L**), where R_4 is analogous to R_2 of Formula I above, were obtained from compound of formula (**XLIX**) using compounds of formula (**LI**) in a solvent such as DME in the presence of a Pd catalyst such as Pd(PPh3)4, an additive or catalyst such as copper iodide at a temperature ranging from about 120 °C to about 150 °C.

In one group of embodiments, provided herein is a compound of Formula I of Examples 1-482 with structures and names as set forth in the Examples section below. In another group of embodiments, provided herein is a compound of Formula I of Examples 1-367 with structures and names as set forth in the Examples section below. In yet another embodiment, provided herein is a compound of Formula I of Examples 368-482 with structures and names as set forth in the Examples section below. In an additional embodiment, provided herein is a compound of Formula IA of Examples 483-495 with structures and names as set forth in the Examples section below. In one group of embodiments, provided herein is a compound of Formula I having structures and names as set forth in Table 2 below.

EXAMPLES

Abbreviations

Term	Acronym
Acetic Acid	HOAc
Acetonitrile	ACN
Apparent	app
Aqueous	aq
Atmosphere	atm
2-(1H-9-Azobenzotriazole-1-yl)-1,1,3,3-tetramethylaminium hexafluorophosphate	HATU
O-(Benzotriazol-1-yl)-*N,N,N',N'*-tetramethyluronium nhexafluorophosphate	HBTU
1-Ethyl-3-(3-dimethylaminopropyl)carbodiimide	EDCI
Hydroxybenzotriazole	HOBt
Benzyl	Bn
2,2'-bis(diphenylphosphino)-1,1'-binaphthalene	BINAP
[1,1'-Bis(di-*tert*-butylphosphino)ferrocene]dichloropalladium(II)	$PdCl_2$(dtbpf)
Broad	br
tert-Butylcarbamoyl	Boc/Boc
Dichloromethane	DCM
Diisopropylethylamine	DIPEA
1,2-Dimethoxyethane	DME
N,N-Dimethylformamide	DMF
Dimethylsulfoxide	DMSO

Term	Acronym
Doublet	d
Electrospray ionization	ESI
Enantiomeric excess	ee
Ethanol	EtOH
Ethyl Acetate	EtOAc, or EA
Grams	g
Hertz	Hz
High-pressure liquid chromatography	HPLC
Hours	h
Liquid chromatography and mass spectrometry	LCMS
Mass spectrometry	MS
Mass to charge ratio	m/z
Methanol	MeOH
Microliter	µL
Milligrams	mg
Milliliter	mL
Millimoles	mmol
Minute	min
Molar	M
Multiplet	m
Normal	N
Nuclear magnetic resonance	NMR
Palladium on carbon	Pd/C
Palladium hydroxide on carbon	$Pd(OH)_2/C$
Parts per million	ppm
Phenyl	Ph
Propylphosphonic anhydride	T3P
Retention time	R_t
Room temperature	rt
Quartet	q
Singlet	s
Supercritical Fluid Chromatography	SFC
Temperature	T
Thin layer chromatography	TLC
Times	X
Triethylamine	TEA
Trifluoroacetic acid	TFA
Triplet	t
Diphenylphosphoryl azide	DPPA
Diisopropyl azodicarboxylate	DIAD

Chemistry:

In obtaining the compounds described in the examples below and the corresponding analytical data, the following experimental and analytical protocols were followed unless otherwise indicated.

Unless otherwise stated, reaction mixtures were magnetically stirred at room temperature (rt) under a nitrogen atmosphere. Where solutions were "dried," they were generally dried over a drying agent such as Na_2SO_4 or $MgSO_4$, filtered and concentrated. Where mixtures, solutions, and extracts were "concentrated", they were typically concentrated on a rotary evaporator under reduced pressure. Reactions under microwave irradiation conditions were carried out in a Biotage Initiator or CEM Discover instrument.

Melting point determinations were performed in open capillary tubes on a FP62 or MP50 apparatus (Mettler-Toledo). Melting points were measured with a temperature gradient of 10 °C/minute. Maximum temperature was 300 °C. The melting point was read from a digital display.

Normal-phase flash column chromatography (FCC) was performed on silica gel (SiO_2) using prepackaged cartridges, eluting with the indicated solvents.

Where compounds were purified by "Prep HPLC" the method employed was either:

Preparative reverse-phase high performance liquid chromatography (HPLC) was performed on a Gilson HPLC with an Xterra Prep RP_{18} (5 μm, 30 x 100 mm, or 50 X 150 mm) column, and a gradient of 10 to 99% acetonitrile/water (20 mM NH_4OH) over 12 to 18 min, and a flow rate of 30 mL/min.

or

Preparative reverse-phase high performance liquid chromatography (HPLC) was performed on a Agilent 1100 Series HPLC with an XBridge C18 column (5 μm, 30 x 100mm), mobile phase of 5%ACN in 20mM NH4OH (hold for 2min) then ramp 5-99%ACN over 15 min, hold at 99% ACN for 5 min. and a flow rate of 40 mL/min.

or

Preparative reverse-phase high performance liquid chromatography (HPLC) was performed on a Agilent 1100 Series HPLC with an XBridge C18 column (5 μm, 50 x 100mm), mobile phase of 5%ACN in 20mM NH4OH (hold for 2min) then ramp 5-99%ACN over 15 min, hold at 99% ACN for 5 min. and a flow rate of 80 mL/min.

or

Preparative reverse-phase high performance liquid chromatography (HPLC) was performed on a Gilson HPLC with an Xterra Prep RP_{18} (5 μm, 30 x 100 mm, or 50 X 150 mm)

column, and a gradient of 10 to 99% acetonitrile/water (20 mM NH_4OH) over 12 to 18 min, and a flow rate of 30 mL/min.

Where compounds were purified by "Agilent Prep Method X" the method employed was either:

Preparative reverse-phase high performance liquid chromatography (HPLC) was performed on a Agilent 1100 Series HPLC with an XBridge C18 OBD column (5 µm, 30 x 100mm), mobile phase of 5% ACN in 20mM NH_4OH was held for 2 min, then a gradient of 5-99% ACN over 15 min, then held at 99% ACN for 5 min, with a flow rate of 40 mL/min.

or

Preparative reverse-phase high performance liquid chromatography (HPLC) was performed on a Agilent 1100 Series HPLC with an XBridge C18 OBD column (5 µm, 50 x 100mm), mobile phase of 5% ACN in 20mM NH_4OH was held for 2min, then a gradient of 5-99% ACN over 15 min, then held at 99% ACN for 5 min, with a flow rate of 80 mL/min.

Analytical chromatography data was acquired using an Agilent 1100 HPLC, with an Inertsil ODS-3 3mm 4.6 x 50mm column, purchased from GL Sciences (Part # 1010L050W046). Samples were run using a gradient profile of 10 – 99% acetonitrile (ACN) in water, each containing 0.05% trifluoroacetic acid (TFA) over 1.6 minutes, then holding at 99% acetonitrile for 0.3 minutes. Flow rate was 5 mL/min and column temperature was set to 50 °C (Method A).

Mass spectra (MS) were obtained on an Agilent series 1100 MSD using electrospray ionization (ESI) in positive mode unless otherwise indicated. Calculated (calcd.) mass corresponds to the exact mass.

Nuclear magnetic resonance (NMR) spectra were obtained on Bruker model DRX spectrometers. The format of the 1H NMR data below is: chemical shift in ppm downfield of the tetramethylsilane reference (multiplicity, coupling constant J in Hz, integration). Definitions for multiplicity are as follows: s = singlet, d = doublet, t= triplet, q = quartet, m = multiplet, br = broad. For compounds that are present as a mixture of rotamers the ratio is represented so that the total is 1, e.g. 0.80:0.20. Alternatively, 1H NMR data may be reported for only the major rotamer as indicated, or the data may be reported for one or more rotamers such that the total is less than 1. It will be understood that for compounds comprising an exchangeable proton, said proton may or may not be visible on an NMR spectrum depending on the choice of solvent used for running the NMR spectrum and the concentration of the compound in the solution.

Chemical names were generated using ChemDraw Ultra 12.0 (CambridgeSoft Corp., Cambridge, MA) or ACD/Name Version 10.01 (Advanced Chemistry).

Where compounds were purified by "SFC Chromatography" the method employed was either:

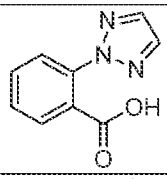
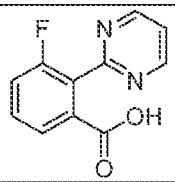
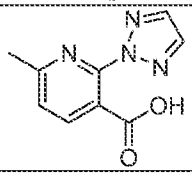
on preparative APS 1010 system with autoprep otion from Berger instrument, consisted of two varian SD-1 pumps (walnut creek, CA, USA), one of which was extensively modified to pump CO_2, a special pump head heat exchanger, a julabo FT 401 chiller (labortechnik GmbH, Sellback, Germany), a model SCM 2500 phase separator (berger instruments) with selection valve and set of collection vessels in a Bodan robot. A model Knauer 2500 UV detector with high pressure flow cell (berlin, germany). Samples were applied using a six-port injection valve (Valco, Houston, TX, USA)) with a 5 ml sample loop and a model YP-300 syringue pump (cavro, san Jose, CA).

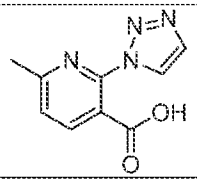
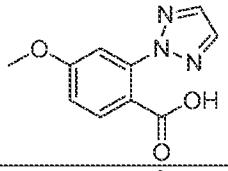
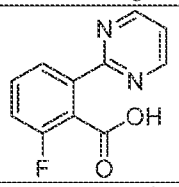
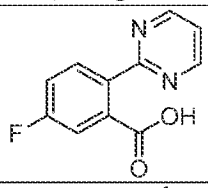
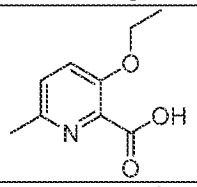
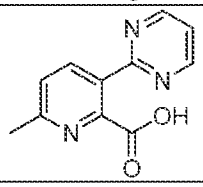
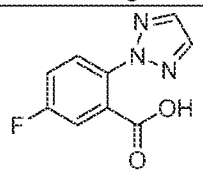
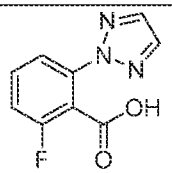
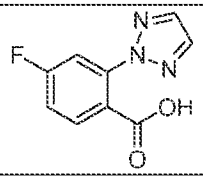
or

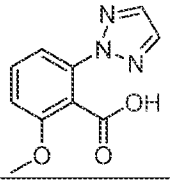
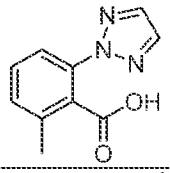
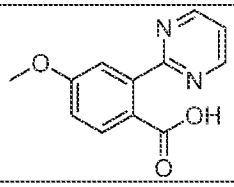
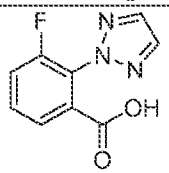
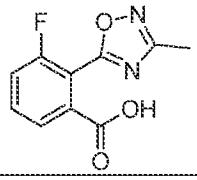
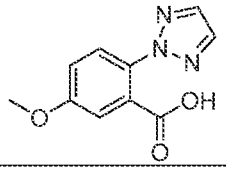
On a SFC-PICLAB-PREP 200 (PIC SOLUTION, Avignon, France). Modifier was pump with a model K1800 Knauer (Berlin, germany), with 100ml Pump Head. The CO_2 was pump with 2 lewa pumps (Leonberg Germany). Cooling of the pump head and the CO2 line was achieved by a coil alimented by a Huber chiller (Offenburg / Germany). Sample injections were made using 6 switching valves (Valco, Houston, TX, USA) and a 5 ml sample loop. The system is managed by a PLC automation system.

Examples 301, 307, 313, 319, 321-367, 396, 464-482, and 483-495 are suitable for preparation using methods analogous to the methods described in the synthetic schemes and in the Examples section.

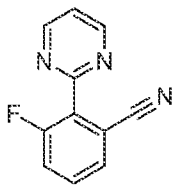
Intermediates

Intermediate	Name	Structure	Reference
A-1	2-(2H-1,2,3-triazol-2-yl)benzoic acid		Prepared according to WO 2011/050198 Intermediate 2.
A-2	3-fluoro-2-(pyrimidin-2-yl)benzoic acid		Prepared according to WO 2011/050198 Intermediate 50.
A-3	6-methyl-2-(2H-1,2,3-triazol-2-yl)nicotinic acid		Prepared according to WO 2011/050198 Intemediate 70

Intermediate	Name	Structure	Reference
A-4	6-methyl-2-(1H-1,2,3-triazol-1-yl)nicotinic acid		Prepared according to WO 2011/050198 Intemediate 71
A-5	4-methoxy-2-(2H-1,2,3-triazol-2-yl)benzoic acid		Prepared according to WO 2011/050198 Intemediate 54
A-6	2-fluoro-6-(pyrimidin-2-yl)benzoic acid		Prepared according to WO 2011/050198 Intermediate 14.
A-7	5-fluoro-2-(pyrimidin-2-yl)benzoic acid.		Prepared according to WO 2011/050198 Intermediate 13.
A-8	3-ethoxy-6-methylpicolinic acid		WO 2010/063663 Description 39
A-9	6-methyl-3-(pyrimidin-2-yl)picolinic acid		WO 2010/063663 Description 69
A-10	5-fluoro-2-(2H-1,2,3-triazol-2-yl)benzoic acid		Prepared according to WO 2011/050198 Intermediate 1.
A-11	2-fluoro-6-(2H-1,2,3-triazol-2-yl)benzoic acid		Prepared according to WO 2011/050198 Intermediate 12.
A-12	4-fluoro-2-(2H-1,2,3-triazol-2-yl)benzoic acid		Prepared according to WO 2011/050198 Intermediate 4.

Intermediate	Name	Structure	Reference
A-13	2-methoxy-6-(2H-1,2,3-triazol-2-yl)benzoic acid		Prepared analogous to Intermediate A-X using 2-bromo-6-(2H-1,2,3-triazol-2-yl)benzoic acid
A-14	2-methyl-6-(2H-1,2,3-triazol-2-yl)benzoic acid		Prepared according to WO 2011/050198 Intermediate 82.
A-15	4-methoxy-2-(pyrimidin-2-yl)benzoic acid		Prepared according to WO 2011/050198 Intermediate 88.
A-16	3-fluoro-2-(2H-1,2,3-triazol-2-yl)benzoic acid		Prepared according to WO 2011/050198 Intermediate 5.
A-17	3-fluoro-2-(3-methyl-1,2,4-oxadiazol-5-yl)benzoic acid		Prepared according to WO 2011/050198 Intermediate 63.
A-18	5-methoxy-2-(2H-1,2,3-triazol-2-yl)benzoic acid		Prepared according to WO 2011/050198 Intermediate 10

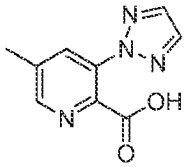
Synthesis of 3-fluoro-2-(pyrimidin-2-yl)benzonitrile (Intermediate in the synthesis of intermediate A-2)



To a solution of 3-fluoro-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzonitrile (4.98 g, 19.1 mmol) and 2-bromopyrimidine (3.85 g, 23 mmol) in THF (96 mL) was added Na_2CO_3 (6 g, 57.4 mmol) followed by water (43 mL). The reaction mixture was degassed with N_2 for 10 minutes. $PdCl_2$(dtbpf) (374 mg, 0.57 mmol) was added and the reaction mixture was stirred at 80 °C for 5h. The solution was cooled to room temperature and a mixture of EtOAc and water was

added. The aqueous was extracted twice with EtOAc and the combined organic layers were dried over MgSO4, filtered and evaporated. The title compound was precipitated by dissolving the residue in a minimum amount of EtOAc and then adding hexanes. The solid was filtered, washed with hexanes and dried to afford the title compound (2.46 g, 64%). MS (ESI) mass calcd. for $C_{11}H_6FN_3$, 199.1; m/z found 200.1 $[M+H]^+$. ^1H NMR (400 MHz, Chloroform-d) δ 9.02 – 8.91 (m, 2H), 7.65 (dt, J = 7.7, 1.0 Hz, 1H), 7.60 – 7.52 (m, 1H), 7.51 – 7.43 (m, 1H), 7.41 (t, J = 4.9 Hz, 1H).

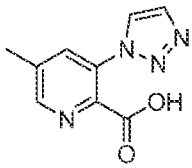
Intermediate A-19: 5-methyl-3-(2H-1,2,3-triazol-2-yl)picolinic acid.



Step A: 5-methyl-3-(2H-1,2,3-triazol-2-yl)picolinonitrile. To 3-bromo-5-methylpicolinonitrile (1.5 g, 7.6 mmol) in DMF (19 mL) was added K_2CO_3 (1.2 g, 8.4 mmol) and 2H-1,2,3-triazole (440 µL, 7.6 mmol). The mixture was heated to 100 °C for 16 h, cooled to rt and extracted with EtOAc (2X). The combined organics were dried (Na_2SO_4) and concentrated. Purification via silica gel chromatography (5-60% EtOAc in hexanes) gave the title compound (490 mg, 35%) ^1H NMR (500 MHz, $CDCl_3$) 8.58 – 8.53 (m, 1H), 8.29 – 8.24 (m, 1H), 7.98 (s, 2H), 2.54 (s, 3H) and 5-methyl-3-(1H-1,2,3-triazol-1-yl)picolinonitrile (387 mg, 27%).

Step B: 5-methyl-3-(2H-1,2,3-triazol-2-yl)picolinate. To a solution of the the title compound of Step A (489 mg, 2.6 mmol) in EtOH (7 mL) was added 4 N NaOH (660 µL, 2.6 mmol). The mixture was heated at 100°C for 24 h. The reaction mixture was concentrated in vacuo to a white solid which was used without further purification in subsequent steps. MS (ESI) mass calcd. for $C_9H_8N_4O_2$, 204.1; m/z found 205.0 $[M+H]^+$.

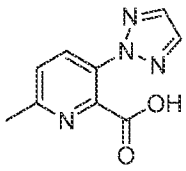
Intermediate A-20: 5-methyl-3-(1H-1,2,3-triazol-1-yl)picolinic acid.



Step A: 5-methyl-3-(1H-1,2,3-triazol-1-yl)picolinonitrile. The title compound was prepared in Intermediate A-19 Step A. ^{1}H NMR (500 MHz, $CDCl_3$) 8.65 (dd, J = 1.8, 0.9 Hz, 1H), 8.41 (d, J = 1.2 Hz, 1H), 8.18 – 8.15 (m, 1H), 7.95 (d, J = 1.2 Hz, 1H), 2.58 (s, 3H).

Step B: 5-methyl-3-(1H-1,2,3-triazol-1-yl)picolinic acid. Prepared analogous to Intermediate A-19 substituting 5-methyl-3-(2H-1,2,3-triazol-2-yl)picolinonitrile with the title compound of Step A. MS (ESI) mass calcd. for $C_9H_8N_4O_2$, 204.1; m/z found 205.0 $[M+H]^+$.

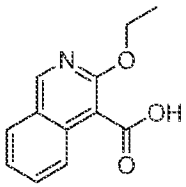
Intermediate A-21: 6-methyl-3-(2H-1,2,3-triazol-2-yl)picolinic acid.



Step A: 6-methyl-3-(2H-1,2,3-triazol-2-yl)picolinonitrile. To 3-bromo-6-methylpicolinonitrile (2.2 g, 11 mmol) in DMF (28 mL) was added K_2CO_3 (1.7 g, 12 mmol) and 2H-1,2,3-triazole (650 µL, 11 mmol). The mixture was heated to 100 °C for 36 h, cooled to rt and extracted with EtOAc. The combined organics were dried (Na_2SO_4) and concentrated. Purification via silica gel chromatography (10-100% EtOAc in hexanes) gave the title compound (1g, 48%).

Step B: 6-methyl-3-(2H-1,2,3-triazol-2-yl)picolinic acid. To a solution of the the title compound of Step A (730 mg, 4 mmol) in EtOH (10 mL) was added 4 N NaOH (1 mL, 4 mmol). The mixture was heated at 100°C for 24 h. The reaction mixture was concentrated in vacuo to a white solid which was used without further purification in subsequent steps.

Intermediate A-22: 3-ethoxyisoquinoline-4-carboxylic acid.



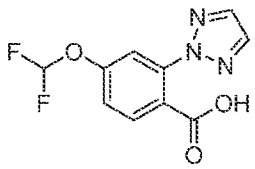
Step A: ethyl 3-hydroxyisoquinoline-4-carboxylate. To a suspension of ethyl 3-aminoisoquinoline-4-carboxylate (583 mg, 2.70 mmol) in 6.8 mL of H_2SO_4 5N cooled to 0 °C was added sodium nitrite (223 mg, 3.24 mmol, dissolved in 1 mL of water). The reaction mixture was stirred at 0 °C for 2.5 h and then $NaOH_{(aq)}$ 1N was added until pH=7. The aqueous phase

was extracted twice with DCM and the combined organic phases were dried over $MgSO_4$, filtered and evaporated to give the title compound of Step A which was used without further purification in the next step (583 mg, 99%). MS (ESI) mass calcd. for $C_{12}H_{11}NO_3$, 217.1; m/z found 218.1 $[M+H]^+$.

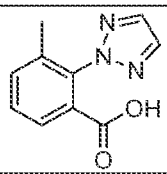
Step B: ethyl 3-ethoxyisoquinoline-4-carboxylate. To the title compound of Step A (583 mg, 2.68 mmol) in THF (13 mL) was added triphenylphosphine (1.06 g, 4.03 mmol), ethanol (0.24 mL, 4.03 mmol) and DIAD (0.79 mL, 4.03 mmol). The reaction mixture was stirred at room temperature for 16h and then the solvent was evaporated. The crude was purified via silica gel chromatography (0-30% EtOAc in hexanes) to afford the title compound of Step B (498 mg, 76%). MS (ESI) mass calcd. for $C_{14}H_{15}NO_3$, 245.1; m/z found 246.1 $[M+H]^+$. ^1H NMR (500 MHz, Chloroform-d) δ 8.97 (s, 1H), 7.91 – 7.82 (m, 2H), 7.65 – 7.60 (m, 1H), 7.42 – 7.36 (m, 1H), 4.59 – 4.48 (m, 4H), 1.48 – 1.39 (m, 6H).

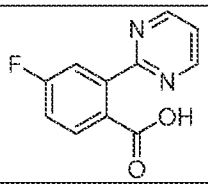
Step C: 3-ethoxyisoquinoline-4-carboxylic acid. The title compound of Step B (492 mg, 2 mmol) dissolved in MeOH (15 mL) was added $NaOH_{(aq)}$ 2M (2.5 mL). The reaction mixture was stirred at 60 °C for 16h and then $NaOH_{(aq)}$ 4M (2 mL) was added and the mixture was stirred at 70 °C for 4h. MeOH was evaporated and the aqueous phase was cooled to 0 °C and acidified with the addition of $HCl_{(aq)}$ 6N. The solid was filtered, washed with cold water and dried to afford the tilte compound (285 mg, 65%). MS (ESI) mass calcd. for $C_{12}H_{11}NO_3$, 217.1; m/z found 218.1 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d6) δ 13.36 (s, 1H), 9.15 (s, 1H), 8.13 – 8.06 (m, 1H), 7.82 – 7.70 (m, 2H), 7.54 – 7.47 (m, 1H), 4.50 (q, J = 7.0 Hz, 2H), 1.35 (t, J = 7.0 Hz, 3H).

Intermediate A-23: 4-(difluoromethoxy)-2-(2H-1,2,3-triazol-2-yl)benzoic acid

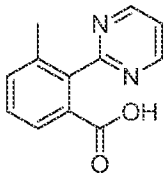


Prepared analogous to Intermediate A-19 substituting 2-bromo-6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridine with 4-(difluoromethoxy)-2-fluorobenzonitrile.

Intermediate	Name	Structure	Reference
A-24	3-methyl-2-(2H-1,2,3-triazol-2-yl)benzoic acid		Prepared according to WO 2011/050198 Intermediate 82

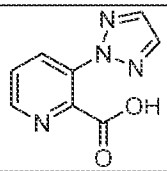
A-25	4-fluoro-2-(pyrimidin-2-yl)benzoic acid		Prepared according to WO 2011/050198 Intermediate 87

Intermediate A-26: 3-methyl-2-(pyrimidin-2-yl)benzoic acid

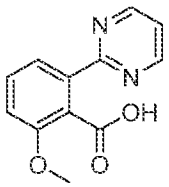


Step A: methyl 3-methyl-2-(pyrimidin-2-yl)benzoate. In a microwave vial was dissolved methyl 3-methyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoate (619 mg, 2.24 mmol) and 2-chloropyrimidine (314 mg, 2.69 mmol) in 2-MeTHF (10 mL). Na_2CO_3 (713 mg, 6.73 mmol) was then added followed by water (3.4 mL) and the reaction mixture was degassed with N_2 for 45 minutes. $Pd(dppf)Cl_2$ (66 mg, 0.09 mmol) and the reaction mixture was heated at 75 °C for 28h. More $Pd(dppf)Cl_2$ (33 mg, 0.045 mmol) was added and the reaction mixture was heated at 150 °C for 3.5h. The mixture was filtered through a pad of celite and rinsed with EtOAc and water. The layers were separated and the aqueous was extracted once with EtOAc. The combined organic layers were dried over $MgSO_4$, filtered and evaporated. The crude was purified via silica gel chromatography (0-50% EtOAc in hexanes) to afford the title compound (116 mg, 23%). MS (ESI) mass calcd. for $C_{13}H_{12}N_2O_2$, 228.1; m/z found 229.1 $[M+H]^+$. ^1H NMR (500 MHz, CDCl3) 8.95 – 8.76 (m, 2H), 7.99 – 7.75 (m, 1H), 7.50 – 7.44 (m, 1H), 7.43 – 7.37 (m, 1H), 7.32 – 7.24 (m, 1H), 3.64 (s, 3H), 2.15 (s, 3H).

Step B: 3-methyl-2-(pyrimidin-2-yl)benzoic acid. Prepared analogous to intermediate A-31 step B to give title compound. MS (ESI) mass calcd. for $C_{12}H_{10}N_2O_2$, 214.1; m/z found 215.1 $[M+H]^+$.

Intermediate	Name	Structure	Reference
A-27	3-(2H-1,2,3-triazol-2-yl)picolinic acid		Prepared according to WO 2011/050198 Intermediate 72

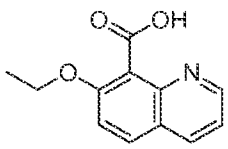
Intermediate A-28: 2-methoxy-6-(pyrimidin-2-yl)benzoic acid



Step A: Methyl 2-methoxy-6-(pyrimidin-2-yl)benzoate. In a microwave vial was dissolved methyl 2-methoxy-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoate (500 mg, 1.71 mmol), commercially available from Combi-Blocks (CAS # 1146214-77-8), and 2-bromopyrimidine (344 mg, 2.05 mmol) in THF (8.5 mL). Na_2CO_3 (544 mg, 5.14 mmol) was then added followed by water (4 mL) and the reaction mixture was degassed with N_2 for 10 minutes. $PdCl_2$(dtbpf) (45 mg, 0.069 mmol) was then added and the reaction mixture was heated at 80 °C for 4h. The mixture was cooled to room temperature and water and EtOAc added. The reaction mixture was extracted with EtOAc (3×). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated. The crude was purified via silica gel chromatography (0-70% EtOAc in hexanes) to afford the title compound (265 mg, 63%). MS (ESI) mass calcd. for $C_{13}H_{12}N_2O_3$, 244.1; m/z found 245.1 $[M+H]^+$. 1H NMR (400 MHz, Chloroform-d) 8.78 (d, J = 4.9 Hz, 2H), 7.99 (dd, J = 7.9, 0.9 Hz, 1H), 7.49 (t, J = 8.1 Hz, 1H), 7.19 (t, J = 4.8 Hz, 1H), 7.09 (dd, J = 8.3, 0.9 Hz, 1H), 3.90 (s, 3H), 3.89 (s, 3H).

Step B: 2-methoxy-6-(pyrimidin-2-yl)benzoic acid. To a solution of the title compound of Step A (265 mg, 1.09 mmol) in THF (4 mL) was added 2 N NaOH (2 mL). The mixture was heated at 50°C for 72 h. The reaction mixture was concentrated in vacuo to a white solid which was used without further purification in subsequent steps. MS (ESI) mass calcd. for $C_{12}H_{10}N_2O_3$, 230.1; m/z found 231.1 $[M+H]^+$. 1H NMR (500 MHz, DMSO-d_6) 12.63 (s, 1H), 8.86 (d, J = 4.9 Hz, 2H), 7.77 (dd, J = 7.9, 1.0 Hz, 1H), 7.51 (t, J = 8.1 Hz, 1H), 7.45 (t, J = 4.9 Hz, 1H), 7.25 (dd, J = 8.4, 1.0 Hz, 1H), 3.83 (s, 3H).

Intermediate A-29: 7-ethoxyquinoline-8-carboxylic acid



Step A: 7-methoxyquinoline-8-carboxylic acid. In 1g separate batches a mixture of 2-amino-6methoxybenzoic acid (11g, 66 mmol) and acrolein (4.8 mL, 72 mmol) in 1,4-dioxane (66 mL) was heated in a microwave reactor for 20 min at 200 °C. After combining the reactions, the mixture was concentrated and purified via silica gel chromatography (0-10% MeOH in

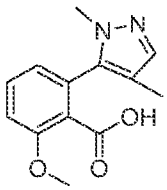
DCM) to give the title compound (2.8g, 20%). MS (ESI) mass calcd. for $C_{11}H_{19}NO_3$, 203.1; m/z found 204.0 $[M+H]^+$.

Step B: 7-hydroxyquinoline-8-carboxylic acid. The title compound of Step A (2.9 g, 14.1 mmol) in HBr (14 mL) was heated at 90 °C for 1h. The mixture was then concentrated washed with PhCH3 and used without further purificaition in subsequent steps.

Step C: ethyl 7-ethoxyquinoline-8-carboxylate. To the title compound of Step B (800 mg, 3.9 mmol) and K2CO3 (1.4 g, 10.4 mmol) in DMF (15 mL) was added iodoethane (560 µL, 6.9 mmol). After stirring overnight at rt, the reaction was concentrated and purified via silica gel chromatography (0-30% EtOAc in hexanes) to give the title compound. MS (ESI) mass calcd. for $C_{14}H_{15}NO_3$, 245.1; m/z found 246.0 $[M+H]^+$.

Step D: 7-ethoxyquinoline-8-carboxylic acid. To the title compound of Step C (1.3 g, 5.4 mmol) in THF (22 mL) and H_2O (11 mL) was added LiOH hydrate (675 mg, 16.5 mmol) and MeOH. The mixture was heated at 67 °C for 12h. Additional LiOH hydrate (675 mg, 16.5 mmol) was added and the heating was continued at 70 °C for 1 day. Additional LiOH hydrate (1.4 g, 33 mmol) was added and the heating was continued at 75 °C for 1 day. The reaction was allowed to cool to rt, acidified to pH=3 with 1N HCl (aq) and concentrated. Purification via prep HPLC gave the title compound (1 g, 84%). MS (ESI) mass calcd. for $C_{12}H_{11}NO_3$, 217.1; m/z found 218.0 $[M+H]^+$.

Intermediate A-30: 2-(1,4-dimethyl-1H-pyrazol-5-yl)-6-methoxybenzoic acid

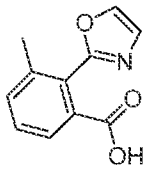


Step A: Ethyl 2-(1,4-dimethyl-1H-pyrazol-5-yl)-6-methoxybenzoate. In a microwave vial was dissolved ethyl 2-bromo-6-methoxybenzoate (500 mg, 1.54 mmol) and 1,4-dimethyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (377 mg, 1.70 mmol) in DME (10 mL) and water (2 mL). Na_2CO_3 (259 mg, 3.09 mmol) was then added followed by $Pd(PPh_3)_4$ (89 mg, 0.077 mmol) and the reaction mixture was degassed with N_2 for 10 minutes. The reaction mixture was then heated at 100 °C for 1h in the microwave. The mixture was cooled to room temperature, filtered through Celite and washed with EtOAc and DCM. The crude solution was concentrated in vacuo and directly purified via silica gel chromatography (10-80% EtOAc in hexanes) to afford the title compound (402 mg, 95%). MS (ESI) mass calcd. for $C_{15}H_{18}N_2O_3$,

274.1; m/z found 275.2 $[M+H]^+$. 1H NMR (400 MHz, Chloroform-d) 7.45 (dd, J = 8.4, 7.6 Hz, 1H), 7.29 (s, 1H), 7.04 (dd, J = 8.5, 0.9 Hz, 1H), 6.84 (dd, J = 7.6, 0.9 Hz, 1H), 4.07 (qd, J = 7.2, 1.5 Hz, 2H), 3.90 (s, 3H), 3.61 (s, 3H), 1.86 (s, 3H), 1.01 (t, J = 7.1 Hz, 3H).

Step B: 2-(1,4-dimethyl-1H-pyrazol-5-yl)-6-methoxybenzoic acid. Prepared analogous to intermediate A-28 step B to give title compound. MS (ESI) mass calcd. for $C_{13}H_{14}N_2O_3$, 246.1; m/z found 247.2 $[M+H]^+$. ^{1}H NMR (500 MHz, DMSO-d_6) 7.50 (dd, J = 8.5, 7.6 Hz, 1H), 7.25 (s, 1H), 7.21 (dd, J = 8.5, 0.9 Hz, 1H), 6.85 (dd, J = 7.6, 0.9 Hz, 1H), 3.84 (s, 3H), 3.49 (s, 3H), 1.79 (s, 3H).

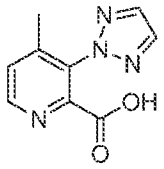
Intermediate A-31: 3-methyl-2-(oxazol-2-yl)benzoic acid



Step A: ethyl 3-methyl-2-(oxazol-2-yl)benzoate. In a microwave vial was dissolved ethyl 2-iodo-3-methylbenzoate (627 mg, 2.16 mmol) and 2-(tributylstannyl)oxazole (0.54 mL, 0.07 mmol) in DME (2.59 mL). The solution was degassed with N_2 for 5 minutes then CuI (21 mg, 0.11 mmol) and $Pd(PPh_3)_4$ (125 mg, 0.11 mmol) were added. The reaction was purged with N_2 and heated at 150 °C for 1h. The reaction was cooled to rt, filtered through a pad of celite and purified via silica gel chromatography (0-40% EtOAc in hexanes) to give the title compound of step A (333 mg, 67%). MS (ESI) mass calcd. for $C_{13}H_{13}NO_3$, 231.1; m/z found 232.1 $[M+H]^+$. ^{1}H NMR (500 MHz, Chloroform-d) 7.89 – 7.82 (m, 1H), 7.79 (d, J = 0.8 Hz, 1H), 7.48 – 7.43 (m, 2H), 7.30 (d, J = 0.9 Hz, 1H), 4.17 (q, J = 7.1 Hz, 2H), 2.27 (s, 3H), 1.18 (t, J = 7.1 Hz, 3H).

Step B: 3-methyl-2-(oxazol-2-yl)benzoic acid. To the title compound of step A (166 mg, 0.72 mmol) was added MeOH (7.2 mL) and 1M $NaOH_{(aq)}$ (7.2 mL). MeOH was evaporated and then 1 M $HCl_{(aq)}$ was added. To the solution was added DCM and the aqueous was extracted with DCM (3X). The combined organic layers were dried over $MgSO_4$, filtered and evaporated to give the title compound (145 mg). MS (ESI) mass calcd. for $C_{11}H_9NO_3$, 203.1; m/z found 204.1 $[M+H]^+$. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.20 (s, 1H), 7.79 – 7.68 (m, 1H), 7.65 – 7.49 (m, 2H), 7.35 (s, 1H), 4.34 (s, 1H), 2.20 (s, 3H).

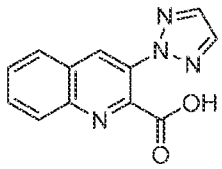
Intermediate A-32: 4-methyl-3-(2H-1,2,3-triazol-2-yl)picolinic acid.



Step A: 4-methyl-3-(2H-1,2,3-triazol-2-yl)picolinonitrile. In a microwave vial was dissolved 2*H*-1,2,3-triazole (0.22 mL, 3.8 mmol) and CuI (26 mg) in DMF (4 mL). The reaction mixture was degassed with N_2 and 3-bromo-4-methylpicolonitrile (300 mg, 1.5 mmol) was added followed by trans-N,N'-dimethyl-1,2-cyclohexanediamine (41 µL, 0.3 mmol) and Cs_2CO_3 (844 mg, 2.6 mmol). The reaction mixture was heated at 120 °C for 1h in a microwave reactor. Then H2O was added and the mixture extracted with EtOAc. The combined organic layers were dried ($MgSO_4$). Purification via silica gel chromatography (0-50% EtOAc in heptane) gave the title compound (112 mg, 27%). MS (ESI) mass calcd. for $C_9H_7N_5$, 185.2; m/z found 186 $[M+H]^+$.

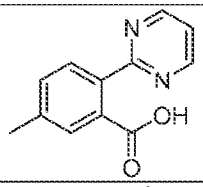
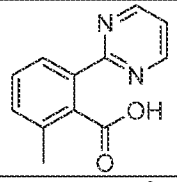
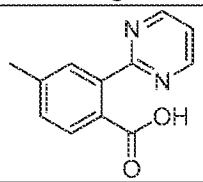
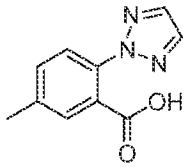
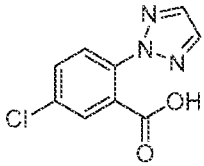
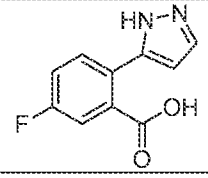
Step B: 4-methyl-3-(2H-1,2,3-triazol-2-yl)picolinic acid. Prepared analogous to Intermediate A-19 substituting 5-methyl-3-(2H-1,2,3-triazol-2-yl)picolinonitrile with the title compound of Step A. The reaction mixture was acidified to pH=4 before concentrating. MS (ESI) mass calcd. for $C_{11}H_9NO_3$, 203.1; m/z found 204.1 $[M+H]^+$.

Intermediate A-33: 3-(2H-1,2,3-triazol-2-yl)quinoline-2-carboxylic acid

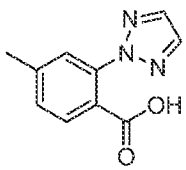


Step A: ethyl 3-(2H-1,2,3-triazol-2-yl)quinoline-2-carboxylate. Prepared analogous to Intermediate A-40 Step A substituting 2-bromo-4-methylbenzoic acid with ethyl 3-iodoquinoline-2-carboxylate (WO 2011093365) in <10% yield. MS (ESI) mass calcd. for $C_{14}H_{12}N_4O_2$, 268.3; m/z found 269.0 $[M+H]^+$.

Step B: 3-(2H-1,2,3-triazol-2-yl)quinoline-2-carboxylic acid. To the title compound of Step A (134 mg, 0.5 mmol) in MeOH (1 mL) was added aqueous 2M NaOH (1 mL). After 1h at rt, the reaction was heated to 50 °C for 1h, cooled to rt, acidified with 1N HCl, concentrated and used in subsequent steps without further purification. MS (ESI) mass calcd. for $C_{12}H_8N_4O_2$, 240.2; m/z found 241.0 $[M+H]^+$.

Intermediate	Name	Structure	Reference
A-34	5-methyl-2-(pyrimidin-2-yl)benzoic acid		Prepared according to WO 2011/050198 Intermediate 50.
A-35	2-methyl-6-(pyrimidin-2-yl)benzoic acid		Prepared according to intermediate A-34 or A-2
A-36	4-methyl-2-(pyrimidin-2-yl)benzoic acid		Prepared according to intermediate A-34 or A-2
A-37	5-methyl-2-(2H-1,2,3-triazol-2-yl)benzoic acid		Prepared according to WO 2011/050198 Intermediate 8.
A-38	5-chloro-2-(2H-1,2,3-triazol-2-yl)benzoic acid		Prepared according to WO 2011/050198 Intermediate 9.
A-39	5-fluoro-2-(1H-pyrazol-5-yl)benzoic acid		Prepared according to WO 2011/050198 Intermediate 51.

Intermediate A-40: 4-methyl-2-(2*H*-1,2,3-triazol-2-yl)benzoic acid.

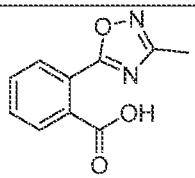


Step A: 4-methyl-2-(2*H*-1,2,3-triazol-2-yl)benzoic acid and 4-methyl-2-(1*H*-1,2,3-triazol-1-yl)benzoic acid. In a microwave vial was dissolved 2*H*-1,2,3-triazole (0.34 mL, 5.81 mmol) and CuI (40 mg, 0.21 mmol) in DMF (5 mL). The reaction mixture was degassed with N_2 for 10 minutes and 2-bromo-4-methylbenzoic acid (500 mg, 2.33 mmol) was added followed by trans-N,N'-dimethyl-1,2-cyclohexanediamine (62 µL, 0.40 mmol) and Cs_2CO_3 (1.29 g, 3.95 mmol). The reaction mixture was stirred at 100 °C for 20 minutes using a microwave oven before being

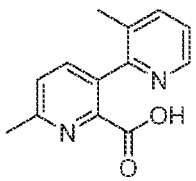
partitioned between water, $HCl_{(aq)}$ (pH=3) and EtOAc. The organic layer was dried over $MgSO_4$, filtered and evaporated to give the crude product mixture which was used in the next step without any further purification.

Step B: methyl 4-methyl-2-(2*H*-1,2,3-triazol-2-yl)benzoate. To the title compound of step A (945 mg, 4.65 mmol) in DMF (28 mL) was added K2CO3 (1.3 g, 9.3 mmol) and iodomethane (0.3 mL, 4.7 mmol). The reaction mixture was stirred at room temperature for 16h under N2. The solvent was evaporated and the residue was dissolved with a saturated solution of NaHCO3. The aqueous phase was extracted with DCM and the organic layer was dried over MgSO4, filtered and evaporated. The crude material was purified via silica gel chromatography (0% to 30% EtOAc/heptane) to afford the title compound (470 mg, 47%).

Step C: Prepared analogous to Intermediate A-31 step B substituting ethyl 3-methyl-2-(oxazol-2-yl)benzoate with the title compound of Step B and used without further purification in subsequent steps.

Intermediate	Name	Structure	Reference
A-41	2-(3-methyl-1,2,4-oxadiazol-5-yl)benzoic acid		Prepared analogous to intermediate A-17

Intermediate A-42: 3,6'-dimethyl-[2,3'-bipyridine]-2'-carboxylic acid.



Step A: 3-bromo-6-methylpicolinic acid. To 3-bromo-6-methylpicolinonitrile (4g, 20.3 mmol) in EtOH (40 mL) in a sealed tube was added aqueous 4M NaOH (15 mL). The reaction was heated at 90 °C for 24h. Additional aqueous 4M NaOH was added and heating continued at 90 °C for 24h. The reaction was cooled to rt, acidified to pH=3 with 1N HCl (aq), concentrated and used without further purification in subsequent steps. MS (ESI) mass calcd. for $C_7H_6BrNO_2$, 216.0; m/z found 218 $[M+H]^+$.

Step B: Methyl 3-bromo-6-methylpicolinate. To the title compound of step A (10.3 g, 20 mmol) in MeOH (50 mL) was added thionyl chloride (4.4 mL, 60 mmol). The reaction was heated at reflux overnight, cooled to rt and concentrated. Purification via silica gel

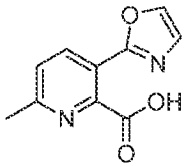
chromatography (0-15% EtOAc in heptane) gave the title compound (1.9g, 40%). MS (ESI) mass calcd. for $C_8H_8BrNO_2$, 230.1; m/z found 232 $[M+H]^+$.

Step C: 3-methyl-2-(tributylstannyl)pyridine. To 2-bromo-3-methylpyridine (1.3 mL, 11.7 mmol) in THF (35 mL) at -78 °C was added *n*-BuLi (2.5 M in hexanes, 5.6 mL, 14 mmol). After 30 min, tri-*n*-butyltin chloride (3.8 mL, 14 mmol) was added. After 1h at – 78 °C, the reaction was allowed to warm to rt. EtOAc was added and the reaction mixture was washed with 10% aq KF. The organic layer was dried (MgSO4). Purification via silica gel chromatography (0-15% EtOAc in heptane) gave the title compound (1.2g, 27%). MS (ESI) mass calcd. for $C_{18}H_{33}NSn$, 382.2; m/z found 384.0 $[M+H]^+$.

Step D: methyl 3,6'-dimethyl-[2,3'-bipyridine]-2'-carboxylate. To the title compound of step B (509 mg, 2.2 mmol) and the title compound of step C (1.1g, 2.9 mmol) in PhCH3 (6.6 mL) was added Pd(PPh3)4 (225 mg, 0.2 mmol). The reaction was degassed with N_2 and heated at 150 °C for 1.5 h using microwave reactor. The reaction was cooled to rt, diluted with H2O and extracted with EtOAc. The organic layer was dried (MgSO4). Purification via silica gel chromatography (0-100% EtOAc in heptane) gave the title compound (101 mg, 18%). MS (ESI) mass calcd. for $C_{14}H_{14}N_2O_2$, 242.3; m/z found 243 $[M+H]^+$.

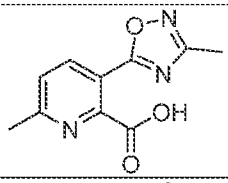
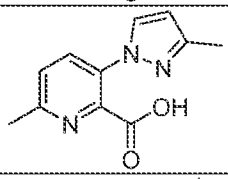
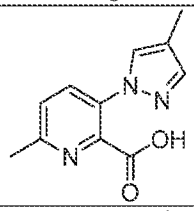
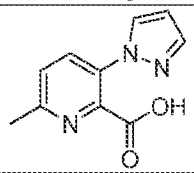
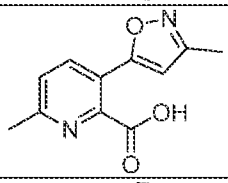
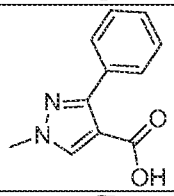
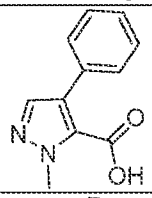
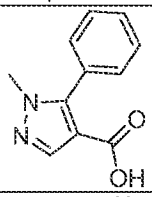
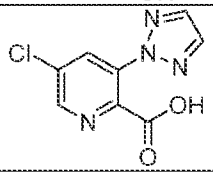
Step E: 3,6'-dimethyl-[2,3'-bipyridine]-2'-carboxylic acid. Prepared analogous to intermediate A-33 step B substituting ethyl 3-(2H-1,2,3-triazol-2-yl)quinoline-2-carboxylate with the title compound of step D. MS (ESI) mass calcd. for $C_{13}H_{12}N_2O_2$, 228.2; m/z found 229 $[M+H]^+$.

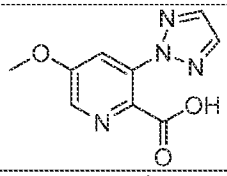
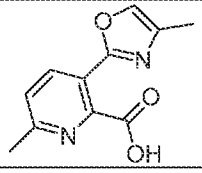
Intermediate A-43: 6-methyl-3-(oxazol-2-yl)picolinic acid



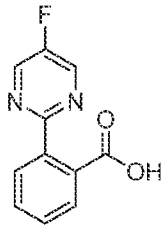
Prepared analogous to Intermediate A-31 substituting ethyl 2-iodo-3-methylbenzoate with methyl 3-iodo-6-methylpicolinate. MS (ESI) mass calcd. for $C_{10}H_8N_2O_3$, 204.2; m/z found 161 $[M-CO2]^+$.

Intermediate	Name	Structure	Reference

Intermediate	Name	Structure	Reference
A-44	6-methyl-3-(3-methyl-1,2,4-oxadiazol-5-yl)picolinic acid		WO 2010/063663 Description 64
A-45	6-methyl-3-(3-methyl-1H-pyrazol-1-yl)picolinic acid		WO 2010/063663 Description 71
A-46	6-methyl-3-(4-methyl-1H-pyrazol-1-yl)picolinic acid		WO 2010/063663
A-47	6-methyl-3-(1H-pyrazol-1-yl)picolinic acid		WO 2010/063663 Description 73
A-48	6-methyl-3-(3-methylisoxazol-5-yl)picolinic acid		WO 2010/063663 Description 117
A-49	1-methyl-3-phenyl-1H-pyrazole-4-carboxylic acid		Purchased
A-50	1-methyl-4-phenyl-1H-pyrazole-5-carboxylic acid		Purchased
A-51	1-methyl-5-phenyl-1H-pyrazole-4-carboxylic acid		Purchased
A-52	5-chloro-3-(2H-1,2,3-triazol-2-yl)picolinic acid		WO 2012/145581 Intermediate 105

Intermediate	Name	Structure	Reference
A-53	5-methoxy-3-(2H-1,2,3-triazol-2-yl)picolinic acid		WO 2012/145581 Intermediate 105
A-54	6-methyl-3-(4-methyloxazol-2-yl)picolinic acid		

Intermediate A-55: 2-(5-fluoropyrimidin-2-yl)benzoic acid.



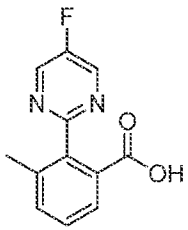
Step A: 5-fluoro-2-iodopyrimidine. To a solution of 2-chloro-5-fluoropyrimidine (4 mL, 32 mmol) in propionitrile (33 mL) was added chlorotrimethylsilane (12 mL, 97 mmol) and sodium iodide (15 g, 97 mmol), and the reaction mixture was heated to 150 °C for 1 h. Upon completion of the reaction, the reaction mixture was cooled to room temperature and the solvent removed. The residue was taken up in EtOAc and a solution of saturated $NaHCO_3$. The organic layer was dried over $MgSO_4$, filtered and evaporated. Purification via silica gel chromatography (0-20% EtOAc in hexanes) gave the title compound (2.82 g, 39%).

Step B: 2-(5-fluoropyrimidin-2-yl)benzonitrile. In a microwave vial was dissolved cyanophenylboronic acid (500 mg, 3.40 mmol) in THF (15 mL), and the reaction mixture was degassed with N_2. Then, the title compound of step A (915 mg, 4.08 mmol), Na_2CO_3 (1.08 g, 10.2 mmol), water (5 mL), and $PdCl_2$(dtbpf) (CAS 95408-45-0) (89 mg, 0.14 mmol) were added, and the reaction mixture was stirred at room temperature for 1 h and then heated via microwave heating to 75 °C for 2 h. The mixture was cooled to room temperature and water and EtOAc added. The reaction mixture was extracted with EtOAc. The combined organic layers were dried over $MgSO_4$, filtered and concentrated. The crude was purified via silica gel chromatography (0-30% EtOAc in hexanes) to afford the title compound (280 mg, 41%). MS (ESI) mass calcd. for $C_{11}H_6FN_3$, 199.1; m/z found 200.0 $[M+H]^+$.

Step C: 2-(5-fluoropyrimidin-2-yl)benzoic acid. A solution of the title compound of step B (1.24 g, 6.22 mmol) in H_2SO_4 (6 mL) and water (6 mL) was stirred at 80 °C for 1 h. Then, the

reaction mixture was cooled to 0 °C and the aqueous phase extracted with DCM (2X). A solution of 20 M NaOH (11 mL) was added to the aqueous layer until pH ~3-4. The aqueous layer was extracted again with EtOAc and DCM. The combined organic layers were dried over $MgSO_4$, filtered and concentrated to afford the title compound (672 mg, 50%). MS (ESI) mass calcd. for $C_{11}H_7FN_2O_2$, 218.1; m/z found 219.1 $[M+H]^+$.

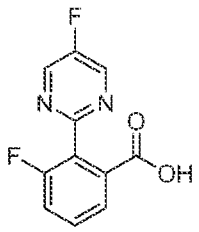
Intermediate A-56: 2-(5-fluoropyrimidin-2-yl)-3-methylbenzoic acid.



Step A: Methyl 2-(5-fluoropyrimidin-2-yl)-3-methylbenzoate. A solution of methyl 3-methyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoate (CAS 887234-98-2) (3 g, 11 mmol) in THF (30 mL) was degassed with N_2. Then, 2-chloro-5-fluoropyrimidine (1.6 mL, 13.04 mmol), Na_2CO_3 (3.45 g, 32.6 mmol), water (10 mL), and $Pd(dppf)Cl_2$ (354 mg, 0.434 mmol) were added, and the reaction mixture was stirred at 100 °C overnight. The mixture was cooled to room temperature and water and EtOAc added. The reaction mixture was extracted with EtOAc. The combined organic layers were dried over $MgSO_4$, filtered and concentrated. The crude was purified via silica gel chromatography (0-40% EtOAc in hexanes) to afford the title compound (1.07 g, 40%).

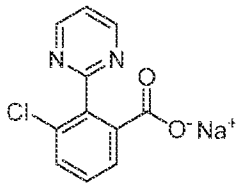
Step B: 2-(5-fluoropyrimidin-2-yl)-3-methylbenzoic acid. To a solution of the title compound of Step A (1.46 g, 5.93 mmol) in MeOH (20 mL) was added 1 M NaOH (12 mL), and the reaction mixture was stirred at room temperature overnight. The solvent was removed and the crude was diluted with water until pH = 10. The aqueous layer was extracted with EtOAc. The aqueous layer was further acidified with 12 M $HCl_{(aq)}$ until pH = 2 and extracted with EtOAc. The combined organic layers were dried over $MgSO_4$, filtered and concentrated to afford the title compound (1.19 g, 83%). MS (ESI) mass calcd. for $C_{12}H_9FN_2O_2$, 232.1; m/z found 233.1 $[M+H]^+$.

Intermediate A-57: 3-fluoro-2-(5-fluoropyrimidin-2-yl)benzoic acid.



Prepared analogous to Intermediate A-55, substituting cyanophenylboronic acid with (2-cyano-6-fluorophenyl)boronic acid (CAS 656235-44-8). MS (ESI) mass calcd. for $C_{11}H_6F_2N_2O_2$, 236.0; m/z found 237.1 $[M+H]^+$.

Intermediate A-58: Sodium 3-chloro-2-(pyrimidin-2-yl)benzoate.

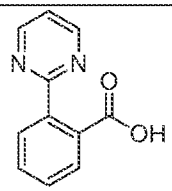
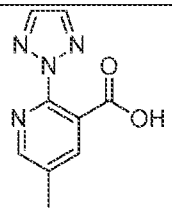
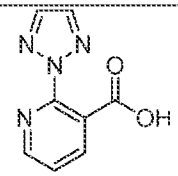
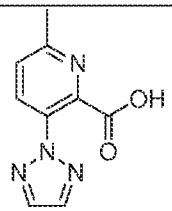
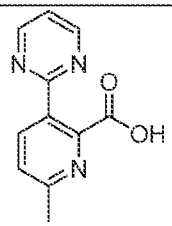
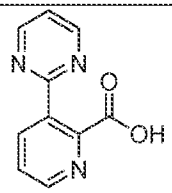
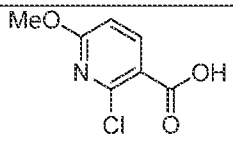


Step A: Methyl 2-(pyrimidin-2-yl)benzoate. Prepared analogous to Example 260 step B substituting 2-(tributylstannyl)oxazole with 2-(tributylstannyl)pyrimidine. MS (ESI) mass calcd. for $C_{12}H_{10}N_2O_2$, 214.1; m/z found 215.1 $[M+H]^+$. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.84 - 8.78 (m, 2H), 8.06 - 7.99 (m, 1H), 7.76 - 7.71 (m, 1H), 7.60 (td, J = 7.6, 1.4 Hz, 1H), 7.52 (td, J = 7.5, 1.3 Hz, 1H), 7.24 (t, J = 4.9 Hz, 1H), 3.75 (s, 3H).

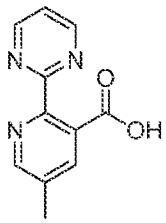
Step B: Methyl 3-chloro-2-(pyrimidin-2-yl)benzoate. In a microwave vial was combined compound of step A (314 mg, 1.47 mmol), $Pd(OAc)_2$ (49 mg, 0.07 mmol), copper (II) trifluoroacetate (425 mg, 1.47 mmol) and calcium chloride (651 mg, 5.87 mmol). The vial was capped and acetic acid (21 mL) was added. The reaction mixture was stirred at 110 °C for 24h and solvent was evaporated. The residue was taken up in EtOAc and a solution of saturated $NaHCO_3$. The aqueous phase was extracted 3 times with EtOAc and the combined organic layers were dried over $MgSO_4$, filtered and evaporated. Purification via silica gel chromatography (0-40% EtOAc in hexanes) gave the title compound (77 mg, 21%). MS (ESI) mass calcd. for $C_{12}H_9ClN_2O_2$, 248.0; m/z found 249.1. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.86 (d, J = 4.9 Hz, 2H), 8.00 (dd, J = 7.9, 1.2 Hz, 1H), 7.68 (dd, J = 8.1, 1.2 Hz, 1H), 7.46 (t, J = 8.0 Hz, 1H), 7.33 (t, J = 4.9 Hz, 1H), 3.65 (s, 3H).

Step C: Sodium 3-chloro-2-(pyrimidin-2-yl)benzoate. To a solution of compound of step B (103 mg, 0.42 mmol) in THF (2 mL) was added 3.75M NaOH in water (0.44 mL, 1.66 mmol). The reaction mixture was stirred at 50 °C for 48h and solvent was evaporated. The residue was

taken up in water and lyophilized to give the title compound (106 mg, 100%). MS (ESI) mass calcd. for $C_{11}H_7ClN_2O_2$, 234.0; m/z found 235.0. ^{1}H NMR (500 MHz, CD3OD) δ 8.80 (d, *J* = 5.0 Hz, 2H), 7.88 (dd, *J* = 7.7, 1.2 Hz, 1H), 7.52 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.48 – 7.38 (m, 2H).

Intermediate	Name	Structure	Reference
A-59	2-(pyrimidin-2-yl)benzoic acid		Commercially available, CAS 400892-62-8
A-60	5-methyl-2-(2H-1,2,3-triazol-2-yl)nicotinic acid		Prepared analogous to WO 2011/050200 Intermediate 47, Example 160
A-61	2-(2H-1,2,3-triazol-2-yl)nicotinic acid		Commercially available, CAS 1369497-44-8
A-62	6-methyl-3-(2H-1,2,3-triazol-2-yl)picolinic acid		2012/089606 Intermediate D40.
A-63	6-methyl-3-(pyrimidin-2-yl)picolinic acid		WO 2010/122151 Intermediate D28
A-64	3-(pyrimidin-2-yl)picolinic acid		WO 2010/122151 Intermediate D105
A-65	2-chloro-6-methoxynicotinic acid		Commercially available, CAS 1227515-71-0

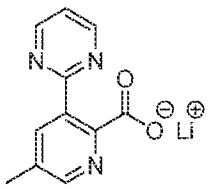
Intermediate A-66: 5-methyl-2-(pyrimidin-2-yl)nicotinic acid.



Step A: Methyl 5-methyl-2-(pyrimidin-2-yl)nicotinate. To a sealed tube containing methyl 2-chloro-5-methylnicotinate (CAS 65169-43-9) (745 mg, 4.01 mmol), CuI (38 mg, 0.2 mmol), LiCl (169 mg, 4.01 mmol), and $Pd(PPh_3)_4$ (231 mg, 0.2 mmol) in toluene (15 mL) was added 2-(tributylstannyl)pyrimidine (1.5 mL, 4.4 mmol), and the reaction mixture was heated at 120 °C overnight. The reaction mixture was diluted with water and extracted with DCM. The combined organic layers were dried over $MgSO_4$, filtered and evaporated. Purification via silica gel chromatography (0-50% EtOAc in hexanes) gave the title compound (494 mg, 52%). MS (ESI) mass calcd. for $C_{12}H_{11}N_3O_2$, 229.1; m/z found 229.99.

Step B: 5-methyl-2-(pyrimidin-2-yl)nicotinic acid. To a solution of the title compound of step A (466 mg, 2.03 mmol) in MeOH (10 mL) was added 10 M NaOH (1 mL), and the reaction mixture was stirred at room temperature for 2 h. The solvent was removed and the crude residue was diluted with water and acidified with 6 M $HCl_{(aq)}$ until pH = 3. The aqueous layer was saturated with solid NaCl and extracted with 20% *i*PrOH in $CHCl_3$ (3X). The combined organic layers were dried over $MgSO_4$, filtered and concentrated to afford the title compound (432 mg, 99%). MS (ESI) mass calcd. for $C_{11}H_9N_3O_2$, 215.1; m/z found 216.1 $[M+H]^+$. ^1H NMR (500 MHz, Methanol-d_4) δ 8.90 (br. s, 2H), 8.64 (br. s, 1H), 8.17 (s, 1H), 7.55 (br. s, 1H), 2.51 (s, 3H).

Intermediate A-67: Lithium 5-methyl-3-(pyrimidin-2-yl)picolinate.

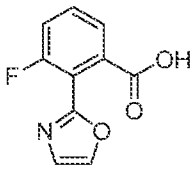


Step A: Methyl 5-methyl-3-(pyrimidin-2-yl)picolinate. Prepared analogous to intermediate A-66, step A substituting methyl 2-chloro-5-methylnicotinate with methyl 3-bromo-5-methylpicolinate. MS (ESI) mass calcd. for $C_{12}H_{11}N_3O_2$, 229.1; m/z found 230.0 $[M+H]^+$

Step B: Lithium 5-methyl-3-(pyrimidin-2-yl)picolinate. To a solution of the title compound of step A (592 mg, 2.58 mmol) in THF (5 mL) was added 4 M LiOH (0.8 mL) and

water (1.5 mL), and the reaction mixture was stirred at room temperature for 2.5 h. The solvent was removed and the crude reaction mixture placed under vacuum overnight to give the title compound (591 mg), which was used in the next step without further purification. MS (ESI) mass calcd. for $C_{11}H_9N_3O_2$, 215.1; m/z found 216.1 $[M+H]^+$. ^1H NMR (500 MHz, Methanol-d_4) δ 8.83 (d, J = 4.9 Hz, 2H), 8.39 (br. s, 1H), 8.23 - 8.18 (m, 1H), 7.38 (t, J = 4.9 Hz, 1H), 2.44 (s, 3H).

Intermediate A-68: 3-fluoro-2-(oxazol-2-yl)benzoic acid.



Step A: 2-bromo-N-(2,2-dimethoxyethyl)-6-fluorobenzamide. To a solution of 2-bromo-6-fluorobenzoic acid (2 g, 9.1 mmol) in DMF (27 mL) was added HBTU (5.20 g, 13.7 mmol) and DIPEA (4.7 mL, 27 mmol), and the reaction mixture was stirred for 10 min. Then, 2,2-dimethoxyethylamine (1.3 mL, 11.9 mmol) was added and the reaction mixture stirred at room temperature for 12 h. The reaction mixture was diluted with EtOAc and washed with saturated aqueous $NaHCO_3$. The combined organic layers were dried over $MgSO_4$, filtered and concentrated. Purification via silica gel chromatography (0-25% EtOAc in hexanes) gave the title compound (2.3 g, 82%).

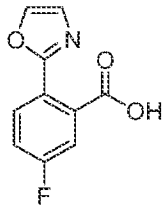
Step B: 2-(2-bromo-6-fluorophenyl)oxazole. To P_2O_5 (6.4 g, 22.6 mmol) was added methanesulfonic acid (52 mL, 801 mmol), and the reaction mixture was stirred at room temperature for 1 h. Then, the title compound of step A (2.3 g, 7.54 mmol) was added to the reaction mixture, and the mixture heated to 140 °C for 2 h. DCM was added and the mixture was slowly poured into a saturated solution of aqueous $NaHCO_3$ on ice. The mixture was extracted with DCM. The combined organic layers were dried over $MgSO_4$, filtered and concentrated. Purification via silica gel chromatography (0-10% EtOAc in hexanes) gave the title compound (1.5 g, 82%). MS (ESI) mass calcd. for C_9H_5BrFNO, 240.95; m/z found 242.0 $[M+H]^+$.

Step C: Methyl 3-fluoro-2-(oxazol-2-yl)benzoate. A solution of the title compound of step B (2.18 g, 8.99 mmol), $Pd(OAc)_2$ (40 mg, 0.18 mmol), 1,1'-bis(diphenylphosphino)ferrocene (199 mg, 0.36 mmol), and Et_3N (3.7 mL, 27 mmol) in 1:1 MeOH/1,4-dioxane (36 mL) was degassed with N_2 for 15 min. Then, the mixture was stirred at 95 °C under an atmosphere of carbon monoxide overnight. The reaction mixture was diluted with EtOAc and washed with a solution of $NaHCO_3$. The organic layer was separated, dried over

$MgSO_4$, filtered, and concentrated. Purification via silica gel chromatography (0-12% EtOAc in hexanes) gave the title compound (1.7 g, 83%). MS (ESI) mass calcd. for $C_{11}H_8FNO_3$, 221.1; m/z found 222.0 $[M+H]^+$.

Step D: 3-fluoro-2-(oxazol-2-yl)benzoic acid. To a solution of the title compound of step C (1.65 g, 7.46 mmol) in MeOH (22 mL) was added 2 M NaOH (7.5 mL), and the reaction mixture was stirred at room temperature overnight. The reaction mixture was acidified with 1 M $HCl_{(aq)}$ and the solvents evaporated in vacuo. The mixture was diluted with water and extracted with DCM. The combined organic were dried over $MgSO_4$, filtered and concentrated to afford the title compound (905 mg, 58%). MS (ESI) mass calcd. for $C_{10}H_6FNO_3$, 207.0; m/z found 208.0 $[M+H]^+$. MP = 182 °C.

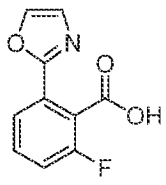
Intermediate A-69: 5-fluoro-2-(oxazol-2-yl)benzoic acid.



Step A: Methyl 5-fluoro-2-(oxazol-2-yl)benzoate. To a solution of methyl 2-bromo-5-fluorobenzoate (1.1 g, 4.8 mmol) and 2-(tri-n-butylstannyl)oxazole (1.3 mL, 6.2 mmol) in toluene (14 mL) was added $Pd(PPh_3)_4$ (550 mg, 0.476 mmol), and the reaction mixture was heated via microwave heating to 150 °C for 30 min. The reaction mixture was diluted with water and extracted with EtOAc. The combined organic layers were dried over $MgSO_4$, filtered and concentrated. Purification via silica gel chromatography (0-40% EtOAc in hexanes, followed by a second column 0-10% EtOAc in hexanes) gave the title compound (553 mg, 52%). MS (ESI) mass calcd. for $C_{11}H_6FNO_3$, 221.1; m/z found 222.1 $[M+H]^+$.

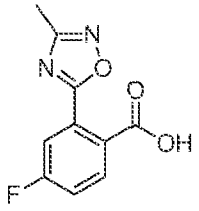
Step B: 5-fluoro-2-(oxazol-2-yl)benzoic acid. Prepared analogous to intermediate 68, step D, to give the title compound (858 mg, 99%). MS (ESI) mass calcd. for $C_{10}H_6FNO_3$, 207.0; m/z found 208.1 $[M+H]^+$.

Intermediate A-70: 2-fluoro-6-(oxazol-2-yl)benzoic acid.



Prepared analogous to intermediate 68, substituting 2-bromo-6-fluorobenzoic acid with 2-bromo-3-fluorobenzoic acid. MS (ESI) mass calcd. for $C_{10}H_6FNO_3$, 207.0; m/z found 208.0 $[M+H]^+$.

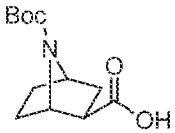
Intermediate A-71: 4-fluoro-2-(3-methyl-1,2,4-oxadiazol-5-yl)benzoic acid.



Step A: 5-(2-bromo-5-fluorophenyl)-3-methyl-1,2,4-oxadiazole. To a solution of 2-bromo-5-fluorobenzoyl chloride (2.17 g, 9.13 mmol) in THF (18 mL) was added DIPEA (1.7 mL, 10 mmol). Then, acetamide oxime (676 mg, 9.13 mmol) was added portionwise, and the reaction mixture was stirred at 70 °C for 16 h. The reaction mixture was diluted with EtOAc and washed with a saturated solution of $NaHCO_3$. The combined organic layers were dried over $MgSO_4$, filtered and concentrated. Purification via silica gel chromatography (0-20% EtOAc in hexanes) gave the title compound (2.35 g, 57%). MS (ESI) mass calcd. for $C_9H_6BrFN_2O$, 255.96; m/z found 257.0 $[M+H]^+$.

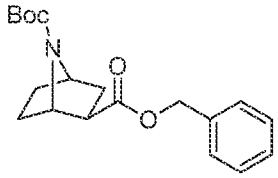
Step B: 4-fluoro-2-(3-methyl-1,2,4-oxadiazol-5-yl)benzoic acid. Prepared analogous to intermediate 68, steps C and D, to give the title compound. MS (ESI) mass calcd. for $C_{10}H_7FN_2O_3$, 222.0; m/z found 223.0 $[M+H]^+$.

Intermediate B-1: (±)-7-(tert-butoxycarbonyl)-7-azabicyclo[2.2.1]heptane-2-carboxylic acid.

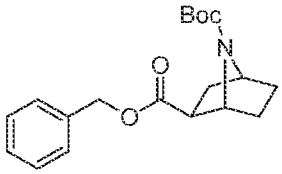


Prepared as described in in WO 2004/074 292 A1. ^1H NMR ($CDCl_3$): 4.54 (d, J = 4.6 Hz, 1H), 4.33 – 4.24 (m, 1H), 2.61 – 2.18 (m, 4H), 1.90 – 1.71 (m, 2H), 1.68 – 1.57 (m, 1H), 1.56 – 1.35 (m, 10H).

Intermediates (+)-B-2 and (-)-B-2: (1S,2R,4R)-2-benzyl 7-tert-butyl 7-azabicyclo[2.2.1]heptane-2,7-dicarboxylate.



and (1R,2S,4S)-2-benzyl 7-tert-butyl-7-azabicyclo[2.2.1]heptane-2,7-dicarboxylate

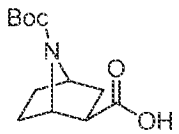


The title compounds were obtained by chiral SFC (CHIRALPAK IC 5 µM 250 X 20mm) resolution of Intermediate B-3 (17 g) using 80% CO_2/20% *i*PrOH as the mobile phase to give (-)-B-3 enantiomer A (7.5 g, 1st eluting enantiomer) and enantiomer (+)-B3 (7.3 g, 2nd eluting enantiomer).

Intermediate (-)-B-2: (-)-2-benzyl 7-tert-butyl-7-azabicyclo[2.2.1]heptane-2,7-dicarboxylate. Enantiomer A, $[\alpha]^{D}_{25}$ -25.2 (*c* 2.8, $CHCl_3$).

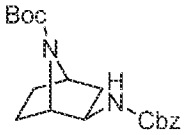
Intermediate (+)-B-2: (+)-2-benzyl 7-tert-butyl-7-azabicyclo[2.2.1]heptane-2,7-dicarboxylate. Enantiomer B, $[\alpha]^{D}_{25}$ +25.0 (*c* 2.8, $CHCl_3$). ^{1}H NMR ($CDCl_3$): 7.39 – 7.30 (m, 5H), 5.19 – 5.08 (m, 2H), 4.55 (s, 1H), 4.30 (s, 1H), 2.59 (dd, *J* = 8.9, 5.0 Hz, 1H), 2.36 – 2.24 (m, 1H), 1.90 – 1.70 (m, 2H), 1.68 – 1.57 (m, 1H), 1.52 – 1.34 (m, 11H).

Intermediate B-3: (1S,2R,4R)-7-(tert-butoxycarbonyl)-7-azabicyclo[2.2.1]heptane-2-carboxylic acid



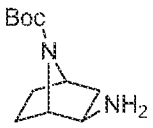
To intermediate (+)-B-2 (3.5g, 10.6 mmol) in EtOH (100 mL) was added 10 wt% Pd/C wet Degussa (750 mg). The reaction was purged with N_2 followed by H_2, then allowed to proceed under an atmosphere of H_2 (balloon). Upon completion, the reaction was filtered and concentrated to give the title compound (2.4g, 94%) that was used without further purification. ^{1}H NMR ($CDCl_3$): 4.62 – 4.52 (m, 1H), 4.35 – 4.26 (m, 1H), 2.59 (ddd, *J* = 8.9, 5.0, 1.5 Hz, 1H), 2.29 – 2.19 (m, 1H), 1.91 – 1.71 (m, 2H), 1.68 – 1.58 (m, 1H), 1.54 – 1.35 (m, 11H).

Intermediate B-4: (1S,2R,4R)-tert-butyl 2-(((benzyloxy)carbonyl)amino)-7-azabicyclo[2.2.1]heptane-7-carboxylate.



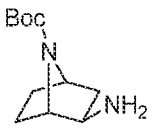
To intermediate B-3 (2.4g, 9.9 mmol) in $PhCH_3$ (32 mL) was added TEA (1.5 mL, 10.9 mmol). After heating in an oil bath to 70 °C, DPPA (2.4 mL, 10.9 mmol) in $PhCH_3$ (3 mL) was added. After 1h, BnOH (1.0 g, 9.5 mmol) was added and the oil bath temperature increased to 90 °C. After an additional 18h, the reaction was cooled to rt, diluted with EtOAc and washed with saturated $NaHCO_3$ (aq). The aqueous layer was extracted with EtOAc (1X). The combined organics were washed with brine and dried (Na_2SO_4). Purification via silica gel chromatography (10-50% EtOAc in hexanes) gave gave the title compound (2.8g, 78%). ^{1}H NMR (CDCl3): 7.39 – 7.28 (m, 5H), 5.20 – 4.84 (m, 3H), 4.30 – 4.06 (m, 3H), 3.86 – 3.68 (m, 1H), 1.93 (dd, J = 13.4, 8.1 Hz, 1H), 1.85 – 1.63 (m, 2H), 1.54 – 1.29 (m, 11H).

Intermediate B-5: (+)-(1S,2R,4R)-tert-butyl 2-amino-7-azabicyclo[2.2.1]heptane-7-carboxylate.



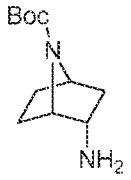
To intermediate B-4 (400 mg, 1.2 mmol) in EtOH (5 mL) was added 10 wt% Pd/C wet Degussa (85 mg). The reaction was purged with N_2 followed by H_2, then allowed to proceed under an atmosphere of H_2 (balloon). Upon completion, the reaction was filtered and concentrated to give the title compound (244 mg, 99%) that was used without further purification. MS (ESI) mass calcd. for $C_{11}H_{20}N_2O_2$, 212.1; m/z found 213.1 $[M+H]^+$. $[\alpha]^D_{25}$ +9.8 (c 4.9, $CHCl_3$) ^{1}H NMR (CDCl3): 4.25 – 4.13 (m, 1H), 3.94 – 3.82 (m, 1H), 2.96 (dd, J = 7.8, 3.0 Hz. 1H), 1.85 – 1.25 (m, 15H).

Intermediate B-6: (±)-tert-butyl 2-amino-7-azabicyclo[2.2.1]heptane-7-carboxylate.

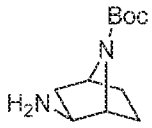


Prepared analogous to intermediate B-5 substituting intermediate B-4 with (±)-7-(tert-butoxycarbonyl)-7-azabicyclo[2.2.1]heptane-2-carboxylic acid (intermediate B-1).

Intermediate B-7: (±)-tert-butyl 2-amino-7-azabicyclo[2.2.1]heptane-7-carboxylate.

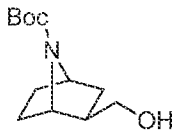


Intermediate B-8: (-)-(1R,2S,4S)-tert-butyl 2-amino-7-azabicyclo[2.2.1]heptane-7-carboxylate.



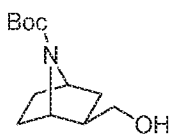
Prepared analogous to intermediate B-5 substituting enantiomer (1S,2R,4R)-2-benzyl 7-tert-butyl 7-azabicyclo[2.2.1]heptane-2,7-dicarboxylate (intermediate (+)-B-2) with enantiomer (1R,2S,4S)-2-benzyl 7-tert-butyl-7-azabicyclo[2.2.1]heptane-2,7-dicarboxylate (intermediate (-)-B-2).

Intermediate B-9: (1S,2R,4R)-tert-butyl 2-(hydroxymethyl)-7-azabicyclo[2.2.1]heptane-7-carboxylate.



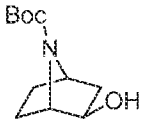
To intermediate (+)-B-2 (504 mg, 1.5 mmol) in THF (12 mL) at 0 °C was added Dibal-H (1M in THF, 4.6 mL). After 1h, additional Dibal-H was added. The reaction allowed to warm to rt and quenched with Rochelle's Salt (20 wt%). EtOAc was added and the mixture allowed to stir until 2 clear layers had formed. The aqueous layer was extracted with EtOAc (2X). The combined organics were washed with brine and dried (Na_2SO_4). Purification via silica gel chromatography (10-50% EtOAc in hexanes) gave the title compound (171 mg, 49%). MS (ESI) mass calcd. for $C_{12}H_{21}NO_3$, 227.2; m/z found 228.2 $[M+H]^+$, 172.2 $[M-55]^+$. ^1H NMR (CDCl3): 4.26 – 4.12 (m, 2H), 3.45 – 3.32 (m, 2H), 3.00 – 2.04 (m, 1H). 1.95 – 1.90 (m, 1H), 1.83 – 1.73 (m, 2H), 1.53 – 1.37 (m, 12H), 1.32 – 1.28 (m, 1H).

Intermediate B-10: (±)-tert-butyl 2-(hydroxymethyl)-7-azabicyclo[2.2.1]heptane-7-carboxylate.



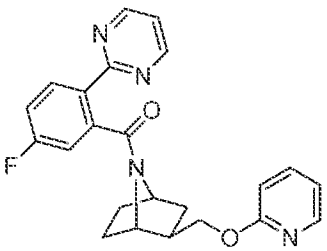
As in Org. Syn., 1997, *74*, 212, Tet. Lett. 1997, *38*, 6829 and Biorg. Med. Chem. Lett. 2006, *14*, 8219. ^{1}H NMR ($CDCl_3$): 4.25 – 4.13 (m, 2H), 3.47 – 3.32 (m, 2H), 1.98 – 1.68 (m, 4H), 1.56 – 1.26 (m, 13H).

Intermediate B-11: (±)-*tert*-Butyl 2-hydroxy-7-azabicyclo[2.2.1]heptane-7-carboxylate.



To a solution of (±)-tert-butyl 7-azabicyclo[2.2.1]hept-5-ene-7-carboxylate (3.4g, 17.4 mmol; *Helvetica Chimica Acta*, **2004**, *87*, 2764) in THF (50 mL) was added borane THF complex (27 mL, ~1M in THF). The solution was stirred at room temperature for ~2h and then the excess borane was quenched by slow addition of water (7 mL, bubbling observed). 6M NaOH (25 mL) was then added followed by slow dropwise addition of H_2O_2 (15 mL, 30%;). The resulting solution was stirred at room temperature overnight. The excess H_2O_2 was then quenched by slow addition of solid sodium meta-bisulfite. This mixture was diluted with water (200 mL) and extracted with DCM (3x75 mL). The combined organics were dried over Na_2SO_4, filtered and the solvent removed. Purification via silica gel chromatography (0-100 % EtOAc in hexanes) gave the title compound (2.74 g) as a clear colorless oil that slowly solidified. MS (ESI): mass calcd. for $C_{11}H_{19}NO_3$, 213.2; m/z found, 158.1 $[M+2H-t\text{Bu}]^+$. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.28 - 4.20 (t, J = 4.9 Hz, 1H), 4.16 - 4.06 (d, J = 5.2 Hz, 1H), 3.91 - 3.80 (td, J = 7.4, 6.4, 1.9 Hz, 1H), 2.00 - 1.88 (s, 1H), 1.88 - 1.80 (m, 1H), 1.78 - 1.69 (m, 1H), 1.69 - 1.55 (m, 2H), 1.50 - 1.40 (s, 9H), 1.31 - 1.20 (m, 2H).

Example 1: (5-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



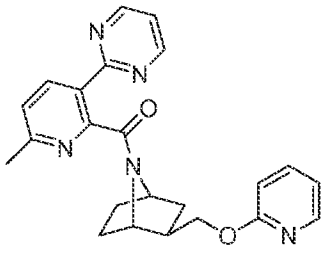
Step A: (1S,2R,4R)-tert-butyl 2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptane-7-carboxylate. To intermediate B-9 (170 mg, 0.75 mmol) in DMF (3 mL) at 0 °C was added NaH (36 mg, 60 wt% in mineral oil, 0.9 mmol). After 30 min, 2-fluoropyridine (102 mg, 1.0 mmol)

in DMF (0.5 mL) was added dropwise and the 0 °C ice bath was removed. The flask was then heated to 90 °C in an oil bath. After 2h, 1/2 saturated NH_4Cl was added and the reaction extracted with EtOAc (2X). The combined organics were washed with brine and dried (Na_2SO_4). Purification via silica gel chromatography (5-30% EtOAc in hexanes) gave the title compound (172 mg, 76%) as a white solid. MS (ESI) mass calcd. for $C_{17}H_{24}N_2O_3$, 304.2; m/z found 305.1 $[M+H]^+$. ^1H NMR ($CDCl_3$): 8.13 (dd, J = 5.1, 2.0 Hz, 1H), 7.55 (ddd, J = 8.7, 7.1, 2.0 Hz, 1H), 6.84 (dd, J = 7.0, 5.0 Hz, 1H), 6.73 (d, J = 8.3 Hz, 1H), 4.35 – 4.15 (m, 2H), 4.15 – 3.99 (m, 2H), 2.26 – 2.14 (m, 1H), 1.90 – 1.68 (m, 2H), 1.64 – 1.55 (m, 1H), 1.54 – 1.31 (m, 12H).

Step B: (1S,2R,4R)-tert-butyl-2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptane-7-carboxylate. To the title compound from Step A (130 mg, 0.4 mmol) in EtOAc was added 4M HCl in dioxane. After 3h, the reaction was concentrated, neutralized with 5% Na_2CO_3 and extracted with DCM. The combined organics were dried (Na_2SO_4) to give the title compound from step B as a white solid that was used without further purification. MS (ESI) mass calcd. for $C_{12}H_{16}N_2O$,204.1; m/z found 205.1 $[M+H]^+$.

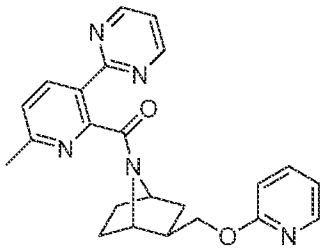
Step C: (5-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone. To the title compound of Step B (50 mg, 0.18 mmol) in DMF (1.4 mL) was added DIPEA (0.078 mL, 0.45 mmol), intermediate A-7 (43 mg, 0.2 mmol) and HATU (75 mg, 0.2 mmol). Upon completion of the reaction, purification was performed using Agilent prep method A to give the title compound. MS (ESI) mass calcd. for $C_{23}H_{21}FN_4O_2$,404.2; m/z found 405.2 $[M+H]^+$. ^1H NMR ($CDCl_3$): 8.78 (d, J = 4.9 Hz, 1H), 8.71 (d, J = 4.8 Hz, 1H), 8.26 – 8.21 (m, 2H), 7.60 – 7.50 (m, 1H), 7.23 – 7.00 (m, 3H), 6.90 – 6.82 (m, 1H), 6.78 – 6.71 (m, 0.5H), 6.59 – 6.51 (m, 0.5H), 4.88 – 4.78 (m, 1H), 4.26 – 4.09 (m, 1H), 4.09 – 3.95 (m, 1H), 3.92 – 3.79 (m, 1H), 2.39 – 2.18 (m, 1H), 2.04 – 1.86 (m, 1H), 1.81 – 1.31 (m, 5H).

Example 2: (±)-(6-methyl-3-(pyrimidin-2-yl)pyridin-2-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.

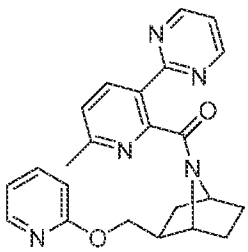


Prepared analogous to Example 1 substituting intermediate B-9 with intermediate B-10, 5-fluoro-2-(pyrimidin-2-yl)benzoic acid with intermediate A-9 and HATU with HBTU to give the title compound. MS (ESI) mass calcd. for $C_{23}H_{23}N_5O_2$, 401.2; m/z found 402.2 $[M+H]^+$. ^1H NMR (DMSO-D_6): 8.92 (d, J = 4.9 Hz, 1H), 8.84 (d, J = 4.9 Hz, 1H), 8.32 (t, J = 8.3 Hz, 1H), 8.24 (dd, J = 5.0, 1.4 Hz, 0.5H), 8.15 (dd, J = 5.0, 1.5 Hz, 0.5H), 7.76 – 7.69 (m, 0.5H), 7.69 – 7.62 (m,0.5H), 7.52 – 7.42 (m, 1.5H), 7.34 (d, J = 8.1 Hz, 0.5H), 7.05 – 6.92 (m, 1H), 6.87 (d, J = 8.3 Hz, 0.5H), 6.68 (d, J = 8.3 Hz, 0.5H), 4.60 – 4.56 (m, 1H), 4.19 (td, J = 10.3, 3.7 Hz, 1H), 4.06 (dt, J = 10.4, 5.3 Hz, 1H), 3.86 (t, J = 4.0 Hz, 0.5H), 3.77 (d, J = 4.1 Hz, 0.5H), 2.56 (s, 1.5H), 2.39 – 2.15 (m, 1H), 2.06 (s, 1.5H), 1.88 – 1.33 (m, 6H).

Example 3A: (6-methyl-3-(pyrimidin-2-yl)pyridin-2-yl)((1S*,2R*,4R*)-2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



and Example 3B: (6-methyl-3-(pyrimidin-2-yl)pyridin-2-yl)((1R*,2S*,4S*)-2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.

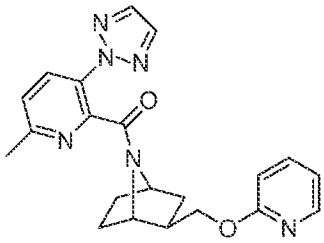


The title compounds were obtained by chiral SFC (CHIRALPAK AD-H 5 μM 250 X 20mm) resolution of Example 2 (538 mg) using 70% CO_2/30% EtOH as the mobile phase to give enantiomer A (230 mg, 1st eluting enantiomer) and enantiomer B (226 mg, 2nd eluting enantiomer). The enantiomeric purity was confirmed by analytical SFC using a CHIRALPAK AD (250x4.6 mm) and a mobile phase of 70% CO_2, 30% EtOH containing 0.3 % $iPrNH_2$ over 7 minutes. (Example 3A: >98% single enantiomer, 4.00 min retention time; Example 3B >98% single enantiomer, 5.12 min retention time). Example 3A: MS (ESI) mass calcd. for $C_{23}H_{23}N_5O_2$, 401.2; m/z found 402.1 $[M+H]^+$. ^1H NMR ($CDCl_3$): 8.83 (d, J = 4.8 Hz, 0.8H), 8.72 (d, J = 4.8 Hz, 1.2H), 8.43 – 8.37 (m, 1H), 8.19 – 8.09 (m, 1H), 7.59 – 7.48 (m, 1H), 7.28 (d, J =

8.0 Hz, 0.4H), 7.19 – 7.16 (m, 1.6H), 6.88 – 6.81 (m, 1H), 6.76 (dt, J = 8.4, 1.0 Hz, 0.4H), 6.57 (dt, J = 8.3, 0.9 Hz, 0.6H), 4.92 – 4.84 (m, 1H), 4.38 – 4.23 (m, 1H), 4.17 (ddd, J = 15.4, 10.3, 5.7 Hz, 1H), 3.97 – 3.87 (m, 1H), 2.62 (s, 1H), 2.39 – 2.18 (m, 2.5H), 2.11 – 1.81 (m, 2H), 1.74 (dd, J = 12.3, 8.6 Hz, 0.5H), 1.68 – 1.36 (m, 4H).

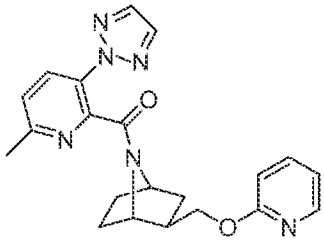
Example 3B: MS (ESI) mass calcd. for $C_{23}H_{23}N_5O_2$, 401.2; m/z found 402.1 $[M+H]^+$.

Example 4: (±)-(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.

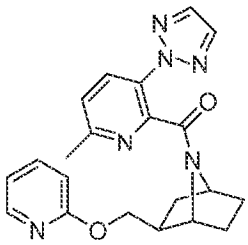


Prepared analogous to Example 1 substituting intermediate B-9 with intermediate B-10, intermediate A-7 with intermediate A-21 and HATU with HBTU to give the title compound. MS (ESI) mass calcd. for $C_{21}H_{22}N_6O_2$, 390.2; m/z found 391.2 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$): 8.20 – 8.07 (m, 2H), 7.84 – 7.75 (m, 2H), 7.61 – 7.49 (m, 1H), 7.31 (d, J = 8.4 Hz, 0.4H), 7.19 (d, J = 8.4 Hz, 0.6H), 6.87 – 6.83 (m, 1H), 6.76 (dt, J = 8.4, 0.9 Hz, 0.4H), 6.57 (dt, J = 8.3, 0.9 Hz, 0.6H),4.91 – 4.81 (m, 1H), 4.32 – 4.07 (m, 2H), 3.96 – 3.84 (m, 1H), 2.62 (s, 1.2H), 2.40 – 2.17 (m, 2.8H), 2.13 – 1.94 (m, 1H), 1.94 – 1.68 (m, 1.8H), 1.68 – 1.37 (m, 3.2H).

Example 5A: (6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)((1S,2R,4R)-2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.

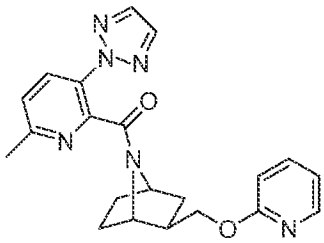


and Example 5B: (6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)((1R,2S,4S)-2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



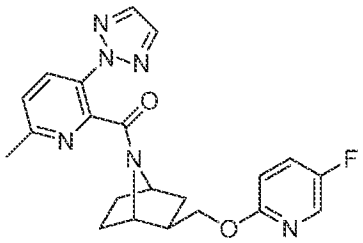
The title compounds were obtained by chiral SFC (CHIRALPAK AD-H 5 μM 250 X 20mm) resolution of Example 4 (555 mg) using 70% CO_2/30% EtOH as the mobile phase to give enantiomer A (264 mg, 1st eluting enantiomer) and enantiomer B (248 mg, 2nd eluting enantiomer). The enantiomeric purity was confirmed by analytical SFC using a CHIRALPAK AD (250x4.6mm) and a mobile phase of 70% CO_2, 30% EtOH containing 0.3 % $iPrNH_2$ over 7 minutes. (Example 5A: >98% single enantiomer, 2.80 min retention time; Example 5B >98% single enantiomer, 3.90 min retention time). Example 5A: MS (ESI) mass calcd. for $C_{21}H_{22}N_6O_2$, 390.2; m/z found 391.2 $[M+H]^+$. Example 5B: MS (ESI) mass calcd. for $C_{21}H_{22}N_6O_2$, 390.2; m/z found 391.2 $[M+H]^+$.

Example 6: (6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)((1S,2R,4R)-2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Prepared analogous to Example 1 substituting intermediate A-7 with intermediate A-21. MS (ESI) mass calcd. for $C_{21}H_{22}N_6O_2$, 390.2; m/z found 391.2 $[M+H]^+$. $[\alpha]_D^{20}$ +11.4° (*c* 0.88, $CHCl_3$). ^1H NMR ($CDCl_3$): 8.19 – 8.06 (m, 2H), 7.83 – 7.73 (m, 2H), 7.61 – 7.48 (m, 1H), 7.30 (d, J = 8.4 Hz, 0.4H), 7.19 (d, J = 8.4 Hz, 0.6H), 6.89 – 6.81 (m, 1H), 6.78 – 6.73 (m, 0.4H), 6.61 – 6.52 (m, 0.6H), 4.91 – 4.81 (m, 1H), 4.32 – 4.08 (m, 2H), 3.96 – 3.84 (m, 1H), 2.62 (s, 1.2H), 2.39 – 2.18 (m, 2.8H), 2.11 – 1.94 (m, 1.5H), 1.94 – 1.37 (m, 4.5H).

Example 7: (±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)methanone.



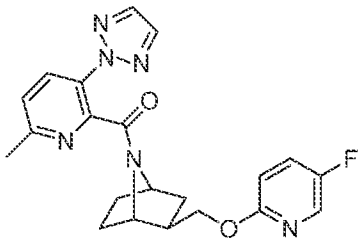
Step A Method A: (±)-tert-butyl 2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptane-7-carboxylate. Tri-n-butylphosphine (1.8 mL, 7.8 mmol) was added to intermediate B-10 (830 mg, 3.7 mmol) and 5-fluoropyridin-2(1H)-one (500 mg, 4.4 mmol) in THF (11 mL) under nitrogen bubbling at rt. After 5 min of stirring, DEAD (1.4 mL, 7.1 mmol) was added and the mixture was stirred at 50°C for 18 hours. The mixture was concentrated and purified silica gel chromatography (0-15% EtOAc in Heptane) to give the title compound of step A (590 mg, 45%) as a white solid.

Step A Method B: (±)-tert-butyl 2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptane-7-carboxylate. Prepared analogous to Example B-6 substituting intermediate B-9 with (±)-B-9 and 2-fluoropyridine with 2,5-difluoropyridine. MS (ESI) mass calcd. for $C_{17}H_{23}FN_2O_3$, 322.2; m/z found 323.0 $[M+H]^+$. ^1H NMR ($CDCl_3$): 8.02 – 7.87 (m, 1H), 7.41 – 7.27 (m, 1H), 6.70 (dd, J = 9.1, 3.6 Hz, 1H), 4.39 – 4.10 (m, 2H), 4.09 – 3.89 (m, 2H), 2.25 – 2.09 (m, 1H), 1.91 – 1.26 (m, 15H).

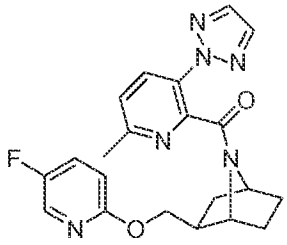
Step B: (±)-2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptane. Prepared analogous to Example 1 substituting (±)-tert-butyl-2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptane-7-carboxylate with the title compound from Step A. ^1H NMR ($CDCl_3$): 7.96 (d, J = 3.1 Hz, 1H), 7.33 (ddd, J = 9.0, 7.6, 3.1 Hz, 1H), 6.70 (dd, J = 9.0, 3.6 Hz, 1H), 4.09 – 3.98 (m, 2H), 3.72 – 3.56 (m, 2H), 2.22 – 1.99 (m, 3H), 1.72 – 1.53 (m, 3H), 1.49 – 1.34 (m, 1H).

Step C: (±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)methanone. Prepared analogous to Example 1 substituting 5-fluoro-2-(pyrimidin-2-yl)benzoic acid with 6-methyl-3-(2H-1,2,3-triazol-2-yl)picolinic acid. MS (ESI) mass calcd. for $C_{21}H_{21}FN_6O_2$, 408.2; m/z found 409.2.

Example 8A: ((1S,2R,4R)-2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)methanone.

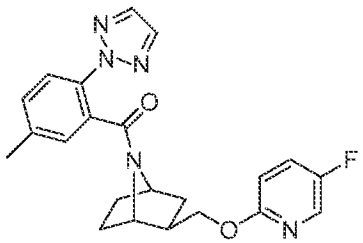


and Example 8B: ((1R,2S,4S)-2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)methanone.



The title compounds were obtained by chiral SFC (CHIRALPAK AD-H 5 μM 250 X 20mm) resolution of Example 7 (259 mg) using 70% CO_2/30% mixture of EtOH/*i*-PrOH (50/50 v/v) as the mobile phase to give enantiomer A (72 mg, 1st eluting enantiomer) and enantiomer B (84 mg, 2nd eluting enantiomer). The enantiomeric purity was confirmed by analytical SFC using a CHIRALPAK AD-H (250x4.6mm) and a mobile phase of 70% CO_2, 15% EtOH, 15% iPrOH containing 0.3 % $iPrNH_2$ over 7 minutes. (Example 8A: 100% single enantiomer, 3.10 min retention time; Example 8B 100% single enantiomer, 4.58 min retention time). Example 8A: MS (ESI) mass calcd. for $C_{21}H_{21}FN_6O_2$, 408.2; m/z found 409.2 $[M+H]^+$. Example 8B: MS (ESI) mass calcd. for $C_{21}H_{21}FN_6O_2$, 408.2; m/z found 409.2 $[M+H]^+$.

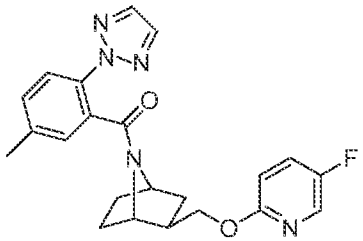
Example 9: (±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(5-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone.



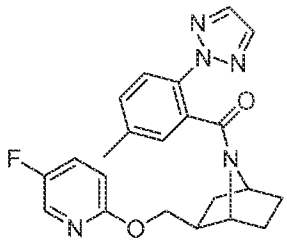
Prepared analogous to Example 7 substituting intermediate A-21 with intermediate A-37. MS (ESI) mass calcd. for $C_{22}H_{22}FN_5O_2$, 407.2; m/z found 408.3 $[M+H]^+$. ^1H NMR ($CDCl_3$): 8.03 – 7.95 (m, 1H), 7.81 – 7.70 (m, 3H), 7.38 – 7.11 (m, 3H), 6.72 (dd, J = 9.0, 3.6 Hz, 0.5H),

6.52 (dd, J = 9.0, 3.5 Hz, 0.5H), 4.86 – 4.74 (m, 1H), 4.15 – 3.68 (m, 3H), 2.46 – 2.37 (s, 1.6H), 2.32 – 1.78 (m, 4.4H), 1.72 – 1.22 (m, 4H).

Example 10A: ((1S,2R,4R)-2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(5-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone.

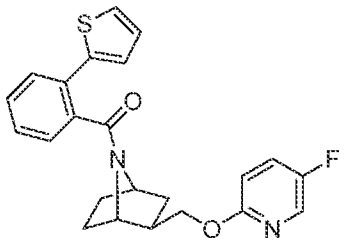


and Example 10B: ((1R,2S,4S)-2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(5-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone.



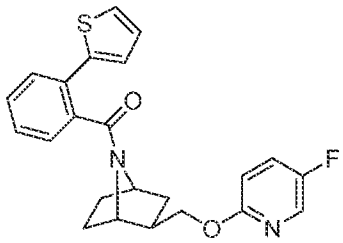
The title compounds were obtained by chiral SFC (CHIRALPAK AD-H 5 μM 250 X 20mm) resolution of Example 9 (290 mg) using 60% CO_2/40% *i*-PrOH as the mobile phase to give enantiomer A (140 mg, 1st eluting enantiomer) and enantiomer B (134 mg, 2nd eluting enantiomer). The enantiomeric purity was confirmed by analytical SFC using a CHIRALPAK AD-H (250x4.6mm) and a mobile phase of 60% CO_2, 40% iPrOH containing 0.3 % $iPrNH_2$ over 7 minutes. (Example 10A: >98% single enantiomer, 2.42 min retention time; Example 10B >98% single enantiomer, 3.20 min retention time).

Example 11: (±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(2-(thiophen-2-yl)phenyl)methanone.

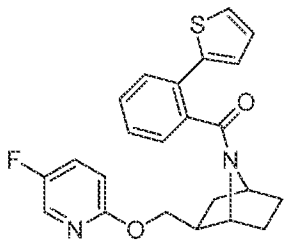


To (±)-2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptane (35 mg, 0.2 mmol) in DCM (2.5 mL) was added TEA (25 µL, 0.2 mmol)) followed by 2-(thiophen-2-yl)benzoyl chloride (40 mg, 0.2 mmol) in DCM (2.5 mL). After 18h, the reaction was diluted with DCM and washed with H_2O. The aqueous layer was extracted DCM (1X). The combined organics were dried (Na_2SO_4). Purification via silica gel chromatography (50-100% EtOAc in hexanes) gave the title compound (37mg, 57%). MS (ESI) mass calcd. for $C_{23}H_{21}FN_2O_2S$, 408.1; m/z found 409.1 $[M+H]^+$.

Example 12A: ((1S*,2R*,4R*)-2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(2-(thiophen-2-yl)phenyl)methanone.



and Example 12B: ((1R*,2S*,4S*)-2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(2-(thiophen-2-yl)phenyl)methanone.

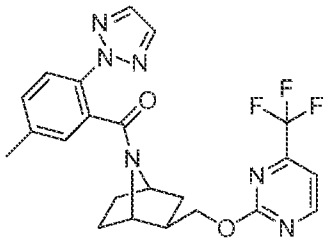


The title compounds were obtained by chiral SFC (CHIRALPAK AS-H 5 µM 250 X 20mm at 40 °C) resolution of Example 11 using 4.2 mL/min MeOH with 0.2% TEA, 37 mL/min CO_2 as the mobile phase to give enantiomer A (1st eluting enantiomer) and enantiomer B (2nd eluting enantiomer).

Example 12A: MS (ESI) mass calcd. for $C_{23}H_{21}FN_2O_2S$, 408.2; m/z found 409.2 $[M+H]^+$. ^1H NMR ($CDCl_3$): 7.97 (dd, J = 11.0, 3.0 Hz, 1H), 7.54 – 7.20 (m, 6.5H), 7.01 (dd, J = 5.0, 3.7 Hz, 1.5H), 6.71 (dd, J = 9.1, 3.5 Hz, 0.5H), 6.45 (dd, J = 9.0, 3.6 Hz, 0.5H), 4.83 – 4.63 (m, 1H), 4.18 – 3.38 (m, 3H), 2.70-0.40 (m, 7H).

Example 12B: MS (ESI) mass calcd. for $C_{23}H_{21}FN_2O_2S$, 408.2; m/z found 409.2 $[M+H]^+$. ^1H NMR ($CDCl_3$): 7.97 (dd, J = 11.0, 3.0 Hz, 1H), 7.54 – 7.20 (m, 6.5H), 7.01 (dd, J = 5.0, 3.7 Hz, 1.5H), 6.71 (dd, J = 9.1, 3.5 Hz, 0.5H), 6.45 (dd, J = 9.0, 3.6 Hz, 0.5H), 4.83 – 4.63 (m, 1H), 4.18 – 3.38 (m, 3H), 2.70-0.40 (m, 7H).

Example 13: (±)-(5-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((4-(trifluoromethyl)pyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



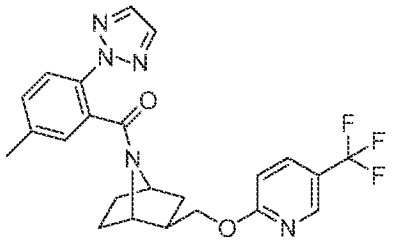
Step A: (±)-7-azabicyclo[2.2.1]heptan-2-ylmethanol hydrochloride. To intermediate B-10 (1.1g, 4.9 mmol) in MeOH (1 mL) was added 4M HCl in dioxane (3 mL). After 6h, the reaction was concentrated to give the title compound that was used without further purification.

Step B: ((±)-2-(hydroxymethyl)-7-azabicyclo[2.2.1]heptan-7-yl)(5-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone. To the title compound of Step A in DMF was added TEA, 5-methyl-2-(2H-1,2,3-triazol-2-yl)benzoic acid and HATU. After 18h, H_2O was added and the mix extracted with EtOAc (2X). The combined organics were washed with brine and dried (Na_2SO_4). Silica gel chromatography (1-7% 2M NH_3/MeOH in DCM) gave the title compound (371 mg, 46%). MS (ESI) mass calcd. for $C_{17}H_{20}N_4O_2$,312.2; m/z found 313.2 $[M+H]^+$.

Step C: (±)-(5-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((4-(trifluoromethyl)pyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone. To the title compound of step B (33 mg, 0.1 mmol) in THF (2 mL) was added NaO*t*Bu (16 mg, 0.16 mmol). The reaction was then heated at reflux for 15 min and 2-chloro-4-trifluoromethylpyrimidine (19 mg, 0.16 mmol) was added. The reaction was heated at reflux temperature for 1h, cooled to rt, diluted with H_2O and extracted with DCM (2X). The combined organics were dried (Na_2SO_4). Purification via silica gel chromatography (0.5-4% 2M NH_3/MeOH in DCM gave the title compound (28 mg, 57%). MS (ESI) mass calcd. for $C_{22}H_{21}F_3N_6O_2$, 457.2; m/z found 458.2 $[M+H]^+$. ^1H NMR ($CDCl_3$): 8.82 – 8.72 (m, 1H), 7.86 – 7.69 (m, 3H), 7.36 – 7.10 (m, 3H), 4.85 (m, 1H), 4.47 (t, J = 10.1 Hz, 0.5H), 4.20 – 3.98 (m,

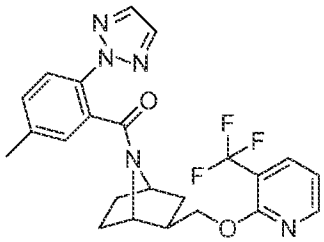
1.5H), 3.90 (d, J = 4.7 Hz, 0.5H), 3.78 (t, J = 4.5 Hz, 0.5H), 2.51 – 2.20 (m, 3H), 2.14 – 1.82 (m, 2H), 1.78 – 1.17 (m, 5H).

Example 14: (±)-(5-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((5-(trifluoromethyl)pyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



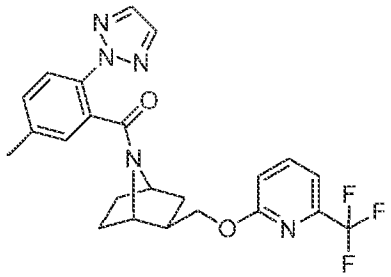
Prepared analogous to Example 13 substituting 2-chloro-4-(trifluoromethyl)pyrimidine with 2-chloro-5-(trifluoromethyl)pyridine. MS (ESI) mass calcd. for $C_{23}H_{22}F_3N_5O_2$, 457.2; m/z found 458.2 $[M+H]^+$.

Example 15: (±)-(5-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((3-(trifluoromethyl)pyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



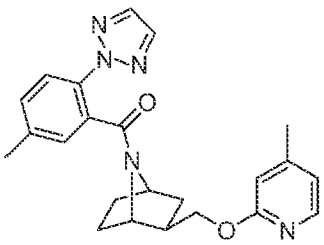
Prepared analogous to Example 13 substituting 2-chloro-4-(trifluoromethyl)pyrimidine with 2-chloro-3-(trifluoromethyl)pyridine. MS (ESI) mass calcd. for $C_{23}H_{22}F_3N_5O_2$, 457.2; m/z found 458.2 $[M+H]^+$. ^1H NMR ($CDCl_3$): 8.36 – 8.26 (m, 1H), 7.91 – 7.69 (m, 4H), 7.36 – 7.29 (m, 0.5H), 7.25 – 7.16 (m, 1H), 7.13 – 7.07 (m, 0.5H), 6.97 (dd, J = 7.5, 5.1 Hz, 1H), 4.87 – 4.70 (m, 1H), 4.53 – 4.34 (m, 0.5H), 4.25 – 4.06 (m, 1H), 3.92 (t, J = 10.9 Hz, 0.5H), 3.85 – 3.71 (m, 1H), 2.46 – 2.40 (m, 1.5H), 2.39 – 2.19 (m, 1.5H), 2.04 – 1.79 (m, 3H), 1.72 – 1.19 (m, 4H).

Example 16: (±)-(5-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((6-(trifluoromethyl)pyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



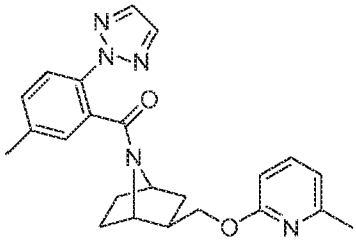
Prepared analogous to Example 13 substituting 2-chloro-4-(trifluoromethyl)pyrimidine with 2-chloro-6-(trifluoromethyl)pyridine. MS (ESI) mass calcd. for $C_{23}H_{22}F_3N_5O_2$, 457.2; m/z found 458.2 $[M+H]^+$. ^1H NMR ($CDCl_3$): 7.87 – 7.63 (m, 4H), 7.37 – 7.11 (m, 3H), 6.92 (d, J = 8.4 Hz, 0.5H), 6.73 (d, J = 8.4 Hz, 0.5H), 4.88 – 4.75 (m, 1H), 4.20 – 3.84 (m, 2H), 3.81 – 3.67 (m, 1H), 2.49 – 2.36 (s, 2H), 2.34 – 2.13 (m, 1H), 2.08 – 1.77 (m, 3H), 1.76 – 1.10 (m, 4H).

Example 17: (±)-(5-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((4-methylpyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



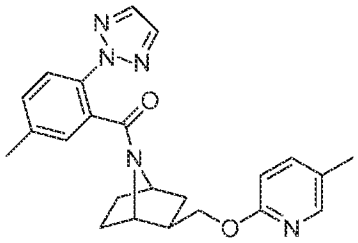
Prepared analogous to Example 13 substituting 2-chloro-4-(trifluoromethyl)pyrimidine with 2-chloro-4-(methyl)pyridine. MS (ESI) mass calcd. for $C_{23}H_{25}N_5O_2$, 403.2; m/z found 404.2 $[M+H]^+$. ^1H NMR ($CDCl_3$): 8.10 – 7.91 (m, 1H), 7.87 (d, J = 3.7 Hz, 2H), 7.82 – 7.70 (m, 1H), 7.50 – 7.42 (m, 1H), 7.34 – 7.24 (m, 0.5H), 7.16 – 7.08 (m, 0.5H), 6.90 – 6.80 (m, 1H), 6.77 – 6.66 (m, 0.4H), 6.59 – 6.45 (m, 0.6H), 4.68 (q, J = 4.0, 3.3 Hz, 1H), 4.16 – 3.71 (m, 3H), 2.49 – 2.18 (m, 5H), 1.94 – 1.17 (m, 8H).

Example 18: (±)-(5-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((6-methylpyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



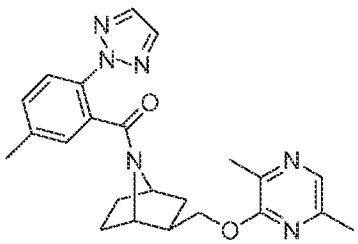
Prepared analogous to Example 13 substituting 2-chloro-4-(trifluoromethyl)pyrimidine with 2-chloro-6-(methyl)pyridine. MS (ESI) mass calcd. for $C_{23}H_{25}N_5O_2$, 403.2; m/z found 404.2 $[M+H]^+$. ^1H NMR ($CDCl_3$): 7.89 (d, J = 1.3 Hz, 2H), 7.82 – 7.66 (m, 1.5H), 7.61 (dd, J = 8.3, 7.3 Hz, 0.5H), 7.43 (ddd, J = 8.3, 1.9, 0.9 Hz, 0.5H), 7.35 – 7.26 (m, 1H), 7.16 – 7.09 (m, 0.5H), 6.88 (dd, J = 16.1, 7.3 Hz, 1H), 6.76 (d, J = 8.4 Hz, 0.5H), 6.53 (d, J = 8.3 Hz, 0.5H), 4.74 – 4.64 (m, 1H), 4.24 – 4.04 (m, 1H), 4.02 – 3.76 (m, 2H), 2.55 – 2.21 (m, 5H), 2.05 – 1.23 (m, 8H).

Example 19: (±)-(5-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((5-methylpyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



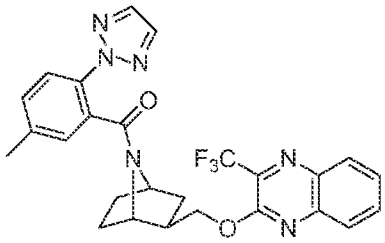
Prepared analogous to Example 13 substituting 2-chloro-4-(trifluoromethyl)pyrimidine with 2-chloro-5-(methyl)pyridine. MS (ESI) mass calcd. for $C_{23}H_{25}N_5O_2$, 403.2; m/z found 404.2 $[M+H]^+$. ^1H NMR ($CDCl_3$): 8.10 – 7.58 (m, 4H), 7.43 – 7.29 (m, 1.5H), 7.26 – 7.11 (m, 1.5H), 6.66 (d, J = 8.4 Hz, 0.5H), 6.45 (d, J = 8.4 Hz, 0.5H), 4.86 – 4.71 (m, 1H), 4.17 – 3.66 (m, 3H), 2.46 – 2.38 (s, 1.2H), 2.31 – 2.14 (m, 3.8H), 2.01 – 1.79 (m, 2H), 1.71 – 1.18 (m, 6H).

Example 20: (±)-(2-(((3,6-dimethylpyrazin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(5-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone.



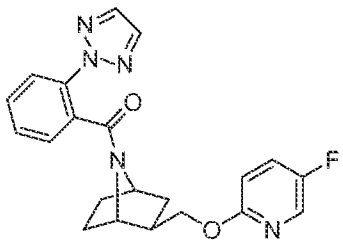
Prepared analogous to Example 13 substituting 2-chloro-4-(trifluoromethyl)pyrimidine with 3-chloro-2,5-dimethylpyrazine. MS (ESI) mass calcd. for $C_{23}H_{26}N_6O_2$, 418.2; m/z found 419.2 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) 7.88 – 7.84 (m, 1H), 7.81 – 7.72 (m, 2.5H), 7.36 – 7.12 (m, 2H), 7.11 – 7.06 (m, 0.5H), 4.86 – 4.75 (m, 1H), 4.26 – 4.15 (m, 0.5H), 4.08 (dd, *J* = 11.0, 5.5 Hz, 1H), 3.86 – 3.71 (m, 1.5H), 2.48 – 2.34 (m, 6H), 2.34 – 2.13 (m, 3H), 1.96 – 1.25 (m, 7H).

Example 21: (±)-(5-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((3-(trifluoromethyl)quinoxalin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



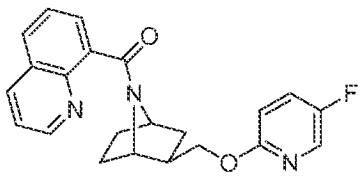
Prepared analogous to Example 13 substituting 2-chloro-4-(trifluoromethyl)pyrimidine with 2-chloro-3-(trifluoromethyl)quinoxaline. MS (ESI) mass calcd. for $C_{26}H_{23}F_3N_6O_2$, 508.2; m/z found 509.2 $[M+H]^+$. ^1H NMR ($CDCl_3$): 8.16 – 8.09 (m, 1H), 7.97 – 7.62 (m, 6H), 7.37 – 7.23 (m, 1H), 7.19 – 7.06 (m, 1H), 4.87 (t, J = 4.7 Hz, 0.5H), 4.80 (d, J = 4.8 Hz, 0.5H), 4.71 – 4.56 (m, 0.5H), 4.38 – 4.22 (m, 1H), 4.16 – 4.01 (m, 0.5H), 3.87 – 3.73 (m, 1H), 2.49 – 2.23 (m, 4H), 2.05 – 1.24 (m, 6H).

Example 22: (±)-(2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



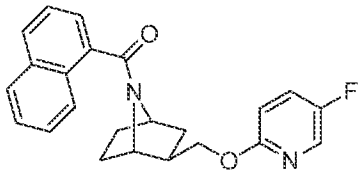
Prepared analogous to Example 7 substituting intermediate A-21 with intermediate A-1. MS (ESI) mass calcd. for $C_{21}H_{20}FN_5O_2$, 393.2; m/z found 394.2 $[M+H]^+$. ^1H NMR (400 MHz, MeOD) 8.02 – 7.78 (m, 4H), 7.62 – 7.53 (m, 0.5H), 7.49 – 7.28 (m, 3H), 7.13 – 7.01 (m, 0.5H), 6.75 (dd, J = 9.0, 3.6 Hz, 0.5H), 6.51 (dd, J = 9.0, 3.6 Hz, 0.5H), 4.85 – 4.71 (m, 1H), 4.21 – 4.03 (m, 1H), 4.02 – 3.72 (m, 2H), 2.39 – 2.09 (m, 1H), 2.04 – 1.16 (m, 6H).

Example 23: (±)-2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(quinolin-8-yl)methanone.



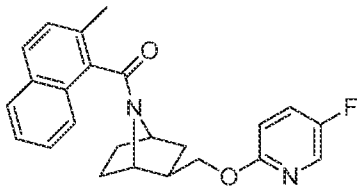
Prepared analogous to Example 22 substituting intermediate A-1 with quinoline-8-carboxylic acid. MS (ESI) mass calcd. for $C_{22}H_{20}FN_3O_2$, 377.2; m/z found 378.2 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$): 8.95 – 8.69 (m, 1H), 8.16 (dd, J = 8.3, 1.8 Hz, 0.4H), 8.11 – 7.81 (m, 2H), 7.81 – 7.67 (m, 1H), 7.64 – 7.51 (m, 1H), 7.47 – 7.09 (m, 2.6H), 6.79 (dd, J = 9.0, 3.6 Hz, 0.5H), 6.25 (s, 0.5H), 5.08 – 4.96 (m, 1H), 4.29 (s, 0.7H), 4.13 – 3.94 (m, 1.3H), 3.65 – 3.45 (m, 1H), 2.47 – 2.02 (m, 2H), 2.02 – 1.30 (m, 5H).

Example 24: (±)-2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(naphthalen-1-yl)methanone.



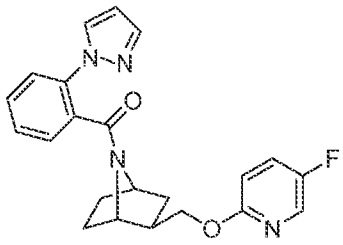
Prepared analogous to Example 22 substituting intermediate A-1 with 1-naphthoic acid. MS (ESI) mass calcd. for $C_{23}H_{21}FN_2O_2$, 376.2; m/z found 377.2 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$): 8.10 – 7.95 (m, 1.5H), 7.92 – 7.83 (m, 1.5H), 7.81 – 7.71 (m, 1H), 7.58 – 7.31 (m, 4H), 7.25 – 7.13 (m, 1H), 6.77 (dd, J = 9.0, 3.6 Hz, 0.5H), 6.36 – 6.24 (m, 0.5H), 5.04 – 4.92 (m, 1H), 4.30 – 4.13 (m, 1H), 4.07 – 3.84 (m, 1H), 3.81 – 3.64 (m, 1H), 2.44 – 2.30 (m, 0.5H), 2.27 – 2.00 (m, 1.5H), 1.89 – 1.37 (m, 5H).

Example 25: (±)-2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(2-methylnaphthalen-1-yl)methanone.



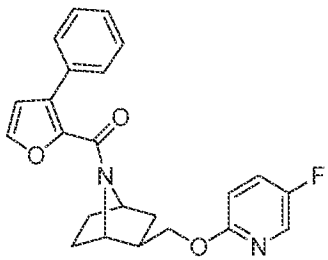
Prepared analogous to Example 22 substituting intermediate A-1 with 2-methyl-1-naphthoic acid. ^1H NMR ($CDCl_3$): 8.06 – 7.86 (m, 1H), 7.85 – 7.62 (m, 2.6H), 7.60 – 7.54 (m, 0.2H), 7.49 – 7.21 (m, 3.4H), 7.13 (m, 0.8H), 6.77 (ddd, J = 12.7, 9.0, 3.6 Hz, 0.6H), 6.43 (dd, J = 9.0, 3.6 Hz, 0.2H), 6.03 (dd, J = 9.0, 3.6 Hz, 0.2H), 5.11 – 4.99 (m, 0.9H), 4.38 – 4.09 (m, 1.2H), 4.08 – 3.82 (m, 0.7H), 3.69 – 3.43 (m, 1.2H), 2.58 – 2.27 (m, 3.5H), 2.23 – 1.97 (m, 1.5H), 1.92 – 1.28 (m, 5H).

Example 26: (±)-2-(1H-pyrazol-1-yl)phenyl)(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



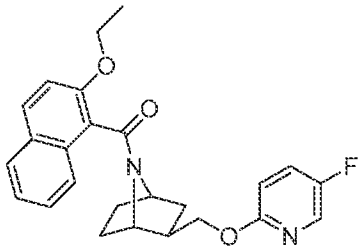
Prepared analogous to Example 22 substituting intermediate A-1 with 2-(1H-pyrazol-1-yl)benzoic acid. MS (ESI) mass calcd. for $C_{22}H_{21}FN_4O_2$, 392.2; m/z found 393.2 $[M+H]^+$. ^1H NMR ($CDCl_3$): 7.98 (dd, J = 8.3, 3.1 Hz, 1H), 7.91 – 7.83 (m, 1H), 7.69 (d, J = 1.9 Hz, 1H), 7.64 – 7.23 (m, 4.5H), 6.99 (t, J = 7.4 Hz, 0.5H), 6.71 (dd, J = 9.0, 3.6 Hz, 0.5H), 6.47 – 6.34 (m, 1.5H), 4.79 – 4.63 (m, 1H), 4.03 – 3.65 (m, 2H), 3.66 – 3.54 (m, 1H), 2.27 – 2.03 (m, 1H), 1.86 – 0.74 (m, 6H).

Example 27: (±)-2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(3-phenylfuran-2-yl)methanone.



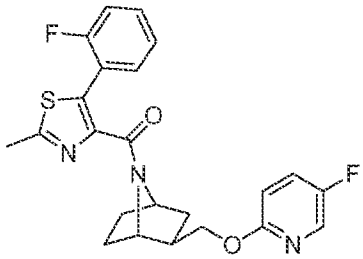
Prepared analogous to Example 22 substituting intermediate A-1 with 3-phenylfuran-2-carboxylic acid. MS (ESI) mass calcd. for $C_{22}H_{21}FN_2O_3$, 392.2; m/z found 393.2 $[M+H]^+$. ^1H NMR ($CDCl_3$): 8.05 – 7.82 (m, 1H), 7.59 – 7.44 (m, 7H), 6.77 – 6.40 (m, 2H), 4.85 – 4.61 (m, 1H), 4.45 – 4.29 (m, 0.5H), 4.24 – 4.08 (m, 0.5H), 4.06 – 3.76 (m, 2H), 2.32 – 2.11 (m, 1H), 2.01 – 0.83 (m, 6H).

Example 28: (±)-(2-ethoxynaphthalen-1-yl)(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



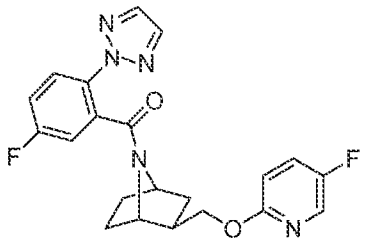
Prepared analogous to Example 22 substituting intermediate A-1 with 2-ethoxy-1-naphthoic acid. MS (ESI) mass calcd. for $C_{25}H_{25}FN_2O_3$, 420.2; m/z found 421.2 $[M+H]^+$. ^1H NMR ($CDCl_3$): 8.03 (d, J = 3.0 Hz, 0.2H), 7.95 (dd, J = 8.1, 3.1 Hz, 0.5H), 7.86 – 7.70 (m, 2.6H), 7.69 – 7.63 (m, 0.3H), 7.60 – 7.55 (m, 0.3H), 7.50 – 7.00 (m, 4.2H), 6.76 (ddd, J = 9.3, 6.1, 3.6 Hz, 0.5H), 6.44 (dd, J = 9.0, 3.5 Hz, 0.2H), 6.03 (dd, J = 9.0, 3.6 Hz, 0.2H), 5.08 – 4.97 (m, 1H), 4.35 – 3.92 (m, 3.3H), 3.91 – 3.76 (m, 0.5H), 3.68 – 3.52 (m, 1.2H), 2.44 – 2.27 (m, 0.8H), 2.20 – 1.93 (m, 2H), 1.85 – 1.18 (m, 7.2H).

Example 29: (±)-(5-(2-fluorophenyl)-2-methylthiazol-4-yl)(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



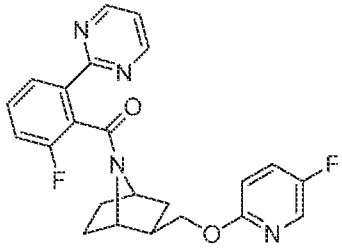
Prepared analogous to Example 22 substituting intermediate A-1 with 5-(2-fluorophenyl)-2-methylthiazole-4-carboxylic acid. MS (ESI) mass calcd. for $C_{23}H_{21}F_2N_3O_2S$, 441.2; m/z found 442.2 $[M+H]^+$. ^1H NMR ($CDCl_3$): 7.99 – 7.93 (m, 1H), 7.53 – 7.44 (m, 1H), 7.36 – 7.09 (m, 3.5H), 7.04 (ddd, J = 9.8, 8.5, 1.2 Hz, 0.5H), 6.66 (ddd, J = 15.9, 9.0, 3.6 Hz, 1H), 4.79 – 4.68 (m, 1H), 4.27 – 4.21 (m, 0.5H), 4.07 (t, J = 4.6 Hz, 0.5H), 3.96 – 3.73 (m, 2H), 2.74 (s, 1.5H), 2.42 (s, 1.5H), 2.23 – 2.11 (m, 1H), 1.89 – 1.57 (m, 2H), 1.54 – 1.24 (m, 3.5H), 0.92 – 0.81 (m, 0.5H).

Example 30: (±)-(5-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



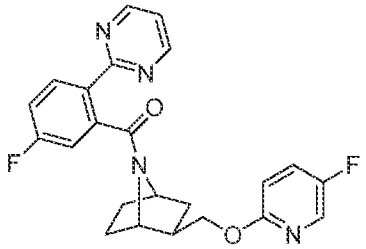
Prepared analogous to Example 22 substituting intermediate A-1 with intermediate A-10. MS (ESI) mass calcd. for $C_{21}H_{19}F_2N_5O_2$, 411.2; m/z found 412.2 $[M+H]^+$. ^1H NMR ($CDCl_3$): 7.98 (dd, J = 7.4, 3.0 Hz, 1H), 7.86 (ddd, J = 21.7, 8.9, 4.7 Hz, 1H), 7.81 – 7.75 (m, 1.5H), 7.38 – 7.03 (m, 3.5H), 6.72 (dd, J = 9.0, 3.6 Hz, 0.5H), 6.52 (dd, J = 9.0, 3.6 Hz, 0.5H), 4.85 – 4.75 (m, 1H), 4.17 – 4.02 (m, 1H), 4.02 – 3.83 (m, 1H), 3.83 – 3.75 (m, 1H), 2.34 – 2.15 (m, 1H), 2.03 – 1.80 (m, 1H), 1.74 – 1.20 (m, 5H).

Example 31: (±)-(2-fluoro-6-(pyrimidin-2-yl)phenyl)(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



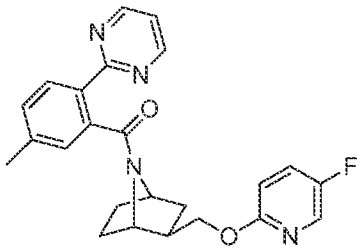
Prepared analogous to Example 22 substituting intermediate A-1 with intermediate A-6. MS (ESI) mass calcd. for $C_{23}H_{20}F_2N_4O_2$, 422.2; m/z found 423.2 $[M+H]^+$. ^1H NMR ($CDCl_3$): 8.93 – 8.61 (m, 1.8H), 8.15 – 7.92 (m, 1.6H), 7.56 – 7.05 (m, 4.3H), 6.94 (t, J = 8.6 Hz, 0.3H), 6.73 (ddd, J = 8.9, 5.2, 3.5 Hz, 0.6H), 6.59 – 6.35 (m, 0.4H), 4.99 – 4.79 (m, 1H), 4.31 (t, J = 9.9 Hz, 0.3H), 4.25 – 3.63 (m, 2.7H), 2.47 – 1.11 (m, 7H).

Example 32: (±)-(5-fluoro-2-(pyrimidin-2-yl)phenyl)(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



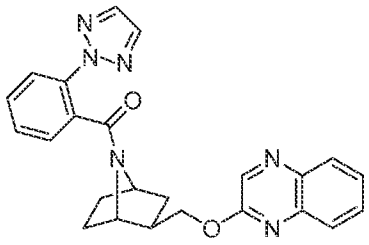
Prepared analogous to Example 22 substituting intermediate A-1 with 5-fluoro-2-(pyrimidin-2-yl)benzoic acid. MS (ESI) mass calcd. for $C_{23}H_{20}F_2N_4O_2$, 422.2; m/z found 423.2 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) 8.78 (d, J = 4.9 Hz, 1H), 8.72 (d, J = 4.8 Hz, 1H), 8.22 (ddd, J = 20.6, 8.7, 5.5 Hz, 1H), 8.01 – 7.93 (m, 1H), 7.37 – 7.27 (m, 1H), 7.23 – 7.13 (m, 1.5H), 7.13 – 6.99 (m, 1.5H), 6.72 (dd, J = 9.0, 3.5 Hz, 0.5H), 6.52 (dd, J = 9.0, 3.5 Hz, 0.5H), 4.90 – 4.75 (m, 1H), 4.25 – 3.91 (m, 2H), 3.91 – 3.78 (m, 1H), 2.39 – 2.15 (m, 1H), 2.08 – 1.13 (m, 6H).

Example 33: (±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(5-methyl-2-(pyrimidin-2-yl)phenyl)methanone.



Prepared analogous to Example 22 substituting intermediate A-1 with 5-methyl-2-(pyrimidin-2-yl)benzoic acid. MS (ESI) mass calcd. for $C_{24}H_{23}FN_4O_2$, 418.2; m/z found 419.2 $[M+H]^+$. ^1H NMR ($CDCl_3$): 8.81 – 8.68 (m, 2H), 8.09 (dd, J = 9.9, 8.0 Hz, 1H), 7.98 (dd, J = 8.6, 3.1 Hz, 1H), 7.41 – 7.24 (m, 1.5H), 7.22 – 7.16 (m, 1H), 7.16 – 7.09 (m, 1.5H), 6.73 (dd, J = 9.1, 3.6 Hz, 0.5H), 6.52 (dd, J = 9.0, 3.6 Hz, 0.5H), 4.88 – 4.77 (m, 1H), 4.21 – 4.01 (m, 1H), 4.01 – 3.89 (m, 1H), 3.88 – 3.76 (m, 1H), 2.42 (s, 1.6H), 2.35 – 2.10 (m, 1H), 2.07 – 1.81 (m, 2.4H), 1.81 – 1.16 (m, 5H).

Example 34: (±)-(2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((quinoxalin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.

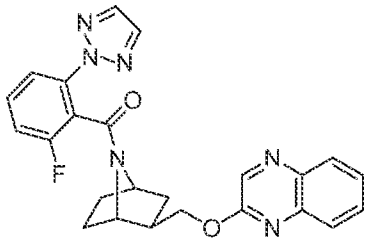


Step A: (±)-2-(-7-azabicyclo[2.2.1]heptan-2-ylmethoxy)quinoxaline. To intermediate B-10 (240 mg, 1.1 mmol) in THF (4 mL) was added NaOtBu (130 mg, 1.4 mmol). The reaction was heated at reflux for 15 min and 2-chloroquinoxaline (207 mg, 1.3 mmol) was added. After

45 min, the reaction was cooled to rt and ½ saturated NH_4Cl (aq) was added. The solution was made slightly basic with 5% Na2CO3 (aq) and extracted with DCM (3X). The combined organics were dried (Na_2SO_4). The resulting compound was treated with TFA in DCM. After the reaction was complete, the reaction was concentrated, neutralized with 5% Na_2CO_3 and extracted with DCM. The combined organics were dried (Na_2SO_4). Purification via silica gel chromatography (1-7% (2M NH_3 in MeOH)/DCM) gave the title compound (208 mg, 78%). MS (ESI) mass calcd. for $C_{15}H_{17}N_3O$, 255.1; m/z found 256.2 $[M+H]^+$.

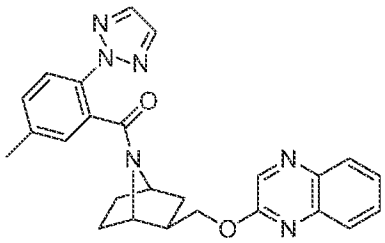
Step B: (±)-(2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((quinoxalin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone. Prepared analogous to Example 7 substituting 6-methyl-3-(2H-1,2,3-triazol-2-yl)picolinic acid with intermediate A-1 and (±)-2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptane with the title compound of Step A. MS (ESI) mass calcd. for $C_{24}H_{22}N_6O_2$, 426.2; m/z found 427.2 $[M+H]^+$. ^1H NMR ($CDCl_3$): 8.49 (s, 0.5H), 8.31 – 8.21 (s, 0.5H), 8.08 – 7.98 (m, 1H), 7.95 – 7.75 (m, 3.4H), 7.75 – 7.66 (m, 1.1H), 7.65 – 7.50 (m, 1.7H), 7.50 – 7.39 (m, 1.1H), 7.36 – 7.28 (m, 1H), 7.24 – 7.13 (m, 0.7H), 4.92 – 4.80 (m, 1H), 4.47 – 4.28 (m, 1H), 4.22 – 4.07 (m, 1H), 3.87 – 3.77 (m, 1H), 2.46 – 2.23 (m, 1.7H), 2.07 – 1.83 (m, 1.3H), 1.82 – 1.29 (m, 4H).

Example 35: (±)-(2-fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl)(2-((quinoxalin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



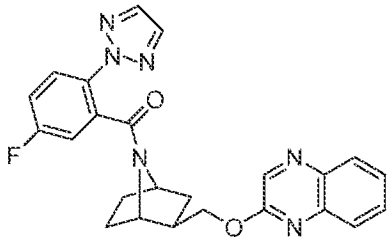
Prepared analogous to Example 34 substituting intermediate A-1 with intermediate A-11. MS (ESI) mass calcd. for $C_{24}H_{21}FN_6O_2$, 444.2; m/z found 445.2 $[M+H]^+$. ^1H NMR ($CDCl_3$): 8.52 – 8.47 (m, 0.5H), 8.27 – 8.21 (m, 0.4H), 8.07 – 7.95 (m, 1H), 7.91 – 7.09 (m, 7.8H), 6.72 – 6.63 (m, 0.3H), 4.98 – 4.87 (m, 1H), 4.63 – 4.54 (dd, J = 10.7, 9.1 Hz, 0.5H), 4.46 – 4.29 (m, 1H), 4.20 – 4.04 (m, 0.5H), 3.96 – 3.76 (m, 1H), 2.51 – 2.23 (m, 1H), 2.17 – 1.88 (m, 1H), 1.84 – 1.19 (m, 5H).

Example 36: (±)-(5-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((quinoxalin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



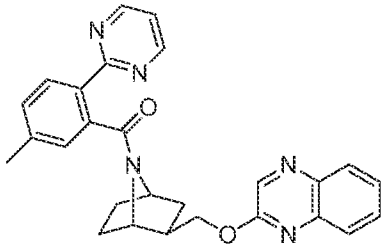
Prepared analogous to Example 34 substituting intermediate A-1 with intermediate A-37. MS (ESI) mass calcd. for $C_{25}H_{24}N_6O_2$, 440.2; m/z found 441.2 $[M+H]^+$. ^1H NMR ($CDCl_3$): 8.49 (s, 0.5H), 8.26 (s, 0.5H), 8.03 (ddd, J = 8.3, 4.4, 1.4 Hz, 1H), 7.90 – 7.74 (m, 3H), 7.74 – 7.65 (m, 1H), 7.59 (dddd, J = 8.3, 7.0, 4.8, 1.4 Hz, 1H), 7.33 (ddd, J = 8.3, 1.9, 0.9 Hz, 0.6H), 7.29 – 7.22 (m, 1H), 7.21 – 7.10 (m, 1.4H), 4.90 – 4.79 (m, 1H), 4.46 – 3.98 (m, 2H), 3.91 – 3.72 (m, 1H), 2.47 – 2.20 (m, 4H), 2.05 – 1.22 (m, 6H).

Example 37: (±)-(5-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((quinoxalin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



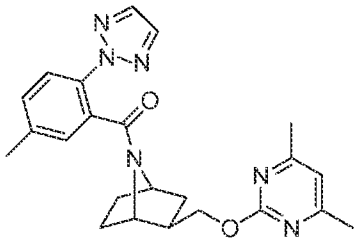
Prepared analogous to Example 34 substituting intermediate A-1 with intermediate A-10. MS (ESI) mass calcd. for $C_{24}H_{21}FN_6O_2$, 444.2; m/z found 445.2 $[M+H]^+$. ^1H NMR ($CDCl_3$): 8.55 – 8.44 (m, 0.5H), 8.36 – 8.23 (m, 0.5H), 8.08 – 8.00 (m, 1H), 7.90 – 7.55 (m, 5H), 7.49 – 7.09 (m, 3H), 4.91 – 4.82 (m, 1H), 4.50 – 4.29 (m, 1H), 4.23 – 4.07 (m, 1H), 3.82 (dd, J = 10.0, 5.0 Hz, 1H), 2.48 – 2.25 (m, 1H), 2.09 – 1.88 (m, 1H), 1.82 – 1.31 (m, 5H).

Example 38: (±)-(5-methyl-2-(pyrimidin-2-yl)phenyl)(2-((quinoxalin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Prepared analogous to Example 34 substituting intermediate A-1 with intermediate A-34. MS (ESI) mass calcd. for $C_{27}H_{25}N_5O_2$, 451.2; m/z found 452.2 $[M+H]^+$. ^1H NMR ($CDCl_3$): 8.87 – 8.79 (m, 1H), 8.75 – 8.68 (m, 1H), 8.49 (s, 0.5H), 8.27 (s, 0.5H), 8.14 – 7.98 (m, 2H), 7.85 (ddd, J = 16.5, 8.3, 1.5 Hz, 1H), 7.74 – 7.66 (m, 1H), 7.64 – 7.54 (m, 1H), 7.35 – 7.29 (m, 0.5H), 7.24 – 7.19 (m, 0.5H), 7.18 – 7.07 (m, 2H), 4.94 – 4.83 (m, 1H), 4.52 – 4.07 (m, 2H), 3.93 – 3.82 (m, 1H), 2.51 – 2.20 (m, 2.6H), 2.08 – 1.83 (m, 1.4H), 1.81 – 1.12 (m, 6H).

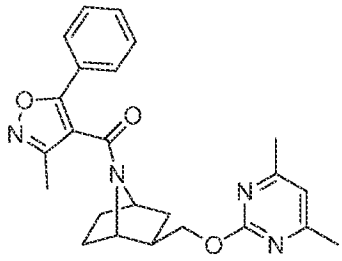
Example 39: (±)-(2-(((4,6-dimethylpyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(5-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone.



Step A: (±)-2-(((4,6-dimethylpyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptane. Prepared analogous to Example 34 substituting 2-chloroquinoxaline with 2-chloro-4,6-dimethylpyrimidine. ^1H NMR ($CDCl_3$): 6.65 (s, 1H), 4.21 – 3.99 (m, 2H), 3.74 – 3.56 (m, 2H), 2.39 (s, 6H), 2.14 (ddd, *J* = 9.0, 5.1, 3.7 Hz, 1H), 1.86 (s, 2H), 1.67 – 1.49 (m, 2H), 1.47 – 1.30 (m, 2H).

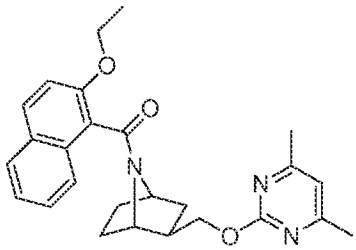
Step B: (±)-(2-(((4,6-dimethylpyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(5-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone. Prepared analogous to Example 7 substituting 6-methyl-3-(2H-1,2,3-triazol-2-yl)picolinic acid with 5-methyl-2-(2H-1,2,3-triazol-2-yl)benzoic acid and (±)-2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptane with the title compound of Step A. MS (ESI) mass calcd. for $C_{23}H_{26}N_6O_2$, 418.2; m/z found 419.2 $[M+H]^+$. ^1H NMR ($CDCl_3$): 7.83 – 7.70 (m, 2.5H), 7.35 – 7.10 (m, 2.5H), 6.71 – 6.65 (m, 1H), 4.87 – 4.72 (m, 1H), 4.34 (dd, J = 10.5, 8.8 Hz, 0.5H), 4.14 – 3.89 (m, 2H), 3.79 – 3.70 (m, 0.5H), 2.48 – 2.18 (m, 7.5H), 2.07 – 1.83 (m, 2.5H), 1.79 – 1.18 (m, 6H).

Example 40: (±)-2-(((4,6-dimethylpyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(3-methyl-5-phenylisoxazol-4-yl)methanone.



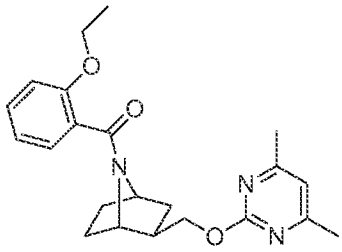
Prepared analogous to Example 39 substituting 5-methyl-2-(2H-1,2,3-triazol-2-yl)benzoic acid with 3-methyl-5-phenylisoxazole-4-carboxylic acid. MS (ESI) mass calcd. for $C_{24}H_{26}N_4O_3$, 418.2; m/z found 419.2 $[M+H]^+$. ^1H NMR ($CDCl_3$): 7.67 (m, 2H), 7.50 – 7.31 (m, 3H), 6.69 (d, J = 6.7 Hz, 1H), 4.74 (dd, J = 10.8, 5.1 Hz, 1H), 4.17 (dd, J = 10.8, 9.2 Hz, 0.5H), 3.85 – 3.78 (m, 1H), 3.70 (d, J = 4.9 Hz, 0.5H), 3.64 – 3.42 (m, 1H), 2.55 (s, 1.4H), 2.49 (s, 1.6H), 2.43 (s, 3H), 2.39 (s, 3H), 2.29 – 2.07 (m, 1H), 1.90 – 1.55 (m, 2H), 1.53 – 1.06 (m, 3H), 0.76 – 0.53 (m, 1H).

Example 41: (±)-(2-(((4,6-dimethylpyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(2-ethoxynaphthalen-1-yl)methanone.



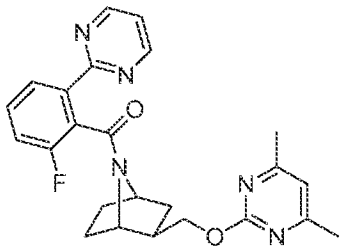
Prepared analogous to Example 39 substituting 5-methyl-2-(2H-1,2,3-triazol-2-yl)benzoic acid with 2-ethoxy-1-naphthoic acid. ^1H NMR ($CDCl_3$): 7.91 – 7.70 (m, 2.5H), 7.67 – 7.54 (m, 0.5H), 7.49 – 7.38 (m, 0.8H), 7.37 – 7.28 (m, 0.8H), 7.27 – 7.16 (m, 0.9H), 7.10 – 7.02 (m, 0.5H), 6.70 (s, 0.2H), 6.65 (s, 0.5H), 6.53 (s, 0.3H), 5.09 – 4.95 (m, 1H), 4.56 – 4.47 (m, 0.5H), 4.28 – 3.87 (m, 3.3H), 3.79 – 3.55 (m, 1.2H), 2.46 – 2.35 (m, 4.5H), 2.28 (s, 1.5H), 2.21 – 1.95 (m, 2H), 1.85 – 1.51 (m, 3.5H), 1.51 – 1.24 (m, 4.5H).

Example 42: (±)-(2-(((4,6-dimethylpyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(2-ethoxyphenyl)methanone).



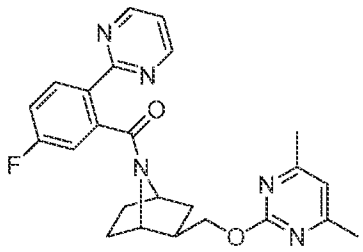
Prepared analogous to Example 39 substituting 5-methyl-2-(2H-1,2,3-triazol-2-yl)benzoic acid with 2-ethoxybenzoic acid. MS (ESI) mass calcd. for $C_{22}H_{27}N_3O_3$, 381.2; m/z found 382.2 $[M+H]^+$. ^1H NMR ($CDCl_3$): 7.34 – 7.27 (m, 1H), 7.21 – 7.12 (m, 1H), 6.98 – 6.92 (m, 0.5H), 6.89 (d, J = 8.2 Hz, 0.5H), 6.78 (d, J = 8.3 Hz, 0.5H), 6.72 – 6.63 (m, 1.5H), 4.89 – 4.78 (m, 1H), 4.36 (dd, J = 10.6, 8.7 Hz, 0.5H), 4.14 – 3.71 (m, 4.5H), 2.45 – 2.16 (m, 6.5H), 2.06 – 1.82 (m, 1.5H), 1.82 – 1.28 (m, 8H).

Example 43: (±)-(2-(((4,6-dimethylpyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(2-fluoro-6-(pyrimidin-2-yl)phenyl)methanone.



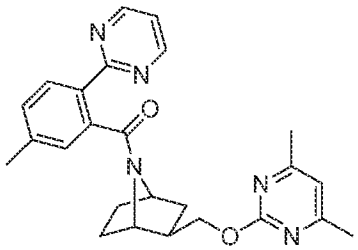
Prepared analogous to Example 39 substituting 5-methyl-2-(2H-1,2,3-triazol-2-yl)benzoic acid with 2-fluoro-6-(pyrimidin-2-yl)benzoic acid. MS (ESI) mass calcd. for $C_{24}H_{24}FN_5O_2$, 433.2; m/z found 434.2 $[M+H]^+$. ^1H NMR ($CDCl_3$): 9.02 – 8.90 (m, 0.7H), 8.82 – 8.65 (m, 1.3H), 8.14 – 7.95 (m, 1H), 7.58 – 7.31 (m, 1H), 7.31 – 7.07 (m, 1.7H), 6.97 – 6.86 (m, 0.3H), 6.75 – 6.51 (m, 1H), 4.96 – 4.83 (m, 1H), 4.55 (dd, J = 10.3, 9.0 Hz, 0.25H), 4.36 (dd, J = 10.6, 8.9 Hz, 0.25H), 4.21 – 3.78 (m, 2.5H), 2.48 – 1.17 (m, 13H).

Example 44: (±)-(2-(((4,6-dimethylpyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(5-fluoro-2-(pyrimidin-2-yl)phenyl)methanone.



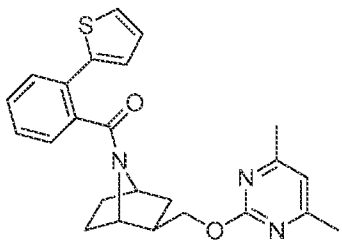
Prepared analogous to Example 39 substituting 5-methyl-2-(2H-1,2,3-triazol-2-yl)benzoic acid with 5-fluoro-2-(pyrimidin-2-yl)benzoic acid. MS (ESI) mass calcd. for $C_{24}H_{24}FN_5O_2$, 433.2; m/z found 434.2 $[M+H]^+$. ^1H NMR ($CDCl_3$): 8.88 – 8.78 (m, 1H), 8.72 (d, J = 4.8 Hz, 1H), 8.26 (dd, J = 8.7, 5.5 Hz, 0.5H), 8.22 – 8.16 (m, 0.5H), 7.29 – 7.09 (m, 2H), 7.06 – 6.97 (m, 1H), 6.68 (s, 1H), 4.88 – 4.81 (m, 1H), 4.40 (t, J = 9.7 Hz, 0.5H), 4.25 (t, J = 10.8 Hz, 0.5H), 4.05 (dd, J = 10.2, 6.2 Hz, 0.5H), 3.99 – 3.91 (m, 1H), 3.89 – 3.80 (m, 0.5H), 2.45 – 2.21 (m, 7H), 2.05 – 1.87 (m, 1H), 1.81 – 1.30 (m, 5H).

Example 45: (±)-(2-(((4,6-dimethylpyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(5-methyl-2-(pyrimidin-2-yl)phenyl)methanone.



Prepared analogous to Example 39 substituting 5-methyl-2-(2H-1,2,3-triazol-2-yl)benzoic acid with 5-methyl-2-(pyrimidin-2-yl)benzoic acid. MS (ESI) mass calcd. for $C_{25}H_{27}N_5O_2$, 429.2; m/z found 430.2 $[M+H]^+$. ^1H NMR ($CDCl_3$): 8.83 (d, J = 5.0 Hz, 1H), 8.71 (d, J = 4.8 Hz, 1H), 8.09 (dd, J = 13.6, 8.0 Hz, 1H), 7.33 – 7.10 (m, 3H), 6.68 (d, J = 1.4 Hz, 1H), 4.90 – 4.79 (m, 1H), 4.41 (dd, J = 10.4, 8.8 Hz, 0.5H), 4.20 (t, J = 10.6 Hz, 0.5H), 4.07 – 3.94 (m, 1.5H), 3.80 (t, J = 4.7 Hz, 0.5H), 2.49 – 2.19 (m, 7H), 2.04 – 1.89 (m, 3H), 1.87 – 1.47 (m, 4.5H), 1.45 – 1.29 (m, 1.5H).

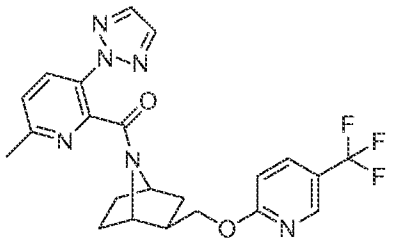
Example 46: (±)-(2-(((4,6-dimethylpyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(2-(thiophen-2-yl)phenyl)methanone.



Prepared analogous to Example 11 substituting (±)-2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptane with (±)-2-(((4,6-dimethylpyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptane. MS (ESI) mass calcd. for $C_{24}H_{25}N_3O_2S$, 419.2; m/z

found 420.2 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$): 7.55 – 6.83 (m, 7H), 6.75 – 6.62 (m, 1H), 4.87 – 4.62 (m, 1H), 4.09 – 3.38 (m, 3H), 2.54 – 2.32 (m, 6H), 2.32 – 2.03 (m, 1H), 1.97 – 0.87 (m, 6H).

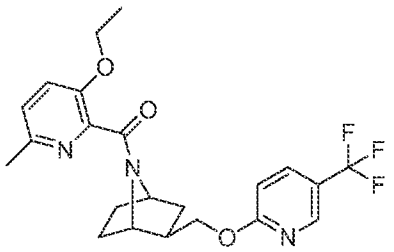
Example 47: (±)-(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-(((5-(trifluoromethyl)pyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Step A: (±)-2-(((5-(trifluoromethyl)pyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptane. Prepared analogous to Example 49 substituting 5-bromo-2-fluoropyridine with 2-fluoro-5-(trifluoromethyl)pyridine. MS (ESI) mass calcd. for $C_{13}H_{15}F_3N_2O$, 272.1; m/z found 273.1, $[M+H]^+$.

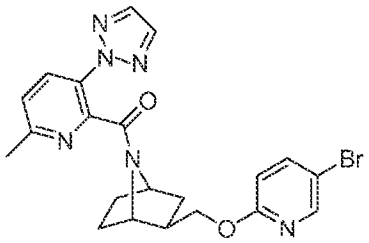
Step B: (±)-(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-(((5-(trifluoromethyl)pyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone. Prepared analogous to Example 1 substituting 5-fluoro-2-(pyrimidin-2-yl)benzoic acid with 6-methyl-3-(2H-1,2,3-triazol-2-yl)picolinic acid and (1S,2R,4R)-tert-butyl-2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptane-7-carboxylate with the title compound of Step A. MS (ESI) mass calcd. for $C_{22}H_{21}F_3N_6O_2$, 458.2; m/z found 459.2 $[M+H]^+$. ^1H NMR ($CDCl_3$): 8.47 – 8.37 (m, 1H), 8.12 (dd, J = 13.2, 8.4 Hz, 1H), 7.85 – 7.69 (m, 3H), 7.32 (dd, J = 8.4, 0.6 Hz, 0.5H), 7.22 (dd, J = 8.4, 0.6 Hz, 0.5H), 6.88 – 6.82 (m, 0.5H), 6.69 – 6.59 (m, 0.5H), 4.93 – 4.81 (m, 1H), 4.39 – 4.18 (m, 2H), 3.94 – 3.87 (m, 1H), 2.65 – 2.60 (s, 1.2H), 2.39 – 2.22 (m, 2.8H), 2.11 – 1.33 (m, 6H).

Example 48: (±)-(3-ethoxy-6-methylpyridin-2-yl)(2-(((5-(trifluoromethyl)pyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Prepared analogous to Example 47 substituting 6-methyl-3-(2H-1,2,3-triazol-2-yl)picolinic acid with 3-ethoxy-6-methylpicolinic acid. MS (ESI) mass calcd. for $C_{22}H_{24}F_3N_3O_3$, 435.2; m/z found 436.2 $[M+H]^+$. ^1H NMR ($CDCl_3$): 8.43 – 8.35 (m, 1H), 7.79 – 7.68 (m, 1H), 7.18 – 7.07 (m, 1H), 7.07 – 6.96 (m, 1H), 6.86 (d, J = 8.7 Hz, 0.5H), 6.64 (d, J = 8.7 Hz, 0.5H), 4.92 – 4.86 (m, 1H), 4.29 – 4.20 (m, 1H), 4.19 – 4.10 (m, 1H), 4.10 – 3.83 (m, 2H), 3.74 (t, J = 3.9 Hz, 1H), 2.52 – 2.47 (s, 1.5H), 2.41 – 2.32 (m, 0.5H), 2.28 – 2.18 (m, 2H), 2.07 – 1.84 (m, 2H), 1.78 – 1.63 (m, 1H), 1.62 – 1.41 (m, 3H), 1.37 (dt, J = 11.8, 7.0 Hz, 3H).

Example 49: (±)-(2-(((5-bromopyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)methanone.

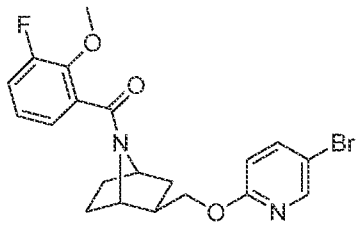


Step A: (±)-2-(((5-bromopyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptane. To intermediate B-10 (175 mg, 0.8 mmol) in DMF (3.5 mL) at 0 °C was added NaH (60 wt% in mineral oil, 37 mg, 0.9 mmol). After 30 min, 5-bromo-2-fluoropyridine (190 mg, 1.1 mmol) in DMF (0.5 mL) was added dropwise and the 0 °C ice bath was removed. After 2h, brine was added and the reaction extracted with EtOAc (2X). The combined organics were washed with brine and dried (Na_2SO_4) to give a clear oil which was treated with TFA and DCM (1:1, 10 mL). After 2h, the reaction was concentrated, dissolved in DCM and neutralized with 5% Na2CO3 (aq). The combined organics were extracted with DCM (3X) and dried (Na_2SO_4) to give the title compound that was used in subsequent reactions without further purification. MS (ESI) mass calcd. for $C_{12}H_{15}BrN_2O$, 282.0; m/z found 283.1, 285.1 $[M+H]^+$. NMR (500 MHz, $CDCl_3$): 8.17 (d, *J* = 2.5 Hz, 1H), 7.63 (dd, *J* = 8.8, 2.5 Hz, 1H), 6.65 (d, *J* = 8.8 Hz, 1H), 4.08 – 3.99 (m, 2H), 3.65 (t, *J* = 4.5 Hz, 1H), 3.59 (d, *J* = 4.1 Hz, 1H), 2.12 – 2.06 (m, 1H), 1.87 (s, 1H), 1.68 – 1.52 (m, 2H), 1.45 – 1.13 (m, 3H), 0.95 – 0.76 (m, 1H).

Step B: Prepared analogous to Example 1 substituting 5-fluoro-2-(pyrimidin-2-yl)benzoic acid with 6-methyl-3-(2H-1,2,3-triazol-2-yl)picolinic acid and (1S,2R,4R)-tert-butyl-2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptane-7-carboxylate with the title compound of Step A. MS (ESI) mass calcd. for $C_{21}H_{21}BrN_6O_2$, 468.1; m/z found 469.1, 471.1 $[M+H]^+$. ^1H NMR ($CDCl_3$): 8.20 (d, J = 2.6 Hz, 0.4H), 8.16 (d, J = 2.6 Hz, 0.6H), 8.13 (d, J = 8.3 Hz, 0.4H), 8.10

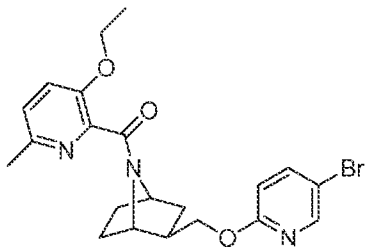
(d, J = 8.4 Hz, 0.6H), 7.82 – 7.77 (m, 2H), 7.64 (dd, J = 8.8, 2.6 Hz, 0.4H), 7.60 (dd, J = 8.8, 2.6 Hz, 0.6H), 7.33 – 7.29 (m, 0.4H), 7.22 (d, J = 8.4 Hz, 0.6H), 6.69 (d, J = 8.8 Hz, 0.4H), 6.50 (d, J = 8.8 Hz, 0.6H), 4.84 (dd, J = 11.1, 5.2 Hz, 1H), 4.30 – 4.04 (m, 2H), 3.93 – 3.85 (m, 1H), 2.62 (s, 1.3H), 2.38 – 2.17 (m, 2.7H), 2.11 – 1.95 (m, 1H), 1.94 – 1.77 (m, 1H), 1.77 – 1.40 (m, 4H).

Example 50: (±)-(2-(((5-bromopyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-methoxyphenyl)methanone.



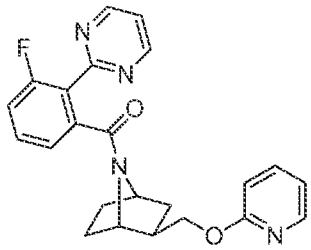
Prepared analogous to Example 49 substituting 6-methyl-3-(2H-1,2,3-triazol-2-yl)picolinic acid with 3-fluoro-2-methoxybenzoic acid. MS (ESI) mass calcd. for $C_{20}H_{20}BrFN_2O_3$, 434.1; m/z found 435.1, 437.1 $[M+H]^+$. ^1H NMR ($CDCl_3$): 8.19 – 8.12 (m, 1H), 7.61 (ddd, J = 26.6, 8.8, 2.5 Hz, 1H), 7.16 – 6.98 (m, 2H), 6.96 (dt, J = 7.6, 1.3 Hz, 0.5H), 6.85 – 6.81 (m, 0.5H), 6.69 (dd, J = 8.8, 0.8 Hz, 0.5H), 6.46 (d, J = 8.7 Hz, 0.5H), 4.88 – 4.77 (m, 1H), 4.17 – 4.06 (m, 1H), 4.03 – 3.86 (m, 4H), 3.81 – 3.75 (m, 1H), 2.37 – 2.22 (m, 1H), 2.04 – 1.40 (m, 6H).

Example 51: (±)-(2-(((5-bromopyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(3-ethoxy-6-methylpyridin-2-yl)methanone.



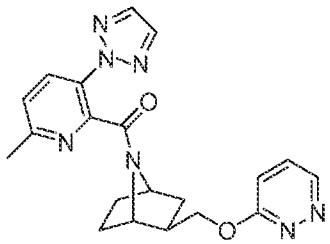
Prepared analogous to Example 49 substituting 6-methyl-3-(2H-1,2,3-triazol-2-yl)picolinic acid with 3-ethoxy-6-methylpicolinic acid. MS (ESI) mass calcd. for $C_{21}H_{24}BrN_3O_3$, 445.1; m/z found 446.1, 448.1 $[M+H]^+$. ^1H NMR ($CDCl_3$): 8.17 – 8.11 (m, 1H), 7.61 (ddd, J = 19.5, 8.8, 2.6 Hz, 1H), 7.16 – 7.06 (m, 1H), 7.05 – 6.96 (m, 1H), 6.69 (dd, J = 8.8, 0.7 Hz, 0.5H), 6.47 (dd, J = 8.8, 0.7 Hz, 0.5H), 4.90 – 4.84 (m, 1H), 4.20 – 4.10 (m, 1H), 4.09 – 3.82 (m, 3H), 3.78 – 3.72 (m, 1H), 2.50 (s, 1.4H), 2.38 – 2.25 (m, 2.6H), 2.04 – 1.84 (m, 2H), 1.75 – 1.40 (m, 4H), 1.60 – 1.40 (m, 3H), 1.36 (dt, J = 7.8, 7.0 Hz, 3H).

Example 52: (±)-(3-fluoro-2-(pyrimidin-2-yl)phenyl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Prepared analogous to Example 1 substituting 5-fluoro-2-(pyrimidin-2-yl)benzoic acid with 3-fluoro-2-(pyrimidin-2-yl)benzoic acid and intermediate B-9 with intermediate B-10. MS (ESI) mass calcd. for $C_{23}H_{21}FN_4O_2$, 404.2; m/z found 405.2 $[M+H]^+$. ^1H NMR ($CDCl_3$): 8.81 (dd, J = 18.0, 4.9 Hz, 2H), 8.20 – 8.12 (m, 1H), 7.56 (ddd, J = 8.3, 7.1, 2.0 Hz, 1H), 7.45 (td, J = 8.0, 5.1 Hz, 0.5H), 7.28 – 7.22 (m, 1.5H), 7.21 – 7.08 (m, 1.5H), 7.05 – 6.96 (m, 0.5H), 6.88 (dddd, J = 13.2, 7.1, 5.1, 1.0 Hz, 1H), 6.71 (dt, J = 8.4, 0.9 Hz, 0.5H), 6.61 (dt, J = 8.4, 0.9 Hz, 0.5H), 4.70 – 4.61 (m, 1H), 4.15 – 4.07 (m, 1H), 4.06 – 3.89 (m, 2H), 2.26 (ddt, J = 15.3, 8.3, 4.5 Hz, 1H), 1.93 – 1.27 (m, 6H).

Example 53: (±)-(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-((pyridazin-3-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.

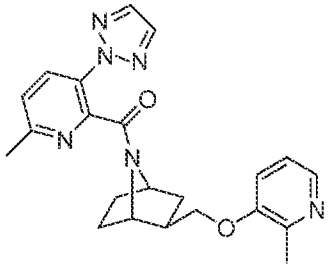


Step A: (±)-tert-butyl 2-((pyridazin-3-yloxy)methyl)-7-azabicyclo[2.2.1]heptane-7-carboxylate. To intermediate B-10 (266 mg, 1.2 mmol) in THF (4 mL) at 0 °C was added NaH (60 wt% in mineral oil, 70 mg, 1.8 mmol). After 15 min, 3-chloropyridazine (160 mg, 1.4 mmol) was added. The reaction allowed to warm to rt. After 18h, H_2O was added and the mixture extracted with EtOAc. The organic layer was dried. Purification via silica gel chromatography (0-30% EtOAc in heptane) gave the title compound (300 mg, 90%). MS (ESI) mass calcd. for $C_{16}H_{23}N_3O_3$, 305.2; m/z found 306.0 $[M+H]^+$.

Step B: (±)-2-((pyridazin-3-yloxy)methyl)-7-azabicyclo[2.2.1]heptane hydrochloride. To the title compound from step A (300 mg, 1 mmol) in 1,4-dioxane (3 mL) was added 6N HCl in iPrOH (1 mL). The reaction was heated to 70 °C for 3h, cooled to rt and concentrated to give the title compound that was used without further purification. MS (ESI) mass calcd. for $C_{11}H_{15}N_3O$, 205.1; m/z found 206.0 $[M+H]^+$.

Step C: (±)-(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-((pyridazin-3-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone. To 6-methyl-3-(2H-1,2,3-triazol-2-yl)picolinic acid (270 mg, 1.3 mmol) in DMF (3 mL) was added DIPEA (630 µL, 3.6 mmol), HBTU (590 mg, 1.5 mmol) and the title compound from step B (250 mg, 1 mmol). After stirring overnight, saturated $NaHCO_3$ (aq) was added and the mixture extracted with EtOAc (3X). The combined organics were dried (MgSO4). Purification by reverse phase chromatography gave material that was triturated with Et_2O/pentane to give the title compound (115 mg, 28%) as a beige solid. MS (ESI) mass calcd. for $C_{20}H_{21}N_7O_2$, 391.2; m/z found 392.2 $[M+H]^+$. ^1H NMR (DMSO-D_6): 8.91 (dd, J = 8.5, 4.4 Hz, 1H), 8.23 – 8.04 (m, 3H), 7.69 – 7.52 (m, 1.5H), 7.41 (d, J = 8.4 Hz, 0.5H), 7.28 (d, J = 8.9 Hz, 0.5H), 7.10 (d, J = 8.9 Hz, 0.5H), 4.60 (t, J = 4.8 Hz, 1H), 4.40 – 4.19 (m, 2H), 3.87 (t, J = 4.3 Hz, 0.5H), 3.79 (d, J = 4.3 Hz, 0.5H), 2.58 (s, 1.5H), 2.46 – 2.24 (m, 1H), 2.06 (s, 1.5H), 1.81 – 1.34 (m, 6H).

Example 54: (±)-(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-(((2-methylpyridin-3-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Step A: (±)-tert-butyl-2-(((methylsulfonyl)oxy)methyl)-7-azabicyclo[2.2.1]heptane-7-carboxylate. To intermediate B-10 (545 mg, 2.4 mmol) in DCM (12 mL) at 0 °C was added TEA (333 µL, 2.4 mmol) followed by MsCl (190 µL, 2.4 mmol). After 2h, brine was added and the mixture was extracted with DCM (2X). The combined organics were dried (Na_2SO_4) to give the title compound (650 mg, 89%) that was used without further purification. MS (ESI) mass calcd. for $C_{12}H_{23}NO_5S$, 305.1; m/z found 249.9 $[M-55]^+$.

Step B: (±)-tert-butyl 2-(((2-methylpyridin-3-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptane-7-carboxylate. To 2-methylpyridin-3-ol in DMF was added KOH. The solution was stirred for 30

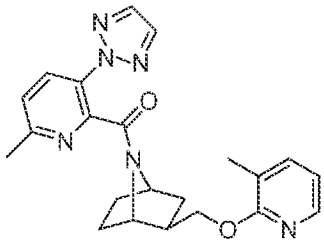
min at rt, then the title compound from step A was added and the reaction was heated at 80 °C. After 5h, H_2O was added and the mixture extracted with EtOAc. The combined organic layers were dried (MgSO4). Purification via silica gel chromatography (0-7% MeOH in DCM) gave the title compound (201 mg, 90%). MS (ESI) mass calcd. for $C_{18}H_{26}N_2O_3$, 318.2; m/z found 319.0 $[M+1]^+$.

Step C: (±)-2-(((2-methylpyridin-3-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptane. Prepared analogous to example 53 step B substituting (±)-tert-butyl 2-((pyridazin-3-yloxy)methyl)-7-azabicyclo[2.2.1]heptane-7-carboxylate with (±)-tert-butyl 2-(((2-methylpyridin-3-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptane-7-carboxylate. MS (ESI) mass calcd. for $C_{13}H_{18}N_2O$, 218.1; m/z found 219.1 $[M+1]^+$.

Step D: (±)-(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-(((2-methylpyridin-3-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.

Prepared analogous to example 53 step C substituting (±)-2-((pyridazin-3-yloxy)methyl)-7-azabicyclo[2.2.1]heptane hydrochloride with (±)-2-(((2-methylpyridin-3-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptane. MS (ESI) mass calcd. for $C_{22}H_{24}N_6O_2$, 404.2; m/z found 405.2 $[M+H]^+$. ^1H NMR (DMSO-D_6): 8.22 – 7.92 (m, 4H), 7.55 (d, J = 8.4 Hz, 0.3H), 7.45 – 7.33 (m, 1H), 7.32 – 7.10 (m, 1.7H), 4. 60 – 4.57 (m, 1H), 3.92 – 3.67 (m, 3H), 2.57 (s, 0.9H), 2.42 – 2.18 (m, 1.9H), 2.08 (s, 2.1H), 1.95 (s, 2.1H), 1.80 – 1.31 (m, 6H).

Example 55: (±)-(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-(((3-methylpyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Step A: (±)-tert-butyl 2-(((2-methylpyridin-3-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptane-7-carboxylate. Prepared analogous to Example 7 Step A Method A substituting PBu3 with PPh3, DEAD with DIAD, 5-fluoropyridin-2(1H)-one with 3-methylpyridin-2-ol and performing the reaction at rt. MS (ESI) mass calcd. for $C_{18}H_{26}N_2O_3$, 318.2; m/z found 319.0 $[M+H]^+$.

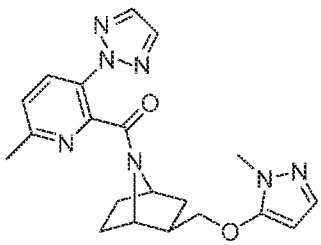
Step B: (±)-2-(((2-methylpyridin-3-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptane. Prepared analogous to Example 53 Step B substituting (±)-tert-butyl 2-((pyridazin-3-yloxy)methyl)-7-azabicyclo[2.2.1]heptane-7-carboxylate with (±)-tert-butyl 2-(((2-methylpyridin-3-

yl)oxy)methyl)-7-azabicyclo[2.2.1]heptane-7-carboxylate. MS (ESI) mass calcd. for $C_{13}H_{18}N_2O$, 218.1; m/z found 219.0 $[M+H]^+$.

Step C: (±)-(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-(((3-methylpyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.

Prepared analogous to Example 53 Step C substituting (±)-2-((pyridazin-3-yloxy)methyl)-7-azabicyclo[2.2.1]heptane hydrochloride with (±)-2-(((2-methylpyridin-3-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptane. MS (ESI) mass calcd. for $C_{22}H_{24}N_6O_2$, 404.2; m/z found 405.2 $[M+H]^+$.

Example 56: (±)-(2-(((1-methyl-1H-pyrazol-5-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)methanone.

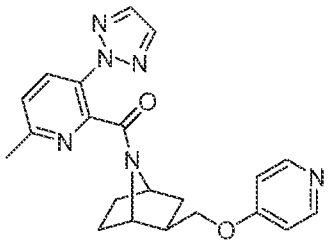


Step A: (±)-tert-butyl 2-(((1-methyl-1H-pyrazol-5-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptane-7-carboxylate. Prepared analogous to Example 7 Step A Method A substituting THF with $PhCH_3$ and 5-fluoropyridin-2(1H)-one with 1-methyl-1H-pyrazol-5-ol. MS (ESI) mass calcd. for $C_{16}H_{25}N_3O_3$, 307.2; m/z found 308.0 $[M+H]^+$.

Step B: (±)-2-(((1-methyl-1H-pyrazol-5-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptane. Prepared analogous to Example 53 Step B substituting (±)-tert-butyl 2-((pyridazin-3-yloxy)methyl)-7-azabicyclo[2.2.1]heptane-7-carboxylate the title compound of Step A. MS (ESI) mass calcd. for $C_{11}H_{17}N_3O$, 207.1; m/z found 208.0 $[M+H]^+$.

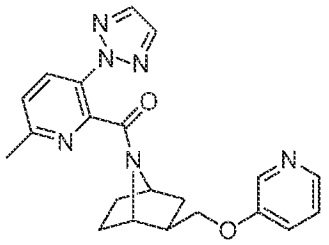
Step C: (±)-(2-(((1-methyl-1H-pyrazol-5-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)methanone. Prepared analogous to Example 53 Step C substituting (±)-2-((pyridazin-3-yloxy)methyl)-7-azabicyclo[2.2.1]heptane hydrochloride with the title compound of Step B. MS (ESI) mass calcd. for $C_{20}H_{23}N_7O_2$, 393.2; m/z found 394.2 $[M+H]^+$. ^1H NMR (DMSO-D_6): 8.18 – 8.05 (m, 3H), 7.56 (d, J = 8.4 Hz, 0.4H), 7.49 (d, J = 8.4 Hz, 0.6H), 7.23 (d, J = 1.7 Hz, 0.4H), 7.19 (d, J = 1.7 Hz, 0.6H), 5.70 (d, J = 1.8 Hz, 0.4H), 5.59 (d, J = 1.8 Hz, 0.6H), 4.59 – 4.56 (m, 1H), 3.96 – 3.76 (m, 3H), 3.57 (s, 1.2H), 3.34 (s, 1.8H), 2.58 (s, 1.2H), 2.39 – 2.17 (m, 2.8H), 1.87 – 1.27 (m, 6H).

Example 57: (±)-(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-((pyridin-4-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



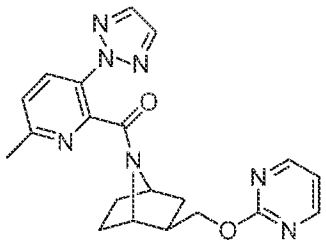
Prepared analogous to Example 54 subsituting 2-methylpyridin-3-ol with pyridin-4-ol. MS (ESI) mass calcd. for $C_{21}H_{22}N_6O_2$, 390.2; m/z found 391.2 $[M+H]^+$. ^1H NMR (DMSO-D_6): 8.41 (d, J = 5.5 Hz, 0.8H), 8.36 (d, J = 5.5 Hz, 1.2H), 8.20 – 8.02 (m, 3H), 7.55 (d, J = 8.4 Hz, 0.4H), 7.40 (d, J = 8.4 Hz, 0.6H), 7.00 (d, J = 6.2 Hz, 0.8H), 6.88 (d, J = 6.2 Hz, 1.2H), 4.64 – 4.51 (m, 1H), 4.02 – 3.78 (m, 2.4H), 3.75 (d, J = 4.4 Hz, 0.6H), 2.57 (s, 1.2H), 2.39 – 2.20 (m, 1H), 2.04 (s, 1.8H), 1.87 – 1.30 (m, 6H).

Example 58: (±)-(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-((pyridin-3-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



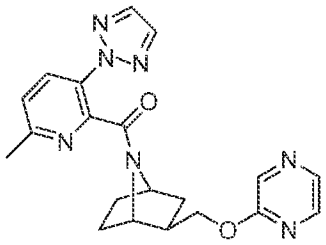
Prepared analogous to Example 54 subsituting 2-methylpyridin-3-ol with pyridin-3-ol. MS (ESI) mass calcd. for $C_{21}H_{22}N_6O_2$, 390.2; m/z found 391.2 $[M+H]^+$. ^1H NMR (DMSO-D_6): 8.33 (d, J = 2.7 Hz, 0.4H), 8.21 – 8.05 (m, 4.6H), 7.55 (d, J = 8.4 Hz, 0.4H), 7.46 – 7.25 (m, 2.6H), 4.58 (t, J = 4.8 Hz, 1H), 3.95 – 3.80 (m, 2.4H), 3.77 (d, J = 4.4 Hz, 0.6H), 2.57 (s, 1.2H), 2.38 – 2.18 (m, 1H), 2.02 (s, 1.8H), 1.85 – 1.31 (m, 6H).

Example59: (±)-(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-((pyrimidin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



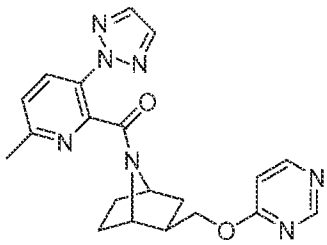
Prepared analogous to Example 53 substituting 2-chloropyridazine with 2-chloropyrimidine. MS (ESI) mass calcd. for $C_{20}H_{21}N_7O_2$, 391.2; m/z found 392.2 $[M+H]^+$. ^1H NMR (DMSO-D_6): 8.65 (d, J = 4.8 Hz, 0.8H), 8.59 (d, J = 4.8 Hz, 1.2H), 8.22 – 8.02 (m, 3H), 7.56 (d, J = 8.4 Hz, 0.4H), 7.44 (d, J = 8.4 Hz, 0.6H), 7.19 – 7.13 (m, 1H), 4.59 (t, J = 4.5 Hz, 0.6H), 4.55 (d, J = 4.4 Hz, 0.4H), 4.24 – 4.04 (m, 2H), 3.85 (t, J = 4.3 Hz, 0.4H), 3.78 (d, J = 4.0 Hz, 0.6H), 2.58 (s, 1.2H), 2.39 – 2.21 (m, 1H), 2.11 (s, 1.8H), 1.86 – 1.29 (m, 6H).

Example 60: (±)-(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-((pyrazin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Prepared analogous to Example 53 substituting 2-chloropyridazine with 2-pyrazine. MS (ESI) mass calcd. for $C_{20}H_{21}N_7O_2$, 391.2; m/z found 392.2 $[M+H]^+$.

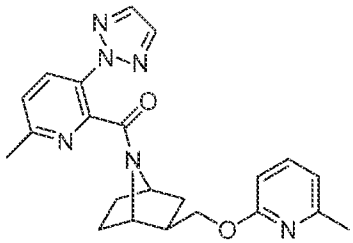
Example 61: (±)-(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-((pyrimidin-4-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Prepared analogous to Example 55 substituting 3-methylpyridin-2-ol with pyrimidin-4-ol. MS (ESI) mass calcd. for $C_{20}H_{21}N_7O_2$, 391.2; m/z found 392.2 $[M+H]^+$. The product is present as a mixture of conformers (ratio ca. 50:50) ^1H NMR (300 MHz, DMSO) 8.84 (s, 0.5H), 8.77 (s, 0.5H), 8.53 (d, J = 5.8 Hz, 0.5H), 8.49 (d, J = 5.8 Hz, 0.5H), 8.22 – 8.01 (m, 3H), 7.55 (d, J = 8.4

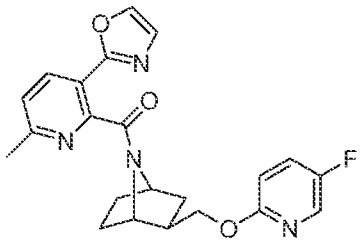
Hz, 0.5H), 7.43 (d, *J* = 8.4 Hz, 0.5H), 7.00 (d, *J* = 5.7 Hz, 0.5H), 6.85 (d, *J* = 5.8 Hz, 0.5H), 4.58 (t, *J* = 3.7 Hz, 0.5H), 4.53 (d, *J* = 4.2 Hz, 0.5H), 4.25 – 4.04 (m, 2H), 3.85 (t, *J* = 3.7 Hz, 0.5H), 3.75 (d, *J* = 3.9 Hz, 0.5H), 2.57 (s, 1.5H), 2.40 – 2.16 (m, 1H), 2.12 (s, 1.5H), 1.85 – 1.31 (m, 6H).

Example 62: (±)-(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-(((6-methylpyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



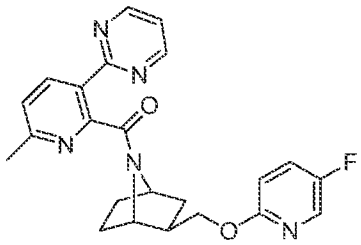
Prepared analogous to Example 55 substituting 3-methylpyridin-2-ol with 6-methylpyridin-2-ol. MS (ESI) mass calcd. for $C_{22}H_{24}N_6O_2$, 404.2; m/z found 405.2 $[M+H]^+$. ^1H NMR (DMSO-D_6): 8.17 (d, *J* = 8.4 Hz, 0.5H), 8.12 (d, *J* = 8.4 Hz, 0.5H), 8.10 (s, 1H), 8.06 (s, 1H), 7.63 – 7.49 (m, 1.5H), 7.41 (d, *J* = 8.4 Hz, 0.5H), 6.85 (d, *J* = 7.2 Hz, 0.5H), 6.81 (d, *J* = 7.2 Hz, 0.5H), 6.64 (d, *J* = 8.2 Hz, 0.5H), 6.46 (d, *J* = 8.2 Hz, 0.5H), 4.58 (t, *J* = 4.4 Hz, 0.5H), 4.54 (d, *J* = 4.5 Hz, 0.5H), 4.16 – 3.95 (m, 2H), 3.83 (t, *J* = 4.4 Hz, 0.5H), 3.74 (d, *J* = 4.4 Hz, 0.5H), 2.58 (s, 1.5H), 2.43 (s, 1.5H), 2.37 (s, 1.5H), 2.33 – 2.14 (m, 1H), 2.11 (s, 1.5H), 1.85 – 1.31 (m, 6H).

Example 63: (±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(oxazol-2-yl)pyridin-2-yl)methanone.



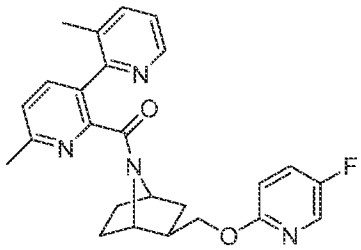
Prepared analogous to Example 7 substituting intermediate A-21 with intermediate A-43. MS (ESI) mass calcd. for $C_{22}H_{21}FN_4O_3$, 408.2; m/z found 409.2 $[M+H]^+$.

Example 64: (±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(pyrimidin-2-yl)pyridin-2-yl)methanone.



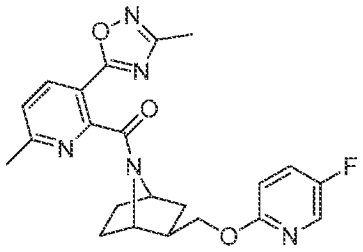
Prepared analogous to Example 7 substituting intermediate A-21 with 6-methyl-3-(pyrimidin-2-yl)picolinic acid. MS (ESI) mass calcd. for $C_{23}H_{22}FN_5O_2$, 419.2; m/z found 420.2 $[M+H]^+$. ^1H NMR (DMSO-D_6): 8.91 (d, J = 4.9 Hz, 0.8H), 8.84 (d, J = 4.9 Hz, 1.2H), 8.33 – 8.29 (m, 1H), 8.22 (d, J = 3.1 Hz, 0.4H), 8.13 (d, J = 3.1 Hz, 0.6H), 7.76 – 7.59 (m, 1H), 7.53 – 7.41 (m, 1.4H), 7.35 (d, J = 8.1 Hz, 0.6H), 6.94 (dd, J = 9.1, 3.6 Hz, 0.4H), 6.75 (dd, J = 9.1, 3.6 Hz, 0.6H), 4.59 (t, J = 4.1 Hz, 0.6H), 4.56 (d, J = 3.8 Hz, 0.4H), 4.16 (dd, J = 14.6, 6.2 Hz, 1H), 4.08 – 3.97 (m, 1H), 3.87 (br s, 0.4H), 3.76 (d, J = 3.9 Hz, 0.6H), 2.56 (s, 1.2H), 2.39 – 2.15 (m, 1H), 2.10 (s, 1.8H), 1.91 – 1.32 (m, 6H).

Example 65: (±)-(3,6'-dimethyl-[2,3'-bipyridin]-2'-yl)(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



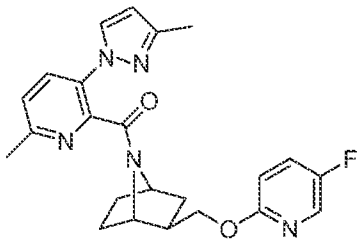
Prepared analogous to Example 7 substituting intermediate A-21 with 3,6'-dimethyl-[2,3'-bipyridine]-2'-carboxylic acid. MS (ESI) mass calcd. for $C_{25}H_{25}FN_4O_2$, 432.2; m/z found 433.2 $[M+H]^+$. ^1H NMR (DMSO-D_6): 8.33 (t, J = 5.1 Hz, 1H), 8.16 (s, 1H), 7.79 – 7.60 (m, 3H), 7.40 (d, J = 7.9 Hz, 0.5H), 7.32 – 7.23 (m, 1H), 7.20 (dd, J = 7.6, 4.8 Hz, 0.5H), 6.85 (dd, J = 9.1, 3.6 Hz, 0.5H), 6.80 (dd, J = 9.1, 3.6 Hz, 0.5H), 4.39 (brs, 0.5H), 4.35 (d, J = 4.1 Hz, 0.5H), 4.19 (t, J = 10.3 Hz, 0.5H), 4.04 (dd, J = 10.4, 5.2 Hz, 0.5H), 3.90 (d, J = 4.8 Hz, 0.5H), 3.85 (t, J = 4.0 Hz, 0.5H), 3.75 – 3.53 (m, 1H), 2.56 (s, 1.5H), 2.22 2.17 (m, 3.5H), 2.11 (s, 1.5H), 1.90 – 1.81 (m, 0.5H), 1.79 – 1.17 (m, 6H).

Example 66: (±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(3-methyl-1,2,4-oxadiazol-5-yl)pyridin-2-yl)methanone.



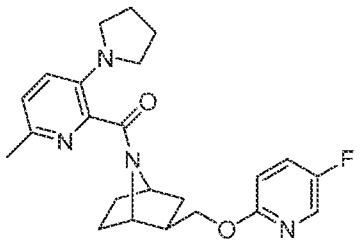
Prepared analogous to Example 7 substituting intermediate A-21 with 6-methyl-3-(3-methyl-1,2,4-oxadiazol-5-yl)picolinic acid. MS (ESI) mass calcd. for $C_{22}H_{22}FN_5O_3$, 423.2; m/z found 424.2 $[M+H]^+$. ^1H NMR (DMSO-D_6): 8.33 (d, J = 8.1 Hz, 0.4H), 8.28 (d, J = 8.1 Hz, 0.6H), 8.14 (d, J = 3.1 Hz, 0.4H), 8.10 (d, J = 3.1 Hz, 0.6H), 7.76 – 7.60 (m, 1H), 7.58 (d, J = 8.2 Hz, 0.4H), 7.47 (d, J = 8.2 Hz, 0.6H), 6.95 (dd, J = 3.6, 9.2 Hz, 0.4H), 6.72 (dd, J = 3.6, 9.2 Hz, 0.6H), 4.67 (t, J = 4.5 Hz, 0.6H), 4.62 (d, J = 4.6 Hz, 0.4H), 4.16 – 3.92 (m, 2H), 3.81 (t, J = 4.3 Hz, 0.4H), 3.73 (d, J = 4.6 Hz, 0.6H), 2.60 (s, 1.2H), 2.41 (s, 1.2H), 2.38 (s, 1.8H), 2.37 – 2.19 (m, 1H), 2.18 (s, 1.8H), 1.90 – 1.30 (m, 6 H).

Example 67: (±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(3-methyl-1H-pyrazol-1-yl)pyridin-2-yl)methanone.



Prepared analogous to Example 7 substituting intermediate A-21 with 6-methyl-3-(3-methyl-1H-pyrazol-1-yl)picolinic acid. MS (ESI) mass calcd. for $C_{23}H_{24}FN_5O_2$, 421.2; m/z found 422.2 $[M+H]^+$. MP=123.2°C.

Example 68: (±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(pyrrolidin-1-yl)pyridin-2-yl)methanone.

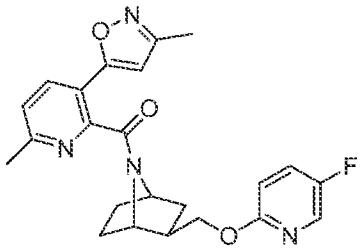


Step A: 6-methyl-3-(pyrrolidin-1-yl)picolinonitrile. To 2-bromo-6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridine (720 mg, 3.7 mmol), pyrollidine (450 µL, 5.5 mmol), $Pd(OAc)_2$ (25 mg, 11 mol%), XPhos (122 mg, 25 mol%) and Cs_2CO_3 (2.4 g, 7.3 mmol) in a sealed tube was added PhCH3. The vessel was sealed and heated at 100 °C overnight. After cooling to rt, the reaction was diluted with EtOAc and H_2O. The organic layer was dried (MgSO4) and concentrated. Purification via silica gel chromatography (0-50% EtOAc in DCM) gave the title compound (186 mg, 27%).

Step B: 6-methyl-3-(pyrrolidin-1-yl)picolinic acid. To the title compound of Step A (162 mg, 0.9 mmol) in EtOH (2.6 mL) was added 4M KOH (650 µL, 2.6 mmol). The reaction was then heated at 90 °C for 18h. Additional 4M KOH (1.5 mL,6 mmol) was added and heating continued overnight. The reaction was then cooled to rt, acidified with 1N HCl (aq), concentrated and used without further purification in the next step.

Step C: (±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(pyrrolidin-1-yl)pyridin-2-yl)methanone Prepared analogous to Example 7 substituting intermediate A-9 with the title compound from Step B. MS (ESI) mass calcd. for $C_{23}H_{27}FN_4O_2$, 410.2; m/z found 411.2 $[M+H]^+$. ^1H NMR (DMSO-D_6): 8.14 (d, J = 3.0 Hz, 0.5H), 8.10 (d, J = 3.0 Hz, 0.5H), 7.68 – 7.38 (m, 2H), 6.92 (dd, J = 9.1, 3.6 Hz, 0.5H), 6.71 (dd, J = 9.1, 3.6 Hz, 0.5H), 4.66 (br s, 0.5H), 4.60 (br s, 0.5H), 4.08 – 3.01 (m, 7H), 2.45 (s, 1.5H), 2.40 – 2.01 (m, 2.5H), 1.94 – 1.30 (m, 10H).

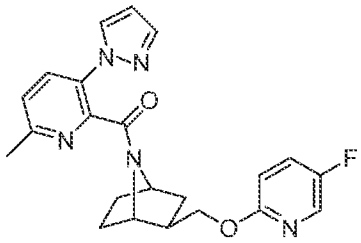
Example 69: # (±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(3-methylisoxazol-5-yl)pyridin-2-yl)methanone.



Prepared analogous to Example 7 substituting intermediate A-21 with 6-methyl-3-(3-methylisoxazol-5-yl)picolinic acid. MS (ESI) mass calcd. for $C_{23}H_{23}FN_4O_3$, 422.2; m/z found 423.2 $[M+H]^+$. ^1H NMR (DMSO-D_6): 8.11 (dt, J = 10.0, 5.4 Hz, 2H), 7.77 – 7.55 (m, 1H), 7.50 (d, J = 8.2 Hz, 0.4H), 7.38 (d, J = 8.2 Hz, 0.6H), 6.94 (dd, J = 9.1, 3.6 Hz, 0.4H), 6.70 (dd, J = 9.1, 3.6 Hz, 0.6H), 6.62 (d, J = 1.6 Hz, 1H), 4.67 (t, J = 4.6 Hz, 0.6H), 4.61 (d, J = 4.7 Hz, 0.4H),

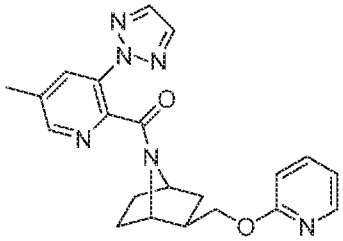
3.98-3.88 (m, 2H), 3.60 (t, *J* = 4.5 Hz, 0.4H), 3.54 (d, *J* = 3.8 Hz, 0.6H), 2.55 (s, 1.2H), 2.38 – 2.14 (m, 4H), 2.12 (s, 1.8H), 1.86 – 1.13 (m, 6H).

Example 70: (±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(1H-pyrazol-1-yl)pyridin-2-yl)methanone.



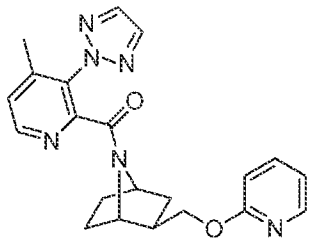
Prepared analogous to Example 63 substituting 6-methyl-3-(oxazol-2-yl)picolinic acid with 6-methyl-3-(1H-pyrazol-1-yl)picolinic acid. MS (ESI) mass calcd. for $C_{22}H_{22}FN_5O_2$, 407.2; m/z found 408.2 $[M+H]^+$. ^1H NMR (DMSO-D_6): 8.17 (d, *J* = 3.1 Hz, 0.5H), 8.13 (d, *J* = 3.1 Hz, 0.5H), 8.08 (t, *J* = 2.4 Hz, 1H), 7.95 (t, *J* = 8.5 Hz, 1H), 7.74 – 7.61 (m, 2H), 7.49 (d, *J* = 8.3 Hz, 0.5H), 7.36 (d, *J* = 8.4 Hz, 0.5H), 6.91 (dd, *J* = 9.1, 3.6 Hz, 0.5H), 6.72 (dd, *J* = 9.1, 3.6 Hz, 0.5H), 6.52 – 6.49 (m, 0.5H), 6.49 – 6.46 (m, 0.5H), 4.55 (t, *J* = 4.5 Hz, 0.5H), 4.50 (d, *J* = 4.7 Hz, 0.5H), 3.94 (d, *J* = 7.6 Hz, 2H), 3.67 (t, *J* = 4.2 Hz, 0.5H), 3.59 (d, *J* = 4.5 Hz, 0.5H), 2.54 (s, 1.5H), 2.30 – 2.11 (m, 1H), 2.07 (s, 1.5H), 1.76 – 1.14 (m, 6H).

Example 71: (±)-(5-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



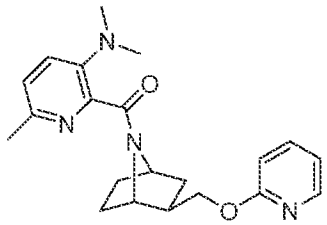
Prepared analogous to Example 2 substituting intermediate A-9 with 5-methyl-3-(2H-1,2,3-triazol-2-yl)picolinic acid. MS (ESI) mass calcd. for $C_{21}H_{22}N_6O_2$, 390.2; m/z found 391.0 $[M+H]^+$. MP= 159.7°C

Example 72: (±)-(4-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Prepared analogous to Example 2 substituting intermediate A-9 with 4-methyl-3-(2H-1,2,3-triazol-2-yl)picolinic acid. MS (ESI) mass calcd. for $C_{21}H_{22}N_6O_2$, 390.2; m/z found 391.0 $[M+H]^+$.MP=114.5°C

Example 73: (±)-(3-(dimethylamino)-6-methylpyridin-2-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.

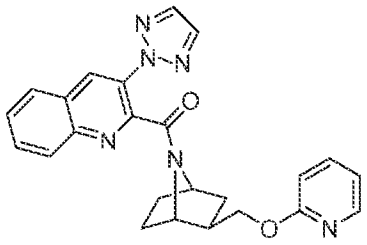


Step A: 3-(dimethylamino)-6-methylpicolinamide. A mixture of 3-bromo-6-methylpicolinonitrile (1g, 5 mmol) and dimethylamine (2 mL) were heated in a microwave reactor for 2h at 140 °C. The mixture was then concentrated and purified via silica gel chromatography (0-5% MeOH in DCM) to give the title compound (249 mg, 27%). MS (ESI) mass calcd. for $C_9H_{13}N_3O$, 179.1; m/z found 180.0 $[M+H]^+$.

Step B: 3-(dimethylamino)-6-methylpicolinic acid. To the title compound of Step A (91 mg, 0.5 mmol) in EtOH (1 mL) was added 4M KOH (0.5 µL). The reaction was then heated at 90 °C for 18h. The reaction was then cooled to rt, acidified with 1N HCl (aq) to pH=3, concentrated and used without further purification in the next step.

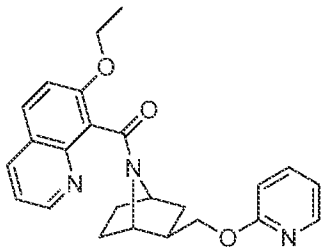
Step C: Prepared analogous to Example 2 substituting intermediate A-9 with the title compound of Step B. MS (ESI) mass calcd. for $C_{21}H_{26}N_4O_2$, 366.2; m/z found 367 $[M+H]^+$.

Example 74: (±)-(3-(2H-1,2,3-triazol-2-yl)quinolin-2-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



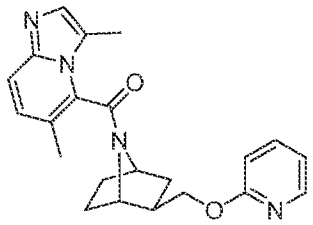
Prepared analogous to Example 2 substituting intermediate A-9 with 3-(2H-1,2,3-triazol-2-yl)quinoline-2-carboxylic acid. MS (ESI) mass calcd. for $C_{24}H_{22}N_6O_2$, 426.2; m/z found 427.2 $[M+H]^+$. ^1H NMR (DMSO-D_6): 8.93 (s, 0.5H), 8.87 (s, 0.5H), 8.26 – 8.09 (m, 2H), 7.96 – 7.86 (m, 0.5H), 7.82 – 7.51 (m, 5H), 7.33 (d, J = 8.4 Hz, 0.5H), 7.00 (t, J = 6.0 Hz, 1H), 6.87 (d, J = 8.3 Hz, 0.5H), 6.52 (d, J = 8.3 Hz, 0.5H), 4.70 – 4.57 (m, 1H), 4.33 (t, J = 10.5 Hz, 0.5H), 4.24 – 4.05 (m, 1.5H), 4.00 (br t, J = 3.8 Hz, 0.5H), 3.93 (d, J = 3.6 Hz, 0.5H), 2.44 – 2.20 (m, 1H), 2.01 – 1.35 (m, 6H).

Example 75: (±)-(7-ethoxyquinolin-8-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Prepared analogous to Example 2 substituting intermediate A-9 with intermediate A-29. MS (ESI) mass calcd. for $C_{24}H_{25}N_3O_3$, 403.2; m/z found 404.2 $[M+H]^+$. ^1H NMR (DMSO-D_6): 9.02 – 8.54 (m, 1.6H), 8.42 (d, J = 7.9 Hz, 0.8H), 8.31 – 7.83 (m, 2.2H), 7.83 – 6.75 (m, 3.8H), 6.64 – 6.46 (m, 0.2H), 6.24 (m, 0.4H), 4.86 – 4.62 (m, 1.2H), 4.46 – 4.01 (m, 3.6H), 3.61 – 3.23 (m, 1.2H), 2.44 – 2.06 (m, 1H), 2.06 – 1.15 (m, 9H).

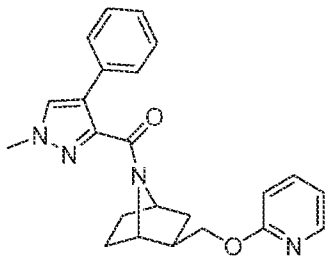
Example 76: (±)-(3,6-dimethylimidazo[1,2-a]pyridin-5-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Step A: 3,6-dimethylimidazo[1,2-a]pyridine-5-carboxylic acid. Prepared analogous to Example 82 substituting chloroacetaldehyde with 2-bromopropanal. MS (ESI) mass calcd. for $C_{10}H_{10}N_2O_2$, 190.1; m/z found 191.0 $[M+H]^+$.

Step B: (±)-(3,6-dimethylimidazo[1,2-a]pyridin-5-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone. Prepared analogous to Example 2 substituting intermediate A-9 with the title compound of Step A. MS (ESI) mass calcd. for $C_{22}H_{24}N_4O_2$, 376.2; m/z found 377.2 $[M+H]^+$. The product is present as a mixture of conformers (ratio ca. 85:15). ^{1}H NMR (300 MHz, DMSO) 8.18 (dd, J = 4.5, 1.4 Hz, 0.85H), 7.91 (d, J = 5.1 Hz, 0.15H), 7.74 (td, J = 7.1, 1.8 Hz, 0.85H), 7.53 (d, J = 9.1 Hz, 0.85H), 7.50 – 7.39 (m, 0.15H), 7.36 (s, 1H), 7.12 (dd, J = 6.3 Hz, 1H), 7.06 – 6.95 (m, 0.85H), 6.88 (d, J = 8.4 Hz, 0.85H), 6.72 (d, J = 8.6 Hz, 0.15H), 6.62 (d, J = 7.4 Hz, 0.15H), 6.46 (d, J = 8.5 Hz, 0.15H), 4.77 (d, J = 4.4 Hz, 0.85H), 4.72 (d, J = 3.6 Hz, 0.15H), 4.25 – 4.10 (m, 1H), 4.10 – 3.98 (m, 1H), 3.78 (br s, 0.85H), 3.69 (br s, 0.15H), 2.48 – 2.38 (m, 1.85H), 2.36 (s, 2H), 2.30 (s, 2H), 2.25 – 2.21 (m, 0.85H), 2.20 – 2.16 (m, 0.3H), 1.98 – 1.32 (m, 6H).

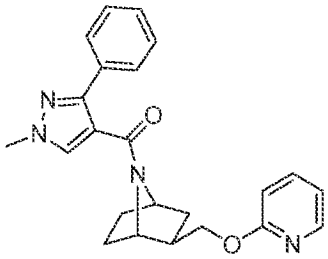
Example 77: (±)-(1-methyl-4-phenyl-1H-pyrazol-3-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Prepared analogous to Example 2 substituting intermediate A-9 with 1-methyl-4-phenyl-1H-pyrazole-3-carboxylic acid. MS (ESI) mass calcd. for $C_{23}H_{24}N_4O_2$, 388.2; m/z found 389.2 $[M+H]^+$. ^{1}H NMR (DMSO-D_6): 8.18 (d, J = 3.8 Hz, 0.5H), 8.08 (d, J = 3.9 Hz, 0.5H), 8.03 (s, 0.5H), 7.92 (s, 0.5H), 7.76 – 7.62 (m, 1H), 7.46 – 7.16 (m, 5H), 7.04 – 6.90 (m, 1H), 6.84 (d, J = 8.3 Hz, 0.5H), 6.71 (d, J = 8.3 Hz, 0.5H), 4.60 (t, J = 4.6 Hz, 0.5H), 4.56 (d, J = 4.7 Hz, 0.5H),

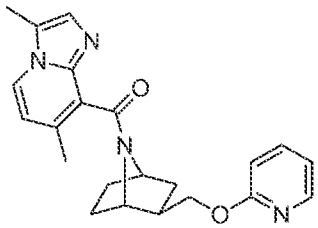
4.15 (br s, 1H), 4.06 (br s, 1H), 3.98 – 3.83 (m, 2.5H), 3.55 (s, 1.5H), 2.29– 2.15 (m, 1H), 1.79 – 1.22 (m, 6H).

Example 78: (±)-(1-methyl-3-phenyl-1H-pyrazol-4-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Prepared analogous to Example 2 substituting intermediate A-9 with 1-methyl-3-phenyl-1H-pyrazole-4-carboxylic acid. MS (ESI) mass calcd. for $C_{23}H_{24}N_4O_2$, 388.2; m/z found 389.2 $[M+H]^+$. ^1H NMR (DMSO-D_6): 8.16 (br s, 1H), 8.09 – 7.75 (m, 1H), 7.70 (t, J = 7.2 Hz, 1H), 7.58 (d, J = 7.0 Hz, 2H), 7.47 – 7.20 (m, 3H), 7.10 – 6.90 (m, 1H), 6.92 – 6.52 (br s, 1H), 4.48 (br s, 1H), 4.21 – 3.44 (m, 6H), 2.17 (br s, 1H), 1.86 – 1.05 (m, 6H).

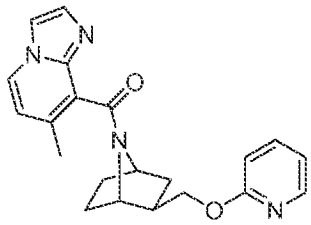
Example 79: (±)-((3,7-dimethylimidazo[1,2-a]pyridin-8-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Step A: Prepared analogous to Example 76 substituting 6-amino-3-methylpicolinic acid with 2-amino-4-methylnicotinic acid.

Step B: (±)-((3,7-dimethylimidazo[1,2-a]pyridin-8-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone. Prepared analogous to Example 2 substituting intermediate A-9 with 3,7-dimethylimidazo[1,2-a]pyridine-8-carboxylic acid. MS (ESI) mass calcd. for $C_{22}H_{24}N_4O_2$, 376.2; m/z found 377.2 $[M+H]^+$. ^1H NMR (DMSO-D_6): 8.24 – 8.03 (m, 2H), 7.80 – 7.68 (m, 0.5H), 7.61 (br s, 0.5H), 7.30 (s, 1H), 7.06 – 6.27 (m, 3H), 4.70 (t, J = 4.3 Hz, 1H), 4.32 – 3.67 (m, 2H), 3.42 (m, 2H), 2.45 (s, 2H), 2.38 – 2.02 (m, 4H), 2.02 – 1.18 (m, 6H).

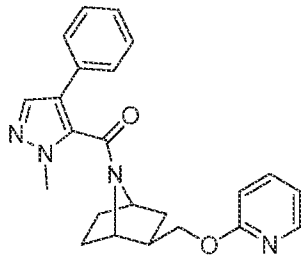
Example 80: (±)-(7-methylimidazo[1,2-a]pyridin-8-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Step A: 7-methylimidazo[1,2-a]pyridine-8-carboxylic acid. Prepared analogous to Example 82 substituting 6-amino-3-methylpicolinic acid with 2-amino-4-methylnicotinic acid.

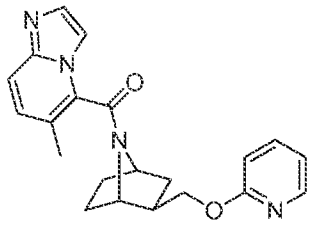
Step B: (±)-(7-methylimidazo[1,2-a]pyridin-8-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone. Prepared analogous to Example 2 substituting intermediate A-9 with the title compound of Step A. MS (ESI) mass calcd. for $C_{21}H_{22}N_4O_2$, 362.2; m/z found 363.2 $[M+H]^+$. ^1H NMR (DMSO-D_6): 8.46 (d, J = 6.9 Hz, 0.5H), 8.38 (d, J = 6.3 Hz, 0.5H), 8.17 (d, J = 3.6 Hz, 0.5H), 8.12 (d, J = 3.8 Hz, 0.5H), 7.91 (s, 1H), 7.79 – 7.39 (m, 2H), 7.14 – 6.70 (m, 2H), 6.70 – 6.33 (m, 1H), 4.71 (br s, 1H), 4.45 – 3.66 (m, 2H), 3.63 – 3.22 (m, 2H), 2.44 – 2.02 (m, 3H), 2.02 – 1.08 (m, 6H).

Example 81: (±)-(1-methyl-4-phenyl-1H-pyrazol-5-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Prepared analogous to Example 2 substituting intermediate A-9 with 1-methyl-4-phenyl-1H-pyrazole-5-carboxylic acid. MS (ESI) mass calcd. for $C_{23}H_{24}N_4O_2$, 388.2; m/z found 389.2 $[M+H]^+$. ^1H NMR (DMSO-D_6): 8.19 (d, J = 3.8 Hz, 0.6H), 8.09 (d, J = 4.0 Hz, 0.4H), 7.79 – 7.57 (m, 2H), 7.43 – 7.19 (m, 5H), 7.05 – 6.91 (m, 1H), 6.84 (d, J = 8.3 Hz, 0.6H), 6.62 (d, J = 8.3 Hz, 0.4H), 4.62 (t, J = 4.5 Hz, 0.4H), 4.57 (d, J = 4.5 Hz, 0.6H), 3.96 – 3.87 (m, 2H), 3.85 (s, 1.8H), 3.79 (s, 1.2H), 3.58 (t, J = 4.3 Hz, 0.6H), 3.52 (d, J = 4.7 Hz, 0.4H), 2.28 – 2.02 (m, 1H), 1.76 – 1.07 (m, 6H).

Example 82: (±)-((6-methylimidazo[1,2-a]pyridin-5-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.

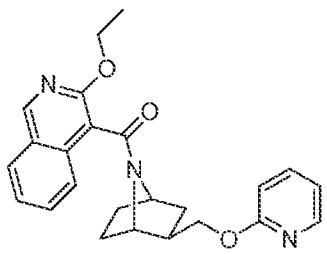


Step A: 6-amino-3-methylpicolinic acid. To methyl 6-amino-3-bromopicolinate (500 mg, 2.2 mmol), tetramethylstannane (900 µL, 6.5 mmol) and LiCl (354 mg, 8.7 mmol) in DMF (6 mL) was added $Pd(PPh_3)_4$ (76 mg, 10 mol%). The reaction mixture was heated at 110 °C for 3h. Additional tetramethylstannane, LiCl and $Pd(PPh_3)_4$ were added and heating continued for 6h. Purification via silica gel chromatography (0-20% MeOH in DCM) gave the title compound.

Step B: 6-methylimidazo[1,2-a]pyridine-5-carboxylic acid. To the title compound of Step A (340 mg, 2.2 mmol) in H_2O (7 mL) was added 1M aq. NaOH (2.2 mL, 2.2 mmol) and chloroacetaldehyde (210 µL, 3.4 mmol) and the reaction mixture heated in a microwave reactor at 150 °C for 2h. Additional 1M aq. NaOH (2.2 mL, 2.2 mmol) and chloroacetaldehyde (210 µL, 3.4 mmol) were added and heating continued at 150 °C for 2h. The reaction was purified via prep HPLC to give the title compound (282 mg, 72%). MS (ESI) mass calcd. for $C_9H_8N_2O_2$, 176.1; m/z found 177.0 $[M+H]^+$.

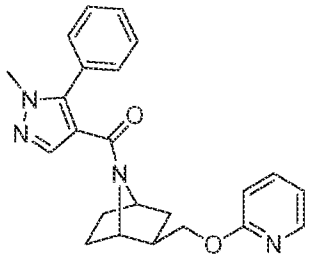
Step C: (±)-((6-methylimidazo[1,2-a]pyridin-5-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone. Prepared analogous to Example 2 substituting intermediate A-9 with 6-methylimidazo[1,2-a]pyridine-5-carboxylic acid. The product is present as a mixture of conformers (ratio ca. 80:20) ^{1}H NMR (300 MHz, DMSO) 8.44 – 8.13 (m, 1.6H), 8.13 – 7.86 (m, 3H), 7.86 – 7.41 (m, 1.2H), 6.97 (br d, J = 33.5 Hz, 1.6H), 6.68 (br d, J = 1.0 Hz, 0.2H), 6.39 (br d, J = 1.0 Hz, 0.4H), 4.80 (d, J = 16.5 Hz, 1.6H), 4.09 – 4.06 (m, 0.2H), 3.58 (s, 2H), 3.46 – 3.30 (m, 0.2H), 2.47 – 2.07 (m, 4H), 2.07 – 1.02 (m, 6H).

Example 83: (±)-(3-ethoxyisoquinolin-4-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



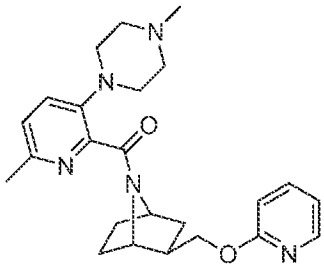
Prepared analogous to Example 164 substituting intermediate B-9 with intermediate B-10. MS (ESI) mass calcd. for $C_{24}H_{25}N_3O_3$, 403.2; m/z found 404.2 $[M+H]^+$.

Example 84: (±)-(1-methyl-5-phenyl-1H-pyrazol-4-yl)(-2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Prepared analogous to Example 2 substituting intermediate A-9 with intermediate A-51. MS (ESI) mass calcd. for $C_{23}H_{24}N_4O_2$, 388.2; m/z found 389.2 $[M+H]^+$.

Example 85: (±)-(6-methyl-3-(4-methylpiperazin-1-yl)pyridin-2-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



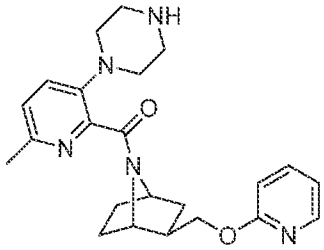
Step A: 6-methyl-3-(4-methylpiperazin-1-yl)picolinonitrile. Prepared analogous to Example 68 substituting pyrollidine with 1-methylpiperazine. MS (ESI) mass calcd. for $C_{12}H_{16}N_4$, 216.1; m/z found 217.0 $[M+H]^+$.

Step B: 6-methyl-3-(4-methylpiperazin-1-yl)picolinic acid. Prepared analogous to Example 68 substituting 6-methyl-3-(pyrrolidin-1-yl)picolinonitrile with the title compound of Step A. MS (ESI) mass calcd. for $C_{12}H_{17}N_3O_2$, 235.1; m/z found 236.0 $[M+H]^+$.

Step C: Prepared analogous to Example 2 substituting intermediate A-9 with the title compound of Step B. MS (ESI) mass calcd. for $C_{24}H_{31}N_5O_2$, 421.2; m/z found 422.2 $[M+H]^+$ ^1H NMR (DMSO-D_6): 8.19 – 8.14 (m, 0.5H), 8.12 (dd, J = 5.0, 1.5 Hz, 0.5H), 7.78 – 7.68 (m, 0.5H), 7.68 – 7.59 (m, 0.5H), 7.52 (d, J = 8.4 Hz, 0.5H), 7.37 (d, J = 8.4 Hz, 0.5H), 7.23 (d, J = 8.4 Hz, 0.5H), 7.07 (d, J = 8.3 Hz, 0.5H), 6.97 (ddd, J = 12.3, 6.7, 5.4 Hz, 1H), 6.87 (d, J = 8.3 Hz, 0.5H), 6.59 (d, J = 8.3 Hz, 0.5H), 4.63 (t, J = 4.5 Hz, 0.5H), 4.59 (d, J = 3.9 Hz, 0.5H), 4.19

– 3.81 (m, 2H), 3.46 (t, J = 3.9 Hz, 0.5H), 3.39 (d, J = 4.7 Hz, 0.5H), 3.07 – 2.92 (m, 2H), 2.92 – 2.78 (m, 2H), 2.46 – 2.27 (m, 6H), 2.22 – 2.05 (m, 3.5H), 1.97 (s, 1.5H), 1.94 – 1.27 (m, 6H).

Example 86: (±)-(6-methyl-3-(piperazin-1-yl)pyridin-2-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



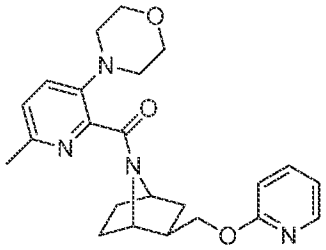
Step A: tert-butyl 4-(2-cyano-6-methylpyridin-3-yl)piperazine-1-carboxylate. Prepared analogous to Example 68 substituting pyrollidine with tert-butyl piperazine-1-carboxylate. MS (ESI) mass calcd. for $C_{16}H_{22}N_4O_2$, 302.2; m/z found 303.0 $[M+H]^+$.

Step B: 3-(4-(tert-butoxycarbonyl)piperazin-1-yl)-6-methylpicolinic acid. Prepared analogous to Example 68 substituting 6-methyl-3-(pyrrolidin-1-yl)picolinonitrile with the title compound of Step A. MS (ESI) mass calcd. for $C_{16}H_{23}N_3O_4$, 321.2; m/z found 322.0 $[M+H]^+$.

Step C: tert-butyl 4-(6-methyl-2-((±)-2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptane-7-carbonyl)pyridin-3-yl)piperazine-1-carboxylate. Prepared analogous to example 2 substituting intermediate A-9 with the title compound of Step B.

Step D: (±)-(6-methyl-3-(piperazin-1-yl)pyridin-2-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone. To the title compound from step C (182 mg, 0.4 mmol) in 1,4-dioxane (1 mL) was added 6N HCl in iPrOH (400 µL). The reaction was heated to 70 °C for 3h, cooled to rt, concentrated and purified via reverse phase chromatography. The mixture was dissolved with a saturated NaHCO3 (aq) and extracted with DCM (x3). The organic layers were dried over MgSO4 and concentrated. The crude product was triturated with diethyl ether and n-pentane to give the title compound (5 mg, 3%). MS (ESI) mass calcd. for $C_{23}H_{29}N_5O_2$, 407.2; m/z found 408.2 $[M+H]^+$. ^{1}H NMR (DMSO-D_6): 8.17 (d, J = 4.0 Hz, 0.4H), 8.12 (d, J = 3.8 Hz, 0.6H), 7.72 (t, J = 7.6 Hz, 0.4H), 7.63 (t, J = 6.9 Hz, 0.6H), 7.48 (d, J = 8.3 Hz, 0.4H), 7.34 (d, J = 8.3 Hz, 0.6H), 7.22 (d, J = 8.3 Hz, 0.4H), 7.06 (d, J = 8.3 Hz, 0.6H), 7.02 – 6.90 (m, 1H), 6.86 (d, J = 8.1 Hz, 0.4H), 6.58 (d, J = 8.3 Hz, 0.6H), 4.63 – 4.60 (m, 1H), 4.14 – 3.92 (m, 2H), 3.86 (t, J = 10.4 Hz, 1H), 2.99 – 2.65 (m, 8H), 2.39 (s, 1H), 2.34 – 2.28(m, 1H), 2.18 – 2.11(m, 1H), 1.96 – 1.88 (m, 2H), 1.86 – 1.20 (m, 6H).

Example 87: (±)-(6-methyl-3-morpholinopyridin-2-yl)((1S,2R,4R)-2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.

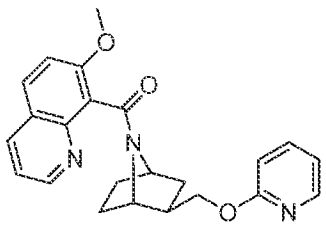


Step A: 6-methyl-3-morpholinopicolinonitrile. Prepared analogous to Example 68 substituting pyrollidine with morpholine. MS (ESI) mass calcd. for $C_{11}H_{13}N_3O$, 203.1; m/z found 204.0 $[M+H]^+$.

Step B: 6-methyl-3-morpholinopicolinic acid. Prepared analogous to Example 68 substituting 6-methyl-3-(pyrrolidin-1-yl)picolinonitrile with the title compound of Step A. MS (ESI) mass calcd. for $C_{11}H_{14}N_2O_3$, 222.1; m/z found 223.0 $[M+H]^+$.

Step C: Prepared analogous to Example 2 substituting intermediate A-9 with the title compound of Step B. MS (ESI) mass calcd. for $C_{23}H_{28}N_4O_3$, 408.2; m/z found 409.2 $[M+H]^+$.

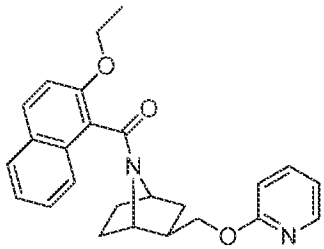
Example 88: (±)-(7-methoxyquinolin-8-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Step A: 7-methoxyquinoline-8-carboxylic acid. In 1g separate batches a mixture of 2-amino-6-methoxybenzoic acid (11g, 66 mmol) and acrolein (4.8 mL, 72 mmol) in 1,4-dioxane (66 mL) was heated in a microwave reactor for 20 min at 200 °C. After combining the reactions, the mixture was concentrated and purified via silica gel chromatography (0-10% MeOH in DCM) to give the title compound (2.8g, 20%). MS (ESI) mass calcd. for $C_{11}H_{19}NO_3$, 203.1; m/z found 204.0 $[M+H]^+$.

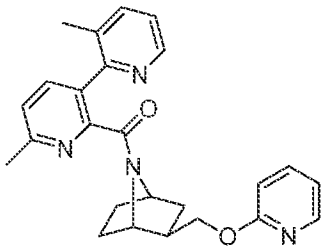
Step B: Prepared analogous to Example 2 substituting intermediate A-9 with the title compound of Step A. MS (ESI) mass calcd. for $C_{23}H_{23}N_3O_3$, 389.2; m/z found 390.2 $[M+H]^+$.

Example 89: (±)-(2-ethoxynaphthalen-1-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



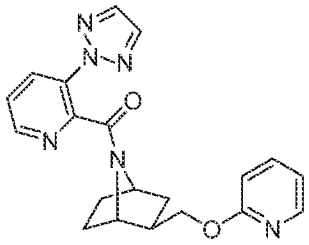
Prepared analogous to Example 2 substituting intermediate A-9 with 2-ethoxy-1-naphthoic acid. MS (ESI) mass calcd. for $C_{25}H_{26}N_2O_3$, 402.2; m/z found 403.2 $[M+H]^+$.

Example 90: (±)-(3,6'-dimethyl-[2,3'-bipyridin]-2'-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



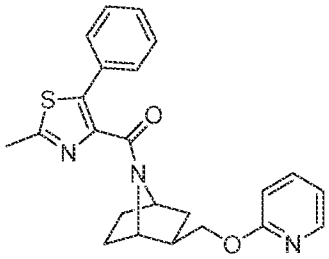
Prepared analogous to Example 2 substituting intermediate A-9 with 3,6'-dimethyl-[2,3'-bipyridine]-2'-carboxylic acid. MS (ESI) mass calcd. for $C_{25}H_{26}N_4O_2$, 414.2; m/z found 415.2 $[M+H]^+$.

Example 91: (±)-(3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



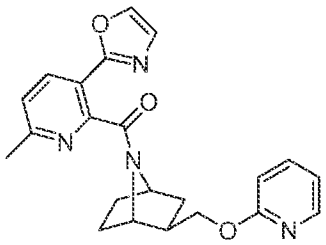
Prepared analogous to Example 2 substituting intermediate A-9 with 3-(2H-1,2,3-triazol-2-yl)picolinic acid. MS (ESI) mass calcd. for $C_{20}H_{20}N_6O_2$, 376.2; m/z found 377.2 $[M+H]^+$. ^1H NMR (DMSO-D_6): 8.70 (d, J = 3.6 Hz, 0.5H), 8.40 – 7.99 (m, 4.5H), 7.82 – 7.47 (m, 2H), 7.02 – 6.85 (m, 1H), 6.86 (d, J = 8.2 Hz, 0.6H), 6.64 (d, J = 8.1 Hz, 0.4H), 4.62 – 4,65 (m, 1H), 4.20 – 3,97 (m, 3H), 2.35 – 2.24 (m, 1H), 2.00 – 1.09 (m, 6H).

Example 92: (±)-(2-methyl-5-phenylthiazol-4-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



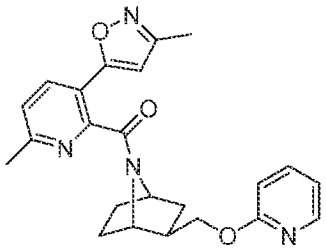
Prepared analogous to Example 2 substituting intermediate A-9 with 2-methyl-5-phenylthiazole-4-carboxylic acid. MS (ESI) mass calcd. for $C_{23}H_{23}N_3O_2S$, 405.2; m/z found 406.2 $[M+H]^+$. ^1H NMR (DMSO-D_6) 8.18 (dd, J = 5.0, 1.4 Hz, 0.5H), 8.10 (dd, J = 5.0, 1.4 Hz, 0.5H), 7.77 – 7.61 (m, 1H), 7.52 – 7.29 (m, 5H), 7.04 – 6.89 (m, 1H), 6.82 (d, J = 8.3 Hz, 0.5H), 6.69 (d, J = 8.3 Hz, 0.5H), 4.57 (t, J = 4.5 Hz, 0.5H), 4.52 (d, J = 4.7 Hz, 0.5H), 3.90 – 3.79 (m, 2.5H), 3.69 (t, J = 10.6 Hz, 0.5H), 2.69 (s, 1.5H), 2.28 (s, 1.5H), 2.25 – 2.06 (m, 1H), 1.72 – 1.04 (m, 6H).

Example 93: (±)-(6-methyl-3-(oxazol-2-yl)pyridin-2-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



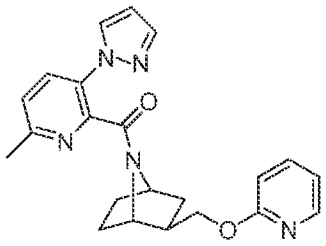
Prepared analogous to Example 2 substituting intermediate A-9 with intermediate A-43. MS (ESI) mass calcd. for $C_{22}H_{22}N_4O_3$, 390.2; m/z found 391.2 $[M+H]^+$. ^1H NMR (DMSO-D_6): 8.22 (dt, J = 14.0, 7.8 Hz, 2.5H), 8.12 (dd, J = 5.0, 1.4 Hz, 0.5H), 7.78 – 7.68 (m, 0.5H), 7.68 – 7.59 (m, 0.5H), 7.49 (d, J = 8.2 Hz, 0.5H), 7.41 – 7.29 (m, 1.5H), 6.97 (ddd, J = 14.7, 6.5, 5.2 Hz, 1H), 6.87 (d, J = 8.4 Hz, 0.5H), 6.63 (d, J = 8.3 Hz, 0.5H), 4.66 (t, J = 4.6 Hz, 0.5H), 4.62 (d, J = 4.8 Hz, 0.5H), 4.22 – 3.93 (m, 2H), 3.70 (t, J = 4.4 Hz, 0.5H), 3.61 (d, J = 4.0 Hz, 0.5H), 2.55 (s, 1.5H), 2.40 – 2.14 (m, 1H), 2.08 (s, 1.5H), 1.93 – 1.23 (m, 6H).

Example 94: (±)-(6-methyl-3-(3-methylisoxazol-5-yl)pyridin-2-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



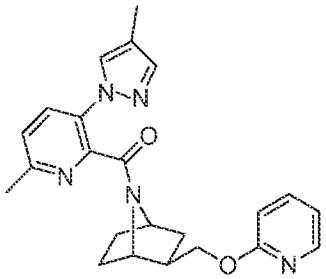
Prepared analogous to Example 2 substituting intermediate A-9 with 6-methyl-3-(3-methylisoxazol-5-yl)picolinic acid. MS (ESI) mass calcd. for $C_{23}H_{24}N_4O_3$, 404.2; m/z found 405.0 $[M+H]^+$. ^1H NMR (DMSO-D_6): 8.20 – 8.02 (m, 2H), 7.73 (t, J = 6.9 Hz, 0.4H), 7.65 (t, J = 7.7 Hz, 0.6H), 7.50 (d, J = 8.1 Hz, 0.4H), 7.37 (d, J = 8.2 Hz, 0.6H), 7.03 – 6.91 (m, 1H), 6.87 (d, J = 8.3 Hz, 0.4H), 6.68 – 6.58 (m, 1.6H), 4.68 (t, J = 4.6 Hz, 0.6H), 4.62 (d, J = 4.7 Hz, 0.4H), 4.01-3.93 (m, 2H), 3.60 (t, J = 4.4, 0.4H), 3.55 (d, J = 3.1, 0.6H), 2.55 (s, 1.2H), 2.36 – 2.14 (m, 4H), 2.09 (s, 1.8H), 1.88 – 1.07 (m, 6H).

Example 95: (±)-(6-methyl-3-(1H-pyrazol-1-yl)pyridin-2-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



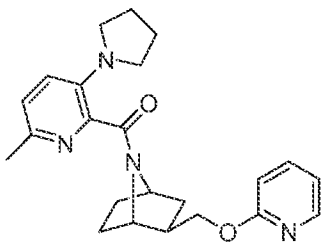
Prepared analogous to Example 2 substituting intermediate A-9 with 6-methyl-3-(1H-pyrazol-1-yl)picolinic acid. ^1H NMR (DMSO-D_6): 8.19 (dd, J = 5.0, 1.4 Hz, 0.5H), 8.14 (dd, J = 5.1, 1.5 Hz, 0.5H), 8.08 (t, J = 2.9 Hz, 1H), 7.97 (d, J = 8.3 Hz, 0.5H), 7.93 (d, J = 8.3 Hz, 0.5H), 7.76 – 7.61 (m, 2H), 7.49 (d, J = 8.4 Hz, 0.5H), 7.34 (d, J = 8.4 Hz, 0.5H), 6.97 (td, J = 7.3, 5.2 Hz, 1H), 6.84 (d, J = 8.3 Hz, 0.5H), 6.65 (d, J = 8.3 Hz, 0.5H), 6.53 – 6.48 (m, 0.5H), 6.48 – 6.43 (m, 0.5H), 4.55 (t, J = 4.5 Hz, 0.5H), 4.51 (d, J = 4.7 Hz, 0.5H), 4.02 – 3.93 (m, 2H), 3.67 (t, J = 4.1 Hz, 0.5H), 3.60 (d, J = 4.5 Hz, 0.5H), 2.54 (s, 1.5H), 2.31 – 2.11 (m, 1H), 2.04 (s, 1.5H), 1.75 – 1.16 (m, 6H).

Example 96: (±)-(6-methyl-3-(4-methyl-1H-pyrazol-1-yl)pyridin-2-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



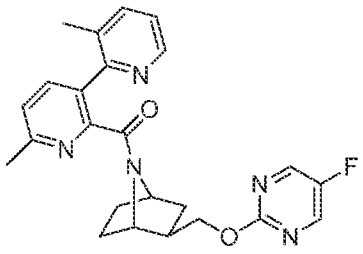
Prepared analogous to Example 2 substituting intermediate A-9 with 6-methyl-3-(4-methyl-1H-pyrazol-1-yl)picolinic acid. MS (ESI) mass calcd. for $C_{23}H_{25}N_5O_2$, 403.2; m/z found 404.2 $[M+H]^+$.

Example 97: (±)-(6-methyl-3-(pyrrolidin-1-yl)pyridin-2-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Prepared analogous to Example 2 substituting intermediate A-9 with 6-methyl-3-(pyrrolidin-1-yl)picolinic acid (Example 68, Step B). MS (ESI) mass calcd. for $C_{23}H_{28}N_4O_2$, 392.2; m/z found 393.2 $[M+H]^+$. The product is present as a mixture of conformers (ratio ca. 50:50). ^{1}H NMR (300 MHz, DMSO) 8.14 (dd, J = 5.1, 1.4 Hz, 0.5H), 8.11 (dd, J = 5.1, 1.4 Hz, 0.5H), 7.76 – 7.59 (m, 1H), 7.06 (q, J = 8.6 Hz, 1H), 7.01 – 6.90 (m, 2H), 6.85 (d, J = 8.3 Hz, 0.5H), 6.69 (d, J = 8.3 Hz, 0.5H), 4.61 (t, J = 4.6 Hz, 0.5H), 4.58 (d, J = 4.7 Hz, 0.5H), 4.19 – 3.91 (m, 2.5H), 3.88 (d, J = 4.6 Hz, 0.5H), 3.28 – 3.11 (m, 3H), 3.10 – 2.98 (m, 1H), 2.41 – 2.18 (m, 2.5H), 2.06 (s, 1.5H), 1.95 – 1.28 (m, 10H).

Example 98: (±)-(3,6'-dimethyl-[2,3'-bipyridin]-2'-yl)(2-(((5-fluoropyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.

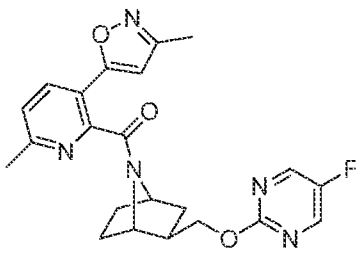


Step A: (±)-tert-butyl 2-(((5-fluoropyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptane-7-carboxylate. To intermediate B-10 (500 mg, 2.2 mmol) in THF (11 mL) at 0 °C was added NaH (176 mg, 60 wt% in mineral oil, 4.4 mmol). After 15 min, 2-chloro-5-fluoropyrimidine (0.3 mL, 2.4 mmol) was added dropwise and the 0 °C ice bath was removed. After 12h, H_2O was added and the reaction extracted with EtOAc. The combined organics dried (Na_2SO_4). Purification via silica gel chromatography (5-30% EtOAc in heptane) gave the title compound (490 mg, 69%) as a white solid. MS (ESI) mass calcd. for $C_{16}H_{22}F_3N_3O_3$, 323.4; m/z found 224.1 $[M-100]^+$.

Step B: (±)-2-(((5-fluoropyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptane. To the title compound from step A (474 mg, 1.5 mmol) in 1,4-dioxane (1.5 mL) was added 6N HCl in iPrOH (1.5 mL). The reaction was heated to 40 °C for 1.5h and concentrated to give the title compound that was used without further purification in subsequent steps. MS (ESI) mass calcd. for $C_{11}H_{14}FN_3O$, 223.1; m/z found 224.0 $[M+H]^+$.

Step C: (±)-(3,6'-dimethyl-[2,3'-bipyridin]-2'-yl)(2-(((5-fluoropyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone. Prepared analogous to example 2 substituting intermediate A-9 with 3,6'-dimethyl-[2,3'-bipyridine]-2'-carboxylic acid and intermediate B-10 with the title compound of Step B. MS (ESI) mass calcd. for $C_{24}H_{24}FN_5O_2$, 433.2; m/z found 434.2 $[M+H]^+$. ^1H NMR (DMSO-D_6): 8.71 (s, 2H), 8.32 (t, J = 4.5 Hz, 1H), 7.74 (d, J = 7.9 Hz, 1H), 7.66 (t, J = 7.3 Hz, 1H), 7.40 (d, J = 7.9 Hz, 0.5H), 7.33 – 7.14 (m, 1.5H), 4.39 (br s, 0.5H), 4.34 (d, J = 4.0 Hz, 0.5H), 4.27 (t, J = 10.4 Hz, 0.5H), 4.10 (dd, J = 5.2, 1.0 Hz, 0.5H), 3.90 (d, J = 4.8 Hz, 0.5H), 3.85 (t, J = 3.1 Hz, 0.5H), 3.69 (d, J = 7.9 Hz, 1H), 2.55 (s, 1.5H), 2.31 – 2.20 (m, 0.5H), 2.18 (s, 1.5H), 2.16 (s, 1.5H), 2.12 (s, 1.5H) , 2.01 – 1.82 (m, 0.5H), 1.81 – 1.14 (m, 6H).

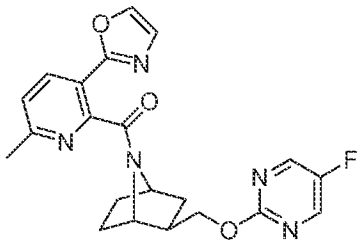
Example 99: (±)-(2-(((5-fluoropyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(3-methylisoxazol-5-yl)pyridin-2-yl)methanone.



Prepared analogous to example 98 substituting 3,6'-dimethyl-[2,3'-bipyridine]-2'-carboxylic acid with 6-methyl-3-(3-methylisoxazol-5-yl)picolinic acid. MS (ESI) mass calcd.

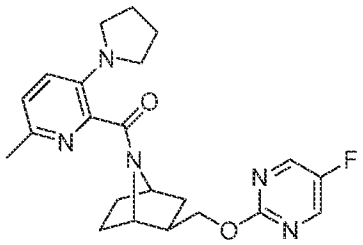
for $C_{22}H_{22}FN_5O_3$, 423.2; m/z found 424.2 $[M+H]^+$. ^1H NMR (DMSO-D_6): 8.71 (s, 1H), 8.66 (s, 1H), 8.12 (d, J = 8.1 Hz, 0.4H), 8.09 (d, J = 8.2 Hz, 0.6H), 7.50 (d, J = 8.2 Hz, 0.4H), 7.40 (d, J = 8.2 Hz, 0.6H), 6.64-6.63 (m, 1H), 4.68 (t, J = 4.6 Hz, 0.6H), 4.60 (d, J = 4.7 Hz, 0.4H), 4.11 – 3.90 (m, 2H), 3.62 (t, J = 4.2 Hz, 0.4H), 3.55 (d, J = 4.1 Hz, 0.5H), 2.55 (s, 1.2H), 2.40-2.15 (m, 4H), 2.16 (s, 1.8H), 1.88 – 1.12 (m, 6H).

Example 100: (±)-(2-(((5-fluoropyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(oxazol-2-yl)pyridin-2-yl)methanone.



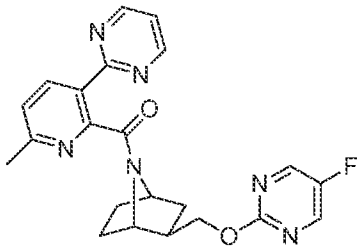
Prepared analogous to example 98 substituting 3,6'-dimethyl-[2,3'-bipyridine]-2'-carboxylic acid with intermediate A-43. MS (ESI) mass calcd. for $C_{21}H_{20}FN_5O_3$, 409.2; m/z found 410.2 $[M+H]^+$. ^1H NMR (DMSO-D_6): 8.74 (s, 0.8H), 8.66 (s, 1.2H), 8.31 – 8.16 (m, 2H), 7.50 (d, J = 8.2 Hz, 0.4H), 7.38 (t, J = 8.9 Hz, 1.6H), 4.67 (t, J = 4.5 Hz, 0.6H), 4.62 (d, J = 4.7 Hz, 0.4H), 4.23 (t, J = 10.1 Hz, 0.4H), 4.07 (dt, J = 10.0, 6.2 Hz, 1.6H), 3.72 (t, J = 4.2 Hz, 0.4H), 3.62 (d, J = 4.4 Hz, 0.6H), 2.56 (s, 1.2H), 2.43 – 2.19 (m, 1H), 2.16 (s, 1.8H), 1.93 – 1.23 (m, 6H).

Example 101: (±)-(2-(((5-fluoropyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(pyrrolidin-1-yl)pyridin-2-yl)methanone.



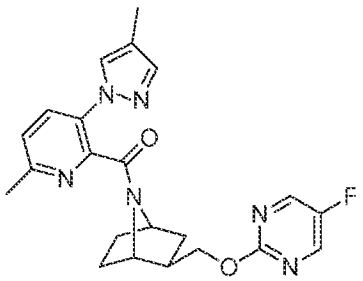
Prepared analogous to example 98 substituting 3,6'-dimethyl-[2,3'-bipyridine]-2'-carboxylic acid with 6-methyl-3-(pyrrolidin-1-yl)picolinic acid (Example 68, Step B). MP=130 °C.

Example 102: (±)-(2-(((5-fluoropyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(pyrimidin-2-yl)pyridin-2-yl)methanone.



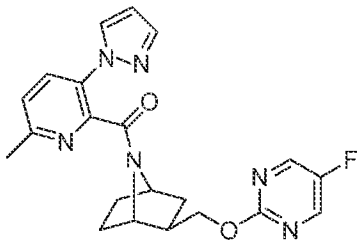
Prepared analogous to example 98 substituting 3,6'-dimethyl-[2,3'-bipyridine]-2'-carboxylic acid with intermediate A-9. MS (ESI) mass calcd. for $C_{22}H_{21}FN_6O_2$, 420.2; m/z found 421.2 $[M+H]^+$ ^1H NMR (DMSO-D_6): 8.93 (d, J = 4.9 Hz, 0.8H), 8.88 (d, J = 4.9 Hz, 1.2H), 8.79 (s, 0.8H), 8.72 (s, 1.2H), 8.37 – 8.33 (m, 1H), 7.55 – 7.47 (m, 1.2H), 7.40 (d, J = 8.1 Hz, 0.6H), 4.67 – 4.61 (br s, 0.6H), 4.59 (d, J = 4.0 Hz, 0.4H), 4.33 – 4.22 (m, 1H), 4.18 – 4.07 (m, 1H), 3.91 (br s, 0.4H), 3.81 (d, J = 3.4 Hz, 0.6H), 2.59 (s, 1.4H), 2.48 – 2.25 (m, 1H), 2.15 (s, 1.8H), 1.93 – 1.34 (m, 6H).

Example 103: (±)-(2-(((5-fluoropyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(4-methyl-1H-pyrazol-1-yl)pyridin-2-yl)methanone.



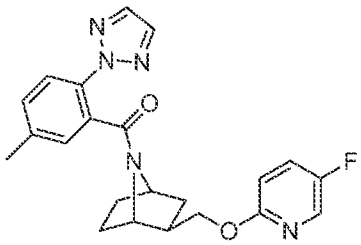
Prepared analogous to example 98 substituting 3,6'-dimethyl-[2,3'-bipyridine]-2'-carboxylic acid with 6-methyl-3-(4-methyl-1H-pyrazol-1-yl)picolinic acid. MP=151.2 °C. ^1H NMR (DMSO-D_6): 8.73 (s, 1H), 8.69 (s, 1H), 7.92 (d, J = 5.0 Hz, 0.5H), 7.90 (d, J = 5.0 Hz, 0.5H), 7.85 (d, J = 2.3 Hz, 1H), 7.51 – 7.54 (m, 1.5H), 7.35 (d, J = 8.4 Hz, 0.5H), 4.57 (t, J = 4.5 Hz, 0.5H), 4.51 (d, J = 4.7 Hz, 0.5H), 4.08 – 3.90 (m, 2H), 3.66 (t, J = 4.0 Hz, 0.5H), 3.60 (d, J = 4.0 Hz, 0.5H), 2.53 (s, 1.5H), 2.35 – 2.14 (m, 1H), 2.10 (s, 1.5H), 2.07 (s, 1.5H), 2.04 (s, 1.5H), 1.77 – 1.14 (m, 6H).

Example 104: (±)-(2-(((5-fluoropyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(1H-pyrazol-1-yl)pyridin-2-yl)methanone.



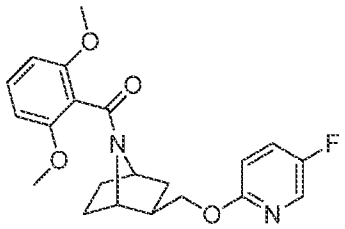
Prepared analogous to example 98 substituting 3,6'-dimethyl-[2,3'-bipyridine]-2'-carboxylic acid with 6-methyl-3-(1H-pyrazol-1-yl)picolinic acid. MS (ESI) mass calcd. for $C_{21}H_{21}FN_6O_2$, 408.2; m/z found 409.2 $[M+H]^+$. MP-119.2 °C.

Example 105: (±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(5-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone.



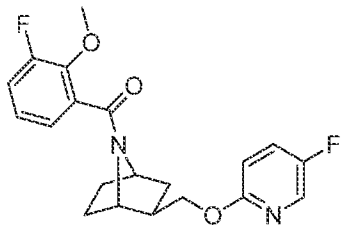
Prepared analogous to Example 7 substituting 6-methyl-3-(2H-1,2,3-triazol-2-yl)picolinic acid with 5-methyl-2-(2H-1,2,3-triazol-2-yl)benzoic acid. (ESI) mass calcd. for $C_{22}H_{22}FN_5O_2$, 407.2; m/z found 408.2 $[M+H]^+$. ^1H NMR (MeOD): 8.08-7.96 (m, 1H), 7.88 (s, 2H), 7.81-7.73 (m, 1H), 7.56-7.12 (m, 3H), 6.85-6.62 (m, 1H), 4.70-4.67 (m, 1H), 4.25-3.74 (m, 3H), 2.51-1.97 (m, 4H), 1.96-1.31 (m, 6H).

Example 106: (±)-(2,6-dimethoxyphenyl)(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



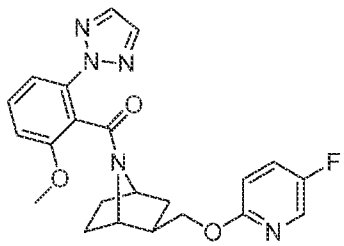
Prepared analogous to example 105 substituting 5-methyl-2-(2H-1,2,3-triazol-2-yl)benzoic acid with 2,6-dimethoxybenzoic acid. MS (ESI) mass calcd. for $C_{21}H_{23}FN_2O_4$, 386.2; m/z found 386.9 $[M+H]^+$. ^1H NMR (MeOD): 8.02-7.93 (m, 1H), 7.57-7.40 (m, 1H), 7.39-7.21 (m, 1H), 6.87-6.63 (m, 2H), 6.62-6.38 (m, 1H), 4.83-4.65 (m, 1H), 4.49-4.07 (m, 1H), 4.07-3.52 (m, 8H), 2.48-2.09 (m, 1H), 2.06-1.07 (m, 6H).

Example 107: (±)-((3-fluoro-2-methoxyphenyl)(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



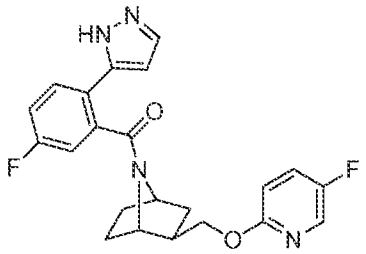
Prepared analogous to example 105 substituting 5-methyl-2-(2H-1,2,3-triazol-2-yl)benzoic acid with 3-fluoro-2-methoxybenzoic acid. MS (ESI) mass calcd. for $C_{20}H_{20}F_2N_2O_3$, 374.1; m/z found 375.1 $[M+H]^+$. ^1H NMR (MeOD): 8.01-7.90 (m, 1H), 7.56-7.38 (m, 1H), 7.28-7.06 (m, 2H), 7.02-6.53 (m, 2H), 4.82-4.66 (m, 1H), 4.50-3.73 (m, 6H), 2.85-2.22 (m, 1H), 2.21-1.10 (m, 6H).

Example 108: (±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(2-methoxy-6-(2H-1,2,3-triazol-2-yl)phenyl)methanone.



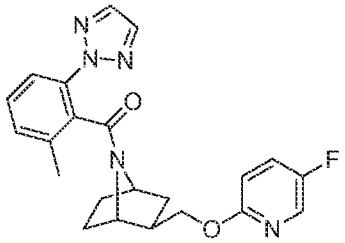
Prepared analogous to example 105 substituting 5-methyl-2-(2H-1,2,3-triazol-2-yl)benzoic acid with 2-methoxy-6-(2H-1,2,3-triazol-2-yl)benzoic acid. MS (ESI) mass calcd. for $C_{22}H_{22}FN_5O_3$, 423.2; m/z found 424.2 $[M+H]^+$. ^1H NMR (MeOD): 8.10-7.74 (m, 3H), 7.66-7.41 (m, 3H), 7.25-6.88 (m, 1H), 6.88-6.43 (m, 1H), 4.78-4.64 (m, 1H), 4.51-3.57 (m, 6H), 2.48-0.94 (m, 7H).

Example 109: (±)-(5-fluoro-2-(1H-pyrazol-5-yl)phenyl)(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



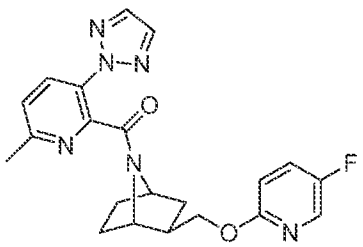
Prepared analogous to example 105 substituting 5-methyl-2-(2H-1,2,3-triazol-2-yl)benzoic acid with 5-fluoro-2-(1H-pyrazol-5-yl)benzoic acid. MS (ESI) mass calcd. for $C_{22}H_{20}F_2N_4O_2$, 410.2; m/z found 411.2 $[M+H]^+$. ^1H NMR (MeOD): 8.11-7.90 (m, 1H), 7.80-7.59 (m, 2H), 7.58-7.40 (m, 1H), 7.36-6.94 (m, 2H), 6.88-6.47 (m, 2H), 4.78-4.58 (m, 1H), 4.41-3.47 (m, 3H), 2.69-0.60 (m, 8H).

Example 110: (±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(2-methyl-6-(2H-1,2,3-triazol-2-yl)phenyl)methanone.



Prepared analogous to example 105 substituting 5-methyl-2-(2H-1,2,3-triazol-2-yl)benzoic acid with 2-methyl-6-(2H-1,2,3-triazol-2-yl)benzoic acid. MS (ESI) mass calcd. for $C_{22}H_{22}FN_5O_2$, 407.2; m/z found 408.2 $[M+H]^+$. ^1H NMR (MeOD): 8.11-7.62 (m, 4H), 7.59-6.48 (m, 4H), 4.78-4.68 (m, 1H), 4.50-3.37 (m, 3H), 2.80-0.82 (m, 10H).

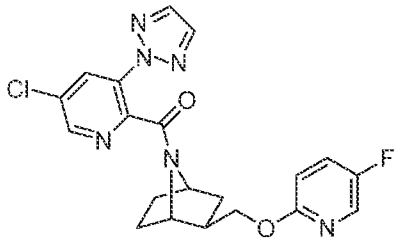
Example 111: (±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)methanone.



Prepared analogous to example 105 substituting 5-methyl-2-(2H-1,2,3-triazol-2-yl)benzoic acid with 6-methyl-3-(2H-1,2,3-triazol-2-yl)picolinic acid. MS (ESI) mass calcd. for $C_{21}H_{21}FN_6O_2$, 408.2; m/z found 409.2 $[M+H]^+$. ^1H NMR (MeOD): 8.28-8.19 (m, 1H), 8.06-7.88

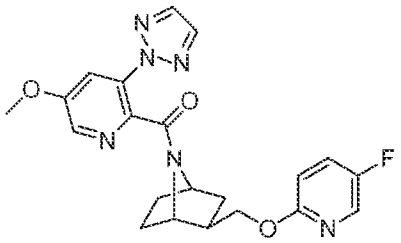
(m, 3H), 7.57-7.35 (m, 2H), 6.89-6.60 (m, 1H), 4.76-4.73 (m, 1H), 4.32-4.02 (m, 2H), 3.93-3.80 (m, 1H), 2.70-2.20 (m, 4H), 2.05-1.42 (m, 6H).

Example 112: (±)-(5-chloro-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



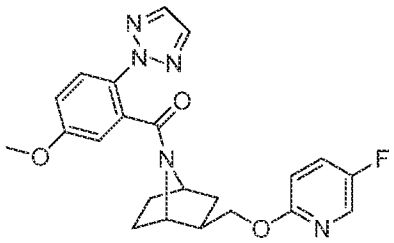
Prepared analogous to example 105 substituting 5-methyl-2-(2H-1,2,3-triazol-2-yl)benzoic acid with sodium 5-chloro-3-(2H-1,2,3-triazol-2-yl)picolinate. MS (ESI) mass calcd. for $C_{20}H_{18}ClFN_6O_2$, 428.1; m/z found 429.1 $[M+H]^+$. ^1H NMR (MeOD): 8.74-8.17 (m, 4H), 8.13-7.96 (m, 2H), 7.59-7.46 (m, 1H), 4.90-4.18 (m, 3H), 3.99 (s, 1H), 2.98-2.39 (m, 1H), 2.10-1.19 (m, 6H).

Example 113: (±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(5-methoxy-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)methanone.



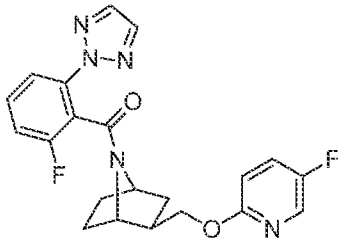
Prepared analogous to example 105 substituting 5-methyl-2-(2H-1,2,3-triazol-2-yl)benzoic acid with sodium 5-methoxy-3-(2H-1,2,3-triazol-2-yl)picolinate. MS (ESI) mass calcd. for $C_{21}H_{21}FN_6O_3$, 424.2; m/z found 425.1 $[M+H]^+$. ^1H NMR (MeOD): 8.37-7.79 (m, 5H), 7.56-7.40 (m, 1H), 6.87-6.59 (m, 1H), 4.73 (s, 1H), 4.30-3.82 (m, 6H), 2.48-2.11 (m, 1H), 2.07-1.42 (m, 6H).

Example 114: (±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(5-methoxy-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone.



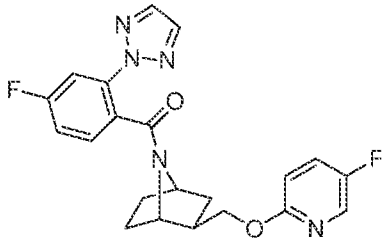
Prepared analogous to example 105 substituting 5-methyl-2-(2H-1,2,3-triazol-2-yl)benzoic acid with sodium 5-methoxy-2-(2H-1,2,3-triazol-2-yl)benzoate. MS (ESI) mass calcd. for $C_{22}H_{22}FN_5O_3$, 423.2; m/z found 424.2 $[M+H]^+$. ^1H NMR (MeOD): 8.18-7.68 (m, 4H), 7.58-7.38 (m, 1H), 7.24-6.85 (m, 2H), 6.85-6.57 (m, 1H), 4.78-4.55 (m, 1H), 4.23-3.40 (m, 6H), 2.77-2.18 (m, 1H), 2.13-1.11 (m, 6H).

Example 115: (±)-(2-fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Prepared analogous to example 105 substituting 5-methyl-2-(2H-1,2,3-triazol-2-yl)benzoic acid with 2-fluoro-6-(2H-1,2,3-triazol-2-yl)benzoic acid. MS (ESI) mass calcd. for $C_{21}H_{19}F_2N_5O_2$, 411.2; m/z found 412.2 $[M+H]^+$. ^1H NMR (MeOD): 8.11-7.71 (m, 4H), 7.69-7.24 (m, 3H), 6.98-6.43 (m, 1H), 4.83-4.67 (m, 1H), 4.53-3.34 (m, 3H), 2.50-0.96 (m, 7H).

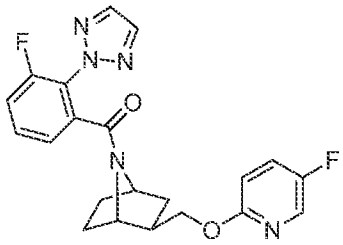
Example 116: (±)-(4-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Prepared analogous to example 105 substituting 5-methyl-2-(2H-1,2,3-triazol-2-yl)benzoic acid with 4-fluoro-2-(2H-1,2,3-triazol-2-yl)benzoic acid. MS (ESI) mass calcd. for

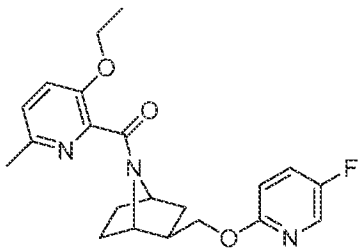
$C_{21}H_{19}F_2N_5O_2$, 411.2; m/z found 412.2 $[M+H]^+$. ^1H NMR (MeOD): 8.11-7.71 (m, 4H), 7.69-7.24 (m, 3H), 6.98-6.43 (m, 1H), 4.83-4.67 (m, 1H), 4.53-3.34 (m, 3H), 2.50-0.96 (m, 7H).

Example 117: (±)-(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



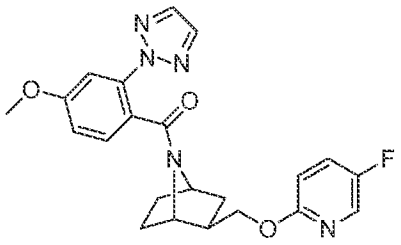
Prepared analogous to example 105 substituting 5-methyl-2-(2H-1,2,3-triazol-2-yl)benzoic acid with 3-fluoro-2-(2H-1,2,3-triazol-2-yl)benzoic acid. MS (ESI) mass calcd. for $C_{21}H_{19}F_2N_5O_2$, 411.2; m/z found 412.2 $[M+H]^+$. ^1H NMR (MeOD): 8.14-7.85 (m, 3H), 7.70-7.18 (m, 4H), 6.81-6.65 (m, 1H), 4.67-4.32 (m, 1H), 4.24-3.79 (m, 3H), 2.42-2.24 (m, 1H), 1.97-1.32 (m, 6H).

Example 118: (±)-(3-ethoxy-6-methylpyridin-2-yl)(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



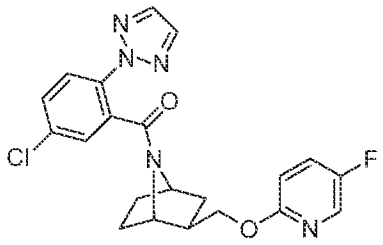
Prepared analogous to example 105 substituting 5-methyl-2-(2H-1,2,3-triazol-2-yl)benzoic acid with 3-ethoxy-6-methylpicolinic acid. MS (ESI) mass calcd. for $C_{21}H_{24}FN_3O_3$, 385.2; m/z found 385.9 $[M+H]^+$. ^1H NMR (MeOD): 8.23-7.90 (m, 1H), 7.57-7.11 (m, 3H), 6.87-6.53 (m, 1H), 4.85-4.69 (m, 1H), 4.51-3.56 (m, 5H), 2.84-2.09 (m, 4H), 2.06-1.49 (m, 5H), 1.47-1.05 (m, 4H).

Example 119: (±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(4-methoxy-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone.



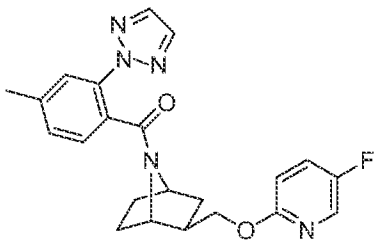
Prepared analogous to example 105 substituting 5-methyl-2-(2H-1,2,3-triazol-2-yl)benzoic acid with 4-methoxy-2-(2H-1,2,3-triazol-2-yl)benzoic acid. MS (ESI) mass calcd. for $C_{22}H_{22}FN_5O_3$, 423.2; m/z found 424.2 $[M+H]^+$. ^1H NMR (MeOD): 8.12-7.81 (m, 3H), 7.58-7.22 (m, 3H), 7.15-6.57 (m, 2H), 4.75-4.58 (m, 1H), 4.48-3.74 (m, 6H), 2.83-2.08 (m, 1H), 2.02-0.98 (m, 6H).

Example 120: (±)-(5-chloro-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Prepared analogous to example 105 substituting 5-methyl-2-(2H-1,2,3-triazol-2-yl)benzoic acid with 5-chloro-2-(2H-1,2,3-triazol-2-yl)benzoic acid. MS (ESI) mass calcd. for $C_{21}H_{19}ClFN_5O_3$, 427.2; m/z found 428.2 $[M+H]^+$. ^1H NMR (MeOD): 8.13-7.77 (m, 4H), 7.70-7.31 (m, 3H), 6.87-6.60 (m, 1H), 4.80-4.60 (m, 1H), 4.51-3.67 (m, 3H), 2.84-2.22 (m, 1H), 2.07-1.11 (m, 6H).

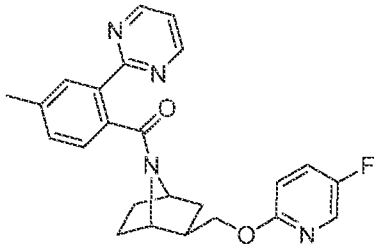
Example 121: (±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(4-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone.



Prepared analogous to example 105 substituting 5-methyl-2-(2H-1,2,3-triazol-2-yl)benzoic acid with 4-methyl-2-(2H-1,2,3-triazol-2-yl)benzoic acid. MS (ESI) mass calcd. for

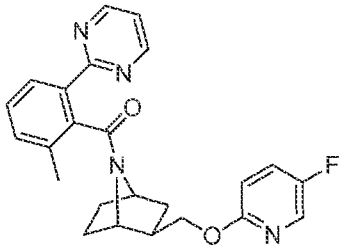
$C_{22}H_{22}FN_5O_2$, 407.2; m/z found 408.2 $[M+H]^+$. ^1H NMR (MeOD): 8.10-7.84 (m, 3H), 7.76-7.69 (m, 1H), 7.56-6.87 (m, 3H), 6.87-6.53 (m, 1H), 4.75-4.59 (m, 1H), 4.49-3.65 (m, 3H), 2.80-2.09 (m, 4H), 2.01-1.00 (m, 6H).

Example 122: (±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(4-methyl-2-(pyrimidin-2-yl)phenyl)methanone.



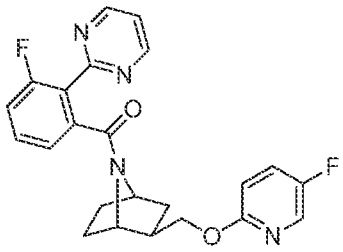
Prepared analogous to example 105 substituting 5-methyl-2-(2H-1,2,3-triazol-2-yl)benzoic acid with 4-methyl-2-(pyrimidin-2-yl)benzoic acid. MS (ESI) mass calcd. for $C_{24}H_{23}FN_4O_2$, 418.2; m/z found 419.2 $[M+H]^+$. ^1H NMR (MeOD): 8.94-8.89 (m, 1H), 8.84-8.81 (m, 1H), 8.08-7.94 (m, 2H), 7.60-7.46 (m, 1H), 7.45-7.33 (m, 2H), 7.22-6.99 (m, 1H), 6.90-6.58 (m, 1H), 4.78-4.62 (m, 1H), 4.52-3.78 (m, 3H), 2.73-2.19 (m, 4H), 2.07-1.05 (m, 6H).

Example 123: (±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(2-methyl-6-(pyrimidin-2-yl)phenyl)methanone.



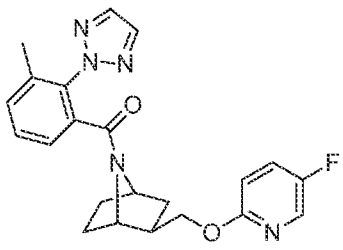
Prepared analogous to example 105 substituting 5-methyl-2-(2H-1,2,3-triazol-2-yl)benzoic acid with 2-methyl-6-(pyrimidin-2-yl)benzoic acid. MS (ESI) mass calcd. for $C_{24}H_{23}FN_4O_2$, 418.2; m/z found 419.2 $[M+H]^+$. ^1H NMR (MeOD): 8.99-8.63 (m, 2H), 8.14-7.70 (m, 2H), 7.61-7.27 (m, 4H), 7.15-6.45 (m, 1H), 4.86-4.65 (m, 1H), 4.55-3.44 (m, 3H), 2.53-2.35 (m, 3H), 2.34-0.78 (m, 7H).

Example 124: (±)-(3-fluoro-2-(pyrimidin-2-yl)phenyl)(-2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



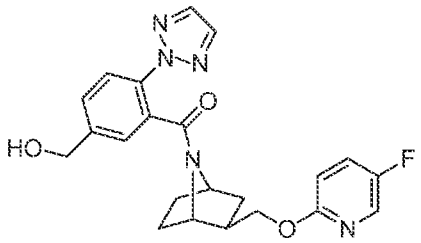
Prepared analogous to example 105 substituting 5-methyl-2-(2H-1,2,3-triazol-2-yl)benzoic acid with 3-fluoro-2-(pyrimidin-2-yl)benzoic acid. MS (ESI) mass calcd. for $C_{23}H_{20}F_2N_4O_2$, 422.2; m/z found 422.8 $[M+H]^+$. ^1H NMR (MeOD): 9.03-8.62 (m, 2H), 8.19-7.82 (m, 1H), 7.67-7.11 (m, 5H), 6.85-6.62 (m, 1H), 4.54 (s, 1H), 4.26-3.76 (m, 3H), 2.33 (s, 1H), 2.01-1.32 (m, 6H).

Example 125: (±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(3-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone.



Prepared analogous to example 105 substituting 5-methyl-2-(2H-1,2,3-triazol-2-yl)benzoic acid with 3-methyl-2-(2H-1,2,3-triazol-2-yl)benzoic acid. MS (ESI) mass calcd. for $C_{22}H_{22}FN_5O_2$, 407.2; m/z found 408.2 $[M+H]^+$. ^1H NMR (MeOD): 8.05-7.95 (m, 1H), 7.93-7.84 (m, 2H), 7.57-7.05 (m, 4H), 6.81-6.65 (m, 1H), 4.61-3.98 (m, 2H), 3.97-3.75 (m, 2H), 2.38-2.23 (m, 1H), 2.19-2.14 (m, 3H), 1.97-1.32 (m, 6H).

Example 126: (±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(5-(hydroxymethyl)-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone.



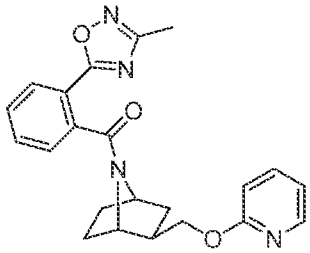
Step A: (±)-(5-bromo-2-(2H-1,2,3-triazol-2-yl)phenyl)(-2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone. Prepared analogous to example 105

substituting 5-methyl-2-(2H-1,2,3-triazol-2-yl)benzoic acid with 5-bromo-2-(2H-1,2,3-triazol-2-yl)benzoic acid.

Step B: (±)-methyl 3-(-2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptane-7-carbonyl)-4-(2H-1,2,3-triazol-2-yl)benzoate. The title compound of step A (100 mg, 0.2 mmol) and $Pd(dppf)Cl_2$ (35 mg) in MeOH (10 mL) was heated to 120 °C for 24h in a sealed tube under an atmosphere of CO. The reaction was allowed to cool to rt and filtered. The filtrate was concentrated and purified via preparative TLC to give the title compound (20 mg, 21%).

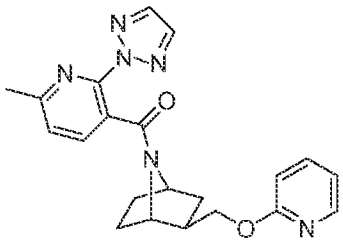
Step C: (±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(5-(hydroxymethyl)-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone. To the title compound of step B (40 mg, 0.1 mmol)) in MeOH (0.2 mL) and THF (6 mL) at 0 °C was added $NaBH_4$ (4 mg, 0.1 mmol). After stirring overnight at rt, the reaction was concentrated and purified directly via silica gel chromatography (EtOAc in petroleum ethers) to give the title compound. MS (ESI) mass calcd. for $C_{21}H_{21}FN_6O_2$, 408.2; m/z found 409.2 $[M+H]^+$. ^1H NMR (MeOD): 8.07-7.82 (m, 4H), 7.66-7.29 (m, 3H), 6.85-6.60 (m, 1H), 4.70 (d, J = 8.7 Hz, 2H), 4.50-3.73 (m, 4H), 2.43-2.20 (m, 1H), 2.04-1.28 (m, 6H).

Example 127: (±)-(2-(3-methyl-1,2,4-oxadiazol-5-yl)phenyl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



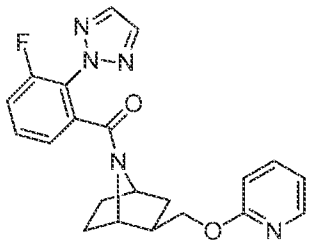
Prepared analogous to Example 2 substituting intermediate A-9 with 2-(3-methyl-1,2,4-oxadiazol-5-yl)benzoic acid. MS (ESI) mass calcd. for $C_{22}H_{22}N_4O_3$, 390.2; m/z found 391.1 $[M+H]^+$. ^1H NMR (MeOD): 8.12-8.00 (m, 2H), 7.75-7.58 (m, 2H), 7.55-7.49 (m, 1H), 7.38-7.28 (m, 1H), 6.95-6.91 (m, 1H), 6.85-6.55 (m, 1H), 4.81-4.78 (m, 1H), 4.27-4.14 (m, 1H), 4.01-3.97 (m, 1H), 3.77-3.75 (m, 1H), 2.44-2.26 (m, 4H), 2.10-1.95 (m, 1H), 1.87-1.62 (m, 3H), 1.56-1.46 (m, 2H).

Example 128: (±)-(6-methyl-2-(2H-1,2,3-triazol-2-yl)pyridin-3-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



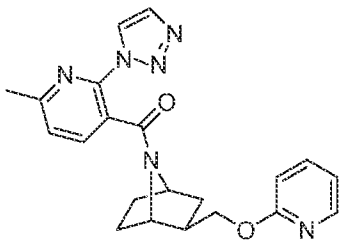
Prepared analogous to Example 127 substituting 2-(3-methyl-1,2,4-oxadiazol-5-yl)benzoic acid with 6-methyl-2-(2H-1,2,3-triazol-2-yl)nicotinic acid. MS (ESI) mass calcd. for $C_{21}H_{22}N_6O_2$, 390.2; m/z found 391.2 $[M+H]^+$. ^1H NMR (MeOD): 8.15-8.09 (m, 1H), 7.99 (s, 2H), 7.91-7.71 (m, 1H), 7.69-6.92 (m, 3H), 6.83-6.59 (m, 1H), 4.71-4.68 (m, 1H), 4.22-4.09 (m, 1H), 4.01-3.76 (m, 2H), 2.64-2.52 (m, 3H), 2.43-2.23 (m, 1H), 2.00-1.36 (m, 6H).

Example 129: (±)-(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Prepared analogous to Example 127 substituting 2-(3-methyl-1,2,4-oxadiazol-5-yl)benzoic acid with 3-fluoro-2-(2H-1,2,3-triazol-2-yl)benzoic acid. MS (ESI) mass calcd. for $C_{21}H_{20}FN_5O_2$, 393.2; m/z found 394.0 $[M+H]^+$. ^1H NMR (MeOD): 8.14-8.12 (m, 1H), 7.95-7.93 (m, 2H), 7.69-7.46 (m, 2H), 7.40-7.31 (m, 1H), 7.22-7.12 (m, 1H), 6.99-6.91 (m, 1H), 6.80-6.66 (m, 1H), 4.57-4.56 (m, 1H), 4.04-3.88 (m, 3H), 2.38-2.27 (m, 1H), 1.85-1.43 (m, 6H).

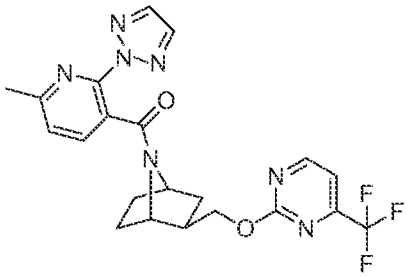
Example 130: (±)-(6-methyl-2-(1H-1,2,3-triazol-1-yl)pyridin-3-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Prepared analogous to Example 127 substituting 2-(3-methyl-1,2,4-oxadiazol-5-yl)benzoic acid with 6-methyl-2-(1H-1,2,3-triazol-1-yl)nicotinic acid. MS (ESI) mass calcd. for

$C_{21}H_{22}N_6O_2$, 390.2; m/z found 391.2 $[M+H]^+$. ^1H NMR (MeOD): 8.62-8.61 (m, 1H), 8.12-8.09 (m, 1H), 7.99-7.73 (m, 2H), 7.71-7.62 (m, 1H), 7.50-6.91 (m, 2H), 6.87-6.61 (m, 1H), 4.74-4.71 (m, 1H), 4.17-3.79 (m, 3H), 2.64-2.53 (m, 3H), 2.46-2.26 (m, 1H), 2.06-1.90 (m, 1H), 1.83-1.38 (m, 5H).

Example 131: (±)-(6-methyl-2-(2H-1,2,3-triazol-2-yl)pyridin-3-yl)(2-(((4-(trifluoromethyl)pyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.

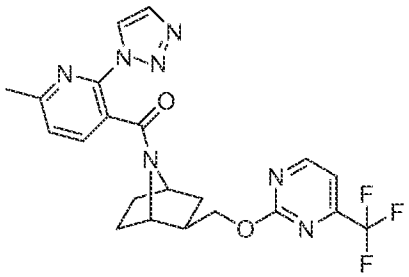


Step A: (±)-tert-butyl 2-(((4-(trifluoromethyl)pyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptane-7-carboxylate. To intermediate B-10 (500 mg, 2.2 mmol) in THF (5 mL) at 0 °C was added NaH (6.6 mmol). After 30 min at rt, 2-chloro-4-(trifluoromethyl)pyrimidine (1.8 g, 9.9 mmol). The flask was then heated to 50 °C in an oil bath. After 3h, H_2O was added and the reaction extracted with EtOAc (2X). Purification via silica gel chromatography (20% EtOAc in petroleum ethers) gave the title compound (752 mg, 92%).

Step B: (±)-2-(((4-(trifluoromethyl)pyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptane hydrochloride. To the title compound of step A (752 mg, 2 mmol) in MeOH (6 mL) was added HCl.

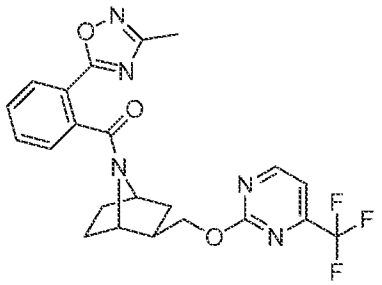
Step C: (±)-tert-butyl 2-(((4-(trifluoromethyl)pyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptane-7-carboxylate. Prepared analogous to example 127 substituting 2-(3-methyl-1,2,4-oxadiazol-5-yl)benzoic acid with 6-methyl-2-(2H-1,2,3-triazol-2-yl)nicotinic acid with the title compound of step B. MS (ESI) mass calcd. for $C_{21}H_{20}F_3N_7O_2$, 459.2; m/z found 460.2 $[M+H]^+$. ^1H NMR (MeOD): 8.89-8.82 (m, 1H), 8.02-7.82 (m, 3H), 7.48-7.14 (m, 2H), 4.75-4.71 (m, 1H), 4.44-4.07 (m, 2H), 3.91-3.84 (m, 1H), 2.64-2.56 (m, 3H), 2.48-2.30 (m, 1H), 2.02-1.43 (m, 6H).

Example 132: (±)-(6-methyl-2-(1H-1,2,3-triazol-1-yl)pyridin-3-yl)(2-(((4-(trifluoromethyl)pyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



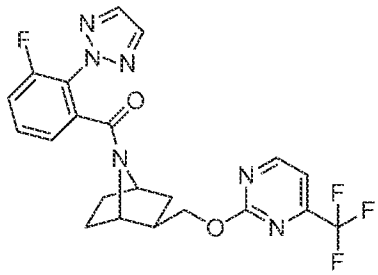
Prepared analogous to Example 131 substituting 6-methyl-2-(2H-1,2,3-triazol-2-yl)nicotinic acid with 6-methyl-2-(1H-1,2,3-triazol-1-yl)nicotinic acid. MS (ESI) mass calcd. for $C_{21}H_{20}F_3N_7O_2$, 459.2; m/z found 460.2 $[M+H]^+$. ^1H NMR (MeOD): 8.86-8.83 (m, 1H), 8.63-8.61 (m, 1H), 8.03-7.84 (m, 2H), 7.49-7.15 (m, 2H), 4.76-4.72 (m, 1H), 4.41-4.31 (m, 1H), 4.27-4.04 (m, 1H), 3.90-3.84 (m, 1H), 2.63-2.54 (m, 3H), 2.47-2.30 (m, 1H), 2.03-1.43 (m, 6H).

Example 133: (±)-(2-(3-methyl-1,2,4-oxadiazol-5-yl)phenyl)(2-(((4-(trifluoromethyl)pyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



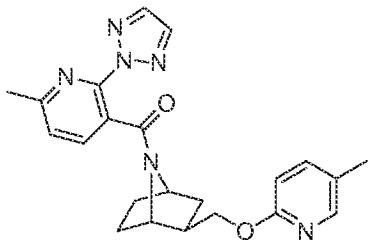
Prepared analogous to Example 131 substituting 6-methyl-2-(2H-1,2,3-triazol-2-yl)nicotinic acid with 2-(3-methyl-1,2,4-oxadiazol-5-yl)benzoic acid. MS (ESI) mass calcd. for $C_{22}H_{20}F_3N_5O_2$, 459.2; m/z found 460.2 $[M+H]^+$. ^1H NMR (MeOD): 8.88-8.80 (m, 1H), 8.08-8.00 (m, 1H), 7.74-7.62 (m, 1H), 7.63-7.51 (m, 1H), 7.48-7.37 (m, 2H), 4.83-4.80 (m, 1H), 4.49-4.33 (m, 1H), 4.23-4.11 (m, 1H), 3.81-3.77 (m, 1H), 2.53-2.36 (m, 4H), 2.07-2.98 (m, 1H), 1.90-1.51 (m, 5H).

Example 134: (±)-(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((4-(trifluoromethyl)pyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



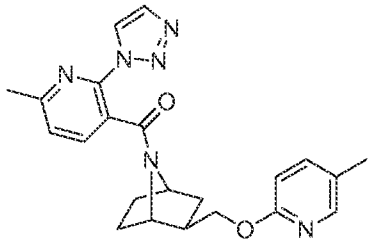
Prepared analogous to Example 131 substituting 6-methyl-2-(2H-1,2,3-triazol-2-yl)nicotinic acid with 3-fluoro-2-(2H-1,2,3-triazol-2-yl)benzoic acid. MS (ESI) mass calcd. for $C_{21}H_{18}F_4N_6O_2$, 462.2; m/z found 463.2 $[M+H]^+$. ^{1}H NMR (MeOD): 8.89-8.84 (m, 1H), 7.96-7.94 (m, 2H), 7.69-7.28 (m, 4H), 4.61-4.58 (m, 1H), 4.29-4.06 (m, 2H), 3.97-3.93 (m, 1H), 2.46-2.37 (m, 1H), 1.88-1.40 (m, 6H).

Example 135: (±)-(6-methyl-2-(2H-1,2,3-triazol-2-yl)pyridin-3-yl)(2-(((5-methylpyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Prepared analogous to Example 131 substituting 2-chloro-4-(trifluoromethyl)pyrimidine with 2-chloro-5-methylpyridine. MS (ESI) mass calcd. for $C_{22}H_{24}N_6O_2$, 404.2; m/z found 405.2 $[M+H]^+$. ^{1}H NMR (MeOD): 7.99-7.71 (m, 4H), 7.51-7.00 (m, 2H), 6.73-6.50 (m, 1H), 4.69 (d, J = 3.6 Hz, 1H), 4.17-4.04 (m, 1H), 3.96-3.72 (m, 2H), 2.64-2.53 (m, 3H), 2.43-2.20 (m, 4H), 2.03-1.35 (m, 6H).

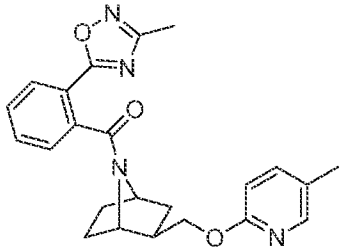
Example 136: (±)-(6-methyl-2-(1H-1,2,3-triazol-1-yl)pyridin-3-yl)(2-(((5-methylpyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Prepared analogous to Example 135 substituting 6-methyl-2-(2H-1,2,3-triazol-2-yl)nicotinic acid with 6-methyl-2-(1H-1,2,3-triazol-1-yl)nicotinic acid. MS (ESI) mass calcd. for

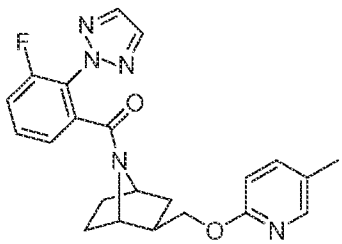
$C_{22}H_{24}N_6O_2$, 404.2; m/z found 405.2 $[M+H]^+$. ^1H NMR (MeOD): 8.62-8.55 (m, 1H), 8.19-7.88 (m, 3H), 7.75-7.47 (m, 2H), 7.05-6.52 (m, 1H), 4.72-4.71 (m, 1H), 4.08-4.02 (m, 1H), 3.98-3.74 (m, 2H), 2.64-2.53 (m, 3H), 2.37-2.24 (m, 4H), 1.96 (brs, 1H), 1.82-1.35 (m, 5H).

Example 137: (±)-(2-(3-methyl-1,2,4-oxadiazol-5-yl)phenyl)(2-(((5-methylpyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



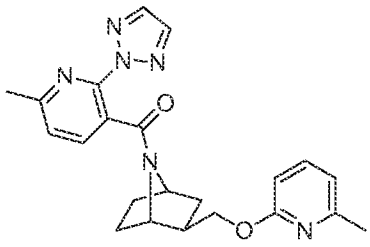
Prepared analogous to Example 135 substituting 6-methyl-2-(2H-1,2,3-triazol-2-yl)nicotinic acid with 2-(3-methyl-1,2,4-oxadiazol-5-yl)benzoic acid. MS (ESI) mass calcd. for $C_{23}H_{24}N_4O_3$, 404.2; m/z found 405.2 $[M+H]^+$. ^1H NMR (MeOD): 8.09-8.00 (m, 1H), 7.92-7.88 (m, 1H), 7.75-7.63 (m, 1H), 7.55-7.43 (m, 2H), 7.38-7.29 (m, 1H), 6.76-6.47 (m, 1H), 4.81-4.77 (m, 1H), 4.22-4.09 (m, 1H), 3.95 (d, J = 8.1 Hz, 1H), 3.76-3.74 (m, 1H), 2.44-2.20 (m, 7H), 2.07-1.97 (m, 1H), 1.86-1.62 (m, 3H), 1.55-1.42 (m, 2H).

Example 138: (±)-(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((5-methylpyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



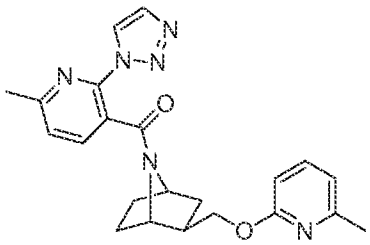
Prepared analogous to Example 135 substituting 6-methyl-2-(2H-1,2,3-triazol-2-yl)nicotinic acid with 3-fluoro-2-(2H-1,2,3-triazol-2-yl)benzoic acid. MS (ESI) mass calcd. for $C_{22}H_{22}FN_5O_2$, 407.2; m/z found 408.2 $[M+H]^+$. ^1H NMR (MeOD): 7.96-7.93 (m, 3H), 7.69-7.49 (m, 2H), 7.40-7.33 (m, 1H), 7.22-7.13 (m, 1H), 6.71-6.58 (m, 1H), 4.58-4.55 (m, 1H), 4.02-3.83 (m, 3H), 2.37-2.23 (m, 4H), 1.85-1.41 (m, 6H).

Example 139: (±)-(6-methyl-2-(2H-1,2,3-triazol-2-yl)pyridin-3-yl)(2-(((6-methylpyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



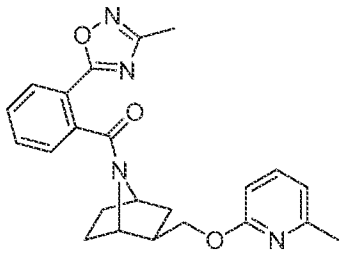
Prepared analogous to Example 135 substituting 2-chloro-4-(trifluoromethyl)pyrimidine with 2-chloro-6-methylpyridine. MS (ESI) mass calcd. for $C_{22}H_{24}N_6O_2$, 404.2; m/z found 405.2 $[M+H]^+$. ^{1}H NMR (MeOD): 7.99 (s, 2H), 7.91-7.69 (m, 1H), 7.56-6.77 (m, 3H), 6.60-6.38 (m, 1H), 4.70-4.69 (m, 1H), 4.21-4.05 (m, 1H), 3.98-3.77 (m, 2H), 2.64-2.51 (m, 3H), 2.43-2.20 (m, 4H), 2.03-1.37 (m, 6H).

Example 140: (±)-(6-methyl-2-(1H-1,2,3-triazol-1-yl)pyridin-3-yl)(2-(((6-methylpyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Prepared analogous to Example 139 substituting 6-methyl-2-(2H-1,2,3-triazol-2-yl)nicotinic acid with 6-methyl-2-(1H-1,2,3-triazol-1-yl)nicotinic acid. MS (ESI) mass calcd. for $C_{22}H_{24}N_6O_2$, 404.2; m/z found 405.2 $[M+H]^+$. ^{1}H NMR (MeOD): 8.34 (d, J = 7.1 Hz, 1H), 7.77-7.42 (m, 3H), 7.28-6.35 (m, 3H), 4.82-4.79 (m, 1H), 4.24-3.94 (m, 2H), 3.87-3.81 (m, 1H), 2.63-2.22 (m, 7H), 2.15-1.98 (m, 1H), 1.84-1.34 (m, 5H).

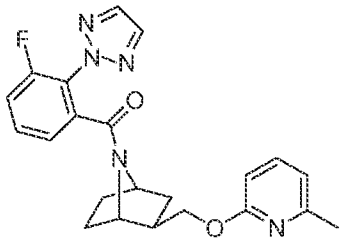
Example 141: (±)-(2-(3-methyl-1,2,4-oxadiazol-5-yl)phenyl)(2-(((6-methylpyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Prepared analogous to Example 139 substituting 6-methyl-2-(2H-1,2,3-triazol-2-yl)nicotinic acid with 2-(3-methyl-1,2,4-oxadiazol-5-yl)benzoic acid. MS (ESI) mass calcd. for

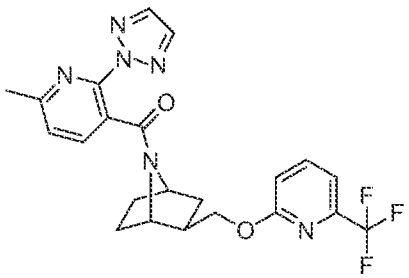
$C_{23}H_{24}N_4O_3$, 404.2; m/z found 405.2 $[M+H]^+$. ^1H NMR (MeOD): 8.10-8.00 (m, 1H), 7.75-7.63 (m, 1H), 7.57-7.47 (m, 2H), 7.37-7.26 (m, 1H), 6.79 (dd, J = 7.2, 2.8 Hz, 1H), 6.64-6.35 (m, 1H), 4.81-4.78 (m, 1H), 4.25-4.11 (m, 1H), 3.98-3.95 (m, 1H), 3.79-3.74 (m, 1H), 2.42-2.25 (m, 7H), 2.08-1.95 (m, 1H), 1.86-1.63 (m, 3H), 1.58-1.44 (m, 2H).

Example 142: (±)-(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((6-methylpyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



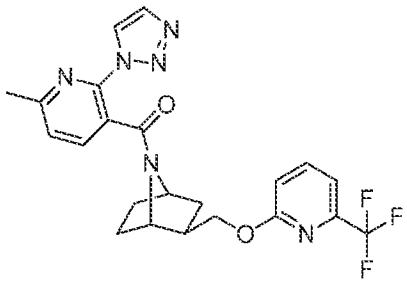
Prepared analogous to Example 139 substituting 6-methyl-2-(2H-1,2,3-triazol-2-yl)nicotinic acid with 3-fluoro-2-(2H-1,2,3-triazol-2-yl)benzoic acid. MS (ESI) mass calcd. for $C_{22}H_{22}FN_5O_2$, 407.2; m/z found 408.2 $[M+H]^+$. ^1H NMR (MeOD): 7.95-7.93 (m, 2H), 7.68-7.47 (m, 2H), 7.40-7.31 (m, 1H), 7.21-7.09 (m, 1H), 6.80 (t, J = 8.3 Hz, 1H), 6.58-6.46 (m, 1H), 4.56 (s, 1H), 4.01 (d, J = 7.3 Hz, 1H), 3.91 (d, J = 7.4 Hz, 2H), 2.43 (d, J = 2.5 Hz, 3H), 2.38-2.28 (m, 1H), 1.83-1.45 (m, 6H).

Example 143: (±)-(6-methyl-2-(2H-1,2,3-triazol-2-yl)pyridin-3-yl)(2-(((6-(trifluoromethyl)pyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



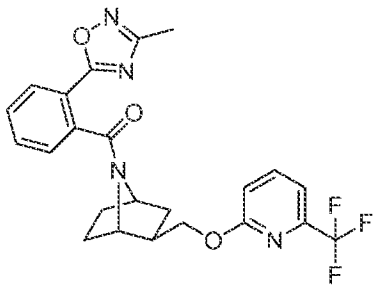
Prepared analogous to Example 131 substituting 2-chloro-4-(trifluoromethyl)pyrimidine with 2-chloro-6-(trifluoromethyl)pyridine. MS (ESI) mass calcd. for $C_{22}H_{21}F_3N_6O_2$, 458.2; m/z found 459.2 $[M+H]^+$. ^1H NMR (MeOD): 7.91 (s, 1H), 7.84 (s, 1H), 7.73-7.65 (m, 2H), 7.29-7.25 (m, 2H), 6.93-6.69 (m, 1H), 4.85-4.82 (m, 1H), 4.25-4.16 (m, 1H), 3.98-3.96 (m, 1H), 3.79-3.69 (m, 1H), 2.69-2.56 (m, 3H), 2.38-2.16 (m, 1H), 2.05-1.24 (m, 6H).

Example 144: (±)-(6-methyl-2-(1H-1,2,3-triazol-1-yl)pyridin-3-yl)(2-(((6-(trifluoromethyl)pyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



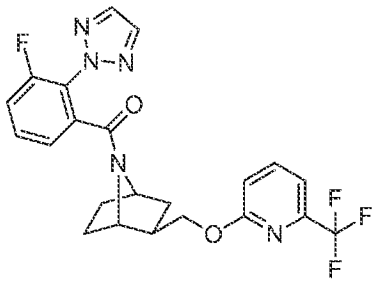
Prepared analogous to Example 143 substituting 6-methyl-2-(2H-1,2,3-triazol-2-yl)nicotinic acid with 6-methyl-2-(1H-1,2,3-triazol-1-yl)nicotinic acid. MS (ESI) mass calcd. for $C_{22}H_{21}F_3N_6O_2$, 458.2; m/z found 459.2 $[M+H]^+$. ^1H NMR (MeOD): 8.61 (t, J = 1.1 Hz, 1H), 8.00-7.72 (m, 3H), 7.49-6.83 (m, 3H), 4.75-4.71 (m, 1H), 4.31-4.10 (m, 1H), 4.08-3.95 (m, 1H), 3.89-3.77 (m, 1H), 2.64-2.52 (m, 3H), 2.43-2.27 (m, 1H), 2.06-1.89 (m, 1H), 1.82-1.37 (m, 5H).

Example 145: (±)-(2-(3-methyl-1,2,4-oxadiazol-5-yl)phenyl)(2-(((6-(trifluoromethyl)pyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



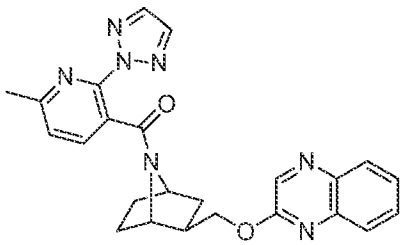
Prepared analogous to Example 143 substituting 6-methyl-2-(2H-1,2,3-triazol-2-yl)nicotinic acid with 2-(3-methyl-1,2,4-oxadiazol-5-yl)benzoic acid. MS (ESI) mass calcd. for $C_{23}H_{21}FN_4O_3$, 458.2; m/z found 459.2 $[M+H]^+$. ^1H NMR (MeOD): 8.10-8.01 (m, 1H), 7.88-7.77 (m, 1H), 7.75-7.63 (m, 1H), 7.54-7.49 (m, 1H), 7.39-7.25 (m, 2H), 7.07-6.78 (m, 1H), 4.82-4.79 (m, 1H), 4.35-4.24 (m, 1H), 4.10-4.07 (m, 1H), 3.78-3.74 (m, 1H), 2.48-2.29 (m, 4H), 2.09-1.96 (m, 1H), 1.88-1.63 (m, 3H), 1.58-1.47 (m, 2H).

Example 146: (±)-(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((6-(trifluoromethyl)pyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



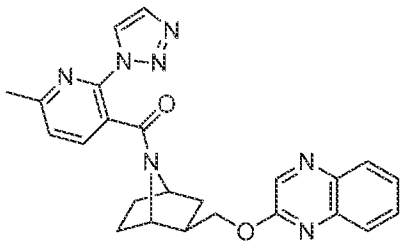
Prepared analogous to Example 143 substituting 6-methyl-2-(2H-1,2,3-triazol-2-yl)nicotinic acid with 3-fluoro-2-(2H-1,2,3-triazol-2-yl)benzoic acid. MS (ESI) mass calcd. for $C_{22}H_{19}F_4N_5O_2$, 461.2; m/z found 462.0 $[M+H]^+$. ^1H NMR (MeOD): 7.95-7.93 (m, 2H), 7.86-7.80 (m, 1H), 7.68-7.12 (m, 4H), 7.02-6.86 (m, 1H), 4.59-4.56 (m, 1H), 4.10-3.86 (m, 3H), 2.38-2.30 (m, 1H), 1.95-1.45 (m, 6H).

Example 147: (±)-(6-methyl-2-(2H-1,2,3-triazol-2-yl)pyridin-3-yl)(2-((quinoxalin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



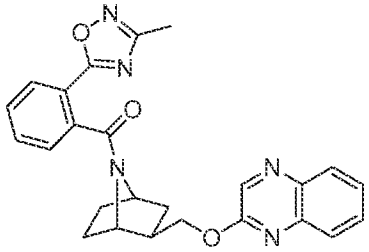
Prepared analogous to Example 131 substituting 2-chloro-4-(trifluoromethyl)pyrimidine with 2-chloroquinoxaline. MS (ESI) mass calcd. for $C_{24}H_{23}N_7O_2$, 441.2; m/z found 442.2 $[M+H]^+$. ^1H NMR (MeOD): 8.47-8.04 (m, 2H), 7.98-7.69 (m, 5H), 7.65-7.56 (m, 1H), 7.45-6.73 (m, 1H), 4.77-4.71 (m, 1H), 4.46-4.10 (m, 2H), 3.91-3.79 (m, 1H), 2.64-2.32 (m, 4H), 2.03-1.38 (m, 6H).

Example 148: (±)-(6-methyl-2-(1H-1,2,3-triazol-1-yl)pyridin-3-yl)(2-((quinoxalin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



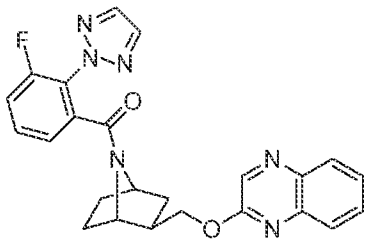
Prepared analogous to Example 147 substituting 6-methyl-2-(2H-1,2,3-triazol-2-yl)nicotinic acid with 6-methyl-2-(1H-1,2,3-triazol-1-yl)nicotinic acid. MS (ESI) mass calcd. for $C_{24}H_{23}N_7O_2$, 441.2; m/z found 441.2 $[M+H]^+$. ^1H NMR (MeOD): 8.61-8.59 (m, 1H), 8.46-8.25 (m, 1H), 8.04-7.55 (m, 6H), 7.48-6.74 (m, 1H), 4.78-4.74 (m, 1H), 4.43-4.30 (m, 1H), 4.21-4.18 (m, 1H), 3.92-3.82 (m, 1H), 2.63-2.34 (m, 4H), 2.08-1.89 (m, 1H), 1.88-1.39 (m, 5H).

Example 149: (±)-(2-(3-methyl-1,2,4-oxadiazol-5-yl)phenyl)(2-((quinoxalin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



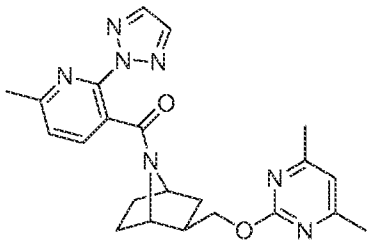
Prepared analogous to Example 147 substituting 6-methyl-2-(2H-1,2,3-triazol-2-yl)nicotinic acid with 2-(3-methyl-1,2,4-oxadiazol-5-yl)benzoic acid. MS (ESI) mass calcd. for $C_{25}H_{23}N_5O_3$, 441.2; m/z found 442.2 $[M+H]^+$. ^1H NMR (MeOD): 8.48-8.20 (m, 1H), 8.08-7.91 (m, 2H), 7.83-7.12 (m, 6H), 4.86-4.81 (m, 1H), 4.50-4.36 (m, 1H), 4.26-4.18 (m, 1H), 3.80-3.77 (m, 1H), 2.55-2.34 (m, 4H), 2.09-1.97 (m, 1H), 1.91-1.64 (m, 3H), 1.61-1.50 (m, 2H).

Example 150: (±)-(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((quinoxalin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



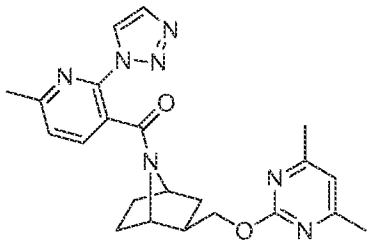
Prepared analogous to Example 147 substituting 6-methyl-2-(2H-1,2,3-triazol-2-yl)nicotinic acid with 3-fluoro-2-(2H-1,2,3-triazol-2-yl)benzoic acid. MS (ESI) mass calcd. for $C_{24}H_{21}FN_6O_2$, 444.2; m/z found 445.1 $[M+H]^+$. ^1H NMR (MeOD): 8.47-8.33 (m, 1H), 8.01-7.60 (m, 6H), 7.54-6.92 (m, 3H), 4.65-4.60 (m, 1H), 4.31-4.13 (m, 2H), 3.96-3.95 (m, 1H), 2.52-2.40 (m, 1H), 1.96-1.44 (m, 6H).

Example 151: (±)-(2-(((4,6-dimethylpyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-2-(2H-1,2,3-triazol-2-yl)pyridin-3-yl)methanone.



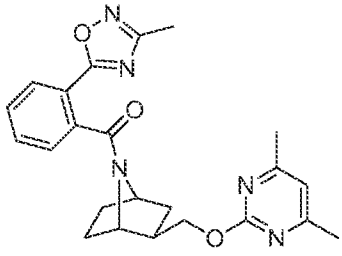
Prepared analogous to Example 131 substituting 2-chloro-4-(trifluoromethyl)pyrimidine with 2-chloro-4,6-dimethylpyrimidine. MS (ESI) mass calcd. for $C_{22}H_{25}N_7O_2$, 419.2; m/z found 420.2 $[M+H]^+$. ^{1}H NMR (MeOD): 8.02-7.99 (m, 2H), 7.94-7.46 (m, 1H), 7.48-7.10 (m, 1H), 6.87 (s, 1H), 4.72-4.71 (m, 1H), 4.38-3.97 (m, 2H), 3.89-3.84 (m, 1H), 2.65-2.17 (m, 10H), 1.98-1.37 (m, 6H).

Example 152: (±)-(2-(((4,6-dimethylpyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-2-(1H-1,2,3-triazol-1-yl)pyridin-3-yl)methanone.



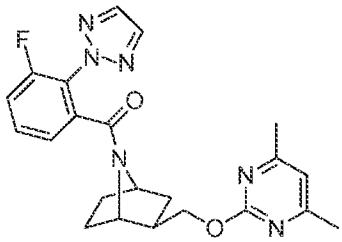
Prepared analogous to Example 151 substituting 6-methyl-2-(2H-1,2,3-triazol-2-yl)nicotinic acid with 6-methyl-2-(1H-1,2,3-triazol-1-yl)nicotinic acid. MS (ESI) mass calcd. for $C_{22}H_{25}N_7O_2$, 419.2; m/z found 420.2 $[M+H]^+$. ^{1}H NMR (MeOD): 8.62-8.61 (m, 1H), 7.98-7.78 (m, 2H), 7.50-7.11 (m, 1H), 6.86 (d, J = 9.7 Hz, 1H), 4.75-4.71 (m, 1H), 4.25-4.23 (m, 1H), 4.16-3.84 (m, 2H), 2.64-2.55 (m, 3H), 2.46-2.25 (m, 7H), 2.06-1.88 (m, 1H), 1.85-1.39 (m, 5H).

Example 153: (±)-(2-(((4,6-dimethylpyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(2-(3-methyl-1,2,4-oxadiazol-5-yl)phenyl)methanone.



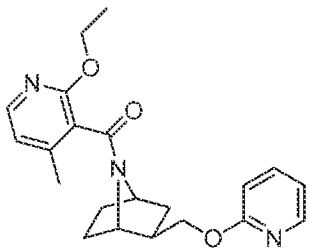
Prepared analogous to Example 151 substituting 6-methyl-2-(2H-1,2,3-triazol-2-yl)nicotinic acid with 2-(3-methyl-1,2,4-oxadiazol-5-yl)benzoic acid.MS (ESI) mass calcd. for $C_{23}H_{25}N_5O_3$, 419.2; m/z found 420.2 $[M+H]^+$. ^1H NMR (MeOD): 8.10-8.01 (m, 1H), 7.76-7.64 (m, 1H), 7.58-7.51 (m, 1H), 7.42-7.36 (m, 1H), 6.86 (s, 1H), 4.83-4.80 (m, 1H), 4.42-4.22 (m, 1H), 4.13-4.00 (m, 1H), 3.83-3.76 (m, 1H), 2.49-2.28 (m, 10H), 2.08-1.98 (m, 1H), 1.89-1.65 (m, 3H), 1.58-1.48 (m, 2H).

Example 154: (±)-(2-(((4,6-dimethylpyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone.



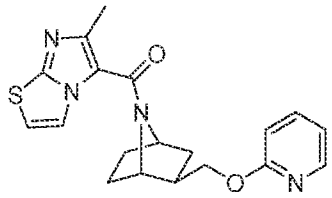
Prepared analogous to Example 151 substituting 6-methyl-2-(2H-1,2,3-triazol-2-yl)nicotinic acid with 3-fluoro-2-(2H-1,2,3-triazol-2-yl)benzoic acid. MS (ESI) mass calcd. for $C_{22}H_{23}FN_6O_2$, 422.2; m/z found 423.1 $[M+H]^+$. ^1H NMR (MeOD): 7.96-7.95 (m, 2H), 7.69-7.22 (m, 3H), 6.87 (d, J = 5.8 Hz, 1H), 4.58-4.56 (m, 1H), 4.19-3.89 (m, 3H), 2.42-2.34 (m, 7H), 1.90-1.37 (m, 6H).

Example 155: (±)-(2-ethoxy-4-methylpyridin-3-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



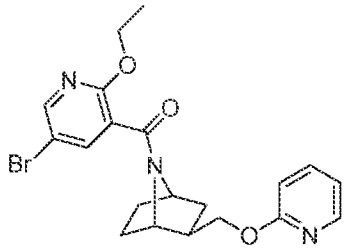
Prepared analogous to Example 1 substituting intermediate B-9 with B-10 and 5-fluoro-2-(pyrimidin-2-yl)benzoic acid with 2-ethoxy-4-methylnicotinic acid. MS (ESI) mass calcd. for $C_{21}H_{25}N_3O_3$, 367.2; m/z found 368.3 $[M+H]^+$. ^1H NMR ($CDCl_3$): 8.13 - 8.05 (m, 1H), 7.99 – 7.87 (m, 1H), 7.58 – 7.46 (m, 1H), 6.87 – 6.79 (m, 1H), 6.76 – 6.67 (m, 1H), 6.55 – 6.49 (m, 1H), 4.92 – 4.84 (m, 1H), 4.43 – 3.64 (m, 5H), 2.43 – 1.22 (m, 13 H).

Example 156: (±)-(6-methylimidazo[2,1-b]thiazol-5-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



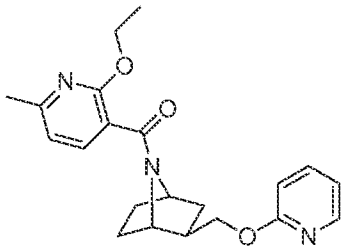
Prepared analogous to Example 1 substituting intermediate B-9 with B-10 and 5-fluoro-2-(pyrimidin-2-yl)benzoic acid with 6-methylimidazo[2,1-b]thiazole-5-carboxylic acid. ^{1}H NMR ($CDCl_3$): 8.05 - 7.98 (m, 1H), 7.79 (d, J = 4.5 Hz, 1H), 7.54 - 7.47 (m, 1H), 6.84 - 6.78 (m, 1H), 6.76 (d, J = 4.5 Hz, 1H), 6.62 (d, J = 8.4 Hz, 1H), 4.54 - 4.35 (m, 2H), 4.11 - 4.03 (m, 1H), 4.02 - 3.88 (m, 1H), 2.46 (s, 3H), 2.39 - 2.28 (m, 1H), 2.07 - 1.97 (m, 1H), 1.80 - 1.70 (m, 2H), 1.65 - 1.52 (m, 3H).

Example 157: (±)-(5-bromo-2-ethoxypyridin-3-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



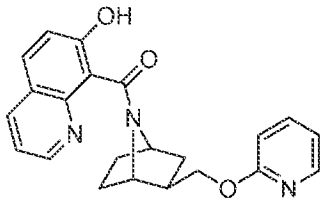
Prepared analogous to Example 1 substituting intermediate B-9 with B-10 and 5-fluoro-2-(pyrimidin-2-yl)benzoic acid with 5-bromo-2-ethoxynicotinic acid. MS (ESI) mass calcd. for $C_{20}H_{22}BrN_3O_3$, 431.1; m/z found 432.2 $[M+H]^+$. ^{1}H NMR ($CDCl_3$): 8.33 - 8.07 (m, 2H), 7.74 (d, J = 2.5 Hz, 0.5H), 7.61 (d, J = 2.5 Hz, 0.5H), 7.59 - 7.49 (m, 1H), 6.89 - 6.81 (m, 1H), 6.75 (d, J = 8.3 Hz, 0.5H), 6.55 (d, J = 8.4 Hz, 0.5H), 4.86 - 4.80 (m, 1H), 4.48 - 3.78 (m, 5H), 2.43 - 2.33 (m, 0.5H), 2.32 – 2.23 (m, 0.5H), 2.03 - 1.39 (m, 6H), 1.37 - 1.29 (m, 3H).

Example 158: (±)-(2-ethoxy-6-methylpyridin-3-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



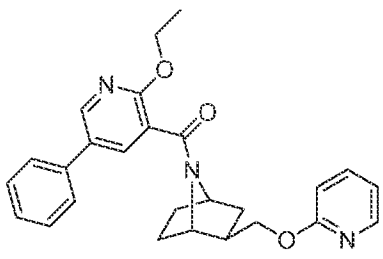
Prepared analogous to Example 1 substituting intermediate B-9 with intermediate B-10 and 5-fluoro-2-(pyrimidin-2-yl)benzoic acid with 2-ethoxy-6-methylnicotinic acid. MS (ESI) mass calcd. for $C_{21}H_{25}N_3O_3$, 367.2; m/z found 368.3 $[M+H]^+$. ^1H NMR ($CDCl_3$): 8.14 - 8.08 (m, 1H), 7.57 - 7.47 (m, 1.5H), 7.38 (d, J = 7.4 Hz, 0.5H), 6.86 - 6.82 (m, 1H), 6.74 (d, J = 8.3 Hz, 0.5H), 6.72 (d, J = 7.4 Hz, 0.5H), 6.51 (d, J = 8.3 Hz, 0.5H), 6.46 (d, J = 7.4 Hz, 0.5H), 4.84 - 4.79 (m, 1H), 4.44 - 4.34 (m, 1.5H), 4.27 - 4.09 (m, 1.5H), 4.06 - 4.01 (m, 0.5H), 3.92 - 3.80 (m, 1.5H), 2.43 (s, 1.5H), 2.38 - 2.32 (m, 2H), 2.26 - 2.20 (m, 0.5H), 2.01 - 1.40 (m, 6H), 1.36 - 1.28 (m, 3H).

Example 159: (±)-(7-hydroxyquinolin-8-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



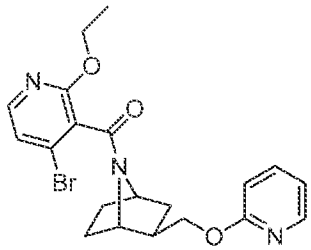
Prepared analogous to Example 1 substituting intermediate B-9 with intermediate B-10 and 5-fluoro-2-(pyrimidin-2-yl)benzoic acid with 7-hydroxyquinoline-8-carboxylic acid (intermediate A-29 step B). MS (ESI) mass calcd. for $C_{22}H_{21}N_3O_3$, 375.2; m/z found 376.3 $[M+H]^+$. ^1H NMR ($CDCl_3$): 8.88 - 8.66 (m, 1H), 8.19 - 7.93 (m, 2H), 7.80 - 7.41 (m, 2H), 7.26 - 6.25 (series of m, 4H), 5.10 - 4.87 (m, 1H), 4.34 - 3.60 (m, 3H), 2.51 – 1.00 (series of m, 7H).

Example 160: (±)-(2-ethoxy-5-phenylpyridin-3-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



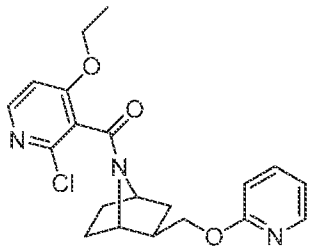
Prepared analogous to Example 1 substituting intermediate B-9 with intermediate B-10 and 5-fluoro-2-(pyrimidin-2-yl)benzoic acid with 2-ethoxy-5-phenylnicotinic acid. MS (ESI) mass calcd. for $C_{26}H_{27}N_3O_3$, 429.2; m/z found 430.2 $[M+H]^+$. ^1H NMR ($CDCl_3$): 8.40 and 8.30 (2d, J = 2.5 Hz, 1H), 8.15 - 8.12 and 7.98 - 7.94 (2m, 1H), 7.87 and 7.74 (2d, J = 2.5 Hz, 1H), 7.59 - 7.28 (m, 6H), 6.88 - 6.83 and 6.72 - 6.68 (2m, 1H), 6.76 and 6.47 (2d, J = 8.3 Hz, 1H), 4.89 - 4.84 (m, 1H), 4.34 - 3.84 (series of m, 5H), 2.43 - 2.34 and 2.32 - 2.23 (m, 1H), 2.06 - 1.45 (series of m, 6H), 1.42 - 1.32 (m, 3H).

Example 161: (±)-(4-bromo-2-ethoxypyridin-3-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Prepared analogous to Example 1 substituting intermediate B-9 with intermediate B-10 and 5-fluoro-2-(pyrimidin-2-yl)benzoic acid with 4-bromo-2-ethoxynicotinic acid. MS (ESI) mass calcd. for $C_{20}H_{22}BrN_3O_3$, 431.1; m/z found 432.2 $[M+H]^+$. ^1H NMR ($CDCl_3$): 8.15 - 8.08 (m, 1H), 7.96 - 7.87 (m, 1H), 7.60 - 7.49 (m, 1H), 7.11 – 6.92 (series of m, 1H), 6.88 - 6.82 (m, 1H), 6.78 - 6.52 (series of m, 1H), 4.94 – 4.87 (m, 1H), 4.47 – 3.67 (series of m, 5H), 2.45 - 1.41 (series of m, 7H), 1.38 - 1.27 (m, 3H).

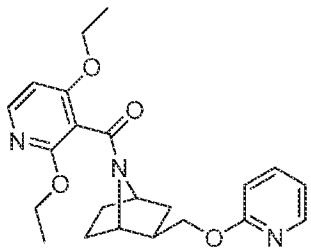
Example 162: (±)-(2-chloro-4-ethoxypyridin-3-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Prepared analogous to Example 1 substituting intermediate B-9 with intermediate B-10 and 5-fluoro-2-(pyrimidin-2-yl)benzoic acid with 2-chloro-4-ethoxynicotinic acid. MS (ESI) mass calcd. for $C_{20}H_{22}ClN_3O_3$, 387.1; m/z found 388.3 $[M+H]^+$. ^1H NMR ($CDCl_3$):8.27 - 8.17 (m, 1H), 8.15 - 8.07 (m, 1H), 7.60 - 7.48 (m, 1H), 6.88-6.82 (m, 1H), 6.80 - 6.73 (m, 1H), 6.58 -

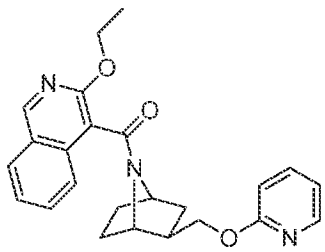
6.49 (m, 1H), 4.93 - 4.87 (m, 1H), 4.27 - 4.02 (m, 3H), 3.92 - 3.58 (series of m, 2H), 2.44 – 1.35 (series of m, 10H).

Example 163: (±)-(2,4-diethoxypyridin-3-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



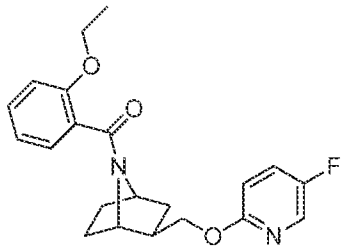
Prepared analogous to Example 1 substituting intermediate B-9 with intermediate B-10 and 5-fluoro-2-(pyrimidin-2-yl)benzoic acid with 2,4-diethoxynicotinic acid. MS (ESI) mass calcd. for $C_{22}H_{27}BrN_3O_4$, 397.2; m/z found 398.2 $[M+H]^+$. ^1H NMR ($CDCl_3$): 8.15 - 8.07 (m, 1H), 8.03 - 7.94 (m, 1H), 7.60 - 7.46 (m, 1H), 6.87 - 6.80 (m, 1H), 6.77 - 6.73 (m, 0.5H), 6.56 - 6.45 (m, 1H), 6.30 - 6.27 (m, 0.5 H) 4.88 – 4.83 (m, 1H), 4.50 - 3.51 (series of m, 7H), 2.40 - 1.15 (series of m, 13H).

Example 164: (3-ethoxyisoquinolin-4-yl)((1S,2R,4R)-2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



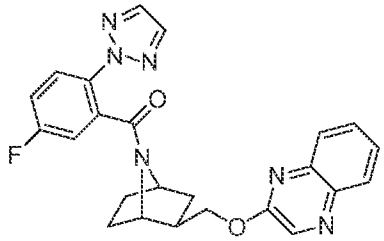
Prepared analogous to Example 1 substituting 5-fluoro-2-(pyrimidin-2-yl)benzoic acid with intermediate A-22. MS (ESI) mass calcd. for $C_{24}H_{25}N_3O_3$, 403.2; m/z found 404.2 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) 8.97 – 8.89 (m, 0.7H), 8.87 – 8.81 (m, 0.3H), 8.22 – 8.07 (m, 0.7H), 7.95 – 7.85 (m, 1H), 7.82 (dq, J = 8.6, 0.9 Hz, 0.2H), 7.78 – 7.69 (m, 0.6H), 7.69 – 7.47 (m, 2H), 7.43 – 7.28 (m, 1.2H), 7.10 (ddd, J = 8.0, 6.8, 1.0 Hz, 0.3H), 6.93 – 6.68 (m, 1.5H), 6.52 – 6.46 (m, 0.2H), 6.16 – 6.09 (m, 0.3H), 5.02 (td, J = 9.5, 4.6 Hz, 1H), 4.65 – 3.99 (m, 3.5H), 3.92 (dd, J = 10.5, 5.6 Hz, 0.25H), 3.74 – 3.58 (m, 1.25H), 2.52 – 2.29 (m, 0.5H), 2.27 – 1.93 (m, 2H), 1.86 – 0.78 (m, 7.5H).

Example 165: (±)-(2-ethoxyphenyl)(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



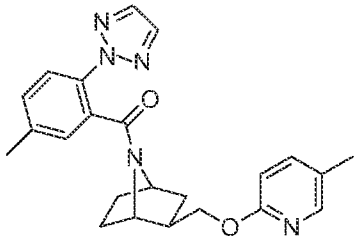
Prepared analogous to Example 7 substituting 6-methyl-3-(2H-1,2,3-triazol-2-yl)picolinic acid with 2-ethoxybenzoic acid. ^{1}H NMR (400 MHz, $CDCl_3$): 7.95 (dd, J = 7.3, 3.1 Hz, 1H), 7.37 – 7.18 (m, 2.5H), 7.14 (dd, J = 7.4, 1.7 Hz, 0.5H), 6.95 (td, J = 7.5, 0.9 Hz, 0.5H), 6.90 (dd, J = 8.4, 1.0 Hz, 0.5H), 6.83 – 6.68 (m, 1.5H), 6.47 (dd, J = 9.0, 3.6 Hz, 0.5H), 4.88 – 4.80 (m, 1H), 4.17 – 3.72 (m, 5H), 2.40 – 2.28 (m, 0.5H), 2.26 – 2.14 (m, 0.5H), 2.07 – 1.85 (m, 2H), 1.83 – 1.17 (m, 7H).

Example 166: (±)-(5-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((quinoxalin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



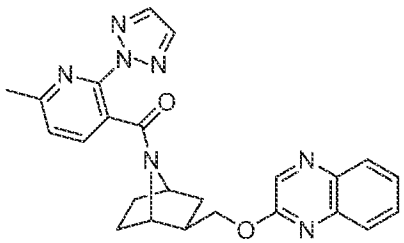
Prepared analogous to Example 2 substituting 6-methyl-3-(2H-1,2,3-triazol-2-yl)picolinic acid with intermediate A-10 and 2-fluoropyridine with 2-chloroquinoxaline. MS (ESI) mass calcd. for $C_{24}H_{21}FN_6O_2$, 444.2; m/z found 445.2 $[M+H]^+$. ^{1}H NMR (400 MHz, $CDCl_3$): 8.49 (s, 0.4H), 8.30 (s, 0.4H), 8.04 (ddd, J = 8.2, 6.9, 1.5 Hz, 1H), 7.90 – 7.76 (m, 2.5H), 7.75 – 7.66 (m, 1.5H), 7.65 – 7.55 (m, 1.5H), 7.44 (dd, J = 8.5, 5.8 Hz, 0.5H), 7.32 (dd, J = 8.5, 5.8 Hz, 0.5H), 7.29 – 7.22 (m, 0.2H), 7.21 – 7.10 (m, 1H), 6.49 (s, 0.5H), 4.93 – 4.84 (m, 1H), 4.52 – 4.30 (m, 1H), 4.23 – 4.07 (m, 1H), 3.87 – 3.78 (m, 1H), 2.48 – 2.25 (m, 1.8H), 2.10 – 1.88 (m, 1.2H), 1.83 – 1.31 (m, 4H).

Example 167: (±)-5-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((5-methylpyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



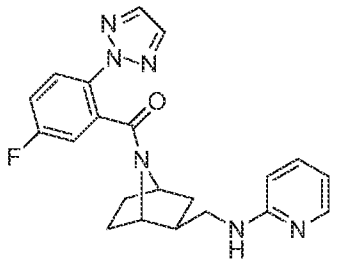
Prepared analogous to Example 13 substituting 2-chloro-4-trifluoromethylpyrimidine with 2-fluoro-5-methylpyridine. MS (ESI) mass calcd. for $C_{23}H_{25}N_5O_2$, 403.2; m/z found 404.2 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$): 7.99 – 7.92 (m, 1H), 7.81 – 7.68 (m, 2.5H), 7.42 – 7.29 (m, 1.5H), 7.26 – 7.21 (m, 0.5H), 7.21 – 7.10 (m, 1H), 6.66 (d, J = 8.4 Hz, 0.5H), 6.45 (d, J = 8.4 Hz, 0.5H), 4.85 – 4.73 (m, 1H), 4.16 – 3.68 (m, 3H), 2.42 (s, 1.3H), 2.34 – 2.14 (m, 3.7H), 2.02 – 1.79 (m, 2.5H), 1.72 – 1.21 (m, 5.5H).

Example 168: (±)-(6-methyl-2-(2H-1,2,3-triazol-2-yl)pyridin-3-yl)(2-((quinoxalin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



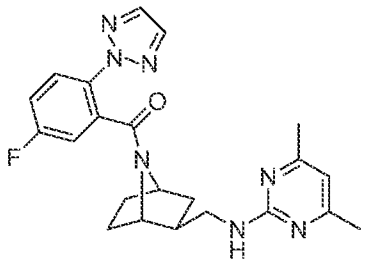
Prepared analogous to Example 1 substituting intermediate B-9 with intermediate B-10, 2-fluoropyridine with 2-chloroquinoxaline and 5-fluoro-2-(pyrimidin-2-yl)benzoic acid with intermediate A-3 to give the title compound. MS (ESI) mass calcd. for $C_{24}H_{23}N_7O_2$, 441.2; m/z found 442.2 $[M+H]^+$. 1H NMR CD_3OD: 8.47-8.04 (m, 2H), 7.98-7.69 (m, 5H), 7.65-7.56 (m, 1H), 7.45-6.73 (m, 1H), 4.77-4.71 (m, 1H), 4.46-4.10 (m, 2H), 3.91-3.79 (m, 1H), 2.64-2.32 (m, 4H), 2.03-1.38 (m, 6H).

Example 169: (±)-(5-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((pyridin-2-ylamino)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



Prepared analogous to example 170 substituting 2-chloro-4,6-dimethylpyrimidine with 2-fluoropyridine. MS (ESI) mass calcd. for $C_{21}H_{21}FN_6O$, 392.2; m/z found 393.1 $[M+H]^+$. 1H NMR (CD3OD): 8.02-7.83 (m, 4H), 7.47-7.23 (m, 3H), 6.59-6.38 (m, 2H), 4.73-4.55 (m, 1H), 3.87-3.70 (m, 1H), 3.24-2.80 (m, 2H), 2.27-2.03 (m, 1H), 1.97-1.34 (m, 6H).

Example 170: (±)-(2-(((4,6-dimethylpyrimidin-2-yl)amino)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(5-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone



Step A: (±)-tert-butyl 2-(((methylsulfonyl)oxy)methyl)-7-azabicyclo[2.2.1]heptane-7-carboxylate. To intermediate B-10 (2.6g, 11.5 mmol) and TEA (1.7g, 17.2 mmol) in DCM (15 mL) at 0 °C was added MsCl (1.6g, 13.7 mmol) dropwise over 10 minutes. This ice bath was removed and the reaction was allowed to stir at rt for 12h and H_2O was added. The layers were separated and the organic layer was washed with brine and dried (Na_2SO_4). Purification via silica gel chromatography(15% EtOAc in petroleum ethers) gave the title compound (3.5g).

Step B: (±)-tert-butyl 2-(azidomethyl)-7-azabicyclo[2.2.1]heptane-7-carboxylate. To the title compound of step A (3.4g, 11.1 mmol) in DMF (15 mL) was added sodium azide (2.1g, 33.4 mmol). The mixture was heated at 100 °C overnight, cooled to rt, poured into H2O and extracted with DCM. The combined organics were washed with brine and dried (Na2SO4). Purification via silica gel chromatography (10% EtOAc in petroleum ethers) gave the title compound (2.6g).

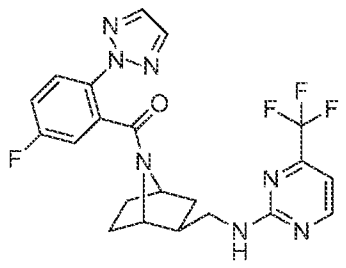
Step C: (±)-2-(azidomethyl)-7-azabicyclo[2.2.1]heptane. To the title compound of step B in DCM was added TFA. After 3h at rt, the reaction mixture was concentrated to give the title compound (1.7g) as the TFA salt.

Step D: (±)-2-(azidomethyl)-7-azabicyclo[2.2.1]heptan-7-yl)(5-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone. Prepared analogous to example 22 substituting 2-(2H-1,2,3-triazol-2-yl)benzoic acid with 5-fluoro-2-(2H-1,2,3-triazol-2-yl)benzoic acid and using the title compound of step C.

Step E: 2-(aminomethyl)-7-azabicyclo[2.2.1]heptan-7-yl)(5-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone. The title compound of step D in MeOH was placed under an atmosphere of hydrogen in the presence of 10 wt% Pd/C for 4h. The catalyst was removed by filtration. Purification via silica gel chromatography (7% MeOH in DCM) gave the title compound.

Step F: (±)-(2-(((4,6-dimethylpyrimidin-2-yl)amino)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(5-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone. To the title compound of step E (30 mg) in NMP (3 mL) was added 2-chloro-4,6-dimethylpyrimidine (16 mg) and Cs_2CO_3 (43 mg). The reaction was heated to 180 °C for 2h. After cooling to rt, H2O was addd and the mixture extracted with EtOAc. Purification via prep-HPLC gave the title compound. MS (ESI) mass calcd. for $C_{22}H_{24}FN_7O$, 421.2; m/z found 422.2 $[M+H]^+$. 1H NMR (CD3OD) 7.90-7.73 (m, 3H), 7.34-7.14 (m, 2H), 6.31-6.26 (m, 1H), 4.62-4.41 (m, 1H), 3.74-3.57 (m, 1H), 3.46-3.22 (m, 1H), 3.18-2.93 (m, 1H), 2.40-1.91 (m, 7H), 1.85-1.20 (m, 6H).

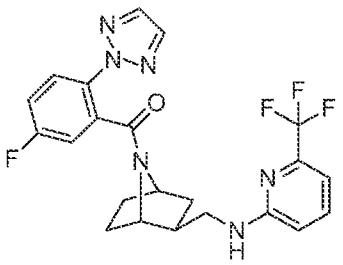
Example 171: (±)-(5-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((4-(trifluoromethyl)pyrimidin-2-yl)amino)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



Prepared analogous to example 170 substituting 2-chloro-4,6-dimethylpyrimidine with 2-chloro-4-(trifluoromethyl)pyrimidine. MS (ESI) mass calcd. for $C_{21}H_{19}F_4N_7O$, 461.2; m/z found 462.1 $[M+H]^+$. 1H NMR (CD3OD): 8.51 (s, 1H), 7.99-7.83 (m, 3H), 7.46-7.16 (m, 2H), 6.88 (d,

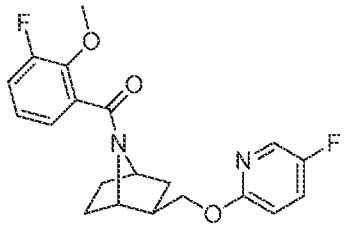
J = 4.9 Hz, 1H), 4.74-4.53 (m, 1H), 3.87-3.66 (m, 1H), 3.34 (s, 1H), 3.30-3.02 (m, 1H), 2.33-2.08 (m, 1H), 1.97-1.32 (m, 6H).

Example 172: (±)-(5-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((6-(trifluoromethyl)pyridin-2-yl)amino)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



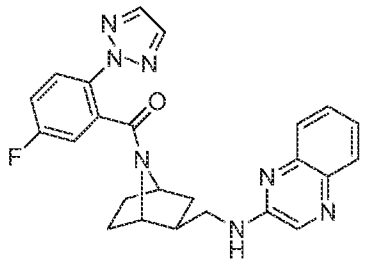
Prepared analogous to example 170 substituting 2-chloro-4,6-dimethylpyrimidine with 2-chloro-6-(trifluoromethyl)pyridine. MS (ESI) mass calcd. for $C_{22}H_{20}F_4N_6O$, 460.2; m/z found 461.2 $[M+H]^+$. 1H NMR (CD3OD): 8.07-7.84 (m, 3H), 7.60-7.22 (m, 3H), 6.90 (d, J = 7.2 Hz, 1H), 6.74-6.58 (m, 1H), 4.77-4.58 (m, 1H), 3.90-3.72 (m, 1H), 3.30-3.05 (m, 2H), 2.37-2.12 (m, 1H), 1.99-1.37 (m, 6H).

Example 173: (±)-(3-fluoro-2-methoxyphenyl)(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



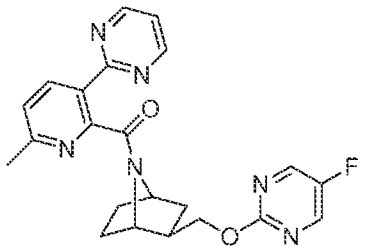
Prepared analogous to Example 7 substituting 6-methyl-3-(2H-1,2,3-triazol-2-yl)picolinic acid with 3-fluoro-2-methoxybenzoic acid. MS (ESI) mass calcd. for $C_{20}H_{20}F_2N_2O_3$, 374.1; m/z found 375.1 $[M+H]^+$. 1H NMR (CD3OD): 8.01-7.90 (m, 1H), 7.56-7.38 (m, 1H), 7.28-7.06 (m, 2H), 7.02-6.53 (m, 2H), 4.82-4.66 (m, 1H), 4.50-3.73 (m, 6H), 2.85-2.22 (m, 1H), 2.21-1.10 (m, 6H).

Example 174: (±)-(5-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((quinoxalin-2-ylamino)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



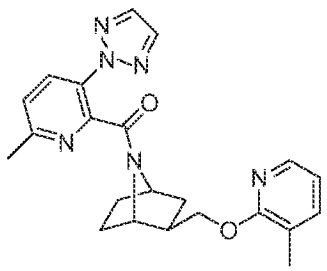
Prepared analogous to example 170 substituting 2-chloro-4,6-dimethylpyrimidine with 2-chloroquinoxaline. MS (ESI) mass calcd. for $C_{24}H_{22}FN_7O$, 443.2; m/z found 444.2 $[M+H]^+$.

Example 175: (±)-(2-(((5-fluoropyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(pyrimidin-2-yl)pyridin-2-yl)methanone



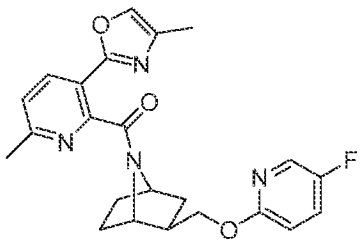
Prepared analogous to example 98 substituting 3,6'-dimethyl-[2,3'-bipyridine]-2'-carboxylic acid with intermediate A-9. MS (ESI) mass calcd. for $C_{22}H_{21}FN_6O_2$, 420.2; m/z found 421 $[M+H]^+$.

Example 176: (±)-(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-(((3-methylpyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



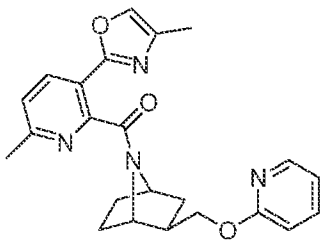
Prepared analogous to example 7 substituting 5-fluoropyridin-2(1H)-one with 3-methylpyridin-2-ol. MS (ESI) mass calcd. for $C_{22}H_{24}N_6O_2$, 404.2; m/z found 405 [M+H

Example 177: (±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(4-methyloxazol-2-yl)pyridin-2-yl)methanone



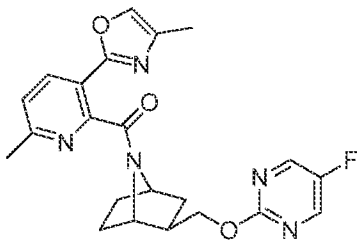
Prepared analogous to Example 7 substituting 6-methyl-3-(2H-1,2,3-triazol-2-yl)picolinic acid with intermediate A-54. MS (ESI) mass calcd. for $C_{23}H_{23}FN_4O_3$, 422.2; m/z found 423 $[M+H]^+$.

Example 178 (6-methyl-3-(4-methyloxazol-2-yl)pyridin-2-yl)((1S,2R,4R)-2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



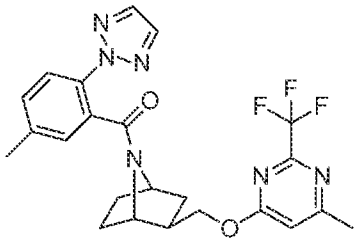
Prepared analogous to Example 1 substituting intermediate A-7 with intermediate A-54. MS (ESI) mass calcd. for $C_{23}H_{24}N_4O_3$, 404.2; m/z found 405 $[M+H]^+$.

Example 179: ((1S,2R,4R)-2-(((5-fluoropyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(4-methyloxazol-2-yl)pyridin-2-yl)methanone



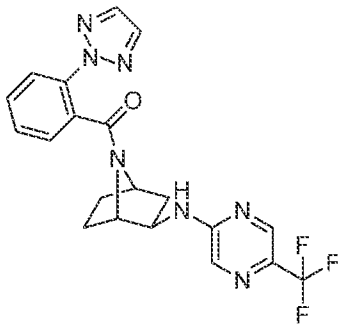
Prepared analogous to Example 98 substituting intermediate 3,6'-dimethyl-[2,3'-bipyridine]-2'-carboxylic acid with intermediate A-54. MS (ESI) mass calcd. for $C_{22}H_{22}FN_5O_3$, 423.2; m/z found 424 $[M+H]^+$

Example 180: (±)-(5-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((6-methyl-2-(trifluoromethyl)pyrimidin-4-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Prepared analogous to Example 13 substituting 2-chloro-4-(trifluoromethyl)pyrimidine with 4-chloro-6-methyl-2-(trifluoromethyl)pyrimidine. MS (ESI) mass calcd. for $C_{23}H_{23}F_3N_6O_2$, 472.2; m/z found 473.2 $[M+H]^+$. ^1H NMR ($CDCl_3$): 7.88 – 7.72 (m, 3H), 7.38 – 7.12 (m, 2H), 6.74 – 6.70 (s, 0.6H), 6.55 – 6.50 (s, 0.4H), 4.89 – 4.75 (m, 1H), 4.30 – 3.87 (m, 2H), 3.85 – 3.46 (m, 1H), 2.56 – 2.49 (m, 3H), 2.46 – 2.39 (s, 2H), 2.32 – 1.80 (m, 3H), 1.74 – 1.11 (m, 5H).

Example 181: (2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



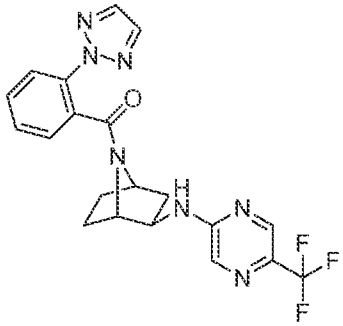
Step A: (1S,2R,4R)-tert-butyl 2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptane-7-carboxylate. To intermediate B-5 (1.6g, 7.3 mmol) and K_2CO_3 (1.5g, 10 mmol) in DMF (11 mL) was added 2-chloro-5-(trifluoromethyl)pyrazine (1.1 mL, 8.8 mmol). After heating at 70 °C for 2h, the mixture was cooled to rt, diluted with EtOAc and H_2O. The aqueous layer was extracted with EtOAc (3X). The combined organics were washed with 4% (aq) and dried ($MgSO_4$). Purification via silica gel chromatography (0-40% EtOAc in hexanes) gave the title compound (1.8g, 67%). MS (ESI) mass calcd. for $C_{16}H_{21}F_3N_4O_2$, 358.2; m/z found

359.2 $[M+H]^+$ 1H NMR (CDCl3): 8.32 (s, 1H), 7.86 – 7.82 (m, 1H), 5.33 (s, 1H), 4.38 – 4.15 (m, 2H), 4.10 – 3.96 (m, 1H), 2.14 – 1.98 (m, 1H), 1.93 – 1.67 (m, 2H), 1.61 – 1.36 (m, 12H).

Step B: (1S,2R,4R)-N-(5-(trifluoromethyl)pyrazin-2-yl)-7-azabicyclo[2.2.1]heptan-2-amine. To the title compound of step A (200 mg, 0.6 mmol) in EtOAc (1 mL) was added 4M HCl in dioxane (3 mL). After 2h, the reaction was concentrated, neutralized with 5% Na_2CO_3 (aq) and extracted with DCM (2X). The combined organics were dried (Na_2SO_4) to give the title compound of step B that was used without further purification. MS (ESI) mass calcd. for $C_{11}H_{13}F_3N_4$, 258.1; m/z found 259.1 $[M+H]^+$.

Step C: (2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone. To the title compound of step B (140 mg, 0.5 mmol) and intermediate A-1 (113 mg, 0.6 mmol) in DMF (4 mL) was added DIPEA (230 µL, 1.4 mmol) and HATU (155 mg, 0.6 mmol). Upon completion of the reaction, purification was performed using Agilent prep method X to give the title compound (172 mg, 74%). MS (ESI) mass calcd. for $C_{20}H_{18}F_3N_7O$, 429.2; m/z found 430 $[M+H]^+$. 1H NMR (CDCl3): 8.32 (s, 0.3H), 8.17 (s, 0.7H), 7.99 – 7.89 (m, 1.5H), 7.88 – 7.77 (m, 1.5H), 7.62 – 7.30 (m, 4H), 6.24 – 6.15 (m, 0.3H), 4.86 (s, 0.7H), 4.76 (d, J = 5.4 Hz, 0.3H), 4.45 – 4.23 (m, 1H), 4.08 – 3.90 (m, 1H), 2.23 – 1.34 (m, 6H).

Example 182: (±)-((2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



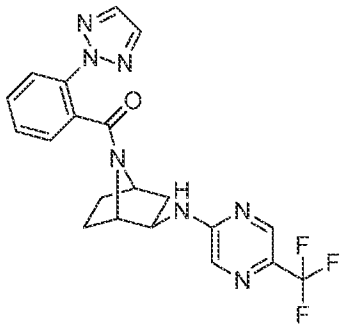
Step A: (±)-tert-butyl 2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptane-7-carboxylate. Prepared analogous to Example 181 step A substituting intermediate B-5 with intermediate B-6.

Step B: (±)-N-(5-(trifluoromethyl)pyrazin-2-yl)-7-azabicyclo[2.2.1]heptan-2-amine. Prepared analogous to Example 181 step B substituting (1S,2R,4R)-tert-butyl 2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptane-7-carboxylate with (±)-tert-butyl 2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptane-7-carboxylate.

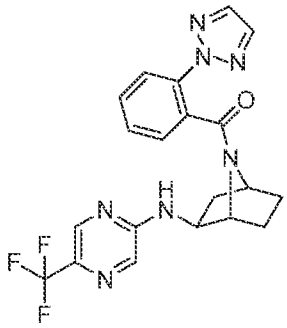
Step C: (±)-((2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.

To 2-(2H-1,2,3-triazol-2-yl)benzoic acid (125 mg, 0.6 mmol) and DMF (4 mL) was added (*i*-Pr)$_2$NEt (0.23 mL, 1.3 mmol) and HBTU (155 mg, 0.6 mmol). After 10 min, the title compound from step B (146 mg. 0.4 mmol) was added. After stirring overnight at rt, saturated $NaHCO_3$ (aq.) was added and the mixture extracted with EtOAc (3X). The combined organics were dried ($MgSO_4$) and concentrated. Purification via preparative HPLC gave the title compound (89 mg, 47%) as a beige solid. MS (ESI) mass calcd. for $C_{20}H_{18}F_3N_7O$, 429.2; m/z found 430 $[M+H]^+$. 1H NMR (DMSO-D_6): 8.47 (s, 0.3H), 8.24 (s, 0.7H), 8.14 – 8.05 (m, 2.2H), 8.02 (s, 0.7H), 7.85 (d, J = 7.2 Hz, 1.3H), 7.72 – 7.55 (m, 1.7H), 7.49 – 7.34 (m, 1.4H), 7.13 (t, J = 7.4 Hz, 0.7H), 4.58 (t, J = 4.3 Hz, 0.7H), 4.44 (d, J = 4.7 Hz, 0.3H), 4.04 – 3.93 (m, 0.3H), 3.82 (t, J = 4.1 Hz, 0.3H), 3.79 – 3.70 (m, 0.7H), 3.54 (d, J = 4.8 Hz, 0.7H), 2.07 – 1.90 (m, 1H), 1.85 – 1.07 (m, 5H).

Example 183a: (2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



and Example 183 b: (2-(2H-1,2,3-triazol-2-yl)phenyl)((1R,2S,4S)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



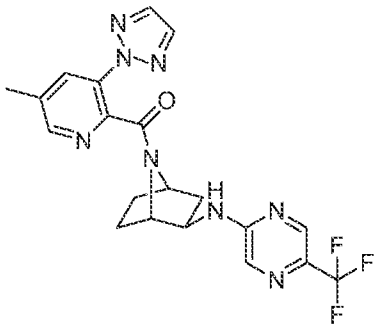
The title compounds were obtained by chiral SFC (CHIRALPAK OD-H 5 μM 250 X 20mm) resolution of Example 182 (81 mg) using 70% CO_2/30% EtOH as the mobile phase to give

enantiomer A (37 mg, 1st eluting enantiomer, example 183a) and enantiomer B (38 mg, 2nd eluting enantiomer, example 183b). Example 183a: >98% single enantiomer, 2.45 min retention time; Example 183b >98% single enantiomer, 3.33 min retention time.

Example 183a: Enantiomer A: MS (ESI) mass calcd. for $C_{20}H_{18}F_3N_7O$, 429.2; m/z found 430 $[M+H]^+$.

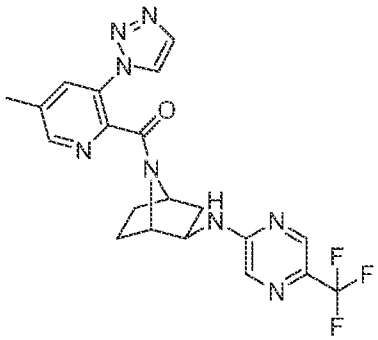
Example 183b: Enantiomer B: MS (ESI) mass calcd. for $C_{20}H_{18}F_3N_7O$, 429.2; m/z found 430 $[M+H]^+$.

Example 184: (±)-(5-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



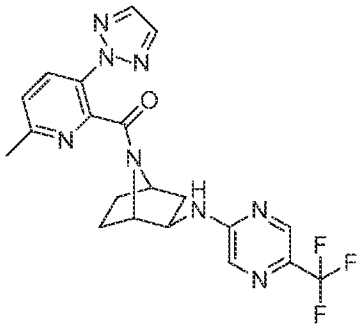
Prepared analogous to Example 182 substituting intermediate A-1 with intermediate A-19 and HBTU with HATU. MS (ESI) mass calcd. for $C_{20}H_{19}F_3N_8O$, 444.2; m/z found 445.1 $[M+H]^+$.

Example 185: (±)-(5-methyl-3-(1H-1,2,3-triazol-1-yl)pyridin-2-yl)(2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



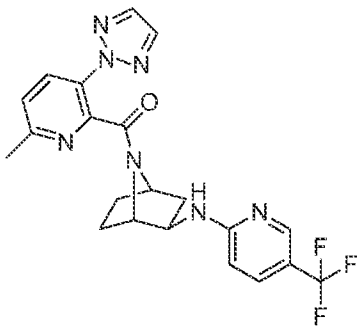
Prepared analogous to Example 184 substituting intermediate A-19 with intermediate A-20. MS (ESI) mass calcd. for $C_{20}H_{19}F_3N_8O$, 444.2; m/z found 445.1 $[M+H]^+$. HPLC R_t=1.13.

Example 186: (±)-(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Prepared analogous to Example 184 substituting intermediate A-19 with intermediate A-21. MS (ESI) mass calcd. for $C_{20}H_{19}F_3N_8O$, 444.2; m/z found 445.1 $[M+H]^+$. ^1H NMR ($CDCl_3$): 8.36 – 8.32 (s, 0.2H), 8.27 – 8.23 (s, 0.8H), 8.22 – 8.18 (d, J = 8.4 Hz, 0.2H), 8.13 – 8.08 (d, J = 8.3 Hz, 0.8H), 7.93 – 7.84 (m, 2H), 7.79 – 7.75 (m, 0.8H), 7.40 – 7.36 (d, J = 8.4 Hz, 0.2H), 7.36 – 7.31 (d, J = 8.4 Hz, 0.8H), 7.26 – 7.22 (m, 0.2H), 6.26 – 6.19 (d, J = 8.5 Hz, 0.2H), 4.96 – 4.86 (t, J = 4.8 Hz, 0.8H), 4.83 – 4.75 (d, J = 5.4 Hz, 0.2H), 4.36 – 4.19 (m, 1H), 4.13 – 3.92 (d, J = 5.0 Hz, 1H), 2.69 – 2.56 (m, 3H), 2.29 – 2.14 (dd, J = 13.1, 7.5 Hz, 1H), 2.14 – 1.87 (m, 2H), 1.81 – 1.78 (m, 1H), 1.63 – 1.56 (m, 2H).

Example 187: (±)-(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



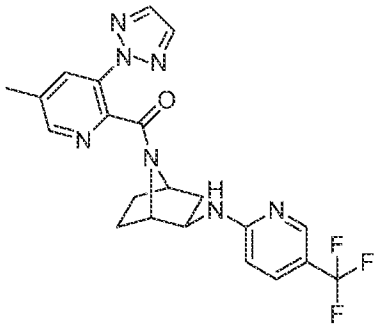
Step A: (±)-tert-butyl 2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptane-7-carboxylate. To intermediate B-6 (150 mg, 0.7 mmol) in DMSO (10 mL) was added DIPEA (244 µL, 1.4 mmol) and 2-chloro-5-(trifluoromethyl)pyridine (170 µL, 1.4 mmol). After heating at 100 °C for 4h, the mixture was cooled to rt and saturated $NaHCO_3$ (aq) was added. The mixture was extracted with DCM (3X). The combined organics were washed with brine and dried ($MgSO_4$). Purification via silica gel chromatography (0-13%

EtOAc in heptanes) gave the title compound. MS (ESI) mass calcd. for $C_{17}H_{22}F_3N_7O_2$, 357.2; m/z found 358.0 $[M+H]^+$.

Step B: (±)-N-(5-(trifluoromethyl)pyridin-2-yl)-7-azabicyclo[2.2.1]heptan-2-amine hydrochloride. To the title compound from step A (262 mg, 0.7 mmol) in 1,4-dioxane (10 mL) was added 6N HCl in iPrOH (700 µL). The reaction was heated to 70 °C for 2h, cooled to rt, concentrated and used without further purification in subsequent steps.

Step C: (±)-(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone. Prepared analogous to Example 182 substituting intermediate A-1 with intermediate A-21 and (±)-N-(5-(trifluoromethyl)pyrazin-2-yl)-7-azabicyclo[2.2.1]heptan-2-amine with the title compound of step B. MP=193.9 °C. ^{1}H NMR (DMSO-D_6): 8.38 (s, 0.3H), 8.24 – 8.16 (m, 1H), 8.15 – 8.11 (m, 2H), 8.05 (d, *J* = 8.3 Hz, 0.7H), 7.69 (dd, *J* = 8.9, 2.3 Hz, 0.3H), 7.63 (dd, *J* = 8.9, 2.4 Hz, 0.7H), 7.57 (d, *J* = 8.4 Hz, 0.3H), 7.37 (d, *J* = 8.4 Hz, 0.7H), 7.33 (d, *J* = 5.8 Hz, 0.7H), 7.14 (d, *J* = 4.5 Hz, 0.3H), 6.75 (d, *J* = 8.9 Hz, 0.3H), 6.61 (d, *J* = 8.9 Hz, 0.7H), 4.60 (t, *J* = 4.5 Hz, 0.7H), 4.51 (d, *J* = 4.8 Hz, 0.3H), 3.99 – 3.90 (m, 0.6H), 3.89 – 3.77 (m, 1.4H), 2.60 (s, 0.9H), 2.23 (s, 2.1H), 1.99 (dd, *J* = 12.6, 7.6 Hz, 1H), 1.83 – 1.21 (m, 5H).

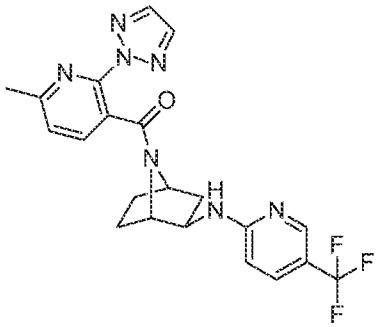
Example 188: (±)-(5-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Prepared analogous to Example 187 substituting intermediate A-21 with intermediate A-19. MS (ESI) mass calcd. for $C_{21}H_{20}F_3N_7O$, 443.2; m/z found 444.1 $[M+H]^+$. ^{1}H NMR ($CDCl_3$): 8.49 – 8.44 (dd, J = 1.9, 0.9 Hz, 0.2H), 8.41 – 8.32 (m, 1H), 8.28 – 8.21 (m, 0.8H), 8.18 – 8.11 (m, 0.2H), 8.06 – 7.98 (m, 0.8H), 7.94 – 7.86 (m, 2H), 7.60 – 7.53 (dd, J = 8.8, 2.4 Hz, 0.2H), 7.45 – 7.35 (dd, J = 8.9, 2.4 Hz, 0.8H), 6.71 – 6.59 (d, J = 8.7 Hz, 0.8H), 6.45 – 6.37 (d, J = 8.8 Hz, 0.2H), 6.27 – 6.17 (d, J = 8.8 Hz, 0.8H), 5.82 – 5.72 (m, 0.2H), 4.95 – 4.84 (t, J = 4.6 Hz, 0.8H), 4.82 – 4.74 (d, J = 5.2 Hz, 0.2H), 4.36 – 4.18 (m, 1H), 4.08 – 3.97 (m, 1H), 2.51 – 2.47 (s,

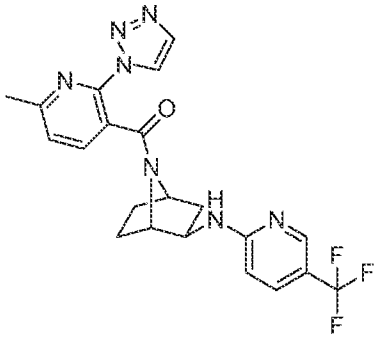
0.7H), 2.45 – 2.41 (m, 2.3H), 2.22 – 2.14 (dd, J = 13.0, 7.7 Hz, 0.8H), 2.11 – 1.90 (m, 2.2H), 1.82 – 1.40 (m, 3H).

Example 189: (±)-(6-methyl-2-(2H-1,2,3-triazol-2-yl)pyridin-3-yl)(2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Prepared analogous to Example 187 substituting intermediate A-21 with intermediate A-3. MS (ESI) mass calcd. for $C_{21}H_{20}F_3N_7O$, 443.2; m/z found 444.1 $[M+H]^+$. ^1H NMR ($CDCl_3$): 8.40 – 8.33 (s, 0.4H), 8.26 – 8.19 (d, J = 2.0 Hz, 0.6H), 7.98 – 7.88 (m, 2H), 7.78 – 7.71 (d, J = 7.7 Hz, 0.4H), 7.64 – 7.55 (m, 1H), 7.41 – 7.27 (m, 1.6H), 7.20 – 7.08 (m, 0.7H), 6.43 – 6.35 (d, J = 8.8 Hz, 0.3H), 6.13 – 6.01 (d, J = 8.7 Hz, 0.7H), 5.74 – 5.56 (m, 0.3H), 4.90 – 4.81 (m, 0.7H), 4.78 – 4.71 (d, J = 5.3 Hz, 0.3H), 4.38 – 4.14 (m, 1H), 3.99 – 3.85 (m, 1H), 2.78 – 2.55 (m, 3H), 2.24 – 2.10 (dd, J = 13.2, 7.9 Hz, 1H), 2.08 – 1.39 (m, 5H).

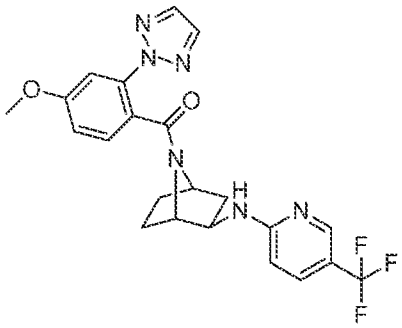
Example 190: (±)-(6-methyl-2-(1H-1,2,3-triazol-1-yl)pyridin-3-yl)(2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Prepared analogous to Example 187 substituting intermediate A-21 with intermediate A-4. MS (ESI) mass calcd. for $C_{21}H_{20}F_3N_7O$, 443.2; m/z found 444.1 $[M+H]^+$. ^1H NMR ($CDCl_3$): 8.50 – 8.46 (m, 0.6H), 8.37 – 8.34 (d, J = 1.2 Hz, 0.4H), 8.34 – 8.31 (s, 0.6H), 8.24 – 8.17 (s, 0.4H), 7.90 – 7.84 (m, 1H), 7.75 – 7.69 (d, J = 7.7 Hz, 0.6H), 7.65 – 7.60 (d, J = 7.8 Hz, 0.4H), 7.55 – 7.47 (dd, J = 8.7, 2.4 Hz, 0.7H), 7.36 – 7.27 (m, 1.3H), 7.22 – 7.14 (m, 0.4H), 6.94 – 6.83

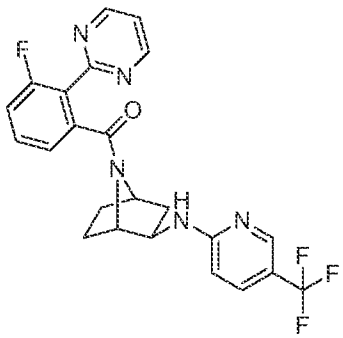
(d, J = 8.7 Hz, 0.6H), 6.29 – 6.11 (d, J = 8.9 Hz, 1H), 4.91 – 4.74 (d, J = 5.3 Hz, 1H), 4.55 – 4.28 (m, 1H), 4.04 – 3.90 (m, 1H), 2.66 – 2.62 (s, 1.9H), 2.59 – 2.55 (s, 1.1H), 2.23 – 2.15 (dd, J = 13.1, 8.1 Hz, 0.5H), 2.06 – 1.79 (m, 2.5H), 1.77 – 1.68 (m, 1H), 1.55 – 1.47 (m, 2H).

Example 191: (±)-(4-methoxy-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Prepared analogous to Example 187 substituting intermediate A-21 with intermediate A-5. MS (ESI) mass calcd. for $C_{22}H_{21}F_3N_6O_2$, 458.2; m/z found 459.1 $[M+H]^+$. ^1H NMR ($CDCl_3$): 8.38 – 8.32 (s, 0.3H), 8.26 – 8.19 (s, 0.7H), 7.93 – 7.87 (s, 1.3H), 7.87 – 7.80 (s, 0.7H), 7.60 – 7.53 (m, 0.4H), 7.49 – 7.43 (d, J = 2.5 Hz, 0.4H), 7.40 – 7.26 (m, 2.7H), 7.00 – 6.93 (dd, J = 8.5, 2.5 Hz, 0.4H), 6.90 – 6.80 (d, J = 8.4 Hz, 0.7H), 6.43 – 6.35 (d, J = 8.7 Hz, 0.4H), 6.12 – 6.04 (d, J = 8.8 Hz, 0.7H), 5.77 – 5.67 (m, 0.3H), 4.84 – 4.79 (m, 0.7H), 4.74 – 4.68 (m, 0.3H), 4.36 – 4.15 (m, 1H), 4.02 – 3.95 (m, 1H), 3.94 – 3.87 (s, 1H), 3.87 – 3.81 (s, 2H), 2.20 – 2.11 (dd, J = 13.0, 8.0 Hz, 0.7H), 2.07 – 1.99 (dd, J = 12.9, 7.6 Hz, 0.3H), 1.99 – 1.83 (s, 2H), 1.79 – 1.34 (m, 3H).

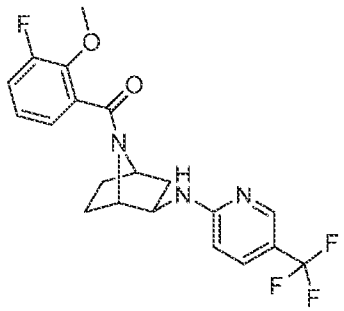
Example 192: (±)-(3-fluoro-2-(pyrimidin-2-yl)phenyl)(2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Prepared analogous to Example 187 substituting intermediate A-21 with intermediate A-6. MS (ESI) mass calcd. for $C_{23}H_{19}F_4N_5O$, 457.2; m/z found 458.1 $[M+H]^+$. ^1H NMR ($CDCl_3$):

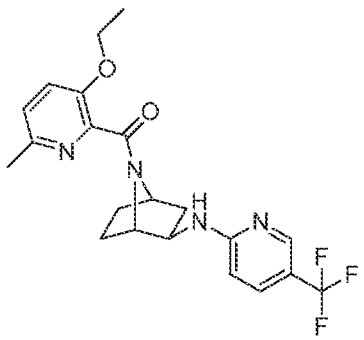
8.91 - 8.76 (m, 2H), 8.36 - 8.18 (m, 1H), 7.68 - 7.52 (m, 1H), 7.40 - 7.27 (m, 3H), 7.24 - 7.14 (m, 2H), 6.29 - 6.15 (m, 1H), 4.78 - 4.66 (t, J = 4.9 Hz, 1H), 4.44 - 4.30 (m, 1H), 4.16 - 4.02 (d, J = 5.0 Hz, 1H), 2.19 - 2.11 (dd, J = 12.9, 8.2 Hz, 1H), 2.08 - 1.97 (m, 1H), 1.97 - 1.85 (m, 1H), 1.77 - 1.60 (m, 2H), 1.54 - 1.49 (m, 1H).

Example 193: (±)-((3-fluoro-2-methoxyphenyl)(2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Prepared analogous to Example 187 substituting intermediate A-21 with 3-fluoro-2-methoxybenzoic acid. MS (ESI) mass calcd. for $C_{20}H_{19}F_4N_3O_2$, 409.1; m/z found 410.4 $[M+H]^+$. ^{1}H NMR (MeOD): 8.39 (s, 0.3H), 8.18 (s, 0.7H), 7.69 (dd, *J* = 8.9, 2.3 Hz, 0.3H), 7.60 (dd, *J* = 8.9, 2.4 Hz, 0.7H), 7.36 (ddd, *J* = 11.7, 7.6, 2.1 Hz, 0.3H), 7.30 – 7.05 (m, 2.3H), 7.01 (d, *J* = 7.6 Hz, 0.7H), 6.85 – 6.73 (m, 0.7H), 6.68 (d, *J* = 8.8 Hz, 0.3H), 6.59 (d, *J* = 8.9 Hz, 0.7H), 4.66 (br s, 0.7H), 4.54 (d, *J* = 4.8 Hz, 0.3H), 4.00 – 3.90 (m, 0.3H), 3.89 – 3.77 (m, 3.7H), 3.75 (t, *J* = 4.3 Hz, 0.3H), 3.64 (br s, 0.7H), 2.08 – 1.91 (m, 1H), 1.80 – 1.37 (m, 5H).

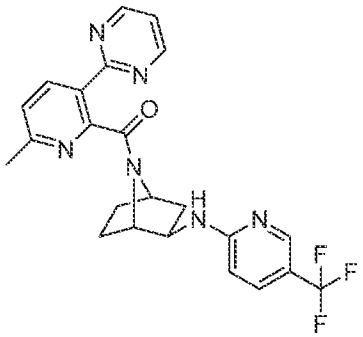
Example 194: (±)-(3-ethoxy-6-methylpyridin-2-yl)(2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Prepared analogous to Example 187 substituting intermediate A-21 with intermediate A-8. MP=147 °C. ^{1}H NMR (DMSO-D_6): 8.38 (s, 0.3H), 8.16 (s, 0.7H), 7.68 (dd, *J* = 8.9, 2.3 Hz, 0.3H), 7.59 (dd, *J* = 8.9, 2.4 Hz, 0.7H), 7.46 (d, *J* = 8.6 Hz, 0.3H), 7.36 – 7.18 (m, 2H), 7.05 (d, *J*

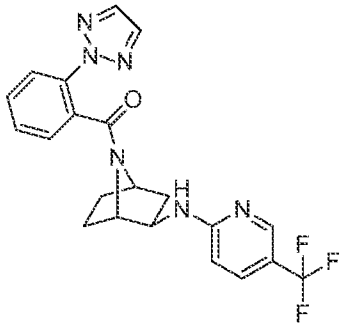
= 8.6 Hz, 0.7H), 6.71 (d, *J* = 8.9 Hz, 0.3H), 6.57 (d, *J* = 8.9 Hz, 0.7H), 4.65 (br s, 0.7H), 4.55 (d, *J* = 2.8 Hz, 0.3H), 4.13 – 3.84 (m, 2.3H), 3.83 – 3.72 (m, 0.7H), 3.67 (d, *J* = 3.5 Hz, 1H), 2.41 (s, 0.9H), 2.16 (s, 2.1H), 2.04 – 1.91 (m, 1H), 1.80 – 1.37 (m, 5H), 1.31 – 1.19 (m, 3H).

Example 195: (±)-(6-methyl-3-(pyrimidin-2-yl)pyridin-2-yl)(2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Prepared analogous to Example 187 substituting intermediate A-21 with intermediate A-9. MS (ESI) mass calcd. for $C_{23}H_{21}F_3N_6O$, 454.2; m/z found 455 $[M+H]^+$. ^1H NMR (DMSO-D_6): 8.95 – 8.81 (m, 2H), 8.37 (s, 0.3H), 8.32 (d, *J* = 8.0 Hz, 0.3H), 8.25 – 8.13 (m, 1.4H), 7.68 (dd, *J* = 8.8, 2.1 Hz, 0.3H), 7.60 (dd, *J* = 8.9, 2.2 Hz, 0.7H), 7.52 – 7.39 (m, 2H), 7.30 (d, *J* = 8.1 Hz, 0.7H), 7.25 (d, *J* = 3.7 Hz, 0.3H), 6.75 (d, *J* = 8.8 Hz, 0.3H), 6.54 (d, *J* = 8.9 Hz, 0.7H), 4.61 (t, *J* = 4.2 Hz, 0.7H), 4.51 (d, *J* = 4.2 Hz, 0.3H), 4.01 – 3.82 (m, 2H), 2.58 (s, 0.9H), 2.24 (s, 2.1H), 2.07 – 1.95 (m, 1H), 1.86 – 1.32 (m, 5H).

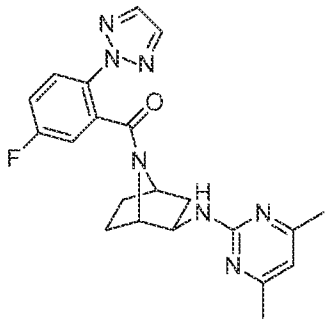
Example 196: (±)-(2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Prepared analogous to Example 187 substituting intermediate A-21 with intermediate A-1. MS (ESI) mass calcd. for $C_{21}H_{19}F_3N_6O$, 428.2; m/z found 409.2 $[M+H]^+$. ^1H NMR (MeOD): 8.38 (s, 0.3H), 8.16 (s, 0.7H), 8.08 (s, 2H), 7.85 (d, *J* = 7.2 Hz, 0.3H), 7.74 – 7.53 (m, 3H), 7.46 – 7.35 (m, 1.3H), 7.31 (d, *J* = 6.1 Hz, 0.7H), 7.14 (t, *J* = 7.5 Hz, 0.7H), 6.68 (d, *J* = 8.9 Hz,

0.3H), 6.62 (d, J = 8.9 Hz, 0.7H), 4.57 (t, J = 4.5 Hz, 0.7H), 4.41 (d, J = 4.8 Hz, 0.3H), 4.04 – 3.95 (m, 0.3H), 3.88 – 3.76 (m, 1H), 3.55 (br s, 0.7H), 1.97 (dd, J = 12.7, 8.0 Hz, 1H), 1.79 – 1.23 (m, 5H).

Example 197: (±)-(2-((4,6-dimethylpyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(5-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone.



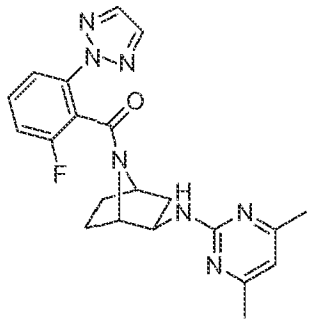
Step A: (±)-tert-butyl 2-((4,6-dimethylpyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptane-7-carboxylate. To a microwave vial was weighed intermediate B-6 (210 mg, 1 mmol), 2-chloro-4,6-dimethylpyrimidine (212 mg, 1.5 mmol), sodium tert-butoxide (142 mg, 1.5 mmol), $Pd(dba)_2$ (28 mg, 5 mol%), Ctc-Q-Phos (44 mg, 10 mol). The vial was capped, evacuated and refilled with N_2 (2X). Then PhCH3 (1 mL) was added and the reaction was heated at 125 °C for 4h. The reaction allowed to cool to rt, applied directly purified via silica gel chromatography 1-7% 2M NH3/MeOH in DCM to give P1 (125 mg, 40%). MS (ESI) mass calcd. for $C_{17}H_{26}N_4O_2$, 318.2; m/z found 319.3 $[M+H]^+$ ^{1}H NMR ($CDCl_3$): 6.31 (s, 1H), 5.18 – 4.94 (m, 1H), 4.35 – 4.13 (m, 2H), 4.08 (td, J = 7.9, 3.2 Hz, 1H), 2.27 (s, 6H), 1.97 (dd, J = 12.9, 7.8 Hz, 1H), 1.82 – 1.62 (m, 2H), 1.62 – 1.30 (m, 12H).

Step B: (±)-N-(4,6-dimethylpyrimidin-2-yl)-7-azabicyclo[2.2.1]heptan-2-amine. To the title compound of step A (125 mg, 0.4 mmol) in DCM (3 mL) was added TFA (3 mL). After starting material was consumed, the reaction was concentrated, neutralized with 5% Na_2CO_3 and extracted with DCM. The combined organics were dried (Na_2SO_4) to give the title compound that was used in subsequent reactions without further purification. MS (ESI) mass calcd. for $C_{12}H_{18}N_4$, 218.2; m/z found 219.2 $[M+H]^+$.

Step C: (±)-(2-((4,6-dimethylpyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(5-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone. Prepared analogous to Example 181 substituting intermediate A-1 with intermediate A-10 and (1S,2R,4R)-N-(5-(trifluoromethyl)pyrazin-2-yl)-7-azabicyclo[2.2.1]heptan-2-amine with the title compound of step B. MS (ESI) mass calcd. for $C_{21}H_{22}FN_7O$, 407.2; m/z found 408.2 $[M+H]^+$. ^{1}H NMR

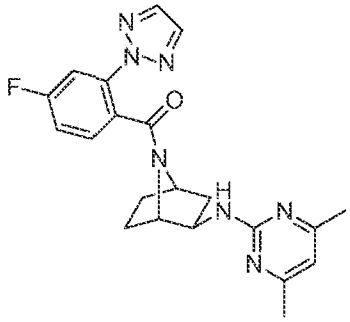
($CDCl_3$): 8.23 – 7.67 (m, 2.5H), 7.54 – 6.93 (m, 2.5H), 6.40 – 6.19 (m, 1H), 4.89 – 4.65 (m, 1H), 4.41 – 3.66 (m, 2H), 2.39 – 1.34 (m, 12H).

Example 198: (±)-(2-((4,6-dimethylpyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(2-fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl)methanone.



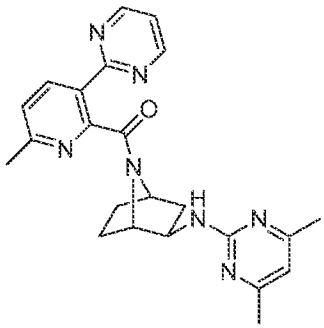
Prepared analogous to Example 197 substituting intermediate A-10 with intermediate A-11. MS (ESI) mass calcd. for $C_{21}H_{22}FN_7O$, 407.2; m/z found 408.2 $[M+H]^+$.

Example 199: (±)-(2-((4,6-dimethylpyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(4-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone.



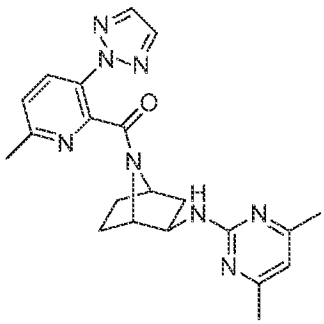
Prepared analogous to Example 197 substituting intermediate A-10 with intermediate A-12. MS (ESI) mass calcd. for $C_{21}H_{22}FN_7O$, 407.2; m/z found 408.2 $[M+H]^+$. ^1H NMR (MeOD): 8.23 – 7.33 (m, 4H), 7.22 – 6.75 (m, 1H), 6.42 – 6.21 (m, 1H), 4.91 – 4.73 (m, 1H), 4.44 – 4.01 (m, 1H), 3.97 – 3.71 (m, 1H), 2.41 – 1.30 (m, 12H).

Example 200: (±)-(2-((4,6-dimethylpyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(pyrimidin-2-yl)pyridin-2-yl)methanone.



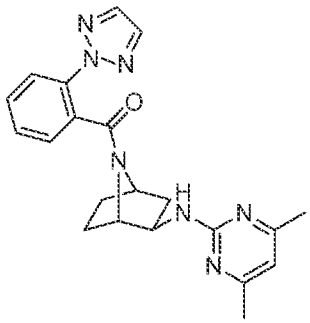
Prepared analogous to Example 187 substituting 2-chloro-5-(trifluoromethyl)pyridine with 2-chloro-4,6-dimethylpyrimidine and intermediate A-21 with intermediate A-9. MS (ESI) mass calcd. for $C_{23}H_{25}N_7O$, 415.2; m/z found 416 $[M+H]^+$. ^1H NMR (DMSO-D_6): 9.05 (d, J = 4.9 Hz, 0.6H), 8.90 (d, J = 4.9 Hz, 1.4H), 8.37 (d, J = 8.1 Hz, 0.3H), 8.28 (d, J = 8.0 Hz, 0.7H), 7.57 – 7.45 (m, 1.3H), 7.41 (d, J = 8.1 Hz, 0.7H), 7.09 (d, J = 7.8 Hz, 0.7H), 6.46 (s, 0.3H), 6.43 – 6.29 (m, 1H), 4.62 (br s, 0.7H), 4.51 (d, J = 4.4 Hz, 0.3H), 4.15 – 3.97 (m, 1H), 3.97 – 3.92 (m, 0.3H), 3.89 (d, J = 3.7 Hz, 0.7H), 2.59 (s, 0.9H), 2.50 (s, 2.1H), 2.26 (s, 1.8H), 2.14 (s, 4.2H), 2.05 (dd, J = 12.5, 7.6 Hz, 1H), 1.99 – 1.37 (m, 5H).

Example 201: (±)-(2-((4,6-dimethylpyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)methanone.



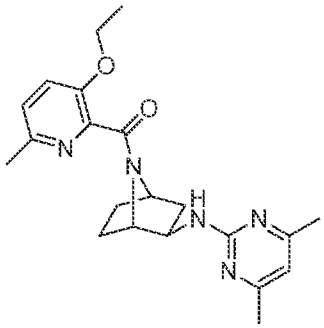
Prepared analogous to Example 200 substituting intermediate A-9 with intermediate A-21. MP=171.9 °C. ^1H NMR (DMSO-D_6): 8.28 – 8.17 (m, 1.2H), 8.17 – 8.09 (m, 1.8H), 7.57 (d, J = 8.4 Hz, 0.4H), 7.46 (d, J = 8.4 Hz, 0.6H), 6.89 (d, J = 7.0 Hz, 0.6H), 6.46 (s, 0.4H), 6.42 (d, J = 7.5 Hz, 0.4H), 6.35 (s, 0.6H), 4.59 (t, J = 4.2 Hz, 0.6H), 4.50 (d, J = 4.9 Hz, 0.4H), 4.08 (td, J = 7.8, 3.0 Hz, 0.4H), 4.00 – 3.86 (m, 1.6H), 2.60 (s, 1.2H), 2.45 (s, 1.8H), 2.26 (s, 2.4H), 2.15 (s, 3.6H), 1.97 (ddd, J = 16.3, 12.6, 7.9 Hz, 1H), 1.83 – 1.35 (m, 5H).

Example 202: (±)-(2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((4,6-dimethylpyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



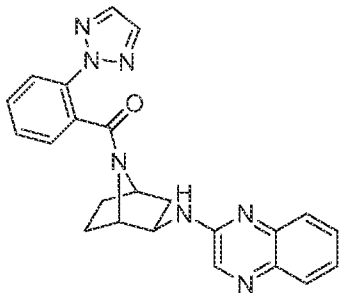
Prepared analogous to Example 200 substituting intermediate A-9 with intermediate A-1. MP=154.2 °C. ^{1}H NMR (DMSO-D_6): 8.12 (s, 1H), 8.07 (s, 1H), 7.85 (d, J = 7.7 Hz, 0.5H), 7.77 (d, J = 6.8 Hz, 0.5H), 7.72 – 7.61 (m, 1H), 7.58 (dd, J = 10.7, 4.2 Hz, 0.5H), 7.49 – 7.39 (m, 1H), 7.15 (t, J = 7.5 Hz, 0.5H), 6.99 (d, J = 6.1 Hz, 0.5H), 6.87 (br s, 0.5H), 6.43 (s, 0.5H), 6.33 (s, 0.5H),), 4.51 (t, J = 4.1 Hz, 0.5H), 4.37 (d, J = 3.9 Hz, 0.5H), 4.12 – 3.97 (m, 0.5H), 3.88 – 3.72 (m, 1H), 3.68 (d, J = 4.4 Hz, 0.5H), 2.24 (s, 3H), 2.15 (s, 3H), 1.97 – 1.21 (m, 6H).

Example 203: (±)-(2-((4,6-dimethylpyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-ethoxy-6-methylpyridin-2-yl)methanone.



Prepared analogous to Example 200 substituting intermediate A-9 with intermediate A-8. MS (ESI) mass calcd. for $C_{21}H_{27}N_5O_2$, 381.2; m/z found 382.5 $[M+H]^+$. MP=137.8 °C. ^{1}H NMR (DMSO-D_6): 7.20 – 7.01 (m, 2H), 6.45 (d, J = 8.5 Hz, 0.7H), 6.31 (s, 0.3H), 6.24 (s, 0.7H), 5.31 (d, J = 8.6 Hz, 0.3H), 4.91 (t, J = 4.5 Hz, 0.7H), 4.80 (d, J = 5.1 Hz, 0.3H), 4.32 – 4.14 (m, 1.7H), 4.14 – 3.98 (m, 1.3H), 3.80 (t, J = 4.7 Hz, 0.3H), 3.75 (d, J = 4.6 Hz, 0.7H), 2.53 (s, 2.1H), 2.49 (s, 0.9H), 2.26 (s, 1.8H), 2.22 (s, 4.2H), 2.20 – 2.08 (m, 1H), 2.05 – 1.49 (m, 5H), 1.48 – 1.40 (m, 3H).

Example 204: (±)-(2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(quinoxalin-2-ylamino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.

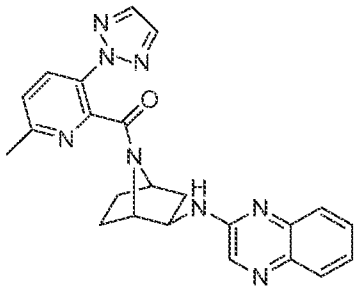


Step A: (±)-tert-butyl 2-(quinoxalin-2-ylamino)-7-azabicyclo[2.2.1]heptane-7-carboxylate. To intermediate B-6 (500 mg, 2.4 mmol) in dry DMA (7 mL) was added K_2CO_3 (650 mg, 4.7 mmol) and 2-chloroquinoxaline (580 mg, 3.5 mmol). After heating at 80 °C for 48h, the mixture was cooled to rt and saturated $NaHCO_3$ (aq) was added. The mixture was extracted with EtOAc (3X). The combined organics were washed with brine and dried ($MgSO_4$). Purification via silica gel chromatography (0-25% EtOAc in heptanes) gave the title compound. MS (ESI) mass calcd. for $C_{19}H_{24}N_4O_2$, 340.2; m/z found 341.0 $[M+H]^+$.

Step B: N-((±)-7-azabicyclo[2.2.1]heptan-2-yl)quinoxalin-2-amine hydrochloride. To the title compound from step A (343 mg, 1 mmol) in 1,4-dioxane (10 mL) was added 6N HCl in iPrOH (1 mL). The reaction was heated to 70 °C for 2h, cooled to rt, concentrated and used without further purification in subsequent steps.

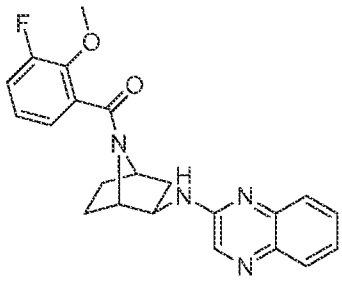
Step C: (±)-(2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(quinoxalin-2-ylamino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone. Prepared analogous to Example 187 substituting intermediate A-21 with intermediate A-1 and (±)-N-(5-(trifluoromethyl)pyridin-2-yl)-7-azabicyclo[2.2.1]heptan-2-amine hydrochloride with the title compound from step B. MS (ESI) mass calcd. for $C_{23}H_{21}N_7O$, 411.2; m/z found 412 $[M+H]^+$. ^1H NMR (DMSO-D_6): 8.38 (s, 0.3H), 8.31 (s, 0.7H), 8.08 (s, 2H), 7.88 – 7.73 (m, 1.3H), 7.72 – 7.20 (m, 7H), 7.14 – 7.04 (m, 0.7H), 4.60 (t, J = 4.4 Hz, 0.7H), 4.54 (d, J = 4.7 Hz, 0.3H), 4.15 – 4.03 (m, 0.3H), 3.97 – 3.87 (m, 0.7H), 3.82 (t, J = 3.9 Hz, 0.3H), 3.65 (d, J = 3.2 Hz, 0.7H), 2.12 – 1.96 (m, 1H), 1.84 – 1.28 (m, 5H).

Example 205: (±)-(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-(quinoxalin-2-ylamino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



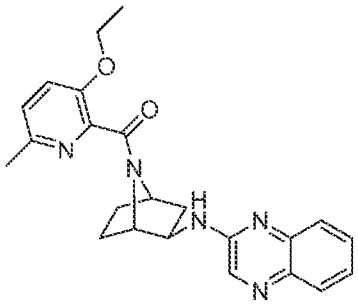
Prepared analogous to Example 204 substituting with intermediate A-1 with intermediate A-21. MP=260.8 °C. ^{1}H NMR (DMSO-D_6): 8.44 (s, 0.3H), 8.32 (s, 0.7H), 8.19 (d, J = 8.4 Hz, 0.3H), 8.13 (s, 2H), 7.96 (d, J = 8.3 Hz, 0.7H), 7.83 – 7.72 (m, 1H), 7.68 – 7.27 (m, 4.3H), 7.19 (d, J = 8.4 Hz, 0.7H), 4.64 (br s, 1H), 4.06 – 3.86 (m, 2H), 2.61 (s, 0.9H), 2.09 (s, 2.1H), 2.06 – 1.99 (m, 1H), 1.88 – 1.62 (m, 2H), 1.62 – 1.38 (m, 3H).

Example 206: (±)-(3-fluoro-2-methoxyphenyl)(2-(quinoxalin-2-ylamino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



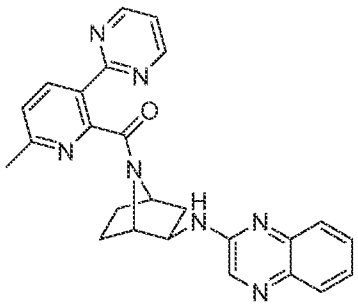
Prepared analogous to Example 204 substituting intermediate A-1 with 3-fluoro-2-methoxybenzoic acid. MP=179.2 °C. ^{1}H NMR (DMSO-D_6): 8.38 (s, 0.3H), 8.27 (s, 0.7H), 7.80 (d, J = 8.0 Hz, 0.3H), 7.73 (d, J = 8.0 Hz, 0.7H), 7.65 – 7.52 (m, 1.4H), 7.52 – 7.28 (m, 2.7H), 7.28 – 7.15 (m, 0.7H), 7.09 (d, J = 7.6 Hz, 0.7H), 6.96 (ddd, J = 11.7, 8.2, 1.4 Hz, 0.7H), 6.75 (td, J = 7.9, 4.8 Hz, 0.7H), 4.75 – 4.63 (m, 1H), 4.11 – 4.01 (m, 0.4H), 3.99 – 3.90 (m, 0.7H), 3.86 (br s, 0.9H), 3.83 – 3.73 (m, 2.1H), 2.06 (dt, J = 16.7, 8.4 Hz, 1H), 1.87 – 1.45 (m, 6H).

Example 207: (±)-(3-ethoxy-6-methylpyridin-2-yl)(2-(quinoxalin-2-ylamino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



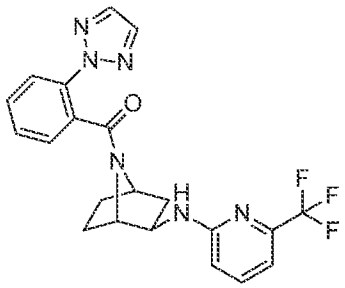
Prepared analogous to Example 204 substituting with intermediate A-1 with intermediate A-8. MS (ESI) mass calcd. for $C_{23}H_{25}N_5O_2$, 403.2; m/z found 404 [M+H]+. MP=184.9 C. ^{1}H NMR (DMSO-D_6): 8.41 (s, 0.3H), 8.26 (s, 0.7H), 7.79 (d, J = 8.1 Hz, 0.3H), 7.72 (d, J = 8.0 Hz, 0.7H), 7.64 – 7.53 (m, 1.7H), 7.50 – 7.22 (m, 2.9H), 7.18 (d, J = 8.6 Hz, 0.7H), 6.86 (d, J = 8.6 Hz, 0.7H), 4.68 (br s, 1H), 4.12 – 3.83 (m, 3H), 3.79 (d, J = 4.1 Hz, 0.7H), 3.71 (br s, 0.3H), 2.41 (s, 0.9H), 2.11 – 1.96 (m, 3.1H), 1.89 – 1.42 (m, 5H), 1.25 (t, J = 6.9 Hz, 3H).

Example 208: (±)-(6-methyl-3-(pyrimidin-2-yl)pyridin-2-yl)(2-(quinoxalin-2-ylamino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Prepared analogous to Example 204 substituting with intermediate A-1 with intermediate A-9. MS (ESI) mass calcd. for $C_{25}H_{23}N_7O$, 437.2; m/z found 438 $[M+H]^+$. ^{1}H NMR (DMSO-D_6): 8.93 – 8.82 (m, 2H), 8.46 (s, 0.3H), 8.33 (d, J = 8.1 Hz, 0.3H), 8.27 (s, 0.7H), 8.14 (d, J = 8.0 Hz, 0.7H), 7.81 – 7.26 (m, 6.3H), 7.17 (d, J = 8.1 Hz, 0.7H), 4.66 (br s, 1H), 4.06 – 3.94 (m, 2H), 2.60 (s, 0.9H), 2.13 – 2.01 (m, 3.1H), 1.92 – 1.36 (m, 5H).

Example 209: (±)-(2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((6-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.

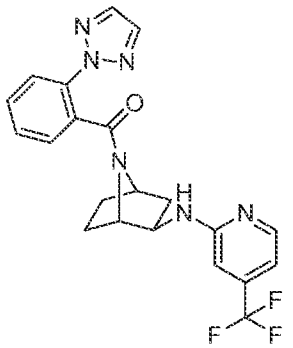


Step A: (±)-tert-butyl-2-((6-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptane-7-carboxylate. To 2-chloro-6-(trifluoromethyl)pyridine (113 mg, 0.6 mmol) in THF (3 mL) was added sodium tert-butoxide (120 mg, 1.2 mmol), Xanphos (26 mg, 7 mol%) and $Pd_2(dba)_3$ (23 mg, 4 mol%) at rt while N_2 was bubbled through the solution. After 10 minutes, intermediate B-6 (132 mg, 0.6 mmol) was added. The reaction mixture was heated at 90 °C for 3h. After allowing to cool to rt, saturated $NaHCO_3$ (aq) the mixture extracted with EtOAc (2X). The combined organics were dried ($MgSO_4$). Purification via silica gel chromatography (0-7% EtOAc in heptane) gave the title compound. MS (ESI) mass calcd. for $C_{17}H_{22}F_3N_3O_2$, 357.2; m/z found 358.4 $[M+H]^+$.

Step B: (±)-N-(6-(trifluoromethyl)pyridin-2-yl)-7-azabicyclo[2.2.1]heptan-2-amine hydrochloride. Prepared analogous to Example 204 substituting (±)-tert-butyl 2-(quinoxalin-2-ylamino)-7-azabicyclo[2.2.1]heptane-7-carboxylate with the title compound of step A.

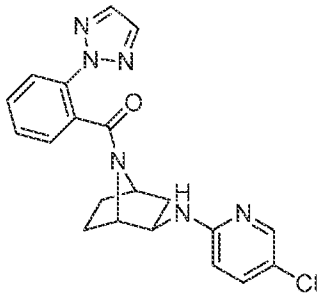
Step C: (±)-tert-butyl-2-((6-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptane-7-carboxylate. Prepared analogous to Example 204 substituting N-((±)-7-azabicyclo[2.2.1]heptan-2-yl)quinoxalin-2-amine hydrochloride with the title compound of step B. MS (ESI) mass calcd. for $C_{21}H_{19}F_3N_6O$, 428.2; m/z found 429. $[M+H]^+$. MP=96.8 °C. ^1H NMR (DMSO-D_6): 8.07 (s, 2H), 7.85 (d, J = 7.9 Hz, 0.3H), 7.74 – 7.51 (m, 2.7H), 7.46 – 7.36 (m, 1.3H), 7.17 – 6.94 (m, 2H), , 6.86 (d, J = 7.2 Hz, 0.7H), 6.82 (d, J = 8.6 Hz, 0.3H), 6.74 (d, J = 8.4 Hz, 0.7H), 4.55 (t, J = 4.5 Hz, 0.7H), 4.41 (d, J = 4.6 Hz, 0.3H), 3.94 – 3.84 (m, 0.3H), 3.84 – 3.71 (m, 1H), 3.61 (d, J = 4.6 Hz, 0.7H), 1.96 (dd, J = 12.6, 8.0 Hz, 1H), 1.80 – 1.21 (m, 5H).

Example 210: (±)-((2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((4-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



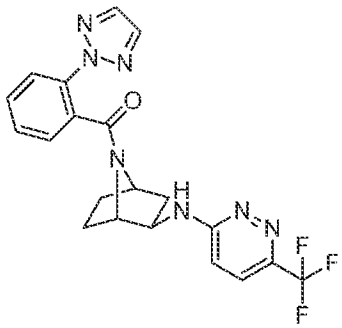
Prepared analogous to Example 209 substituting 2-chloro-6-(trifluoromethyl)pyridine with 2-chloro-4-(trifluoromethyl)pyridine. MP=153.5 °C. MS (ESI) mass calcd. for $C_{21}H_{19}F_3N_6O$, 428.2; m/z found 429 $[M+H]^+$. ^1H NMR (DMSO-D_6): 8.27 (d, J = 5.3 Hz, 0.3H), 8.12 – 7.99 (m, 2.7H), 7.85 (d, J = 7.9 Hz, 0.3H), 7.72 – 7.54 (m, 1.6H), 7.50 – 7.33 (m, 1.4H), 7.13 – 6.92 (m, 2H), 6.82 (d, J = 12.6 Hz, 0.3H), 6.78 (s, 0.7H), 6.67 (d, J = 5.3 Hz, 0.7H), 4.56 (t, J = 4.5 Hz, 0.7H), 4.41 (d, J = 4.6 Hz, 0.3H), 4.04 – 3.93 (m, 0.3H), 3.86 – 3.72 (m, 1H), 3.52 (br s, 0.7H), 1.96 (dd, J = 12.6, 8.0 Hz, 1H), 1.78 – 1.17 (m, 5H).

Example 211: (±)-(2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((5-chloropyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



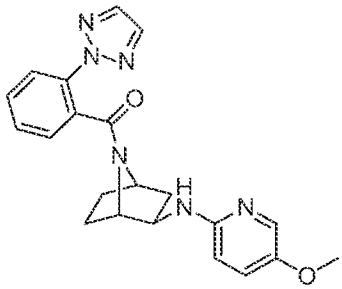
Prepared analogous to Example 209 substituting 2-chloro-6-(trifluoromethyl)pyridine with 5-chloro-2-iodopyridine. MS (ESI) mass calcd. for $C_{20}H_{19}ClN_6O$, 394.1; m/z found 395 $[M+H]^+$. MP=157.0 °C. ^1H NMR (DMSO-D_6): 8.14 – 7.99 (m, 2.3H), 7.87 – 7.79 (m, 1H), 7.71 – 7.52 (m, 1.7H), 7.52 – 7.36 (m, 2.6H), 7.23 – 7.11 (m, 0.7H), 6.80 (d, J = 6.4 Hz, 0.7H), 6.58 (d, J = 9.0 Hz, 0.3H), 6.52 (d, J = 8.9 Hz, 0.7H), 4.53 (t, J = 4.6 Hz, 0.7H), 4.37 (d, J = 4.6 Hz, 0.3H), 3.92 – 3.82 (m, 0.3H), 3.81 – 3.68 (m, 1H), 3.52 (d, J = 4.3 Hz, 0.7H), 1.94 (dd, J = 12.5, 8.1 Hz, 1H), 1.73 – 1.22 (m, 5H).

Example 212: (±)-(2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((6-(trifluoromethyl)pyridazin-3-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



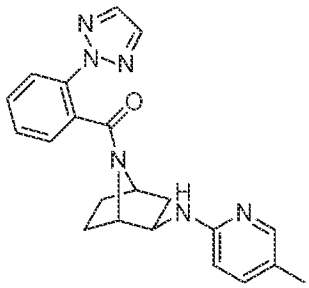
Prepared analogous to Example 209 substituting 2-chloro-6-(trifluoromethyl)pyridine with 3-chloro-6-(trifluoromethyl)pyridazine. MP=134.0 °C. MS (ESI) mass calcd. for $C_{20}H_{18}F_3N_7O$, 429.2; m/z found 430 $[M+H]^+$. ^1H NMR (DMSO-D_6): 8.08 (s, 1.4H), 8.07 (s, 0.6H), 7.85 (d, J = 7.8 Hz, 0.3H), 7.77 – 7.46 (m, 3.6H), 7.44 – 7.31 (m, 1.4H), 7.20 – 7.09 (m, 0.7H), 7.06 (d, J = 9.4 Hz, 0.3H), 6.98 (d, J = 9.3 Hz, 0.7H), 4.59 (t, J = 4.4 Hz, 0.7H), 4.48 (d, J = 4.7 Hz, 0.3H), 3.97 – 3.87 (m, 0.7H), 3.81 (t, J = 4.0 Hz, 0.3H), 3.58 – 3.56 (m, 1H), 2.01 (dd, J = 12.9, 8.0 Hz, 1H), 1.82 – 1.18 (m, 5H).

Example 213: (±)-(2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((5-methoxypyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



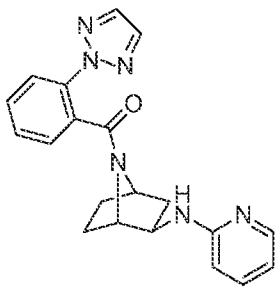
Prepared analogous to Example 209 substituting 2-chloro-6-(trifluoromethyl)pyridine with 2-chloro-5-methoxypyridine. MS (ESI) mass calcd. for $C_{21}H_{22}N_6O_2$, 390.2; m/z found 391 $[M+H]^+$. MP=174.0 °C. ^1H NMR (DMSO-D_6): 8.31 (s, 0.3H), 8.13 – 8.02 (m, 2H), 7.84 (d, J = 8.0 Hz, 0.3H), 7.79 (d, J = 3.0 Hz, 0.3H), 7.71 – 7.61 (m, 1.3H), 7.60 – 7.53 (m, 1H), 7.50 – 7.37 (m, 1.4H), 7.22 – 7.04 (m, 1.7H), 6.52 (d, J = 9.0 Hz, 0.3H), 6.46 (d, J = 9.0 Hz, 0.7H), 6.21 (d, J = 6.9 Hz, 0.7H), 4.52 (t, J = 4.5 Hz, 0.7H), 4.37 (d, J = 4.5 Hz, 0.2H), 3.90 – 3.79 (m, 0.3H), 3.79 – 3.68 (m, 1.9H), 3.64 (s, 2.1H), 3.57 (d, J = 4.0 Hz, 0.7H), 1.98 – 1.84 (m, 1H), 1.76 – 1.21 (m, 5H).

Example 214: (±)-(2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((5-methylpyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



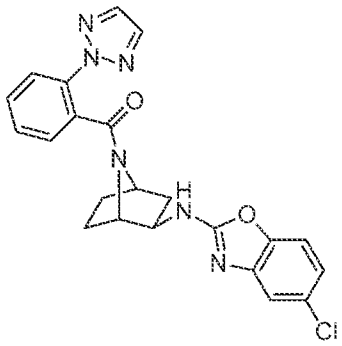
Prepared analogous to Example 209 substituting 2-chloro-6-(trifluoromethyl)pyridine with 2-chloro-5-methylpyridine. MS (ESI) mass calcd. for $C_{21}H_{22}N_6O$, 374.2; m/z found 375.2 $[M+H]^+$. ^1H NMR (DMSO-D_6): 8.32 (s, 0.7H), 8.09 (s, 0.6H), 8.07 (s, 1.4H), 7.89 – 7.80 (m, 0.6H), 7.72 – 7.53 (m, 2.1H), 7.52 – 7.37 (m, 1.3H), 7.27 (dd, J = 8.5, 2.2 Hz, 0.3H), 7.23 – 7.11 (m, 1.3H), 6.47 (d, J = 8.5 Hz, 0.3H), 6.41 (d, J = 8.2 Hz, 0.7H), 6.35 (d, J = 6.9 Hz, 0.7H), 4.53 (t, J = 4.5 Hz, 0.7H), 4.37 (d, J = 4.4 Hz, 0.3H), 3.95 – 3.84 (m, 0.3H), 3.84 – 3.70 (m, 1H), 3.56 (d, J = 4.3 Hz, 0.7H), 2.12 (s, 0.9H), 2.04 (s, 2.1H), 1.99 – 1.86 (m, 1H), 1.78 – 1.24 (m, 5H).

Example 215: (±)-(2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(pyridin-2-ylamino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Prepared analogous to Example 209 substituting 2-chloro-6-(trifluoromethyl)pyridine with 2-iodopyridine. MS (ESI) mass calcd. for $C_{20}H_{20}N_6O$, 360.2; m/z found 361 $[M+H]^+$. MP=167.9 °C. ^1H NMR (DMSO-D_6): 8.12 – 8.00 (m, 2.3H), 7.88 – 7.79 (m, 1H), 7.73 – 7.53 (m, 1.5H), 7.50 – 7.28 (m, 2.5H), 7.13 (t, J = 7.4 Hz, 0.7H), 6.63 – 6.37 (m, 3H), 4.54 (t, J = 4.5 Hz, 0.7H), 4.39 (d, J = 4.4 Hz, 0.3H), 3.92 (td, J = 7.5, 3.2 Hz, 0.3H), 3.86 – 3.73 (m, 1H), 3.58 (d, J = 4.3 Hz, 0.7H), 2.02 – 1.86 (m, 1H), 1.78 – 1.23 (m, 5H).

Example 216: (±)-(2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((5-chlorobenzo[d]oxazol-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.

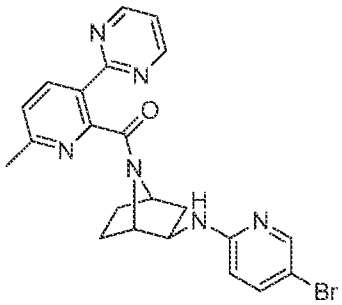


Step A: (±)-tert-butyl 2-((5-chlorobenzo[d]oxazol-2-yl)amino)-7-azabicyclo[2.2.1]heptane-7-carboxylate. To intermediate B-6 (116 mg, 0.6 mmol) in 1,4-dioxane (3 mL) was added DIPEA (190 µL, 1.1 mmol) and 5-chloro-2-(methylsulfinyl)benzo[d]oxazole (235 mg, 1.1 mmol). After heating at 80 °C for 4h, the mixture was cooled to rt and saturated $NaHCO_3$ (aq) was added. The aqueous layer was extracted with EtOAc (3X). The combined organics were dried ($MgSO_4$). Purification via silica gel chromatography (0-10% EtOAc in hexanes) gave the title compound (130 mg, 66%). MS (ESI) mass calcd. for $C_{18}H_{22}ClN_3O_3$, 363.1; m/z found 364.0 $[M+H]^+$.

Step B: N-((±)-7-azabicyclo[2.2.1]heptan-2-yl)-5-chlorobenzo[d]oxazol-2-amine hydrochloride. Prepared analogous to Example 209 substituting (±)-tert-butyl-2-((6-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptane-7-carboxylate with the title compound of step A. MS (ESI) mass calcd. for $C_{13}H_{14}ClN_3O$, 263.1; m/z found 264.0 $[M+H]^+$.

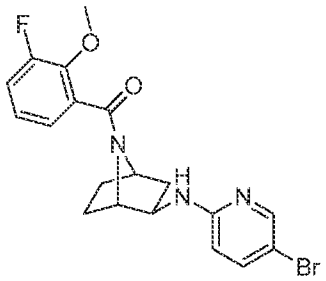
Step C: (±)-(2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((5-chlorobenzo[d]oxazol-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone. Prepared analogous to Example 209 substituting (±)-N-(6-(trifluoromethyl)pyridin-2-yl)-7-azabicyclo[2.2.1]heptan-2-amine hydrochloride with the title compound of step B. MS (ESI) mass calcd. for $C_{22}H_{19}ClN_6O_2$, 434.1; m/z found 435 $[M+H]^+$. ^1H NMR (DMSO-D_6): 8.20 (d, J = 5.6 Hz, 1H), 8.13 – 8.05 (m, 2H), 7.85 (d, J = 7.4 Hz, 0.3H), 7.76 (d, J = 7.3 Hz, 0.3H), 7.72 – 7.55 (m, 1.3H), 7.53 – 7.44 (m, 0.7H), 7.44 – 7.29 (m, 2H), 7.24 (d, J = 2.1 Hz, 0.7H), 7.16 – 7.08 (m, 0.7H), 7.08 – 6.98 (m, 1H), 4.66– 4.47 (m, 1H), 3.97 – 3.86 (m, 0.3H), 3.82 (t, J = 3.9 Hz, 0.3H), 3.79 – 3.66 (m, 1.4H), 2.07 – 1.92 (m, 1H), 1.88 – 1.22 (m, 5H).

Example 217: (±)-(2-((5-bromopyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(pyrimidin-2-yl)pyridin-2-yl)methanone.



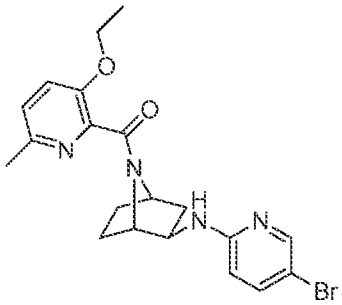
Prepared analogous to Example 209 substituting 2-chloro-6-(trifluoromethyl)pyridine with 5-bromo-2-iodopyridine and intermediate A-1 with intermediate A-9. MS (ESI) mass calcd. for $C_{22}H_{21}BrN_6O$, 464.1; m/z found 466 $[M+H]^+$. MP=221.8 °C. ^{1}H NMR (DMSO-D_6): 8.96 – 8.78 (m, 2H), 8.32 (d, *J* = 8.0 Hz, 0.3H), 8.19 (d, *J* = 8.0 Hz, 0.7H), 8.10 (d, *J* = 2.4 Hz, 0.3H), 7.93 (d, *J* = 2.4 Hz, 0.7H), 7.56 (dd, *J* = 8.9, 2.5 Hz, 0.3H), 7.51 – 7.39 (m, 2H), 7.33 (d, *J* = 8.1 Hz, 0.7H), 6.93 (d, *J* = 7.1 Hz, 0.7H), 6.66 (d, *J* = 5.6 Hz, 0.3H), 6.61 (d, *J* = 9.0 Hz, 0.3H), 6.36 (d, *J* = 8.9 Hz, 0.7H), 4.59 (t, *J* = 4.1 Hz, 0.7H), 4.47 (d, *J* = 4.3 Hz, 0.3H), 3.96 – 3.75 (m, 2H), 2.58 (s, 0.9H), 2.31 (s, 2.1H), 2.07 – 1.91 (m, 1H), 1.88 – 1.30 (m, 5H).

Example 218: (±)-(2-((5-bromopyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-methoxyphenyl)methanone.



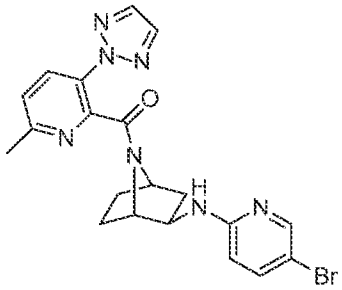
Prepared analogous to Example 217 substituting intermediate A-9 with 3-fluoro-2-methoxybenzoic acid. MS (ESI) mass calcd. for $C_{19}H_{19}BrFN_3O_2$, 419.1; m/z found 420.1 $[M+H]^+$. MP=175.2 °C. ^{1}H NMR (DMSO-D_6): 8.10 (d, *J* = 2.4 Hz, 0.3H), 7.90 (d, *J* = 2.4 Hz, 0.7H), 7.56 (dd, *J* = 8.9, 2.5 Hz, 0.3H), 7.47 (dd, *J* = 8.9, 2.5 Hz, 0.7H), 7.34 (ddd, *J* = 11.7, 7.5, 2.3 Hz, 0.3H), 7.24 – 7.08 (m, 1.3H), 7.02 (d, *J* = 7.6 Hz, 0.7H), 6.87 – 6.66 (m, 1.7H), 6.54 (d, *J* = 8.9 Hz, 0.3H), 6.46 (d, *J* = 8.9 Hz, 0.7H), 4.63 (br s, 0.7H), 4.50 (d, *J* = 4.8 Hz, 0.3H), 3.88 – 3.68 (m, 4.3H), 3.58 (d, *J* = 2.9 Hz, 0.7H), 2.05 – 1.87 (m, 1H), 1.78 – 1.20 (m, 5H).

Example 219: (±)-(2-((5-bromopyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-ethoxy-6-methylpyridin-2-yl)methanone.



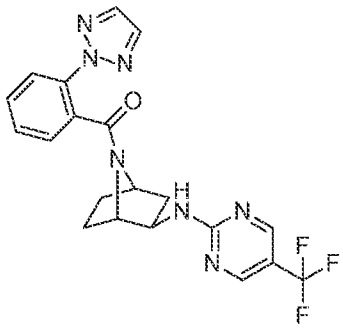
Prepared analogous to Example 217 substituting intermediate A-9 with intermediate A-8. MS (ESI) mass calcd. for $C_{20}H_{23}BrN_4O_2$, 430.1; m/z found 431.1 $[M+H]^+$. MP=134.5 °C. ^1H NMR (DMSO-D_6): 8.10 (d, J = 2.4 Hz, 0.3H), 7.88 (d, J = 2.4 Hz, 0.7H), 7.55 (dd, J = 8.9, 2.5 Hz, 0.3H), 7.50 – 7.41 (m, 1H), 7.30 (d, J = 8.6 Hz, 0.7H), 7.24 (d, J = 8.6 Hz, 0.3H), 7.08 (d, J = 8.6 Hz, 0.7H), 6.76 (d, J = 5.7 Hz, 0.7H), 6.63 (d, J = 5.3 Hz, 0.3H), 6.57 (d, J = 8.9 Hz, 0.3H), 6.43 (d, J = 8.9 Hz, 0.7H), 4.62 (br s, 0.7H), 4.51 (d, J = 2.8 Hz, 0.3H), 4.13 – 3.88 (m, 2H), 3.83 – 3.73 (m, 0.3H), 3.72 – 3.61 (m, 1H), 3.59 (d, J = 3.5 Hz, 0.7H), 2.39 (s, 0.9H), 2.21 (s, 2.1H), 2.02 – 1.85 (m, 1H), 1.75 – 1.33 (m, 5H), 1.25 (td, J = 6.9, 3.6 Hz, 3H).

Example 220: (±)-(2-((5-bromopyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)methanone.



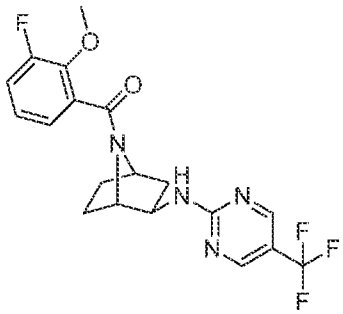
Prepared analogous to Example 217 substituting intermediate A-9 with intermediate A-21. MS (ESI) mass calcd. for $C_{20}H_{20}BrN_7O$, 453.1; m/z found 454.1 $[M+H]^+$. MP=214.9 °C. ^1H NMR (DMSO-D_6): 8.18 (d, J = 8.4 Hz, 0.3H), 8.14 – 8.09 (m, 2.3H), 8.05 (d, J = 8.4 Hz, 0.7H), 7.93 (d, J = 2.4 Hz, 0.7H), 7.62 – 7.53 (m, 0.6H), 7.50 (dd, J = 8.9, 2.5 Hz, 0.7H), 7.40 (d, J = 8.4 Hz, 0.7H), 6.76 (d, J = 6.3 Hz, 0.7H), 6.61 (d, J = 8.9 Hz, 0.3H), 6.52 (d, J = 5.7 Hz, 0.3H), 6.45 (d, J = 8.9 Hz, 0.7H), 4.58 (t, J = 4.5 Hz, 0.7H), 4.47 (d, J = 4.8 Hz, 0.3H), 3.91 (t, J = 4.3 Hz, 0.3H), 3.88 – 3.68 (m, 1.7H), 2.60 (s, 0.9H), 2.31 (s, 2.1H), 2.03 – 1.90 (m, 1H), 1.81 – 1.29 (m, 5H).

Example 221: (±)-(2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



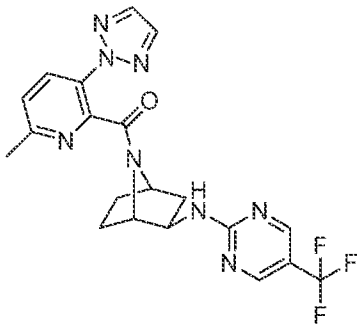
Prepared analogous to Example 220 substituting 5-bromo-2-iodopyridine with 2-chloro-5-(trifluoromethyl)pyrimidine and intermediate A-21 with intermediate A-1. MP=167.1 °C. ^{1}H NMR (DMSO-D_6): 8.75 (s, 0.4H), 8.70 (s, 0.4H), 8.66 (s, 0.6H), 8.53 (s, 0.6H), 8.12 – 8.03 (m, 2.6H), 7.86 (d, J = 7.3 Hz, 0.4H), 7.80 (d, J = 7.2 Hz, 0.4H), 7.72 – 7.54 (m, 1.6H), 7.48 – 7.34 (m, 1.4H), 7.16 (t, J = 7.4 Hz, 0.6H), 4.56 (br s, 0.6H), 4.41 (d, J = 4.3 Hz, 0.4H), 4.08 (dd, J = 11.1, 6.8 Hz, 0.4H), 3.90 – 3.75 (m, 1H), 3.61 (d, J = 4.3 Hz, 0.6H), 2.01 – 1.27 (m, 6H).

Example 222: (±)-(3-fluoro-2-methoxyphenyl)(2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



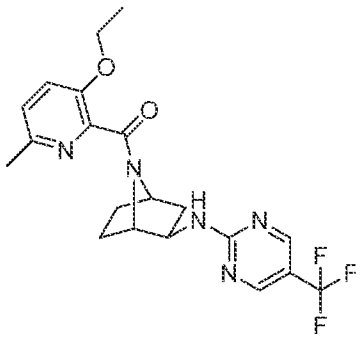
Prepared analogous to Example 221 substituting intermediate A-1 with 3-fluoro-2-methoxybenzoic acid. ^{1}H NMR (DMSO-D_6): 8.72 (br d, J = 22.6 Hz, 0.8H), 8.58 (br d, J = 24.1 Hz, 1.2H), 8.12 (br d, J = 5.6 Hz, 0.4H), 7.99 (br d, J = 5.0 Hz, 0.6H), 7.45 – 7.23 (m, 0.8H), 7.26 – 7.06 (m, 1.2H), 6.97 (d, J = 7.5 Hz, 0.6H), 6.90 – 6.72 (m, 0.6H), 4.65 (br s, 0.6H), 4.53 (d, J = 4.8 Hz, 0.4H), 3.97 (dd, J = 11.4, 6.0 Hz, 0.4H), 3.84 (s, 1.2H), 3.93 – 3.71 (m, 1H), 3.78 (s, 1.8H), 3.69 (br d, J = 2.9 Hz, 0.6H), 2.06 – 1.35 (m, 6H)

Example 223: (±)-(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



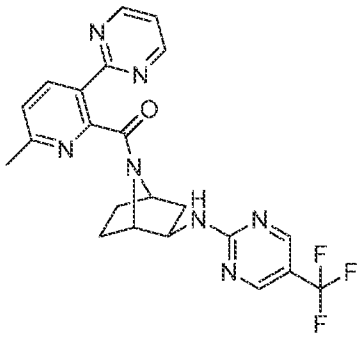
Prepared analogous to Example 221 substituting intermediate A-1 with intermediate A-21. ^{1}H NMR (DMSO-D_6): 8.74 (br d, J = 12.1 Hz, 0.4H), 8.63 (br d, J = 13.2 Hz, 1.2H), 8.26 – 8.01 (m, 3.4H), 7.61 (dd, J = 21.8, 7.4 Hz, 0.4H), 7.43 (d, J = 8.4 Hz, 0.6H), 4.61 (br s, 0.6H), 4.55 (d, J = 5.0 Hz, 0.4H), 4.11 – 4.01 (m, 0.4H), 4.02 – 3.93 (m, 1H), 3.88 (dd, J = 10.1, 6.1 Hz, 0.6H), 3.22 – 3.06 (m, 1H), 2.60 (s, 1H), 2.30 (s, 2H), 2.06 – 1.34 (m, 6H).

Example 224: (±)-(3-ethoxy-6-methylpyridin-2-yl)(2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



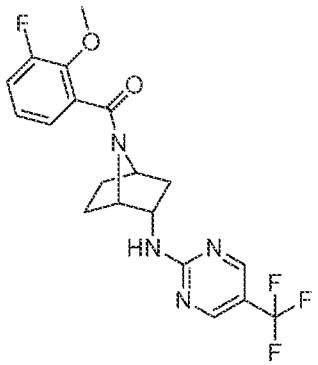
Prepared analogous to Example 221 substituting intermediate A-1 with intermediate A-8. ^{1}H NMR (DMSO-D_6): 8.79 (br d, J = 22.9 Hz, 0.6H), 8.65 (br d, J = 17.4 Hz, 1.4H), 8.21 (d, J = 5.3 Hz, 0.7H), 7.92 (d, J = 5.2 Hz, 0.3H), 7.52 (d, J = 8.6 Hz, 0.3H), 7.42 (d, J = 8.6 Hz, 0.7H), 7.32 (d, J = 8.6 Hz, 0.3H), 7.18 (d, J = 8.6 Hz, 0.7H), 4.71 (br s, 0.7H), 4.64 (br d, J = 4.7 Hz, 0.3H), 4.23 – 3.93 (m, 2.5H), 3.93 – 3.78 (m, 1.4H), 3.78 – 3.55 (m, 1.7H), 3.31 – 3.07 (m, 1.4H), 2.47 (s, 1H), 2.31 (s, 2H), 2.06 – 1.40 (m, 6H).

Example 225: (±)-(6-methyl-3-(pyrimidin-2-yl)pyridin-2-yl)(2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



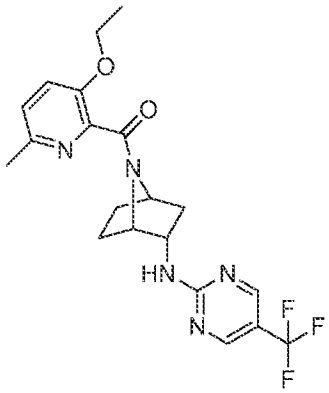
Prepared analogous to Example 221 substituting intermediate A-1 with intermediate A-9. MP=203 °C. MS (ESI) mass calcd. for $C_{22}H_{20}F_3N_7O$, 455.2; m/z found 427.5 $[M+H]^+$. ^1H NMR (DMSO-D_6): 8.94 (d, J = 4.9 Hz, 0.4H), 8.89 (d, J = 4.9 Hz, 1.6H), 8.77 (s, 0.2H), 8.71 (s, 0.2H), 8.61 (s, 1.4H), 8.36 (d, J = 8.1 Hz, 0.2H), 8.24 (d, J = 7.9 Hz, 1.8H), 7.72 (d, J = 6.0 Hz, 0.2H), 7.54 – 7.44 (m, 1.2H), 7.38 (d, J = 8.1 Hz, 0.8H), 4.64 (br s, 0.8H), 4.58 (d, J = 4.6 Hz, 0.2H), 4.06 – 3.90 (m, 2H), 2.60 (s, 0.6H), 2.35 (s, 2.4H), 2.11 – 1.73 (m, 4H), 1.62 – 1.35 (m, 2H).

Example 226: (±)-(3-fluoro-2-methoxyphenyl)(2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



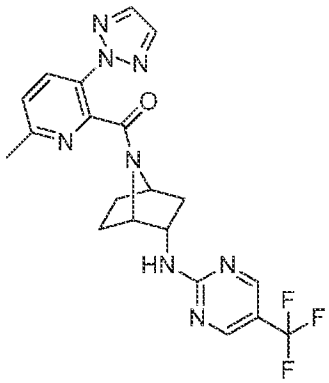
Prepare analogous to Example 222 substituting intermediate B-6 with intermediate B-7. MS (ESI) mass calcd. for $C_{19}H_{18}F_4N_4O_2$, 410.2; m/z found 411.3 $[M+H]^+$. ^1H NMR (DMSO-D_6): 8.75 (s, 0.5H), 8.68 (s, 0.5H), 8.61 (s, 0.5H), 8.57 (s, 0.5H), 8.52 (d, J = 6.3 Hz, 0.5H), 8.44 (d, J = 6.3 Hz, 0.5H), 7.44 – 7.29 (m, 1H), 7.23 – 7.08 (m, 2H), 4.82 (t, J = 3.9 Hz, 0.5H), 4.58 (t, J = 4.5 Hz, 0.5H), 4.34 – 4.12 (m, 1H), 3.94 – 3.81 (m, 3.5H), 3.68 (t, J = 4.2 Hz, 0.5H), 2.31 – 2.11 (m, 1H), 1.93 – 1.40 (m, 5H).

Example 227: (±)-(3-ethoxy-6-methylpyridin-2-yl)(2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



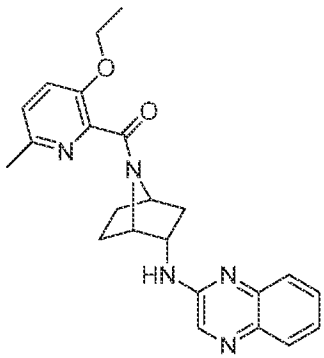
Prepare analogous to Example 224 substituting intermediate B-6 with intermediate B-7. MP=79.7 °C. MS (ESI) mass calcd. for $C_{20}H_{22}F_3N_5O_2$, 421.2; m/z found 422.4 $[M+H]^+$. ^1H NMR (DMSO-D_6): 8.76 (s, 0.5H), 8.68 (s, 0.5H), 8.61 (s, 0.5H), 8.56 (s, 0.5H), 8.52 (d, J = 6.4 Hz, 0.5H), 8.44 (d, J = 6.6 Hz, 0.5H), 7.48 (d, J = 3.2 Hz, 0.5H), 7.45 (d, J = 3.2 Hz, 0.5H), 7.28 (d, J = 3.3 Hz, 0.5H), 7.25 (d, J = 3.3 Hz, 0.5H), 4.83 (t, J = 4.2 Hz, 0.5H), 4.59 (t, J = 4.3 Hz, 0.5H), 4.40 – 4.29 (m, 0.5H), 4.28 – 4.19 (m, 0.5H), 4.16 – 4.01 (m, 2H), 3.79 (t, J = 4.4 Hz, 0.5H), 3.61 (t, J = 4.6 Hz, 0.5H), 2.41 (s, 1.5H), 2.40 (s, 1.5H), 2.30 – 2.09 (m, 1H), 1.93 – 1.41 (m, 5H), 1.34 – 1.23 (m, 3H).

Example 228: (±)-(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



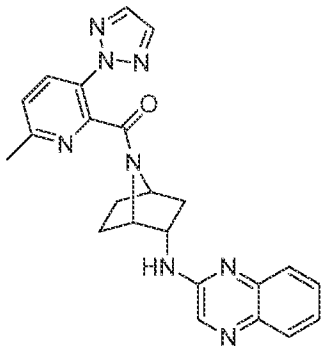
Prepare analogous to Example 223 substituting intermediate B-6 with intermediate B-7. MS (ESI) mass calcd. for $C_{20}H_{19}F_3N_8O$, 444.2; m/z found 445.4 $[M+H]^+$. MP=89.1 °C. ^1H NMR (DMSO-D_6): 8.77 (s, 0.6H), 8.68 (s, 0.6H), 8.61 (s, 0.4H), 8.55 (s, 0.4H), 8.51 (d, J = 6.3 Hz, 0.6H), 8.44 (d, J = 6.3 Hz, 0.4H), 8.24 – 8.16 (m, 1H), 8.13 (s, 1H), 8.12 (s, 1H), 7.63 – 7.52 (m, 1H), 4.81 (t, J = 4.2 Hz, 0.6H), 4.55 (t, J = 4.2 Hz, 0.4H), 4.40 – 4.21 (m, 1H), 4.06 (t, J = 4.4 Hz, 0.4H), 3.79 (t, J = 4.4 Hz, 0.6H), 2.61 (s, 1.2H), 2.58 (s, 1.8H), 2.34 – 2.20 (m, 0.6H), 2.19 – 2.03 (m, 0.6H), 1.94 – 1.50 (m, 4.2H), 1.44 (dd, J = 12.3, 4.6 Hz, 0.6H).

Example 229: (±)-(3-ethoxy-6-methylpyridin-2-yl)(2-(quinoxalin-2-ylamino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Prepare analogous to Example 207 substituting intermediate B-6 with intermediate B-7. MS (ESI) mass calcd. for $C_{23}H_{25}N_5O_2$, 403.2; m/z found 404.5 $[M+H]^+$. MP=115.1 °C. ^1H NMR (DMSO-D_6): 8.37 (s, 0.5H), 8.30 (s, 0.5H), 7.97 (t, J = 5.4 Hz, 1H), 7.80 (d, J = 7.4 Hz, 0.5H), 7.75 (d, J = 7.1 Hz, 0.5H), 7.69 – 7.44 (m, 2.5H), 7.43 – 7.23 (m, 2.5H), 4.99 (t, J = 4.4 Hz, 0.5H), 4.63 (t, J = 4.6 Hz, 0.5H), 4.48 – 4.27 (m, 1H), 4.26 – 4.13 (m, 2H), 3.96 (t, J = 4.4 Hz, 0.5H), 3.64 (t, J = 4.6 Hz, 0.5H), 2.44 (s, 1.5H), 2.41 (s, 1.5H), 2.39 – 2.26 (m, 1H), 1.98 – 1.37 (m, 5H), 1.36 – 1.28 (m, 3H).

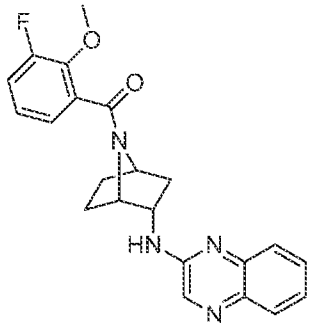
Example 230: (±)-(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-(quinoxalin-2-ylamino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Prepare analogous to Example 205 substituting intermediate B-6 with intermediate B-7. MS (ESI) mass calcd. for $C_{23}H_{22}N_8O$, 426.2; m/z found 427.5 $[M+H]^+$. MP=152.3 °C. ^1H NMR (DMSO-D_6): 8.37 (s, 0.5H), 8.28 – 8.20 (m, 2H), 8.16 – 8.13 (m, 2H), 7.95 (dd, J = 5.6, 3.6 Hz, 1H), 7.79 (d, J = 8.1 Hz, 0.5H), 7.74 (d, J = 8.1 Hz, 0.5H), 7.70 – 7.48 (m, 2.5H), 7.41 – 7.23 (m, 1.5H), 4.98 (t, J = 4.2 Hz, 0.5H), 4.60 (t, J = 4.6 Hz, 0.5H), 4.36 – 4.24 (m, 1H), 4.19 (t, J = 4.5

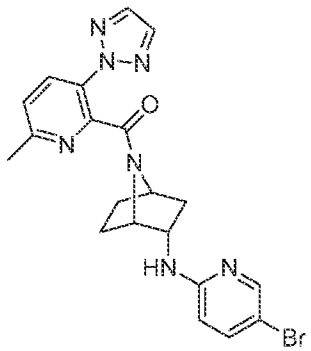
Hz, 0.5H), 3.81 (t, *J* = 4.6 Hz, 0.5H), 2.67 (s, 1.5H), 2.60 (s, 1.5H), 2.43 – 2.17 (m, 1H), 1.97 – 1.25 (m, 5H).

Example 231: (±)-(3-fluoro-2-methoxyphenyl)(2-(quinoxalin-2-ylamino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



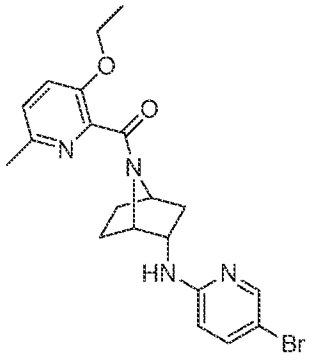
Prepare analogous to Example 206 substituting intermediate B-6 with intermediate B-7. ^{1}H NMR (DMSO-D_6): 8.36 (s, 0.5H), 8.29 (s, 0.5H), 8.08 – 7.95 (m, 1H), 7.85 – 7.69 (m, 1H), 7.69 – 7.49 (m, 1.5H), 7.49 – 7.27 (m, 2H), 7.27 – 7.12 (m, 2.5H), 5.00 (t, *J* = 4.2 Hz, 0.5H), 4.62 (t, *J* = 4.2 Hz, 0.5H), 4.43 – 4.17 (m, 1H), 4.11 (t, *J* = 4.3 Hz, 0.5H), 3.95 (s, 1.5H), 3.88 (s, 1.5H), 3.72 (t, *J* = 4.5 Hz, 0.5H), 2.45 – 2.25 (m, 1H), 1.99 – 1.46 (m, 4H), 1.46 – 1.28 (m, 1H).

Example 232: (±)-(2-((5-bromopyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)methanone.



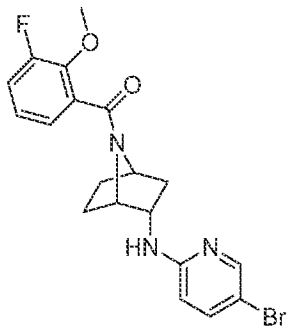
Prepare analogous to Example 220 substituting intermediate B-6 with intermediate B-7. MP=196.0 °C. ^{1}H NMR (DMSO-D_6): 8.25 – 8.16 (m, 1H), 8.16 – 8.10 (m, 2.6H), 7.90 (d, *J* = 2.4 Hz, 0.4H), 7.63 – 7.53 (m, 1.6H), 7.50 (dd, *J* = 8.9, 2.5 Hz, 0.4H), 7.19 (d, *J* = 6.0 Hz, 0.6H), 7.12 (d, *J* = 6.1 Hz, 0.4H), 6.54 (d, *J* = 8.9 Hz, 0.6H), 6.44 (d, *J* = 8.9 Hz, 0.4H), 4.81 (t, *J* = 4.2 Hz, 0.6H), 4.54 (t, *J* = 4.2 Hz, 0.4H), 4.23 – 4.07 (m, 1H), 4.04 (t, *J* = 4.5 Hz, 0.4H), 3.75 (t, *J* = 4.5 Hz, 0.6H), 2.61 (s, 1.2H), 2.58 (s, 1.8H), 2.36 – 2.05 (m, 1H), 1.92 – 1.41 (m, 4H), 1.30 (dd, *J* = 12.4, 4.4 Hz, 0.4H), 1.18 (dd, *J* = 12.2, 4.6 Hz, 0.6H).

Example 233: (±)-(2-((5-bromopyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-ethoxy-6-methylpyridin-2-yl)methanone.



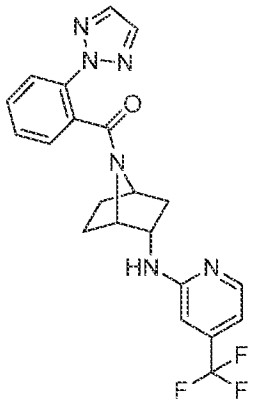
Prepare analogous to Example 219 substituting intermediate B-6 with intermediate B-7. MP=176.1 °C. ^{1}H NMR (DMSO-D_6): 8.11 (d, J = 2.4 Hz, 0.5H), 7.91 (d, J = 2.4 Hz, 0.5H), 7.61 – 7.43 (m, 2H), 7.33 – 7.20 (m, 1.5H), 7.15 (d, J = 6.1 Hz, 0.5H), 6.55 (d, J = 8.9 Hz, 0.5H), 6.46 (d, J = 8.9 Hz, 0.5H), 4.83 (t, J = 4.3 Hz, 0.5H), 4.57 (t, J = 4.6 Hz, 0.5H), 4.20 (d, J = 5.5 Hz, 0.5H), 4.09 (dq, J = 10.2, 6.9 Hz, 2.5H), 3.79 (t, J = 4.3 Hz, 0.5H), 3.58 (t, J = 4.6 Hz, 0.5H), 2.41 (s, 1.5H), 2.40 (s, 1.5H), 2.32 – 2.14 (m, 1H), 1.93 – 1.45 (m, 4H), 1.36 – 1.17 (m, 4H).

Example 234: (±)-(2-((5-bromopyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-methoxyphenyl)methanone.



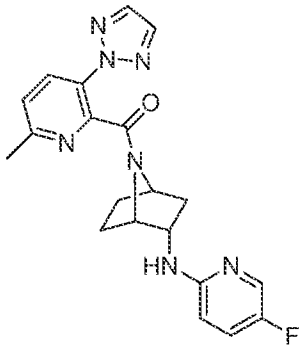
Prepare analogous to Example 217 substituting intermediate B-6 with intermediate B-7. MP=144.5 °C. ^{1}H NMR (DMSO-D_6): 8.11 (d, J = 2.4 Hz, 0.6H), 7.91 (d, J = 2.4 Hz, 0.4H), 7.56 (dd, J = 8.9, 2.5 Hz, 0.6H), 7.50 (dd, J = 8.9, 2.5 Hz, 0.4H), 7.43 – 7.30 (m, 1H), 7.27 – 7.05 (m, 3H), 6.54 (d, J = 8.9 Hz, 0.6H), 6.46 (d, J = 8.9 Hz, 0.4H), 4.83 (t, J = 4.3 Hz, 0.6H), 4.57 (t, J = 4.7 Hz, 0.4H), 4.21 – 3.99 (m, 1H), 3.95 – 3.81 (m, 3.4H), 3.66 (t, J = 4.7 Hz, 0.6H), 2.36 – 2.14 (m, 1H), 1.94 – 1.43 (m, 4H), 1.36 – 1.14 (m, 1H).

Example 235: (±)-((2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((4-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Prepare analogous to Example 210 substituting intermediate B-6 with intermediate B-7. MS (ESI) mass calcd. for $C_{21}H_{19}F_3N_6O$, 428.2; m/z found 429 [M+H]+. MP=274.2 °C. ^{1}H NMR (DMSO-D_6): 8.27 (d, J = 5.2 Hz, 0.5H), 8.13 – 8.01 (m, 2.5H), 7.89 – 7.80 (m, 1H), 7.73 – 7.61 (m, 1H), 7.61 – 7.51 (m, 2H), 7.44 (d, J = 6.1 Hz, 0.5H), 7.38 (d, J = 5.9 Hz, 0.5H), 6.83 – 6.75 (m, 1H), 6.73 – 6.63 (m, 1H), 4.78 (t, J = 3.9 Hz, 0.5H), 4.50 (t, J = 4.6 Hz, 0.5H), 4.27 – 4.04 (m, 1H), 3.96 (t, J = 4.1 Hz, 0.5H), 3.64 (t, J = 4.1 Hz, 0.5H), 2.40 – 2.21 (m, 0.5H), 2.17 – 1.99 (m, 0.5H), 1.88 – 1.32 (m, 4H), 1.27 (dd, J = 12.3, 4.3 Hz, 0.5H), 1.12 (dd, J = 12.2, 4.5 Hz, 0.5H).

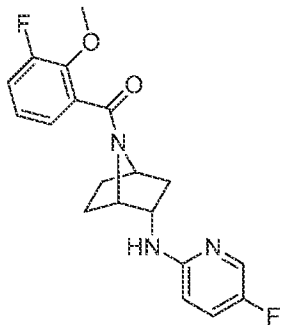
Example 236: (±)-(2-((5-fluoropyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)methanone.



Prepared analogous to Example 209 substituting 2-chloro-6-(trifluoromethyl)pyridine with 5-fluoro-2-iodopyridine and intermediate A-1 with A-21. MP=100.1 °C. MS (ESI) mass calcd. for $C_{20}H_{20}FN_7O$, 393.2; m/z found 394.2 $[M+H]^+$. ^{1}H NMR (DMSO-D_6): 8.24 – 8.15 (m, 1H), 8.12 (s, 1.2H) 8.11 (s, 0.8H), 8.00 (d, J = 2.9 Hz, 0.6H), 7.80 (d, J = 2.8 Hz, 0.4H), 7.63 – 7.51 (m, 1H), 7.43 – 7.26 (m, 1H), 6.94 (d, J = 5.9 Hz, 0.6H), 6.87 (d, J = 6.0 Hz, 0.4H), 6.55

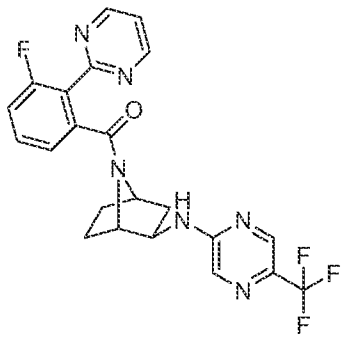
(dd, J = 9.1, 3.6 Hz, 0.6H), 6.45 (dd, J = 9.1, 3.7 Hz, 0.4H), 4.81 (t, J = 4.2 Hz, 0.6H), 4.52 (t, J = 4.6 Hz, 0.4H), 4.19 – 3.99 (m, 1.4H), 3.73 (t, J = 4.6 Hz, 0.6H), 2.60 (s, 1.2H), 2.58 (s, 1.8H), 2.35 – 2.20 (m, 0.6H), 2.19 – 2.05 (m, 0.4H), 1.96 – 1.38 (m, 4H), 1.27 (dd, J = 12.5, 4.2 Hz, 0.6H), 1.15 (dd, J = 12.2, 4.8 Hz, 0.4H).

Example 237: (±)-(3-fluoro-2-methoxyphenyl)(2-((5-fluoropyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Prepared analogous to Example 209 substituting 2-chloro-6-(trifluoromethyl)pyridine with 5-fluoro-2-iodopyridine and intermediate A-1 with 3-fluoro-2-methoxybenzoic acid. MS (ESI) mass calcd. for $C_{19}H_{19}F_2N_3O_2$, 359.1; m/z found 360.2 $[M+H]^+$. MP=134.7 °C. ^{1}H NMR (DMSO-D_6): 8.00 (d, J = 2.9 Hz, 0.5H), 7.80 (d, J = 2.9 Hz, 0.5H), 7.45 – 7.26 (m, 2H), 7.24 – 7.06 (m, 2H), 6.96 (d, J = 6.0 Hz, 0.5H), 6.89 (d, J = 5.8 Hz, 0.5H), 6.56 (dd, J = 9.1, 3.6 Hz, 0.5H), 6.48 (dd, J = 9.2, 3.6 Hz, 0.5H), 4.83 (t, J = 4.3 Hz, 0.5H), 4.56 (t, J = 4.7 Hz, 0.5H), 4.18 – 3.98 (m, 1H), 3.95 – 3.81 (m, 3.5H), 3.64 (t, J = 4.6 Hz, 0.5H), 2.35 – 2.14 (m, 1H), 1.96 – 1.43 (m, 4H), 1.30 – 1.13 (m, 1H).

Example 238: (3-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Step A: (1S,2R,4R)-N-(5-(trifluoromethyl)pyrazin-2-yl)-7-azabicyclo[2.2.1]heptan-2-amine hydrochloride. To the intermediate of Example 181 Step A (100 mg, 0.3 mmol) in DCM

(3 mL) was added 4M HCl in dioxane (0.8 mL). The reaction was allowed to proceed overnight then concentrated neutralized with 5% Na_2CO_3 (aq) and extracted with DCM (2X). The combined organics were dried (Na_2SO_4) to give the title compound of step A that was used without further purification.

Step B: (3-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone. To the title compound of step A (1.44 g, 5.6 mmol) in DCM (56 mL) was added DIPEA (1.25 mL, 7.3 mmol) and intermediate A-2 (1.43 g, 6.1 mmol). Then T3P (50% solution in DMF, 10 mL, 17 mmol) was added dropwise and the reaction heated at 45 °C for 16h. After allowing to cool to rt, DCM was added and the mixture washed with H_2O then saturated $NaHCO_3$ (aq). The combined aq layers were extracted with DCM. The combined organic layers were dried (Na_2SO_4). Purification via silica gel chromatography (10-100% EtOAc in hexanes) gave the title compound (2 g, 78%). MS (ESI) mass calcd. for $C_{22}H_{18}F_4N_6O$, 458.2; m/z found 459.1 $[M+H]^+$. ^1H NMR ($CDCl_3$) 8.91 – 8.73 (m, 2H), 8.35 – 8.22 (m, 1H), 8.19 (s, 1H), 7.66 (s, 1H), 7.44 – 7.13 (m, 4H), 4.79 – 4.68 (m, 1H), 4.46 – 4.35 (m, 1H), 4.12 – 4.03 (m, 1H), 2.22 – 2.00 (m, 2H), 1.99 – 1.84 (m, 1H), 1.79 – 1.45 (m, 3H).

Example 238 was also prepared as follows:

Step A: 3-fluoro-2-(pyrimidin-2-yl)benzonitrile. To a 12-L 4-necked round-bottomed flask equipped with a thermocouple probe, mechanical stirrer, condenser and nitrogen inlet was charged 3-fluorobenzonitrile (140 g, 123.6 mmol), 2-isopropoxy-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (353.7 mL, 1.699 mol), and THF (2.35 L). The mixture was cooled to –78 °C and lithium diisopropylamide (623 mL, 1.246 mol, 2 M) was added over 45 min maintaining a temperature of < –71 °C. The mixture was stirred for 1 h at –76 °C then quenched with sodium bicarbonate$_{(aq)}$ (172 g in 1500 mL water). This mixture was warmed to room temperature to produce an off-white slurry. The slurry was treated with 2-bromopyrimidine (171.8 g, 1.059 mol) and then degassed with bubbling nitrogen. Dichloro[1,1'-bis(di-*t*-butylphosphino)ferrocene]palladium(II) (17 g, 25.8 mmol) was then added and the mixture was heated to 66 °C for 1 h. The mixture was cooled and ethyl acetate (5.6 L) was added. Solids were removed by filtration and washed with ethyl acetate (2 x 300 mL). The layers were cut and the aqueous layer was extracted with ethyl acetate (2 L). The combined organic layers were washed with brine (2 x 1.2 L) and then concentrated. Ethanol (600 mL) was added and the mixture was further concentrated to provide a dark brown liquid (382.0 g, 96% mass recovery, 75.5% desired, 19.1% regioisomer (3-fluoro-4-(pyrimidin-2-yl)benzonitrile). This liquid was warmed in ethanol (600 mL) at 66 °C until homogeneous and then gradually cooled to 20 °C.

The resulting solids were isolated by filtration and washed with cold 1/1 hexanes/ethanol (2 x 100 mL). After drying for 3 hours under air suction, the title compound was obtained as an off-white solid (118 g, 30%, 99.2% desired regioisomer). The mother liquor contained ~20% additional desired product that could be recovered through chromatography and crystallization. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.97 (d, J = 4.9 Hz, 2H), 7.69 – 7.61 (m, 1H), 7.61 – 7.52 (m, 1H), 7.51 – 7.43 (m, 1H), 7.41 (t, J = 5.0 Hz, 1H).

Step B: 3-fluoro-2-(pyrimidin-2-yl)benzoic acid. To a 5-L, 4-necked round-bottomed flask equipped with a thermocouple, mechanical stirrer, condenser, and nitrogen inlet was charged the title compound of Step A (100 g, 502.0 mmol) in THF (500 mL) and methanol (500 mL). The mixture was stirred for 5 min at 20 °C and then sodium hydroxide$_{(aq)}$ (1.0 L, 3 N) was added. The resulting mixture was warmed to 60 °C for 24 h. The mixture was concentrated to 500 mL and the resulting thick aqueous layer was diluted with water (500 mL) and then transferred into a 5-L, 4-necked round-bottomed flask. The flask was cooled to 4 °C and the pH was adjusted from 14.0 to 2-3 with concentrated hydrogen chloride$_{(aq)}$ (260 mL, 37%). The resulting off-white slurry was stirred at 0 °C for 20 min, and then the solids were collected by filtration, washed with water (4 x 200 mL), dried under air suction for 20 h, and then placed in a vacuum oven at 60 °C for 20 h to provide the title compound as an off-white solid (106 g, 97%). ^{1}H NMR (400 MHz, DMSO) δ 13.01 (s, 1H), 8.89 (d, J = 5.0 Hz, 2H), 7.75 (dd, J = 7.7, 1.2 Hz, 1H), 7.69 – 7.54 (m, 2H), 7.52 (t, 1 H). HPLC retention time: 1.765 min.

Step C: (1*S*,2*R*,4*R*)-tert-butyl 2-(((benzyloxy)carbonyl)amino)-7-azabicyclo[2.2.1]-heptane-7-carboxylate. A racemic mixture of tert-butyl 2-(((benzyloxy)carbonyl)amino)-7-azabicyclo[2.2.1]-heptane-7-carboxylate (578 g) was separated on a chiralcel OD column (1000A, 20 um (Daicel), 110 mm diameter, 42 cm length) with a mobile phase of 90:10 heptane:ethanol over 126 injections with a run time of 15 min. Peak shaving was employed in conjuction with 1 recycling. The title compound was isolated through filtration after crystallization upon concentration (249.8 g, 86% of theory). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.28 (m, 5H), 5.20 – 5.00 (m, 3H), 4.23 (s, 1H), 4.12 (d, J = 4.9 Hz, 1H), 3.78 (td, J = 8.0, 2.9 Hz, 1H), 1.93 (dd, J = 13.1, 8.1 Hz, 1H), 1.83 – 1.62 (m, 2H), 1.54 – 1.29 (m, 3H), 1.43 (s, 9H). HPLC retention time: 3.461 min.

Step D: (1*S*,2*R*,4*R*)-*tert*-butyl 2-amino-7-azabicyclo[2.2.1]heptane-7-carboxylate. To a 2.25 L Parr vessel were added (1*S*,2*R*,4*R*)-tert-butyl 2-(((benzyloxy)carbonyl)amino)-7-azabicyclo[2.2.1]heptane-7-carboxylate (91.2 g, 261.4 mmol) and 5% Pd/C (Johnson Matthey A102038-5, (9.6 g, 2.26 mmol). Ethanol (912 mL) was added and the vessel was agitated under a pressure of hydrogen gas (60 psi) for ~2.5 h. Mid-way through that time period the flask was

evacuated and recharged with hydrogen gas (60 psi). The mixture was then filtered to remove residual heterogeneous catalyst. After washing the filter cake with ethanol (90 mL) the filtrate was concentrated under reduced pressure and concentrated again from acetonitrile to provide the title compound as a slightly yellow oil (57 g, quant. yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.2 (bs, 1H), 3.88 (bs, 1H), 2.96 (dd, *J* = 7.6, 3.1 Hz, 1H), 1.81 (dd, *J* = 12.9, 7.8 Hz, 1H), 1.77 – 1.54 (m, 2H), 1.46 (s, 9H), 1.39 – 1.20 (m, 3H).

Step E: (1*S*,2*R*,4*R*)-tert-butyl 2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1] heptane-7-carboxylate. To a 3 L round-bottomed flask equipped with a mechanical stirring mechanism, temperature probe, reflux condenser, heating mantle, and nitrogen inlet was added (1*S*,2*R*,4*R*)-*tert*-butyl 2-amino-7-azabicyclo[2.2.1]heptane-7-carboxylate (56.92 g, 264.4 mmol) in acetonitrile (360 mL). Triethylamine (55.1 mL, 396.6 mmol) and 2-chloro-5-trifluoromethylpyrazine (57.91 g, 317.2 mmol) were added in rapid succession and the mixture was then heated to reflux for 16.5 h. The mixture was cooled to room temperature and concentrated under reduced pressure. The residue (189.57 g) was taken up in ammonium chloride$_{(aq)}$ (500 mL, 13 wt%) and ethyl acetate (500 mL). The layers were mixed and separated and the organic was washed with sodium carbonate$_{(aq)}$ (500 mL, ½ saturated). The organic layer was then dried over magnesium sulphate, filtered, and concentrated to a final mass of 94.73 g. This orange solid was taken up in heptane (500 mL) at 98 °C. The homogeneous solution was allowed to cool slowly to room temperature, filtered, and washed with 100 mL of heptane to provide the title compound as a white solid (79.62 g, 84%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (s, 1H), 7.86 (d, *J* = 1.4 Hz, 1H), 5.45 (bs, 1H), 4.44 – 4.25 (m, 1H), 4.20 (d, *J* = 5.2 Hz, 1H), 4.05 (td, *J* = 7.6, 3.0 Hz, 1H), 2.06 (dd, *J* = 13.1, 7.6 Hz, 1H), 1.92 – 1.70 (m, 2H), 1.61 – 1.38 (m, 3H), 1.44 (s, 9H). HPLC retention time: 3.424 min.

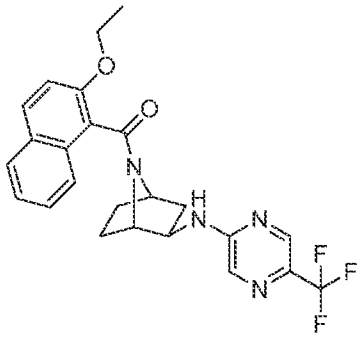
Step F: (1*S*,2*R*,4*R*)-*N*-(5-(trifluoromethyl)pyrazin-2-yl)-7-azabicyclo[2.2.1]heptan-2-amine. In a 2-L round-bottomed flask, (1*S*,2*R*,4*R*)-tert-butyl 2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1] heptane-7-carboxylate (79.52 g, 221.9 mmol) was taken up in IPA (584 mL). Hydrogen chloride (121.0 mL, 665.7 mmol, 5.5 M in IPA) was added and the reaction was warmed to 60 °C for 14 h. After cooling to room temperature, the mixture was poured over isopropyl acetate (1 L) and sodium carbonate$_{(aq)}$ (1 kg, 8.1 wt%). The layers were mixed and separated. The aqueous phase was washed with isopropyl acetate (500 mL), and the combined organics were washed with brine (700 mL), dried over $MgSO_4$, filtered, and concentrated to provide the title compound as a pinkish-white solid (57.11 g, 99%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (s, 1H), 7.84 (d, *J* = 1.4 Hz, 1H), 5.51 (d, *J* = 7.7 Hz, 1H), 3.95 (td, *J* =

7.8, 3.0 Hz, 1H), 3.76 (t, J = 4.4 Hz, 1H), 3.60 (d, J = 4.9 Hz, 1H), 1.95 (m, J = 12.9, 7.8 Hz, 1H), 1.69 – 1.39 (m, 5H). HPLC retention time: 1.938 min.

Step G: (3-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone. A 3 L 3-necked round-bottom flask was fitted with mechanical stirring and a thermometer and charged with the amine from Step F (51.61 g, 200 mmol), acid from Step B (56.69 g, 260 mmol), and 2-MeTHF (1 L). The mixture was stirred at room temperature for several minutes until nearly all the solids had dissolved. Diisopropylethylamine (45.2 mL, 260 mmol) was added followed immediately by T3P (178 mL of a 50% solution in EtOAc, 300 mmol). Mild exotherm to 27 °C observed. The reaction was warmed to 40 °C and allowed to stir 9 h. A dark brown reaction mixture resulted. HPLC and MS analysis indicated complete conversion of the amine. The reaction was quenched by addition of 1:1 sat'd. NH_4Cl/water (1 L) and allowed to cool to room temperature. The layers were separated, and the aqueous layer was extracted once with 2-MeTHF (200 mL). The combined organic layers were washed with 3:1 sat'd. Na_2CO_3/water (1 L). The organic layer was washed with brine (1 L) causing an emulsion which was given several hours to clear. Layers were separated, and the organic layer was dried ($MgSO_4$) and concentrated to a viscous brown oil. This material was combined with material from two prior smaller scale reactions for product purification. Yield calculations are based upon the total combined amount of limiting amine for the three reactions, 221.3 mmol. The combined crude products were first flash chromatographed (1.5 kg silica gel cartridge, initial linear gradient elution of 50% EtOAc/hex to 100% EtOAc then elution with 20% THF/EtOAc and 40% THF/EtOAc, 400 mL/min, material loaded as a CH_2Cl_2 solution). Strong reddish purple colored band and several minor spots co-eluted with the initial fractions of product. The latter, less-colored three quarters of the product-containing fractions were combined and concentrated to a thick red-orange syrup (83 g). This material was treated with activated charcoal (17 g) in acetonitrile (1.1 L) at 46 °C for 30 min. The charcoal was removed by vacuum filtration through a pad of Celite, and the filter cake was washed with warm acetonitrile (500 mL) to provide a straw yellow solution. The solvents were removed in vacuo to give the impure crude product as an off-white foam (~70 g). To crystallize the material, the foam was dissolved in hot EtOAc (175 mL, 77 °C) with mechanical stirring. Heptane was added in portions at 76-80 °C. At 300 mL of added heptane, solids were observed to slowly precipitate. Addition of heptane was continued until a total volume of 650 mL was added. Mixture was allowed to cool to room temperature over 5 h. The product was collected by vacuum filtration and washed with excess heptane and allowed to air dry. The product was dense off-white granular crystals (Form 1). HPLC analysis appeared to indicate a minor

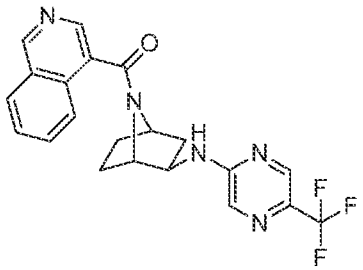
impurity (0.7% peak area, 2.23 min, 220 nm); therefore, a second crystallization was undertaken under identical conditions. During this crystallization, the product was observed to rapidly crystallize in fluffy white needles (Form 2) which "froze" the mixture preventing controlled stirring. Additional heptane was added, and a spatula was used to mechanically break up the mixture and restore stirring of a suspension of crystalline product. Due to continued observance of the minor peak, the product was crystallized twice more with similar crystallization behavior as observed in the second crystallization. It was noted that more EtOAc was necessary to initially dissolve the Form 2 crystals. The final product was dried in a vacuum oven (~10 torr) at 60 °C overnight and then 80 °C overnight to provide crystalline Form 2 (small fluffy white needles). Yield = 54.46 g (54%). By ^{1}H NMR, EtOAc content was 900 ppm, and heptane content was 660 ppm. The remaining product-containing chromatography fractions were concentrated and chromatographed a second time. Mixed fractions were chromatographed a third time. The product fractions were concentrated to give a light orange foam (28.6 g). The foam was decolorized with activated charcoal (5.6 g) in warm acetonitrile (46 °C). Charcoal was removed by vacuum filtration through a pad of Celite. The filter cake was washed with warm acetonitrile, and the filtrate was concentrated and crystallized from EtOAc/heptane as before. With this batch, crystalline Form 2 was generated upon the initial crystallization. Product was collected by vacuum filtration, washed with excess heptane, and dried in a vacuum oven (~10 torr) at 50 °C overnight. Yield = 23.69 g (23%). By 1H NMR, EtOAc content was 3500 ppm, and heptane content was 600 ppm. Total combined yield of two batches = 78.15 g (77%). ^{1}H NMR (400 MHz, $CDCl_3$) Major Rotamer (90%) δ 8.87 (d, J = 4.9 Hz, 2H), 8.35 (m, 1H), 8.18 (s, 1H), 7.65 (d, J = 1.3 Hz, 1H), 7.42 – 7.34 (m, 2H), 7.24 – 7.18 (m, 2H), 4.72 (t, J = 4.8 Hz, 1H), 4.37 (td, J = 8.8, 3.7 Hz, 1H), 4.07 (d, J = 4.9 Hz, 1H), 2.15 (dd, J = 12.8, 8.1 Hz, 1H), 2.09 – 1.98 (m, 1H), 1.97 – 1.84 (m, 1H), 1.76 – 1.58 (m, 1H), 1.56 – 1.44 (m, 2H). Minor Rotamer (10%) unique peaks only δ 8.76 (d, J = 4.88 Hz, 2H), 7.70 (s, 1H), 7.50 – 7.44 (m, 1H), 7.33 – 7.27 (m, 2H), 6.21 (m, 1H), 4.59 (bd, J = 4.1 Hz, 1H), 4.20 – 4.13 (m, 2H).

Example 239: (2-ethoxynaphthalen-1-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



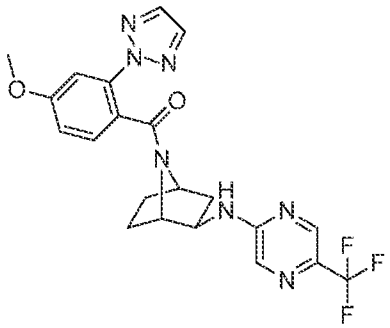
Prepared analogous to Example 181 substituting intermediate A-1 with 2-ethoxy-1-naphthoic acid. MS (ESI) mass calcd. for $C_{24}H_{23}F_3N_4O_2$, 456.2; m/z found 457.2 $[M+H]^+$. ^1H NMR ($CDCl_3$): 8.39 – 8.31 (m, 0.3H), 8.18 (s, 0.5H), 8.08 – 7.98 (m, 0.3H), 7.96 – 7.67 (m, 3.6H), 7.57 – 7.32 (m, 2H), 7.31 – 7.16 (m, 1.3H), 7.10 – 7.04 (m, 0.2H), 6.34 (d, J = 9.1 Hz, 0.5H), 5.90 – 5.75 (m, 0.3H), 5.17 – 4.95 (m, 1H), 4.70 (d, J = 7.1 Hz, 0.2H), 4.49 – 4.07 (m, 2.7H), 3.90 (td, J = 7.4, 2.9 Hz, 0.2H), 3.77 – 3.65 (m, 0.3H), 3.62 – 3.56 (m, 0.2H), 3.39 (d, J = 5.1 Hz, 0.4H), 2.30 – 1.94 (m, 2H), 1.81 – 1.47 (m, 5H), 1.47 – 1.33 (m, 2H).

Example 240: isoquinolin-4-yl((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



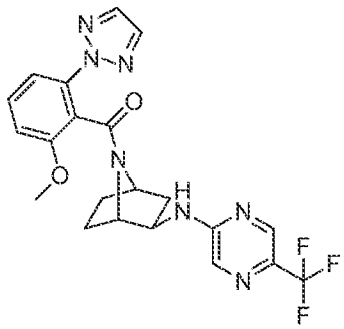
Prepared analogous to Example 181 substituting intermediate A-1 with isoquinoline-4-carboxylic acid. MS (ESI) mass calcd. for $C_{21}H_{18}F_3N_5O$, 413.2; m/z found 414.2 $[M+H]^+$. ^1H NMR ($CDCl_3$): 9.31 (s, 0.5H), 9.13 (s, 0.5H), 8.68 – 8.49 (m, 1H), 8.40 – 7.53 (m, 5.5H), 7.42 (s, 0.5H), 6.20 (s, 0.5H), 4.99 (s, 1.5H), 4.21 (s, 0.5H), 4.06 – 3.77 (m, 1.5H), 2.27 – 1.43 (m, 6H).

Example 241: (4-methoxy-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



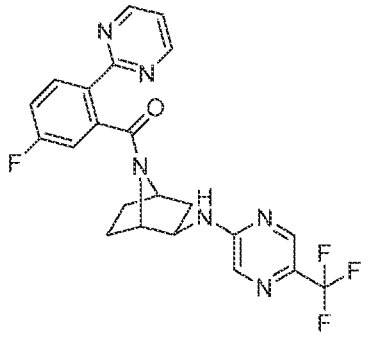
Prepared analogous to Example 181 substituting intermediate A-1 with intermediate A-5. MS (ESI) mass calcd. for $C_{21}H_{20}F_3N_7O_2$, 459.2; m/z found 460.3 $[M+H]^+$. ^1H NMR ($CDCl_3$): 8.31 (s, 0.3H), 8.18 (s, 0.7H), 7.91 (s, 1.5H), 7.87 – 7.77 (m, 1H), 7.54 (s, 0.8H), 7.48 – 7.39 (m, 0.7H), 7.35 – 7.28 (m, 1.7H), 6.97 (dd, J = 8.5, 2.5 Hz, 0.3H), 6.87 (d, J = 8.3 Hz, 0.7H), 6.29 (s, 0.3H), 4.85 – 4.79 (m, 0.7H), 4.75 – 4.70 (m, 0.3H), 4.40 – 4.22 (m, 1H), 4.09 – 4.03 (m, 0.3H), 3.99 (s, 0.7H), 3.94 – 3.83 (m, 3H), 2.19 – 1.41 (m, 6H).

Example 242: (2-methoxy-6-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



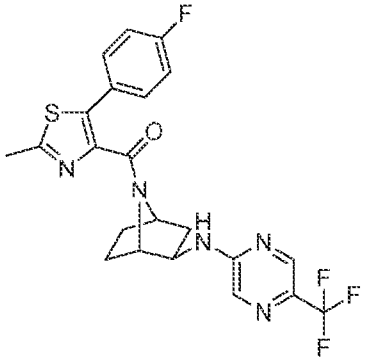
Prepared analogous to Example 181 substituting intermediate A-1 with intermediate A-13. MS (ESI) mass calcd. for $C_{21}H_{20}F_3N_7O_2$, 459.2; m/z found 460.3 $[M+H]^+$. ^1H NMR ($CDCl_3$): 8.37 – 8.30 (m, 0.3H), 8.25 – 8.17 (m, 0.7H), 7.97 – 7.85 (m, 1.5H), 7.84 – 7.74 (m, 0.8H), 7.65 – 7.56 (m, 0.4H), 7.55 – 7.37 (m, 2.7H), 7.05 – 6.94 (m, 1H), 6.17 – 5.98 (m, 0.2H), 5.90 – 5.66 (m, 0.4H), 5.02 – 4.86 (m, 0.7H), 4.86 – 4.71 (m, 0.3H), 4.45 – 4.18 (m, 0.8H), 4.05 (s, 0.7H), 3.97 – 3.75 (m, 3.3H), 3.62 – 3.57 (m, 0.2H), 2.25 – 1.29 (m, 6H).

Example 243: (5-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



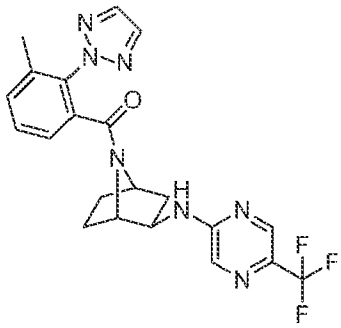
Prepared analogous to Example 181 substituting intermediate A-1 with intermediate A-7. MS (ESI) mass calcd. for $C_{22}H_{18}F_4N_6O$, 458.2; m/z found 459.3 $[M+H]^+$. ^1H NMR ($CDCl_3$): 8.88 – 8.79 (m, 1.7H), 8.77 – 8.69 (m, 0.3H), 8.36 – 8.14 (m, 1.8H), 8.01 (dd, J = 8.6, 5.4 Hz, 1H), 7.81 (s, 0.2H), 7.42 – 7.30 – 7.02 (m, 3.8H), 6.26 (d, J = 7.8 Hz, 0.2H), 4.90 – 4.81 (m, 0.8H), 4.74 (d, J = 5.2 Hz, 0.2H), 4.42 (s, 0.8H), 4.27 (s, 0.2H), 4.12 – 3.96 (m, 1H), 2.29 – 1.39 (m, 6H).

Example 244: (5-(4-fluorophenyl)-2-methylthiazol-4-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



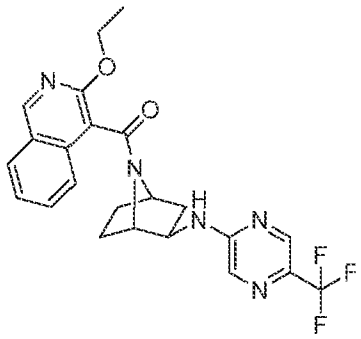
Prepared analogous to Example 181 substituting intermediate A-1 with 5-(4-fluorophenyl)-2-methylthiazole-4-carboxylic acid. MS (ESI) mass calcd. for $C_{22}H_{19}F_4N_5OS$, 477.2; m/z found 478.1 $[M+H]^+$. ^1H NMR ($CDCl_3$): 8.32 – 8.20 (m, 1H), 7.95 – 7.84 (m, 1H), 7.56 – 7.40 (m, 2H), 7.15 – 7.04 (m, 2H), 6.97 – 6.77 (m, 0.8H), 6.01 – 5.88 (m, 0.2H), 4.85 (t, J = 4.5 Hz, 1H), 4.21 – 3.90 (m, 2H), 2.80 – 2.56 (m, 3H), 2.19 – 1.95 (m, 1.7H), 1.93 – 1.31 (m, 4.3H).

Example 245: (3-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



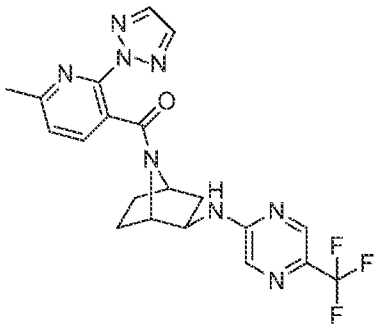
Prepared analogous to Example 181 substituting intermediate A-1 with intermediate A-24. MS (ESI) mass calcd. for $C_{21}H_{20}F_3N_7O$, 443.2; m/z found 444.3 $[M+H]^+$. ^1H NMR ($CDCl_3$): 8.29 – 8.23 (m, 0.2H), 8.21 – 8.15 (m, 0.8H), 7.95 – 7.88 (m, 1.6H), 7.84 – 7.74 (m, 1.3H), 7.62 – 7.39 (m, 1.2H), 7.37 – 7.19 (m, 2.7H), 5.81 (s, 0.2H), 4.79 – 4.65 (m, 0.8H), 4.61 – 4.51 (m, 0.2H), 4.38 – 3.90 (m, 2H), 2.19 (s, 3H), 2.14 – 1.42 (m, 6H).

Example 246: (3-ethoxyisoquinolin-4-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



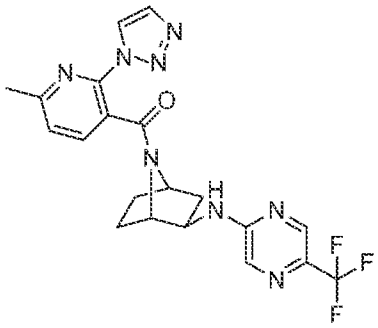
Prepared analogous to Example 181 substituting intermediate A-1 with intermediate A-22. MS (ESI) mass calcd. for $C_{23}H_{22}F_3N_5O_2$, 457.2; m/z found 458.3 $[M+H]^+$. ^1H NMR ($CDCl_3$): 9.01 – 8.92 (m, 0.8H), 8.82 (s, 0.2H), 8.35 (s, 0.5H), 8.22 (s, 0.3H), 8.05 (s, 0.1H), 8.00 – 7.85 (m, 1.6H), 7.84 – 7.71 (m, 1H), 7.71 – 7.54 (m, 1.2H), 7.50 – 7.39 (m, 0.8H), 7.39 – 7.31 (m, 0.4H), 7.18 (s, 0.3H), 6.11 (s, 0.1H), 5.95 (d, J = 8.8 Hz, 0.3H), 5.83 (d, J = 8.0 Hz, 0.4H), 5.15 – 5.06 (m, 0.3H), 5.06 – 4.94 (m, 0.7H), 4.92 – 4.72 (m, 0.5H), 4.68 – 4.41 (m, 1.5H), 4.40 – 4.30 (m, 0.3H), 4.24 – 4.07 (m, 0.4H), 3.89 – 3.81 (m, 0.2H), 3.81 – 3.67 (m, 0.7H), 3.51 (d, J = 5.1 Hz, 0.3H), 2.30 – 1.95 (m, 2.5H), 1.91 – 1.21 (m, 6.5H).

Example 247: (6-methyl-2-(2H-1,2,3-triazol-2-yl)pyridin-3-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



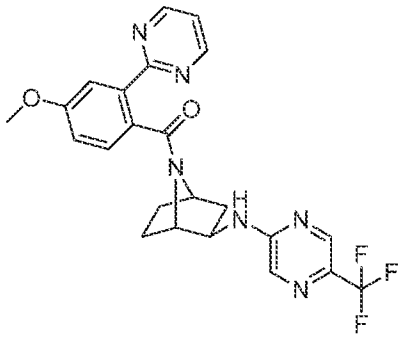
Prepared analogous to Example 181 substituting intermediate A-1 with intermediate A-3. MS (ESI) mass calcd. for $C_{20}H_{19}F_3N_8O$, 444.2; m/z found 445.2 $[M+H]^+$. ^1H NMR ($CDCl_3$): 8.32 (s, 0.4H), 8.18 (s, 0.6H), 7.96 (s, 1.3H), 7.88 (d, J = 4.6 Hz, 1.1H), 7.79 (d, J = 7.7 Hz, 0.5H), 7.73 – 7.52 (m, 1.5H), 7.35 – 7.27 (m, 0.5H), 7.18 (s, 0.7H), 6.28 (s, 0.4H), 4.89 – 4.70 (m, 1H), 4.42 – 4.19 (m, 1H), 4.03 – 3.81 (m, 1H), 2.76 – 2.56 (m, 3H), 2.26 – 1.40 (m, 6H).

Example 248: (6-methyl-2-(1H-1,2,3-triazol-1-yl)pyridin-3-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



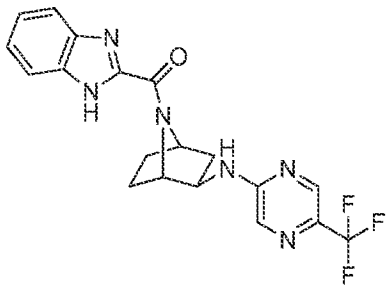
Prepared analogous to Example 181 substituting intermediate A-1 with intermediate A-4. MS (ESI) mass calcd. for $C_{20}H_{19}F_3N_8O$, 444.2; m/z found 445.2 $[M+H]^+$. ^1H NMR ($CDCl_3$): 8.51 – 8.35 (m, 1.6H), 8.29 (s, 0.7H), 8.17 (s, 0.3H), 7.92 – 7.80 (m, 1H), 7.76 – 7.60 (m, 1.3H), 7.35 – 7.18 (m, 1.4H), 6.81 – 6.61 (m, 0.7H), 4.95 – 4.85 (m, 0.3H), 4.84 – 4.75 (m, 0.7H), 4.49 – 4.32 (m, 1H), 4.07 (t, J = 4.4 Hz, 0.7H), 3.93 (s, 0.3H), 2.70 – 2.54 (m, 3H), 2.22 (dd, J = 13.1, 8.0 Hz, 0.4H), 2.14 – 1.46 (m, 5.6H).

Example 249: (4-methoxy-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



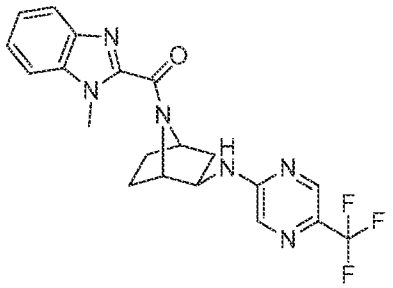
Prepared analogous to Example 181 substituting intermediate A-1 with intermediate A-15. MS (ESI) mass calcd. for $C_{23}H_{21}F_3N_6O_2$, 470.2; m/z found 471.2 $[M+H]^+$. ^1H NMR ($CDCl_3$): 8.89 – 8.69 (m, 2H), 8.38 – 8.12 (m, 2H), 7.81 – 7.74 (m, 0.1H), 7.70 – 7.62 (m, 0.1H), 7.49 – 7.28 (m, 3.8H), 6.91 (dd, J = 8.4, 2.6 Hz, 0.9H), 6.48 – 6.39 (m, 0.1H), 4.85 – 4.77 (m, 0.9H), 4.73 – 4.67 (m, 0.1H), 4.48 – 4.34 (m, 0.9H), 4.24 (s, 0.1H), 4.09 (d, J = 5.0 Hz, 1H), 3.94 – 3.79 (m, 3H), 2.18 (dd, J = 13.0, 8.1 Hz, 1H), 2.13 – 1.37 (m, 5H).

Example 250: (1H-benzo[d]imidazol-2-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



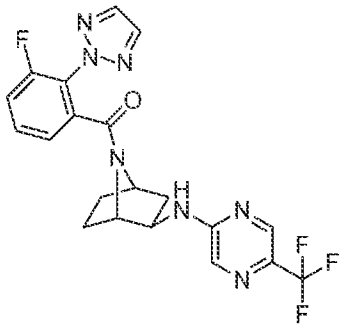
Prepared analogous to Example 181 substituting intermediate A-1 with 1H-benzo[d]imidazole-2-carboxylic acid. MS (ESI) mass calcd. for $C_{19}H_{17}F_3N_6O$, 402.1; m/z found 403.2 $[M+H]^+$. ^1H NMR ($CDCl_3$): 8.35 – 7.61 (m, 3.5H), 7.40 – 7.13 (m, 3.5H), 6.26 – 5.75 (m, 1H), 5.06 – 4.63 (m, 1.5H), 4.27 – 3.95 (m, 1.5H), 2.86 – 2.47 (m, 1H), 2.33 – 1.45 (m, 5H).

Example 251: (1-methyl-1H-benzo[d]imidazol-2-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



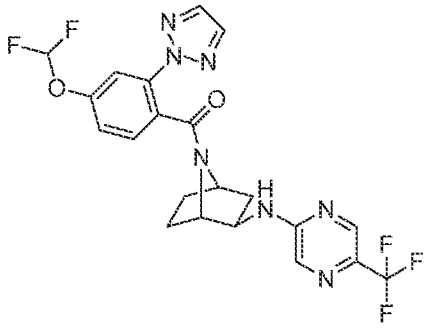
Prepared analogous to Example 181 substituting intermediate A-1 with 1-methyl-1H-benzo[d]imidazole-2-carboxylic acid. MS (ESI) mass calcd. for $C_{20}H_{19}F_3N_6O$, 416.2; m/z found 417.2 $[M+H]^+$.

Example 252: (3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



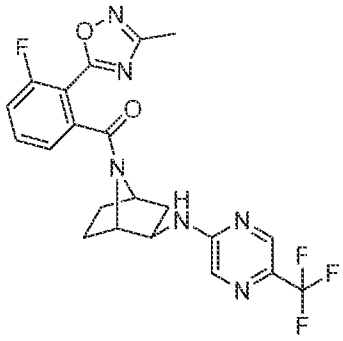
Prepared analogous to Example 181 substituting intermediate A-1 with intermediate A-16. MS (ESI) mass calcd. for $C_{20}H_{17}F_4N_7O$, 447.1; m/z found 448.3 $[M+H]^+$. ^1H NMR ($CDCl_3$): 8.30 (s, 0.3H), 8.19 (s, 0.7H), 7.96 – 7.75 (m, 2.8H), 7.58 – 7.49 (m, 0.3H), 7.45 – 7.11 (m, 3.7H), 5.83 (s, 0.2H), 4.80 – 4.58 (m, 1H), 4.38 – 4.25 (m, 0.8H), 4.24 – 4.13 (m, 0.2H), 4.13 – 4.04 (m, 0.2H), 3.97 (d, J = 4.9 Hz, 0.8H), 2.22 – 2.07 (m, 1H), 2.07 – 1.40 (m, 5H).

Example 253: (4-(difluoromethoxy)-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



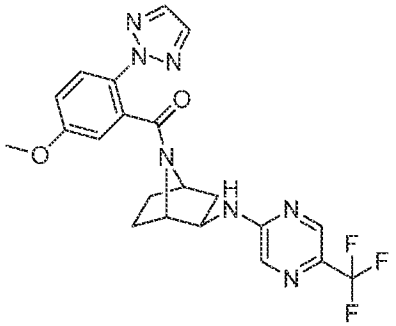
Prepared analogous to Example 181 substituting intermediate A-1 with intermediate A-23. MS (ESI) mass calcd. for $C_{21}H_{18}F_5N_7O_2$, 495.1; m/z found 496.3 $[M+H]^+$. ^1H NMR ($CDCl_3$): 8.32 (s, 0.3H), 8.19 (s, 0.7H), 7.98 – 7.81 (m, 2.4H), 7.77 (d, J = 2.3 Hz, 0.4H), 7.61 (d, J = 2.4 Hz, 0.7H), 7.58 – 7.45 (m, 1H), 7.39 (d, J = 8.4 Hz, 0.7H), 7.21 (dd, J = 8.4, 2.4 Hz, 0.5H), 7.18 – 7.00 (m, 0.9H), 6.59 (td, J = 72.6, 31.4 Hz, 1H), 6.33 – 6.16 (m, 0.4H), 4.92 – 4.70 (m, 1H), 4.43 – 4.19 (m, 1H), 4.09 – 3.83 (m, 1H), 2.30 – 1.44 (m, 6H).

Example 254: (3-fluoro-2-(3-methyl-1,2,4-oxadiazol-5-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Prepared analogous to Example 181 substituting intermediate A-1 with intermediate A-17. MS (ESI) mass calcd. for $C_{21}H_{18}F_4N_6O_2$, 462.1; m/z found 463.3 $[M+H]^+$. ^1H NMR ($CDCl_3$): 8.31 (s, 0.3H), 8.18 (s, 0.7H), 8.09 (s, 0.3H), 7.75 – 7.68 (m, 0.7H), 7.63 (td, J = 8.0, 5.0 Hz, 0.3H), 7.49 (td, J = 7.9, 5.1 Hz, 0.7H), 7.44 – 7.13 (m, 2.6H), 5.79 (d, J = 8.0 Hz, 0.4H), 4.88 – 4.67 (m, 1H), 4.40 – 4.22 (m, 1H), 4.10 – 3.88 (m, 1H), 2.52 (s, 3H), 2.28 – 1.54 (m, 6H).

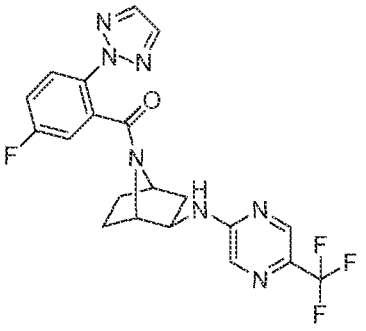
Example 255: (5-methoxy-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Prepared analogous to Example 181 substituting intermediate A-1 with intermediate A-18. MS (ESI) mass calcd. for $C_{21}H_{20}F_3N_7O_2$, 459.2; m/z found 460.3 $[M+H]^+$. ^1H NMR ($CDCl_3$): 8.32 (s, 0.3H), 8.19 (s, 0.7H), 7.96 – 7.76 (m, 2.5H), 7.74 – 7.63 (m, 1H), 7.56 (s, 1H),

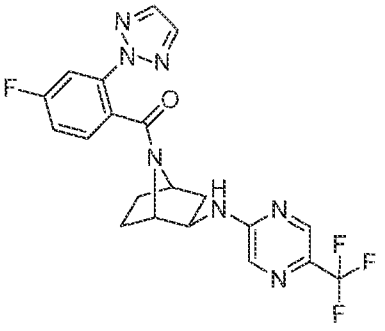
7.07 (dd, J = 8.9, 2.9 Hz, 0.4H), 7.03 – 6.92 (m, 1H), 6.87 (d, J = 2.9 Hz, 0.8H), 6.17 – 6.05 (m, 0.3H), 4.89 – 4.70 (m, 1H), 4.43 – 4.19 (m, 1H), 4.10 – 3.94 (m, 1H), 3.92 – 3.75 (m, 3H), 2.25 – 1.43 (m, 6H).

Example 256: (5-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



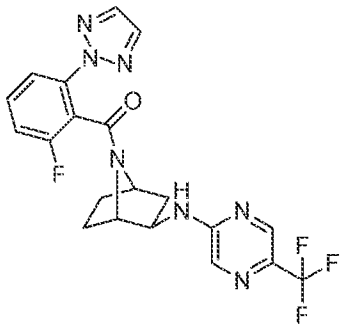
Prepared analogous to Example 181 substituting intermediate A-1 with intermediate A-10. MS (ESI) mass calcd. for $C_{20}H_{17}F_4N_7O$, 447.2; m/z found 448.3 $[M+H]^+$. ^1H NMR ($CDCl_3$): 8.32 (s, 0.3H), 8.20 (s, 0.7H), 8.02 – 7.87 (m, 1.5H), 7.88 – 7.71 (m, 1.5H), 7.54 (s, 0.7H), 7.38 – 7.00 (m, 3H), 6.32 – 6.08 (m, 0.3H), 4.92 – 4.68 (m, 1H), 4.46 – 4.20 (m, 1H), 4.12 – 3.88 (m, 1H), 2.28 – 1.39 (m, 6H).

Example 257: (4-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



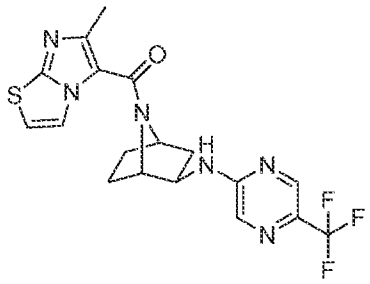
Prepared analogous to Example 181 substituting intermediate A-1 with intermediate A-12. MS (ESI) mass calcd. for $C_{20}H_{17}F_4N_7O$, 447.2; m/z found 448.3 $[M+H]^+$. ^1H NMR ($CDCl_3$): 8.33 (s, 0.3H), 8.20 (s, 0.7H), 8.01 – 7.79 (m, 2.4H), 7.73 (dd, J = 9.4, 2.6 Hz, 0.4H), 7.63 – 7.44 (m, 1.7H), 7.38 (dd, J = 8.5, 5.7 Hz, 0.7H), 7.21 – 6.94 (m, 1.4H), 6.20 (d, J = 8.5 Hz, 0.4H), 4.91 – 4.73 (m, 1H), 4.46 – 4.17 (m, 1H), 4.09 – 3.85 (m, 1H), 2.25 – 1.44 (m, 6H).

Example 258: (2-fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



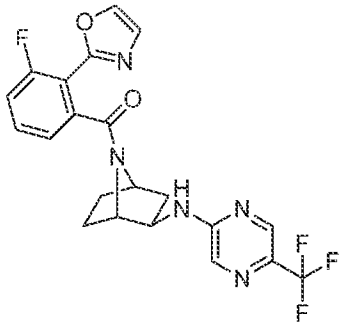
Prepared analogous to Example 181 substituting intermediate A-1 with intermediate A-11. MS (ESI) mass calcd. for $C_{20}H_{17}F_4N_7O$, 447.2; m/z found 448.3 $[M+H]^+$. ^1H NMR ($CDCl_3$): 8.41 – 8.29 (m, 0.3H), 8.20 (s, 0.7H), 8.01 – 7.60 (m, 3H), 7.60 – 7.11 (m, 3.2H), 7.03 – 6.89 (m, 0.2H), 6.20 – 6.06 (m, 0.2H), 5.45 – 5.34 (m, 0.2H), 5.16 – 5.04 (m, 0.2H), 4.99 – 4.75 (m, 1H), 4.49 – 4.16 (m, 1H), 4.13 – 4.00 (m, 0.3H), 3.88 (d, J = 5.2 Hz, 0.5H), 3.69 (d, J = 5.1 Hz, 0.2H), 2.33 – 1.36 (m, 6H).

Example 259: (6-methylimidazo[2,1-b]thiazol-5-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Prepared analogous to Example 181 substituting intermediate A-1 with 6-methylimidazo[2,1-b]thiazole-5-carboxylic acid. MS (ESI) mass calcd. for $C_{18}H_{17}F_3N_6OS$, 422.2; m/z found 423.2 $[M+H]^+$. ^1H NMR ($CDCl_3$): 8.26 (s, 1H), 7.91 – 7.75 (m, 2H), 6.96 – 6.80 (m, 1H), 5.91 (s, 1H), 4.58 (d, J = 5.0 Hz, 1H), 4.42 (t, J = 4.8 Hz, 1H), 4.21 – 4.05 (m, 1H), 2.49 (s, 3H), 2.25 (dd, J = 13.2, 7.5 Hz, 1H), 2.10 – 1.88 (m, 2H), 1.73 – 1.54 (m, 3H).

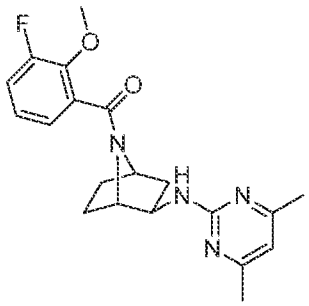
Example 260: (3-fluoro-2-(oxazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



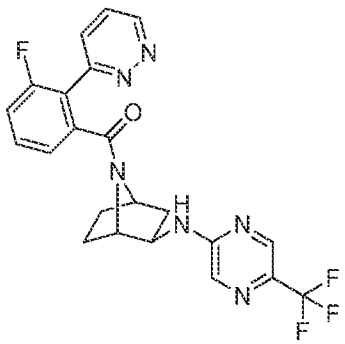
Step A: (3-fluoro-2-iodophenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone. Prepared analogous to Example 238 substituting intermediate A-2 with 3-fluoro-2-iodobenzoic acid. MS (ESI) mass calcd. for $C_{18}H_{15}F_4IN_4O$, 506.0; m/z found 507.2 $[M+H]^+$. ^1H NMR ($CDCl_3$): 8.27– 8.14 (m, 1H), 8.10 – 7.81 (m, 1H), 7.48 – 7.32 (m, 0.5H), 7.23 – 6.83 (m, 2.5H), 6.66 – 5.98 (m, 1H), 4.94 – 4.69 (m, 1H), 4.31 – 4.14 (m, 0.5H), 4.08 – 3.90 (m, 0.5H), 3.90 – 3.75 (m, 0.5H), 3.72 – 3.44 (m, 0.5H), 2.27 – 1.41 (m, 6H).

Step B: (3-fluoro-2-(oxazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone. The title compound of step A (35 mg) and 2-(tributylstannyl)oxazole (17 μL) were dissolved in DME (1 mL). The solution was degassed with N_2 as CuI (1 mg) and $Pd(PPh_3)_4$ (4 mg) was added. The reaction was heated at 120 °C for 3h. Additional CuI and $Pd(PPh_3)_4$ and the reaction purged with N_2. Heating was continued overnight. The reaction was cooled to rt, filtered through a pad of celite and purified via prep HPLC to give the title compound (12 mg, 39%). MS (ESI) mass calcd. for $C_{21}H_{17}F_4N_5O_2$, 447.1; m/z found 448.3 $[M+H]^+$. ^1H NMR ($CDCl_3$): 8.34 (s, 1H), 8.16 (s, 1H), 7.98 – 7.78 (m, 1H), 7.69 (s, 0.8H), 7.60 – 7.06 (m, 4H), 6.80 – 6.61 (m, 0.2H), 4.92 – 4.66 (m, 1H), 4.46 – 4.23 (m, 1H), 4.06 – 3.80 (m, 1H), 2.36 – 1.51 (m, 6H).

Example 261: (2-((4,6-dimethylpyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-methoxyphenyl)methanone.

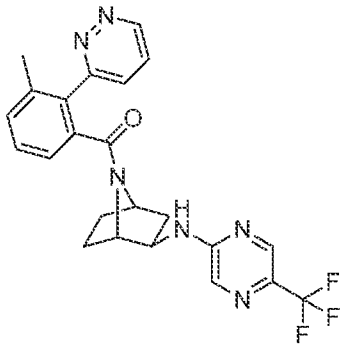


Example 262: (3-fluoro-2-(pyridazin-3-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Prepared analogous to Example 260 substituting 2-(tributylstannyl)oxazole with 3-(tributylstannyl)pyridazine. MS (ESI) mass calcd. for $C_{22}H_{18}F_4N_6O$, 458.1; m/z found 459.1 $[M+H]^+$. ^1H NMR (500 MHz, Chloroform-d) 9.25 – 9.14 (m, 1H), 8.50 (s, 0.5H), 8.28 (s, 0.8H), 8.17 (s, 0.5H), 7.97 – 7.80 (m, 1.5H), 7.72 – 7.59 (m, 1H), 7.55 – 7.41 (m, 1H), 7.34 – 7.18 (m, 2.2H), 6.96 (d, J = 8.1 Hz, 0.5H), 4.79 – 4.72 (m, 0.55H), 4.71 – 4.64 (m, 0.45H), 4.53 – 4.43 (m, 0.6H), 4.38 – 4.28 (m, 0.45H), 4.18 (s, 0.4H), 4.13 – 4.05 (m, 0.55H), 2.30 – 1.47 (m, 6H).

Example 263: (3-methyl-2-(pyridazin-3-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.

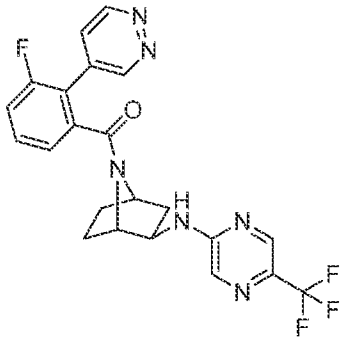


Step A: (2-iodo-3-methylphenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone. Prepared analogous to Example 238 substituting intermediate A-2 with 2-iodo-3-methylbenzoic acid. MS (ESI) mass calcd. for $C_{19}H_{18}F_3IN_4O$, 502.0; m/z found 503.0 $[M+H]^+$. ^1H NMR (400 MHz, Chloroform-d) 8.26 – 8.03 (m, 1.4H), 7.88 – 6.60 (m, 4.6H), 4.93 – 4.58 (m, 1H), 4.32 – 4.15 (m, 0.4H), 3.92 (s, 0.4H), 3.86 – 3.76 (m, 0.6H), 3.57 (s, 0.6H), 2.51 (s, 1.4H), 2.40 (s, 1.6H), 2.21 – 0.66 (m, 6H).

Step B: (3-methyl-2-(pyridazin-3-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone. Prepared analogous to Example 260

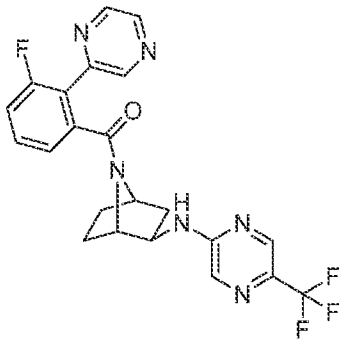
Step B substituting 2-(tributylstannyl)oxazole with 3-(tributylstannyl)pyridazine. MS (ESI) mass calcd. for $C_{23}H_{21}F_3N_6O$, 454.2; m/z found 455.2 $[M+H]^+$. ^1H NMR (400 MHz, Chloroform-d) 9.22 (dd, J = 4.9, 1.7 Hz, 0.25H), 9.19 (dd, J = 4.8, 1.8 Hz, 0.75H), 8.57 (s, 0.75H), 8.27 (s, 0.25H), 8.21 (s, 0.25H), 8.16 (s, 0.75H), 7.97 (s, 0.75H), 7.72 – 7.56 (m, 2H), 7.44 – 7.27 (m, 2.25H), 7.25 – 7.19 (m, 0.75H), 6.40 (d, J = 8.0 Hz, 0.25H), 4.68 – 4.62 (m, 0.75H), 4.59 – 4.54 (m, 0.25H), 4.39 (ddd, J = 9.3, 8.1, 3.9 Hz, 0.75H), 4.28 – 4.15 (m, 0.5H), 4.08 – 4.03 (m, 0.75H), 2.32 (s, 0.75H), 2.21 (s, 2.25H), 2.18 – 1.42 (m, 6H).

Example 264 (3-fluoro-2-(pyridazin-4-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



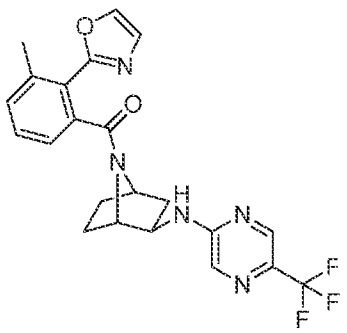
Prepared analogous to Example 260 substituting 2-(tributylstannyl)oxazole with 4-(tributylstannyl)pyridazine. MS (ESI) mass calcd. for $C_{22}H_{18}F_4N_6O$, 458.1; m/z found 459.2 $[M+H]^+$. ^1H NMR (400 MHz, Chloroform-d) 9.38 – 9.20 (m, 2H), 8.28 (s, 0.6H), 8.19 (s, 0.4H), 8.00 (s, 0.6H), 7.94 (s, 0.4H), 7.71 – 7.63 (m, 0.6H), 7.62 – 7.50 (m, 1H), 7.40 – 7.29 (m, 1H), 7.24 – 7.08 (m, 1.4H), 5.24 (s, 0.4H), 4.80 (s, 0.6H), 4.67 (s, 0.4H), 4.61 (d, J = 5.3 Hz, 0.6H), 4.02 – 3.92 (m, 0.6H), 3.85 – 3.75 (m, 0.4H), 3.70 – 3.59 (m, 1H), 1.90 – 2.07 (m, 1H), 1.84 – 0.79 (m, 5H).

Example 265 (3-fluoro-2-(pyrazin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



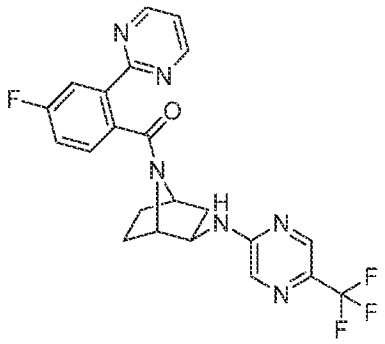
Prepared analogous to Example 260 substituting 2-(tributylstannyl)oxazole with 2-(tributylstannyl)pyrazine. MS (ESI) mass calcd. for $C_{22}H_{18}F_4N_6O$, 458.1; m/z found 459.2 $[M+H]^+$. ^1H NMR (400 MHz, Chloroform-d) 8.99 – 8.94 (m, 1H), 8.69 (d, J = 2.6 Hz, 1H), 8.58 – 8.51 (m, 1H), 8.19 (s, 1H), 8.03 (s, 1H), 7.57 (s, 1H), 7.44 – 7.37 (m, 1H), 7.25 – 7.20 (m, 2H), 4.80 – 4.74 (m, 1H), 4.40 (td, J = 8.6, 3.6 Hz, 1H), 4.05 (d, J = 5.1 Hz, 1H), 2.24 – 2.16 (m, 1H), 1.78 – 1.67 (m, 2H), 1.62 – 1.51 (m, 2H), 1.41 – 1.29 (m, 1H).

Example 266 (3-methyl-2-(oxazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



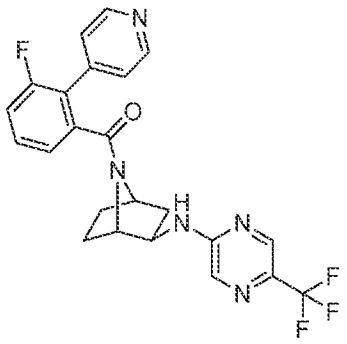
Prepared analogous to Example 263 substituting 3-(tributylstannyl)pyridazine with 2-(tributylstannyl)oxazole. MS (ESI) mass calcd. for $C_{22}H_{20}F_3N_5O_2$, 443.2; m/z found 444.2 $[M+H]^+$. ^1H NMR (500 MHz, Chloroform-d) 8.57 (s, 1H), 8.14 (s, 1H), 7.88 (d, J = 0.9 Hz, 1H), 7.79 (d, J = 1.4 Hz, 1H), 7.33 – 7.23 (m, 3H), 7.20 – 7.14 (m, 1H), 4.82 – 4.75 (m, 1H), 4.29 (td, J = 8.5, 3.7 Hz, 1H), 3.94 (d, J = 4.9 Hz, 1H), 2.28 (s, 3H), 2.16 – 1.45 (m, 6H).

Example 267 (4-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



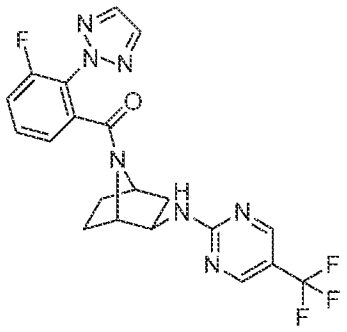
Prepared analogous to Example 238 substituting intermediate A-2 with intermediate A-25. MS (ESI) mass calcd. for : $C_{22}H_{18}F_4N_6O$, 458.1; m/z found 459.2 $[M+H]^+$. ^1H NMR (500 MHz, Chloroform-d) 8.89 – 8.81 (m, 1.7H), 8.80 – 8.73 (m, 0.3H), 8.33 – 7.87 (m, 2H), 7.80 (s, 0.2H), 7.74 – 7.66 (m, 0.8H), 7.56 – 7.31 (m, 2.8H), 7.21 – 7.14 (m, 0.2H), 7.14 – 7.06 (m, 0.8H), 6.58 (s, 0.2H), 4.88 – 4.78 (m, 0.8H), 4.72 (d, J = 5.2 Hz, 0.2H), 4.40 (s, 0.8H), 4.26 (s, 0.2H), 4.10 – 3.97 (m, 1H), 2.27 – 1.39 (m, 6H).

Example 268 (3-fluoro-2-(pyridin-4-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



Prepared analogous to Example 260 substituting 2-(tributylstannyl)oxazole with 4-(tributylstannyl)pyridine. MS (ESI) mass calcd. for : $C_{23}H_{19}F_4N_5O$, 457.2; m/z found 458.2 $[M+H]^+$. ^1H NMR (500 MHz, Chloroform-d) 8.78 – 8.61 (m, 2H), 8.28 (s, 0.6H), 8.15 (s, 0.4H), 7.87 (s, 1H), 7.72 – 7.28 (m, 4.2H), 7.23 – 7.02 (m, 1.4H), 5.49 (s, 0.4H), 4.67 – 4.60 (m, 0.4H), 4.56 (d, J = 5.3 Hz, 0.6H), 3.99 – 3.89 (m, 0.6H), 3.82 – 3.72 (m, 0.4H), 3.65 – 3.58 (m, 0.6H), 3.56 (d, J = 5.4 Hz, 0.4H), 2.00 – 0.80 (m, 6H).

Example 269 (3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



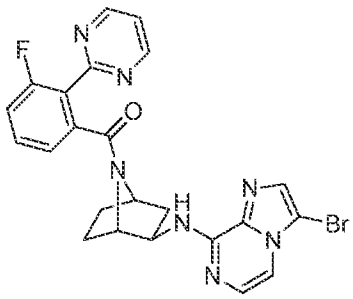
Step A: (1S,2R,4R)-tert-butyl 2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptane-7-carboxylate. To intermediate B-5 (250 mg, 1.2 mmol) and K_2CO_3 (244 mg, 1.8 mmol) in DMF (1.7 mL) was added 2-chloro-5-(trifluoromethyl)pyrimidine (258 mg, 1.4 mmol). After heating at 70 °C for 17h, the mixture was cooled to rt, diluted with EtOAc and H_2O. The aqueous layer was extracted with EtOAc (3X). The combined organics were washed with 4% $MgSO_4$ (aq) and dried ($MgSO_4$). Purification via silica gel chromatography (0-30% EtOAc in hexanes) gave the title compound (356 mg, 84%). MS (ESI) mass calcd. for $C_{16}H_{21}F_3N_4O_2$, 358.2; m/z found 359.2 $[M+H]^+$. ^1H NMR (500 MHz, Chloroform-d) 8.58 – 8.37 (m, 2H), 5.70 (s, 1H), 4.30 (s, 1H), 1.78 – 1.68 (m, 1H), 4.25 – 4.17 (m, 1H), 1.89 – 1.79 (m, 1H), 4.12 – 4.03 (m, 1H), 2.03 (dd, J = 13.1, 7.8 Hz, 1H), 1.63 – 1.37 (m, 12H).

Step B: (1S,2R,4R)-N-(5-(trifluoromethyl)pyrimidin-2-yl)-7-azabicyclo[2.2.1]heptan-2-amine. To the title compound of step A (355 mg, 1 mmol) in DCM (9.7 mL) was added 4M HCl in dioxane (1.2 mL). The reaction was allowed to proceed overnight then concentrated and neutralized with 5% Na_2CO_3 (aq) and extracted with DCM (2X). The combined organics were dried (Na_2SO_4) to give the title compound of step B that was used without further purification.

Step C: (3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone. To the title compound of step B (25 mg, 0.1 mmol) in DCM (1 mL) was added DIPEA (22 µL, 0.13 mmol) and intermediate A-16 (22 mg, 0.1 mmol). Then T3P (50% solution in DMF, 0.17 mL, 0.29 mmol) was added dropwise and the reaction heated at 45 °C for 12h. After allowing to cool to rt, DCM was added and the mixture washed with H_2O then saturated $NaHCO_3$ (aq). The combined aq layers were extracted with DCM. The combined organic layers were dried (Na_2SO_4). Purification was performed using Agilent prep method X to give the title compound (35 mg, 80%). MS (ESI) mass calcd. for: $C_{20}H_{17}F_4N_7O$, 447.1; m/z found 448.2 $[M+H]^+$. ^1H NMR (400 MHz, Chloroform-d) 8.50 (s, 0.9H), 8.41 (s, 1.1H), 8.09 (s, 0.9H), 7.95 (s, 1.1H), 7.56 – 7.47 (m, 0.5H), 7.44 – 7.32 (m, 1H), 7.33 – 7.23 (m, 1.5H), 7.20 – 7.14 (m, 0.5H), 6.18 (d, J = 8.6 Hz,

0.5H), 4.83 – 4.74 (m, 0.5H), 4.67 (d, *J* = 5.2 Hz, 0.5H), 4.34 – 4.19 (m, 1H), 4.11 – 4.04 (m, 0.5H), 3.99 (d, *J* = 4.8 Hz, 0.5H), 2.21 – 1.44 (m, 6H).

Example 270 ((1S,2R,4R)-2-((3-bromoimidazo[1,2-a]pyrazin-8-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-(pyrimidin-2-yl)phenyl)methanone

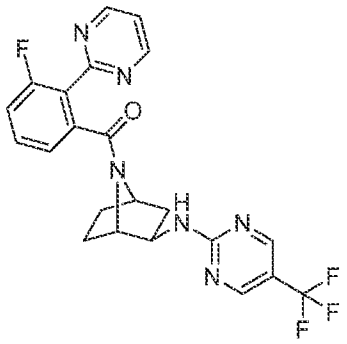


Step A: (1S,2R,4R)-tert-butyl 2-((3-bromoimidazo[1,2-a]pyrazin-8-yl)amino)-7-azabicyclo[2.2.1]heptane-7-carboxylate. Prepared analogous to Example 269 step A substituting 2-chloro-5-(trifluoromethyl)pyrimidine with 3-bromo-8-chloroimidazo[1,2-a]pyrazine. MS (ESI) mass calcd. for : $C_{17}H_{22}BrN_5O_2$, 407.1; m/z found 408.1 $[M+H]^+$. ^1H NMR (500 MHz, Chloroform-d) 7.45 (s, 1H), 7.43 (d, *J* = 4.7 Hz, 1H), 7.40 (d, *J* = 4.7 Hz, 1H), 6.15 (s, 1H), 4.37 – 4.27 (m, 2H), 4.27 – 4.21 (m, 1H), 2.08 (dd, *J* = 13.0, 7.8 Hz, 1H), 1.90 – 1.33 (m, 14H).

Step B: N-((1S,2R,4R)-7-azabicyclo[2.2.1]heptan-2-yl)-3-bromoimidazo[1,2-a]pyrazin-8-amine. Prepared analogous to Example 269 step B using title compound of step A.

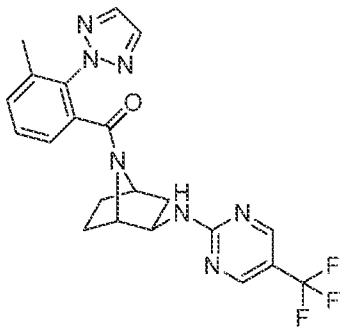
Step C: ((1S,2R,4R)-2-((3-bromoimidazo[1,2-a]pyrazin-8-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-(pyrimidin-2-yl)phenyl)methanone. Prepared analogous to Example 269 step C substituting intermediate A-16 with intermediate A-2. MS (ESI) mass calcd. for : $C_{23}H_{19}BrFN_7O$, 507.1; m/z found 508.1 $[M+H]^+$. ^1H NMR (400 MHz, Chloroform-d) 8.92 (d, *J* = 4.9 Hz, 0.7H), 8.88 (d, *J* = 4.9 Hz, 1.3H), 7.53 – 7.03 (m, 7.6H), 5.82 (d, *J* = 7.6 Hz, 0.4H), 4.81 – 4.75 (m, 0.6H), 4.71 (d, *J* = 5.1 Hz, 0.4H), 4.47 – 4.37 (m, 0.6H), 4.31 – 4.22 (m, 0.4H), 4.13 – 4.07 (m, 0.6H), 4.06 – 3.99 (m, 0.4H), 2.26 – 1.36 (m, 6H).

Example 271 (3-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



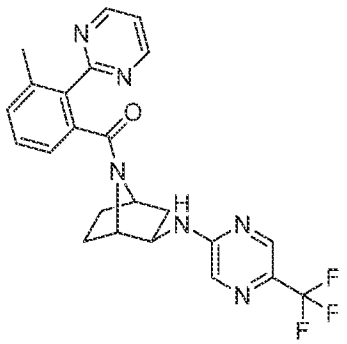
Prepared analogous to Example 269 substituting intermediate A-16 with intermediate A-2. MS (ESI) mass calcd. for : $C_{22}H_{18}F_4N_6O$, 458.1; m/z found 459.2 $[M+H]^+$. ^1H NMR (400 MHz, Chloroform-d) 8.90 (d, J = 5.0 Hz, 2H), 8.49 (s, 1H), 8.44 – 8.31 (m, 2H), 7.43 – 7.32 (m, 2H), 7.26 – 7.14 (m, 2H), 4.80 – 4.75 (m, 1H), 4.45 – 4.37 (m, 1H), 4.09 (d, J = 5.0 Hz, 1H), 2.22 (dd, J = 12.9, 8.0 Hz, 1H), 2.11 – 1.51 (m, 5H).

Example 272 (3-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



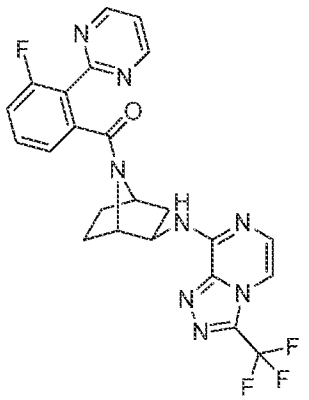
Prepared analogous to Example 269 substituting intermediate A-16 with intermediate A-24. MS (ESI) mass calcd. for : $C_{21}H_{20}F_3N_7O$, 443.2; m/z found 444.2 $[M+H]^+$. ^1H NMR (400 MHz, Chloroform-d) 8.49 (s, 0.8H), 8.41 (s, 1.2H), 8.02 (s, 0.8H), 7.91 (s, 1.2H), 7.47 – 7.39 (m, 1H), 7.38 – 7.28 (m, 2H), 7.23 – 7.16 (m, 0.6H), 5.98 (d, J = 8.4 Hz, 0.4H), 4.77 – 4.68 (m, 0.6H), 4.60 (d, J = 5.1 Hz, 0.4H), 4.29 – 4.17 (m, 1H), 4.11 – 4.03 (m, 0.4H), 3.99 (d, J = 5.0 Hz, 0.6H), 2.27 (s, 1.3H), 2.24 (s, 1.7H), 2.18 – 1.41 (m, 6H).

Example 273 (3-methyl-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



Prepared analogous to Example 238 substituting intermediate A-2 with intermediate A-26. MS (ESI) mass calcd. for : $C_{23}H_{21}F_3N_6O$, 454.2; m/z found 455.1 $[M+H]^+$. ^1H NMR (400 MHz, Chloroform-d) 8.85 (d, J = 5.0 Hz, 2H), 8.50 (d, J = 9.2 Hz, 1H), 8.17 (s, 1H), 7.66 (d, J = 1.3 Hz, 1H), 7.37 (t, J = 5.0 Hz, 1H), 7.31 – 7.18 (m, 3H), 4.73 – 4.67 (m, 1H), 4.35 (td, J = 8.7, 3.7 Hz, 1H), 4.14 – 4.09 (m, 1H), 2.29 (s, 3H), 2.19 – 1.45 (m, 6H).

Example 274 (3-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((3-(trifluoromethyl)-[1,2,4]triazolo[4,3-a]pyrazin-8-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



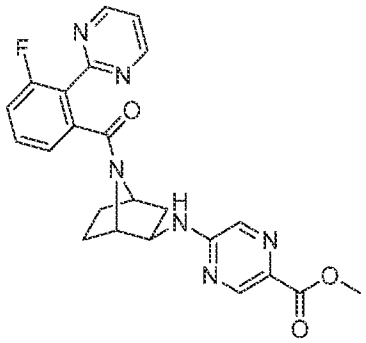
Step A: (1S,2R,4R)-tert-butyl 2-((3-(trifluoromethyl)-[1,2,4]triazolo[4,3-a]pyrazin-8-yl)amino)-7-azabicyclo[2.2.1]heptane-7-carboxylate. Prepared analogous to Example 269 step A substituting 2-chloro-5-(trifluoromethyl)pyrimidine with 8-chloro-3-(trifluoromethyl)-[1,2,4]triazolo[4,3-a]pyrazine. MS (ESI) mass calcd. for : $C_{17}H_{21}F_3N_6O_2$, 398.2; m/z found 399.2 $[M+H]^+$. ^1H NMR (500 MHz, Chloroform-d) 7.51 – 7.48 (m, 1H), 7.48 – 7.45 (m, 1H), 6.58 (d,

J = 7.6 Hz, 1H), 4.41 – 4.25 (m, 3H), 1.94 – 1.83 (m, 1H), 2.12 (dd, J = 13.1, 7.8 Hz, 1H), 1.83 – 1.70 (m, 2H), 1.59 – 1.52 (m, 1H), 1.50 – 1.41 (m, 10H).

Step B: N-((1S,2R,4R)-7-azabicyclo[2.2.1]heptan-2-yl)-3-(trifluoromethyl)-[1,2,4]triazolo[4,3-a]pyrazin-8-amine. Prepared analogous to Example 269 step B using title compound of step A.

Step C: (3-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((3-(trifluoromethyl)-[1,2,4]triazolo[4,3-a]pyrazin-8-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone. Prepared analogous to Example 269 step C substituting intermediate A-16 with intermediate A-2. MS (ESI) mass calcd. for : $C_{23}H_{18}F_4N_8O$, 498.2; m/z found 499.2 $[M+H]^+$. ^{1}H NMR (400 MHz, Chloroform-d) 8.99 (d, J = 4.9 Hz, 0.6H), 8.95 (d, J = 5.0 Hz, 1.4H), 8.72 (s, 0.7H), 7.55 – 7.28 (m, 4.6H), 7.21 – 7.10 (m, 1.4H), 6.18 (d, J = 7.5 Hz, 0.3H), 4.88 – 4.80 (m, 0.7H), 4.75 (d, J = 5.1 Hz, 0.3H), 4.67 (s, 0.7H), 4.33 (s, 0.3H), 4.16 – 4.06 (m, 1H), 2.27 (dd, J = 12.7, 8.2 Hz, 0.7H), 2.11 (dd, J = 13.0, 8.1 Hz, 0.3H), 2.04 – 1.41 (m, 5H).

Example 275 methyl 5-(((1S,2R,4R)-7-(3-fluoro-2-(pyrimidin-2-yl)benzoyl)-7-azabicyclo[2.2.1]heptan-2-yl)amino)pyrazine-2-carboxylate

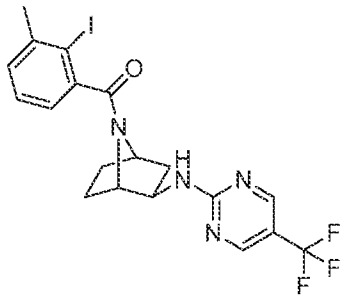


Step A: (1S,2R,4R)-tert-butyl 2-((5-(methoxycarbonyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptane-7-carboxylate. Prepared analogous to Example 269 step A substituting 2-chloro-5-(trifluoromethyl)pyrimidine with methyl 5-chloropyrazine-2-carboxylate. MS (ESI) mass calcd. for : $C_{17}H_{24}N_4O_4$, 348.2; m/z found 349.2 $[M+H]^+$. ^{1}H NMR (400 MHz, Chloroform-d) 8.77 (d, J = 1.4 Hz, 1H), 7.88 (d, J = 1.4 Hz, 1H), 5.55 (s, 1H), 4.34 – 4.27 (m, 1H), 4.25 – 4.18 (m, 1H), 4.12 – 4.06 (m, 1H), 3.95 (s, 3H), 2.12 – 2.05 (m, 1H), 1.92 – 1.72 (m, 2H), 1.63 – 1.38 (m, 12H).

Step B: methyl 5-((1S,2R,4R)-7-azabicyclo[2.2.1]heptan-2-ylamino)pyrazine-2-carboxylate. Prepared analogous to Example 269 step B using title compound of step A.

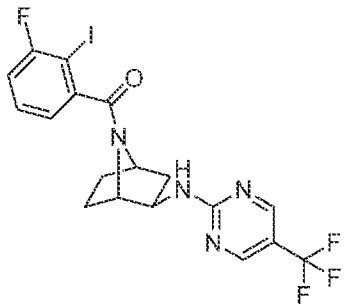
Step C: methyl 5-(((1S,2R,4R)-7-(3-fluoro-2-(pyrimidin-2-yl)benzoyl)-7-azabicyclo[2.2.1]heptan-2-yl)amino)pyrazine-2-carboxylate. Prepared analogous to Example 269 step C substituting intermediate A-16 with intermediate A-2. MS (ESI) mass calcd. for : $C_{23}H_{21}FN_6O_3$, 448.2; m/z found 449.2 $[M+H]^+$. ^1H NMR (500 MHz, Chloroform-d) 8.87 (d, J = 4.9 Hz, 2H), 8.65 (s, 1H), 8.37 (d, J = 9.4 Hz, 1H), 7.67 (s, 1H), 7.42 – 7.34 (m, 2H), 7.24 – 7.17 (m, 2H), 4.77 – 4.70 (m, 1H), 4.48 – 4.39 (m, 1H), 4.07 (d, J = 5.1 Hz, 1H), 3.90 (s, 3H), 2.18 (dd, J = 13.0, 8.1 Hz, 1H), 2.11 – 2.00 (m, 1H), 1.97 – 1.62 (m, 3H), 1.58 – 1.48 (m, 1H).

Example 276 (2-iodo-3-methylphenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



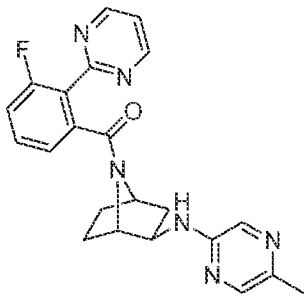
Prepared analogous to Example 269 substituting intermediate A-16 with 2-iodo-3-methylbenzoic acid. MS (ESI) mass calcd. for : $C_{19}H_{18}F_3IN_4O$, 502.0; m/z found 503.0 $[M+H]^+$. ^1H NMR (400 MHz, Chloroform-d) 8.59 – 8.30 (m, 2H), 7.32 – 7.22 (m, 1.4H), 7.19 – 6.96 (m, 1H), 6.93 – 6.83 (m, 0.6H), 6.02 (s, 0.5H), 5.54 (s, 0.5H), 5.01 – 4.91 (m, 0.5H), 4.84 (d, J = 5.1 Hz, 0.5H), 4.28 (s, 0.5H), 4.02 (s, 0.5H), 3.84 – 3.66 (m, 1H), 2.50 (s, 1.5H), 2.43 (s, 1.5H), 2.24 – 1.39 (m, 6H).

Example 277 (3-fluoro-2-iodophenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



Prepared analogous to Example 269 substituting intermediate A-16 with 3-fluoro-2-iodobenzoic acid. MS (ESI) mass calcd. for : $C_{18}H_{15}F_4IN_4O$, 506.0; m/z found 507.0 $[M+H]^+$. ^1H NMR (400 MHz, Chloroform-d) 8.57 – 8.33 (m, 2H), 7.42 – 7.32 (m, 0.5H), 7.16 – 7.02 (m, 1.5H), 6.99 – 6.88 (m, 1H), 5.99 (d, J = 7.6 Hz, 0.5H), 5.55 (s, 0.5H), 5.00 – 4.91 (m, 0.5H), 4.85 (d, J = 5.3 Hz, 0.5H), 4.32 – 4.24 (m, 0.5H), 4.05 – 3.97 (m, 0.5H), 3.81 – 3.71 (m, 1H), 2.22 – 1.93 (m, 2H), 1.91 – 1.43 (m, 4H).

Example 278 (3-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-methylpyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

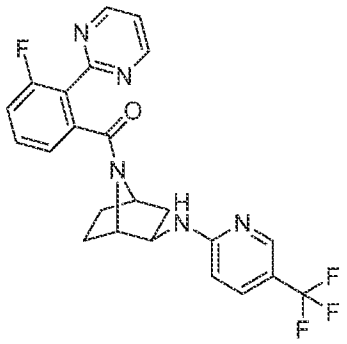


Step A: (1S,2R,4R)-tert-butyl 2-((5-methylpyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptane-7-carboxylate. Prepared analogous to Example 279 step A substituting 2-chloro-5-(trifluoromethyl)pyridine with 2-chloro-5-methylpyrazine. MS (ESI) mass calcd. for : $C_{16}H_{24}N_4O_2$, 304.2; m/z found 305.2 $[M+H]^+$. ^1H NMR (400 MHz, Chloroform-d) 7.86 (s, 1H), 7.78 (d, J = 1.5 Hz, 1H), 4.71 (s, 1H), 4.28 (s, 1H), 4.19 (d, J = 4.9 Hz, 1H), 3.95 – 3.85 (m, 1H), 2.38 (s, 3H), 2.11 – 1.96 (m, 1H), 1.89 – 1.66 (m, 2H), 1.58 – 1.33 (m, 12H).

Step B: (1S,2R,4R)-N-(5-methylpyrazin-2-yl)-7-azabicyclo[2.2.1]heptan-2-amine. Prepared analogous to Example 279 step B using title compound of step A.

Step C: (3-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-methylpyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone. Prepared analogous to Example 279 step C. MS (ESI) mass calcd. for : $C_{22}H_{21}FN_6O$, 404.2; m/z found 405.2 $[M+H]^+$. ^1H NMR (500 MHz, Chloroform-d) 8.87 (d, J = 5.0 Hz, 2H), 7.74 (s, 1H), 7.60 (s, 1H), 7.41 – 7.30 (m, 3H), 7.23 – 7.12 (m, 2H), 4.76 – 4.68 (m, 1H), 4.30 – 4.17 (m, 1H), 4.08 – 4.01 (m, 1H), 2.30 (s, 3H), 2.15 (dd, J = 12.9, 8.1 Hz, 1H), 2.07 – 1.95 (m, 1H), 1.95 – 1.84 (m, 1H), 1.74 – 1.46 (m, 3H).

Example 279 (3-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



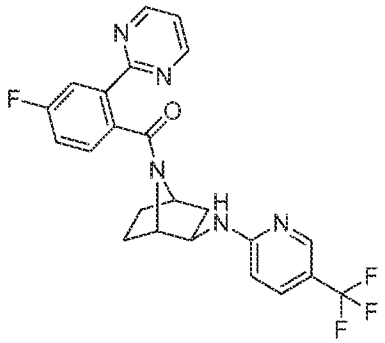
Step A: (1S,2R,4R)-tert-butyl 2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptane-7-carboxylate. In a microwave vial, toluene (8.3 mL) was degassed with N_2 for 10 minutes then $Pd(OAc)_2$ (22 mg, 0.03 mmol) and racemic BINAP (21 mg, 0.03 mmol) were added and the solution was degassed with N_2 for 5 minutes. Then intermediate B-5, 2-chloro-5-(trifluoromethyl)pyridine (150 mg, 0.83 mmol) and sodium tert-butoxide (115 mg, 1.16 mmol) were added and the reaction mixture was stirred at 70 °C. After 15h the reaction mixture was filtered through a pad of celite and solvent was evaporated. Purification via silica gel chromatography (0-40% EtOAc in hexanes) gave the title compound of step A (192 mg, 65%). MS (ESI) mass calcd. for : $C_{17}H_{22}F_3N_3O_2$, 357.2; m/z found 358.2 $[M+H]^+$. ^1H NMR (500 MHz, Chloroform-d) 8.33 (s, 1H), 7.61 – 7.49 (m, 1H), 6.35 (d, J = 8.8 Hz, 1H), 5.06 (s, 1H), 4.29 (s, 1H), 4.20 (s, 1H), 4.03 – 3.91 (m, 1H), 2.04 (dd, J = 13.0, 7.6 Hz, 1H), 1.89 – 1.79 (m, 1H), 1.79 – 1.71 (m, 1H), 1.59 – 1.37 (m, 12H).

Step B: (1S,2R,4R)-N-(5-(trifluoromethyl)pyridin-2-yl)-7-azabicyclo[2.2.1]heptan-2-amine. To the title compound of step A (319 mg, 0.89 mmol) in DCM (8.7 mL) was added 4M HCl in dioxane (1.1 mL). The reaction was allowed to proceed overnight then concentrated and neutralized with 5% Na_2CO_3 (aq) and extracted with DCM (2X). The combined organics were dried (Na_2SO_4) to give the title compound of step B that was used without further purification.

Step C: (3-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone. To the title compound of step B (100 mg, 0.39 mmol) in DCM (3.9 mL) was added DIPEA (87 µL, 0.51 mmol) and intermediate A-2 (100 mg, 0.43 mmol). Then T3P (50% solution in DMF, 0.7 mL, 1.16 mmol) was added dropwise and the reaction heated at 45 °C for 12h. After allowing to cool to rt, DCM was added and the mixture washed with H_2O then saturated $NaHCO_3$ (aq). The combined aq layers were extracted with DCM. The combined organic layers were dried (Na_2SO_4). Purification was performed using Agilent prep method X to give the title compound (61 mg, 34%). MS (ESI) mass calcd. for: $C_{23}H_{19}F_4N_5O$, 457.2; m/z found 458.2 $[M+H]^+$. ^1H NMR (400 MHz, Chloroform-d) 8.88 (d,

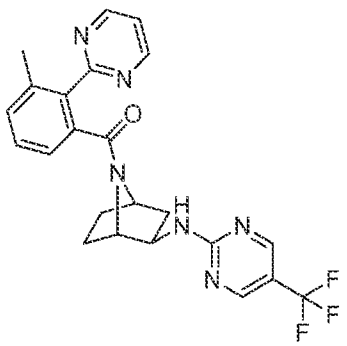
J = 4.9 Hz, 2H), 8.22 (s, 1H), 7.67 (d, *J* = 9.3 Hz, 1H), 7.43 – 7.28 (m, 3H), 7.24 – 7.12 (m, 2H), 6.19 (d, *J* = 8.8 Hz, 1H), 4.76 – 4.68 (m, 1H), 4.43 – 4.32 (m, 1H), 4.08 (d, *J* = 5.0 Hz, 1H), 2.16 (dd, *J* = 12.9, 8.1 Hz, 1H), 2.08 – 1.83 (m, 2H), 1.77 – 1.38 (m, 3H).

Example 280 (4-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



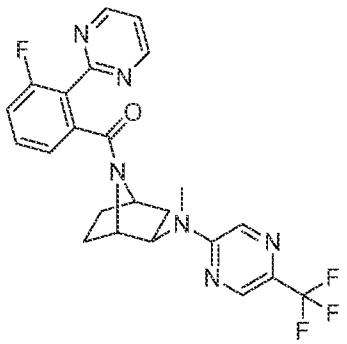
Prepared analogous to Example 279 substituting intermediate A-2 with intermediate A-25. MS (ESI) mass calcd. for : $C_{23}H_{19}F_4N_5O$, 457.2; m/z found 458.2 $[M+H]^+$. ^1H NMR (400 MHz, Chloroform-d) 8.89 – 8.76 (m, 2H), 8.36 (s, 0.2H), 8.26 – 8.19 (m, 0.8H), 8.05 – 7.91 (m, 0.4H), 7.70 (dd, *J* = 9.3, 2.7 Hz, 0.6H), 7.60 – 7.53 (m, 0.3H), 7.48 – 7.40 (m, 0.3H), 7.40 – 7.28 (m, 2.6H), 7.25 – 6.99 (m, 1.6H), 6.36 (d, *J* = 8.7 Hz, 0.2H), 5.96 (d, *J* = 8.8 Hz, 0.8H), 5.70 (s, 0.2H), 4.87 – 4.80 (m, 0.8H), 4.73 (d, *J* = 5.3 Hz, 0.2H), 4.38 (s, 0.8H), 4.17 (s, 0.2H), 4.06 – 4.00 (m, 0.8H), 4.00 – 3.94 (m, 0.2H), 2.21 (dd, *J* = 12.9, 8.0 Hz, 0.8H), 2.12 – 1.35 (m, 5.2H).

Example 281 (3-methyl-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



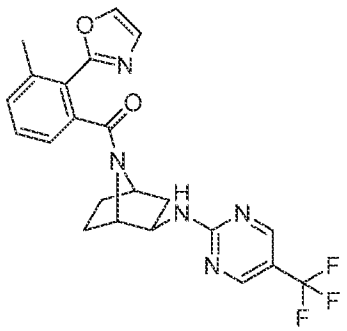
Prepared analogous to Example 269 substituting intermediate A-16 with intermediate A-26. MS (ESI) mass calcd. for : $C_{23}H_{21}F_3N_6O$, 454.2; m/z found 455.3 $[M+H]^+$. ^1H NMR (500 MHz, Chloroform-d) 8.89 – 8.85 (m, 2H), 8.70 (s, 1H), 8.44 – 8.32 (m, 2H), 7.34 – 7.23 (m, 3H), 7.21 – 7.15 (m, 1H), 4.77 – 4.68 (m, 1H), 4.43 – 4.33 (m, 1H), 4.11 (d, J = 5.1 Hz, 1H), 2.36 (s, 3H), 2.19 (dd, J = 12.8, 7.9 Hz, 1H), 2.09 – 1.99 (m, 1H), 1.94 – 1.85 (m, 1H), 1.72 – 1.48 (m, 3H).

Example 282 (3-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-(methyl(5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



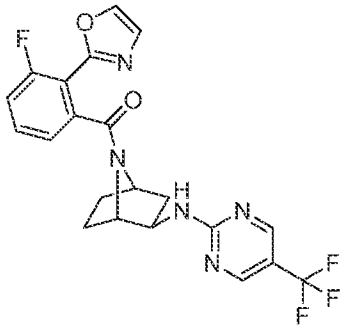
The title compound of Example 238 (63 mg, 0.14 mmol) was dissolved in DMF (1.4 mL) and then sodium tert-butoxide (15 mg, 0.15 mmol) followed by iodomethane (9 µL, 0.14 mmol) were added. After 15h at room temperature the reaction mixture was diluted with EtOAc and water was added. The aqueous phase was extracted twice with EtOAc and the combined organic phases were dried over $MgSO_4$, filtered and evaporated. Purification was performed using Agilent prep method X to give the title compound (40 mg, 62%). MS (ESI) mass calcd. for : $C_{23}H_{20}F_4N_6O$, 472.2; m/z found 473.2 $[M+H]^+$. ^1H NMR (500 MHz, Chloroform-d) 8.81 (d, J = 4.9 Hz, 2H), 8.35 (s, 1H), 8.02 (s, 1H), 7.55 – 7.46 (m, 1H), 7.34 – 7.20 (m, 3H), 4.81 – 4.73 (m, 1H), 4.67 (d, J = 4.3 Hz, 1H), 4.17 – 4.08 (m, 1H), 3.05 (s, 3H), 2.12 (dd, J = 12.8, 8.3 Hz, 1H), 1.98 – 1.44 (m, 5H).

Example 283 (3-methyl-2-(oxazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



Prepared analogous to Example 269 substituting intermediate A-16 with intermediate A-31. MS (ESI) mass calcd. for : $C_{22}H_{20}F_3N_5O_2$, 443.2; m/z found 444.1 $[M+H]^+$. ^1H NMR (400 MHz, Chloroform-d) 8.48 (s, 1H), 8.35 (s, 1H), 7.88 – 7.78 (m, 1H), 7.68 (s, 0.4H), 7.44 – 7.21 (m, 3.6H), 7.15 (dd, J = 6.6, 2.2 Hz, 0.6H), 7.06 – 6.97 (m, 0.4H), 4.84 – 4.78 (m, 0.6H), 4.73 – 4.67 (m, 0.4H), 4.33 (td, J = 8.4, 3.0 Hz, 0.4H), 4.24 (td, J = 8.2, 3.7 Hz, 0.6H), 4.04 – 3.98 (m, 0.4H), 3.97 – 3.89 (m, 0.6H), 2.47 (s, 1.7H), 2.37 (s, 1.3H), 2.19 – 1.41 (m, 6H).

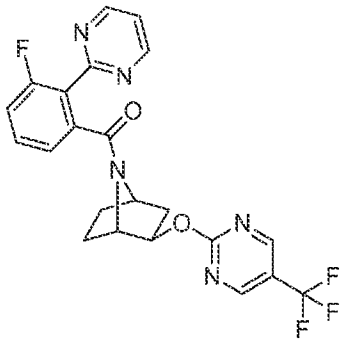
Example 284 (3-fluoro-2-(oxazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



In a microwave vial was dissolved the title compound of Example 277 (30 mg, 0.06 mmol) and 2-(tributylstannyl)oxazole (15 µL, 0.07 mmol) in DME (1 mL). The solution was degassed with N_2 for 5 minutes then CuI (1 mg, 0.0045 mmol) and $Pd(PPh_3)_4$ (5 mg, 0.0045 mmol) were added. The reaction was purged with N_2 and heated at 145 °C for 3h. The reaction was cooled to rt, filtered through a pad of celite and purified via prep HPLC to give the title compound (19 mg, 72%). MS (ESI) mass calcd. for : $C_{21}H_{17}F_4N_5O_2$, 447.1; m/z found 448.1 $[M+H]^+$. ^1H NMR (500 MHz, Chloroform-d) 8.49 (s, 1H), 8.36 (s, 0.8H), 7.85 (s, 0.8H), 7.76 (s,

0.4H), 7.62 – 7.45 (m, 1H), 7.43 – 7.33 (m, 1H), 7.32 – 7.23 (m, 2H), 7.23 – 7.09 (m, 1H), 4.91 – 4.85 (m, 0.4H), 4.78 (d, J = 5.4 Hz, 0.6H), 4.42 (td, J = 8.6, 2.8 Hz, 0.6H), 4.28 (td, J = 8.2, 3.6 Hz, 0.4H), 4.00 – 3.95 (m, 0.6H), 3.89 (d, J = 4.4 Hz, 0.4H), 2.23 – 1.44 (m, 6H).

Example 285 (±)-(3-fluoro-2-(pyrimidin-2-yl)phenyl)(2-((5-(trifluoromethyl)pyrimidin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

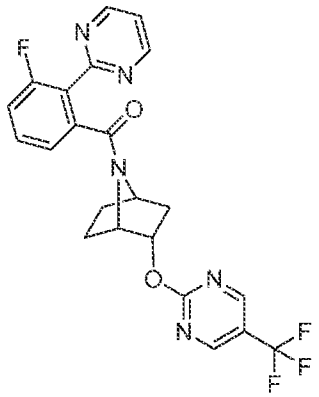


Step A: (±)-tert-butyl 2-((5-(trifluoromethyl)pyrimidin-2-yl)oxy)-7-azabicyclo[2.2.1]heptane-7-carboxylate: To (±)-tert-butyl 2-hydroxy-7-azabicyclo[2.2.1]heptane-7-carboxylate (exo) (52 mg, 0.25 mol) in DMF (5 mL) was added 60 wt% NaH (20 mg, 0.5 mmol) in one portion. The reaction was heated at 80 °C for 5 min, then 2-chloro-5-(trifluoromethyl)pyrimidine (89.7 mg, 0.49 mmol) was added. After heating at 80 °C for 2 hours, water was added and the mixture extracted with DCM (3X). The combined organics were dried (Na_2SO_4) and concentrated. Purification via silica gel chromatography (0-50% EtOAc in hexanes) gave the title compound (20 mg, 23%). MS (ESI) mass calcd. for : $C_{16}H_{20}F_3N_3O_3$, 359.4; m/z found 260.1 $[M\text{-Boc}]^+$.

Step B: (±)-(3-fluoro-2-(pyrimidin-2-yl)phenyl)(2-((5-(trifluoromethyl)pyrimidin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone: To (±)-tert-butyl 2-((5-(trifluoromethyl)pyrimidin-2-yl)oxy)-7-azabicyclo[2.2.1]heptane-7-carboxylate (20 mg, 0.06 mmol0 in DCM (2 mL) was added 2 mL (2M HCl in Et_2O) and stirred at rt for 3 h. The reaction mixture was concentrated and placed under high vacuum for 1 h. To the intermediate in DCM (2 mL) was added intermediate acid (A-2) (13.3 mg, 0.06 mmol), HOBt (13.7 mg, 0.101 mmol), EDCI (19.4 mg, 0.101 mmol) and DIPEA (26 µL, 0.15 mmol). After stirring at rt for 2 h, saturated $NaHCO_3$ (aq.) was added and the mixture was extracted with DCM (3X). The combined organics were dried (Na_2SO_4), and concentrated. Purification via silica gel chromatography (0-100 % EtOAc in hexanes) gave the title compound (9 mg, 38 %). MS (ESI)

mass calcd. for: $C_{22}H_{17}F_4N_5O_2$, 459.1; m/z found 460.1 $[M+H]^+$. ^1H NMR (500 MHz, Chloroform-d) 8.88 (d, J = 4.9 Hz, 1H), 8.81 (d, J = 4.9 Hz, 1H), 8.74 (d, J = 12.6 Hz, 2H), 7.63 - 7.27 (m, 3H), 7.14 (t, J = 8.9 Hz, 1H), 4.99 (dt, J = 8.3, 4.8 Hz, 1H), 4.87 - 4.66 (m, 1H), 4.16 - 3.97 (m, 1H), 2.07 (d, J = 4.3 Hz, 1H), 1.91 (d, J = 32.9 Hz, 1H), 1.85 - 1.68 (m, 2H), 1.66 - 1.60 (m, 1H), 1.51 (dd, J = 7.9, 4.8 Hz, 1H).

Example 286 (±)-(3-fluoro-2-(pyrimidin-2-yl)phenyl)(2-((5-(trifluoromethyl)pyrimidin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

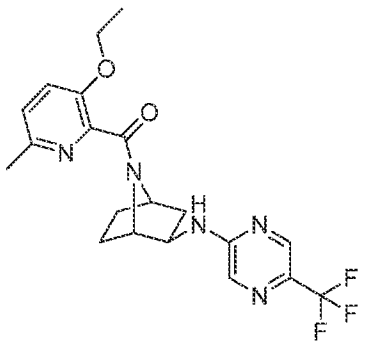


Step A: (±)-tert-butyl 2-((5-(trifluoromethyl)pyrimidin-2-yl)oxy)-7-azabicyclo[2.2.1]heptane-7-carboxylate: To (±)-tert-butyl 2-hydroxy-7-azabicyclo[2.2.1]heptane-7-carboxylate (endo) (150 mg, 0.703 mol) in DMF (8 mL) was added 60 wt% NaH (56.3 mg, 1.41 mmol) in one portion. The reaction was heated at 80 °C for 5 min, then 2-chloro-5-(trifluoromethyl)pyrimidine (257 mg, 1.4 mmol) was added. After heating at 80 °C for 2 hours, water was added and the mixture extracted with DCM (3X). The combined organics were dried (Na_2SO_4) and concentrated. Purification via silica gel chromatography (0-50% EtOAc in hexanes) gave the title compound (130 mg, 51 %). MS (ESI) mass calcd. for: $C_{16}H_{20}F_3N_3O_3$, 359.4; m/z found 260.1 $[M\text{-Boc}]^+$. 1H NMR (400 MHz, Chloroform-d) 8.82 - 8.71 (m, 2H), 5.28 (d, J = 10.0 Hz, 1H), 4.59 (s, 1H), 4.25 (s, 1H), 2.43 (dddd, J = 13.1, 10.1, 5.2, 2.8 Hz, 1H), 2.18 - 2.04 (m, 1H), 1.85 (dd, J = 7.8, 3.8 Hz, 1H), 1.69 (s, 1H), 1.59 (s, 2H), 1.47 (s, 9H).

Step B: (3-fluoro-2-(pyrimidin-2-yl)phenyl)((1R,2S,4S)-2-((5-(trifluoromethyl)pyrimidin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone: To (±)-tert-butyl 2-((5-(trifluoromethyl)pyrimidin-2-yl)oxy)-7-azabicyclo[2.2.1]heptane-7-carboxylate (143 mg, 0.398 mmol) in DCM (3 mL) was added 2M HCl in Et_2O (3 mL). After 3h at rt the reaction

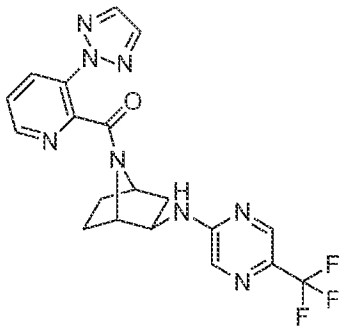
mixture was concentrated and placed under high vacuum for 1 h. To the intermediate in DCM (3 mL) was added carboxcylic acid (A-2) (95.5 mg, 0.438 mmol), HOBt (88.9 mg, 0.658 mmol0, EDCI (126.1 mg, 0.658 mmol) and DIPEA (170 µL, 0.987 mmol). After stirring at rt for 2 h, saturated $NaHCO_3$ (aq.) was added and the mixture was extracted with DCM (3X). The combined organics were dried (Na_2SO_4), and concentrated. Purification via silica gel chromatography (0-100 % EtOAc in hexanes) gave the title compound (78.6 mg, 47%). MS (ESI) mass calcd. for : $C_{22}H_{17}F_4N_5O_2$, 459.1; m/z found 460.1 $[M+H]^+$. 1H NMR (400 MHz, Chloroform-d) d 8.85 (t, J = 5.2 Hz, 2H), 8.76 (d, J = 12.3 Hz, 2H), 7.47 (dd, J = 8.5, 5.4 Hz, 1H), 7.29 (td, J = 5.4, 4.9, 4.3 Hz, 3H), 5.58 - 5.40 (m, 1H), 5.30 (s, 1H), 5.09 - 4.92 (m, 1H), 4.67 (s, 1H), 4.34 (s, 1H), 4.02 (s, 1H), 2.61 - 2.39 (m, 1H), 2.32 - 2.08 (m, 1H), 1.90 (d, J = 13.7 Hz, 1H).

Example 287 (3-ethoxy-6-methylpyridin-2-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



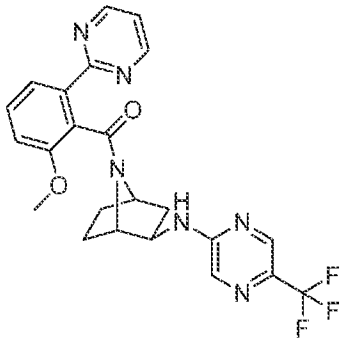
Prepared analogous to Example 238 substituting intermediate A-2 with intermediate A-8. MS (ESI) mass calcd. for : $C_{20}H_{22}F_3N_5O_2$, 421.2; m/z found 422.2 $[M+H]^+$. ^1H NMR (400 MHz, Chloroform-d) 8.31 (s, 0.2H), 8.24 (s, 0.8H), 8.01 – 7.81 (m, 1.8H), 7.25 – 7.09 (m, 2H), 6.15 (d, J = 8.0 Hz, 0.2H), 5.01 – 4.93 (m, 0.8H), 4.87– 4.80 (m, 0.2H), 4.32 – 4.24 (m, 0.2H), 4.18 – 4.02 (m, 2.8H), 3.95 (d, J = 4.6 Hz, 0.8H), 3.88 – 3.82 (m, 0.2H), 2.55 – 2.46 (m, 3H), 2.26 – 1.23 (m, 9H).

Example 288 (3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



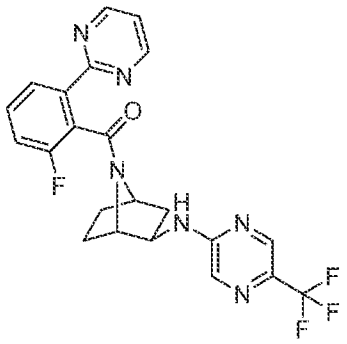
Prepared analogous to Example 238 substituting intermediate A-2 with intermediate A-27. MS (ESI) mass calcd. for : $C_{19}H_{17}F_3N_8O$, 430.1; m/z found 431.2 $[M+H]^+$. ^1H NMR (400 MHz, Chloroform-d) 8.65 (dd, J = 4.7, 1.5 Hz, 0.2H), 8.55 (dd, J = 4.8, 1.5 Hz, 0.8H), 8.39 – 8.32 (m, 0.4H), 8.29 – 8.18 (m, 1.6H), 7.97 – 7.86 (m, 2.2H), 7.70 (s, 0.8H), 7.56 (dd, J = 8.3, 4.7 Hz, 0.2H), 7.50 (dd, J = 8.3, 4.7 Hz, 0.8H), 7.15 (d, J = 8.6 Hz, 0.8H), 6.12 (d, J = 8.6 Hz, 0.2H), 4.97 – 4.89 (m, 0.8H), 4.82 (d, J = 5.2 Hz, 0.2H), 4.29 (td, J = 7.9, 2.8 Hz, 1H), 4.12 – 4.07 (m, 0.2H), 4.04 (d, J = 5.0 Hz, 0.8H), 2.27 – 1.43 (m, 6H).

Example 289 (2-methoxy-6-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



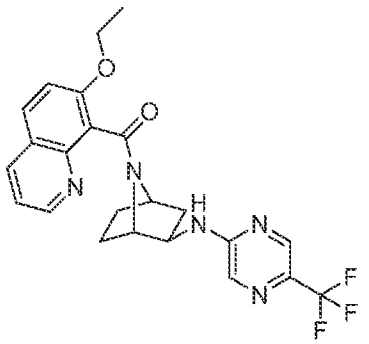
Prepared analogous to Example 238 substituting intermediate A-2 with intermediate A-28. MS (ESI) mass calcd. for : $C_{23}H_{21}F_3N_6O_2$, 470.2; m/z found 471.2$[M+H]^+$. ^1H NMR (400 MHz, Chloroform-d) 8.89 – 8.71 (m, 2H), 8.53 – 8.14 (m, 1.5H), 7.99 – 7.76 (m, 0.5H), 7.60 – 7.29 (m, 3.7H), 7.23 – 6.99 (m, 1H), 6.08 (d, J = 8.9 Hz, 0.2H), 5.78 (d, J = 8.5 Hz, 0.1H), 5.00 – 4.78 (m, 1H), 4.46 – 4.35 (m, 1H), 4.07 (s, 0.5H), 3.91 – 3.79 (m, 3.5H), 2.32 – 1.24 (m, 6H).

Example 290 (2-fluoro-6-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



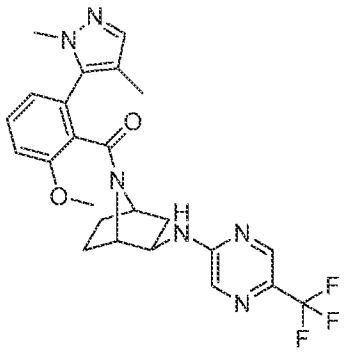
Prepared analogous to Example 238 substituting intermediate A-2 with intermediate A-6. MS (ESI) mass calcd. for : $C_{22}H_{18}F_4N_6O$, 458.1; m/z found 459.2 $[M+H]^+$. ^1H NMR (400 MHz, Chloroform-d) 8.89 – 8.72 (m, 2H), 8.38 – 8.16 (m, 2H), 7.78 (dd, J = 7.8, 1.1 Hz, 1H), 7.55 – 7.44 (m, 1H), 7.43 – 7.35 (m, 1H), 7.34 – 7.14 (m, 2H), 4.93 – 4.85 (m, 1H), 4.50 – 4.39 (m, 1H), 3.98 – 3.88 (m, 1H), 2.31 – 1.11 (m, 6H).

Example 291 (7-ethoxyquinolin-8-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



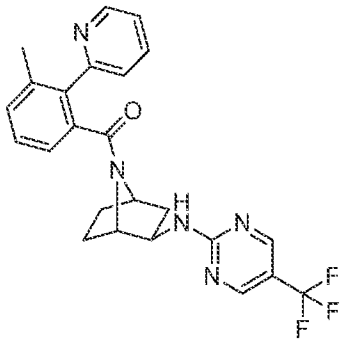
Prepared analogous to Example 238 substituting intermediate A-2 with intermediate A-29. MS (ESI) mass calcd. for : $C_{23}H_{22}F_3N_5O_2$, 457.2 m/z found 458.2 $[M+H]^+$.

Example 292 (2-(1,4-dimethyl-1H-pyrazol-5-yl)-6-methoxyphenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



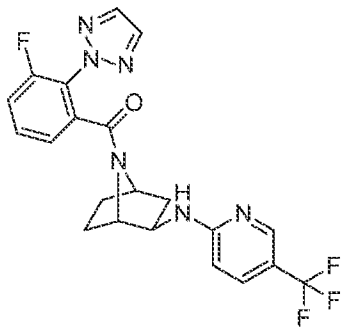
Prepared analogous to Example 238 substituting intermediate A-2 with intermediate A-30. MS (ESI) mass calcd. for : $C_{24}H_{25}F_3N_6O_2$, 486.2 m/z found 487.2 $[M+H]^+$.

Example 293 (3-methyl-2-(pyridin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



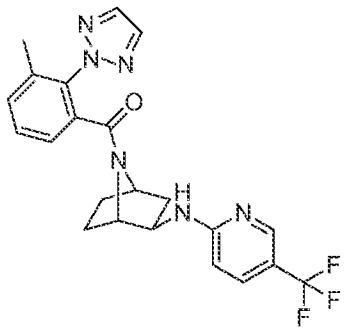
Prepared analogous to Example 284 substituting title compound of Example 277 with title compound of Example 276 and 2-(tributylstannyl)oxazole with 2-(tributylstannyl)pyridine. MS (ESI) mass calcd. for : $C_{24}H_{22}F_3N_5O$, 453.2 m/z found 454.2 $[M+H]^+$. ^1H NMR (400 MHz, Chloroform-d) 8.72 – 8.66 (m, 1H), 8.45 (s, 0.5H), 8.39 (s, 1.5H), 7.86 – 7.75 (m, 1H), 7.52 – 7.44 (m, 1H), 7.38 – 7.20 (m, 4.2H), 7.18 – 7.12 (m, 0.8H), 4.72 – 4.65 (m, 0.8H), 4.49 – 4.45 (m, 0.2H), 4.32 (s, 0.8H), 4.03 – 3.95 (m, 1H), 3.88 – 3.83 (m, 0.2H), 2.26 (s, 2.2H), 2.23 (s, 0.8H), 2.16 (dd, J = 12.8, 7.9 Hz, 0.8H), 1.98 – 1.08 (m, 5.2H).

Example 294 (3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



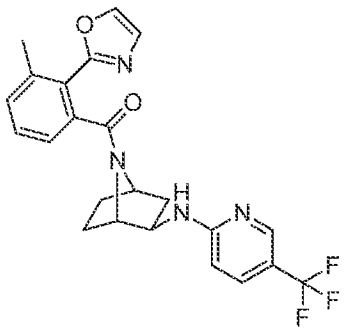
Prepared analogous to Example 279 substituting intermediate A-2 with intermediate A-16. MS (ESI) mass calcd. for : $C_{21}H_{18}F_4N_6O$, 446.1 m/z found 447.2 $[M+H]^+$. ^1H NMR (500 MHz, Chloroform-d) 8.33 (s, 0.2H), 8.23 (s, 0.8H), 7.96 (s, 1.55H), 7.91 (s, 0.45H), 7.57 – 7.48 (m, 0.4H), 7.44 – 7.29 (m, 2H), 7.30 – 7.21 (m, 1H), 7.21 – 7.13 (m, 0.8H), 6.72 (s, 0.6H), 6.36 – 6.25 (m, 1H), 5.34 (s, 0.2H), 4.78 – 4.69 (m, 0.8H), 4.61 (d, J = 5.2 Hz, 0.2H), 4.28 (s, 0.8H), 4.12 (s, 0.2H), 4.05 – 3.95 (m, 1H), 2.17 – 1.41 (m, 6H).

Example 295 (3-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



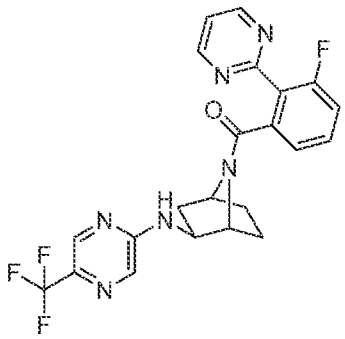
Prepared analogous to Example 279 substituting intermediate A-2 with intermediate A-24. MS (ESI) mass calcd. for : $C_{22}H_{21}F_3N_6O$, 442.1 m/z found 443.2 $[M+H]^+$. ^1H NMR (500 MHz, Chloroform-d) 8.32 (s, 0.2H), 8.23 (s, 0.8H), 7.90 (s, 1.55H), 7.85 (s, 0.45H), 7.57 – 7.25 (m, 3.2H), 7.24 – 7.15 (m, 0.8H), 6.93 (s, 0.8H), 6.38 – 6.27 (m, 1H), 5.22 (s, 0.2H), 4.74 – 4.65 (m, 0.8H), 4.55 (d, J = 4.7 Hz, 0.2H), 4.28 (s, 0.8H), 4.09 (s, 0.2H), 4.03 – 3.95 (m, 1H), 2.20 (s, 3H), 2.13 – 1.38 (m, 6H).

Example 296 (3-methyl-2-(oxazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



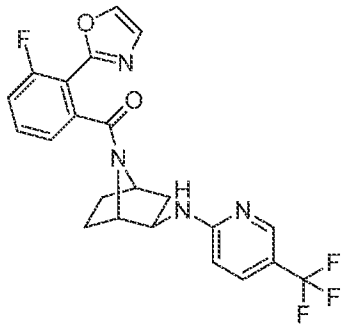
Prepared analogous to Example 279 substituting intermediate A-2 with intermediate A-31. MS (ESI) mass calcd. for : $C_{23}H_{21}F_3N_4O_2$, 442.2 m/z found 443.2 $[M+H]^+$. ^1H NMR (500 MHz, Chloroform-d) 8.19 (s, 1H), 7.91 – 7.80 (m, 2H), 7.32 – 7.21 (m, 4H), 7.19 – 7.13 (m, 1H), 6.32 (d, J = 8.8 Hz, 1H), 4.79 – 4.72 (m, 1H), 4.36 – 4.28 (m, 1H), 3.93 (d, J = 4.6 Hz, 1H), 2.29 (s, 3H), 2.10 (dd, J = 12.9, 8.1 Hz, 1H), 2.00 – 1.85 (m, 2H), 1.76 – 1.64 (m, 2H), 1.55 – 1.46 (m, 1H).

Example 297 (3-fluoro-2-(pyrimidin-2-yl)phenyl)((1R,2S,4S)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



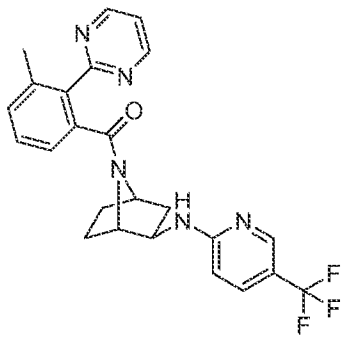
Prepared analogous to Example 238 substituting intermediate B-5 with intermediate B-8. MS (ESI) mass calcd. for $C_{22}H_{18}F_4N_6O$, 458.2; m/z found 459.1 $[M+H]^+$. ^1H NMR (500 MHz, Chloroform-d) 8.91 – 8.84 (m, 2H), 8.27 (s, 1H), 8.19 (s, 1H), 7.65 (d, J = 1.4 Hz, 1H), 7.44 – 7.34 (m, 2H), 7.24 – 7.16 (m, 2H), 4.77 – 4.68 (m, 1H), 4.43 – 4.33 (m, 1H), 4.07 (d, J = 5.1 Hz, 1H), 2.16 (dd, J = 13.0, 8.2 Hz, 1H), 2.10 – 1.99 (m, 1H), 1.98 – 1.86 (m, 1H), 1.78 – 1.65 (m, 2H), 1.58 – 1.48 (m, 1H).

Example 298: (3-fluoro-2-(oxazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



Prepared analogous to Example 320 substituting 2-(tributylstannyl)pyridine with 2-(tributylstannyl)oxazole. MS (ESI) mass calcd. for $C_{22}H_{18}F_4N_4O_2$, 446.1; m/z found 447.1 $[M+H]^+$. ^1H NMR ($CDCl_3$): 8.36 (s, 0.2H), 8.23 - 8.16 (m, 0.8H), 7.90 (s, 0.8H), 7.86 (s, 0.2H), 7.70 - 7.46 (m, 1.2H), 7.43 - 7.20 (m, 2.8H), 7.19 - 7.10 (m, 1.8H), 6.39 (d, J = 8.8 Hz, 0.2H), 6.20 (d, J = 8.8 Hz, 1H), 4.85 - 4.79 (m, 0.8H), 4.72 (d, J = 5.3 Hz, 0.2H), 4.39 - 4.31 (m, 0.8H), 4.26 (s, 0.2H), 3.95 - 3.88 (m, 1H), 2.14 (dd, J = 12.9, 8.2 Hz, 0.8H), 2.06 - 1.41 (m, 5.2H).

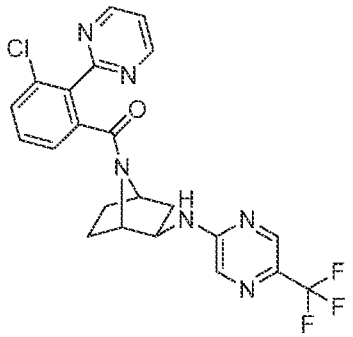
Example 299: (3-methyl-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



Prepared analogous to Example 279 substituting intermediate A-2 with intermediate A-26. Analytical HPLC was obtained on a Agilent 1100 Series using an Inertsil ODS-3 column (3µm, 50 x 3 mm), mobile phase of 5-99% ACN in 0.05% TFA over 1.6 min and then hold at 99% ACN for 0.4 min, at a flow rate of 2.2 mL/min (Temperature = 50 °C). R_t = 1.11 min (major rotamer) at 254 nm. ^1H NMR (500 MHz, $CDCl_3$, Compound present as a mixture of rotamers (0.90:0.10), only major rotamer reported) δ 8.84 (d, J = 4.9 Hz, 2H), 8.22 (s, 1H), 7.82 (d, J = 9.3 Hz, 1H), 7.33 (t, J = 5.0 Hz, 1H), 7.29 - 7.27 (m, 1H), 7.23 (t, J = 7.5 Hz, 1H), 7.21 -

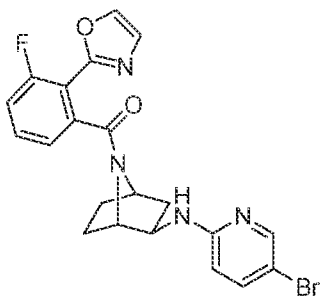
7.17 (m, 1H), 6.21 (d, J = 8.7 Hz, 1H), 4.67 (t, J = 4.8 Hz, 1H), 4.42 - 4.29 (m, 1H), 4.09 (d, J = 5.0 Hz, 1H), 2.31 (s, 3H), 2.12 (dd, J = 12.9, 8.1 Hz, 1H), 2.06 - 1.97 (m, 1H), 1.93 - 1.85 (m, 1H), 1.73 - 1.65 (m, 1H), 1.61 - 1.53 (m, 1H), 1.53 - 1.45 (m, 1H).

Example 300: (3-chloro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

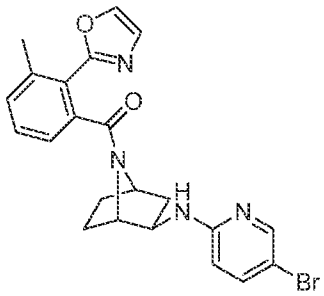


Prepared analogous to Example 238 substituting intermediate A-2 with intermediate A-58. Analytical HPLC was obtained on a Agilent 1100 Series using an Inertsil ODS-3 column (3μm, 50 x 3 mm), mobile phase of 5-99% ACN in 0.05% TFA over 1.6 min and then hold at 99% ACN for 0.4 min, at a flow rate of 2.2 mL/min (Temperature = 50 °C). R_t = 1.26 min (major rotamer) at 254 nm. ^{1}H NMR (500 MHz, $CDCl_3$, Compound present as a mixture of rotamers (0.92:0.08), only major rotamer reported) δ 8.88 (d, J = 5.0 Hz, 2H), 8.26 (d, J = 9.1 Hz, 1H), 8.18 (s, 1H), 7.74 (d, J = 1.4 Hz, 1H), 7.49 (dd, J = 7.2, 2.1 Hz, 1H), 7.41 (t, J = 5.0 Hz, 1H), 7.31 - 7.29 (m, 1H), 4.71 - 4.65 (m, 1H), 4.34 (td, J = 8.7, 3.8 Hz, 1H), 4.05 (d, J = 5.1 Hz, 1H), 2.13 (dd, J = 13.0, 8.1 Hz, 1H), 2.09 - 2.00 (m, 1H), 1.96 - 1.85 (m, 1H), 1.75 - 1.66 (m, 1H), 1.61 - 1.56 (m, 1H), 1.54 - 1.46 (m, 1H).

Example 301: ((1S,2R,4R)-2-((5-bromopyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-(oxazol-2-yl)phenyl)methanone

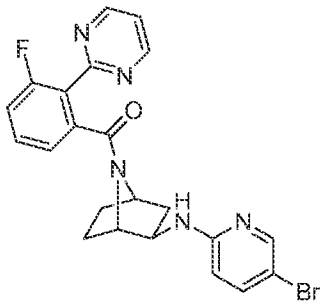


Example 302: ((1S,2R,4R)-2-((5-bromopyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-methyl-2-(oxazol-2-yl)phenyl)methanone



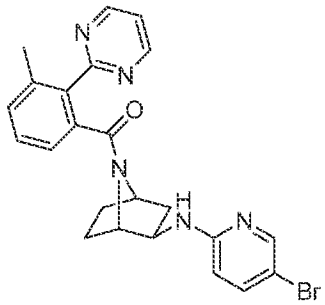
Prepared analogous to Example 305 substituting intermediate A-16 with intermediate A-31. MS (ESI): mass calcd. for $C_{22}H_{21}BrN_4O_2$, 452.1; m/z found, 452.9 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$, Compound present as a mixture of rotamers) δ 7.96 (d, J = 2.5 Hz, 1H), 7.85 (d, J = 0.9 Hz, 1H), 7.28 - 7.26 (series m, 2H), 7.25 - 7.22 (m, 1H), 7.19 (dd, J = 8.9, 2.5 Hz, 1H), 7.17 - 7.13 (m, 1H), 6.23 (d, J = 9.0 Hz, 1H), 4.73 (t, J = 4.5 Hz, 1H), 4.24 - 4.14 (m, 1H), 3.90 (d, J = 4.6 Hz, 1H), 2.29 (s, 3H), 2.07 (dd, J = 12.8, 8.1 Hz, 1H), 1.95 - 1.85 (series of m, 2H), 1.70 - 1.60 (series of m, 2H), 1.52 - 1.44 (m, 1H).

Example 303: ((1S,2R,4R)-2-((5-bromopyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-(pyrimidin-2-yl)phenyl)methanone



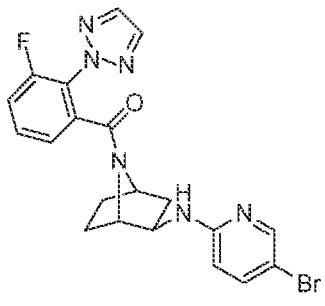
Prepared analogous to Example 305 substituting intermediate A-16 with intermediate A-2. MS (ESI): mass calcd. for $C_{22}H_{19}BrFN_5O$, 467.1; m/z found, 468.1 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$, Compound present as a mixture of rotamers (0.87:0.13), only major rotamer reported) δ 8.87 (d, J = 4.9 Hz, 2H), 8.00 (d, J = 2.5 Hz, 1H), 7.40 - 7.31 (series of m, 2H), 7.24 - 7.20 (m, 1H), 7.19 - 7.14 (series of m, 2H), 6.10 (d, J = 8.9 Hz, 1H), 4.70 (t, J = 4.9 Hz, 1H), 4.28 - 4.19 (m, 1H), 4.06 (d, J = 5.1 Hz, 1H), 2.13 (dd, J = 12.9, 8.1 Hz, 1H), 2.06 - 1.83 (series of m, 2H), 1.73 - 1.46 (series of m, 2H). *1H buried under solvent peak.

Example 304: ((1S,2R,4R)-2-((5-bromopyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-methyl-2-(pyrimidin-2-yl)phenyl)methanone



Prepared analogous to Example 305 substituting intermediate A-16 with intermediate A-26. MS (ESI): mass calcd. for $C_{23}H_{22}BrN_5O$, 463.1; m/z found, 464.1 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$, Compound present as a mixture of rotamers (0.88:0.12), only major rotamer reported) δ 8.82 (d, J = 4.9 Hz, 2H), 8.00 (d, J = 2.5 Hz, 1H), 7.31 (t, J = 4.9 Hz, 1H), 7.28 - 7.26 (m, 1H), 7.25 - 7.16 (m, 3H), 6.12 (d, J = 8.8 Hz, 1H), 4.69 - 4.60 (m, 1H), 4.23 - 4.17 (m, 1H), 4.06 (d, J = 5.1 Hz, 1H), 2.30 (s, 3H), 2.09 (dd, J = 12.8, 8.1 Hz, 1H), 2.04 - 1.95 (m, 1H), 1.92 - 1.82 (m, 1H), 1.69 - 1.61 (m, 1H), 1.58 - 1.42 (m, 2H).

Example 305: ((1S,2R,4R)-2-((5-bromopyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone



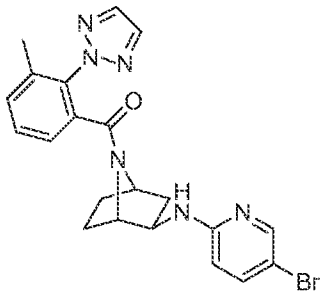
Step A: (1S,2R,4R)-tert-butyl 2-((5-bromopyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptane-7-carboxylate. In a microwave vial, 5-bromo-2-iodopyridine (133 mg, 0.47 mmol) was dissolved in THF (2.4 mL) and sodium tert-butoxide (91 mg, 0.94 mmol) was added followed by Xantphos (20 mg, 0.033mmol) and $Pd_2(dba)_3$ (17 mg, 0.019 mmol). The solution was degassed with N_2 for 10 minutes then intermediate B-5 (100 mg, 0.47 mmol) was added. After 2 days at 90 °C the reaction mixture was filtered through a pad of celite and solvent was evaporated. Purification via silica gel chromatography (0-40% EtOAc in hexanes) gave the

title compound of step A (87 mg, 50%). MS (ESI): mass calcd. for $C_{16}H_{22}BrN_3O_2$, 367.1; m/z found, 368.1 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.10 (d, J = 2.4 Hz, 1H), 7.44 (dd, J = 8.8, 2.5 Hz, 1H), 6.25 (d, J = 8.8 Hz, 1H), 4.70 (s, 1H), 4.27 (s, 1H), 4.21 – 4.14 (m, 1H), 3.90 – 3.81 (m, 1H), 2.00 (dd, J = 13.0, 7.6 Hz, 1H), 1.89 – 1.66 (m, 2H), 1.57 – 1.34 (m, 12H).

Step B: (1S,2R,4R)-N-(5-bromopyridin-2-yl)-7-azabicyclo[2.2.1]heptan-2-amine. Prepared analogous to Example 382 step B. MS (ESI): mass calcd. for $C_{11}H_{14}BrN_3$, 267.0; m/z found, 268.1 $[M+H]^+$.

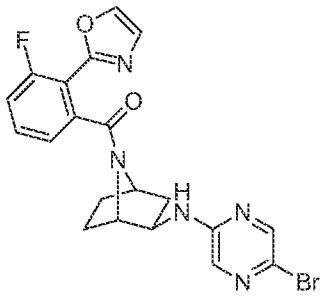
Step C: ((1S,2R,4R)-2-((5-bromopyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone. Prepared analogous to Example 382 step C substituting intermediate A-2 with intermediate A-16. MS (ESI): mass calcd. for $C_{20}H_{18}BrFN_6O$, 456.1; m/z found, 457.1 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$, Compound present as a mixture of rotamers (0.80:0.20), only major rotamer reported) δ 8.00 (d, J = 2.5 Hz, 1H), 7.94 (s, 2H), 7.41 - 7.33 (m, 1H), 7.33 - 7.22 (m, 2H), 7.16 (dt, J = 7.7, 1.1 Hz, 1H), 6.20 (d, J = 8.7 Hz, 1H), 4.77 - 4.67 (m, 1H), 4.20 - 4.10 (m, 1H), 3.97 (d, J = 4.9 Hz, 1H), 2.10 (dd, J = 13.0, 8.1 Hz, 1H), 1.98 - 1.80 (m, 2H), 1.70 - 1.54 (m, 2H), 1.52 - 1.46 (m, 1H).

Example 306: ((1S,2R,4R)-2-((5-bromopyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone

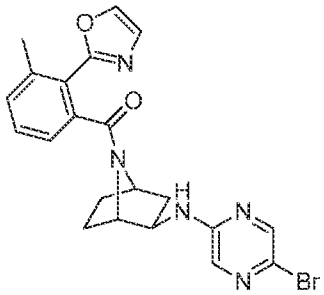


Prepared analogous to Example 305 substituting intermediate A-16 with intermediate A-24. MS (ESI): mass calcd. for $C_{21}H_{21}BrN_6O$, 452.1; m/z found, 452.9 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$, Compound present as a mixture of rotamers) δ 8.00 (d, J = 2.5 Hz, 1H), 7.89 (s, 2H), 7.42 (d, J = 4.3 Hz, 1H), 7.36 - 7.31 (m, 1H), 7.28 - 7.24 (series of m, 2H), 7.22 - 7.16 (m, 1H), 6.24 (d, J = 8.9 Hz, 1H), 4.67 (t, J = 4.7 Hz, 1H), 4.21 - 4.06 (m, 1H), 3.95 (d, J = 5.1 Hz, 1H), 2.20 (s, 3H), 2.07 (dd, J = 12.9, 8.0 Hz, 1H), 1.98 - 1.90 (m, 1H), 1.87 - 1.78 (m, 1H), 1.66 - 1.60 (m, 1H), 1.57 - 1.50 (m, 1H), 1.50 - 1.43 (m, 1H).

Example 307: ((1S,2R,4R)-2-((5-bromopyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-(oxazol-2-yl)phenyl)methanone

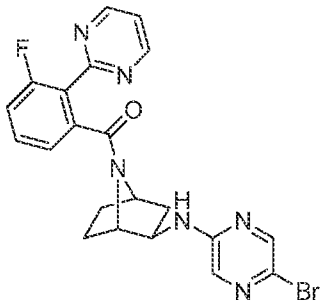


Example 308: ((1S,2R,4R)-2-((5-bromopyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-methyl-2-(oxazol-2-yl)phenyl)methanone



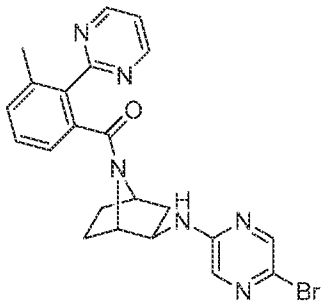
Prepared analogous to Example 311 substituting intermediate A-16 with intermediate A-31. MS (ESI): mass calcd. for $C_{21}H_{20}BrN_5O_2$, 453.1; m/z found, 453.9 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$, Compound present as a mixture of rotamers) δ 8.04 - 7.93 (m, 1H), 7.88 (d, J = 1.4 Hz, 1H), 7.86 (d, J = 0.9 Hz, 1H), 7.54 (d, J = 1.4 Hz, 1H), 7.29 (d, J = 7.5 Hz, 1H), 7.29 - 7.22 (m, 1H), 7.18 - 7.14 (m, 1H), 4.75 (t, J = 4.6 Hz, 1H), 4.17 - 4.09 (m, 1H), 3.90 (d, J = 4.7 Hz, 1H), 2.28 (s, 3H), 2.08 (dd, J = 12.9, 8.1 Hz, 1H), 1.99 - 1.85 (m, 2H), 1.73 - 1.63 (m, 2H), 1.53 - 1.45 (m, 1H).

Example 309: ((1S,2R,4R)-2-((5-bromopyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-(pyrimidin-2-yl)phenyl)methanone



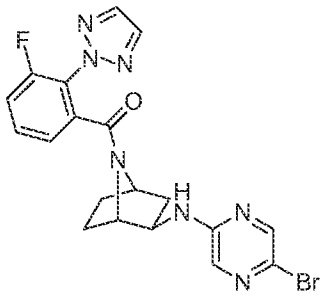
Prepared analogous Example 311 substituting intermediate A-16 with intermediate A-2. MS (ESI): mass calcd. for $C_{21}H_{18}BrFN_6O$, 468.1; m/z found, 469.9 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$, Compound present as a mixture of rotamers) δ 8.86 (d, J = 5.0 Hz, 2H), 7.94 (d, J = 1.4 Hz, 1H), 7.42 (d, J = 1.4 Hz, 1H), 7.40 - 7.35 (m, 2H), 7.25 - 7.20 (m, 1H), 7.19 - 7.15 (m, 1H), 4.76 - 4.66 (m, 1H), 4.27 - 4.16 (m, 1H), 4.04 (d, J = 5.0 Hz, 1H), 2.14 (dd, J = 12.9, 8.1 Hz, 1H), 2.07 - 1.99 (m, 1H), 1.95 - 1.86 (m, 1H), 1.73 - 1.62 (series of m, 2H), 1.54 - 1.47 (m, 1H).

Example 310: ((1S,2R,4R)-2-((5-bromopyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-methyl-2-(pyrimidin-2-yl)phenyl)methanone



Prepared analogous Example 311 substituting intermediate A-16 with intermediate A-26. Analytical HPLC was obtained on a Agilent 1100 Series using an Inertsil ODS-3 column (3μm, 50 x 3 mm), mobile phase of 5-99% ACN in 0.05% TFA over 1.6 min and then hold at 99% ACN for 0.4 min, at a flow rate of 2.2 mL/min (Temperature = 50 °C). R_t = 1.24 min (major rotamer) at 254 nm. ^1H NMR (500 MHz, $CDCl_3$, Compound present as a mixture of rotamers) δ 8.83 (d, J = 4.9 Hz, 2H), 7.92 (d, J = 1.4 Hz, 1H), 7.41 (d, J = 1.4 Hz, 1H), 7.34 (t, J = 5.0 Hz, 1H), 7.30 - 7.27 (m, 1H), 7.24 (t, J = 7.5 Hz, 1H), 7.21 - 7.17 (m, 1H), 4.71 - 4.61 (m, 1H), 4.21 - 4.12 (m, 1H), 4.06 (d, J = 5.0 Hz, 1H), 2.28 (s, 3H), 2.09 (dd, J = 12.9, 8.1 Hz, 1H), 2.06 - 1.97 (m, 1H), 1.93 - 1.84 (m, 1H), 1.66 - 1.62 (m, 1H), 1.61 - 1.54 (m, 1H), 1.51 - 1.43 (m, 1H).

Example 311: ((1S,2R,4R)-2-((5-bromopyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone

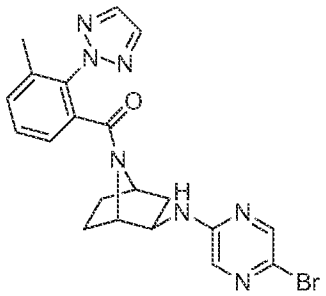


Step A: (1S,2R,4R)-tert-butyl 2-((5-bromopyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptane-7-carboxylate. In a microwave vial was dissolved intermediate B-5 (830 mg, 3.91 mmol) in DMSO (8 mL). K_2CO_3 (811 mg, 5.87 mmol) was added followed by 2,5-dibromopyrazine (1.12 g, 4.70 mmol). The vial was capped and the reaction mixture was heated to 100 °C for 16h. Then water and EtOAc were added and the aqueous phase was extracted twice with EtOAc. The combined organic phases were dried over $MgSO_4$, filtered and evaporated. Purification via silica gel chromatography (0-40% EtOAc in hexanes) gave the title compound (291 mg, 20%). MS (ESI): mass calcd. for $C_{15}H_{21}BrN_4O_2$, 368.1; m/z found, 370.9 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.07 (s, 1H), 7.62 (s, 1H), 4.95 (s, 1H), 4.28 (s, 1H), 4.18 (s, 1H), 3.95 – 3.81 (m, 1H), 2.05 – 1.99 (m, 1H), 1.89 – 1.70 (m, 2H), 1.57 – 1.37 (m, 12H).

Step B: (1S,2R,4R)-N-(5-bromopyrazin-2-yl)-7-azabicyclo[2.2.1]heptan-2-amine. Prepared analogous to Example 390 step B. MS (ESI): mass calcd. for $C_{10}H_{13}BrN_4$, 268.0; m/z found, 270.9 $[M+H]^+$.

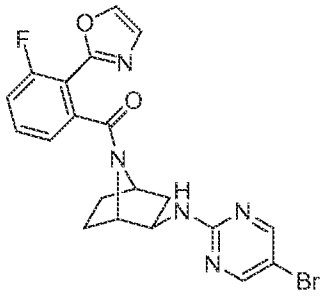
Step C: ((1S,2R,4R)-2-((5-bromopyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone. Prepared analogous to Example 390 step C. MS (ESI): mass calcd. for $C_{19}H_{17}BrFN_7O$, 457.1; m/z found, 459.8 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$, Compound present as a mixture of rotamers) δ 7.94 (s, 3H), 7.54 (d, J = 1.4 Hz, 1H), 7.43 - 7.37 (m, 1H), 7.32 - 7.27 (m, 1H), 7.21 - 7.16 (m, 1H), 4.72 (t, J = 4.8 Hz, 1H), 4.19 - 4.08 (m, 1H), 3.93 (d, J = 5.0 Hz, 1H), 2.10 (dd, J = 13.2, 8.2 Hz, 1H), 1.99 - 1.79 (series of m, 3H), 1.63 - 1.54 (m, 1H), 1.54 - 1.46 (m, 1H).

Example 312: ((1S,2R,4R)-2-((5-bromopyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone

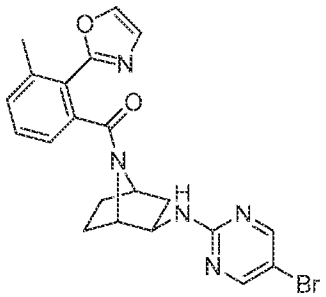


Prepared analogous to Example 311 substituting intermediate A-16 with intermediate A-24. MS (ESI): mass calcd. for $C_{20}H_{20}BrN_7O$, 453.1; m/z found, 453.9 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$, Compound present as a mixture of rotamers) δ 7.93 (d, J = 1.4 Hz, 1H), 7.90 (s, 2H), 7.56 (d, J = 1.4 Hz, 1H), 7.36 - 7.32 (m, 1H), 7.30 (t, J = 7.6 Hz, 1H), 7.23 - 7.18 (m, 1H), 4.68 (t, J = 4.7 Hz, 1H), 4.14 - 4.07 (m, 1H), 3.94 (d, J = 5.1 Hz, 1H), 2.19 (s, 3H), 2.10 - 2.04 (m, 1H), 2.00 - 1.92 (m, 1H), 1.90 - 1.80 (m, 1H), 1.64 - 1.42 (series of m, 3H).

Example 313: ((1S,2R,4R)-2-((5-bromopyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-(oxazol-2-yl)phenyl)methanone



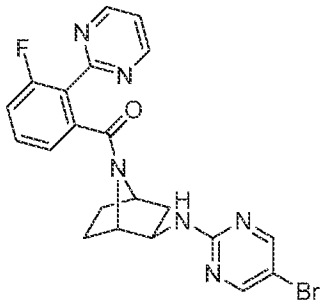
Example 314: ((1S,2R,4R)-2-((5-bromopyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-methyl-2-(oxazol-2-yl)phenyl)methanone



Prepared analogous to Example 317 substituting intermediate A-16 with intermediate A-31. MS (ESI): mass calcd. for $C_{21}H_{20}BrN_5O_2$, 453.1; m/z found, 453.9 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$, Compound present as a mixture of rotamers (0.55:0.45), only major rotamer

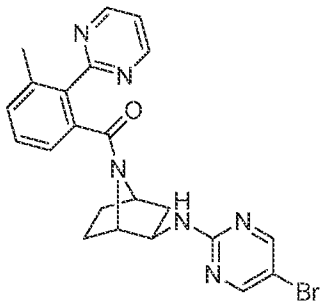
reported) δ 8.16 (s, 2H), 7.80 (s, 1H), 7.40 - 7.35 (m, 1H), 7.31 (s, 1H), 7.26 - 7.22 (series of m, 2H), 4.80 - 4.74 (m, 1H), 4.67 (d, *J* = 5.3 Hz, 1H), 4.11 - 4.03 (m, 1H), 2.37 (s, 3H), 2.10 (dd, *J* = 12.9, 8.0 Hz, 1H), 1.88 - 1.68 (series of m, 3H), 1.61 - 1.39 (series of m, 2H).

Example 315: ((1S,2R,4R)-2-((5-bromopyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-(pyrimidin-2-yl)phenyl)methanone



Prepared analogous to Example 317 substituting intermediate A-16 with intermediate A-2. MS (ESI): mass calcd. for $C_{21}H_{18}BrFN_6O$, 468.1; m/z found, 470.8 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$, Compound present as a mixture of rotamers (0.80:0.20), only major rotamer reported) δ 8.88 (d, *J* = 4.9 Hz, 2H), 8.18 (s, 2H), 7.41 - 7.35 (m, 1H), 7.32 (t, *J* = 4.9 Hz, 1H), 7.25 - 7.19 (m, 1H), 7.16 (dd, *J* = 7.6, 1.1 Hz, 1H), 4.77 - 4.71 (m, 1H), 4.28 - 4.18 (m, 1H), 4.06 (d, *J* = 5.1 Hz, 1H), 2.18 (dd, *J* = 12.9, 7.9 Hz, 1H), 2.02 - 1.79 (m, 2H), 1.56 - 1.49 (m, 1H). *2 H buried under water peak.

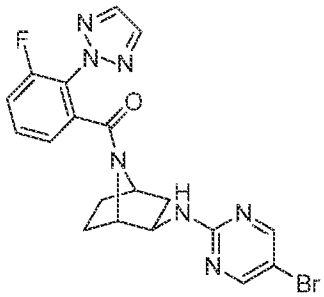
Example 316: ((1S,2R,4R)-2-((5-bromopyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-methyl-2-(pyrimidin-2-yl)phenyl)methanone



Prepared analogous to Example 317 substituting intermediate A-16 with intermediate A-26. Analytical HPLC was obtained on a Agilent 1100 Series using an Inertsil ODS-3 column (3μm, 50 x 3 mm), mobile phase of 5-99% ACN in 0.05% TFA over 1.6 min and then hold at 99% ACN for 0.4 min, at a flow rate of 2.2 mL/min (Temperature = 50 °C). R_t = 0.82 min (major rotamer) at 254 nm. ^1H NMR (500 MHz, $CDCl_3$, Compound present as a mixture of

rotamers) δ 8.86 (d, *J* = 4.9 Hz, 2H), 8.19 (s, 2H), 7.34 - 7.23 (series of m, 3H), 7.20 - 7.16 (m, 1H), 4.69 (t, *J* = 4.6 Hz, 1H), 4.27 - 4.17 (m, 1H), 4.10 - 4.06 (m, 1H), 2.35 (s, 3H), 2.16 (dd, *J* = 12.8, 7.9 Hz, 1H), 2.07 - 1.96 (m, 1H), 1.90 - 1.80 (m, 1H), 1.69 - 1.54 (series of m, 2H), 1.54 - 1.46 (m, 1H).

Example 317: ((1S,2R,4R)-2-((5-bromopyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone



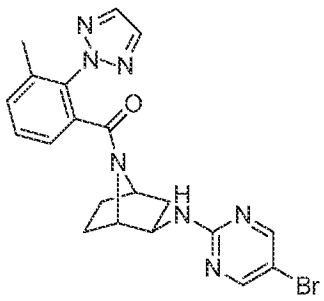
Step A: (1S,2R,4R)-tert-butyl 2-((5-bromopyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptane-7-carboxylate. To a solution of intermediate B-5 (520 mg, 2.45 mmol) in DMA (8.2 mL) was added DIPEA (0.84 mL, 4.90 mmol) followed by 2,5-dibromopyrimidine (661 mg, 2.69 mmol). The reaction mixture was heated at 120 °C for 30 minutes using microwave and was then diluted with water and EtOAc. The aqueous phase was extracted twice with EtOAc and the combined organic layers were washed with a saturated solution of NaCl, dried over $MgSO_4$, filtered and evaporated. Purification via silica gel chromatography (0-40% EtOAc in hexanes) gave the title compound (651 mg, 72%). MS (ESI): mass calcd. for $C_{15}H_{21}BrN_4O_2$, 368.1; m/z found, 370.9 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.28 (s, 2H), 5.56 (s, 1H), 4.29 (s, 1H), 4.23 – 4.15 (m, 1H), 3.99 – 3.91 (m, 1H), 2.03 – 1.93 (m, 1H), 1.87 – 1.63 (m, 2H), 1.62 – 1.32 (m, 12H).

Step B: (1S,2R,4R)-N-(5-bromopyrimidin-2-yl)-7-azabicyclo[2.2.1]heptan-2-amine. To the title compound of step A (812 mg, 2.2 mmol) in DCM (11 mL) was added 4M HCl in dioxane (2.7 mL). After 16h, the reaction was concentrated, neutralized with 5% Na_2CO_3 (aq) and extracted with DCM (2X). The combined organics were dried (Na_2SO_4) to give the title compound of step B that was used without further purification. MS (ESI): mass calcd. for $C_{10}H_{13}BrN_4$, 268.0; m/z found, 270.9 $[M+H]^+$.

Step C: ((1S,2R,4R)-2-((5-bromopyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone. To a solution of the title compound of step B (30 mg, 0.11 mmol) and intermediate A-16 (25 mg, 0.12 mmol) in DCM (1.1 mL) was

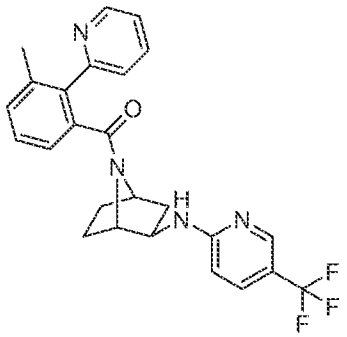
added DIPEA (0.12 mL, 0.67 mmol) followed by HATU (51 mg, 0.13 mmol). The reaction mixture was stirred at room temperature for 16h. Solvent was evaporated and purification via prep HPLC gave the title compound (50 mg, 98%). MS (ESI): mass calcd. for $C_{19}H_{17}BrFN_7O$, 457.1; m/z found, 459.8 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$, Compound present as a mixture of rotamers (0.57:0.43), only major rotamer reported) δ 8.20 (s, 2H), 7.92 (s, 2H), 7.37 - 7.31 (m, 1H), 7.30 - 7.27 (m, 1H), 7.21 - 7.15 (m, 1H), 4.74 (t, J = 4.8 Hz, 1H), 4.13 (td, J = 8.3, 3.2 Hz, 1H), 3.95 (d, J = 5.0 Hz, 1H), 2.11 (dd, J = 13.0, 8.0 Hz, 1H), 1.88 - 1.73 (m, 2H), 1.65 - 1.59 (m, 1H), 1.52 - 1.42 (m, 2H).

Example 318: ((1S,2R,4R)-2-((5-bromopyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone

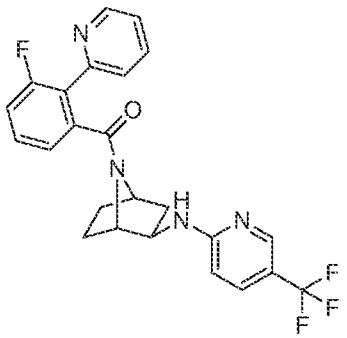


Prepared analogous to Example 317 substituting intermediate A-16 with intermediate A-24. MS (ESI): mass calcd. for $C_{20}H_{20}BrN_7O$, 453.1; m/z found, 453.9 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$, Compound present as a mixture of rotamers (0.59:0.58), only major rotamer reported) δ 8.20 (s, 2H), 7.88 (s, 2H), 7.44 - 7.42 (m, 1H), 7.34 - 7.28 (m, 1H), 7.22 - 7.17 (m, 1H), 4.69 (t, J = 4.9 Hz, 1H), 4.07 (dd, J = 8.2, 3.4 Hz, 1H), 3.96 (d, J = 5.1 Hz, 1H), 2.22 (s, 3H), 2.10 (dd, J = 12.9, 8.0 Hz, 1H), 1.93 - 1.85 (m, 1H), 1.83 - 1.74 (m, 1H), 1.64 - 1.53 (m, 2H), 1.47 - 1.42 (m, 1H).

Example 319: (3-methyl-2-(pyridin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



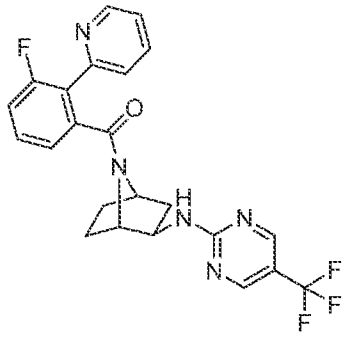
Example 320: (3-fluoro-2-(pyridin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



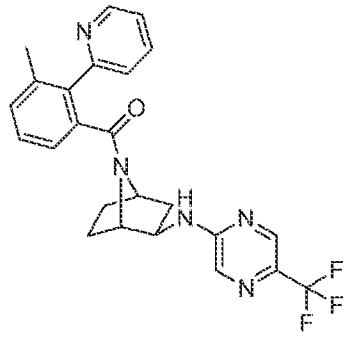
Step A: (3-fluoro-2-iodophenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone. Prepared analogous to Example 279 substituting intermediate A-2 with 3-fluoro-2-iodobenzoic acid. MS (ESI): mass calcd. for $C_{19}H_{16}F_4IN_3O$, 505.0; m/z found 506.0 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.35 (s, 0.5H), 8.24 (s, 0.5H), 7.60 - 7.50 (m, 1H), 7.40 - 7.33 (m, 0.6H), 7.14 - 7.02 (m, 1.4H), 6.98 - 6.92 (m, 0.5H), 6.90 (d, J = 7.4 Hz, 0.5H), 6.47 - 6.37 (m, 1H), 5.36 (s, 0.5H), 4.95 - 4.90 (m, 0.5H), 4.82 (d, J = 5.4 Hz, 0.5H), 4.76 (s, 0.5H), 4.28 - 4.20 (m, 0.5H), 3.99 (s, 0.5H), 3.80 - 3.75 (m, 0.5H), 3.73 (d, J = 4.3 Hz, 0.5H), 2.21 - 2.11 (m, 1H), 2.08 - 1.44 (m, 5H).

Step B: (3-fluoro-2-(pyridin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone. Prepared analogous to Example 260 Step B substituting 2-(tributylstannyl)oxazole with 2-(tributylstannyl)pyridine. MS (ESI): mass calcd. for $C_{24}H_{20}F_4N_4O$, 456.2; m/z found, 457.1 $[M+H]^+$. Analytical HPLC was obtained on a Agilent 1100 Series using a XBridge C18 column (5µm, 100 x 4.6mm), mobile phase of 10-100% ACN in 20 mM NH_4OH over 8 min and then hold at 100% ACN for 3 min, at a flow rate of 1 mL/min (Temperature = 30 °C). R_t = 7.26 min (major rotamer) at 254 nm.

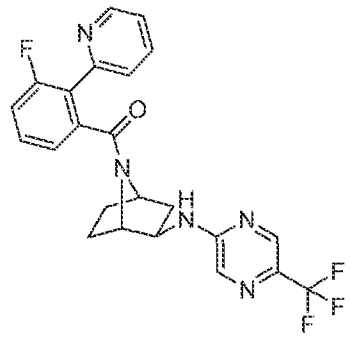
Example 321: (3-fluoro-2-(pyridin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



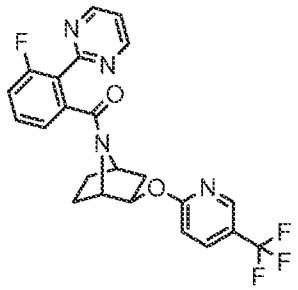
Example 322: (3-methyl-2-(pyridin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



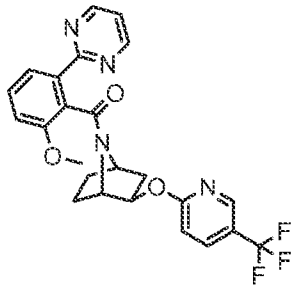
Example 323: (3-fluoro-2-(pyridin-2-yl)phenyl)((2S)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



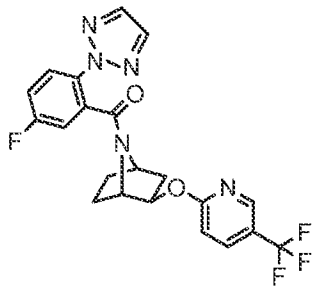
Example 324: (3-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



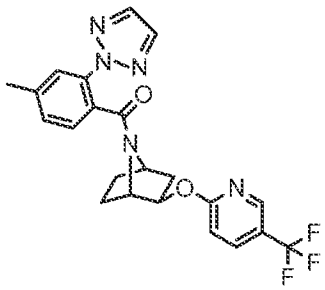
Example 325: (2-methoxy-6-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



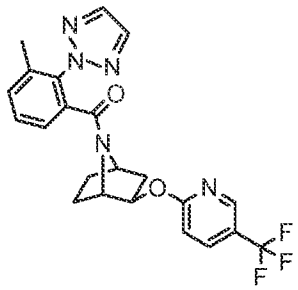
Example 326: (5-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



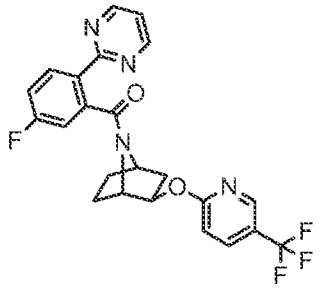
Example 327: (4-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



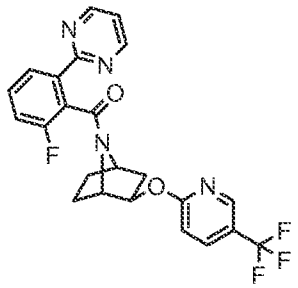
Example 328: (3-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



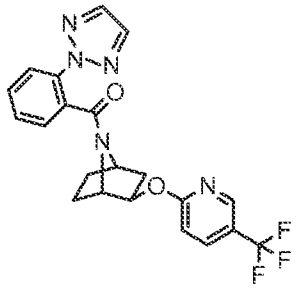
Example 329: (5-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



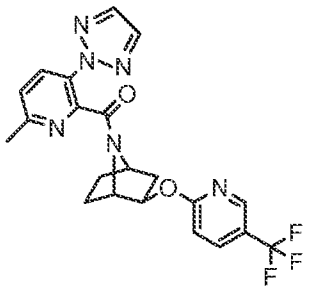
Example 330: (2-fluoro-6-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



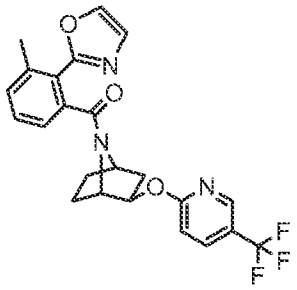
Example 331: (2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



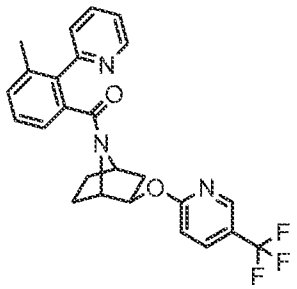
Example 332: (6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



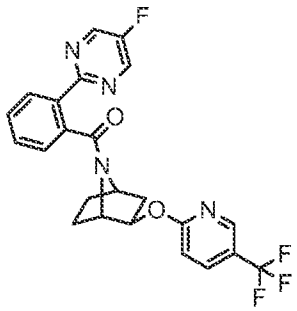
Example 333: (3-methyl-2-(oxazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



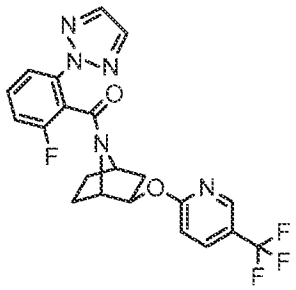
Example 334: (3-methyl-2-(pyridin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



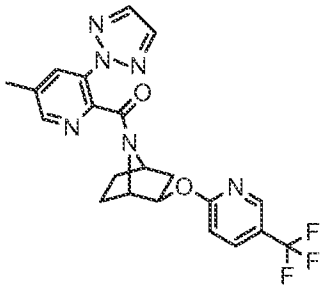
Example 335: (2-(5-fluoropyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



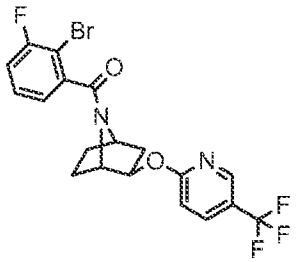
Example 336: (2-fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



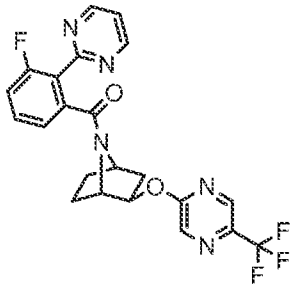
Example 337: (5-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



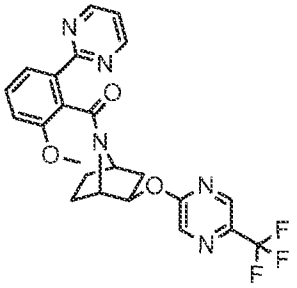
Example 338: (2-bromo-3-fluorophenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



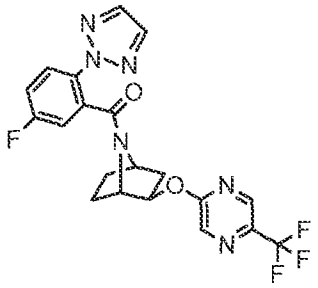
Example 339: (3-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



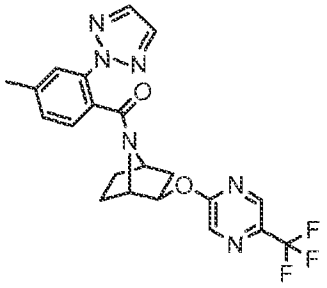
Example 340: (2-methoxy-6-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



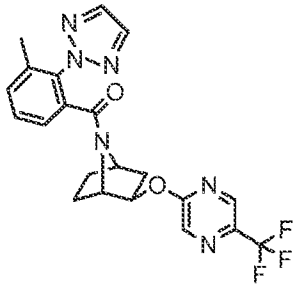
Example 341: (5-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



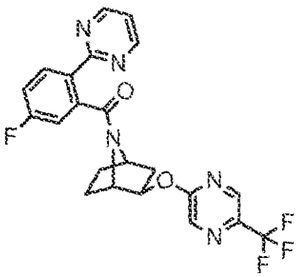
Example 342: (4-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



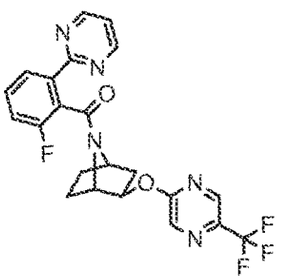
Example 343: (3-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



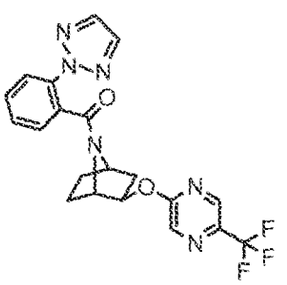
Example 344: (5-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



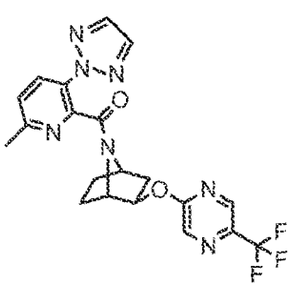
Example 345: (2-fluoro-6-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



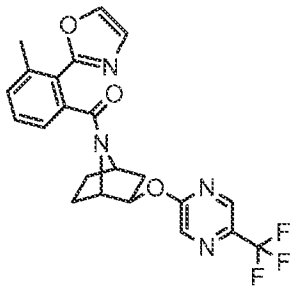
Example 346: (2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



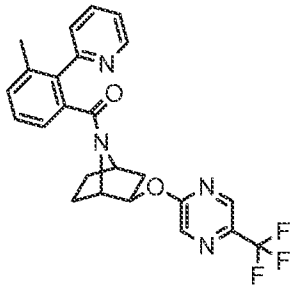
Example 347: (6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



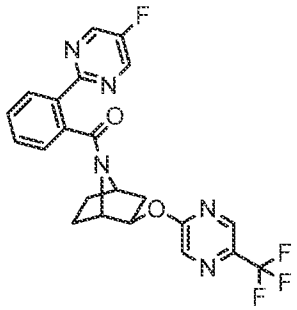
Example 348: (3-methyl-2-(oxazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



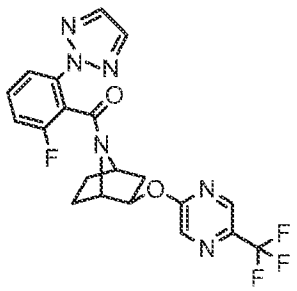
Example 349: (3-methyl-2-(pyridin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



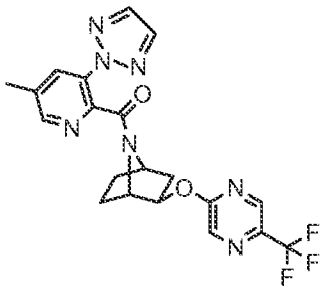
Example 350: (2-(5-fluoropyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



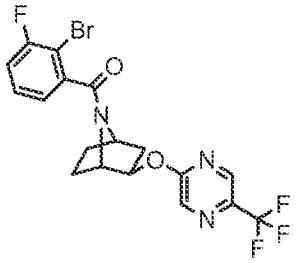
Example 351: (2-fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



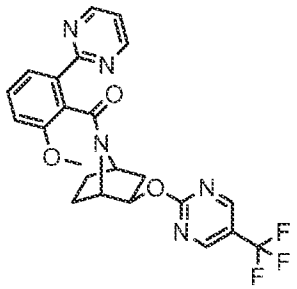
Example 352: (5-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



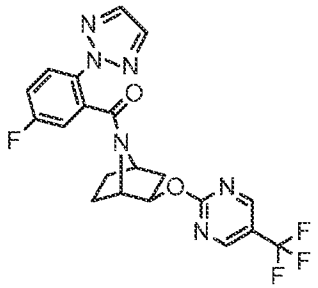
Example 353: (2-bromo-3-fluorophenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



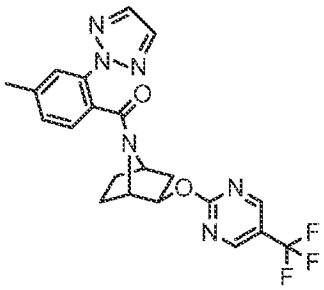
Example 354: (2-methoxy-6-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



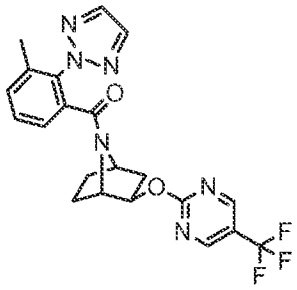
Example 355: (5-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



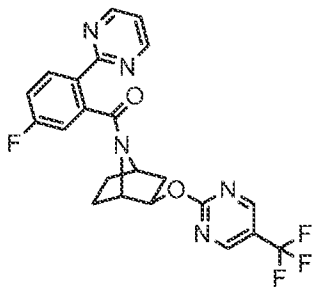
Example 356: (4-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



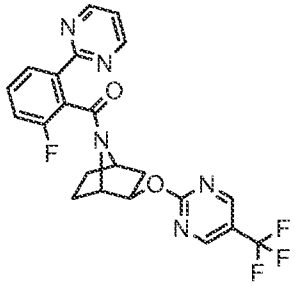
Example 357: (3-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



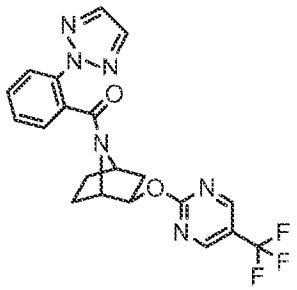
Example 358: (5-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



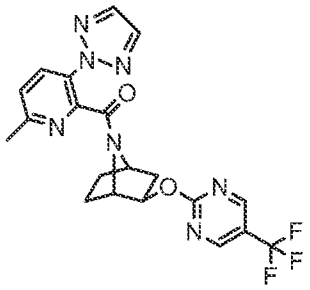
Example 359: (2-fluoro-6-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



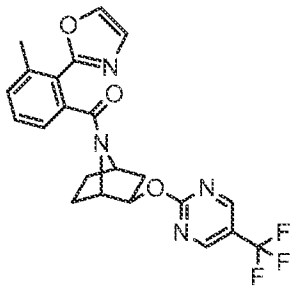
Example 360: (2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



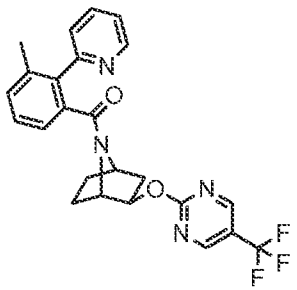
Example 361: (6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



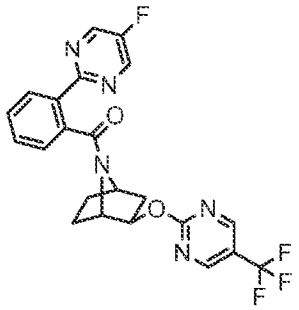
Example 362: (3-methyl-2-(oxazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



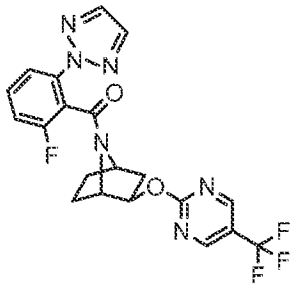
Example 363: (3-methyl-2-(pyridin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



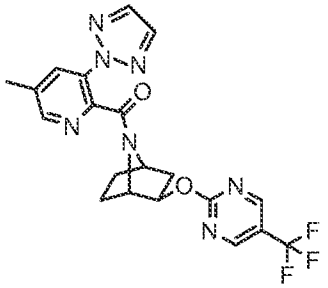
Example 364: (2-(5-fluoropyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



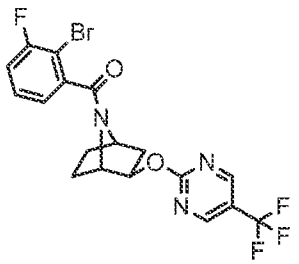
Example 365: (2-fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



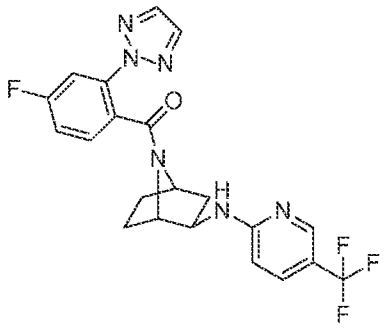
Example 366: (5-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



Example 367: (2-bromo-3-fluorophenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

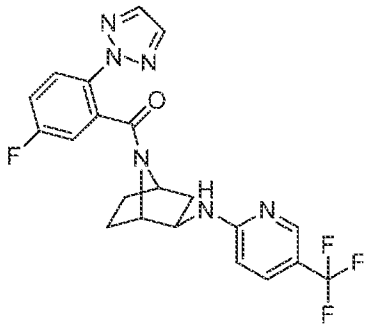


Example 368: (4-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



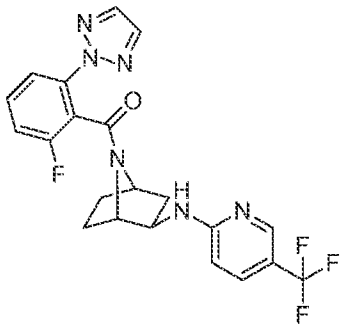
Prepared analogous to Example 279 substituting intermediate A-2 with intermediate A-12. MS (ESI): mass calcd. for $C_{21}H_{18}F_4N_6O$, 446.1; m/z found, 447.1 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$, Compound present as a mixture of rotamers (0.64:0.36), only major rotamer reported) δ 8.22 (s, 1H), 7.91 (s, 2H), 7.57 (dd, J = 9.1, 2.5 Hz, 1H), 7.40 - 7.33 (m, 2H), 6.38 (d, J = 8.7 Hz, 1H), 6.05 (s, 1H), 4.83 (t, J = 4.5 Hz, 1H), 4.24 - 4.16 (m, 1H), 3.93 - 3.88 (m, 1H), 2.22 - 2.10 (m, 1H), 2.09 - 1.86 (m, 2H), 1.68 - 1.61 (m, 2H), 1.57 - 1.50 (m, 1H).

Example 369: (5-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



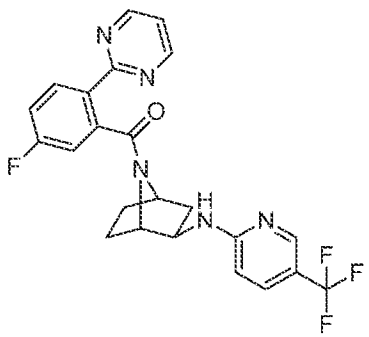
Prepared analogous to Example 279 substituting intermediate A-2 with intermediate A-10. MS (ESI): mass calcd. for $C_{21}H_{18}F_4N_6O$, 446.1; m/z found, 446.9 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$, Compound present as a mixture of rotamers) δ 8.40 - 8.19 (m, 1H), 7.99 - 7.73 (series of m, 3H), 7.58 - 7.31 (m, 1H), 7.31 - 7.10 (series of m, 2H), 7.06 (dd, J = 7.9, 2.9 Hz, 1H), 6.16 - 5.67 (series of m, 1H), 4.90 - 4.68 (series of m, 1H), 4.38 - 3.84 (series of m, 1H), 2.20 - 1.40 (series of m, 6H).

Example 370: (2-fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



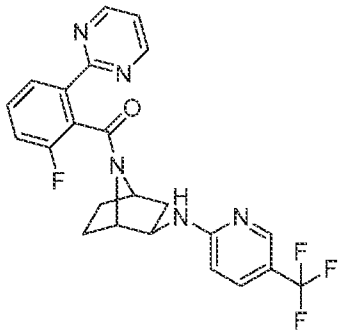
Prepared analogous to Example 279 substituting intermediate A-2 with intermediate A-11. MS (ESI): mass calcd. for $C_{21}H_{18}F_4N_6O$, 446.1; m/z found, 446.9 $[M+H]^+$. Analytical HPLC was obtained on a Agilent 1100 Series using an Inertsil ODS-3 column (3µm, 50 x 3 mm), mobile phase of 5-99% ACN in 0.05% TFA over 1.6 min and then hold at 99% ACN for 0.4 min, at a flow rate of 2.2 mL/min (Temperature = 50 °C). R_t = 1.27 min (major rotamer) at 254 nm.

Example 371: (5-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



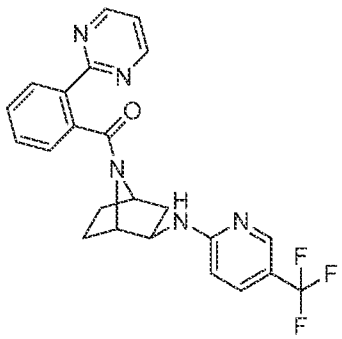
Prepared analogous to Example 279 substituting intermediate A-2 with intermediate A-7. MS (ESI): mass calcd. for $C_{23}H_{19}F_4N_5O$, 457.2; m/z found, 458.2 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$, Compound present as a mixture of rotamers (0.80:0.20), only major rotamer reported) δ 8.82 (d, J = 4.9 Hz, 2H), 8.22 (s, 1H), 8.02 (dd, J = 8.6, 5.4 Hz, 1H), 7.34 - 7.27 (m, 2H), 7.15 (dd, J = 8.3, 2.7 Hz, 1H), 7.04 (dd, J = 8.4, 2.7 Hz, 1H), 6.01 - 5.88 (m, 1H), 4.84 (t, J = 4.5 Hz, 1H), 4.37 (s, 1H), 4.07 - 4.01 (m, 1H), 2.20 (dd, J = 13.0, 8.1 Hz, 1H), 2.00 - 1.89 (m, 2H), 1.80 - 1.51 (series of m, 3H).

Example 372: (2-fluoro-6-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



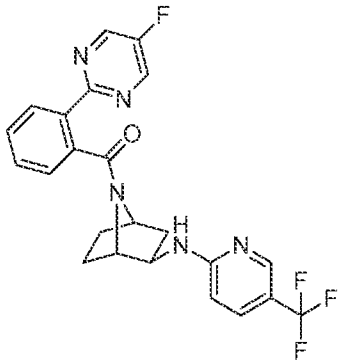
Prepared analogous to Example 279 substituting intermediate A-2 with intermediate A-6. MS (ESI): mass calcd. for $C_{23}H_{19}F_4N_5O$, 457.2; m/z found, 458.2 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$, Compound present as mixture of rotamers) δ 8.85 (d, J = 4.9 Hz, 2H), 8.22 (s, 1H), 7.78 (d, J = 7.7 Hz, 1H), 7.66 (d, J = 9.8 Hz, 1H), 7.48 - 7.43 (m, 1H), 7.37 (t, J = 4.9 Hz, 1H), 7.18 (t, J = 8.8 Hz, 1H), 5.88 (d, J = 8.8 Hz, 1H), 4.88 (t, J = 4.9 Hz, 1H), 4.49 - 4.36 (m, 1H), 3.93 (d, J = 5.0 Hz, 1H), 2.25 (dd, J = 12.9, 7.9 Hz, 1H), 2.18 - 2.08 (m, 1H), 2.03 - 1.93 (m, 1H), 1.81 - 1.67 (m, 2H). *1H buried under solvent peak.

Example 373: (2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



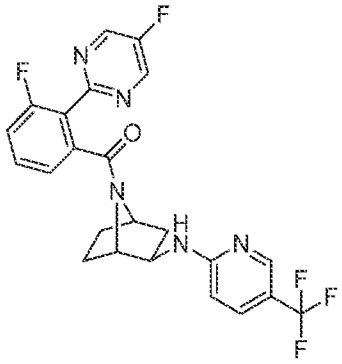
Prepared analogous to Example 279 substituting intermediate A-2 with intermediate A-59. MS (ESI): mass calcd. for $C_{23}H_{20}F_3N_5O$, 439.2; m/z found, 440.0 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$, Compound present as a mixture of rotamers (0.82:0.18), only major rotamer reported) δ 8.83 (d, J = 4.9 Hz, 2H), 8.23 - 8.20 (m, 1H), 7.97 (d, J = 7.7 Hz, 1H), 7.50 - 7.45 (m, 1H), 7.41 - 7.35 (m, 2H), 7.32 (t, J = 4.9 Hz, 1H), 5.94 (d, J = 8.8 Hz, 1H), 4.84 (t, J = 4.5 Hz, 1H), 4.46 - 4.30 (m, 1H), 4.06 (d, J = 4.6 Hz, 1H), 2.20 (dd, J = 12.9, 8.0 Hz, 1H), 1.99 - 1.91 (m, 2H), 1.82 - 1.59 (m, 2H), 1.59 - 1.50 (m, 1H). *1H buried under solvent peak.

Example 374: (2-(5-fluoropyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



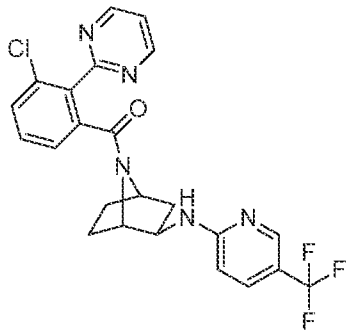
Prepared analogous to Example 279 substituting intermediate A-2 with intermediate A-55. MS (ESI): mass calcd. for $C_{23}H_{19}F_4N_5O$, 457.2; m/z found, 457.9 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.68 (s, 2H), 8.21 (s, 1H), 7.93 (d, J = 7.7 Hz, 1H), 7.48 - 7.42 (m, 1H), 7.38 - 7.30 (m, 3H), 6.00 (d, J = 8.8 Hz, 1H), 4.83 (t, J = 4.6 Hz, 1H), 4.29 (s, 1H), 4.05 (d, J = 4.6 Hz, 1H), 2.18 (dd, J = 13.0, 8.0 Hz, 1H), 2.05 - 1.92 (m, 2H), 1.71 - 1.64 (m, 2H), 1.59 - 1.54 (m, 1H).

Example 375: (3-fluoro-2-(5-fluoropyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



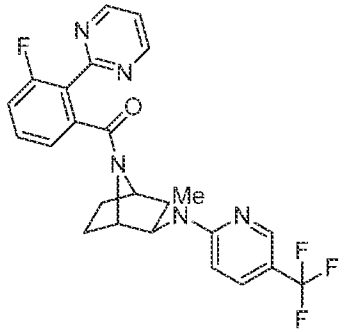
Prepared analogous to Example 279 substituting intermediate A-2 with intermediate A-57. MS (ESI): mass calcd. for $C_{23}H_{18}F_5N_5O$, 475.1; m/z found, 475.9 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.73 (s, 2H), 8.28 - 8.13 (m, 1H), 7.38 - 7.31 (m, 2H), 7.18 - 7.14 (m, 2H), 6.19 (d, J = 8.8 Hz, 1H), 4.72 (t, J = 4.9 Hz, 1H), 4.38 - 4.26 (m, 1H), 4.09 (d, J = 5.0 Hz, 1H), 2.16 (dd, J = 12.9, 8.1 Hz, 1H), 2.07 - 1.98 (m, 1H), 1.95 - 1.86 (m, 1H), 1.75 - 1.66 (m, 1H), 1.66 - 1.57 (m, 1H), 1.57 - 1.48 (m, 1H).

Example 376: (3-chloro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Prepared analogous to Example 279 substituting intermediate A-2 with intermediate A-58. MS (ESI): mass calcd. for $C_{23}H_{19}ClF_3N_5O$, 473.1; m/z found, 474.1 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$, Compound present as a mixture of rotamers (0.92:0.08), only major rotamer reported) δ 8.88 (d, J = 5.0 Hz, 2H), 8.24 - 8.19 (m, 1H), 7.67 - 7.60 (m, 1H), 7.45 (dd, J = 5.9, 3.3 Hz, 1H), 7.39 (t, J = 5.0 Hz, 1H), 7.32 (dd, J = 8.8, 2.5 Hz, 1H), 7.27 (d, J = 2.6 Hz, 1H), 6.29 (d, J = 8.8 Hz, 1H), 4.66 (t, J = 5.1 Hz, 1H), 4.32 (td, J = 8.6, 3.7 Hz, 1H), 4.06 (d, J = 4.9 Hz, 1H), 2.11 (dd, J = 12.9, 8.2 Hz, 1H), 2.05 - 1.97 (m, 1H), 1.92 - 1.84 (m, 1H), 1.74 - 1.67 (m, 1H), 1.59 - 1.53 (m, 1H), 1.53 - 1.46 (m, 1H).

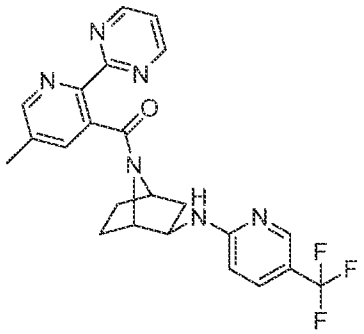
Example 377: (3-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-(methyl(5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



To a solution of compound of Example 279 (19 mg, 0.042 mmol) in DMF (0.42 mL) was added sodium tert-butoxide (5 mg, 0.05 mmol) followed by iodomethane (2.7 µL, 0.044 mmol). The reaction mixture was stirred at room temperature for 12 hours. Solvent was evaporated and purification via prep HPLC gave the title compound (16 mg, 82%). MS (ESI): mass calcd. for $C_{24}H_{21}F_4N_5O$, 471.2; m/z found, 472.2 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$, Compound present

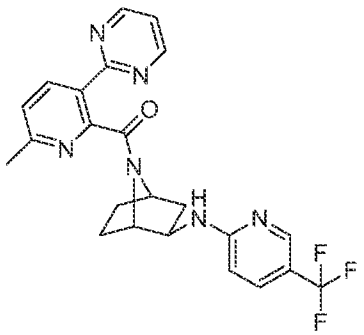
as a mixture of rotamers (0.82:0.18), only major rotamer reported) δ 8.80 (d, *J* = 4.9 Hz, 2H), 8.37 (s, 1H), 7.62 (dd, *J* = 9.1, 2.6 Hz, 1H), 7.51 - 7.44 (m, 1H), 7.32 - 7.22 (series of m, 3H), 6.50 (d, *J* = 9.1 Hz, 1H), 4.93 (dd, *J* = 8.3, 5.0 Hz, 1H), 4.63 (d, *J* = 4.1 Hz, 1H), 4.08 (t, *J* = 4.4 Hz, 1H), 2.93 (s, 3H), 2.09 (dd, *J* = 12.7, 8.3 Hz, 1H), 1.92 - 1.81 (m, 2H), 1.70 - 1.60 (m, 2H), 1.54 - 1.45 (m, 1H).

Example 378: (5-methyl-2-(pyrimidin-2-yl)pyridin-3-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Prepared analogous to Example 279 substituting intermediate A-2 with intermediate A-66. MS (ESI): mass calcd. for $C_{23}H_{21}F_3N_6O$, 454.2; m/z found, 455.2 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$, Compound present as a mixture of rotamers (0.81:0.19), only major rotamer reported) δ 8.89 (d, *J* = 4.9 Hz, 2H), 8.56 (d, *J* = 1.7 Hz, 1H), 8.26 - 8.20 (m, 1H), 7.48 - 7.41 (m, 1H), 7.39 (t, *J* = 4.9 Hz, 1H), 7.35 - 7.28 (m, 1H), 6.01 (d, *J* = 8.8 Hz, 1H), 4.84 (t, *J* = 4.4 Hz, 1H), 4.33 (s, 1H), 3.98 (d, *J* = 4.6 Hz, 1H), 2.31 (s, 3H), 2.20 (dd, *J* = 13.0, 8.1 Hz, 1H), 2.00 - 1.88 (series of m, 2H), 1.79 - 1.50 (series of m, 3H).

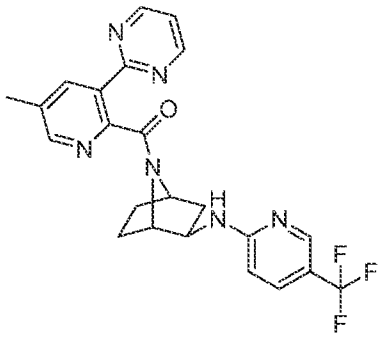
Example 379: (6-methyl-3-(pyrimidin-2-yl)pyridin-2-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Prepared analogous to Example 279 substituting intermediate A-2 with intermediate A-63. MS (ESI): mass calcd. for $C_{23}H_{21}F_3N_6O$, 454.2; m/z found, $[M+H]^+$. ^1H NMR (400 MHz,

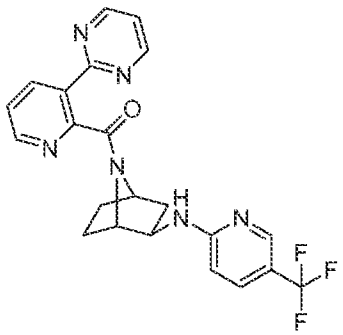
$CDCl_3$, Compound present as a mixture of rotamers (0.89:0.11), only major rotamer reported) δ 8.79 (d, *J* = 4.9 Hz, 1H), 8.31 (d, *J* = 8.1 Hz, 1H), 8.28 - 8.24 (m, 1H), 7.40 (dd, *J* = 8.8, 2.5 Hz, 1H), 7.31 - 7.26 (series of m, 3H), 7.18 (d, *J* = 8.8 Hz, 1H), 6.21 (d, *J* = 8.8 Hz, 1H), 4.89 (t, *J* = 4.7 Hz, 1H), 4.39 - 4.24 (m, 1H), 4.08 (d, *J* = 5.1 Hz, 1H), 2.61 (s, 3H), 2.19 (dd, *J* = 13.0, 7.5 Hz, 1H), 2.11 - 1.93 (series of m, 2H), 1.87 - 1.55 (series of m, 3H).

Example 380: (5-methyl-3-(pyrimidin-2-yl)pyridin-2-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



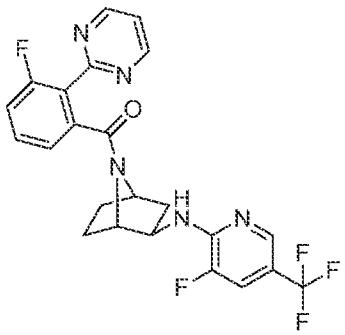
Prepared analogous to Example 279 substituting intermediate A-2 with intermediate A-67. MS (ESI): mass calcd. for $C_{23}H_{21}F_3N_6O$, 454.2; m/z found, 455.2 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$, Compound present as a mixture of rotamers (0.88:0.12), only major rotamer reported) δ 8.83 (d, *J* = 4.9 Hz, 2H), 8.40 (dd, *J* = 2.1, 0.9 Hz, 1H), 8.26 - 8.22 (m, 1H), 8.16 (dd, *J* = 2.0, 0.9 Hz, 1H), 7.36 (dd, *J* = 8.8, 2.5 Hz, 1H), 7.32 (t, *J* = 4.9 Hz, 1H), 7.28 (d, *J* = 9.4 Hz, 1H), 6.14 (d, *J* = 8.8 Hz, 1H), 4.86 (t, *J* = 4.8 Hz, 1H), 4.34 - 4.25 (m, 1H), 4.13 (d, *J* = 5.2 Hz, 1H), 2.41 (s, 3H), 2.19 (dd, *J* = 12.9, 7.7 Hz, 1H), 2.12 - 2.05 (m, 1H), 2.03 - 1.93 (m, 1H), 1.81 - 1.73 (m, 1H), 1.65 - 1.52 (m, 2H).

Example 381: (3-(pyrimidin-2-yl)pyridin-2-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Prepared analogous to Example 279 substituting intermediate A-2 with intermediate A-64. MS (ESI): mass calcd. for $C_{22}H_{19}F_3N_6O$, 440.2; m/z found, 441.2 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$, Compound present as a mixture of rotamers (0.87:0.13), only major rotamer reported) δ 8.83 (d, *J* = 4.9 Hz, 2H), 8.59 (dd, *J* = 4.8, 1.7 Hz, 1H), 8.39 (dd, *J* = 7.9, 1.7 Hz, 1H), 8.26 - 8.22 (m, 1H), 7.43 (dd, *J* = 7.9, 4.8 Hz, 1H), 7.37 (dd, *J* = 8.9, 2.5 Hz, 1H), 7.33 (t, *J* = 4.9 Hz, 1H), 7.23 (d, *J* = 9.4 Hz, 1H), 6.15 (d, *J* = 8.8 Hz, 1H), 4.88 (t, *J* = 4.9 Hz, 1H), 4.35 - 4.26 (m, 1H), 4.11 (d, *J* = 5.2 Hz, 1H), 2.20 (dd, *J* = 13.0, 7.7 Hz, 1H), 2.14 - 2.07 (m, 1H), 2.04 - 1.91 (m, 1H), 1.84 - 1.74 (m, 1H), 1.66 - 1.53 (m, 2H).

Example 382: (3-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((3-fluoro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



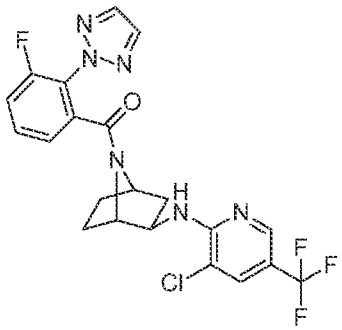
Step A: (1S,2R,4R)-tert-butyl 2-((3-fluoro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptane-7-carboxylate. In a microwave vial was dissolved intermediate B-5 (1.6g, 7.3 mmol) in ACN (11 mL). 2,3-difluoro-5-(trifluoromethyl)pyridine (0.74 mL, 5.82 mmol) was added followed by Et_3N (1 mL, 7.28 mmol). The microwave vial was capped and the reaction mixture was heated to reflux for 16h. Solvent was evaporated and purification via silica gel chromatography (0-20% EtOAc in hexanes) gave the title compound (1.7g, 94%). MS (ESI): mass calcd. for $C_{17}H_{21}F_4N_3O_2$, 375.2; m/z found, 376.2 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$): δ 8.15 (s, 1H), 7.29 (dd, *J* = 10.8, 2.0 Hz, 1H), 5.23 (s, 1H), 4.36 – 4.27 (m, 1H), 4.27 – 4.21 (m, 1H), 4.21 – 4.15 (m, 1H), 2.08 (dd, *J* = 13.1, 7.7 Hz, 1H), 1.91 – 1.80 (m, 1H), 1.80 – 1.70 (m, 1H), 1.63 – 1.48 (m, 2H), 1.43 (s, 10H).

Step B: (1S,2R,4R)-N-(3-fluoro-5-(trifluoromethyl)pyridin-2-yl)-7-azabicyclo[2.2.1]heptan-2-amine. To the title compound of step A (135 mg, 0.36 mmol) in DCM (3.6 mL) was added 4M HCl in dioxane (0.9 mL). After 16h, the reaction was concentrated, neutralized with 5% Na_2CO_3 (aq) and extracted with DCM (2X). The combined organics were dried (Na_2SO_4) to give the title compound of step B that was used without further purification. MS (ESI) mass calcd. for $C_{12}H_{13}F_4N_3$, 275.1; m/z found 276.0 $[M+H]^+$.

Step C: (3-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((3-fluoro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.

To the title compound of step B (98 mg, 0.36 mmol) in DCM (3.6 mL) was added DIPEA (0.08 mL, 0.46 mmol) and intermediate A-2 (93 mg, 0.43 mmol). Then T3P (50% solution in DMF, 0.64 mL, 1.07 mmol) was added dropwise and the reaction heated at 45 °C for 16h. Solvent was evaporated and purification via prep HPLC gave the title compound (133 mg, 79%). MS (ESI): mass calcd. for $C_{23}H_{18}F_5N_5O$, 475.1; m/z found, 476.1 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$, Compound present as a mixture of rotamers (0.83:0.17), major rotamer reported) δ 8.84 (d, J = 5.0 Hz, 2H), 8.05 (s, 1H), 7.59 (br s, 1H), 7.36 - 7.30 (m, 2H), 7.23 - 7.10 (m, 3H), 4.84 - 4.71 (m, 1H), 4.56 - 4.49 (m, 1H), 4.02 (d, J = 4.8 Hz, 1H), 2.20 (dd, J = 12.8, 8.3 Hz, 1H), 2.01 - 1.84 (m, 2H), 1.83 - 1.68 (m, 2H), 1.57 - 1.49 (m, 1H).

Example 383: ((1S,2R,4R)-2-((3-chloro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone.



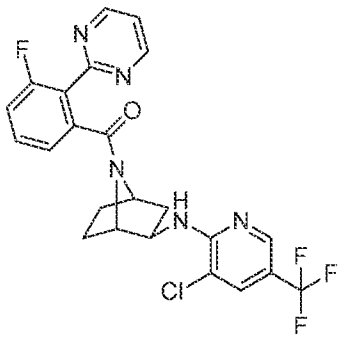
Step A: (1S,2R,4R)-tert-butyl 2-((3-chloro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptane-7-carboxylate. Prepared analogous to Example 382 step A substituting 2,3-difluoro-5-(trifluoromethyl)pyridine with 3-chloro-2-fluoro-5-(trifluoromethyl(pyridine). MS (ESI): mass calcd. for $C_{17}H_{21}ClF_3N_3O_2$, 391.1; m/z found, 392.2 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.26 (s, 1H), 7.62 (s, 1H), 5.65 (s, 1H), 4.39 – 4.22 (m, 2H), 4.22 – 4.13 (m, 1H), 2.09 (dd, J = 13.1, 7.7 Hz, 1H), 1.90 – 1.81 (m, 1H), 1.81 – 1.71 (m, 1H), 1.62 – 1.49 (m, 2H), 1.44 (s, 10H).

Step B: (1S,2R,4R)-N-(3-chloro-5-(trifluoromethyl)pyridin-2-yl)-7-azabicyclo[2.2.1]heptan-2-amine. Prepared analogous to Example 382 step B. MS (ESI): mass calcd. for $C_{12}H_{13}ClF_3N_3$, 291.1; m/z found, 292.1 $[M+H]^+$.

Step C: ((1S,2R,4R)-2-((3-chloro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone. Prepared

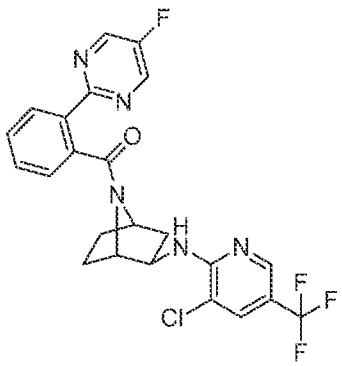
analogous to Example 382 step C substituting intermediate A-2 with intermediate A-16. MS (ESI): mass calcd. for $C_{21}H_{17}ClF_4N_6O$, 480.1; m/z found, 481.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$, Compound present as a mixture of rotamers (0.64:0.36), only major rotamer reported) δ 8.16 (s, 1H), 7.88 (s, 2H), 7.60 (d, J = 2.1 Hz, 1H), 7.43 - 7.30 (m, 1H), 7.25 - 7.21 (m, 1H), 7.18 - 7.12 (m, 1H), 4.77 (t, J = 4.5 Hz, 1H), 4.29 - 4.19 (m, 1H), 3.92 - 3.89 (m, 1H), 2.13 (dd, J = 13.1, 8.1 Hz, 1H), 1.80 - 1.36 (series of m, 5H).

Example 384: ((1S,2R,4R)-2-((3-chloro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-(pyrimidin-2-yl)phenyl)methanone.



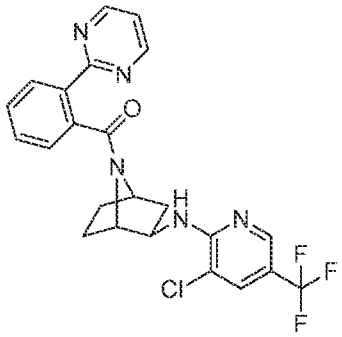
Prepared analogous to Example 383 substituting intermediate A-16 with A-2. MS (ESI): mass calcd. for $C_{23}H_{18}ClF_4N_5O$, 491.1; m/z found, 492.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$, Compound present as a mixture of rotamers (0.74:0.26), only major rotamer reported) δ 8.84 (d, J = 4.8 Hz, 2H), 8.17 (s, 1H), 7.55 (d, J = 2.2 Hz, 1H), 7.32 - 7.26 (series of m, 2H), 7.19 - 7.12 (series of m, 2H), 4.77 (t, J = 4.6 Hz, 1H), 4.46 - 4.31 (m, 1H), 3.98 (d, J = 4.3 Hz, 1H), 2.25 - 2.13 (m, 1H), 1.93 - 1.63 (series of m, 4H), 1.59 - 1.35 (m, 1H).

Example 385: ((1S,2R,4R)-2-((3-chloro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(2-(5-fluoropyrimidin-2-yl)phenyl)methanone.



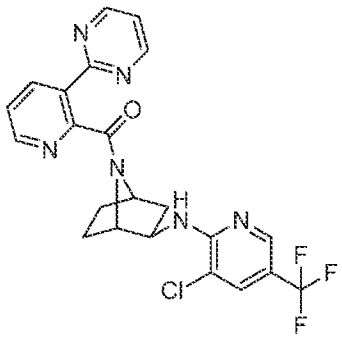
Prepared analogous to Example 383 substituting intermediate A-16 with A-55. MS (ESI): mass mass calcd. for $C_{23}H_{18}ClF_4N_5O$, 491.1; m/z found, 492.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$, Compound present as a mixture of rotamers (0.72:0.28), only major rotamer reported) δ 8.63 (s, 2H), 8.17 - 8.12 (m, 1H), 8.08 - 8.02 (m, 1H), 7.56 (s, 1H), 7.57 - 7.37 (series of m, 2H), 7.37 - 7.29 (m, 1H), 4.93 (t, J = 4.5 Hz, 1H), 4.36 - 4.24 (m, 1H), 3.90 (d, J = 5.0 Hz, 1H), 2.21 (dd, J = 13.0, 8.1 Hz, 1H), 2.00 - 1.51 (series of m, 5H).

Example 386: ((1S,2R,4R)-2-((3-chloro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(2-(pyrimidin-2-yl)phenyl)methanone.



Prepared analogous to Example 383 substituting intermediate A-16 with A-59. MS (ESI): mass calcd. for $C_{23}H_{19}ClF_3N_5O$, 473.1; m/z found, 474.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$, Compound present as a mixture of rotamers (0.74:0.26), only major rotamer reported) δ 8.79 (d, J = 4.9 Hz, 2H), 8.15 - 8.10 (m, 2H), 7.54 - 7.52 (m, 1H), 7.46 - 7.39 (m, 1H), 7.37 - 7.29 (m, 2H), 7.22 (t, J = 4.9 Hz, 1H), 4.93 (t, J = 5.1 Hz, 1H), 4.42 - 4.24 (m, 1H), 3.89 (d, J = 5.0 Hz, 1H), 2.20 (dd, J = 12.9, 8.1 Hz, 1H), 1.99 - 1.47 (series of m, 5H).

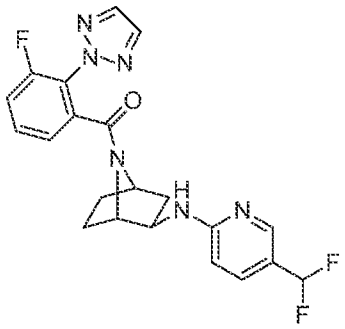
Example 387: ((1S,2R,4R)-2-((3-chloro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-(pyrimidin-2-yl)pyridin-2-yl)methanone.



Prepared analogous to Example 383 substituting intermediate A-16 with A-64. MS (ESI): mass calcd. for $C_{22}H_{18}ClF_3N_6O$, 474.1; m/z found, 475.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$,

Compound present as a mixture of rotamers (0.89:0.11), only major rotamer reported) δ 8.79 (d, *J* = 4.9 Hz, 2H), 8.64 (dd, *J* = 4.8, 1.7 Hz, 1H), 8.50 (dd, *J* = 7.9, 1.7 Hz, 1H), 8.23 - 8.19 (m, 1H), 7.60 (d, *J* = 2.1 Hz, 1H), 7.47 (dd, *J* = 7.9, 4.8 Hz, 1H), 7.38 (d, *J* = 7.8 Hz, 1H), 7.25 (t, *J* = 4.9 Hz, 1H), 4.94 (t, *J* = 4.7 Hz, 1H), 4.38 (td, *J* = 7.6, 2.9 Hz, 1H), 4.12 (d, *J* = 4.8 Hz, 1H), 2.25 (dd, *J* = 12.9, 7.4 Hz, 1H), 2.16 - 1.98 (series of m, 2H), 1.89 - 1.79 (m, 1H), 1.66 - 1.56 (series of m, 2H).

Example 388: ((1S,2R,4R)-2-((5-(difluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone.



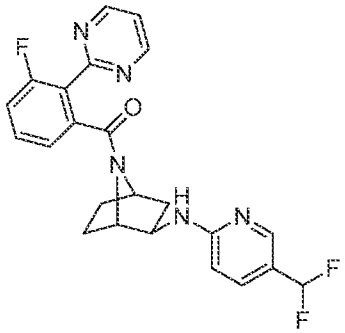
Step A: (1S,2R,4R)-tert-butyl 2-((5-(difluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptane-7-carboxylate. Prepared analogous to Example 279 step A substituting 2-chloro-5-(trifluoromethyl)pyridine with 2-chloro-5-(difluoromethyl)pyridine. MS (ESI): mass calcd. for $C_{17}H_{23}F_2N_3O_2$, 339.2; m/z found, 340.0 $[M+H]^+$. Analytical HPLC was obtained on a Agilent 1100 Series using an Inertsil ODS-3 column (3µm, 50 x 3 mm), mobile phase of 5-99% ACN in 0.05% TFA over 1.6 min and then hold at 99% ACN for 0.4 min, at a flow rate of 2.2 mL/min (Temperature = 50 °C). R_t = 0.601 min at 254 nm.

Step B: (1S,2R,4R)-N-(5-(difluoromethyl)pyridin-2-yl)-7-azabicyclo[2.2.1]heptan-2-amine. Prepared analogous to Example 279 step B. MS (ESI): mass calcd. for $C_{12}H_{15}F_2N_3$, 239.1; m/z found, 240.0 $[M+H]^+$.

Step C: ((1S,2R,4R)-2-((5-(difluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone. Prepared analogous to Example 181 step C substituting intermediate A-1 with intermediate A-16. MS (ESI): mass calcd. for $C_{21}H_{19}F_3N_6O$, 428.2; m/z found, 429.0 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$, Compound present as a mixture of rotamers) δ 8.09 - 8.02 (m, 1H), 7.95 (s, 2H), 7.39 - 7.33 (m, 2H), 7.29 - 7.21 (m, 1H), 7.16 (dt, *J* = 7.6, 1.2 Hz, 1H), 6.48 (t, *J* = 56.3 Hz, 1H), 6.32

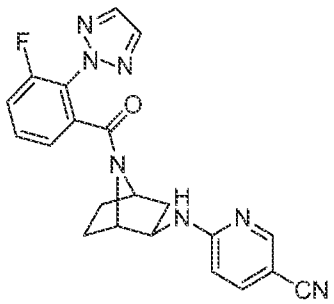
(d, J = 8.8 Hz, 1H), 4.77 - 4.69 (m, 1H), 4.30 - 4.22 (m, 1H), 3.99 (d, J = 4.9 Hz, 1H), 2.12 (dd, J = 13.0, 8.1 Hz, 1H), 1.98 - 1.81 (m, 2H), 1.72 - 1.58 (m, 2H), 1.54 - 1.47 (m, 1H).

Example 389: ((1S,2R,4R)-2-((5-(difluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-(pyrimidin-2-yl)phenyl)methanone.



Prepared analogous to Example 388 substituting intermediate A-16 with intermediate A-2. MS (ESI): mass calcd. for $C_{23}H_{20}F_3N_5O$, 439.2; m/z found, 439.9 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$, Compound present as a mixture of rotamers (0.89:0.11), only major rotamer reported) δ 8.87 (d, J = 5.0 Hz, 2H), 8.09 - 8.02 (m, 1H), 7.51 - 7.43 (m, 1H), 7.37 (t, J = 5.0 Hz, 1H), 7.34 - 7.28 (m, 1H), 7.21 - 7.12 (m, 2H), 6.47 (t, J = 56.3 Hz, 1H), 6.22 (d, J = 8.7 Hz, 1H), 4.78 - 4.65 (m, 1H), 4.35 (td, J = 8.7, 3.7 Hz, 1H), 4.07 (d, J = 4.9 Hz, 1H), 2.15 (dd, J = 12.9, 8.1 Hz, 1H), 2.05 - 1.96 (m, 1H), 1.95 - 1.85 (m, 1H), 1.76 - 1.67 (m, 1H), 1.63 - 1.61 (m, 1H), 1.55 - 1.46 (m, 1H).

Example 390: 6-(((1S,2R,4R)-7-(3-fluoro-2-(2H-1,2,3-triazol-2-yl)benzoyl)-7-azabicyclo[2.2.1]heptan-2-yl)amino)nicotinonitrile.



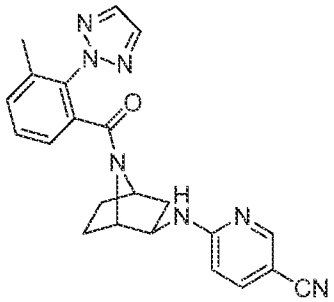
Step A: (1S,2R,4R)-tert-butyl 2-((5-cyanopyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptane-7-carboxylate. To a solution of intermediate B-5 (442 mg, 2.08 mmol) in DMA (7 mL) was added DIPEA (0.72 mL, 4.16 mmol) followed by 2-chloro-5-cyanopyridine (324 mg, 2.29 mmol). The reaction mixture was heated at 120 °C for 90 minutes using microwave and was then diluted with water and EtOAc. The aqueous phase was extracted twice

with EtOAc and the combined organic layers were washed with a saturated solution of NaCl, dried over $MgSO_4$, filtered and evaporated. Purification via silica gel chromatography (0-40% EtOAc in hexanes) gave the title compound (416 mg, 64%). MS (ESI): mass calcd. for $C_{17}H_{22}N_4O_2$, 314.2; m/z found, 315.1 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.36 (d, J = 2.2 Hz, 1H), 7.58 – 7.49 (m, 1H), 6.35 (d, J = 8.7 Hz, 1H), 5.42 (s, 1H), 4.29 (s, 1H), 4.24 – 4.15 (m, 1H), 3.99 (s, 1H), 2.09 – 1.98 (m, 1H), 1.90 – 1.68 (m, 2H), 1.62 – 1.34 (m, 12H).

Step B: 6-((1S,2R,4R)-7-azabicyclo[2.2.1]heptan-2-ylamino)nicotinonitrile. To the title compound of step A (416 mg, 1.32 mmol) in DCM (6.5 mL) was added 4M HCl in dioxane (1.7 mL). After 16h, the reaction was concentrated, neutralized with 5% Na_2CO_3 (aq) and extracted with DCM (2X). The combined organics were dried (Na_2SO_4) to give the title compound of step B that was used without further purification. MS (ESI): mass calcd. for $C_{12}H_{14}N_4$, 214.1; m/z found, 215.0 $[M+H]^+$.

Step C: 6-(((1S,2R,4R)-7-(3-fluoro-2-(2H-1,2,3-triazol-2-yl)benzoyl)-7-azabicyclo[2.2.1]heptan-2-yl)amino)nicotinonitrile. To a solution of the title compound of step B (30 mg, 0.14 mmol) and intermediate A-16 (32 mg, 0.15 mmol) in DCM (1.4 mL) was added DIPEA (0.15 mL, 0.84 mmol) followed by HATU (64 mg, 0.17 mmol). The reaction mixture was stirred at room temperature for 16h. Solvent was evaporated and purification via prep HPLC gave the title compound (44 mg, 78%). MS (ESI): mass calcd. for $C_{21}H_{18}FN_7O$, 403.2; m/z found, 404.0 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$, Compound present as a mixture of rotamers) δ 8.25 (d, J = 2.1 Hz, 1H), 7.96 (s, 2H), 7.40 - 7.27 (series of m, 3H), 7.18 (dt, J = 7.7, 1.1 Hz, 1H), 6.27 (d, J = 8.9 Hz, 1H), 4.79 - 4.68 (m, 1H), 4.39 - 4.24 (m, 1H), 3.97 (d, J = 5.0 Hz, 1H), 2.12 (dd, J = 13.1, 8.2 Hz, 1H), 2.00 - 1.83 (m, 2H), 1.73 - 1.64 (m, 2H), 1.55 - 1.48 (m, 1H).

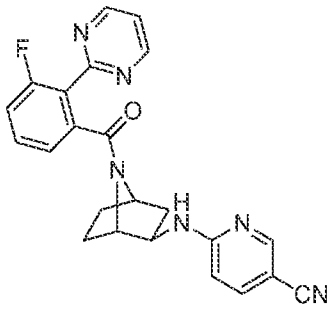
Example 391: 6-(((1S,2R,4R)-7-(3-methyl-2-(2H-1,2,3-triazol-2-yl)benzoyl)-7-azabicyclo[2.2.1]heptan-2-yl)amino)nicotinonitrile.



Prepared analogous to Example 390 substituting intermediate A-16 with A-24. MS (ESI): mass calcd. for $C_{22}H_{21}N_7O$, 399.2; m/z found, 400.0 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$,

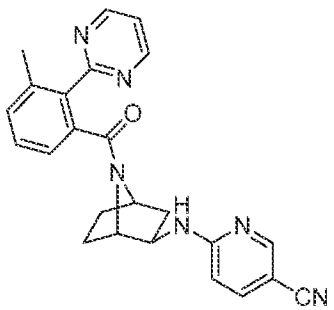
Compound present as a mixture of rotamers (0.81:0.19), only major rotamer reported) δ 8.25 (d, *J* = 2.3 Hz, 1H), 7.90 (s, 2H), 7.39 - 7.27 (series of m, 3H), 7.23 - 7.15 (m, 1H), 6.31 (d, *J* = 9.0 Hz, 1H), 4.68 (t, *J* = 4.8 Hz, 1H), 4.37 - 4.20 (m, 1H), 3.95 (d, *J* = 5.1 Hz, 1H), 2.19 (s, 3H), 2.12 - 2.03 (m, 1H), 1.99 - 1.94 (m, 1H), 1.89 - 1.77 (m, 1H), 1.66 - 1.61 (m, 1H), 1.61 - 1.52 (m, 1H), 1.52 - 1.39 (m, 1H).

Example 392: 6-(((1S,2R,4R)-7-(3-fluoro-2-(pyrimidin-2-yl)benzoyl)-7-azabicyclo[2.2.1]heptan-2-yl)amino)nicotinonitrile.



Prepared analogous to Example 390 substituting intermediate A-16 with A-2. MS (ESI): mass calcd. for $C_{23}H_{19}FN_6O$, 414.2; m/z found, 415.0 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$, Compound present as a mixture of rotamers) δ 8.87 (d, *J* = 5.0 Hz, 2H), 8.25 (d, *J* = 2.2 Hz, 1H), 8.10 - 7.99 (m, 1H), 7.40 (t, *J* = 4.9 Hz, 1H), 7.38 - 7.34 (m, 1H), 7.31 - 7.27 (m, 1H), 7.22 - 7.20 (m, 1H), 7.19 - 7.15 (m, 1H), 6.16 (d, *J* = 8.8 Hz, 1H), 4.79 - 4.67 (m, 1H), 4.48 - 4.30 (m, 1H), 4.07 (d, *J* = 5.0 Hz, 1H), 2.15 (dd, *J* = 13.0, 8.2 Hz, 1H), 2.07 - 2.00 (m, 1H), 1.96 - 1.88 (m, 1H), 1.76 - 1.68 (m, 1H), 1.68 - 1.63 (m, 1H), 1.56 - 1.48 (m, 1H).

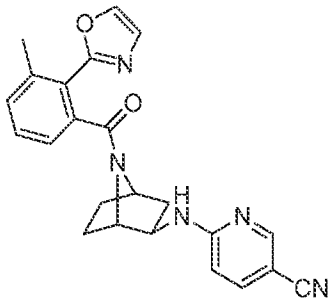
Example 393: 6-(((1S,2R,4R)-7-(3-methyl-2-(pyrimidin-2-yl)benzoyl)-7-azabicyclo[2.2.1]heptan-2-yl)amino)nicotinonitrile.



Prepared analogous to Example 390 substituting intermediate A-16 with A-26. MS (ESI): mass calcd. for $C_{24}H_{22}N_6O$, 410.2; m/z found, 411.0 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$, Compound present as a mixture of rotamers) δ 8.83 (d, *J* = 5.0 Hz, 2H), 8.25 (d, *J* = 2.3 Hz, 1H),

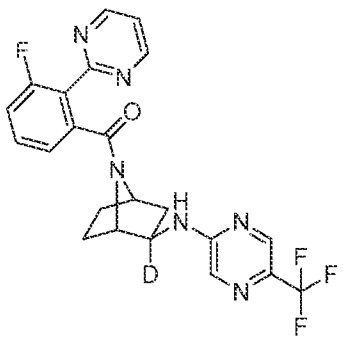
7.35 (t, J = 5.0 Hz, 1H), 7.32 - 7.21 (m, 3H), 7.21 - 7.18 (m, 1H), 6.17 (d, J = 8.8 Hz, 1H), 4.72 - 4.62 (m, 1H), 4.42 - 4.31 (m, 1H), 4.07 (d, J = 5.0 Hz, 1H), 2.30 (s, 3H), 2.11 (dd, J = 12.9, 8.1 Hz, 1H), 2.07 - 1.98 (m, 1H), 1.95 - 1.84 (m, 1H), 1.72 - 1.65 (m, 1H), 1.61 - 1.54 (m, 1H), 1.52 - 1.45 (m, 1H).

Example 394: 6-(((1S,2R,4R)-7-(3-methyl-2-(oxazol-2-yl)benzoyl)-7-azabicyclo[2.2.1]heptan-2-yl)amino)nicotinonitrile.



Prepared analogous to Example 390 substituting intermediate A-16 with A-31. MS (ESI): mass calcd. for $C_{23}H_{21}N_5O_2$, 399.2; m/z found, 400.0 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$, Compound present as a mixture of rotamers (0.89:0.11), only major rotamer reported) δ 8.22 (d, J = 2.2 Hz, 1H), 7.88 (d, J = 0.9 Hz, 1H), 7.32 - 7.22 (series of m, 4H), 7.20 - 7.13 (m, 1H), 6.29 (dd, J = 9.0, 0.8 Hz, 1H), 4.79 - 4.70 (m, 1H), 4.39 - 4.27 (m, 1H), 3.91 (d, J = 4.8 Hz, 1H), 2.28 (s, 3H), 2.09 (dd, J = 12.9, 8.2 Hz, 1H), 2.00 - 1.87 (m, 2H), 1.73 - 1.64 (m, 2H), 1.54 - 1.46 (m, 1H).

Example 395: (3-fluoro-2-(pyrimidin-2-yl)phenyl) ((1S,2R,4R)-(2-^{2}H)-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Step A: (1S,4R)-(2-^{2}H)-tert-butyl 2-(((benzyloxy)carbonyl)amino)-7-azabicyclo[2.2.1]heptane-7-carboxylate. To a solution of intermediate (+)-B-2 (640 mg, 1.9 mmol) in CD_3OD (5.5 mL) was added 0.45M $NaOCD_3$ in CD_3OD (5.8 mL, 2.90 mmol). The reaction mixture was heated to reflux for 2 days and cooled to room temperature. 1N $KHSO_4$

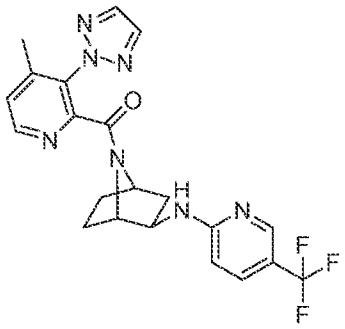
was added and the aqueous phase was extracted 3 times with DCM. The combined organic layers were dried over $MgSO_4$, filtered and evaporated. The material was used in the next step without any further purification. To a solution of the residue in CD_3OD (9.6 mL) cooled to 0 °C was added 2M NaOH in D_2O (3.9 mL, 7.7 mmol). The reaction mixture was stirred for 2h and was then acidified with 1N $KHSO_4$ until pH 2-3. The aqueous phase was extracted 3 times with DCM and the combined organic layers were dried over $MgSO_4$, filtered and evaporated. The material was used in the next step without any further purification. To the residue in $PhCH_3$ (4.8 mL) was added TEA (0.3 mL, 2.1 mmol). After heating in an oil bath to 70 °C, DPPA (0.46 mL, 2.1 mmol) in $PhCH_3$ (1 mL) was added. After 2.5h, BnOH (0.19 mL, 1.8 mmol) was added and the oil bath temperature increased to 90 °C. After an additional 18h, the reaction was cooled to rt, diluted with EtOAc and washed with saturated $NaHCO_3$ (aq). The aqueous layer was extracted with EtOAc (1X). The combined organics were washed with brine and dried ($MgSO_4$). Purification via prep HPLC gave gave the title compound (380 mg, 57%) as a mixture of diastereoisomers (80/20). MS (ESI): mass calcd. for $C_{19}H_{25}DN_2O_4$, 347.2; m/z found, 348.2 $[M+H]^+$. Reporting only the major diastereoisomer. ^1H NMR (500 MHz, $CDCl_3$) δ 7.40 – 7.28 (m, 5H), 5.22 – 4.91 (m, 3H), 4.22 (s, 1H), 4.14 – 4.06 (m, 1H), 1.92 (d, J = 13.1 Hz, 1H), 1.85 – 1.59 (m, 2H), 1.44 (d, J = 7.6 Hz, 12H).

Step B: (1S,2R,4R)- (2-^{2}H)-tert-butyl 2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptane-7-carboxylate. To intermediate of step A (380 mg, 1.1 mmol) in EtOH (6.5 mL) was added 10 wt% Pd/C wet Degussa (79 mg). The reaction was purged with N_2 followed by H_2, then allowed to proceed under an atmosphere of H_2 (balloon). Upon completion, the reaction was filtered and concentrated to give the unprotected amine. MS (ESI): mass calcd. for $C_{11}H_{19}DN_2O_2$, 213.2; m/z found, 214.2 $[M+H]^+$. In a microwave vial was dissolved the residue in ACN (3.7 mL). 5-chloro-2-trifluoromethylpyrazine (0.08 mL, 0.66 mmol) was added followed by Et_3N (0.11 mL, 0.82 mmol). The microwave vial was capped and the reaction mixture was heated to reflux for 16h. Solvent was evaporated and purification via silica gel chromatography (0-30% EtOAc in hexanes) gave the title compound (119 mg, 60%). Only the desired diastereoisomer was isolated. MS (ESI): mass calcd. for $C_{16}H_{20}DF_3N_4O_2$, 359.2; m/z found, 360.2 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.32 (s, 1H), 7.85 (s, 1H), 5.38 (s, 1H), 4.30 (s, 1H), 4.21 (s, 1H), 2.06 (d, J = 13.0 Hz, 1H), 1.95 – 1.68 (m, 2H), 1.66 – 1.35 (m, 12H).

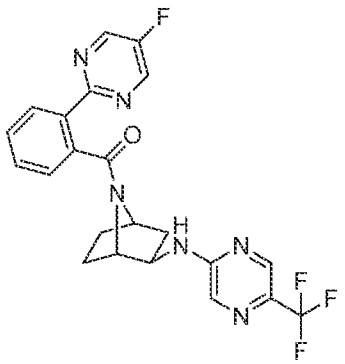
Step C: (3-fluoro-2-(pyrimidin-2-yl)phenyl) ((1S,2R,4R)-(2-^{2}H)-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone. To the title compound of step B (119 mg, 0.33 mmol) in DCM (3.3 mL) was added 4M HCl in dioxane (0.4 mL). After 16h, the reaction was concentrated, neutralized with 5% Na_2CO_3 (aq) and extracted

with DCM (2X). The combined organics were dried (Na_2SO_4) to give the unprotected amine that was used without any further purification in the next step. MS (ESI): mass calcd. for $C_{11}H_{12}DF_3N_4$, 259.1; m/z found, 260.2 $[M+H]^+$. To the residue in DCM (3.3 mL) was added DIPEA (0.07 mL, 0.43 mmol) and intermediate A-2 (86 mg, 0.39 mmol). Then T3P (50% solution in DMF, 0.59 mL, 0.98 mmol) was added dropwise and the reaction heated at 45 °C for 16h. Solvent was evaporated and purification via prep HPLC gave the title compound (107 mg, 71%). MS (ESI): mass calcd. for $C_{22}H_{17}DF_4N_6O$, 459.2; m/z found, 460.2 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$, Compound present as a mixture of rotamers (0.93:0.07), only major rotamer reported) δ 8.88 (d, *J* = 5.0 Hz, 2H), 8.27 (s, 1H), 8.19 (s, 1H), 7.65 (d, *J* = 1.4 Hz, 1H), 7.42 - 7.36 (m, 2H), 7.25 - 7.17 (m, 2H), 4.77 - 4.72 (m, 1H), 4.07 (d, *J* = 5.1 Hz, 1H), 2.17 (d, *J* = 13.0 Hz, 1H), 2.09 - 2.02 (m, 1H), 1.98 - 1.89 (m, 1H), 1.75 - 1.71 (m, 1H), 1.69 - 1.64 (m, 1H), 1.55 - 1.49 (m, 1H).

Example 396: (4-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.

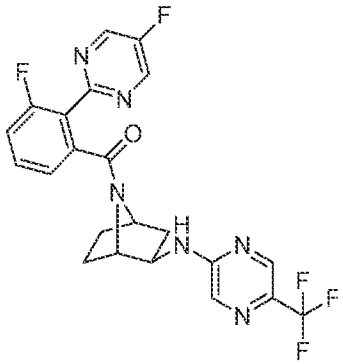


Example 397: (2-(5-fluoropyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



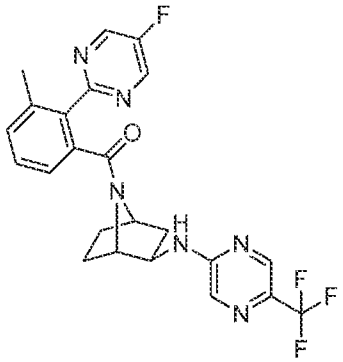
Prepared analogous to Example 238 substituting intermediate A-2 with intermediate A-55. MS (ESI): mass calcd. for $C_{22}H_{18}F_4N_6O$, 458.1; m/z found, 458.9 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.69 (s, 2H), 8.15 (s, 1H), 7.91 (d, *J* = 7.8 Hz, 1H), 7.48 - 7.31 (m, 4H), 4.86 - 4.77 (m, 1H), 4.29 (s, 1H), 4.09 - 3.90 (m, 1H), 2.19 - 1.50 (series of m, 6H).

Example 398: (3-fluoro-2-(5-fluoropyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Prepared analogous to Example 238 substituting intermediate A-2 with intermediate A-57. MS (ESI): mass calcd. for $C_{22}H_{17}F_5N_6O$, 476.1; m/z found, 476.9 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.73 (s, 2H), 8.19 (s, 1H), 7.69 (d, *J* = 9.0 Hz, 1H), 7.64 (d, *J* = 1.5 Hz, 1H), 7.40 - 7.32 (m, 1H), 7.20 - 7.17 (m, 1H), 4.72 (t, *J* = 5.2 Hz, 1H), 4.33 (td, *J* = 8.7, 3.6 Hz, 1H), 4.07 (d, *J* = 5.0 Hz, 1H), 2.16 (dd, *J* = 13.1, 8.1 Hz, 1H), 2.10 - 1.97 (m, 1H), 1.96 - 1.85 (m, 1H), 1.77 - 1.68 (m, 1H), 1.65 - 1.58 (m, 1H), 1.57 - 1.48 (m, 1H).

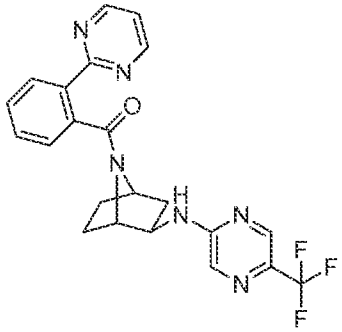
Example 399: (2-(5-fluoropyrimidin-2-yl)-3-methylphenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Prepared analogous to Example 238 substituting intermediate A-2 with intermediate A-56. Analytical HPLC was obtained on a Agilent 1100 Series using an Inertsil ODS-3 column (3μm, 50 x 3 mm), mobile phase of 5-99% ACN in 0.05% TFA over 1.6 min and then hold at

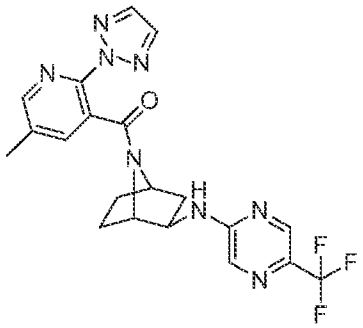
99% ACN for 0.4 min, at a flow rate of 2.2 mL/min (Temperature = 50 °C). R_t = 1.38 min (major rotamer) at 254 nm. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.70 (s, 2H), 8.17 (s, 1H), 7.88 (d, *J* = 9.1 Hz, 1H), 7.63 (s, 1H), 7.26 - 7.18 (m, 2H), 4.73 - 4.65 (m, 1H), 4.36 - 4.26 (m, 1H), 4.11 (d, *J* = 5.2 Hz, 1H), 2.26 (s, 3H), 2.13 (dd, *J* = 13.0, 8.1 Hz, 1H), 2.10 - 2.01 (m, 1H), 1.95 - 1.86 (m, 1H), 1.70 - 1.64 (m, 1H), 1.60 - 1.55 (m, 1H), 1.54 - 1.45 (m, 1H).

Example 400: (2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Prepared analogous to Example 238 substituting intermediate A-2 with intermediate A-59. MS (ESI): mass calcd. for $C_{22}H_{19}F_3N_6O$, 440.2; m/z found, 441.2 $[M+H]^+$. ^{1}H NMR (500 MHz, $CDCl_3$, Compound present as a mixture of rotamers (0.88:0.12), only major rotamer reported) δ 8.84 (d, *J* = 4.9 Hz, 2H), 8.16 (s, 1H), 7.99 - 7.92 (m, 1H), 7.53 - 7.47 (m, 1H), 7.45 - 7.32 (series of m, 4H), 4.85 (t, *J* = 4.8 Hz, 1H), 4.46 - 4.33 (m, 1H), 4.07 (d, *J* = 5.0 Hz, 1H), 2.20 (dd, *J* = 13.0, 8.1 Hz, 1H), 2.06 - 1.91 (m, 2H), 1.86 - 1.66 (m, 2H), 1.59 - 1.52 (m, 1H).

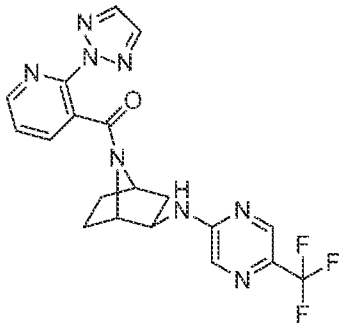
Example 401: (5-methyl-2-(2H-1,2,3-triazol-2-yl)pyridin-3-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Prepared analogous to Example 238 substituting intermediate A-2 with intermediate A-60. MS (ESI): mass calcd. for $C_{20}H_{19}F_3N_8O$, 444.2; m/z found, 445.2 $[M+H]^+$. Analytical HPLC was obtained on a Agilent 1100 Series using an Inertsil ODS-3 column (3μm, 50 x 3 mm), mobile phase of 5-99% ACN in 0.05% TFA over 1.6 min and then hold at 99% ACN for 0.4

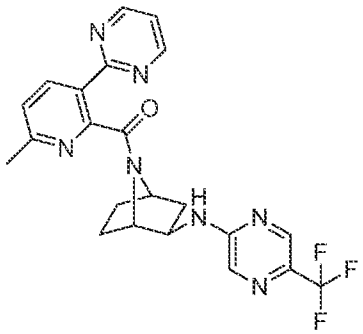
min, at a flow rate of 2.2 mL/min (Temperature = 50 °C). R_t = 1.13 min (major rotamer) at 254 nm.

Example 402: (2-(2H-1,2,3-triazol-2-yl)pyridin-3-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Prepared analogous to Example 238 substituting intermediate A-2 with intermediate A-61. MS (ESI): mass calcd. for $C_{19}H_{17}F_3N_8O$, 430.1; m/z found, 431.1 $[M+H]^+$. Analytical HPLC was obtained on a Agilent 1100 Series using an Inertsil ODS-3 column (3µm, 50 x 3 mm), mobile phase of 5-99% ACN in 0.05% TFA over 1.6 min and then hold at 99% ACN for 0.4 min, at a flow rate of 2.2 mL/min (Temperature = 50 °C). R_t = 1.05 min (major rotamer) at 254 nm.

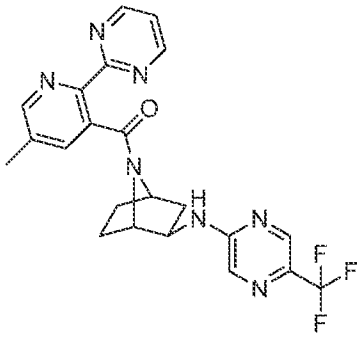
Example 403: (6-methyl-3-(pyrimidin-2-yl)pyridin-2-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Prepared analogous to Example 238 substituting intermediate A-2 with intermediate A-63. MS (ESI): mass calcd. for $C_{22}H_{20}F_3N_7O$, 455.2; m/z found, 456.2 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$, Compound present as a mixture of rotamers, major rotamer reported) δ 8.80 (d, J = 4.9 Hz, 2H), 8.31 (d, J = 8.0 Hz, 1H), 8.23 (s, 1H), 7.82 (d, J = 8.5 Hz, 1H), 7.66 (d, J = 1.4 Hz, 1H), 7.30 (d, J = 1.2 Hz, 1H), 7.30 - 7.28 (m, 1H), 4.94 - 4.87 (m, 1H), 4.35 - 4.25 (m, 1H), 4.14

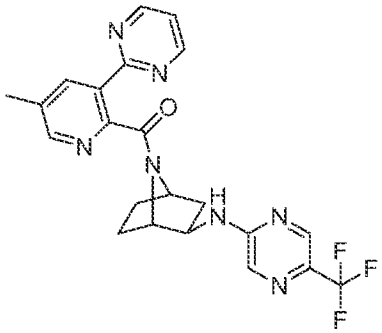
(d, J = 5.3 Hz, 1H), 2.61 (s, 3H), 2.20 (dd, J = 13.1, 7.6 Hz, 1H), 2.16 - 2.09 (m, 1H), 2.06 - 1.97 (m, 1H), 1.84 - 1.76 (m, 1H), 1.63 - 1.58 (m, 2H).

Example 404: (5-methyl-2-(pyrimidin-2-yl)pyridin-3-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Prepared analogous to Example 238 substituting intermediate A-2 with intermediate A-66. MS (ESI): mass calcd. for $C_{22}H_{20}F_3N_7O$, 455.2; m/z found, 456.2 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$, Compound present as a mixture of rotamers (0.79:0.21), only major rotamer reported) δ 8.89 (d, J = 4.9 Hz, 2H), 8.61 (d, J = 2.1 Hz, 1H), 8.18 (s, 1H), 7.54 - 7.46 (m, 2H), 7.41 (t, J = 4.9 Hz, 1H), 4.85 (t, J = 4.5 Hz, 1H), 4.39 (s, 1H), 3.97 (d, J = 4.4 Hz, 1H), 2.37 (s, 3H), 2.22 (dd, J = 13.0, 8.0 Hz, 1H), 2.07 - 1.90 (m, 2H), 1.85 - 1.65 (m, 2H), 1.61 - 1.52 (m, 1H).

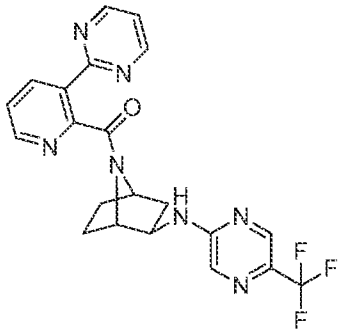
Example 405: (5-methyl-3-(pyrimidin-2-yl)pyridin-2-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Prepared analogous to Example 238 substituting intermediate A-2 with intermediate A-67. MS (ESI): mass calcd. for $C_{22}H_{20}F_3N_7O$, 455.2; m/z found, 456.2 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$, Compound present as a mixture of rotamers (0.90:0.10), only major rotamer reported) δ 8.83 (d, J = 4.9 Hz, 2H), 8.43 - 8.37 (m, 1H), 8.21 (s, 1H), 8.18 - 8.13 (m, 1H), 7.93 - 7.85 (m, 1H), 7.56 (s, 1H), 7.34 (t, J = 4.9 Hz, 1H), 4.93 - 4.84 (m, 1H), 4.31 (td, J = 8.4, 3.0 Hz,

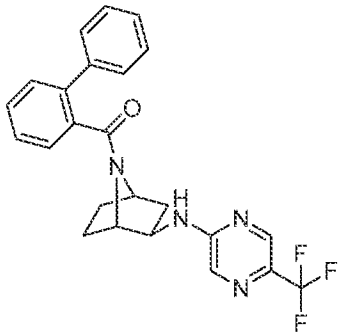
1H), 4.19 (d, *J* = 5.3 Hz, 1H), 2.40 (s, 3H), 2.20 (dd, *J* = 13.1, 7.8 Hz, 1H), 2.17 - 2.11 (m, 1H), 2.03 - 1.94 (m, 1H), 1.84 - 1.76 (m, 1H), 1.64 - 1.53 (series of m, 2H).

Example 406: (3-(pyrimidin-2-yl)pyridin-2-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Prepared analogous to Example 238 substituting intermediate A-2 with intermediate A-64. MS (ESI): mass calcd. for $C_{21}H_{18}F_3N_7O$, 441.2; m/z found, 442.2 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$, Compound present as a mixture of rotamers (0.91:0.09), only major rotamer reported) δ 8.84 (d, *J* = 4.9 Hz, 2H), 8.58 (dd, *J* = 4.8, 1.7 Hz, 1H), 8.38 (dd, *J* = 7.9, 1.7 Hz, 1H), 8.21 (s, 1H), 7.83 (d, *J* = 8.8 Hz, 1H), 7.58 (s, 1H), 7.44 (dd, *J* = 7.9, 4.8 Hz, 1H), 7.34 (t, *J* = 4.9 Hz, 1H), 4.90 (t, *J* = 4.8 Hz, 1H), 4.40 - 4.26 (m, 1H), 4.16 (d, *J* = 5.3 Hz, 1H), 2.21 (dd, *J* = 13.1, 7.8 Hz, 1H), 2.18 - 2.11 (m, 1H), 2.05 - 1.94 (m, 1H), 1.87 - 1.78 (m, 1H), 1.68 - 1.55 (m, 2H).

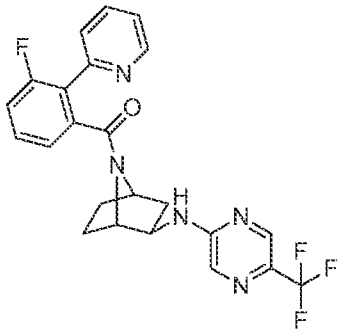
Example 407: [1,1'-biphenyl]-2-yl((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Prepared analogous to Example 238 substituting intermediate A-2 with 2-biphenylcarcoxylic acid. MS (ESI): mass calcd. for $C_{24}H_{21}F_3N_4O$, 438.2; m/z found, 438.9 $[M+H]^+$. Analytical HPLC was obtained on a Agilent 1100 Series using an Inertsil ODS-3 column (3µm, 50 x 3 mm), mobile phase of 5-99% ACN in 0.05% TFA over 1.6 min and then

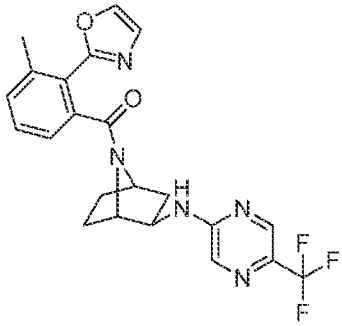
hold at 99% ACN for 0.4 min, at a flow rate of 2.2 mL/min (Temperature = 50 °C). R_t = 1.46 min (major rotamer) at 254 nm.

Example 408: (3-fluoro-2-(pyridin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Prepared analogous to Example 260 substituting 2-(tributylstannyl)oxazole with 2-(tributylstannyl)pyridine. MS (ESI): mass calcd. for $C_{23}H_{19}F_4N_5O$, 457.2; m/z found, 458.2 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$, Compound present as a mixture of rotamers, only major rotamer reported) δ 8.55 (d, *J* = 5.4 Hz, 1H), 8.17 (s, 1H), 7.88 (td, *J* = 7.8, 1.8 Hz, 1H), 7.68 (dd, *J* = 8.0, 3.2 Hz, 1H), 7.59 (s, 1H), 7.43 - 7.38 (m, 1H), 7.37 - 7.31 (m, 1H), 7.20 - 7.14 (m, 2H), 4.78 (t, *J* = 4.9 Hz, 1H), 4.53 - 4.42 (m, 1H), 4.02 (d, *J* = 4.9 Hz, 1H), 2.19 (dd, *J* = 12.9, 8.1 Hz, 1H), 2.11 - 1.86 (series of m, 2H), 1.81 - 1.68 (series of m, 2H), 1.58 - 1.49 (m, 1H).

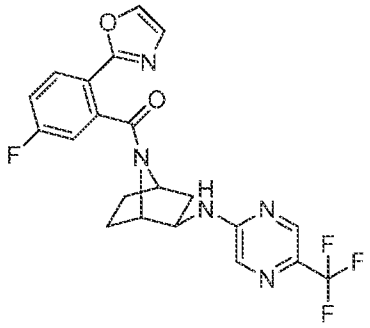
Example 409: (3-methyl-2-(oxazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Prepared analogous to Example 263 substituting 3-(tributylstannyl)pyridazine with 2-(tributylstannyl)oxazole. MS (ESI): mass calcd. for $C_{22}H_{20}F_3N_5O_2$, 443.2; m/z found, 444.2 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$, Compound present as a mixture of rotamers (0.91:0.09), only major rotamer reported) δ 8.14 (s, 1H), 7.88 (d, *J* = 0.9 Hz, 1H), 7.79 (d, *J* = 1.4 Hz, 1H), 7.31 - 7.27 (m, 2H), 7.26 - 7.23 (m, 1H), 7.20 - 7.13 (m, 1H), 4.78 (t, *J* = 4.6 Hz, 1H), 4.33 - 4.26

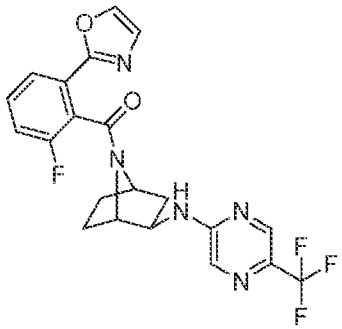
(m, 1H), 3.94 (d, J = 4.9 Hz, 1H), 2.28 (s, 3H), 2.12 (dd, J = 13.0, 8.2 Hz, 1H), 2.06 - 1.88 (series of m, 2H), 1.77 - 1.64 (series of m, 2H), 1.56 - 1.48 (m, 1H).

Example 410: (5-fluoro-2-(oxazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Prepared analogous to Example 238 substituting intermediate A-2 with intermediate A-69. MS (ESI): mass calcd. for $C_{21}H_{17}F_4N_5O_2$, 447.1; m/z found, 448.1 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$, Compound present as a mixture of rotamers (0.65:0.35), only major rotamer reported) δ 8.16 (s, 1H), 7.86 - 7.79 (series of m, 2H), 7.37 - 7.30 (series of m, 2H), 7.19 - 7.09 (m, 1H), 7.04 (dd, J = 8.2, 2.7 Hz, 1H), 4.93 (t, J = 4.4 Hz, 1H), 4.37 - 4.30 (m, 1H), 3.87 - 3.81 (m, 1H), 2.19 (dd, J = 13.1, 8.1 Hz, 1H), 2.05 - 1.68 (series of m, 4H), 1.62 - 1.43 (m, 1H).

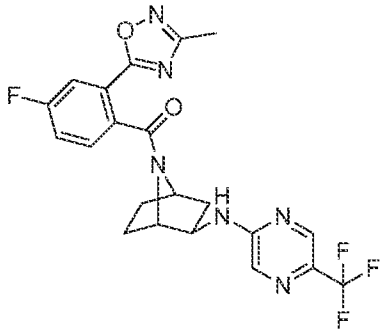
Example 411: (2-fluoro-6-(oxazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Prepared analogous to Example 181 substituting intermediate A-1 with intermediate A-70. MS (ESI): mass calcd. for $C_{21}H_{17}F_4N_5O_2$, 447.1; m/z found, 448.1 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$, Compound present as a mixture of rotamers) δ 8.16 (s, 1H), 7.87 - 7.83 (series of m, 2H), 7.63 (d, J = 7.8 Hz, 1H), 7.47 - 7.40 (m, 1H), 7.36 (d, J = 0.8 Hz, 1H), 7.19 (td, J = 8.6,

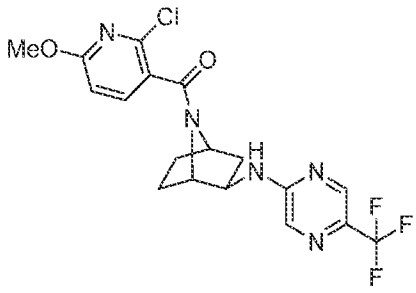
1.1 Hz, 1H), 4.99 (t, *J* = 5.0 Hz, 1H), 4.42 - 4.35 (m, 1H), 3.76 (d, *J* = 5.0 Hz, 1H), 2.21 (dd, *J* = 13.1, 8.0 Hz, 1H), 2.12 - 1.55 (series of m, 5H).

Example 412: (4-fluoro-2-(3-methyl-1,2,4-oxadiazol-5-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Prepared analogous to Example 238 substituting intermediate A-2 with intermediate A-71. MS (ESI): mass calcd. for $C_{21}H_{18}F_4N_6O_2$, 462.1; m/z found, 463.1 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$, Compound present as a mixture of rotamers (0.50:0.50), both rotamers reported) δ 8.32 (s, 0.5H), 8.18 (s, 0.5H), 8.08 (d, *J* = 1.4 Hz, 0.5H), 7.83 (dd, *J* = 8.8, 2.7 Hz, 0.5H), 7.58 (dd, *J* = 8.5, 2.6 Hz, 0.5H), 7.54 (s, 0.5H), 7.52 - 7.37 (m, 1H), 7.32 (td, *J* = 8.1, 2.6 Hz, 0.5H), 7.18 (td, *J* = 8.1, 2.6 Hz, 0.5H), 6.93 (s, 0.5H), 6.17 (d, *J* = 8.3 Hz, 0.5H), 4.88 (t, *J* = 4.5 Hz, 0.5H), 4.80 (d, *J* = 5.3 Hz, 0.5H), 4.39 - 4.21 (m, 1H), 3.91 (t, *J* = 4.7 Hz, 0.5H), 3.84 (d, *J* = 4.4 Hz, 0.5H), 2.50 (two s, 3H), 2.23 - 2.06 (m, 1H), 2.07 - 1.67 (series of m, 4H), 1.64 - 1.46 (series of m, 1H).

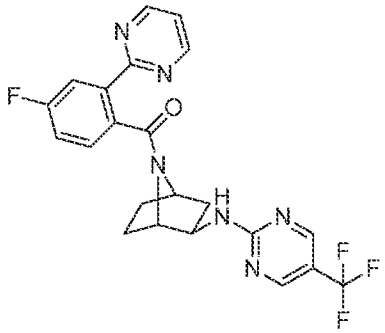
Example 413: (2-chloro-6-methoxypyridin-3-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Prepared analogous to Example 181 substituting intermediate A-1 with intermediate A-65. MS (ESI): mass calcd. for $C_{18}H_{17}ClF_3N_5O_2$, 427.1; m/z found, 427.9 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$, Compound present as a mixture of rotamers) δ 8.35 - 8.12 (m, 1H), 7.98 - 7.89 (m, 1H), 7.71 - 7.48 (m, 1H), 6.84 - 6.35 (m, 1H), 6.29 - 5.68 (m, 1H), 4.92 - 4.73 (m, 1H), 4.30 -

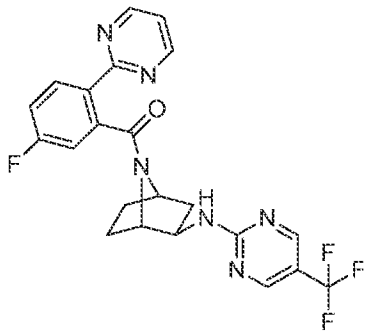
3.73 (series of m, 5H), 2.24 - 2.05 (m, 1H), 2.07 - 1.79 (m, 2H), 1.64 - 1.46 (m, 2H), 1.01 (d, *J* = 6.6 Hz, 1H).

Example 414: (4-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Prepared analogous to Example 269 substituting intermediate A-16 with intermediate A-25. MS (ESI): mass calcd. for $C_{22}H_{18}F_4N_6O$, 458.1; m/z found, 459.2 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$, Compound present as a mixture of rotamers (0.70:0.30), only major rotamer reported) δ 8.85 (d, *J* = 4.9 Hz, 2H), 8.50 (d, *J* = 2.6 Hz, 1H), 8.39 (s, 1H), 7.76 (dd, *J* = 9.5, 2.7 Hz, 1H), 7.35 (dd, *J* = 8.4, 5.4 Hz, 1H), 7.32 (t, *J* = 4.9 Hz, 1H), 7.10 (td, *J* = 8.2, 2.7 Hz, 1H), 4.87 (t, *J* = 4.6 Hz, 1H), 4.48 - 4.35 (m, 1H), 4.04 (d, *J* = 4.5 Hz, 1H), 2.24 (dd, *J* = 12.9, 8.0 Hz, 1H), 1.99 - 1.93 (series of m, 2H), 1.83 - 1.76 (m, 1H), 1.72 - 1.65 (m, 1H), 1.61 - 1.54 (m, 1H).

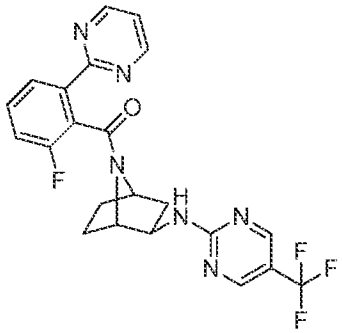
Example 415: (5-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Prepared analogous to Example 269 substituting intermediate A-16 with intermediate A-7. MS (ESI): mass calcd. for $C_{22}H_{18}F_4N_6O$, 458.1; m/z found, 459.1 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$, Compound present as a mixture of rotamers (0.70:0.30), only major rotamer reported) δ 8.82 (d, *J* = 4.9 Hz, 2H), 8.50 (s, 1H), 8.38 (s, 1H), 8.06 (dd, *J* = 8.6, 5.4 Hz, 1H), 7.28 (t, *J* = 4.9 Hz, 1H), 7.21 - 7.15 (m, 1H), 7.04 (dd, *J* = 8.4, 2.6 Hz, 1H), 4.95 - 4.84 (m, 1H),

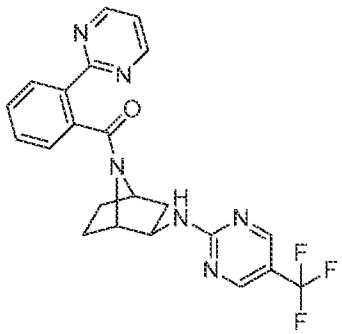
4.48 - 4.28 (m, 1H), 4.11 - 4.05 (m, 1H), 2.24 (dd, *J* = 12.9, 7.9 Hz, 1H), 2.10 - 1.89 (series of m, 2H), 1.82 - 1.63 (series of m, 2H), 1.63 - 1.54 (m, 1H).

Example 416: (2-fluoro-6-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Prepared analogous to Example 269 substituting intermediate A-16 with intermediate A-6. MS (ESI): mass calcd. for $C_{22}H_{18}F_4N_6O$, 458.1; m/z found, 459.2 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$, Compound present as a mixture of rotamers) δ 8.86 (d, *J* = 4.9 Hz, 2H), 8.55 (d, *J* = 9.7 Hz, 1H), 8.40 (s, 1H), 7.82 (d, *J* = 7.9 Hz, 1H), 7.55 - 7.44 (m, 1H), 7.34 (t, *J* = 4.9 Hz, 1H), 7.27 - 7.16 (m, 1H), 4.92 (t, *J* = 4.8 Hz, 1H), 4.52 - 4.41 (m, 1H), 3.99 (d, *J* = 5.2 Hz, 1H), 2.28 (dd, *J* = 12.9, 7.8 Hz, 1H), 2.20 - 2.11 (m, 1H), 2.04 - 1.94 (m, 1H), 1.83 - 1.77 (m, 1H), 1.73 - 1.54 (series of m, 2H).

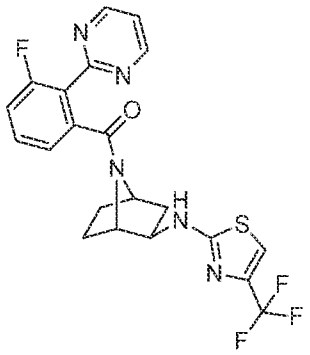
Example 417: (2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Prepared analogous to Example 269 substituting intermediate A-16 with intermediate A-59. MS (ESI): mass calcd. for $C_{22}H_{19}F_3N_6O$, 440.2; m/z found, 441.2 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$, Compound present as a mixture of rotamers (0.74:0.26), only major rotamer reported) δ 8.84 (d, *J* = 4.9 Hz, 2H), 8.50 (s, 1H), 8.38 (s, 1H), 8.03 (dd, *J* = 7.7, 1.3 Hz, 1H), 7.53 - 7.47 (m, 1H), 7.45 - 7.39 (m, 1H), 7.36 (dd, *J* = 7.4, 1.2 Hz, 1H), 7.29 (t, *J* = 4.9 Hz, 1H),

4.88 (t, J = 4.6 Hz, 1H), 4.44 - 4.38 (m, 1H), 4.07 (d, J = 4.5 Hz, 1H), 2.24 (dd, J = 12.9, 7.9 Hz, 1H), 1.99 - 1.96 (m, 1H), 1.84 - 1.76 (m, 1H), 1.73 - 1.65 (series of m, 2H), 1.60 - 1.52 (m, 1H).

Example 418: (3-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((4-(trifluoromethyl)thiazol-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



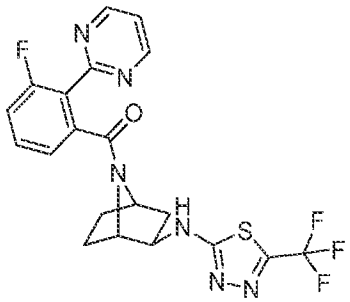
Step A: (1S,2R,4R)-tert-butyl 2-((4-(trifluoromethyl)thiazol-2-yl)amino)-7-azabicyclo[2.2.1]heptane-7-carboxylate. To a solution of intermediate B-5 (107 mg, 0.50 mmol) in ACN (1.7 mL) was added DIPEA (0.22 mL, 1.26 mmol) followed by 2-chloro-4-(trifluoromethyl)thiazole (104 mg, 0.55 mmol). The reaction mixture was heated at 170 °C for 2.5h using microwave. Solvent was evaporated and purification via silica gel chromatography (0-40% EtOAc in hexanes) gave the title compound (37 mg, 20%). MS (ESI): mass calcd. for $C_{15}H_{20}F_3N_3O_2S$, 363.1; m/z found, 364.0 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 6.91 (s, 1H), 5.66 (s, 1H), 4.32 – 4.23 (m, 2H), 3.79 – 3.69 (m, 1H), 2.08 – 2.00 (m, 1H), 1.92 – 1.66 (m, 2H), 1.65 – 1.35 (m, 12H).

Step B: N-((1S,2R,4R)-7-azabicyclo[2.2.1]heptan-2-yl)-4-(trifluoromethyl)thiazol-2-amine. To the title compound of step A (37 mg, 0.10 mmol) in DCM (1 mL) was added 4M HCl in dioxane (0.26 mL). After 16h, the reaction was concentrated, neutralized with 5% Na_2CO_3 (aq) and extracted with DCM (2X). The combined organics were dried (Na_2SO_4) to give the title compound of step B that was used without further purification. MS (ESI): mass calcd. for $C_{10}H_{12}F_3N_3S$, 263.1; m/z found, 264.0 $[M+H]^+$.

Step C: (3-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((4-(trifluoromethyl)thiazol-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone. To the title compound of step B (27 mg, 0.10 mmol) in DCM (1 mL) was added DIPEA (0.04 mL, 0.21 mmol) and intermediate A-2 (25 mg, 0.11 mmol). Then T3P (50% solution in DMF, 0.19 mL, 0.31 mmol) was added dropwise and the reaction heated at 45 °C for 16h. Solvent was evaporated and purification via prep HPLC gave the title compound (16 mg, 34%). MS (ESI): mass calcd. for $C_{21}H_{17}F_4N_5OS$, 463.1; m/z found, 463.9 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.88 (d, J = 4.9 Hz, 2H), 7.45 - 7.40

(m, 1H), 7.38 (t, J = 4.9 Hz, 1H), 7.24 - 7.17 (m, 2H), 6.77 - 6.69 (m, 1H), 4.70 (t, J = 4.9, 1.2 Hz, 1H), 4.22 - 4.16 (m, 2H), 2.16 (dd, J = 13.1, 8.0 Hz, 1H), 2.10 - 2.01 (m, 1H), 1.96 - 1.86 (m, 1H), 1.76 - 1.57 (m, 2H), 1.55 - 1.44 (m, 1H).

Example 419: (3-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)-1,3,4-thiadiazol-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



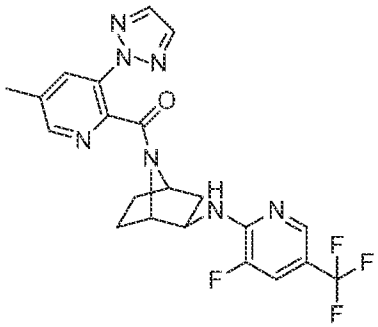
Step A: (1S,2R,4R)-tert-butyl 2-((5-(trifluoromethyl)-1,3,4-thiadiazol-2-yl)amino)-7-azabicyclo[2.2.1]heptane-7-carboxylate. To a solution of intermediate B-5 (71 mg, 0.33 mmol) in ACN (0.85 mL) was added DIPEA (0.14 mL, 0.84 mmol) followed by 2-chloro-5-(trifluoromethyl)-1,3,4-thiadiazole (73 mg, 0.37 mmol). The reaction mixture was heated at 120 °C for 30 minutes using microwave. EtOAc was added and the organic phase was washed with a saturated solution of $NaHCO_3$ followed by a saturated solution of NaCl. The organic phase was dried over $MgSO_4$, filtered and evaporated. Purification via silica gel chromatography (0-40% EtOAc in hexanes) gave the title compound (85 mg, 70%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.82 (s, 1H), 4.38 – 4.22 (m, 2H), 3.96 – 3.82 (m, 1H), 2.11 – 2.00 (m, 1H), 1.92 – 1.79 (m, 1H), 1.79 – 1.66 (m, 2H), 1.43 (s, 11H). MS (ESI): mass calcd. for $C_{14}H_{19}F_3N_4O_2S$, 364.1; m/z found, 365.0 $[M+H]^+$.

Step B: N-((1S,2R,4R)-7-azabicyclo[2.2.1]heptan-2-yl)-5-(trifluoromethyl)-1,3,4-thiadiazol-2-amine. To the title compound of step A (85 mg, 0.23 mmol) in DCM (2.3 mL) was added 4M HCl in dioxane (0.30 mL). After 48h, the reaction was concentrated, neutralized with 5% Na_2CO_3 (aq) and extracted with DCM (2X). The combined organics were dried (Na_2SO_4) to give the title compound of step B that was used without further purification. MS (ESI): mass calcd. for $C_9H_{11}F_3N_4S$, 264.1; m/z found, 265.0 $[M+H]^+$.

Step C: (3-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)-1,3,4-thiadiazol-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone. To the title compound of step B (58 mg, 0.10 mmol) in DCM (2.2 mL) was added DIPEA (0.1 mL, 0.55 mmol) and intermediate A-2 (53 mg, 0.24 mmol). Then T3P (50% solution in DMF, 0.40 mL, 0.66 mmol)

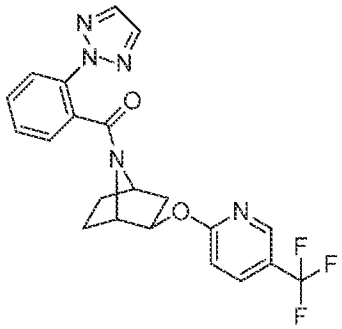
was added dropwise and the reaction heated at 45 °C for 16h. Solvent was evaporated and purification via prep HPLC gave the title compound (63 mg, 62%). MS (ESI): mass calcd. for $C_{20}H_{16}F_4N_6OS$, 464.1; m/z found, 464.9 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.94 (d, J = 9.3 Hz, 1H), 8.87 (d, J = 5.0 Hz, 2H), 7.47 - 7.37 (m, 2H), 7.25 - 7.19 (m, 2H), 4.71 (td, J = 4.8, 1.2 Hz, 1H), 4.33 - 4.18 (m, 2H), 2.17 (dd, J = 13.3, 8.1 Hz, 1H), 2.13 - 2.03 (m, 1H), 1.98 - 1.85 (m, 1H), 1.74 - 1.62 (m, 2H), 1.57 - 1.45 (m, 1H).

Example 420: ((1S,2R,4R)-2-((3-fluoro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(5-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)methanone.



Prepared analogous to Example 382 substituting intermediate A-2 with intermediate A-19. MS (ESI): mass calcd. for $C_{21}H_{19}F_4N_7O$, 461.2; m/z found, 462.2 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.39 (dd, J = 1.9, 0.8 Hz, 1H), 8.12 – 8.08 (m, 2H), 7.86 (s, 2H), 7.26 – 7.22 (m, 1H), 5.77 – 5.70 (m, 1H), 4.97 – 4.91 (m, 1H), 4.38 (td, J = 7.8, 3.0 Hz, 1H), 4.09 – 4.05 (m, 1H), 2.46 (s, 3H), 2.25 (dd, J = 13.0, 7.5 Hz, 1H), 2.13 – 1.97 (m, 2H), 1.88 – 1.80 (m, 1H), 1.66 – 1.60 (m, 2H).

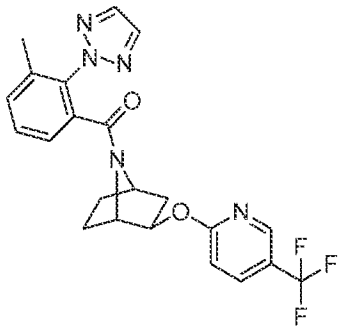
Example 421: (R/S)-(2-(2H-1,2,3-triazol-2-yl)phenyl)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Prepared analogous to Example 433 substituting intermediate A-55 with intermediate A-1. MS (ESI): mass calcd. for $C_{21}H_{18}F_3N_5O_2$, 429.1; m/z found, 429.9 $[M+H]^+$. ^1H NMR (400

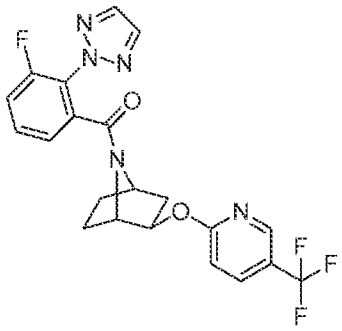
MHz, $CDCl_3$) δ 8.32 - 8.25 (m, 1H), 7.82 - 7.74 (m, 4H), 7.49 - 7.39 (m, 2H), 7.20 (td, *J* = 7.6, 1.2 Hz, 1H), 6.75 (d, *J* = 8.7 Hz, 1H), 4.97 (dd, *J* = 6.6, 2.5 Hz, 1H), 4.88 (t, *J* = 5.0 Hz, 1H), 3.89 (d, *J* = 5.3 Hz, 1H), 2.08 - 1.94 (m, 2H), 1.87 - 1.75 (m, 1H), 1.55 - 1.48 (m, 1H), 1.47 - 1.40 (m, 1H), 1.36 - 1.27 (m, 1H).

Example 422: (R/S)-(3-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Prepared analogous to Example 433 substituting intermediate A-55 with intermediate A-24. MS (ESI): mass calcd. for $C_{22}H_{20}F_3N_5O_2$, 443.2; m/z found, 443.9 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$, Compound present as a mixture of rotamers) δ 8.43 - 8.28 (m, 1H), 7.85 - 7.75 (series of m, 3H), 7.44 - 7.27 (series of m, 2H), 7.18 (t, *J* = 7.6 Hz, 1H), 6.86 - 6.76 (m, 1H), 5.06 - 4.97 (m, 1H), 4.76 - 4.63 (m, 1H), 4.05 - 3.90 (m, 1H), 2.21 - 2.12 (m, 3H), 2.04 - 1.98 (m, 1H), 1.98 - 1.92 (m, 1H), 1.87 - 1.78 (m, 1H), 1.54 - 1.44 (m, 1H), 1.39 - 1.31 (m, 2H).

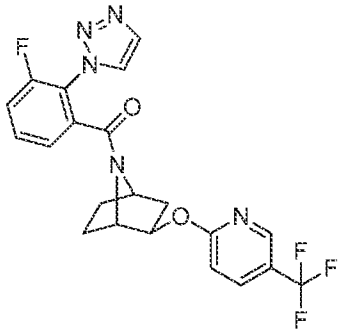
Example 423: (R/S)-(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Prepared analogous to Example 433 substituting intermediate A-55 with intermediate A-16. MS (ESI): mass calcd. for $C_{21}H_{17}F_4N_5O_2$, 447.1; m/z found, 448.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.42 - 8.29 (m, 1H), 7.91 - 7.82 (m, 2H), 7.79 (dd, J = 8.7, 2.5 Hz, 1H), 7.41 -

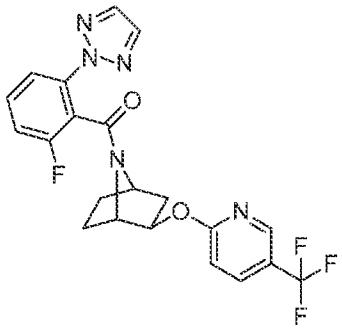
7.19 (m, 3H), 6.84 - 6.75 (m, 1H), 5.07 - 4.96 (m, 1H), 4.82 - 4.68 (m, 1H), 4.03 - 3.86 (m, 1H), 2.08 - 1.91 (m, 2H), 1.77 - 1.47 (m, 2H), 1.44 - 1.31 (m, 2H).

Example 424: (R/S)-(3-fluoro-2-(1H-1,2,3-triazol-1-yl)phenyl)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Prepared analogous to Example 433 substituting intermediate A-55 with 3-fluoro-2-(1H-1,2,3-triazol-1-yl)benzoic acid, obtained during the synthesis of intermediate A-16. MS (ESI): mass calcd. for $C_{21}H_{17}F_4N_5O_2$, 447.1; m/z found, 447.9 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.36 - 8.32 (m, 1H), 7.93 (t, *J* = 1.2 Hz, 1H), 7.84 - 7.79 (m, 2H), 7.41 - 7.27 (m, 3H), 6.88 - 6.84 (m, 1H), 5.04 (dd, *J* = 6.9, 2.3 Hz, 1H), 4.69 (t, *J* = 5.1 Hz, 1H), 4.06 (d, *J* = 5.6 Hz, 1H), 2.12 - 2.01 (m, 1H), 1.99 - 1.90 (m, 1H), 1.87 - 1.78 (m, 1H), 1.71 - 1.59 (m, 1H), 1.41 (d, *J* = 8.4 Hz, 2H).

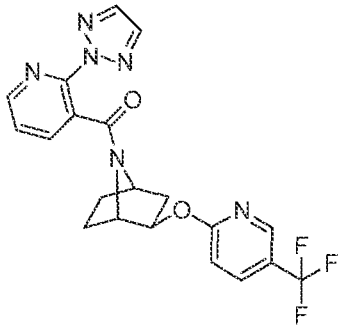
Example 425: (R/S)-(2-fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Prepared analogous to Example 433 substituting intermediate A-55 with intermediate A-11. MS (ESI): mass calcd. for $C_{21}H_{17}F_4N_5O_2$, 447.1; m/z found, 447.9 [M+H]+. 1H NMR (500 MHz, $CDCl_3$, Compound present as a mixture of rotamers) δ 8.47 - 8.24 (m, 1H), 7.86 - 7.66 (series of m, 4H), 7.53 - 7.34 (m, 1H), 7.20 - 6.94 (m, 1H), 6.92 - 6.79 (m, 1H), 5.19 - 4.90

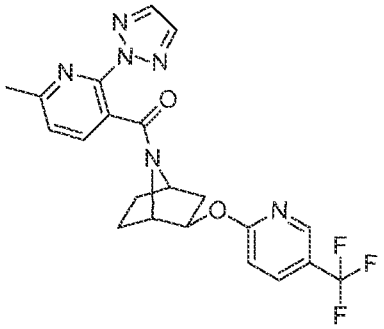
(series of m, 2H), 3.95 - 3.77 (m, 1H), 2.12 - 1.97 (series of m, 2H), 1.96 - 1.56 (series of m, 2H), 1.48 - 1.26 (series of m, 2H).

Example 426: (R/S)-(2-(2H-1,2,3-triazol-2-yl)pyridin-3-yl)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



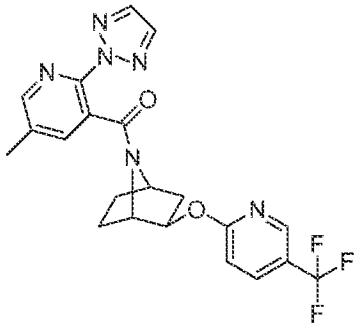
Prepared analogous to Example 433 substituting intermediate A-55 with intermediate A-61. MS (ESI): mass calcd. for $C_{20}H_{17}F_3N_6O_2$, 430.1; m/z found, 430.9 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.55 (dd, J = 4.8, 1.8 Hz, 1H), 8.34 - 8.25 (m, 1H), 7.89 - 7.84 (m, 3H), 7.78 (dd, J = 8.8, 2.5 Hz, 1H), 7.21 (dd, J = 7.6, 4.8 Hz, 1H), 6.73 (d, J = 8.7 Hz, 1H), 4.99 (dd, J = 6.8, 2.4 Hz, 1H), 4.91 (t, J = 4.8 Hz, 1H), 3.88 (d, J = 5.3 Hz, 1H), 2.08 (d, J = 6.9 Hz, 1H), 2.04 - 2.00 (m, 1H), 1.93 - 1.83 (m, 1H), 1.57 - 1.44 (m, 2H), 1.39 - 1.31 (m, 1H).

Example 427: (R/S)-(6-methyl-2-(2H-1,2,3-triazol-2-yl)pyridin-3-yl)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



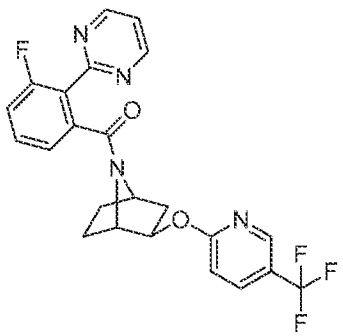
Prepared analogous to Example 433 substituting intermediate A-55 with intermediate A-3. MS (ESI): mass calcd. for $C_{21}H_{19}F_3N_6O_2$, 444.2; m/z found, 444.9 $[M+H]^+$. Analytical HPLC was obtained on a Agilent 1100 Series using an Inertsil ODS-3 column (3µm, 50 x 3 mm), mobile phase of 5-99% ACN in 0.05% TFA over 1.6 min and then hold at 99% ACN for 0.4 min, at a flow rate of 2.2 mL/min (Temperature = 50 °C). R_t = 1.29 min (major rotamer) at 254 nm.

Example 428: (R/S)-(5-methyl-2-(2H-1,2,3-triazol-2-yl)pyridin-3-yl)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



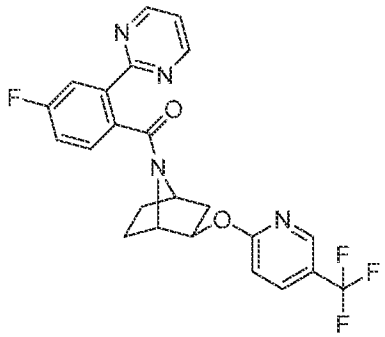
Prepared analogous to Example 433 substituting intermediate A-55 with intermediate A-60. MS (ESI): mass calcd. for $C_{21}H_{19}F_3N_6O_2$, 444.2; m/z found, 444.9 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.35 - 8.32 (m, 1H), 8.32 - 8.30 (m, 1H), 7.85 (s, 2H), 7.83 - 7.77 (m, 1H), 7.63 - 7.57 (m, 1H), 6.74 (d, J = 8.6 Hz, 1H), 4.96 (dd, J = 6.3, 3.0 Hz, 1H), 4.90 (t, J = 4.5 Hz, 1H), 3.91 (d, J = 5.3 Hz, 1H), 2.21 (s, 3H), 2.13 - 1.94 (m, 2H), 1.91 - 1.76 (m, 1H), 1.55 - 1.27 (m, 3H).

Example 429: (R/S)-(3-fluoro-2-(pyrimidin-2-yl)phenyl)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



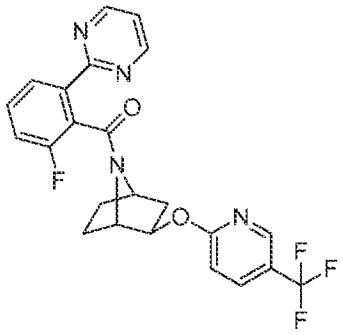
Prepared analogous to Example 433 substituting intermediate A-55 with intermediate A-2. MS (ESI): mass calcd. for $C_{23}H_{18}F_4N_4O_2$, 458.1; m/z found, 458.9 [M+H]. Analytical HPLC was obtained on a Agilent 1100 Series using an Inertsil ODS-3 column (3μm, 50 x 3 mm), mobile phase of 5-99% ACN in 0.05% TFA over 1.6 min and then hold at 99% ACN for 0.4 min, at a flow rate of 2.2 mL/min (Temperature = 50 °C). R_t = 1.37 min (major rotamer) at 254 nm.

Example 430: (R/S)-(4-fluoro-2-(pyrimidin-2-yl)phenyl)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



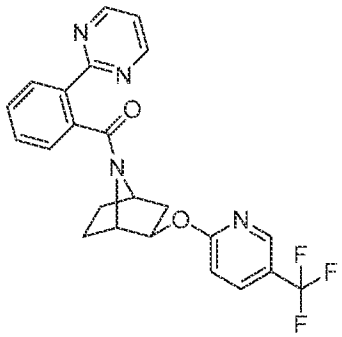
Prepared analogous to Example 433 substituting intermediate A-55 with intermediate A-25. MS (ESI): mass calcd. for $C_{23}H_{18}F_4N_4O_2$, 458.1; m/z found, 458.9 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$, Compound present as a mixture of rotamers, major rotamer reported) δ 8.76 - 8.74 (m, 2H), 8.34 - 8.28 (m, 1H), 7.85 (dd, J = 9.8, 2.6 Hz, 1H), 7.80 - 7.75 (m, 1H), 7.44 - 7.40 (m, 1H), 7.21 (t, J = 4.8 Hz, 1H), 6.95 (td, J = 8.2, 2.7 Hz, 1H), 6.75 (d, J = 8.7 Hz, 1H), 5.00 (dd, J = 6.7, 2.4 Hz, 1H), 4.88 (t, J = 4.8 Hz, 1H), 3.95 (d, J = 5.5 Hz, 1H), 2.08 - 1.99 (m, 1H), 1.88 - 1.81 (m, 1H), 1.68 - 1.58 (m, 1H), 1.53 - 1.45 (m, 1H), 1.41 - 1.32 (m, 1H), 0.86 - 0.81 (m, 1H).

Example 431: (R/S)-(2-fluoro-6-(pyrimidin-2-yl)phenyl)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



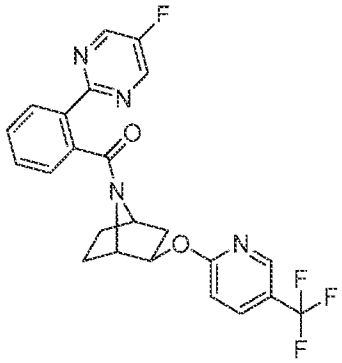
Prepared analogous to Example 433 substituting intermediate A-55 with intermediate A-6. MS (ESI): mass calcd. for $C_{23}H_{18}F_4N_4O_2$, 458.1; m/z found, 458.9 $[M+H]^+$. Analytical HPLC was obtained on a Agilent 1100 Series using an Inertsil ODS-3 column (3µm, 50 x 3 mm), mobile phase of 5-99% ACN in 0.05% TFA over 1.6 min and then hold at 99% ACN for 0.4 min, at a flow rate of 2.2 mL/min (Temperature = 50 °C). R_t = 1.40 min (major rotamer) at 254 nm.

Example 432: (R/S)-(2-(pyrimidin-2-yl)phenyl)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Prepared analogous to Example 433 substituting intermediate A-55 with intermediate A-59. MS (ESI): mass calcd. for $C_{23}H_{19}F_3N_4O_2$, 440.1; m/z found, 441.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) d 8.80 - 8.71 (m, 2H), 8.43 - 8.27 (m, 1H), 8.21 - 8.09 (m, 1H), 7.83 - 7.74 (m, 1H), 7.57 - 7.37 (m, 2H), 7.28 - 7.13 (m, 2H), 6.90 - 6.72 (m, 1H), 5.12 - 4.86 (m, 2H), 4.00 - 3.83 (m, 1H), 2.14 - 1.77 (m, 3H), 1.74 - 1.53 (m, 1H), 1.53 - 1.21 (m, 2H).

Example 433: (R/S)-(2-(5-fluoropyrimidin-2-yl)phenyl)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



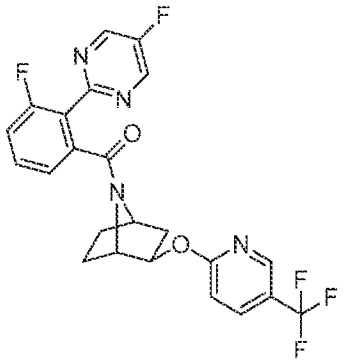
Step A. (R/S)-*tert*-Butyl 2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptane-7-carboxylate. To a solution of intermediate B-11 (1.35 g, 6.33 mmol) and 2-chloro-5-(trifluoromethyl)pyridine (1.35 g, 7.44 mmol) in DMF (20 mL) at rt was added NaH (310 mg, 7.75 mmol) and the mixture stirred at rt overnight. The reaction was diluted with water (200 mL) and extracted with EtOAc (3x50 mL). The combined organics were dried over Na_2SO_4, filtered and the solvent removed. Purification via silica gel chromatography (80g redisep, 0-100 % EtOAc in hexanes) provided 1.68 g of the title compound as a waxy solid. ^1H NMR (400 MHz, $CDCl_3$) δ 8.42 (s, 1H), 7.76 (dd, J = 8.8, 2.6 Hz, 1H), 6.77 (d, J = 8.7 Hz, 1H),

5.03 (dd, J = 6.9, 2.6 Hz, 1H), 4.45 - 4.24 (m, 2H), 2.02 - 1.95 (m, 1H), 1.95 - 1.67 (m, 3H), 1.50 - 1.31 (m, 11H).

Step B. (R/S)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptane. To a solution of (R/S)-*tert*-Butyl 2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptane-7-carboxylate from step A (1.35g, 3.77 mmol) in DCM (20 mL) was added TFA (5 mL). This solution was stirred at rt for ~4h. The solvent was the removed and the residue was then partitioned between 2M Na_2CO_3 (20 mL) and DCM (20 mL). The layers were separated and the aqueous layer was extracted with DCM (2x20 mL). The combined organics were dried over Na_2SO_4, filtered and the solvent removed to reveal 0.98g of the title compound. The material was utilized as is. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.42 (dt, J = 2.0, 1.1 Hz, 1H), 7.75 (dd, J = 8.7, 2.5 Hz, 1H), 6.78 (d, J = 8.7 Hz, 1H), 5.05 (dd, J = 6.7, 2.1 Hz, 1H), 3.73 (q, J = 4.9 Hz, 2H), 2.01 (dd, J = 13.3, 6.7 Hz, 1H), 1.96 - 1.88 (m, 1H), 1.74 - 1.55 (m, 3H), 1.40 - 1.22 (m, 2H).

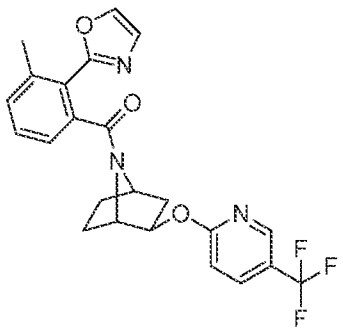
Step C. (R/S)-(2-(5-fluoropyrimidin-2-yl)phenyl)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone. To a 20 mL screw cap vial were added intermediate A-55 (60 mg, 0.27 mmol), (R/S)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptane from step B (56 mg, 0.217 mmol), HOBt (40mg, 0.29 mmol), and EDCI (75 mg, 0.39 mmol). DMF (2 mL) and TEA (50 µL) were then added and vial capped and stirred at rt. overnight. The resulting reddish mixture was diluted with water (25 mL) and extracted with EtOAc (3x10 mL) and the organic layers combined and the solvent removed. Purification via silica gel chromatography (0-100 % EtOAc in hexanes) provided 80.4 mg of the title compound. ^{1}H NMR exhibits a mixture of rotamers. MS (ESI): mass calcd. for $C_{23}H_{18}F_4N_4O_2$, 458.1; m/z found, 459.2 $[M+H]^+$. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.65 - 8.56 (m, 2H), 8.45 - 8.28 (m, 1H), 8.15 - 8.03 (m, 1H), 7.85 - 7.75 (m, 1H), 7.56 - 7.37 (m, 2.5H), 7.25 - 7.22 (m, 0.5H), 6.89 - 6.75 (m, 1H), 5.13 - 4.99 (m, 1H), 4.97 - 4.85 (m, 1H), 4.03 - 3.84 (m, 1H), 2.15 - 1.93 (m, 2H), 1.92 - 1.66 (m, 2H), 1.55 - 1.21 (m, 2H).

Example 434: (R/S)- (3-fluoro-2-(5-fluoropyrimidin-2-yl)phenyl)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



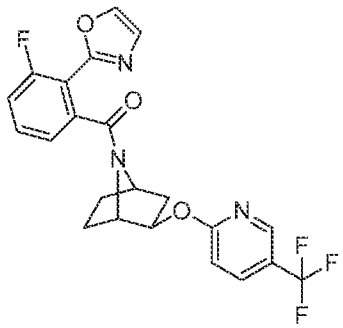
Prepared analogous to Example 433 substituting intermediate A-55 with intermediate A-57. MS (ESI): mass calcd. for $C_{23}H_{17}F_5N_4O_2$, 476.1; m/z found, 476.9 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$, Compound present as a mixture of rotamers, major rotamer reported) δ 8.66 (s, 2H), 8.38 - 8.32 (m, 1H), 7.80 (dt, *J* = 8.8, 2.6 Hz, 1H), 7.33 - 7.27 (m, 1H), 7.25 - 7.19 (m, 1H), 7.18 - 7.11 (m, 1H), 6.84 (d, *J* = 8.7 Hz, 1H), 5.09 - 4.98 (m, 1H), 4.76 (d, *J* = 5.4 Hz, 1H), 4.72 (t, *J* = 4.4 Hz, 1H), 4.12 (d, *J* = 5.5 Hz, 1H), 3.97 (t, *J* = 4.7 Hz, 1H), 2.11 - 1.32 (m, 4H).

Example 435: (R/S)-(3-methyl-2-(oxazol-2-yl)phenyl)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



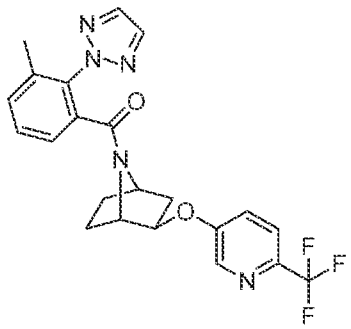
Prepared analogous to Example 433 substituting intermediate A-55 with intermediate A-31. MS (ESI): mass calcd. for $C_{23}H_{20}F_3N_3O_3$, 443.1; m/z found, 443.9 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$, Compound present as a mixture of rotamers, major rotamer reported) δ 8.32 - 8.26 (m, 1H), 7.78 - 7.73 (m, 2H), 7.39 - 7.19 (m, 3H), 7.18 (d, *J* = 7.6 Hz, 1H), 6.76 (d, *J* = 8.7 Hz, 1H), 4.98 (dd, *J* = 6.6, 2.6 Hz, 1H), 4.76 (t, *J* = 4.5 Hz, 1H), 3.93 (d, *J* = 5.0 Hz, 1H), 2.39 (s, 3H), 2.07 - 1.28 (m, 6H).

Example 436: (R/S)-(3-fluoro-2-(oxazol-2-yl)phenyl)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



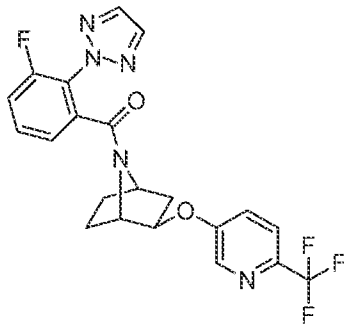
Prepared analogous to Example 433 substituting intermediate A-55 with intermediate A-68. MS (ESI): mass calcd. for $C_{22}H_{17}F_4N_3O_3$, 447.1; m/z found, 448.9 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$, Compound present as a mixture of rotamers (0.69:0.31), major rotamer reported) δ 8.34 - 8.27 (m, 1H), 7.78 - 7.74 (m, 2H), 7.30 - 7.22 (m, 3H), 7.18 - 7.09 (m, 1H), 6.73 (d, *J* = 8.6 Hz, 1H), 4.98 (dd, *J* = 6.8, 2.5 Hz, 1H), 4.85 (t, *J* = 4.7 Hz, 1H), 3.89 (d, *J* = 5.6 Hz, 1H), 2.11 - 1.20 (m, 6H).

Example 437: (R/S)-(3-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)-2-((6-(trifluoromethyl)pyridin-3-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



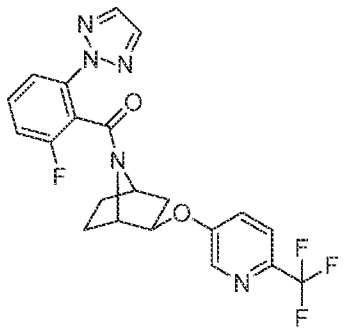
Prepared analogous to Example 433 substituting 2-chloro-5-(trifluoromethyl)pyridine with 5-fluoro-2-(trifluoromethyl)pyridine and intermediate A-55 with intermediate A-24. MS (ESI): mass calcd. for $C_{22}H_{20}F_3N_5O_2$, 443.2; m/z found, 444.9 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$, Compound present as a mixture of rotamers) δ 8.33 - 8.25 (m, 1H), 7.85 - 7.72 (m, 2H), 7.64 - 7.54 (m, 1H), 7.44 - 7.27 (series of m, 3H), 7.23 - 7.12 (m, 1H), 4.82 - 4.66 (m, 1H), 4.44 - 4.35 (m, 1H), 4.06 - 3.95 (m, 1H), 2.16 (s, 3H), 2.06 - 1.92 (series of m, 2H), 1.91 - 1.75 (m, 1H), 1.56 - 1.22 (series of m, 3H).

Example 438: (R/S)-(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)-2-((6-(trifluoromethyl)pyridin-3-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



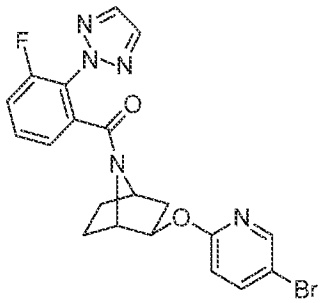
Prepared analogous to Example 437 substituting intermediate A-24 with intermediate A-16. MS (ESI): mass calcd. for $C_{21}H_{17}F_4N_5O_2$, 447.1; m/z found, 447.9 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$, Compound present as a mixture of rotamers) δ 8.33 - 8.23 (m, 1H), 7.89 - 7.78 (m, 2H), 7.66 - 7.55 (m, 1H), 7.42 - 7.27 (series of m, 3H), 7.25 - 7.09 (m, 1H), 4.84 - 4.71 (m, 1H), 4.46 - 4.37 (m, 1H), 3.98 (d, J = 5.5 Hz, 1H), 2.09 - 1.56 (series of m, 4H), 1.48 - 1.26 (series of m, 2H).

Example 439: (R/S)- (2-fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl)-2-((6-(trifluoromethyl)pyridin-3-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Prepared analogous to Example 437 substituting intermediate A-24 with intermediate A-11. MS (ESI): mass calcd. for $C_{21}H_{17}F_4N_5O_2$, 447.1; m/z found, 448.9 $[M+H]^+$. Analytical HPLC was obtained on a Agilent 1100 Series using a XBridge C18 column (5µm, 100 x 4.6mm), mobile phase of 10-100% ACN in 20 mM NH_4OH over 8 min and then hold at 100% ACN for 3 min, at a flow rate of 1 mL/min (Temperature = 30 °C). R_t = 1.29 min (major rotamer) at 254 nm.

Example 440: (R/S)-2-((5-bromopyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone.



Step A: (R/S)-Benzyl 7-azabicyclo[2.2.1]hept-5-ene-7-carboxylate. To a solution of (R/S)-benzyl 2-bromo-7-azabicyclo[2.2.1]heptane-7-carboxylate (2.96g, 9.5 mmol; *J. Org. Chem.* **2007**, *72*, 8656) in THF (65 mL) under N_2 was added 16.5 mL of tBuOK 1M solution in THF. This mixture was stirred at rt. and slowly a suspension forms (~2h) and reaction monitored by LC/MS. Upon completion the mixture was diluted with saturated NH_4Cl (20 mL) solution and water then extracted with EtOAc (3x50 mL). The combined organics were washed with brine and dried over Na_2SO_4 then solvent concentrated to give 1.34g the title compound that was utilized without purification. MS (ESI) mass calcd. for: $C_{14}H_{15}NO_2$, 229.1; m/z found 230.1 [M+H]+

Step B: (R/S)-Benzyl 2-hydroxy-7-azabicyclo[2.2.1]heptane-7-carboxylate. To a solution of (R/S)-Benzyl 7-azabicyclo[2.2.1]hept-5-ene-7-carboxylate (1 g, 4.36 mmol) from step A in THF (25 mL), cooled to 0 °C, was added 1M BH_3 in THF (9.6 mL) drop-wise and the solution was allowed to warm to rt. After 3 h the reaction mixture was cooled in an ice bath and the excess borane quenched with water (2.38 mL), followed by addition of 4M NaOH (2.38 mL), and the drop-wise addition of H_2O_2 (50% by weight, 2.38 mL). The reaction was then removed from the ice bath and warmed to 40 °C for 2 h. The mixture was then cooled to rt. and solid K_2CO_3 (1.0 g) added. THF was removed under vacuum and the reaction diluted with water (100 mL) and extracted with DCM (3X). The combined organics were washed with water, dried with Na_2SO_4, filtered and concentrated. Purification via silica gel chromatography (0-3 % 2M NH_3 in MeOH/DCM) provided 0.9g of the title compound. MS (ESI) mass calcd. for : $C_{14}H_{17}NO_3$, 247.1; m/z found 248.1 $[M+H]^+$ ^1H NMR (400 MHz, $CDCl_3$) δ 7.46 - 7.18 (m, 5H), 5.09 (s, 2H), 4.31 (t, J = 4.7 Hz, 1H), 4.19 (d, J = 5.1 Hz, 1H), 3.86 (ddd, J = 6.7, 4.6, 1.8 Hz, 1H), 1.78 (dd, J = 13.1, 6.8 Hz, 1H), 1.72 - 1.54 (m, 3H), 1.22 (dt, J = 10.2, 2.4 Hz, 2H).

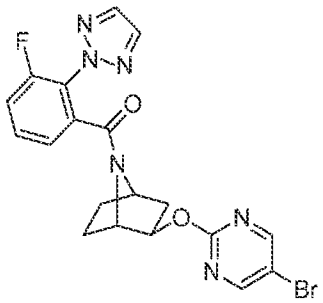
Step C: (R/S)-7-azabicyclo[2.2.1]heptan-2-ol. A solution of (R/S)-benzyl 2-hydroxy-7-azabicyclo[2.2.1]heptane-7-carboxylate (504 mg, 2.038 mmol) from step B in MeOH (20 mL)

was charged with 10% Pd/C (217 mg, 0.204 mmol) and then stirred at rt under an atmosphere of hydrogen. Upon completion the reaction was filtered through a bed of celite and concentrated to give 180 mg of the title compound that was utilized without purification. MS (ESI) mass calcd. for : $C_6H_{11}NO$, 113; m/z found 114.10 $[M+H]^+$

Step D. (3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)((R/S)-2-hydroxy-7-azabicyclo[2.2.1]heptan-7-yl)methanone. To a 20 mL screw cap vial was added intermediate A-16 (400 mg, 1.9 mmol), (R/S)-7-azabicyclo[2.2.1]heptan-2-ol from step C (198 mg, 1.75 mmol), HOBt (425mg, 3.14 mmol), and EDCI (600 mg, 3.13 mmol). DMF (10 mL) and TEA (0.7 mL) were then added and the vial was capped and stirred at rt overnight. The resulting mixture was diluted with water (100 mL) and extracted with EtOAc (3x20 mL) and the organic layers combined and the solvent removed. Purification via silica gel chromatography (40g redisep, 0-100 % EtOAc in hexanes) provided 160 mg of the title compound as a white solid. MS (ESI) mass calcd. for : $C_{15}H_{15}FN_4O_2$, 302.3; m/z found 303.1 $[M+H]^+$.

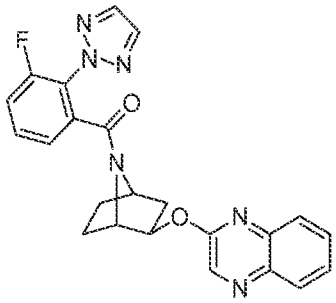
Step E. (R/S)-2-((5-bromopyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone. To a solution of (3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)((R/S)-2-hydroxy-7-azabicyclo[2.2.1]heptan-7-yl)methanone from step D (26.7 mg, 0.08 mmol) and 5-bromo-2-fluoropyridine in DMF (2 mL) at rt was added NaH (8 mg, 0.2 mmol) in a single portion. The mixture was stirred overnight then diluted with water (20 mL) and extracted with EtOAc (3x10 mL). The organic layers were combined and the solvent removed. Purification via silica gel chromatography (0-100 % EtOAc in hexanes) provided 35.7 mg of the title compound as a light tan solid. MS (ESI): mass calcd. for $C_{20}H_{17}BrFN_5O_2$, 457.1; m/z found, 458.0 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) d 8.17 - 8.05 (m, 1H), 7.89 - 7.78 (m, 2H), 7.65 (dd, J = 8.7, 2.6 Hz, 1H), 7.39 - 7.20 (m, 3H), 6.66 - 6.58 (m, 1H), 4.95 - 4.86 (m, 1H), 4.79 - 4.66 (m, 1H), 3.98 - 3.85 (m, 1H), 2.03 - 1.89 (m, 2H), 1.73 - 1.45 (m, 2H), 1.41 - 1.29 (m, 2H).

Example 441: (R/S)-2-((5-bromopyrimidin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone.



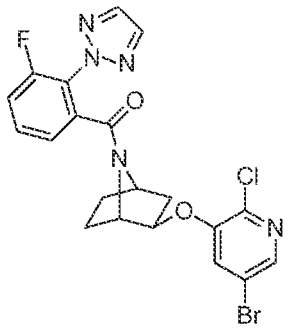
Prepared analogous to Example 440 substituting 5-bromo-2-fluoropyridine with 5-bromo-2-chloropyrimidine. MS (ESI): mass calcd. for $C_{19}H_{16}BrFN_6O_2$, 458.1; m/z found, 459.0 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.54 - 8.47 (m, 2H), 7.91 - 7.83 (m, 2H), 7.49 - 7.45 (m, 1H), 7.39 - 7.31 (m, 1H), 7.26 - 7.20 (m, 1H), 4.89 - 4.81 (m, 1H), 4.74 - 4.70 (m, 1H), 4.01 - 3.89 (m, 1H), 2.05 - 2.00 (m, 1H), 2.00 - 1.69 (m, 3H), 1.46 - 1.28 (m, 2H).

Example 442: (R/S)-(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)-2-(quinoxalin-2-yloxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



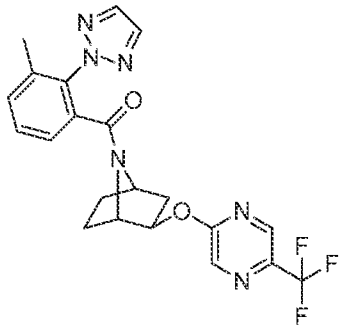
Prepared analogous to Example 440 substituting 5-bromo-2-fluoropyridine with 2-chloroquinoxaline. MS (ESI): mass calcd. for $C_{23}H_{19}FN_6O_2$, 430.2; m/z found, 431.1 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.47 - 8.40 (m, 1H), 8.07 - 7.99 (m, 1H), 7.91 - 7.82 (m, 2H), 7.81 - 7.72 (m, 1H), 7.70 - 7.63 (m, 1H), 7.61 - 7.55 (m, 1H), 7.42 - 7.33 (m, 1H), 7.33 - 7.27 (m, 1H), 7.19 - 7.11 (m, 1H), 5.21 - 5.12 (m, 1H), 4.94 - 4.73 (m, 1H), 4.08 - 3.93 (m, 1H), 2.15 - 2.01 (m, 2H), 1.78 - 1.53 (m, 2H), 1.49 - 1.35 (m, 2H).

Example 443: (R/S)-2-((5-bromo-2-chloropyridin-3-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone.



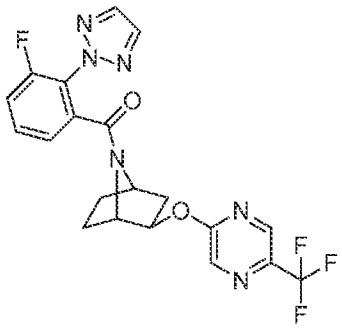
Prepared analogous to Example 440 substituting 5-bromo-2-fluoropyridine with 5-bromo-2-chloro-3-fluoropyridine. MS (ESI): mass calcd. for $C_{20}H_{16}BrClFN_5O_2$, 491.0; m/z found, 491.8 $[M+H]^+$. 1H NMR (400 MHz, $CDCl_3$, Compound present as a mixture of rotamers) δ 8.10 (d, J = 2.0 Hz, 1H), 7.86 (s, 2H), 7.67 (dt, J = 7.7, 1.2 Hz, 1H), 7.48 - 7.39 (m, 1H), 7.39 - 7.28 (m, 1H), 7.10 (d, J = 2.0 Hz, 1H), 4.84 - 4.76 (m, 1H), 4.41 - 4.31 (m, 1H), 4.17 - 4.08 (m, 1H), 2.14 - 2.07 (m, 1H), 2.04 - 1.79 (m, 2H), 1.77 - 1.61 (m, 1H), 1.48 - 1.29 (m, 2H).

Example 444: (R/S)-(3-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)-2-((5-(trifluoromethyl)pyrazin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Prepared analogous to Example 445 substituting intermediate A-16 with intermediate A-24. MS (ESI): mass calcd. for $C_{21}H_{19}F_3N_6O_2$, 444.2; m/z found, 444.9 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$, Compound present as a mixture of rotamers) δ 8.45 - 8.32 (m, 1H), 8.30 - 8.19 (m, 1H), 7.86 - 7.76 (m, 2H), 7.47 - 7.17 (series of m, 3H), 5.04 - 4.94 (series of m, 1H), 4.79 - 4.67 (series of m, 1H), 4.04 - 3.93 (m, 1H), 2.16 (two s, 3H), 2.07 - 1.96 (series of m, 1H), 1.90 - 1.76 (series of m, 2H), 1.55 - 1.30 (series of m, 3H).

Example 445: (R/S)-(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((5-(trifluoromethyl)pyrazin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



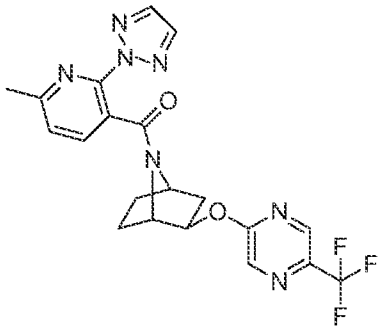
Step A: (R/S)-tert-butyl 2-((5-(trifluoromethyl)pyrazin-2-yl)oxy)-7-azabicyclo[2.2.1]heptane-7-carboxylate. To intermediate B-11 (43 mg, 0.203 mol) in DMF (5 mL) was added NaH (11 mg, 0.26 mmol, 60% dispersion in mineral oil) in one portion, and the reaction mixture was heated at 80 °C for 5 minutes. Then, 2-chloro-5-(trifluoromethyl)pyrazine (59 mg, 0.325 mmol) was added. After heating at 80 °C overnight, water was added and the mixture extracted with DCM (3X). The combined organics were dried (Na_2SO_4) and concentrated. Purification via silica gel chromatography (0-50% EtOAc in hexanes) gave the title compound (30 mg, 41%). MS (ESI) mass calcd. for $C_{16}H_{20}F_3N_3O_3$, 359.2; m/z found 304.1 $[M+2H-t\text{Bu}]^+$.

Step B: (R/S)-2-((5-(trifluoromethyl)pyrazin-2-yl)oxy)-7-azabicyclo[2.2.1]heptane. To the title compound of step A (30 mg, 0.106 mmol) in DCM (2 mL) was added 2M HCl in Et_2O (2 mL), and the reaction mixture was stirred at room temperature for 3 h. The reaction mixture was concentrated and placed under high vacuum for 1 h to give the title compound of step B. MS (ESI) mass calcd. for $C_{11}H_{12}F_3N_3O$, 259.1; m/z found 260.1 $[M+H]^+$.

Step C: (R/S)-(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)(-2-((5-(trifluoromethyl)pyrazin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone. To the title compound of step B (30 mg, 0.101 mmol) in DCM (5 mL) was added intermediate A-16 (23 mg, 0.112 mmol), HOBt (23 mg, 0.168 mmol), EDCI (32 mg, 0.168 mmol) and DIPEA (43 µL, 0.252 mmol). After stirring at room temperature for 2 h, saturated $NaHCO_3$ (aq.) was added and the mixture was extracted with DCM (3X). The combined organics were dried (Na_2SO_4), filtered and concentrated. Purification via silica gel chromatography (0-100 % EtOAc in hexanes) gave the title compound (29 mg, 64 %). MS (ESI): mass calcd. for $C_{20}H_{16}F_4N_6O_2$, 448.1; m/z found, 448.9 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$, Compound present as a mixture of rotamers) δ 8.48 - 8.21 (series of m, 2H), 7.95 - 7.78 (m, 2H), 7.59 - 7.18 (series of m, 3H), 5.09 - 4.95 (m, 1H), 4.85 - 4.71 (m, 1H), 3.96 (d, J =

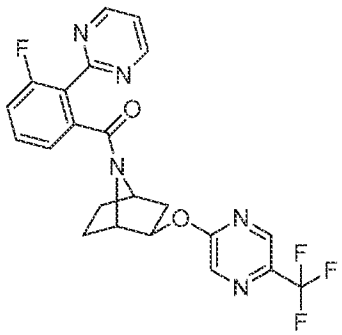
5.2 Hz, 1H), 2.11 - 1.94 (series of m, 2H), 1.90 - 1.61 (series of m, 1H), 1.56 - 1.47 (series of m, 1H), 1.43 - 1.29 (series of m, 2H).

Example 446: (R/S)-(6-methyl-2-(2H-1,2,3-triazol-2-yl)pyridin-3-yl)(2-((5-(trifluoromethyl)pyrazin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



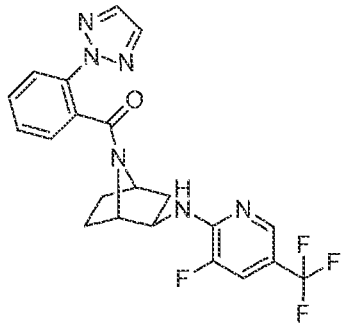
Prepared analogous to Example 445 substituting intermediate A-16 with intermediate A-3. MS (ESI): mass calcd. for $C_{20}H_{18}F_3N_7O_2$, 445.1; m/z found, 445.9 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$, Compound present as a mixture of rotamers) δ 8.31 (series of three s, 2H), 7.93 - 7.83 (m, 2H), 7.83 - 7.70 (m, 1H), 7.36 - 7.04 (m, 1H), 5.10 - 4.86 (series of m, 2H), 3.91 - 3.78 (m, 1H), 2.65 (two s, 3H), 2.14 - 1.65 (series of m, 3H), 1.54 - 1.27 (series of m, 3H).

Example 447: (R/S)-(3-fluoro-2-(pyrimidin-2-yl)phenyl)(2-((5-(trifluoromethyl)pyrazin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



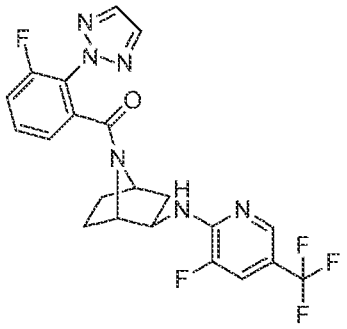
Prepared analogous to Example 445 substituting intermediate A-16 with intermediate A-2. MS (ESI): mass calcd. for $C_{22}H_{17}F_4N_5O_2$, 459.1; m/z found, 459.9 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$, Compound present as a mixture of rotamers) δ 8.85 - 8.79 (m, 2H), 8.49 - 8.31 (m, 1H), 8.30 - 8.17 (m, 1H), 7.53 - 7.27 (series of m, 3H), 7.26 - 7.11 (m, 1H), 5.06 - 4.97 (m, 1H), 4.83 - 4.69 (m, 1H), 4.10 - 4.01 (m, 1H), 2.06 - 2.00 (m, 1H), 1.94 - 1.71 (m, 1H), 1.69 - 1.31 (series of m, 4H).

Example 448: (2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((3-fluoro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



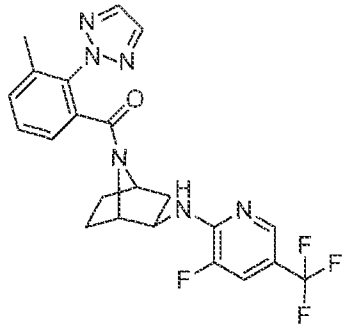
Prepared analogous to Example 382 substituting intermediate A-2 with intermediate A-1. MS (ESI): mass calcd. for $C_{21}H_{18}F_4N_6O$, 446.1; m/z found, 447.2 $[M+H]^+$. Agilent 1100 Series using an Inertsil ODS-3 column (3μm, 50 x 3 mm), mobile phase of 5-99% ACN in 0.05% TFA over 1.6 min and then hold at 99% ACN for 0.4 min, at a flow rate of 2.2 mL/min (Temperature = 50 °C). R_t = 1.39 min at 254 nm.

Example 449: (3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((3-fluoro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



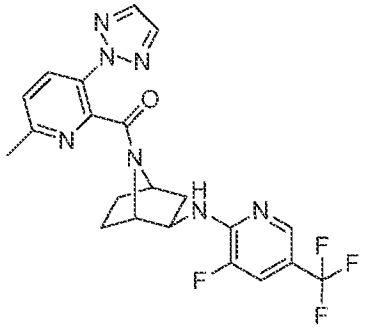
Prepared analogous to Example 382 substituting intermediate A-2 with intermediate A-16. MS (ESI): mass calcd. for $C_{21}H_{17}F_5N_6O$, 464.1; m/z found, 465.2 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.15 (s, 0.4H), 8.06 (s, 0.6H), 7.91 (s, 2H), 7.57 – 7.48 (m, 0.4H), 7.43 – 7.12 (m, 3.6H), 6.48 (s, 0.6H), 5.12 – 5.04 (m, 0.4H), 4.78 (t, J = 4.5 Hz, 0.6H), 4.62 (d, J = 5.2 Hz, 0.4H), 4.40 (s, 0.6H), 4.31 (td, J = 8.0, 3.3 Hz, 0.4H), 4.01 – 3.91 (m, 1H), 2.21 – 2.13 (m, 0.6H), 2.09 – 2.01 (m, 0.4H), 1.96 – 1.41 (m, 5H).

Example 450: ((1S,2R,4R)-2-((3-fluoro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone.



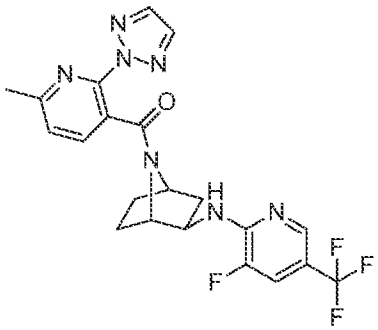
Prepared analogous to Example 382 substituting intermediate A-2 with intermediate A-24. MS (ESI): mass calcd. for $C_{22}H_{20}F_4N_6O$, 460.2; m/z found, 461.2 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.14 (s, 0.3H), 8.06 (s, 0.7H), 7.89 – 7.82 (m, 2H), 7.46 – 7.41 (m, 0.7H), 7.36 – 7.24 (m, 2H), 7.23 – 7.16 (m, 1.3H), 6.84 (s, 0.7H), 5.00 – 4.93 (m, 0.3H), 4.76 – 4.70 (m, 0.7H), 4.55 (d, J = 5.2 Hz, 0.3H), 4.40 (s, 0.7H), 4.30 – 4.22 (m, 0.3H), 3.99 – 3.92 (m, 1H), 2.22 (s, 2H), 2.19 (s, 1H), 2.15 (dd, J = 12.9, 8.2 Hz, 0.7H), 2.03 (dd, J = 13.1, 8.0 Hz, 0.3H), 1.97 – 1.55 (m, 4H), 1.53 – 1.46 (m, 0.7H), 1.46 – 1.39 (m, 0.3H).

Example 451: ((1S,2R,4R)-2-((3-fluoro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)methanone.



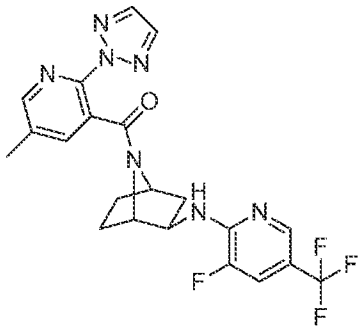
Prepared analogous to Example 382 substituting intermediate A-2 with intermediate A-21. MS (ESI): mass calcd. for $C_{21}H_{19}F_4N_7O$, 461.2; m/z found, 462.2 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.23 – 8.17 (m, 0.4H), 8.14 – 8.08 (m, 1.6H), 7.87 (s, 0.4H), 7.84 (s, 1.6H), 7.39 – 7.30 (m, 1.2H), 7.24 (dd, J = 10.9, 2.0 Hz, 0.8H), 6.69 (d, J = 8.0 Hz, 0.8H), 5.78 (d, J = 8.8 Hz, 0.2H), 4.94 – 4.90 (m, 0.8H), 4.79 (d, J = 5.3 Hz, 0.2H), 4.48 (td, J = 8.3, 3.2 Hz, 0.2H), 4.39 (td, J = 7.9, 2.9 Hz, 0.8H), 4.08 – 4.03 (m, 0.8H), 4.02 – 3.98 (m, 0.2H), 2.64 (s, 0.6H), 2.59 (s, 2.4H), 2.27 – 2.19 (m, 0.8H), 2.12 – 1.92 (m, 2.2H), 1.86 – 1.56 (m, 2.8H), 1.50 – 1.42 (m, 0.2H).

Example 452: ((1S,2R,4R)-2-((3-fluoro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-2-(2H-1,2,3-triazol-2-yl)pyridin-3-yl)methanone.



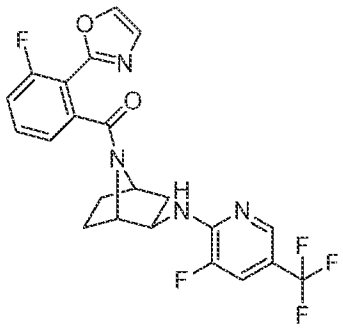
Prepared analogous to Example 382 substituting intermediate A-2 with intermediate A-3. MS (ESI): mass calcd. for $C_{21}H_{19}F_4N_7O$, 461.2; m/z found, 462.2 $[M+H]^+$. Analytical HPLC was obtained on a Agilent 1100 Series using a XBridge C18 column (5µm, 100 x 4.6mm), mobile phase of 10-100% ACN in 20 mM NH_4OH over 8 min and then hold at 100% ACN for 3 min, at a flow rate of 1 mL/min (Temperature = 30 °C). R_t = 6.59 min at 254 nm.

Example 453: ((1S,2R,4R)-2-((3-fluoro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(5-methyl-2-(2H-1,2,3-triazol-2-yl)pyridin-3-yl)methanone.



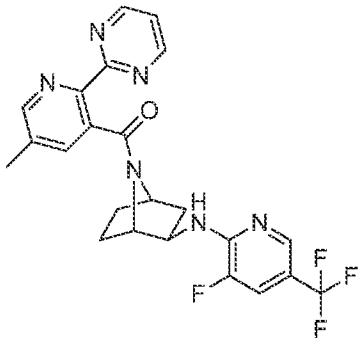
Prepared analogous to Example 382 substituting intermediate A-2 with intermediate A-60. MS (ESI): mass calcd. for $C_{21}H_{19}F_4N_7O$, 461.2; m/z found, 462.2 $[M+H]^+$. Analytical HPLC was obtained on a Agilent 1100 Series using a XBridge C18 column (5µm, 100 x 4.6mm), mobile phase of 10-100% ACN in 20 mM NH_4OH over 8 min and then hold at 100% ACN for 3 min, at a flow rate of 1 mL/min (Temperature = 30 °C). R_t = 6.60 min at 254 nm.

Example 454: (3-fluoro-2-(oxazol-2-yl)phenyl)((1S,2R,4R)-2-((3-fluoro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



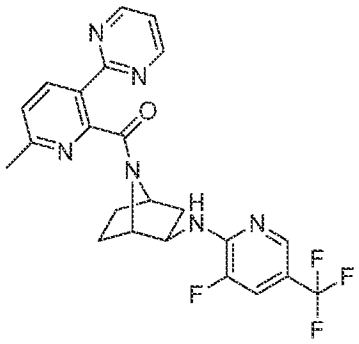
Prepared analogous to Example 382 substituting intermediate A-2 with intermediate A-68. MS (ESI): mass calcd. for $C_{22}H_{17}F_5N_4O_2$, 464.1; m/z found, 465.2 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.18 (s, 0.4H), 8.03 (s, 0.6H), 7.85 – 7.81 (m, 1H), 7.53 – 7.46 (m, 0.4H), 7.41 – 7.27 (m, 2.6H), 7.23 – 7.09 (m, 2.4H), 6.05 (d, J = 8.6 Hz, 0.6H), 4.91 – 4.87 (m, 0.6H), 4.73 (d, J = 5.3 Hz, 0.4H), 4.49 – 4.43 (m, 1H), 3.91 – 3.87 (m, 0.4H), 3.85 (d, J = 4.8 Hz, 0.6H), 2.23 – 2.16 (m, 0.6H), 2.06 – 2.00 (m, 0.4H), 1.99 – 1.82 (m, 2.6H), 1.81 – 1.65 (m, 1.4H), 1.59 – 1.52 (m, 0.6H), 1.49 – 1.42 (m, 0.4H).

Example 455: ((1S,2R,4R)-2-((3-fluoro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(5-methyl-2-(pyrimidin-2-yl)pyridin-3-yl)methanone.



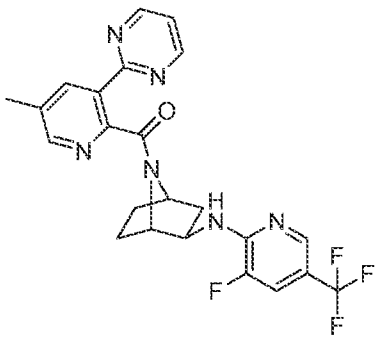
Prepared analogous to Example 382 substituting intermediate A-2 with intermediate A-66. MS (ESI): mass calcd. for $C_{23}H_{20}F_4N_6O$, 472.2; m/z found, 473.2 $[M+H]^+$. Analytical HPLC was obtained on a Agilent 1100 Series using a XBridge C18 column (5µm, 100 x 4.6mm), mobile phase of 10-100% ACN in 20 mM NH_4OH over 8 min and then hold at 100% ACN for 3 min, at a flow rate of 1 mL/min (Temperature = 30 °C). R_t = 6.08 min at 254 nm.

Example 456: ((1S,2R,4R)-2-((3-fluoro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(pyrimidin-2-yl)pyridin-2-yl)methanone



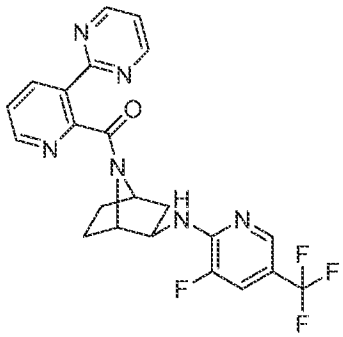
Prepared analogous to Example 382 substituting intermediate A-2 with intermediate A-63. MS (ESI): mass calcd. for $C_{23}H_{20}F_4N_6O$, 472.2; m/z found, 473.2 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.77 (d, J = 4.9 Hz, 2H), 8.36 (d, J = 8.0 Hz, 1H), 8.09 (s, 1H), 7.31 – 7.22 (m, 2H), 7.19 (dd, J = 11.0, 2.0 Hz, 1H), 7.07 (d, J = 8.4 Hz, 1H), 4.95 – 4.90 (m, 1H), 4.46 – 4.40 (m, 1H), 4.08 (d, J = 5.1 Hz, 1H), 2.59 (s, 3H), 2.24 (dd, J = 13.0, 7.6 Hz, 1H), 2.14 – 2.01 (m, 2H), 1.88 – 1.81 (m, 1H), 1.66 – 1.57 (m, 2H).

Example 457: ((1S,2R,4R)-2-((3-fluoro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(5-methyl-3-(pyrimidin-2-yl)pyridin-2-yl)methanone.



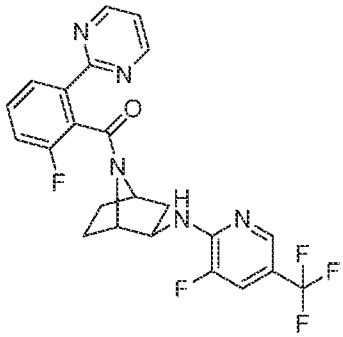
Prepared analogous to Example 382 substituting intermediate A-2 with intermediate A-67. MS (ESI): mass calcd. for $C_{23}H_{20}F_4N_6O$, 472.2; m/z found, 473.2 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.79 (d, J = 4.9 Hz, 2H), 8.44 (dd, J = 2.0, 0.9 Hz, 1H), 8.26 (dd, J = 2.1, 0.9 Hz, 1H), 8.09 (s, 1H), 7.72 (d, J = 8.2 Hz, 1H), 7.30 – 7.24 (m, 1H), 7.19 (dd, J = 11.0, 2.0 Hz, 1H), 4.95 – 4.90 (m, 1H), 4.46 – 4.39 (m, 1H), 4.12 (d, J = 5.3 Hz, 1H), 2.44 (s, 3H), 2.29 – 2.22 (m, 1H), 2.16 – 2.06 (m, 1H), 2.04 – 1.96 (m, 1H), 1.90 – 1.82 (m, 1H), 1.68 – 1.55 (m, 2H).

Example 458: ((1S,2R,4R)-2-((3-fluoro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-(pyrimidin-2-yl)pyridin-2-yl)methanone.



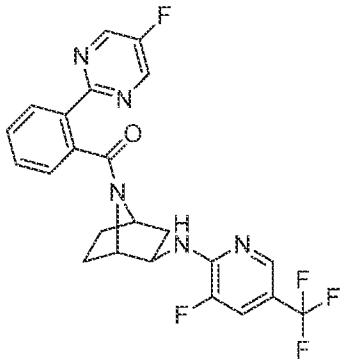
Prepared analogous to Example 382 substituting intermediate A-2 with intermediate A-64. MS (ESI): mass calcd. for $C_{22}H_{18}F_4N_6O$, 458.1; m/z found, 459.2 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.80 (d, J = 4.9 Hz, 2H), 8.62 (dd, J = 4.8, 1.6 Hz, 1H), 8.48 (dd, J = 7.9, 1.7 Hz, 1H), 8.08 (s, 1H), 7.66 (d, J = 8.4 Hz, 1H), 7.46 (dd, J = 8.0, 4.8 Hz, 1H), 7.28 (t, J = 4.9 Hz, 1H), 7.19 (dd, J = 11.0, 2.0 Hz, 1H), 4.96 – 4.91 (m, 1H), 4.47 – 4.41 (m, 1H), 4.11 (d, J = 5.2 Hz, 1H), 2.27 (dd, J = 12.9, 7.5 Hz, 1H), 2.12 (ddd, J = 14.0, 8.7, 4.3 Hz, 1H), 2.06 – 1.97 (m, 1H), 1.91 – 1.83 (m, 1H), 1.68 – 1.59 (m, 2H).

Example 459: ((1S,2R,4R)-2-((3-fluoro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(2-fluoro-6-(pyrimidin-2-yl)phenyl)methanone.



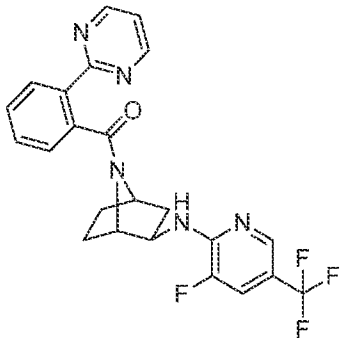
Prepared analogous to Example 382 substituting intermediate A-2 with intermediate A-6. MS (ESI): mass calcd. for $C_{23}H_{18}F_5N_5O$, 475.1; m/z found, 476.2 $[M+H]^+$. Agilent 1100 Series using an Inertsil ODS-3 column (3µm, 50 x 3 mm), mobile phase of 5-99% ACN in 0.05% TFA over 1.6 min and then hold at 99% ACN for 0.4 min, at a flow rate of 2.2 mL/min (Temperature = 50 °C). R_t = 1.41 min at 254 nm.

Example 460: ((1S,2R,4R)-2-((3-fluoro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(2-(5-fluoropyrimidin-2-yl)phenyl)methanone.



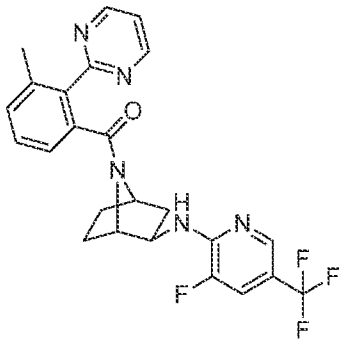
Prepared analogous to Example 382 substituting intermediate A-2 with intermediate A-55. MS (ESI): mass calcd. for $C_{23}H_{18}F_5N_5O$, 475.1; m/z found, 476.2 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.65 (s, 1.6H), 8.60 (s, 0.4H), 8.18 (s, 0.2H), 8.11 (dd, J = 7.6, 1.4 Hz, 0.2H), 8.06 – 7.99 (m, 1.6H), 7.58 – 7.42 (m, 1.8H), 7.41 – 7.30 (m, 2.2H), 7.11 (d, J = 10.9 Hz, 0.8H), 5.49 (d, J = 7.9 Hz, 0.2H), 4.93 – 4.87 (m, 0.8H), 4.75 (d, J = 5.3 Hz, 0.2H), 4.50 (s, 0.8H), 4.42 – 4.36 (m, 0.2H), 4.03 – 3.97 (m, 1H), 2.25 (dd, J = 12.9, 8.2 Hz, 0.8H), 2.11 (dd, J = 12.8, 7.7 Hz, 0.2H), 2.00 – 1.89 (m, 1.6H), 1.88 – 1.78 (m, 0.4H), 1.74 – 1.53 (m, 2.8H), 1.48 – 1.40 (m, 0.2H).

Example 461: ((1S,2R,4R)-2-((3-fluoro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(2-(pyrimidin-2-yl)phenyl)methanone.



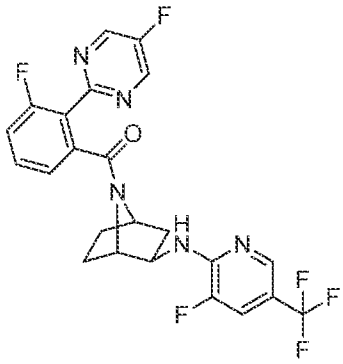
Prepared analogous to Example 382 substituting intermediate A-2 with intermediate A-59. MS (ESI): mass calcd. for $C_{23}H_{19}F_4N_5O$, 457.2; m/z found, 458.2 $[M+H]^+$. Agilent 1100 Series using an Inertsil ODS-3 column (3µm, 50 x 3 mm), mobile phase of 5-99% ACN in 0.05% TFA over 1.6 min and then hold at 99% ACN for 0.4 min, at a flow rate of 2.2 mL/min (Temperature = 50 °C). R_t = 1.38 min at 254 nm.

Example 462: ((1S,2R,4R)-2-((3-fluoro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-methyl-2-(pyrimidin-2-yl)phenyl)methanone.



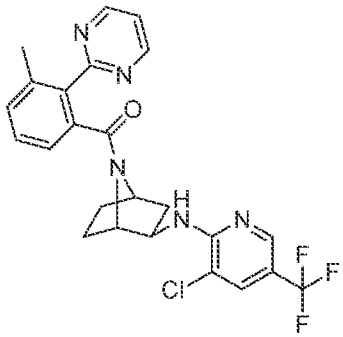
Prepared analogous to Example 382 substituting intermediate A-2 with intermediate A-26. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.80 (d, J = 4.9 Hz, 2H), 8.05 (s, 1H), 7.97 (s, 1H), 7.32 – 7.15 (m, 4H), 7.10 (dd, J = 11.1, 2.0 Hz, 1H), 4.76 – 4.70 (m, 1H), 4.57 – 4.49 (m, 1H), 4.03 (d, J = 4.9 Hz, 1H), 2.33 (s, 3H), 2.17 (dd, J = 12.7, 8.3 Hz, 1H), 2.04 – 1.94 (m, 1H), 1.94 – 1.82 (m, 1H), 1.77 – 1.68 (m, 2H), 1.54 – 1.46 (m, 1H). Agilent 1100 Series using an Inertsil ODS-3 column (3μm, 50 x 3 mm), mobile phase of 5-99% ACN in 0.05% TFA over 1.6 min and then hold at 99% ACN for 0.4 min, at a flow rate of 2.2 mL/min (Temperature = 50 °C). R_t = 1.42 min at 254 nm.

Example 463: (3-fluoro-2-(5-fluoropyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((3-fluoro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.

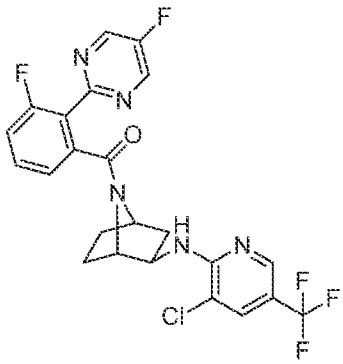


Prepared analogous to Example 382 substituting intermediate A-2 with intermediate A-57. MS (ESI): mass calcd. for $C_{23}H_{17}F_6N_5O$, 493.1; m/z found, 494.1 $[M+H]^+$. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.69 (s, 2H), 8.06 (s, 1H), 7.39 – 7.32 (m, 1H), 7.24 – 7.07 (m, 4H), 4.80 – 4.75 (m, 1H), 4.56 – 4.48 (m, 1H), 4.04 (d, J = 4.9 Hz, 1H), 2.21 (dd, J = 12.9, 8.2 Hz, 1H), 2.01 – 1.94 (m, 1H), 1.94 – 1.86 (m, 1H), 1.79 – 1.69 (m, 2H), 1.58 – 1.50 (m, 1H).

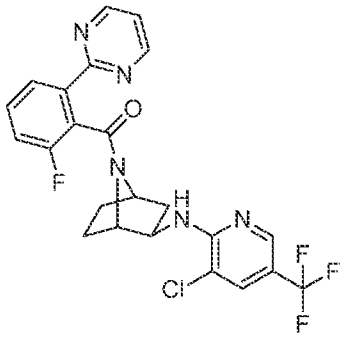
Example 464: ((1S,2R,4R)-2-((3-chloro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-methyl-2-(pyrimidin-2-yl)phenyl)methanone.



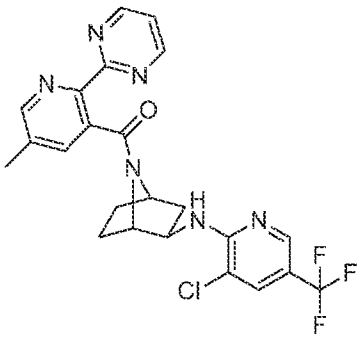
Example: 465: ((1S,2R,4R)-2-((3-chloro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-(5-fluoropyrimidin-2-yl)phenyl)methanone.



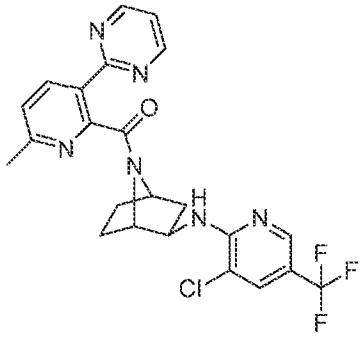
Example 466: ((1S,2R,4R)-2-((3-chloro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(2-fluoro-6-(pyrimidin-2-yl)phenyl)methanone.



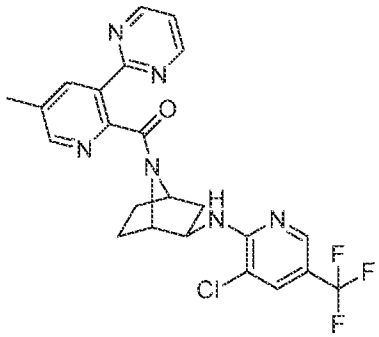
Example 467: ((1S,2R,4R)-2-((3-chloro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(5-methyl-2-(pyrimidin-2-yl)pyridin-3-yl)methanone.



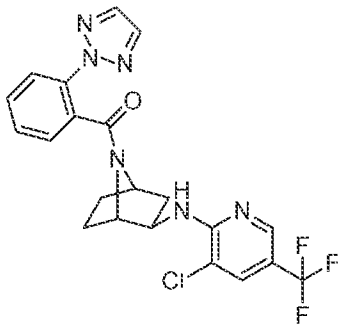
Example 468: ((1S,2R,4R)-2-((3-chloro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(pyrimidin-2-yl)pyridin-2-yl)methanone.



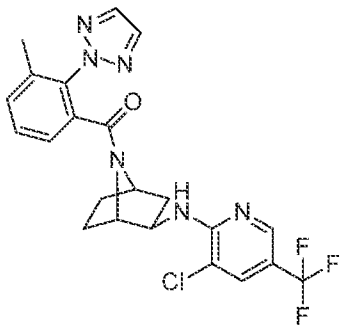
Example 469: ((1S,2R,4R)-2-((3-chloro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(5-methyl-3-(pyrimidin-2-yl)pyridin-2-yl)methanone.



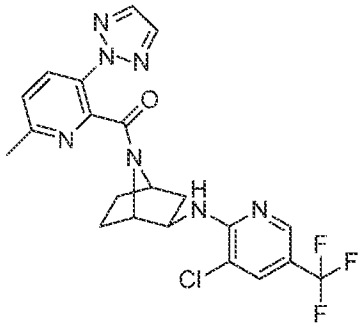
Example 470: (2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((3-chloro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



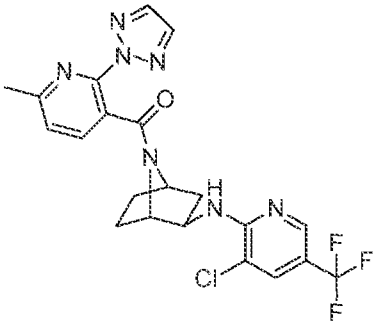
Example 471: ((1S,2R,4R)-2-((3-chloro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone.



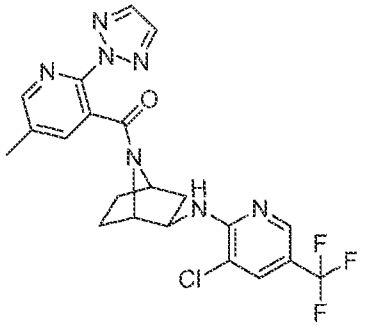
Example 472: ((1S,2R,4R)-2-((3-chloro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)methanone.



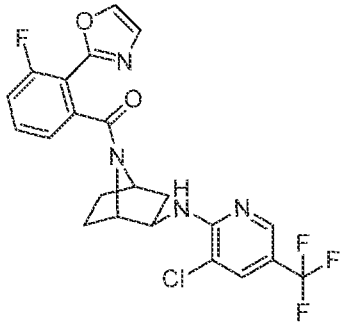
Example 473: ((1S,2R,4R)-2-((3-chloro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-2-(2H-1,2,3-triazol-2-yl)pyridin-3-yl)methanone.



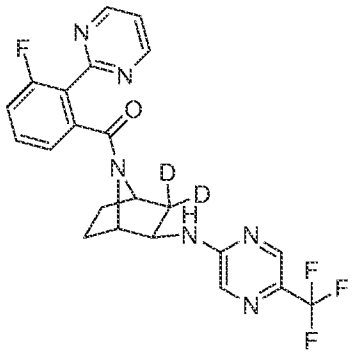
Example 474: ((1S,2R,4R)-2-((3-chloro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(5-methyl-2-(2H-1,2,3-triazol-2-yl)pyridin-3-yl)methanone.



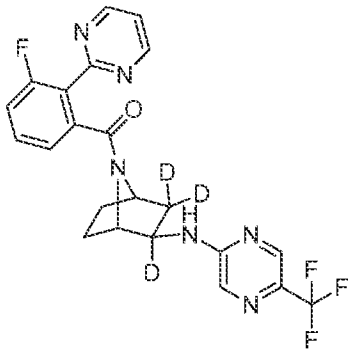
Example 475: ((1S,2R,4R)-2-((3-chloro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-(oxazol-2-yl)phenyl)methanone.



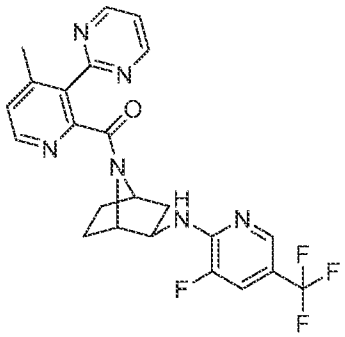
Example 476: (3-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]-(3-^{2}H,^{2}H)-heptan-7-yl)methanone



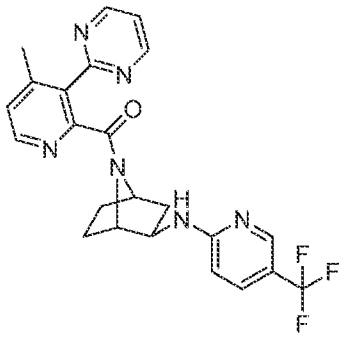
Example 477: (3-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-(2-^{2}H)-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]-(3-^{2}H,^{2}H)-heptan-7-yl)methanone



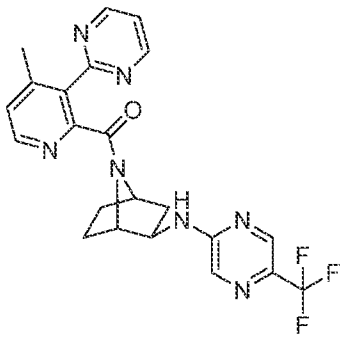
Example 478: ((1S,2R,4R)-2-((3-fluoro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(4-methyl-3-(pyrimidin-2-yl)pyridin-2-yl)methanone.



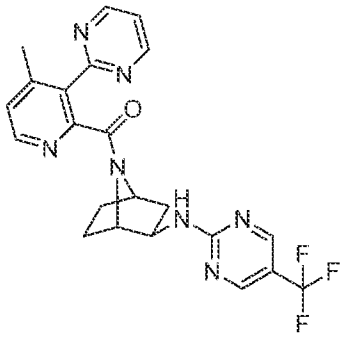
Example 479: (4-methyl-3-(pyrimidin-2-yl)pyridin-2-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



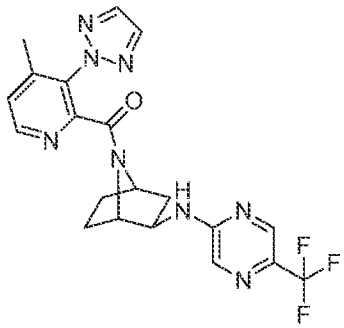
Example 480: (4-methyl-3-(pyrimidin-2-yl)pyridin-2-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



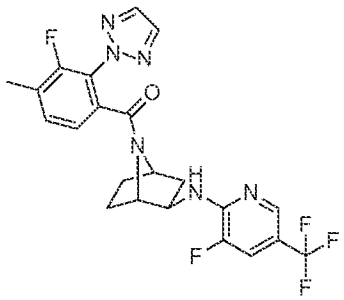
Example 481: (4-methyl-3-(pyrimidin-2-yl)pyridin-2-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



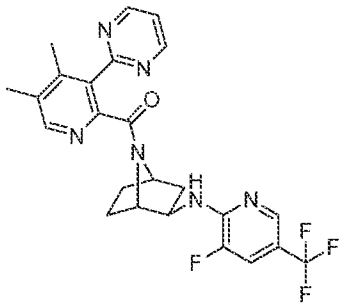
Example 482: (4-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



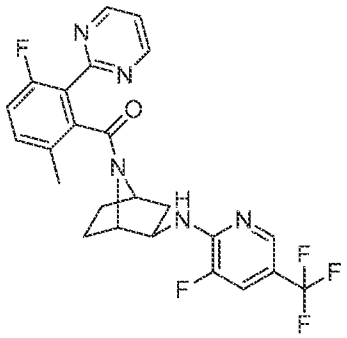
Example 483: (3-fluoro-4-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((3-fluoro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



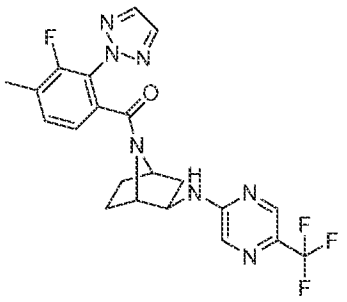
Example 484: (4,5-dimethyl-3-(pyrimidin-2-yl)pyridin-2-yl)((1S,2R,4R)-2-((3-fluoro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



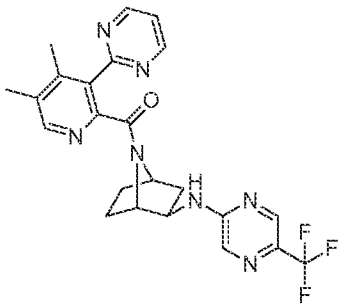
Example 485: ((1S,2R,4R)-2-((3-fluoro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-6-methyl-2-(pyrimidin-2-yl)phenyl)methanone.



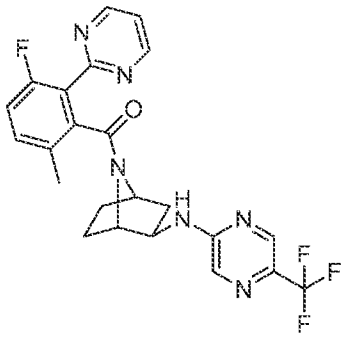
Example 486: (3-fluoro-4-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



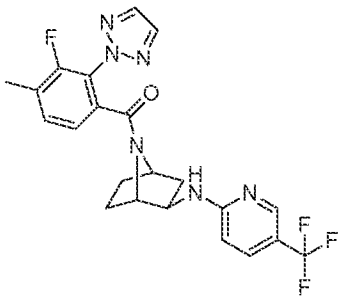
Example 487: (4,5-dimethyl-3-(pyrimidin-2-yl)pyridin-2-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



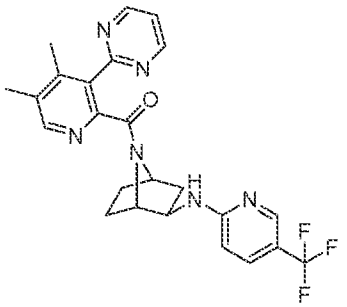
Example 488: (3-fluoro-6-methyl-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



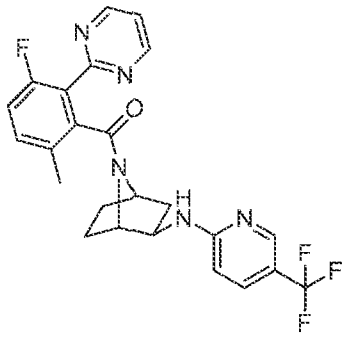
Example 489: (3-fluoro-4-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



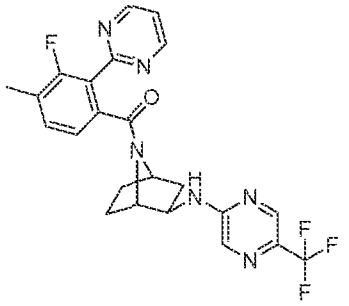
Example 490: (4,5-dimethyl-3-(pyrimidin-2-yl)pyridin-2-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



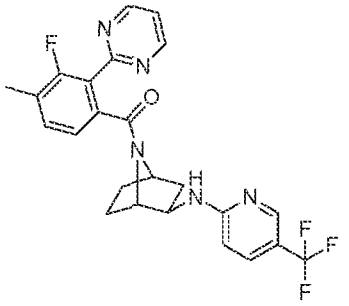
Example 491: (3-fluoro-6-methyl-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



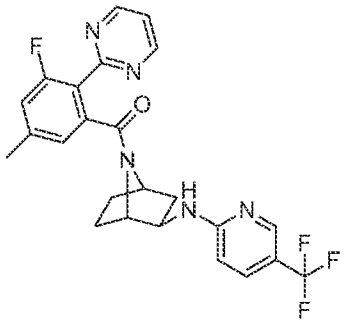
Example 492: (3-fluoro-4-methyl-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



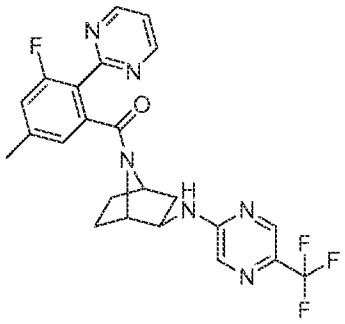
Example 493: (3-fluoro-4-methyl-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone



Example 494: (3-fluoro-5-methyl-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Example 495: (3-fluoro-5-methyl-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone.



Assays:

The *in vitro* affinity of the compounds of the invention for the rat/human orexin 1 and human orexin 2 receptors was determined by competitive radioligand binding using [3H] (1-(5-(2-fluoro-phenyl)-2-methyl-thiazol-4-yl)-1-((S)-2-(5-phenyl-(1,3,4)oxadiazol-2-ylmethyl)-pyrrolidin-1-yl)-methanone)(Langmead et al., 2004) and [3H]EMPA (n-ethyl-2[96-methoxy-pyridin-3-yl)-(toluene-2-sulfonyl)-amino]-N-pyridin-3-ylmethyl acetamide), respectively (Langmead et al., 2004, British Journal of Pharmacology 141:340-346; Malherbe et al., 2004, British Journal of Pharmacology 156:1326-41).

The *in vitro* functional antagonism of the compounds on the human orexin 1 and orexin 2 receptors was determined using fluorometric imaging plate reader (FLIPR) based calcium assays.

Data are analyzed using pc-Sandy macro and graphed on Graphpad Prism 5. For analysis, each concentration point is averaged from triplicate values and the averaged values are plotted on Graphpad Prism. The IC50 is determined by applying the following equation (GraphPad Prism 5.0, SanDiego) for one site competition where X=log (concentration) and Y=specific binding. Top denotes the total [^{3}H]- (1-(5-(2-fluoro-phenyl)-2-methyl-thiazol-4-yl)-

1-((S)-2-(5-phenyl-(1,3,4)oxadiazol-2-ylmethyl)-pyrrolidin-1-yl)-methanone) binding, bottom denotes the nonspecific [^{3}H]- (1-(5-(2-fluoro-phenyl)-2-methyl-thiazol-4-yl)-1-((S)-2-(5-phenyl-(1,3,4)oxadiazol-2-ylmethyl)-pyrrolidin-1-yl)-methanone) binding. Graphpad Prism calculates Ki value from IC50 and the pre-determined Kd values for [^{3}H]- (1-(5-(2-fluoro-phenyl)-2-methyl-thiazol-4-yl)-1-((S)-2-(5-phenyl-(1,3,4)oxadiazol-2-ylmethyl)-pyrrolidin-1-yl)-methanone) and [3H]-EMPA. The Ki for each compound is then uploaded into 3DX. Each run comprises individual compounds in triplicate. The data in Table 1 and Table 2 represent averages from between 2-20 runs.

Rat and human orexin 1 receptor radioligand binding studies

Human Embryonic Kidney 293 cells (HEK293) stably expressing rat orexin 1 receptor (Genebank accession number NM_001525) or Chinese ovary cells (CHO) stably expressing human orexin 1 receptor (Genebank accession number NM_001526) were grown to confluency in DMEM (Hyclone, cat # SH30022), 10% FBS, 1X Pen/Strep, 1X sodium pyruvate, 10 mM HEPES, 600 µg/mL G418 and DMEM/F12 (Gibco, Cat #11039), 10%FBS, 1X Pen/Strep, 600 µg/mL G418 media, respectively on 150 cm2 tissue culture plates, washed with 5 mM EDTA in PBS (HyClone Dulbecco's Phoshpate Buffered Saline 1X with Calcium and Magnesium, Cat # SH30264.01, hereafter referred to simply as PBS) and scraped into 50 ml tubes. After centrifugation (2K xG, 5 min at 4 °C), the supernatant was aspirated and the pellets frozen and stored at –800C. Cells were resuspended in PBS in the presence of 1 tablet of protease inhibitor cocktail (Roche, Cat. #11836145001) per 50 mL. Each cell pellet from a 15 cm plate was resuspended in 10 mL, stored on ice, and homogenized for 45 sec prior to addition to the reactions. Competition binding experiments in 96 well polypropylene plates were performed using [3H]- (1-(5-(2-fluoro-phenyl)-2-methyl-thiazol-4-yl)-1-((S)-2-(5-phenyl-(1,3,4)oxadiazol-2-ylmethyl)-pyrrolidin-1-yl)-methanone) (Moraveck Corporation, specific activity = 35.3 Ci/mmol), diluted to a 10 nM concentration in PBS (4 nM final). Compounds were solubilized in 100% DMSO (Acros Organics, Cat. #61042-1000) and tested over a range of 7 concentrations (from 0.1 nM to 10 µM). The final concentration of DMSO in the reactions is equal to or less than 0.1%. Total and nonspecific binding was determined in the absence and presence of 10 µM almorexant. The total volume of each reaction is 200 µL (20 µL of diluted compounds, 80 µL of [3H]- (1-(5-(2-fluoro-phenyl)-2-methyl-thiazol-4-yl)-1-((S)-2-(5-phenyl-(1,3,4)oxadiazol-2-ylmethyl)-pyrrolidin-1-yl)-methanone) diluted in PBS and 100 µL of the cell suspension). Reactions were run for 60 min at room temperature and terminated by filtration through GF/C

filter plates (PerkinElmer, Cat. #6005174) presoaked in 0.3% polyethylenimine using the cell harvester (PerkinElmer Filtermate). The plates were washed 3 times by aspirating 30 ml PBS through the plates. Plates were dried in 55 °C oven for 60 min, scintillation fluid was added, and the radioactivity was counted on a Topcount (Packard).

IC_{50} values (i.e. concentration of unlabelled compound required to compete for 50% of specific binding to the radioligand) was calculated using the GraphPad Prism software (GraphPad Prism Software Inc., San Diego, CA) with a fit to a sigmoidal dose-response curve. Apparent Ki values were calculated as $Ki = IC_{50}/(1+C/Kd)$, where C is concentration of radioligand and Kd = 4 nM for rat orexin 1 receptor and 6 nM for human orexin 1 receptor.

Human orexin 2 receptor radioligand binding studies

HEK293 stably expressing human orexin 2 receptor (Genebank accession number NM_001526) were grown to confluency in DMEM (Hyclone, cat # SH30022) , 10%FBS, 1X Pen/Strep, 1X NaPyruvate, 10 mM HEPES, 600 ug/ml G418 media on 150 cm^2 tissue culture plates, washed with 5 mM EDTA in PBS (HyClone Dulbecco's Phoshpate Buffered Saline 1X with Calcium and Magnesium, Cat # SH30264.01, hereafter referred to simply as PBS) and scraped into 50 ml tubes. After centrifugation (2K xG, 5 min at 40 °C), the supernatant was aspirated and the pellets frozen and stored at –800 °C. Cells were resuspended in PBS in the presence of 1 tablet of protease inhibitor cocktail (Roche, Cat. #11836145001) per 50 mL. Each cell pellet from a 15 cm plate was resuspended in 10 mL, stored on ice, and homogenized for 45 sec just prior to addition to the reactions. Competition binding experiments in 96 well polypropylene plates were performed using [3H]-EMPA (Moraveck Corporation, specific activity = 29.6 Ci/mmol), diluted to a 5 nM concentration in PBS (2 nM final concentration). Compounds were solubilized in 100% DMSO (Acros Organics, Cat. #61042-1000) and tested over a range of 7 concentration (from 0.1 nM to 10 μM). The final concentration of DMSO in the reactions is equal to or less than 0.1%. Total and nonspecific binding was determined in the absence and presence of 10 μM almorexant. The total volume of each reaction is 200 μL (20 μL of diluted compounds, 80 μL of [3H]-EMPA diluted in PBS and 100 μL of the cell suspension). Reactions were run for 60 min at room temperature and terminated by filtration through GF/C filter plates (PerkinElmer, Cat. #6005174) presoaked in 0.3% polyethylenimine using the cell harvester (PerkinElmer Filtermate). The plates were washed 3 times by aspirating 30 ml PBS through the plates. Plates were dried in 55 °C oven for 60 min, scintillation fluid was added, and the radioactivity was counted on a Topcount (Packard).

IC_{50} values (i.e. concentration of unlabelled compound required to compete for 50% of specific binding to the radioligand) was calculated using the GraphPad Prism software (GraphPad Prism Software Inc., San Diego, CA) with a fit to a sigmoidal dose-response curve. Apparent Ki values were calculated as Ki = IC_{50}/(1+C/Kd), where C is concentration of radioligand and Kd = 2 nM.

Human orexin 1 receptor Ca2+ mobilization assay

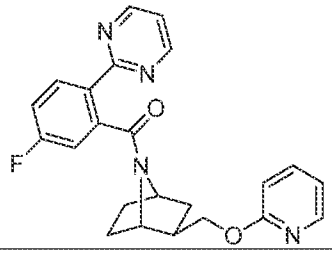
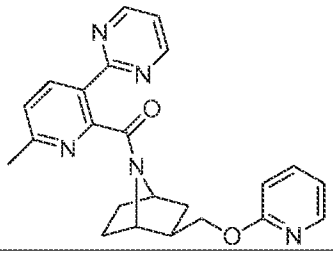
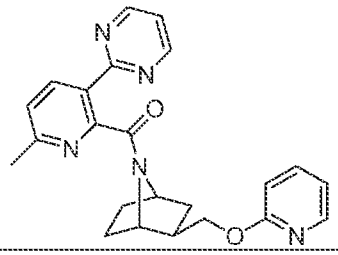
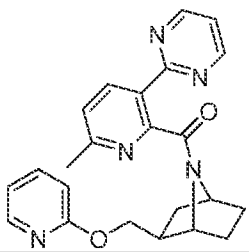
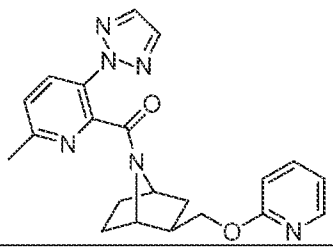
CHO cells stably transfected with the human orexin 1 receptor (Genebank accession number NM_001526) were grown to confluency in DMEM/F12, 10% FBS, 1X pen-strep, 400 µg/ml G418. Cells were seeded on to 384-well Packard viewplates at a density of 10,000 cells/well and incubated overnight at 370C, 5% CO_2. The cells were dye-loaded with BD Calcium Assay kit (BD, cat # 640178) in HBSS (Gibco, cat# 14025-092) with 2.5 mM probenecid and incubated at 37 °C, 5% CO2 for 45 min. Cells were pre-incubated with compounds (diluted in DMEM/F-12) for 15-30 minutes before agonist (orexin A, 10 nM) stimulation. Ligand-induced Ca^{2+} release was measured using a Fluorometric Imaging Plate Reader (FLIPR, Molecular Devices, Sunnyvale, CA). Functional responses were measured as peak fluorescence intensity minus basal. The concentration of agonist that produced a half-maximal response is represented by the EC_{50} value. Antagonistic potency values were converted to apparent pKB values using a modified Cheng-Prusoff correction. Apparent pKB = - log IC_{50}/1+[conc agonist/EC_{50}].

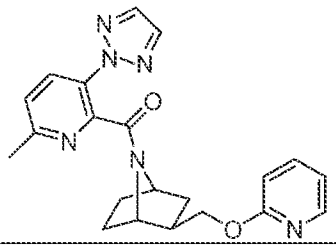
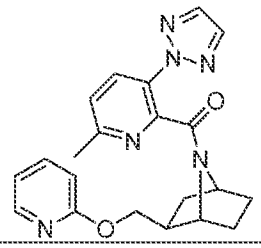
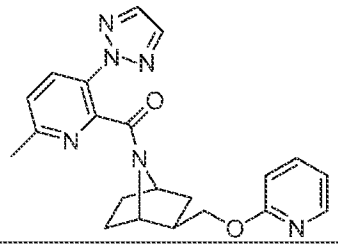
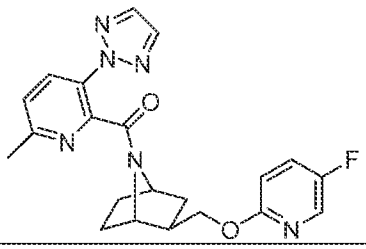
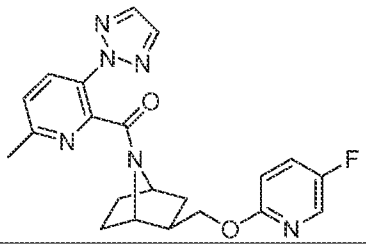
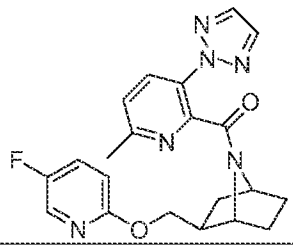
Human orexin 2 receptor Ca2+ mobilization assay

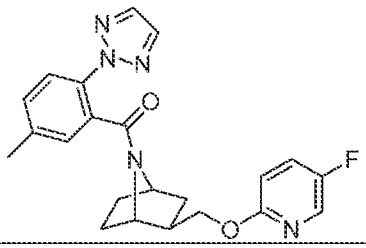
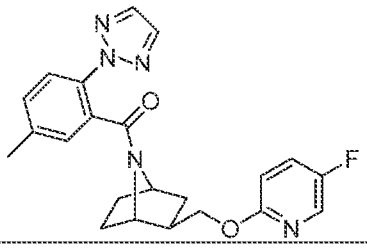
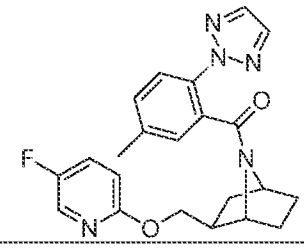
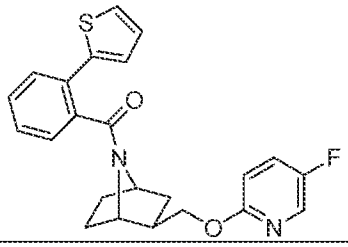
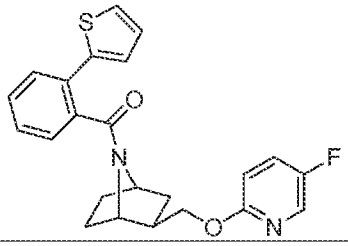
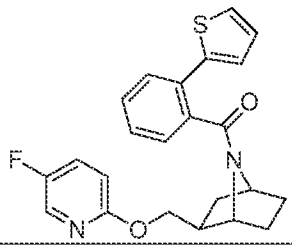
PFSK-1 cells endogenously expressing the human orexin 2 receptor were grown to confluency in RPMI1640 (Hyclone, cat# 30027.02), 10% FBS, 1X pen-strep. Cells were seeded on to 384-well Packard viewplates at a density of 5,000 cells/well and incubated overnight at 370C, 5% CO_2. The cells were dye-loaded with BD Calcium Assay kit (BD, cat # 640178) in HBSS (Gibco, cat# 14025-092) with 2.5 mM probenecid and incubated at 37 °C, 5% CO2 for 45 min. Cells were pre-incubated with compounds (diluted in DMEM/F-12) for 15-30 minutes before agonist (orexin B, 100 nM) stimulation. Ligand-induced Ca^{2+} release was measured using a Fluorometric Imaging Plate Reader (FLIPR, Molecular Devices, Sunnyvale, CA). Functional responses were measured as peak fluorescence intensity minus basal. The concentration of agonist that produced a half-maximal response is represented by the EC_{50} value. Antagonistic potency values were converted to apparent pKB values using a modified Cheng-Prusoff correction. Apparent pKB = - log IC_{50}/1+[conc agonist/EC50].

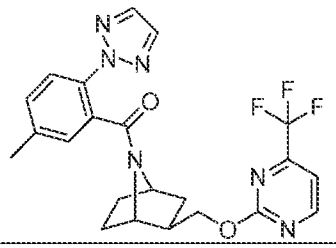
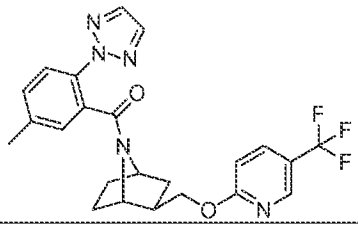
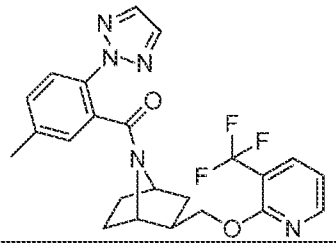
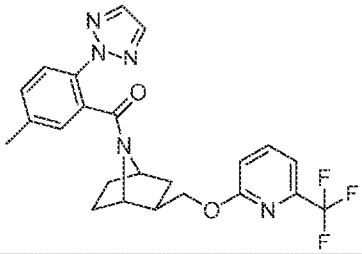
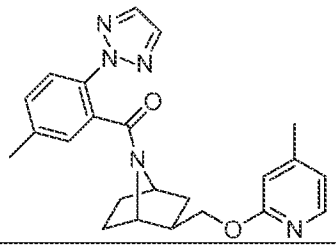
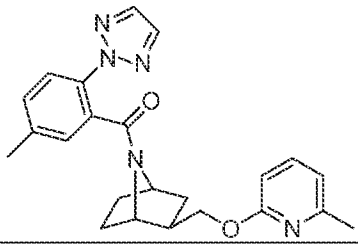
Preferred compounds of the invention are set forth in Table 1 below. Orexin receptor activity of certain compounds of the invention is also set forth in Table 1 below

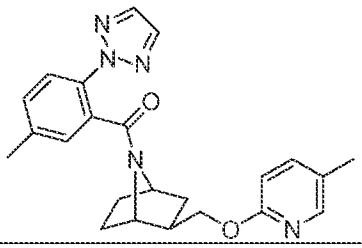
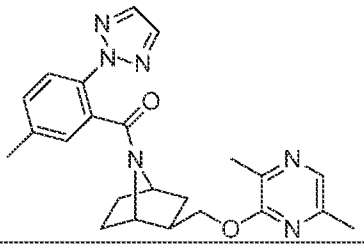
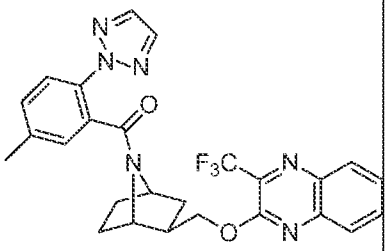
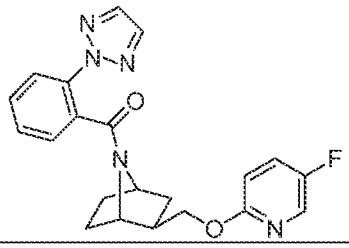
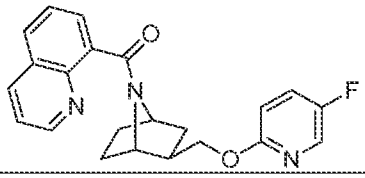
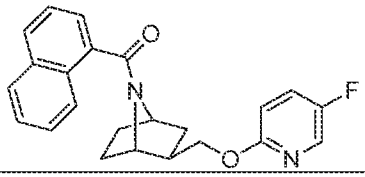
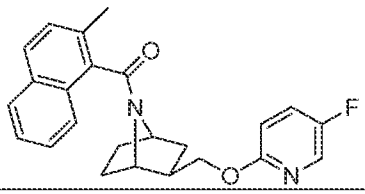
Table 1

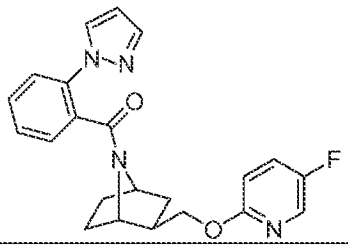
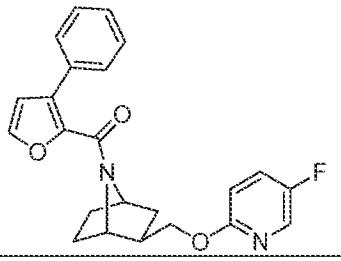
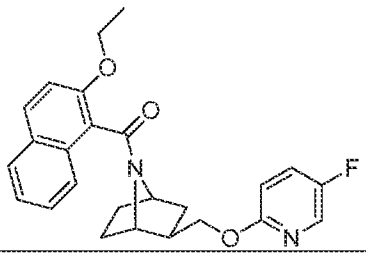
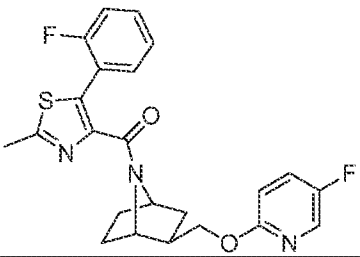
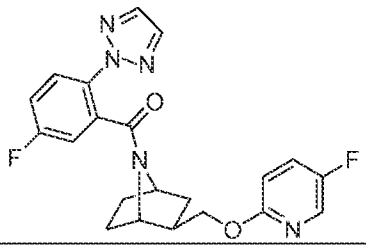
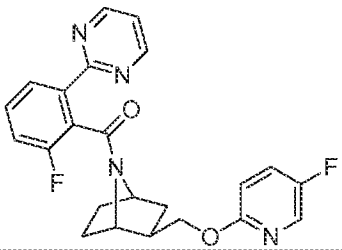
Ex. No.	Compound	rOX1 Ki (nM)	hOX1 Ki (nM)	hOX2 Ki (nM)	Compound Name
1		25	41	276	(5-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
2		31	23	500	(±)-(6-methyl-3-(pyrimidin-2-yl)pyridin-2-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
3A		24	19	268	(6-methyl-3-(pyrimidin-2-yl)pyridin-2-yl)((1S*,2R*,4R*)-2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
3B		>10000		>10000	(6-methyl-3-(pyrimidin-2-yl)pyridin-2-yl)((1R*,2S*,4S*)-2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
4		36	41	927	(±)-(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

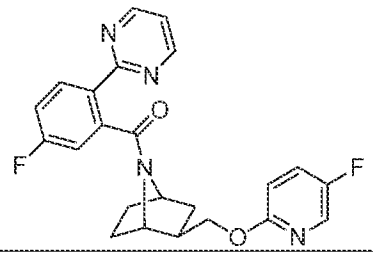
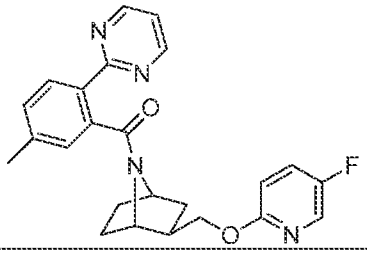
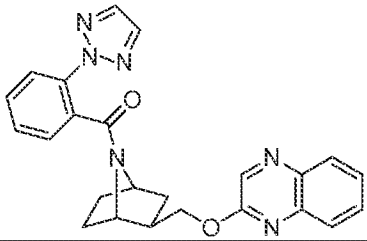
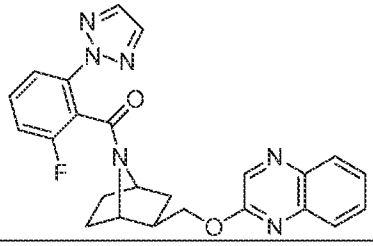
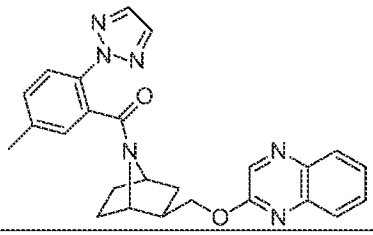
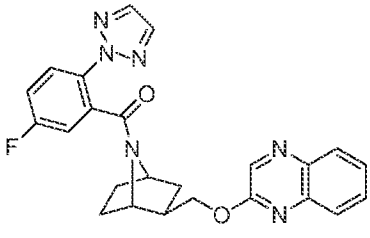
5A		14	15	428	(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)((1S,2R,4R)-2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
5B		>10000		>10000	(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)((1R,2S,4S)-2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
6		14	15	428	(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)((1S,2R,4R)-2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
7		19	19	198	(±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)methanone
8A		9	14	94	((1S,2R,4R)-2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)methanone
8B		>10000		>10000	((1R,2S,4S)-2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)methanone

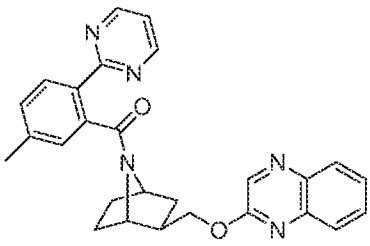
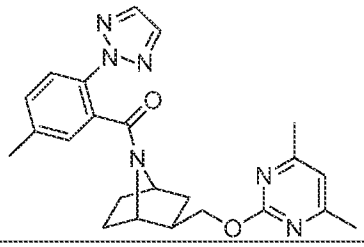
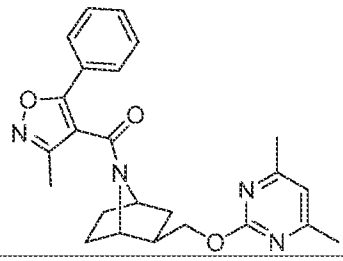
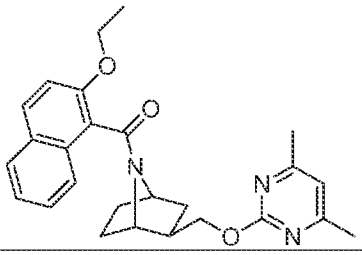
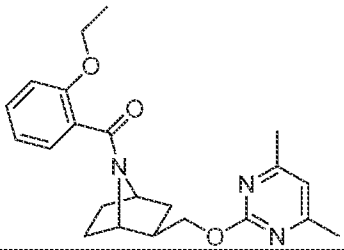
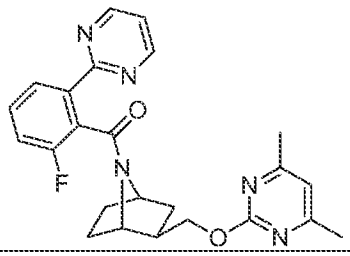
9			9	57	(±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(5-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone
10A		4	3	32	((1S,2R,4R)-2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(5-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone
10B		3937	3200	5148	((1R,2S,4S)-2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(5-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone
11			10	12	(±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(2-(thiophen-2-yl)phenyl)methanone
12A			177	339	((1S*,2R*,4R*)-2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(2-(thiophen-2-yl)phenyl)methanone
12B			3	5	((1R*,2S*,4S*)-2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(2-(thiophen-2-yl)phenyl)methanone

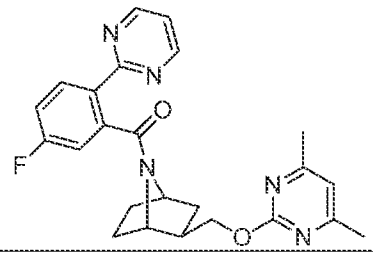
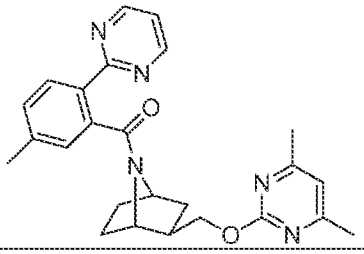
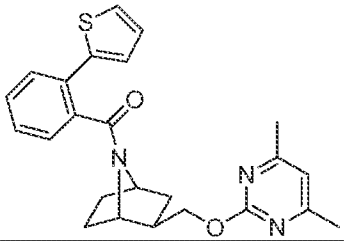
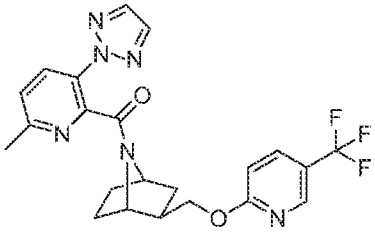
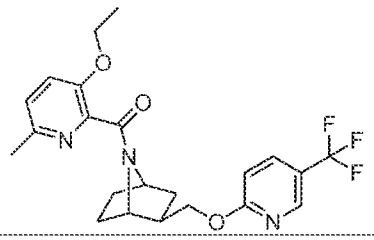
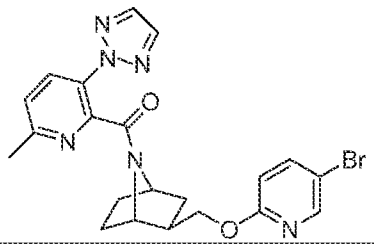
13			118	109	(±)-(5-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((4-(trifluoromethyl)pyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
14			50	71	(±)-(5-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((5-(trifluoromethyl)pyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
15			56	120	(±)-(5-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((3-(trifluoromethyl)pyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
16			20	42	(±)-(5-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((6-(trifluoromethyl)pyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
17			41	69	(±)-(5-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((4-methylpyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
18			12	44	(±)-(5-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((6-methylpyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

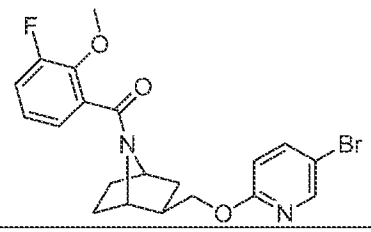
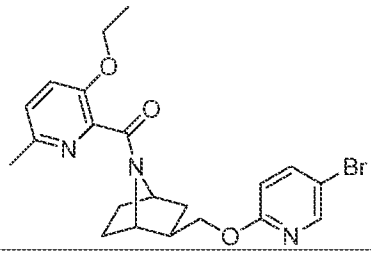
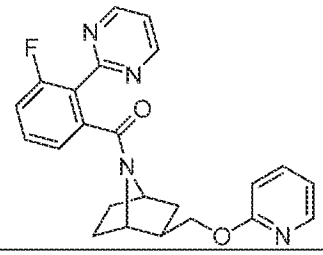
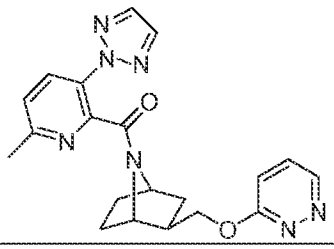
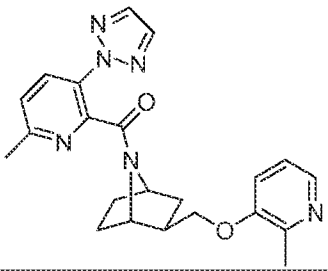
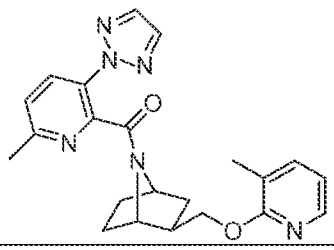
19			12	44	(±)-(5-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((5-methylpyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
20			270	364	(±)-(2-(((3,6-dimethylpyrazin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(5-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone
21			300	487	(±)-(5-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((3-(trifluoromethyl)quinoxalin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
22			47	50	(±)- (2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
23			322	1500	(±)-2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(quinolin-8-yl)methanone
24			122	164	(±)-2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(naphthalen-1-yl)methanone
25			74	160	(±)-2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(2-methylnaphthalen-1-yl)methanone

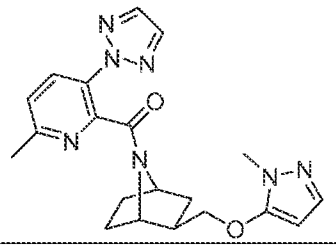
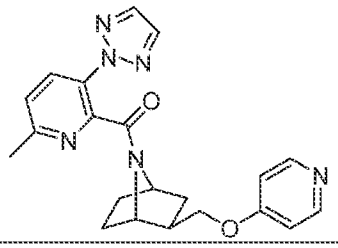
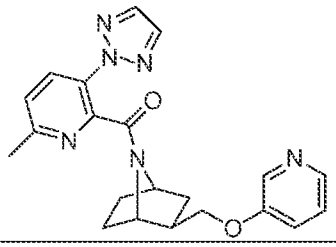
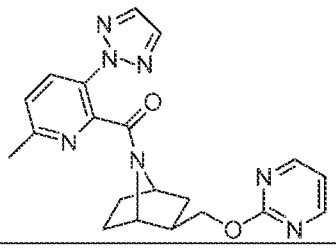
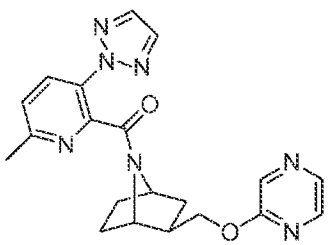
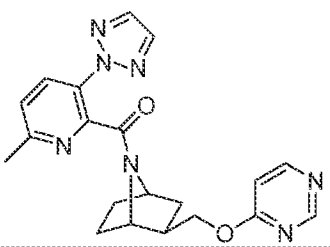
26			117	394	(±)-2-(1H-pyrazol-1-yl)phenyl)(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
27			677	380	(±)-2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(3-phenylfuran-2-yl)methanone
28			14	11	(±)-(2-ethoxynaphthalen-1-yl)(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
29			11	60	(±)-(5-(2-fluorophenyl)-2-methylthiazol-4-yl)(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
30			47	149	(±)-(5-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
31			33	122	(±)-(2-fluoro-6-(pyrimidin-2-yl)phenyl)(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

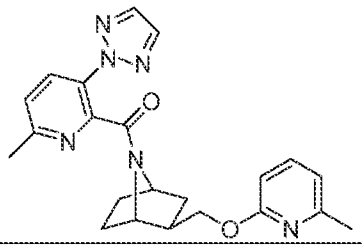
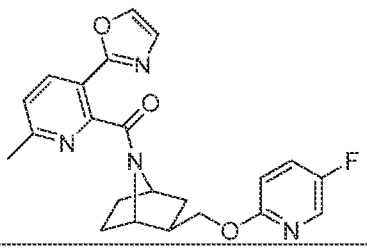
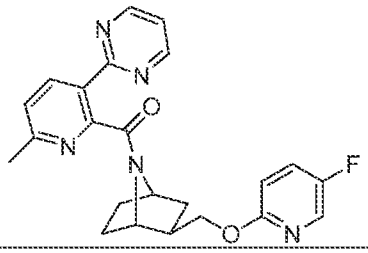
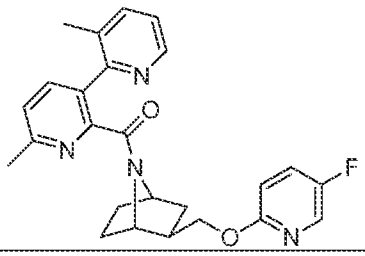
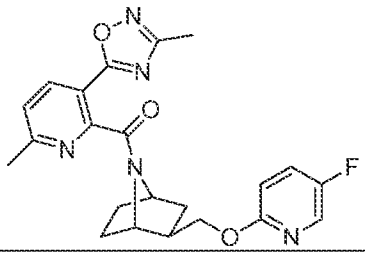
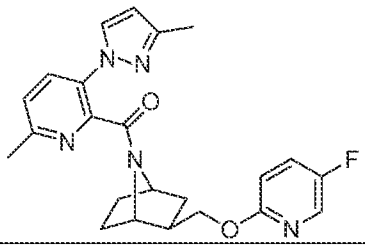
32			21	123	(±)-(5-fluoro-2-(pyrimidin-2-yl)phenyl)(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
33		15	9	39	(±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(5-methyl-2-(pyrimidin-2-yl)phenyl)methanone
34			60	467	(±)-(2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((quinoxalin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
35		69	58	693	(±)-(2-fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl)(2-((quinoxalin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
36			70	107	(±)-(5-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((quinoxalin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
37			300	487	(±)-(5-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((quinoxalin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

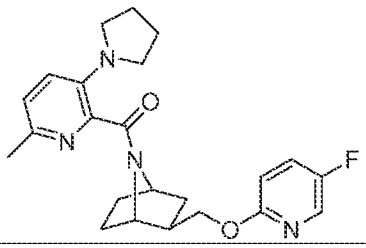
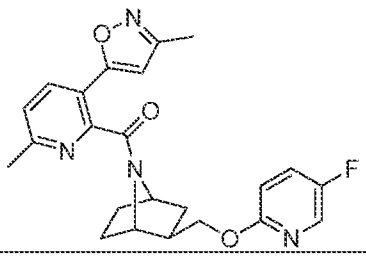
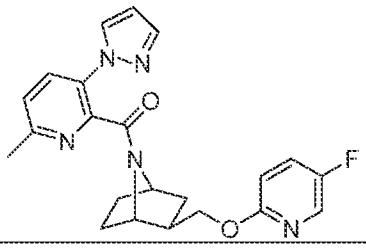
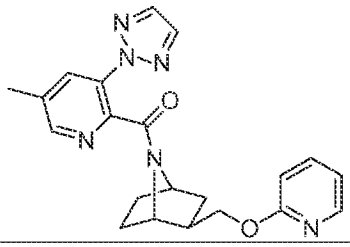
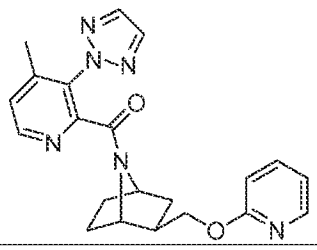
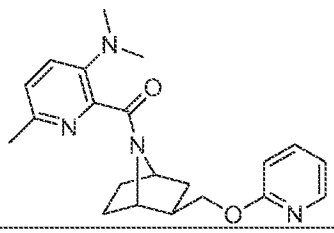
38			120	383	(±)-(5-methyl-2-(pyrimidin-2-yl)phenyl)(2-((quinoxalin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
39			29	27	(±)-(2-(((4,6-dimethylpyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(5-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone
40			5000	1203	(±)-2-(((4,6-dimethylpyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(3-methyl-5-phenylisoxazol-4-yl)methanone
41			35	22	(±)-(2-(((4,6-dimethylpyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(2-ethoxynaphthalen-1-yl)methanone
42			1277	253	(±)-(2-(((4,6-dimethylpyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(2-ethoxyphenyl)methanone)
43			222	92	(±)-(2-(((4,6-dimethylpyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(2-fluoro-6-(pyrimidin-2-yl)phenyl)methanone

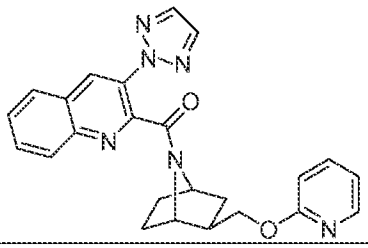
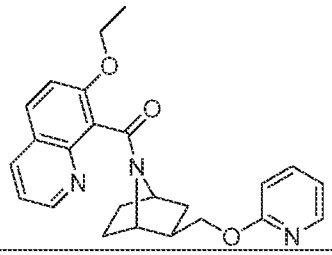
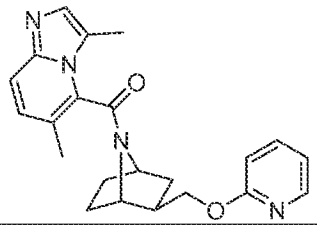
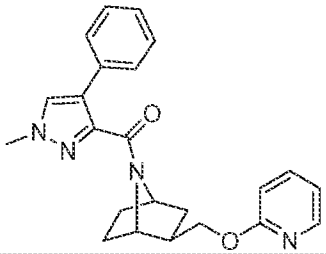
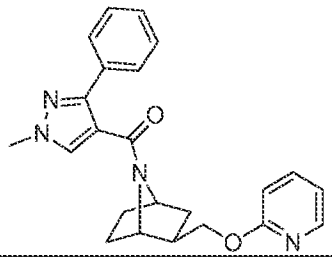
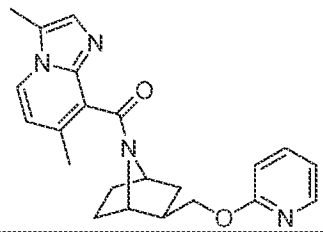
44			400	104	(±)-(2-(((4,6-dimethylpyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(5-fluoro-2-(pyrimidin-2-yl)phenyl)methanone
45			79	59	(±)-(2-(((4,6-dimethylpyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(5-methyl-2-(pyrimidin-2-yl)phenyl)methanone
46			82	10	(±)-(2-(((4,6-dimethylpyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(2-(thiophen-2-yl)phenyl)methanone
47		460		418	(±)-(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-(((5-(trifluoromethyl)pyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
48		3900		4700	(±)-(3-ethoxy-6-methylpyridin-2-yl)(2-(((5-(trifluoromethyl)pyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
49		81	69	192	(±)-(2-(((5-bromopyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)methanone

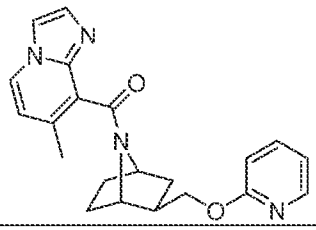
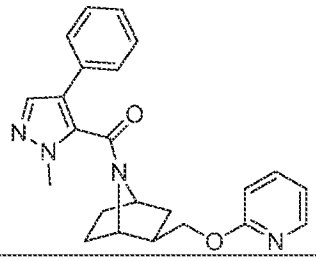
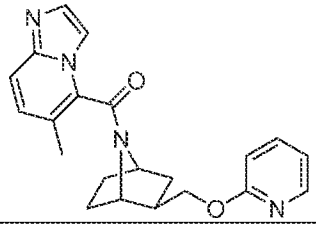
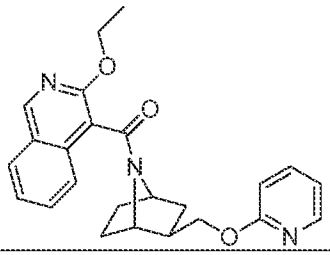
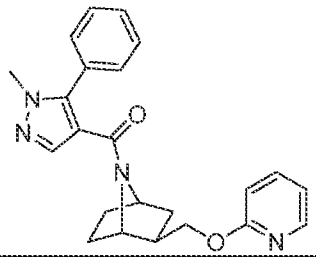
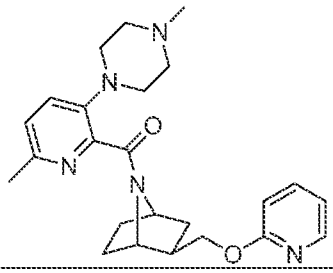
50		460		4399	(±)-(2-(((5-bromopyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-methoxyphenyl)methanone
51		974		1800	(±)-(2-(((5-bromopyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(3-ethoxy-6-methylpyridin-2-yl)methanone
52		350		2300	(±)-(3-fluoro-2-(pyrimidin-2-yl)phenyl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
53		2200		>10000	(±)-(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-((pyridazin-3-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
54		3500		2200	(±)-(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-(((2-methylpyridin-3-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
55		119	150	202	(±)-(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-(((3-methylpyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

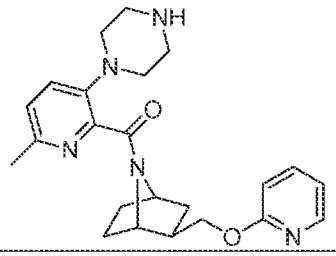
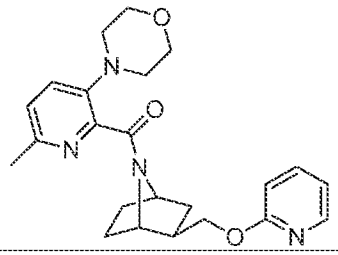
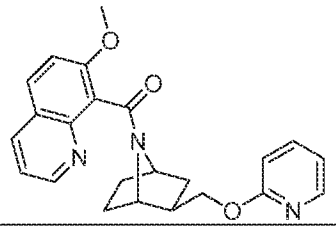
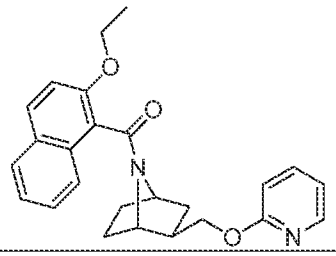
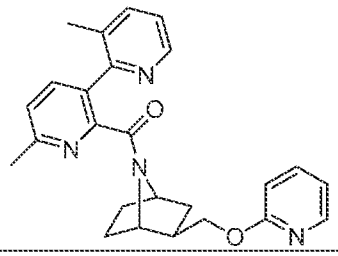
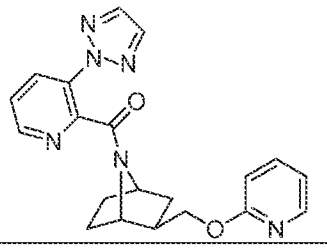
56		>10000		>10000	(±)-(2-(((1-methyl-1H-pyrazol-5-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)methanone
57		1000		7300	(±)-(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-((pyridin-4-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
58		88	117	2400	(±)-(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-((pyridin-3-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
59		2600		4900	(±)-(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-((pyrimidin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
60		7800		>10000	(±)-(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-((pyrazin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
61		2800		>10000	(±)-(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2- ((pyrimidin-4-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

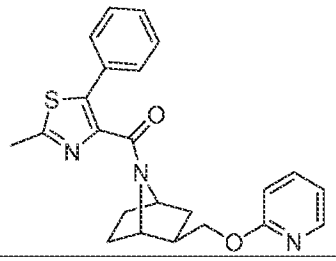
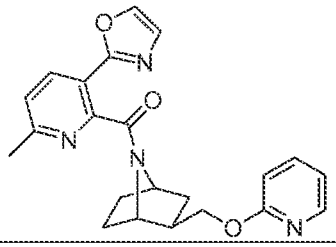
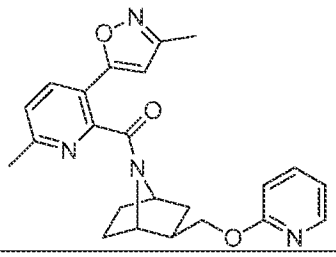
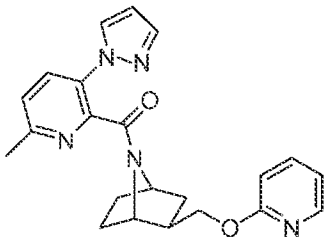
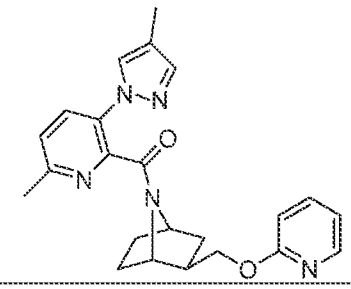
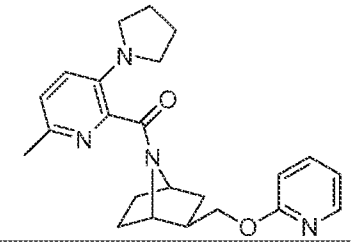
62		74	46	188	(±)-(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-(((6-methylpyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
63		25	25	339	(±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(oxazol-2-yl)pyridin-2-yl)methanone
64		18	24	81	(±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(pyrimidin-2-yl)pyridin-2-yl)methanone
65		1440		6200	(±)-(3,6'-dimethyl-[2,3'-bipyridin]-2'-yl)(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
66		197	293	620	(±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(3-methyl-1,2,4-oxadiazol-5-yl)pyridin-2-yl)methanone
67		48	69	258	(±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(3-methyl-1H-pyrazol-1-yl)pyridin-2-yl)methanone

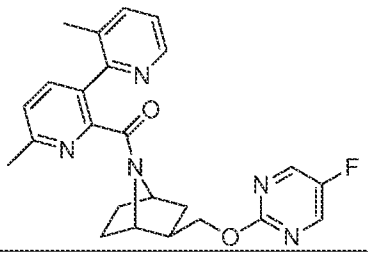
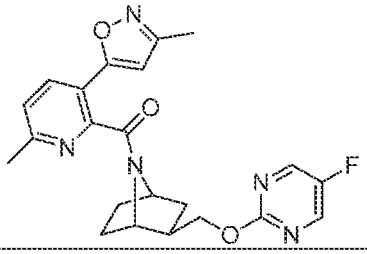
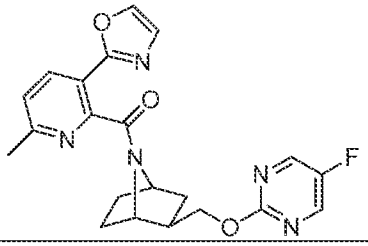
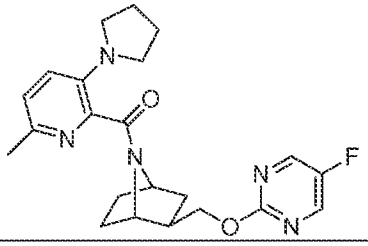
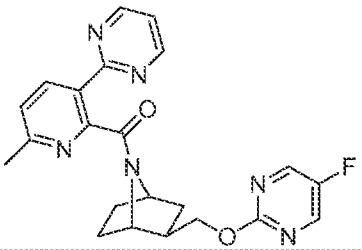
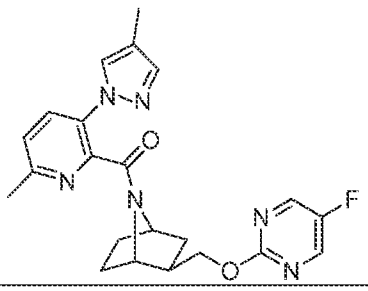
68		27	22	576	(±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(pyrrolidin-1-yl)pyridin-2-yl)methanone
69		40	64	174	(±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(3-methylisoxazol-5-yl)pyridin-2-yl)methanone
70		88	62	624	(±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(1H-pyrazol-1-yl)pyridin-2-yl)methanone
71		1200		3700	(±)-(5-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
72		137	162	2400	(±)- (4-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
73		278		7900	(±)-(3-(dimethylamino)-6-methylpyridin-2-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

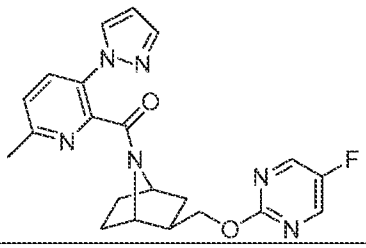
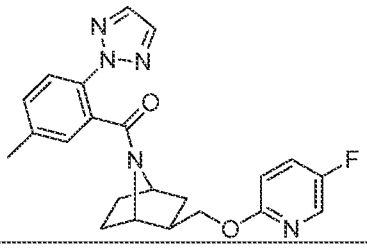
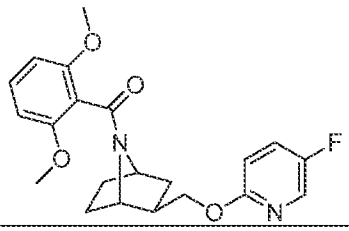
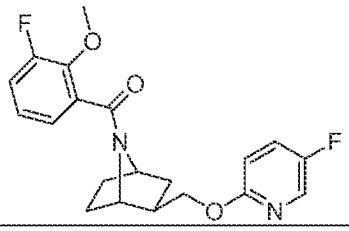
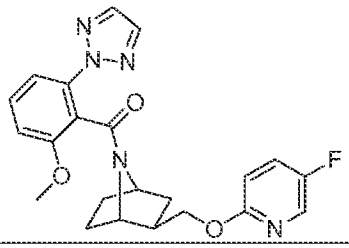
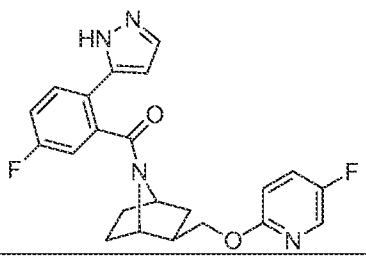
74		359		1700	(±)-(3-(2H-1,2,3-triazol-2-yl)quinolin-2-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
75		18	7	220	(±)-(7-ethoxyquinolin-8-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
76		>10000		>10000	(±)-(3,6-dimethylimidazo[1,2-a]pyridin-5-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
77		103	66	867	(±)-(1-methyl-4-phenyl-1H-pyrazol-3-yl)((1S,2R,4R)-2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
78		418		3100	(±)-(1-methyl-3-phenyl-1H-pyrazol-4-yl)((1S,2R,4R)-2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
79		2400		8500	(±)-((3,7-dimethylimidazo[1,2-a]pyridin-8-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

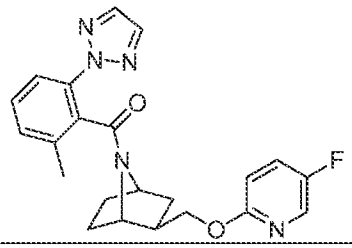
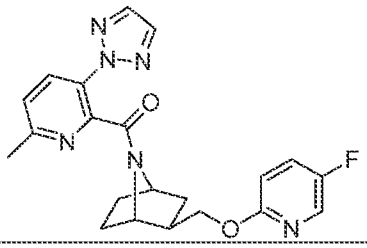
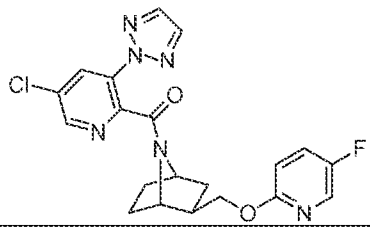
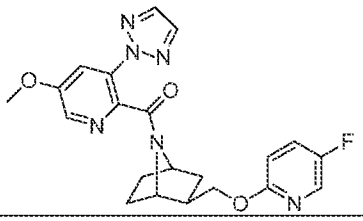
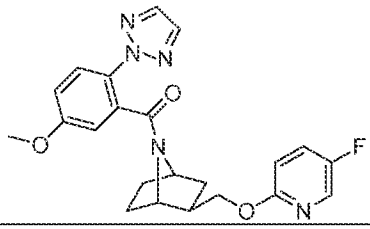
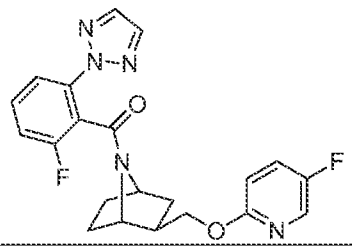
80		1100		>10000	(±)-(7-methylimidazo[1,2-a]pyridin-8-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
81		916		2900	(±)-(1-methyl-4-phenyl-1H-pyrazol-5-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
82		>10000		>10000	(±)-((6-methylimidazo[1,2-a]pyridin-5-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
83		17	12	271	(±)-(3-ethoxyisoquinolin-4-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
84		2600		9701	(±)-(1-methyl-5-phenyl-1H-pyrazol-4-yl)(-2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
85		>10000		>10000	(±)-(6-methyl-3-(4-methylpiperazin-1-yl)pyridin-2-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

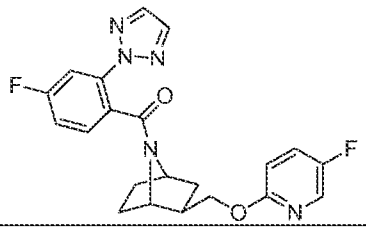
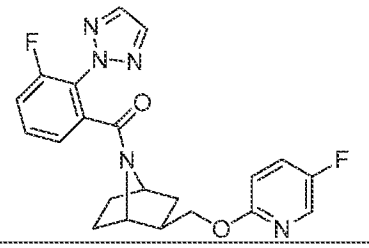
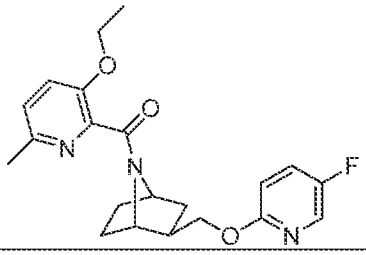
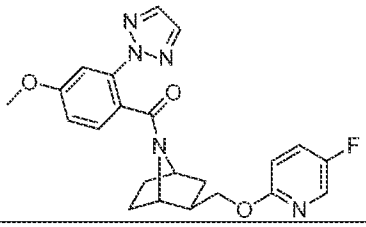
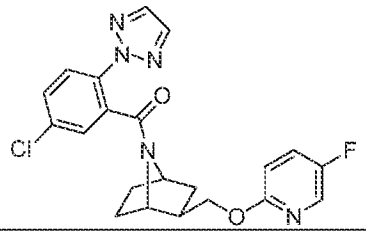
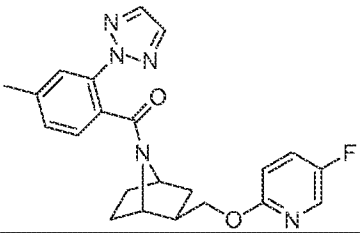
86		>10000		>10000	(±)-(6-methyl-3-(piperazin-1-yl)pyridin-2-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
87		4200		>10000	(±)-(6-methyl-3-morpholinopyridin-2-yl)((1S,2R,4R)-2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
88		47	49	690	(±)-(7-methoxyquinolin-8-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
89		11	10	38	(±)-(2-ethoxynaphthalen-1-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
90		3000		>10000	(±)-(3,6'-dimethyl-[2,3'-bipyridin]-2'-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
91		624		3300	(±)-(3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

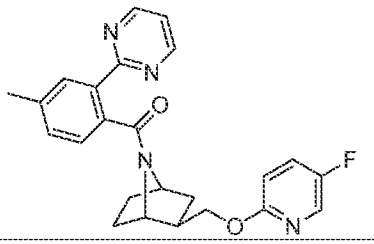
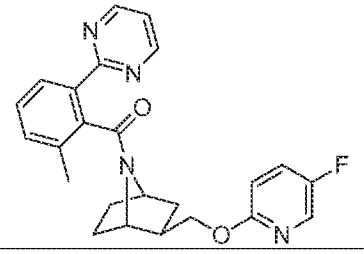
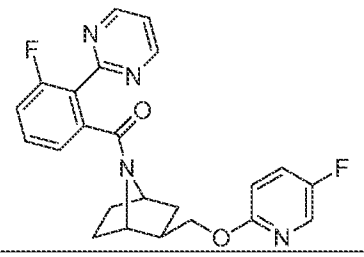
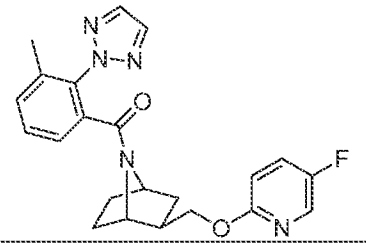
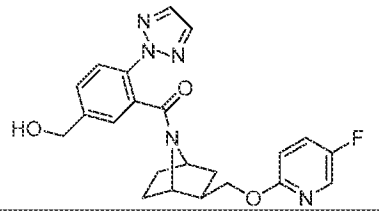
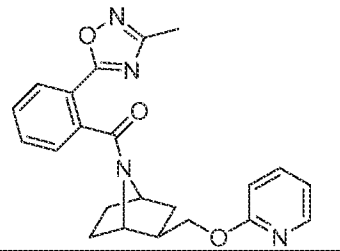
92		20	11	218	(±)-(2-methyl-5-phenylthiazol-4-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
93		40	73	836	(±)-(6-methyl-3-(oxazol-2-yl)pyridin-2-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
94		170	200	2100	(±)-(6-methyl-3-(3-methylisoxazol-5-yl)pyridin-2-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
95		247		3700	(±)-(6-methyl-3-(1H-pyrazol-1-yl)pyridin-2-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
96		70	76	950	(±)-(6-methyl-3-(4-methyl-1H-pyrazol-1-yl)pyridin-2-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
97		35	32	840	(±)-(6-methyl-3-(pyrrolidin-1-yl)pyridin-2-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

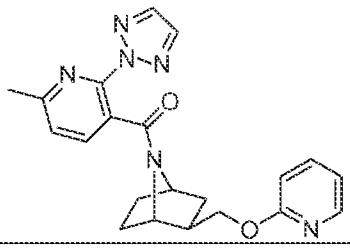
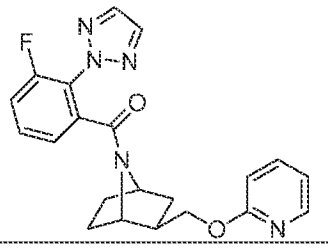
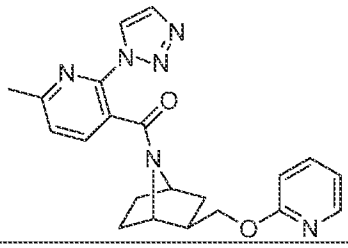
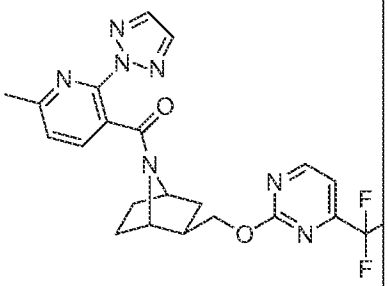
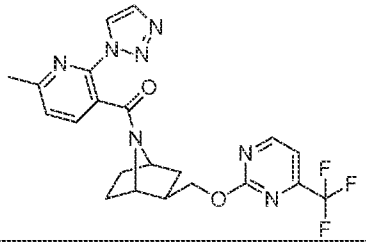
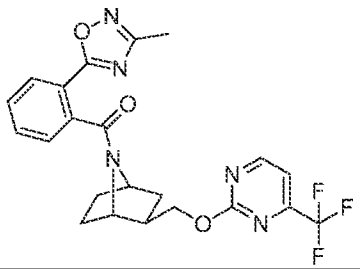
98		>10000		>10000	(±)-(3,6'-dimethyl-[2,3'-bipyridin]-2'-yl)(2-(((5-fluoropyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
99		1500		2900	(±)-(2-(((5-fluoropyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(3-methylisoxazol-5-yl)pyridin-2-yl)methanone
100		950		1800	(±)-(2-(((5-fluoropyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(oxazol-2-yl)pyridin-2-yl)methanone
101		650		1200	(±)-(2-(((5-fluoropyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(pyrrolidin-1-yl)pyridin-2-yl)methanone
102					(±)-(2-(((5-fluoropyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(pyrimidin-2-yl)pyridin-2-yl)methanone
103		1700		3600	(±)-(2-(((5-fluoropyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(4-methyl-1H-pyrazol-1-yl)pyridin-2-yl)methanone

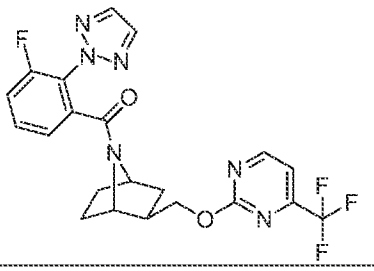
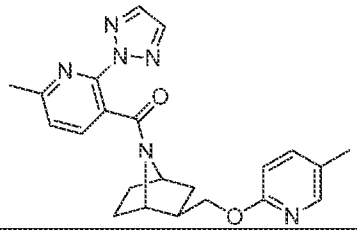
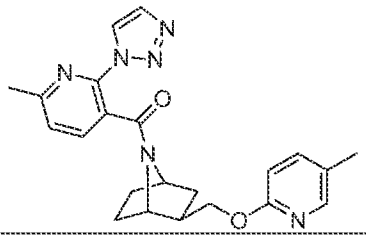
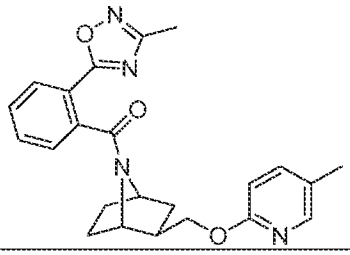
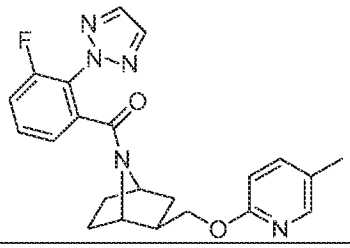
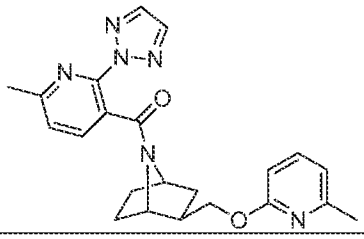
104		1100		4600	(±)-(2-(((5-fluoropyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(1H-pyrazol-1-yl)pyridin-2-yl)methanone
105					(±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(5-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone
106		300		154	(±)-(2,6-dimethoxyphenyl)(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
107		440		2200	(±)-((3-fluoro-2-methoxyphenyl)(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
108		10	12	12	(±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(2-methoxy-6-(2H-1,2,3-triazol-2-yl)phenyl)methanone
109		29	20	99	(±)-(5-fluoro-2-(1H-pyrazol-5-yl)phenyl)(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

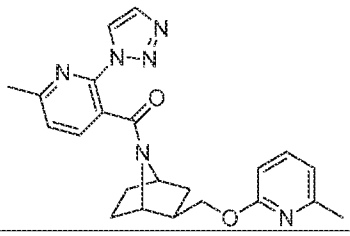
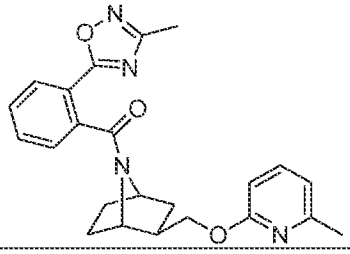
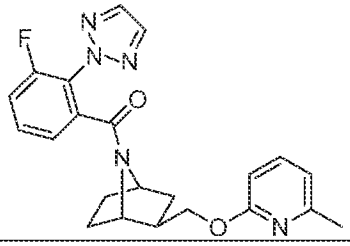
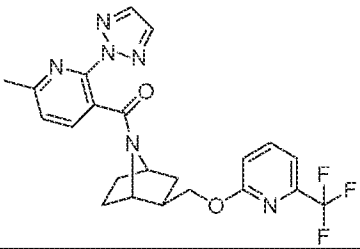
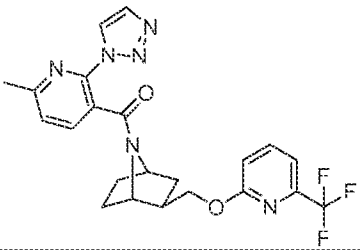
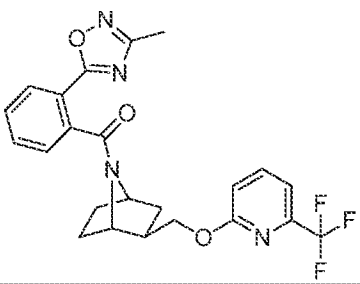
110		54	67	94	(±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(2-methyl-6-(2H-1,2,3-triazol-2-yl)phenyl)methanone
111		19	19	198	(±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)methanone
112		480		1000	(±)-(5-chloro-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
113		3400		4800	(±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(5-methoxy-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)methanone
114		20	48	73	(±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(5-methoxy-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone
115		57	78	108	(±)-(2-fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

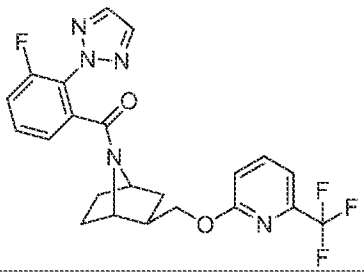
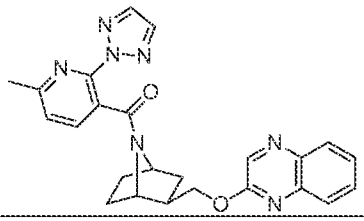
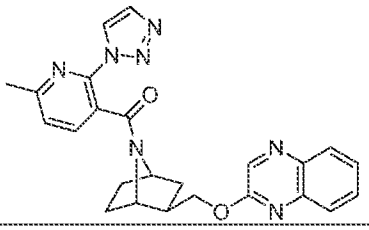
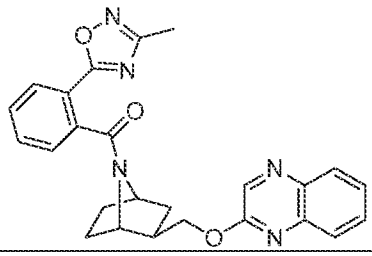
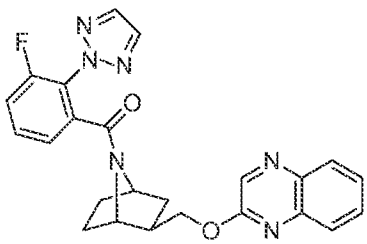
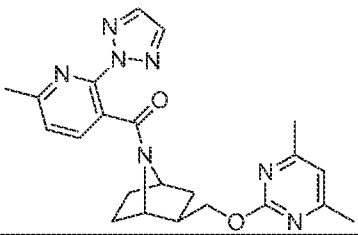
116		142	250	315	(±)-(4-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
117		62	82	245	(±)-(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
118		440		2200	(±)-(3-ethoxy-6-methylpyridin-2-yl)(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
119		500		1300	(±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(4-methoxy-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone
120		15	14	124	(±)-(5-chloro-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
121		78	68	340	(±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(4-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone

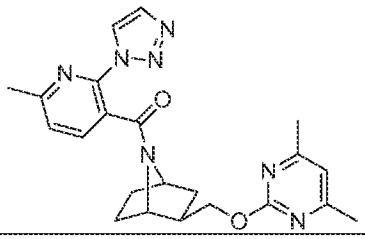
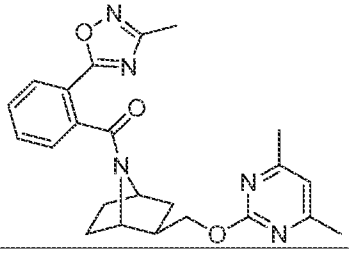
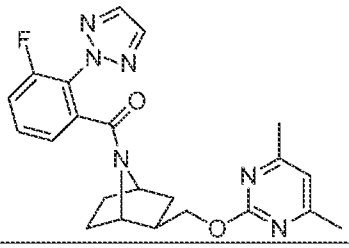
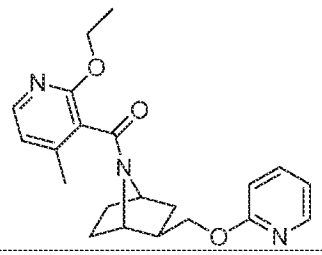
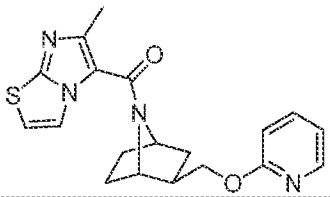
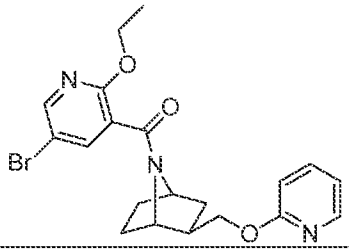
122		118	154	1000	(±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(4-methyl-2-(pyrimidin-2-yl)phenyl)methanone
123		400		286	(±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(2-methyl-6-(pyrimidin-2-yl)phenyl)methanone
124		83	52	355	(±)-(3-fluoro-2-(pyrimidin-2-yl)phenyl)(-2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
125		47	29	132	(±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(3-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone
126		23	27	231	(±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(5-(hydroxymethyl)-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone
127			190	1100	(±)-(2-(3-methyl-1,2,4-oxadiazol-5-yl)phenyl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

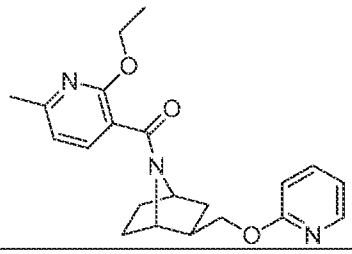
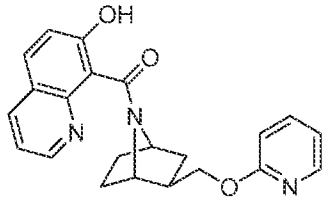
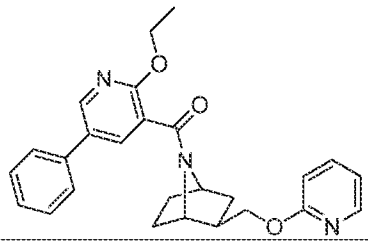
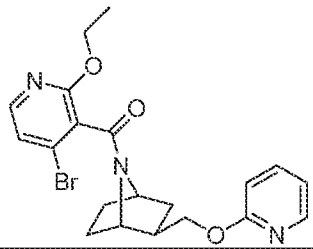
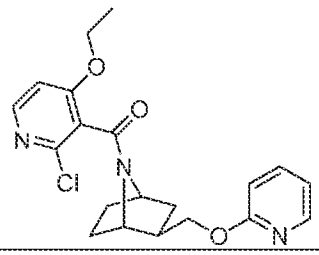
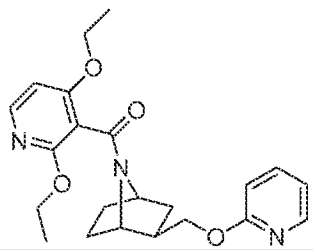
128			5700	10000	(±)-(6-methyl-2-(2H-1,2,3-triazol-2-yl)pyridin-3-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
129			190	1000	(±)-(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
130			3700	7199	(±)-(6-methyl-2-(1H-1,2,3-triazol-1-yl)pyridin-3-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
131			10000	10000	(±)-(6-methyl-2-(2H-1,2,3-triazol-2-yl)pyridin-3-yl)(2-(((4-(trifluoromethyl)pyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
132			10000	7399	(±)-(6-methyl-2-(1H-1,2,3-triazol-1-yl)pyridin-3-yl)(2-(((4-(trifluoromethyl)pyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
133			1400	950	(±)-(2-(3-methyl-1,2,4-oxadiazol-5-yl)phenyl)(2-(((4-(trifluoromethyl)pyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

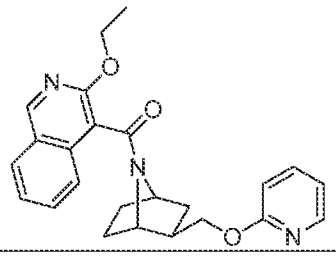
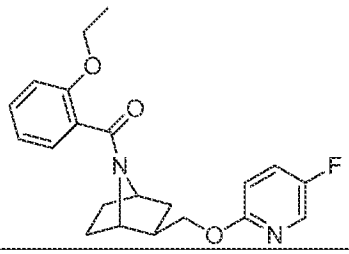
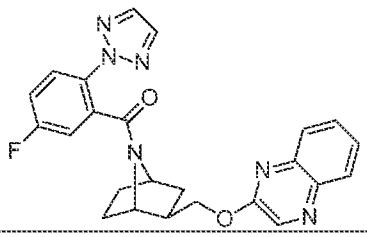
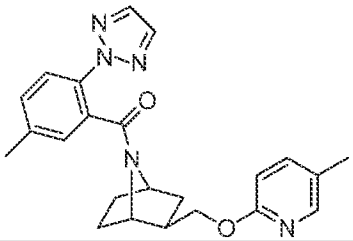
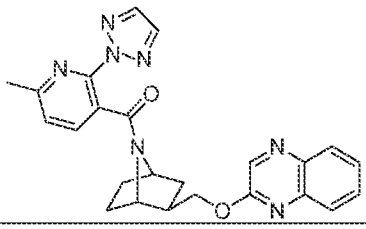
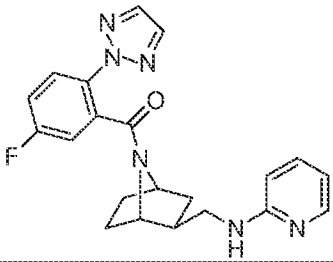
134			1500	690	(±)-(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((4-(trifluoromethyl)pyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
135			5400	3900	(±)-(6-methyl-2-(2H-1,2,3-triazol-2-yl)pyridin-3-yl)(2-(((5-methylpyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
136			6800	1200	(±)-(6-methyl-2-(1H-1,2,3-triazol-1-yl)pyridin-3-yl)(2-(((5-methylpyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
137			950	425	(±)-(2-(3-methyl-1,2,4-oxadiazol-5-yl)phenyl)(2-(((5-methylpyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
138			606	250	(±)-(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((5-methylpyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
139			4399	6500	(±)-(6-methyl-2-(2H-1,2,3-triazol-2-yl)pyridin-3-yl)(2-(((6-methylpyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

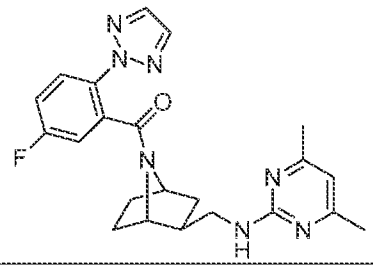
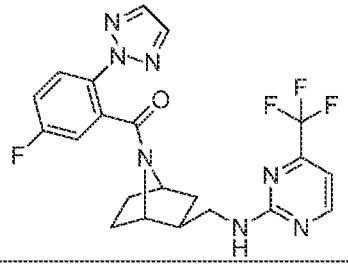
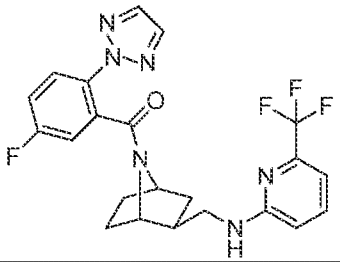
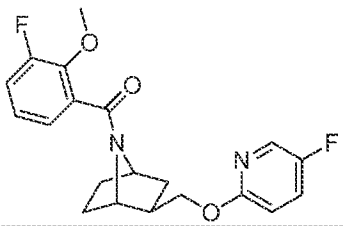
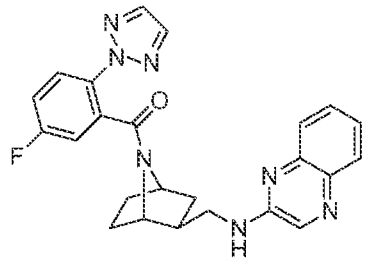
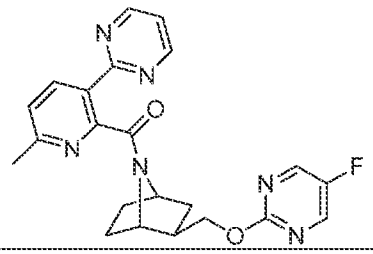
140			3100	2300	(±)-(6-methyl-2-(1H-1,2,3-triazol-1-yl)pyridin-3-yl)(2-(((6-methylpyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
141			280	300	(±)-(2-(3-methyl-1,2,4-oxadiazol-5-yl)phenyl)(2-(((6-methylpyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
142			207	300	(±)-(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((6-methylpyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
143			3900	4600	(±)-(6-methyl-2-(2H-1,2,3-triazol-2-yl)pyridin-3-yl)(2-(((6-(trifluoromethyl)pyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
144			3600	3200	(±)-(6-methyl-2-(1H-1,2,3-triazol-1-yl)pyridin-3-yl)(2-(((6-(trifluoromethyl)pyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
145			340	330	(±)-(2-(3-methyl-1,2,4-oxadiazol-5-yl)phenyl)(2-(((6-(trifluoromethyl)pyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

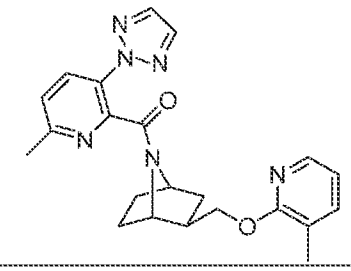
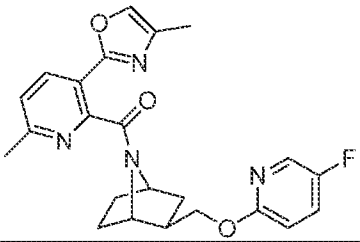
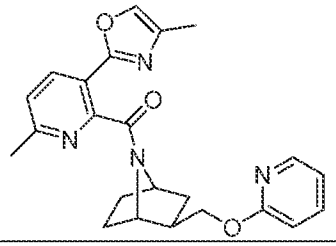
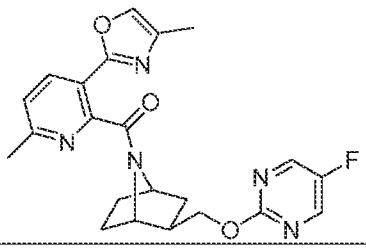
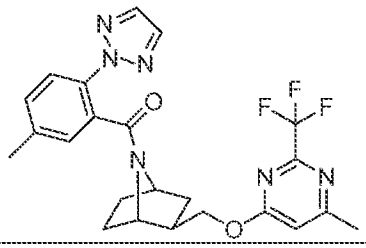
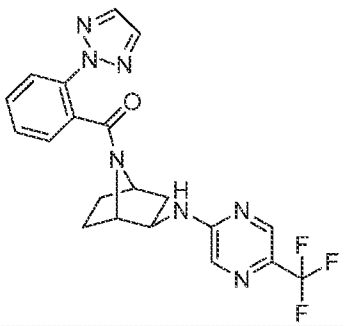
146			180	196	(±)-(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((6-(trifluoromethyl)pyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
147					(±)-(6-methyl-2-(2H-1,2,3-triazol-2-yl)pyridin-3-yl)(2-((quinoxalin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
148			6299	3200	(±)-(6-methyl-2-(1H-1,2,3-triazol-1-yl)pyridin-3-yl)(2-((quinoxalin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
149			220	2000	(±)-(2-(3-methyl-1,2,4-oxadiazol-5-yl)phenyl)(2-((quinoxalin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
150			180	990	(±)-(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((quinoxalin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
151			10000	10000	(±)-(2-(((4,6-dimethylpyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-2-(2H-1,2,3-triazol-2-yl)pyridin-3-yl)methanone

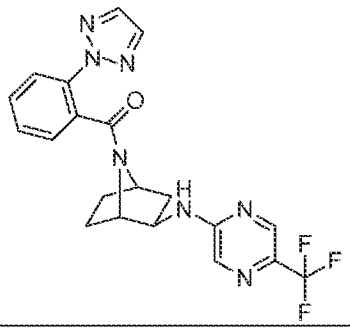
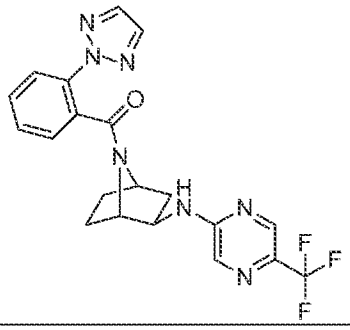
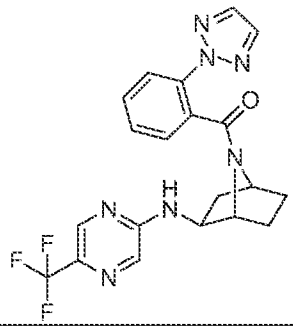
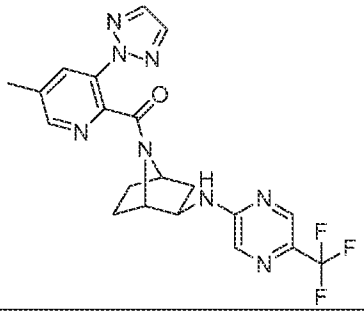
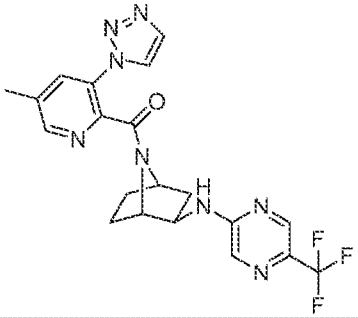
152			10000	5899	(±)-(2-(((4,6-dimethylpyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-2-(1H-1,2,3-triazol-1-yl)pyridin-3-yl)methanone
153			1100	440	(±)-(2-(((4,6-dimethylpyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(2-(3-methyl-1,2,4-oxadiazol-5-yl)phenyl)methanone
154			690	300	(±)-(2-(((4,6-dimethylpyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone
155		1570		3600	(±)-(2-ethoxy-4-methylpyridin-3-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
156		>10000		>10000	(±)-(6-methylimidazo[2,1-b]thiazol-5-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
157		94	134	537	(±)-(5-bromo-2-ethoxypyridin-3-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

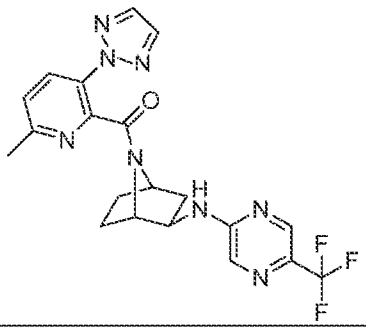
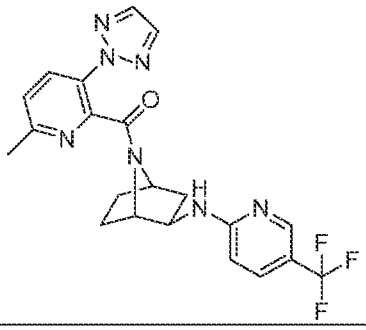
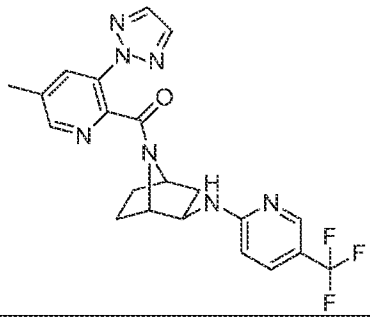
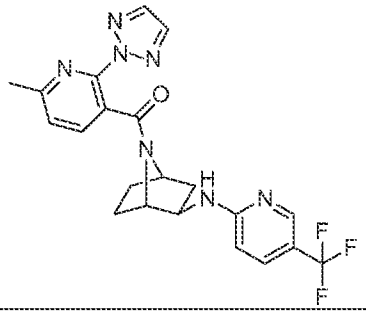
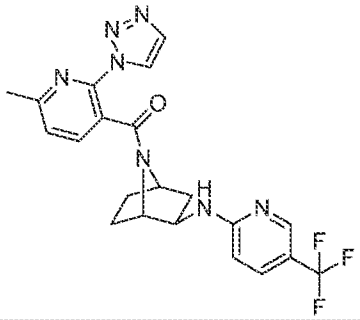
158		2930		1780	(±)-(2-ethoxy-6-methylpyridin-3-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
159		262		786	(±)-(7-hydroxyquinolin-8-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
160		8700		>10000	(±)-(2-ethoxy-5-phenylpyridin-3-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
161		478		1450	(±)-(4-bromo-2-ethoxypyridin-3-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
162		8500		>10000	(±)-(2-chloro-4-ethoxypyridin-3-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
163		150	153	150	(±)-(2,4-diethoxypyridin-3-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

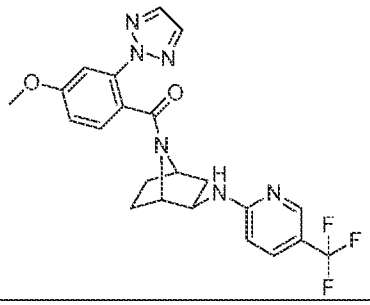
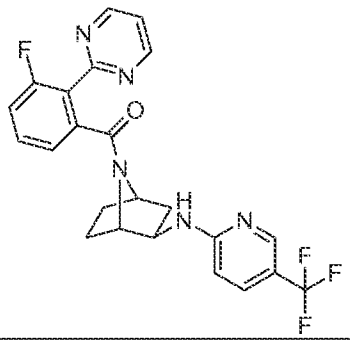
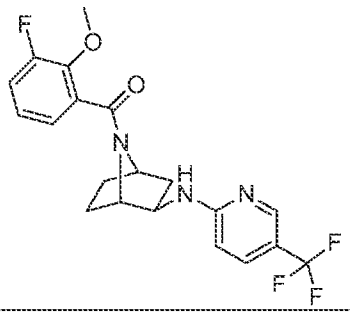
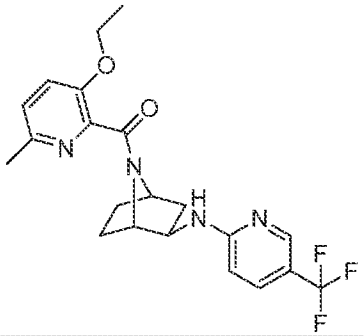
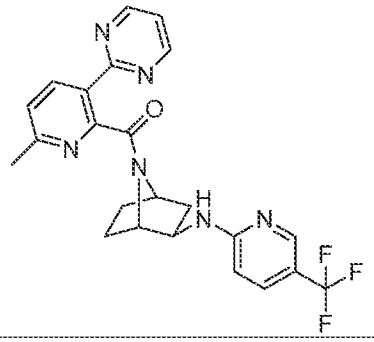
164		9	7	195	(3-ethoxyisoquinolin-4-yl)((1S,2R,4R)-2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
165			409	550	(±)-(2-ethoxyphenyl)(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
166			106	1141	(±)-(5-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((quinoxalin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
167			9	14	(±)-5-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((5-methylpyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
168			2300	7300	(±)-(6-methyl-2-(2H-1,2,3-triazol-2-yl)pyridin-3-yl)(2-((quinoxalin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
169			8999	2526	(±)-(5-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((pyridin-2-ylamino)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

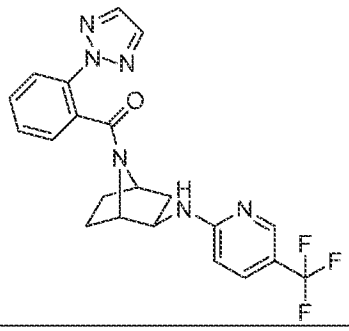
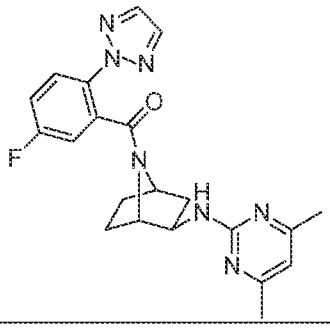
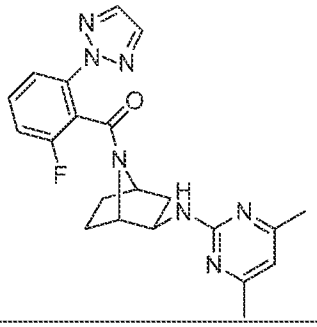
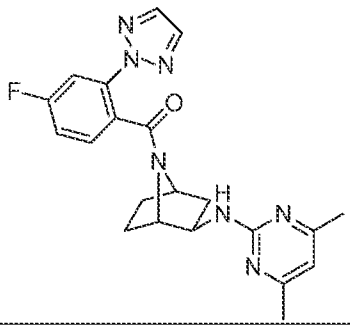
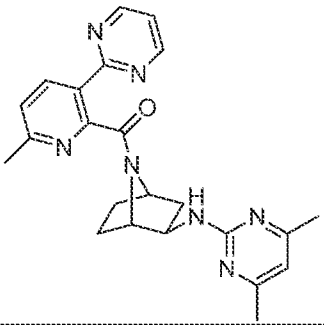
170			1965	512	(±)-(2-(((4,6-dimethylpyrimidin-2-yl)amino)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(5-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone
171			1935		(±)-(5-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((4-(trifluoromethyl)pyrimidin-2-yl)amino)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
172			686		(±)-(5-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((6-(trifluoromethyl)pyridin-2-yl)amino)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
173		1260		3000	(±)-(3-fluoro-2-methoxyphenyl)(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
174		373		1000	(±)-(5-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((quinoxalin-2-ylamino)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
175		2500		4000	(±)-(2-(((5-fluoropyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(pyrimidin-2-yl)pyridin-2-yl)methanone

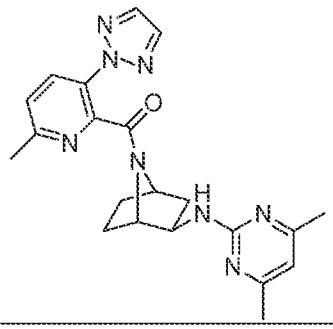
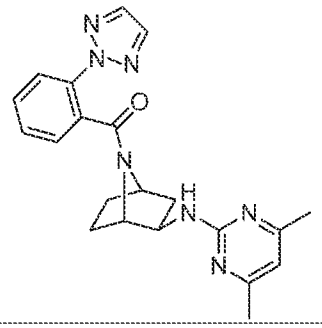
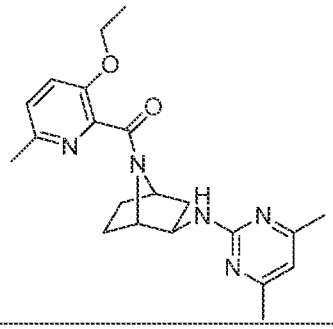
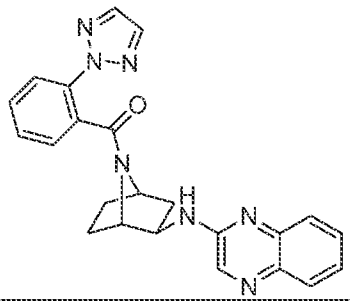
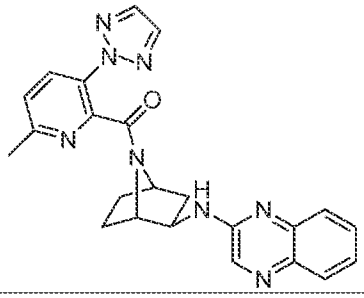
176		119	150	202	(±)-(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-(((3-methylpyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
177		535		4000	(±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(4-methyloxazol-2-yl)pyridin-2-yl)methanone
178		964		>10000	(6-methyl-3-(4-methyloxazol-2-yl)pyridin-2-yl)((1S,2R,4R)-2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
179					((1S,2R,4R)-2-(((5-fluoropyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(4-methyloxazol-2-yl)pyridin-2-yl)methanone
180			33	32	(±)-(5-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((6-methyl-2-(trifluoromethyl)pyrimidin-4-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
181		34	28	700	(2-(2H-1,2,3-triazol-2-yl)phenyl)(1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

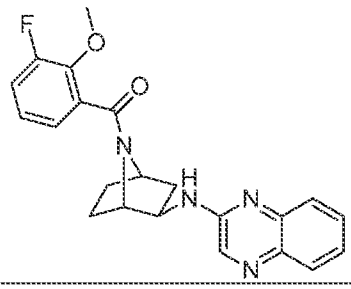
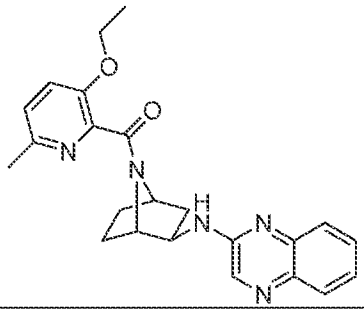
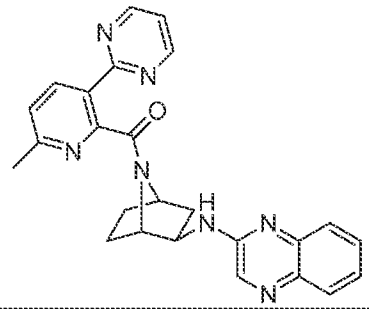
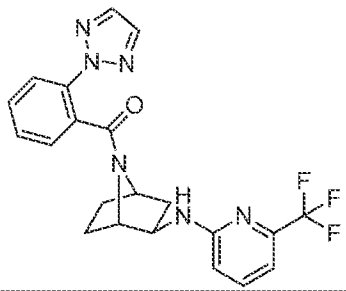
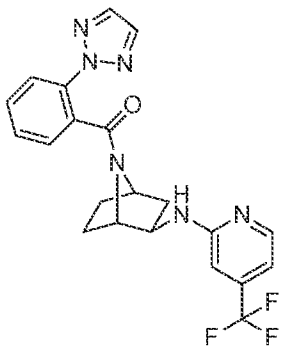
182		47	38	1100	(±)-((2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
183 a		>10000		>10000	(2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
183 b		34	28	700	(2-(2H-1,2,3-triazol-2-yl)phenyl)((1R,2S,4S)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
184		189	349	4100	(±)-(5-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
185		1500		2700	(±)-(5-methyl-3-(1H-1,2,3-triazol-1-yl)pyridin-2-yl)(2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

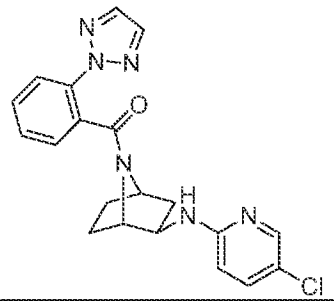
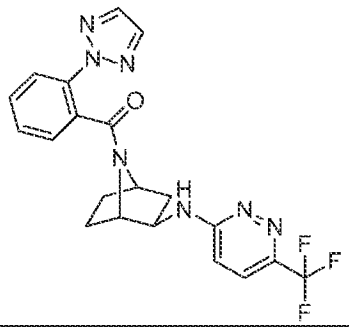
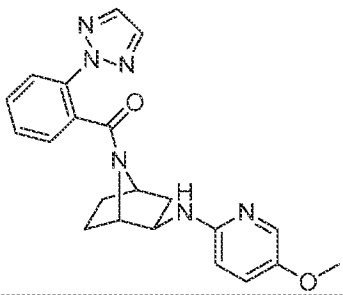
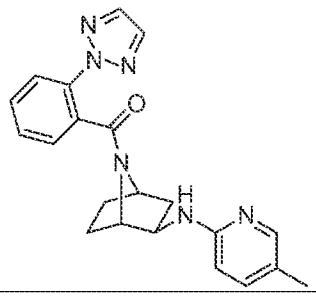
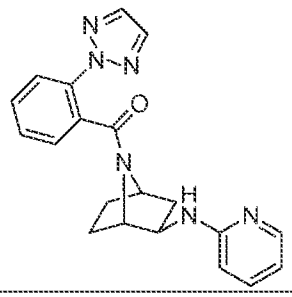
186		134	164	1200	(±)-(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
187		81	48	620	(±)-(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
188		295		1500	(±)-(5-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
189		766		1500	(±)-(6-methyl-2-(2H-1,2,3-triazol-2-yl)pyridin-3-yl)(2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
190		589		1200	(±)-(6-methyl-2-(1H-1,2,3-triazol-1-yl)pyridin-3-yl)(2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

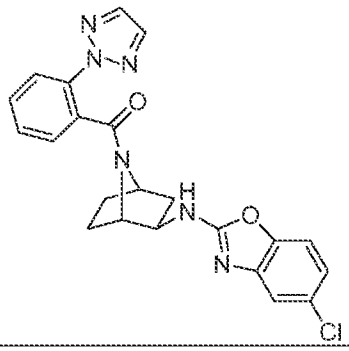
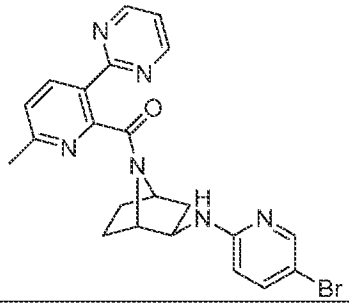
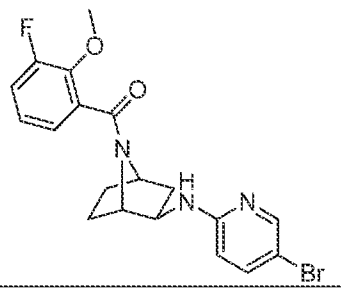
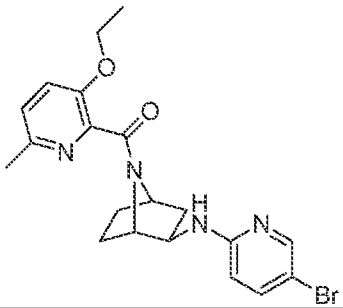
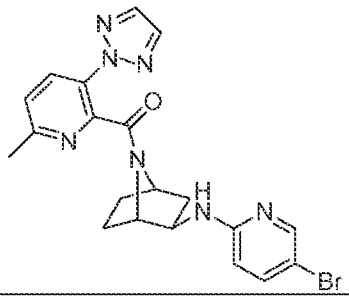
191		257		8800	(±)-(4-methoxy-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
192		60	52	1500	(±)-(3-fluoro-2-(pyrimidin-2-yl)phenyl)(2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
193		2900		>10000	(±)-((3-fluoro-2-methoxyphenyl)(2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
194		450		800	(±)-(3-ethoxy-6-methylpyridin-2-yl)(2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
195		57	37	325	(±)-(6-methyl-3-(pyrimidin-2-yl)pyridin-2-yl)(2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

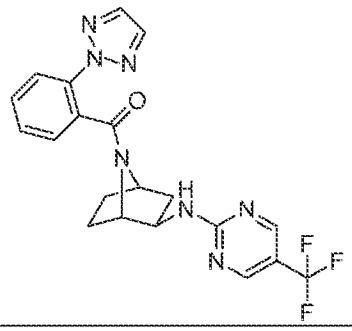
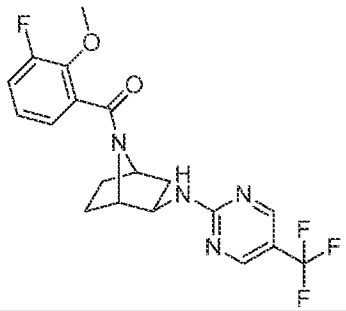
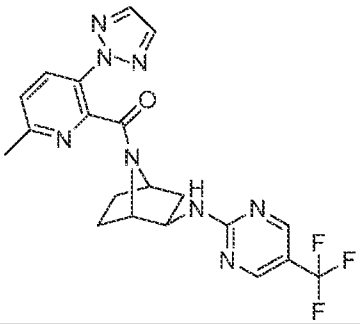
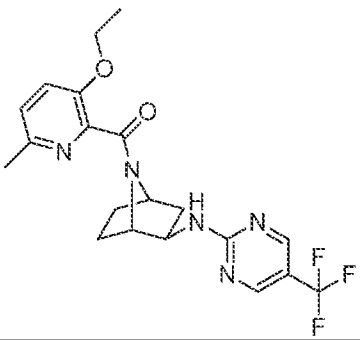
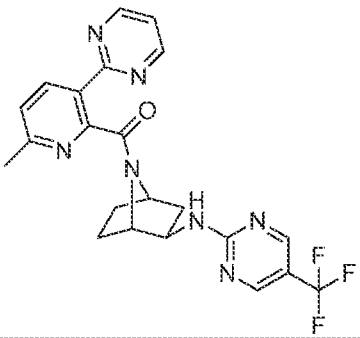
196		59	61	1500	(±)-(2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
197			8999	862	(±)-(2-((4,6-dimethylpyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(5-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone
198			1411	704	(±)-(2-((4,6-dimethylpyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(2-fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl)methanone
199			1634	553	(±)-(2-((4,6-dimethylpyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(4-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone
200		1100		552	(±)-(2-((4,6-dimethylpyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(pyrimidin-2-yl)pyridin-2-yl)methanone

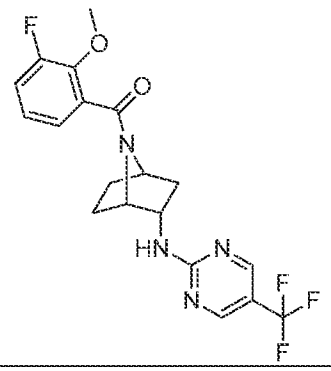
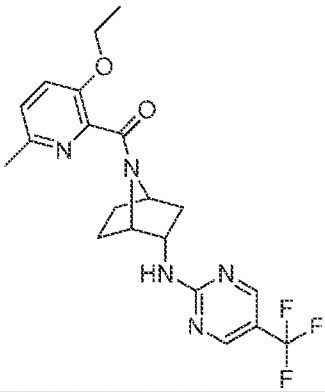
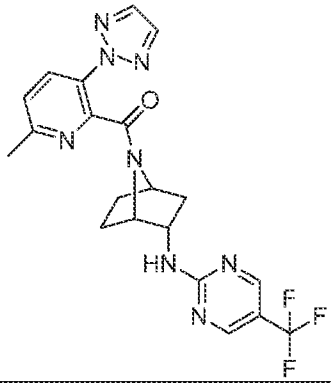
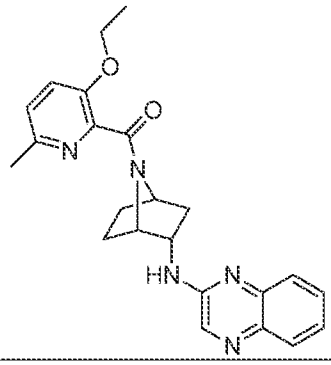
201		3700		1100	(±)-(2-((4,6-dimethylpyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)methanone
202		760		444	(±)-(2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((4,6-dimethylpyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
203		>10000		490	(±)-(2-((4,6-dimethylpyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-ethoxy-6-methylpyridin-2-yl)methanone
204		33	25	220	(±)-(2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(quinoxalin-2-ylamino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
205		79	50	168	(±)-(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-(quinoxalin-2-ylamino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

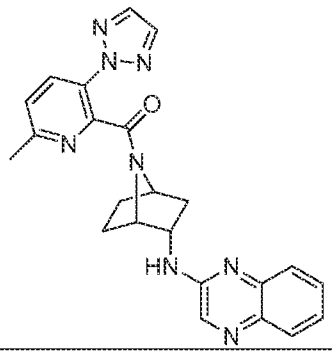
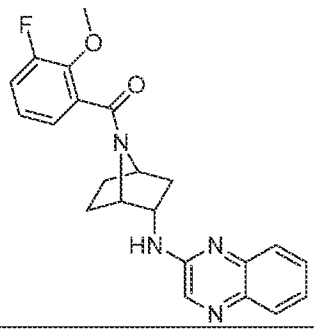
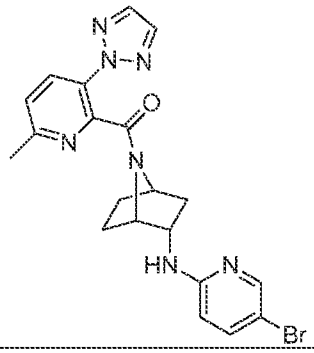
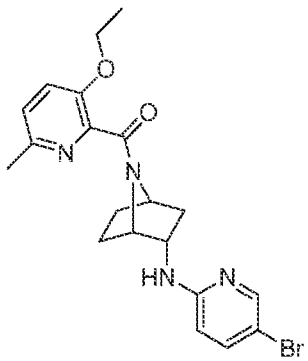
206		1200		1500	(±)-(3-fluoro-2-methoxyphenyl)(2-(quinoxalin-2-ylamino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
207		120	95	64	(±)-(3-ethoxy-6-methylpyridin-2-yl)(2-(quinoxalin-2-ylamino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
208		26	30	90	(±)-(6-methyl-3-(pyrimidin-2-yl)pyridin-2-yl)(2-(quinoxalin-2-ylamino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
209		1100		736	(±)-(2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((6-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
210		211		128	(±)-((2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((4-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

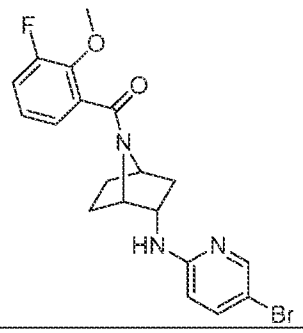
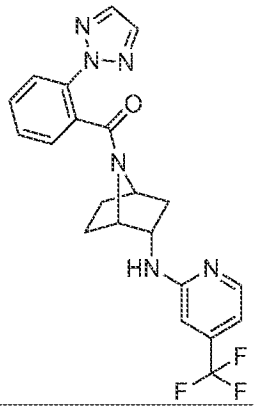
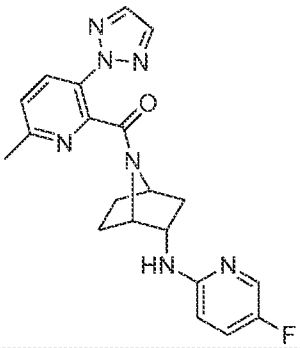
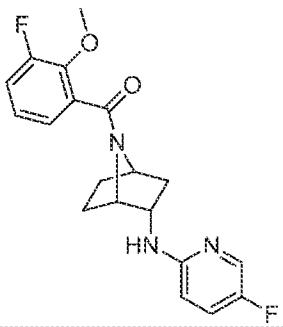
211		110	55	1800	(±)-(2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((5-chloropyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
212		734		4900	(±)-(2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((6-(trifluoromethyl)pyridazin-3-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
213		2800		7501	(±)-(2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((5-methoxypyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
214		500		3100	(±)-(2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((5-methylpyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
215		1700		8999	(±)-(2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(pyridin-2-ylamino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

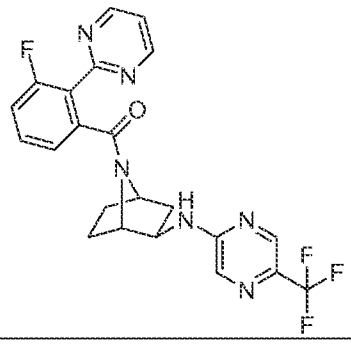
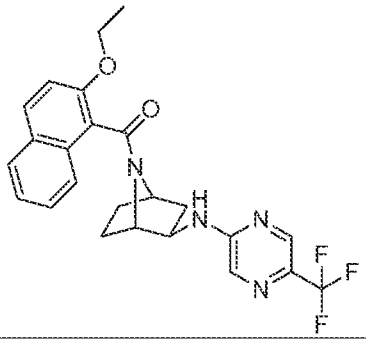
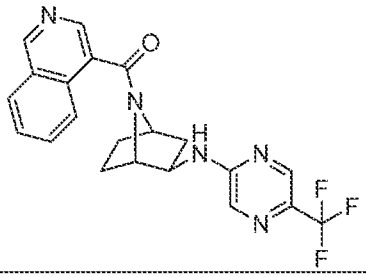
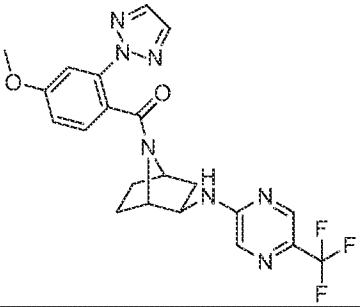
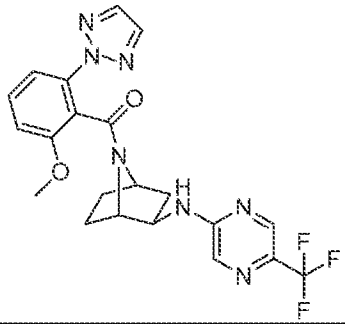
216		99	71	475	(±)-(2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((5-chlorobenzo[d]oxazol-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
217		59	40	770	(±)-(2-((5-bromopyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(pyrimidin-2-yl)pyridin-2-yl)methanone
218		2700		6700	(±)-(2-((5-bromopyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-methoxyphenyl)methanone
219		257		1700	(±)-(2-((5-bromopyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-ethoxy-6-methylpyridin-2-yl)methanone
220		38	26	1100	(±)-(2-((5-bromopyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)methanone

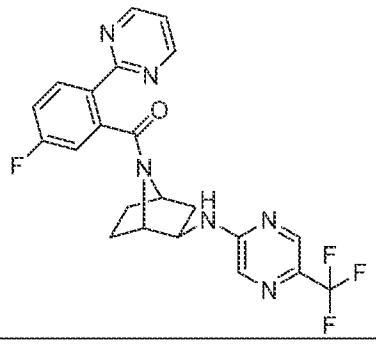
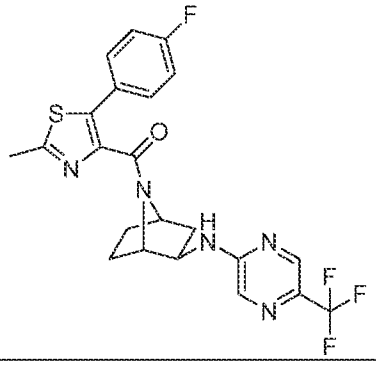
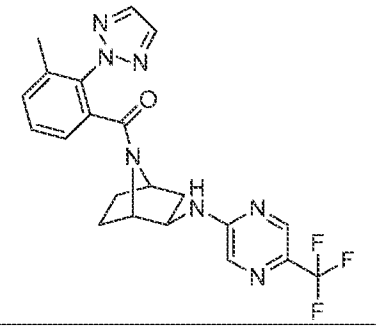
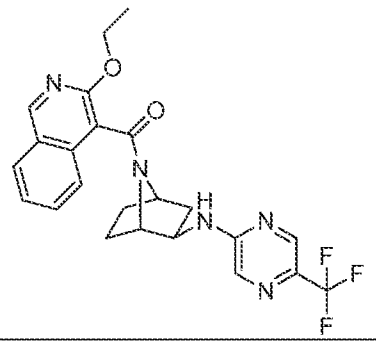
221		172	200	3300	(±)-(2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
222		4800		>10000	(±)-(3-fluoro-2-methoxyphenyl)(2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
223		550		4000	(±)-(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
224		2500		7399	(±)-(3-ethoxy-6-methylpyridin-2-yl)(2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
225		530		3300	(±)-(6-methyl-3-(pyrimidin-2-yl)pyridin-2-yl)(2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

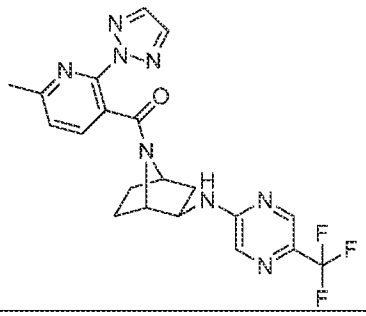
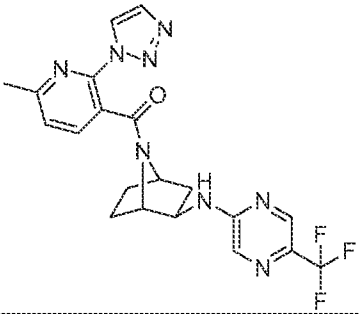
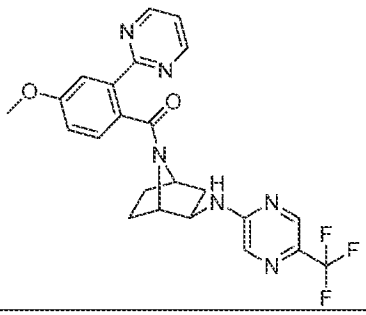
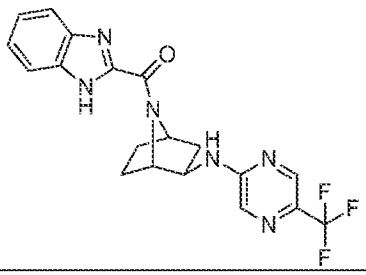
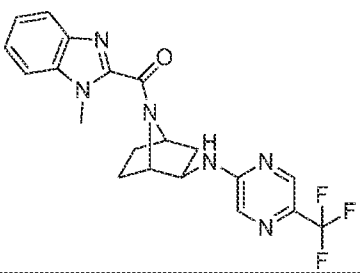
226		>10000		>10000	(±)-(3-fluoro-2-methoxyphenyl)(2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
227		>10000		>10000	(±)-(3-ethoxy-6-methylpyridin-2-yl)(2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
228		>10000		>10000	(±)-(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
229		>10000		>10000	(±)-(3-ethoxy-6-methylpyridin-2-yl)(2-(quinoxalin-2-ylamino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

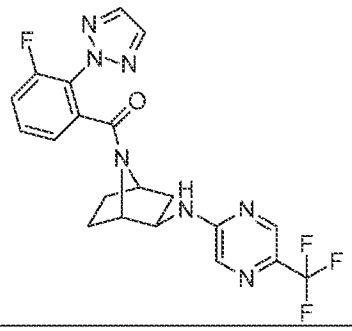
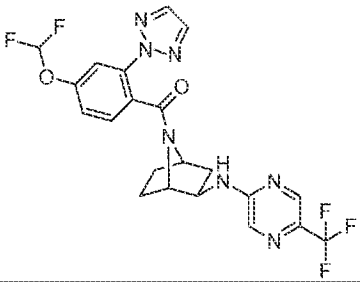
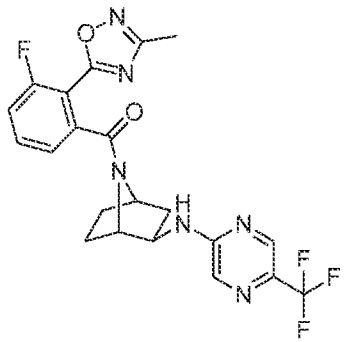
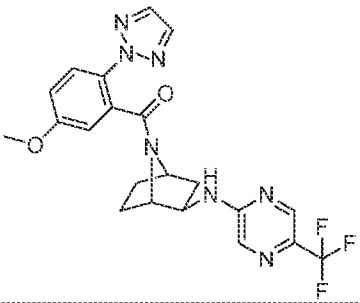
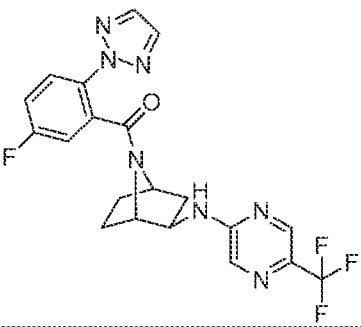
230		>10000		>10000	(±)-(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-(quinoxalin-2-ylamino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
231		>10000		>10000	(±)-(3-fluoro-2-methoxyphenyl)(2-(quinoxalin-2-ylamino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
232					(±)-(2-((5-bromopyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)methanone
233					(±)-(2-((5-bromopyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-ethoxy-6-methylpyridin-2-yl)methanone

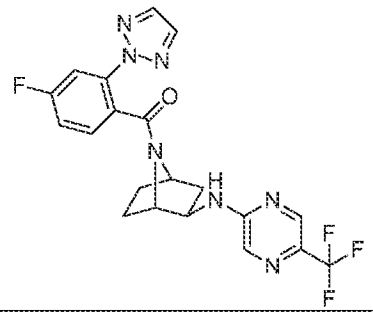
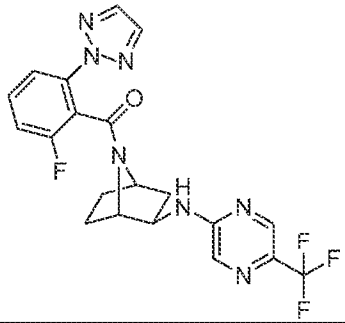
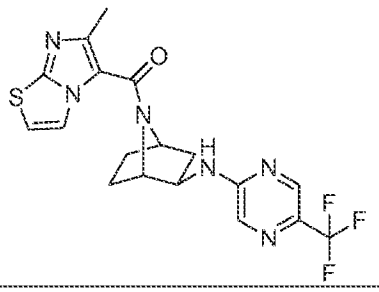
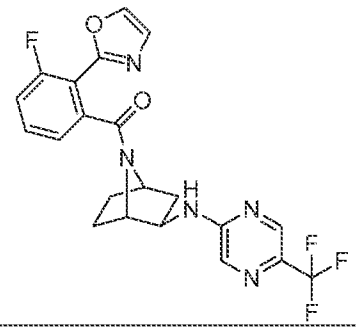
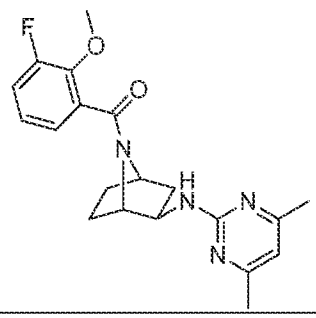
234					(±)-(2-((5-bromopyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-methoxyphenyl)methanone
235		>10000		>10000	(±)-((2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((4-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
236		>10000		>10000	(±)-(2-((5-fluoropyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)methanone
237		>10000		>10000	(±)-(3-fluoro-2-methoxyphenyl)(2-((5-fluoropyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

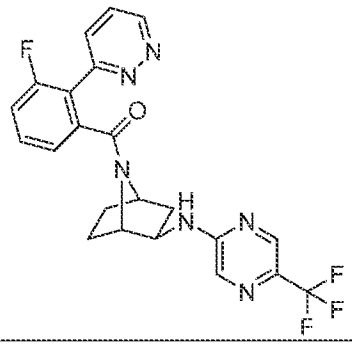
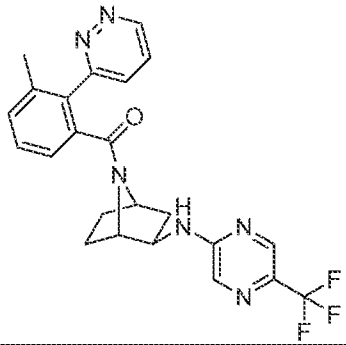
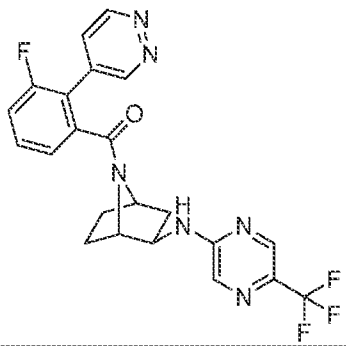
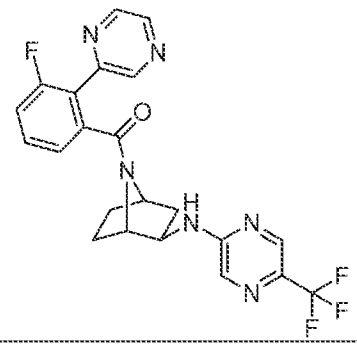
238		16	16	955	(3-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
239		22	19	490	(2-ethoxynaphthalen-1-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
240		400		2100	isoquinolin-4-yl((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
241		134	159	5064	(4-methoxy-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
242		31	41	239	(2-methoxy-6-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

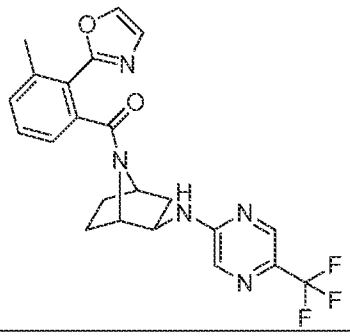
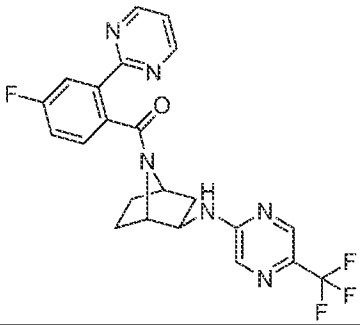
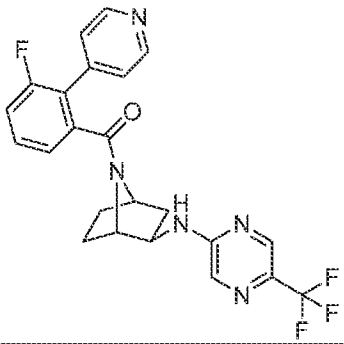
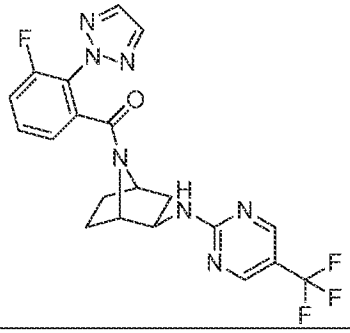
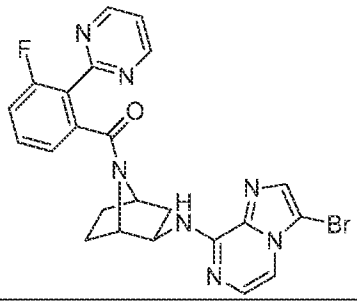
243		34	45	723	(5-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
244		74	46	235	(5-(4-fluorophenyl)-2-methylthiazol-4-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
245		10	7	288	(3-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
246		29	17	1022	(3-ethoxyisoquinolin-4-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

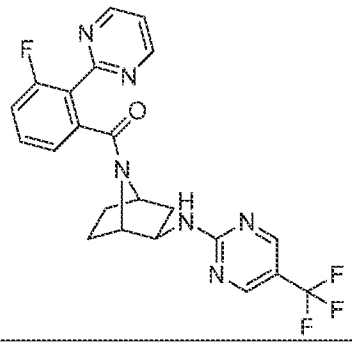
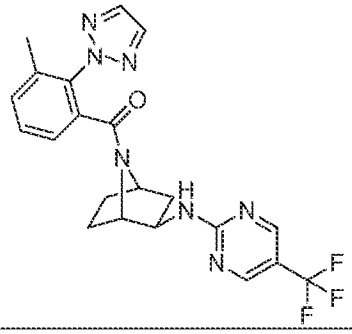
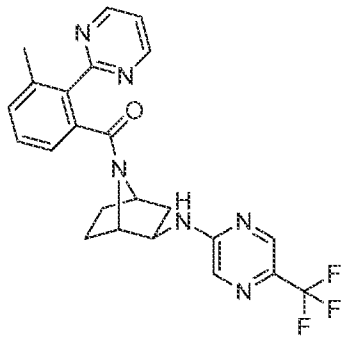
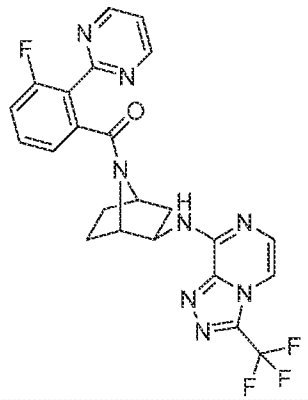
247		420		1130	(6-methyl-2-(2H-1,2,3-triazol-2-yl)pyridin-3-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
248		153	119	>10000	(6-methyl-2-(1H-1,2,3-triazol-1-yl)pyridin-3-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
249		57	54	5600	(4-methoxy-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
250		5649		>10000	(1H-benzo[d]imidazol-2-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
251		520		5300	(1-methyl-1H-benzo[d]imidazol-2-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

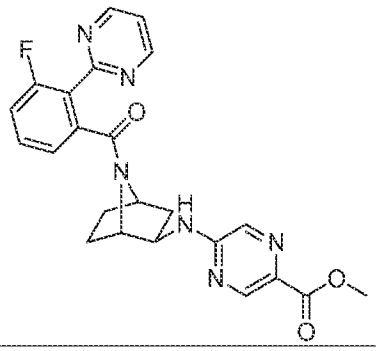
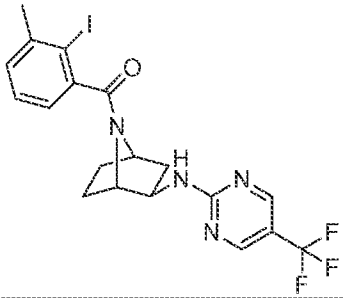
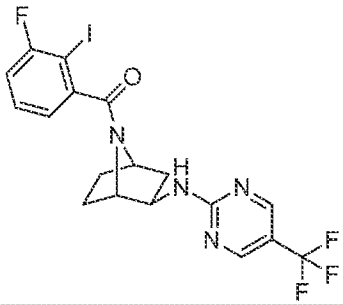
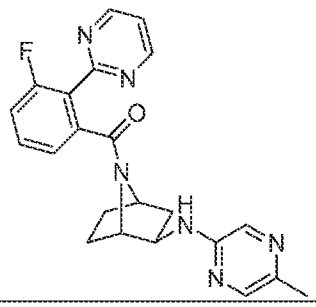
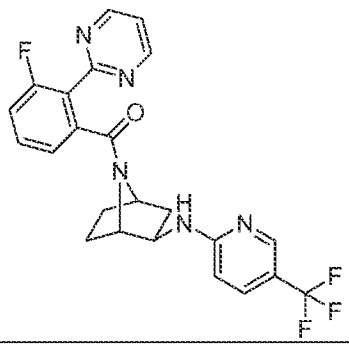
252		45	27	1230	(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
253		155	152	9601	(4-(difluoromethoxy)-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
254		23	20	377	(3-fluoro-2-(3-methyl-1,2,4-oxadiazol-5-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
255		32	29	265	(5-methoxy-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
256		84	60	1100	(5-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

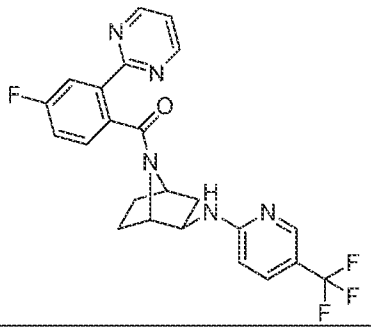
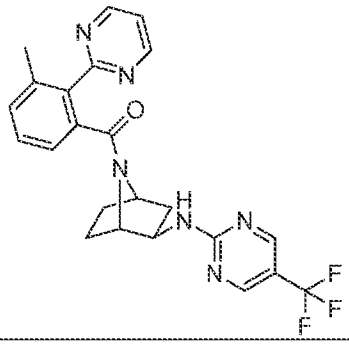
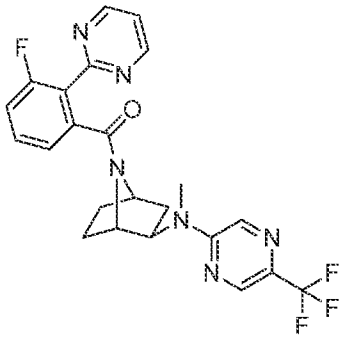
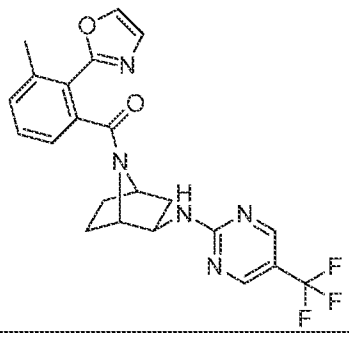
257		85	102	3200	(4-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
258		42	48	690	(2-fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
259		>10000		>10000	(6-methylimidazo[2,1-b]thiazol-5-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
260		14	10	519	(3-fluoro-2-(oxazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
261		>10000		5000	(2-((4,6-dimethylpyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-methoxyphenyl)methanone

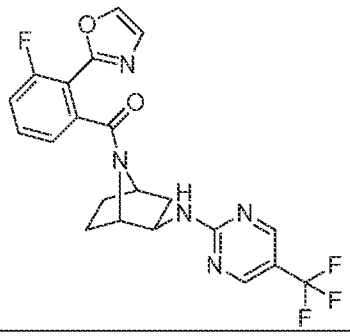
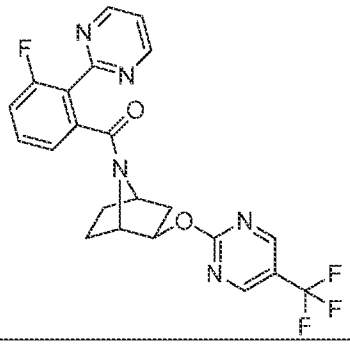
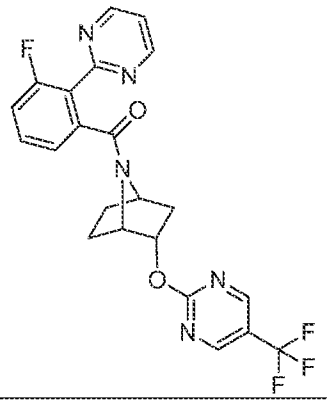
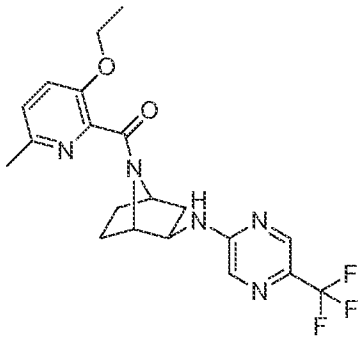
262		106	175	4200	(3-fluoro-2-(pyridazin-3-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
263		44	41	1100	(3-methyl-2-(pyridazin-3-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
264		1400		>10000	(3-fluoro-2-(pyridazin-4-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
265		20	23	188	(3-fluoro-2-(pyrazin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

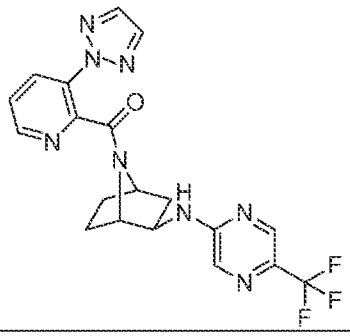
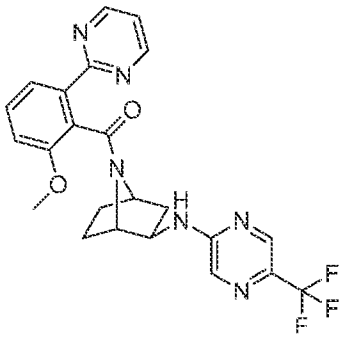
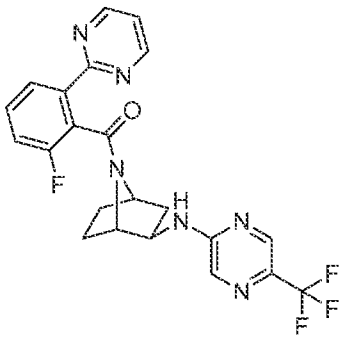
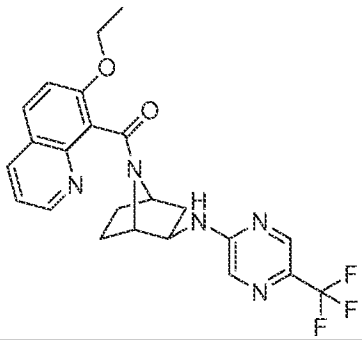
266		5	7	121	(3-methyl-2-(oxazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
267		33	61	1700	(4-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
268		450		3700	(3-fluoro-2-(pyridin-4-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
269		48	111	1700	(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
270		325		145	((1S,2R,4R)-2-((3-bromoimidazo[1,2-a]pyrazin-8-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-(pyrimidin-2-yl)phenyl)methanone

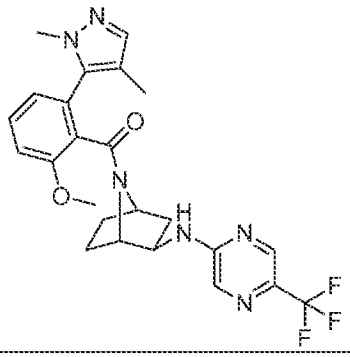
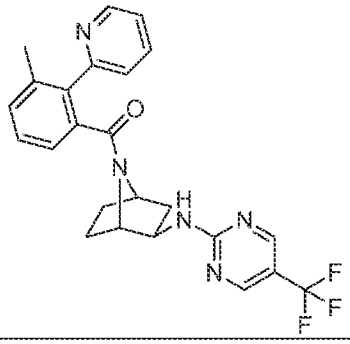
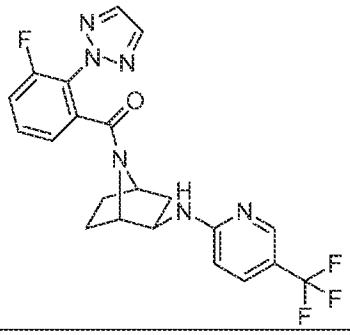
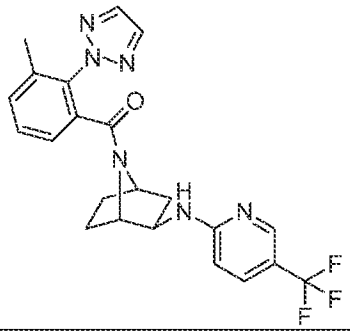
271		41	42	2300	(3-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
272		21	26	742	(3-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
273		17	12	328	(3-methyl-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
274		>10000		2560	(3-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((3-(trifluoromethyl)-[1,2,4]triazolo[4,3-a]pyrazin-8-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

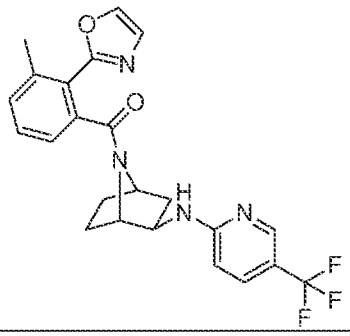
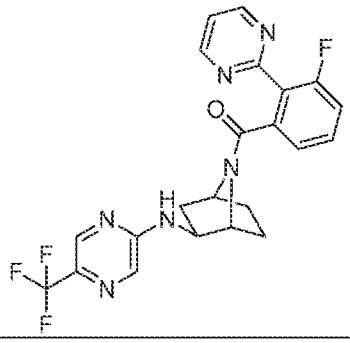
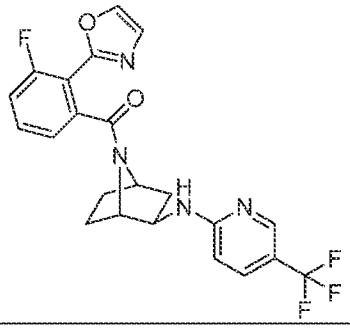
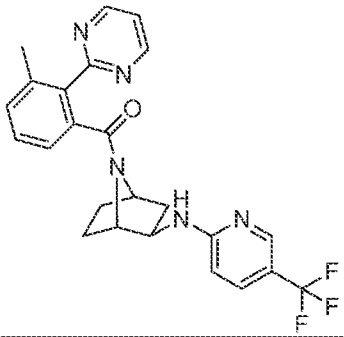
275		>10000		>10000	methyl 5-(((1S,2R,4R)-7-(3-fluoro-2-(pyrimidin-2-yl)benzoyl)-7-azabicyclo[2.2.1]heptan-2-yl)amino)pyrazine-2-carboxylate
276		133	97	2500	(2-iodo-3-methylphenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
277		457		7399	(3-fluoro-2-iodophenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
278		87	77	934	(3-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-methylpyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
279		15	8	1100	(3-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

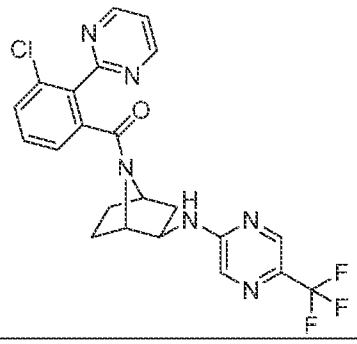
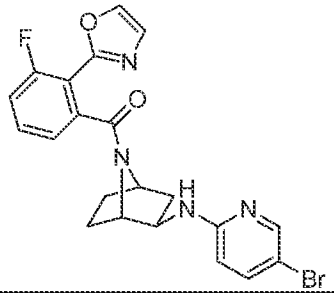
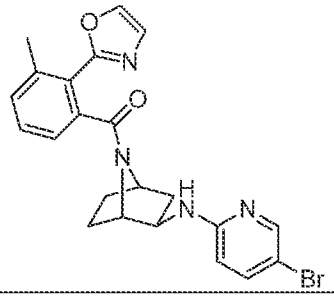
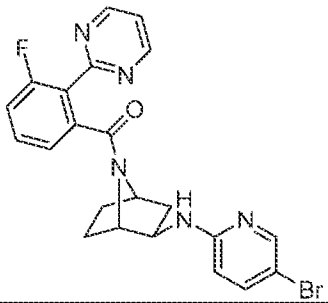
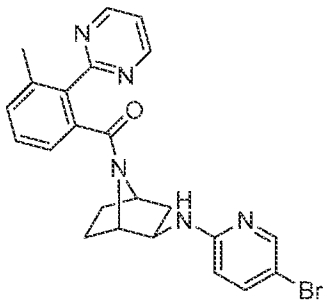
280		39	37	1300	(4-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
281		21	17	1200	(3-methyl-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
282		486		>10000	(3-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-(methyl(5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
283		14	9	417	(3-methyl-2-(oxazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

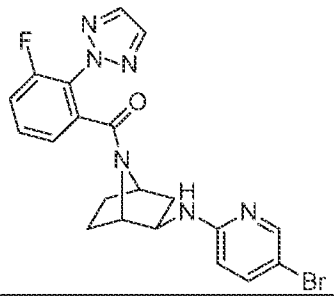
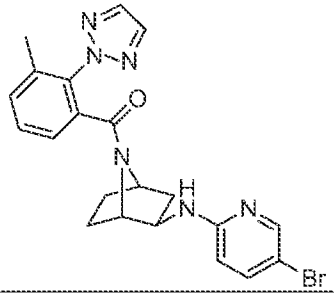
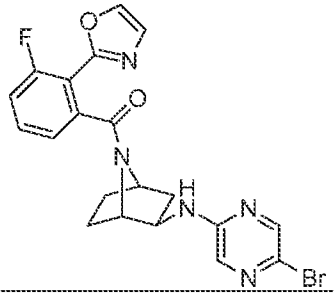
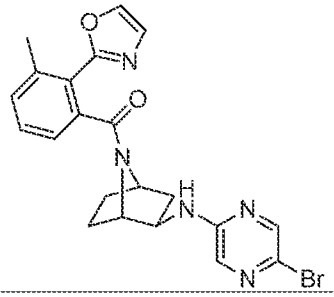
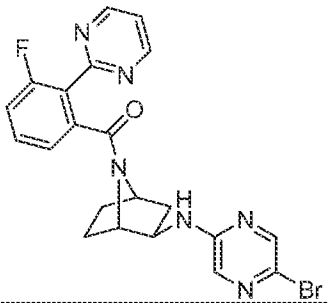
284		29	27	1700	(3-fluoro-2-(oxazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
285		720		>10000	(±)-(3-fluoro-2-(pyrimidin-2-yl)phenyl)(2-((5-(trifluoromethyl)pyrimidin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
286		>10000		>10000	(±)-(3-fluoro-2-(pyrimidin-2-yl)phenyl)(2-((5-(trifluoromethyl)pyrimidin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
287		472		767	(3-ethoxy-6-methylpyridin-2-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

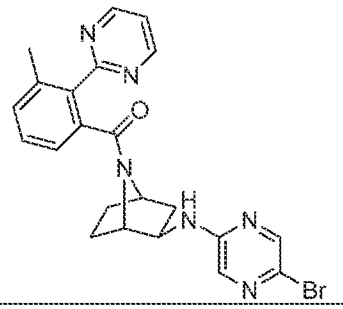
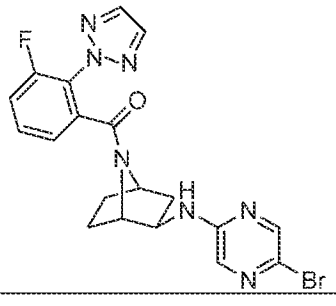
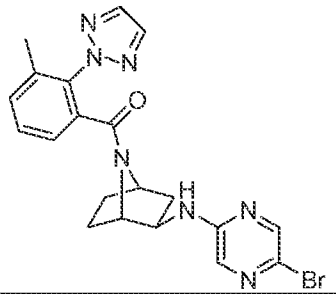
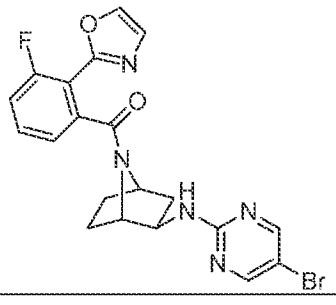
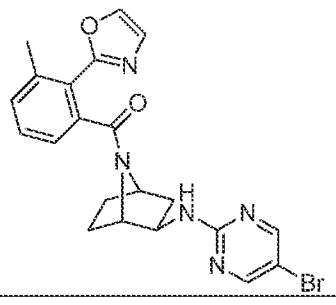
288		94	128	1900	(3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
289		13	32	173	(2-methoxy-6-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
290		21	19	558	(2-fluoro-6-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
291		15	35	425	(7-ethoxyquinolin-8-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

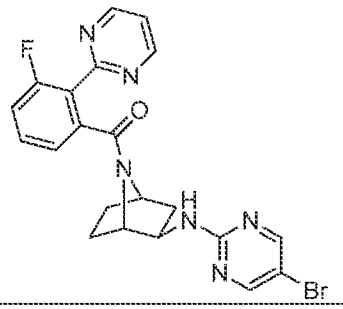
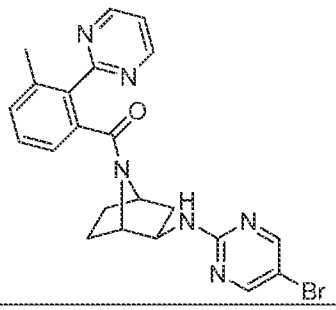
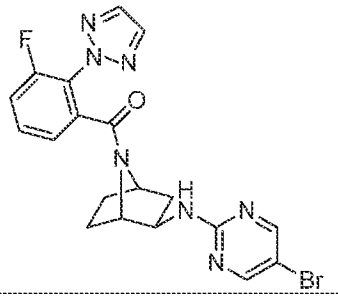
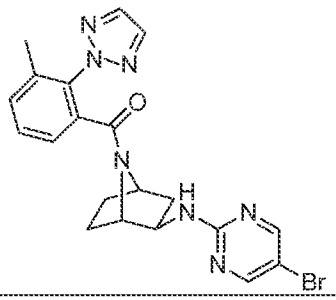
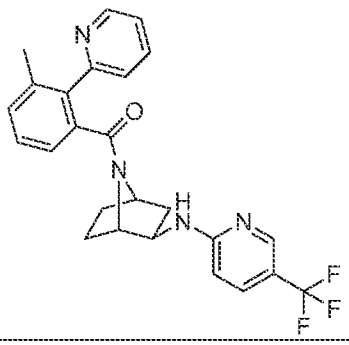
292		>10000		>10000	(2-(1,4-dimethyl-1H-pyrazol-5-yl)-6-methoxyphenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
293		23	37	1100	(3-methyl-2-(pyridin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
294		21	15	1200	(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
295		9	8	257	(3-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

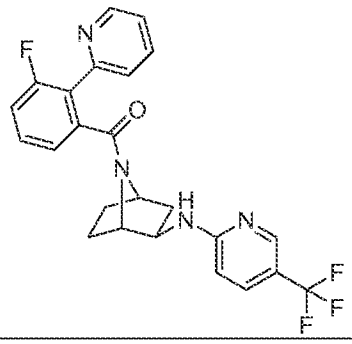
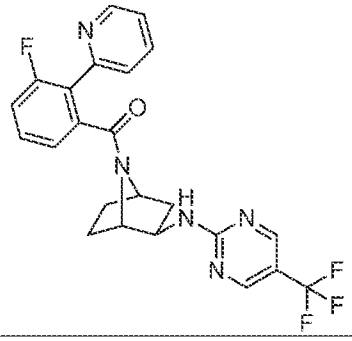
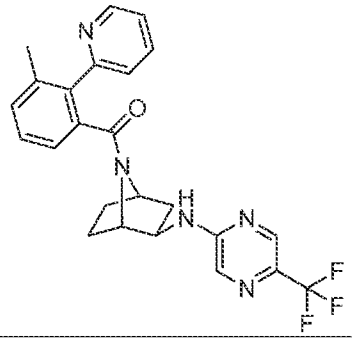
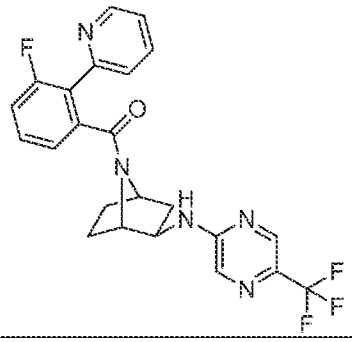
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297		>10000		>10000	(3-fluoro-2-(pyrimidin-2-yl)phenyl)((1R,2S,4S)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
298					(3-fluoro-2-(oxazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
299					(3-methyl-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

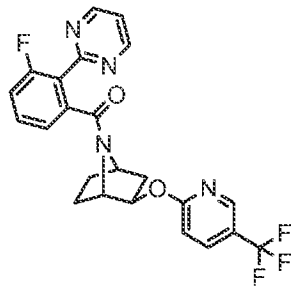
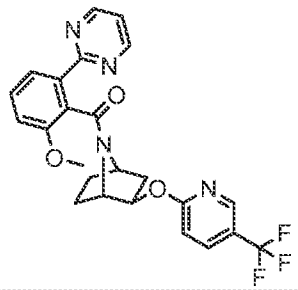
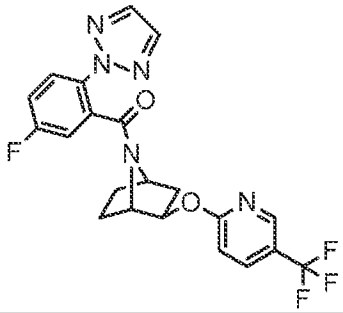
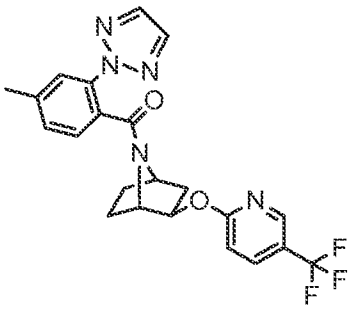
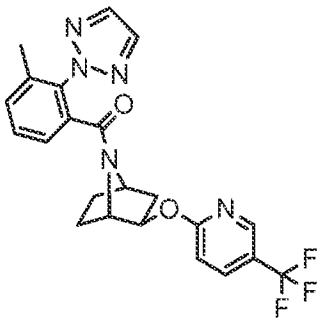
300					(3-chloro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
301					((1S,2R,4R)-2-((5-bromopyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-(oxazol-2-yl)phenyl)methanone
302					((1S,2R,4R)-2-((5-bromopyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-methyl-2-(oxazol-2-yl)phenyl)methanone
303					((1S,2R,4R)-2-((5-bromopyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-(pyrimidin-2-yl)phenyl)methanone
304					((1S,2R,4R)-2-((5-bromopyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-methyl-2-(pyrimidin-2-yl)phenyl)methanone

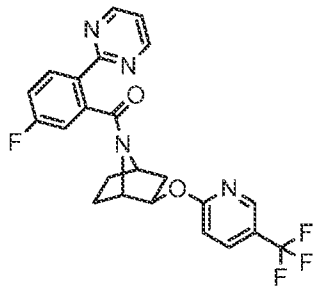
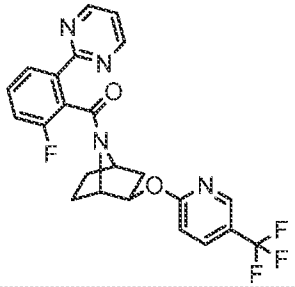
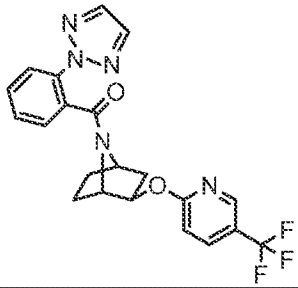
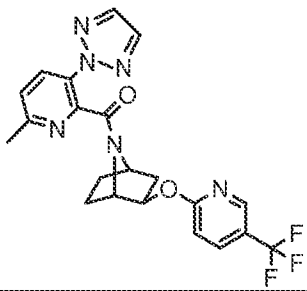
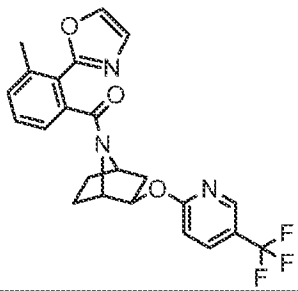
305					((1S,2R,4R)-2-((5-bromopyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone
306					((1S,2R,4R)-2-((5-bromopyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone
307					((1S,2R,4R)-2-((5-bromopyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-(oxazol-2-yl)phenyl)methanone
308					((1S,2R,4R)-2-((5-bromopyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-methyl-2-(oxazol-2-yl)phenyl)methanone
309					((1S,2R,4R)-2-((5-bromopyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-(pyrimidin-2-yl)phenyl)methanone

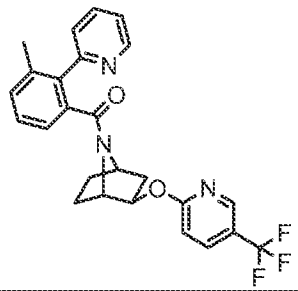
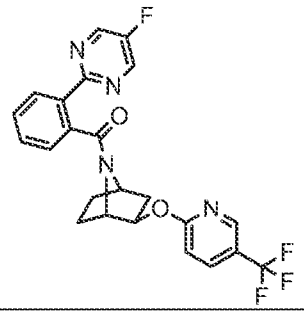
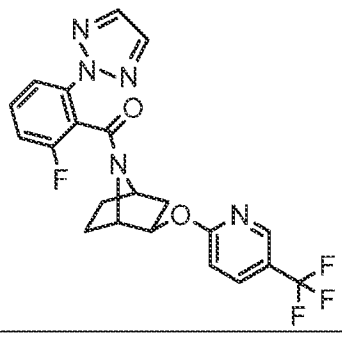
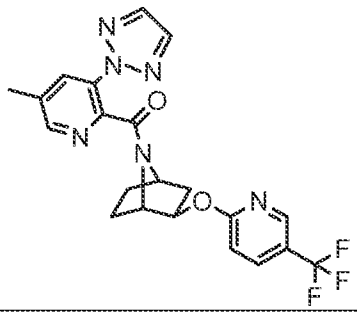
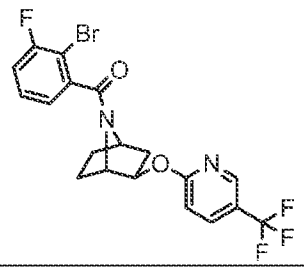
310					((1S,2R,4R)-2-((5-bromopyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-methyl-2-(pyrimidin-2-yl)phenyl)methanone
311					((1S,2R,4R)-2-((5-bromopyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone
312					((1S,2R,4R)-2-((5-bromopyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone
313					((1S,2R,4R)-2-((5-bromopyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-(oxazol-2-yl)phenyl)methanone
314					((1S,2R,4R)-2-((5-bromopyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-methyl-2-(oxazol-2-yl)phenyl)methanone

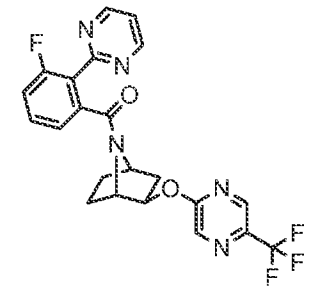
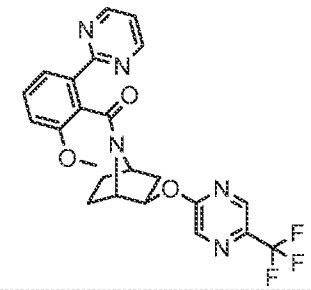
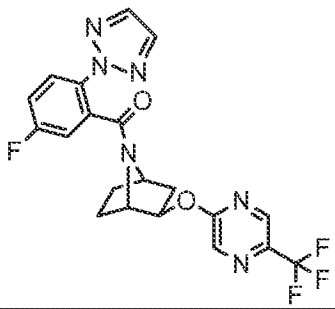
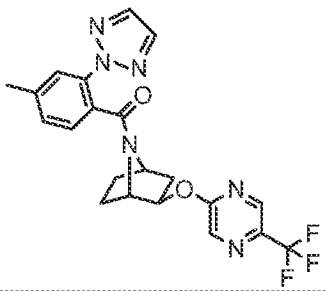
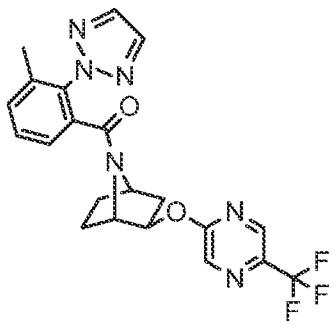
315					((1S,2R,4R)-2-((5-bromopyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-(pyrimidin-2-yl)phenyl)methanone
316					((1S,2R,4R)-2-((5-bromopyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-methyl-2-(pyrimidin-2-yl)phenyl)methanone
317					((1S,2R,4R)-2-((5-bromopyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone
318					((1S,2R,4R)-2-((5-bromopyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone
319					(3-methyl-2-(pyridin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

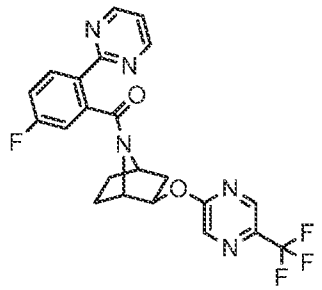
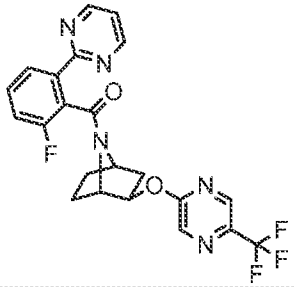
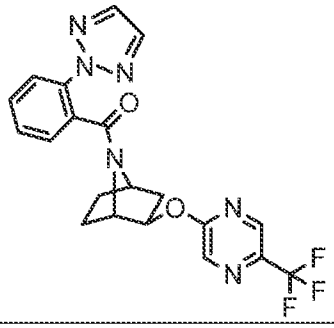
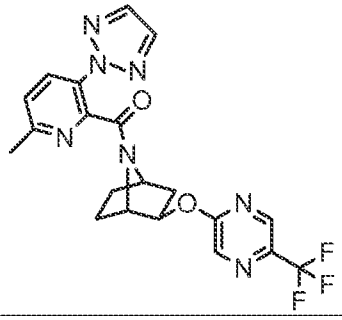
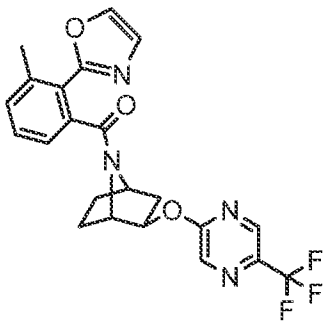
320					(3-fluoro-2-(pyridin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
321					(3-fluoro-2-(pyridin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
322					(3-methyl-2-(pyridin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
323					(3-fluoro-2-(pyridin-2-yl)phenyl)((2S)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

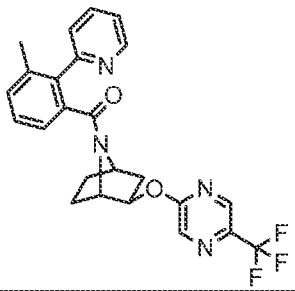
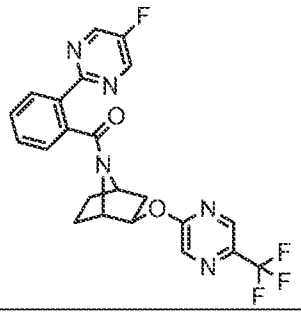
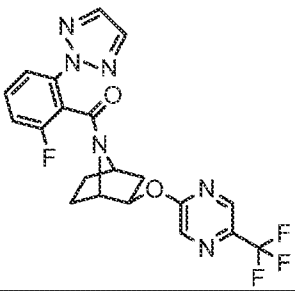
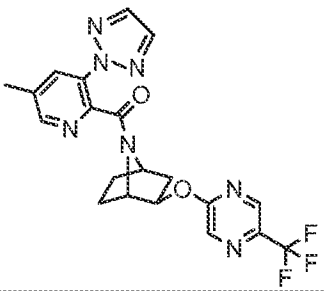
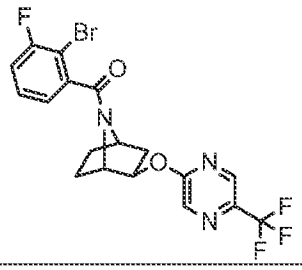
324					(3-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
325					(2-methoxy-6-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
326					(5-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
327					(4-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
328					(3-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

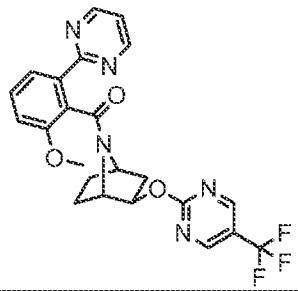
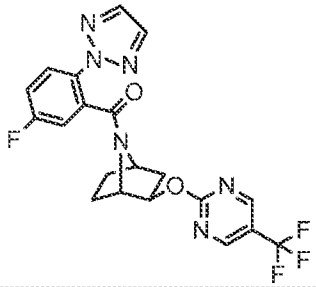
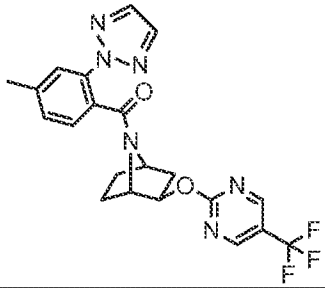
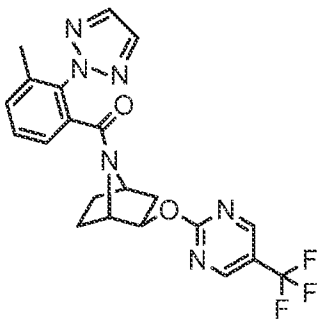
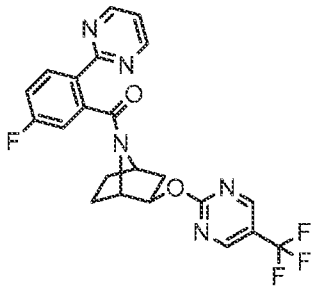
329					(5-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
330					(2-fluoro-6-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
331					(2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
332					(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
333					(3-methyl-2-(oxazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

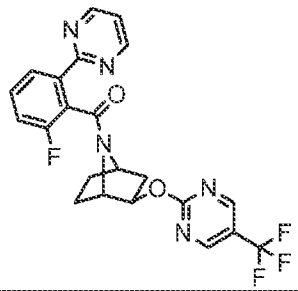
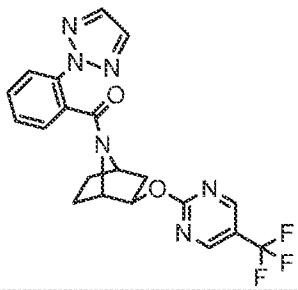
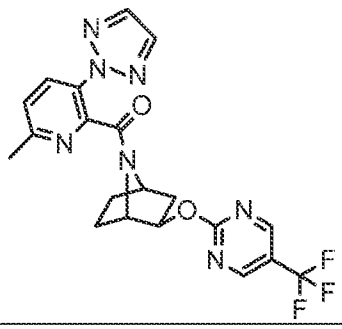
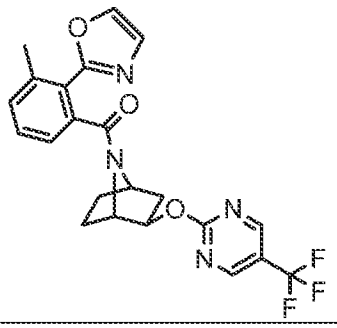
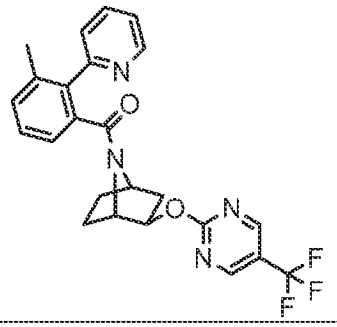
334					(3-methyl-2-(pyridin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
335					(2-(5-fluoropyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
336					(2-fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
337					(5-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
338					(2-bromo-3-fluorophenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

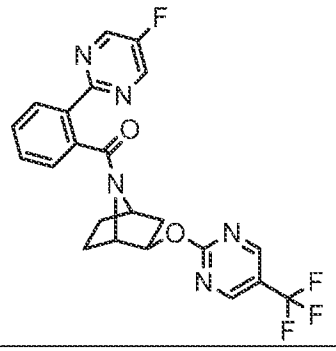
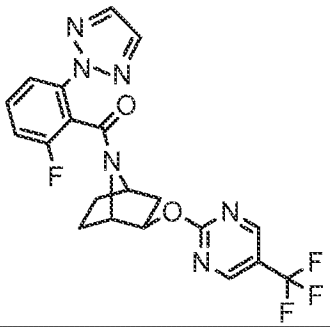
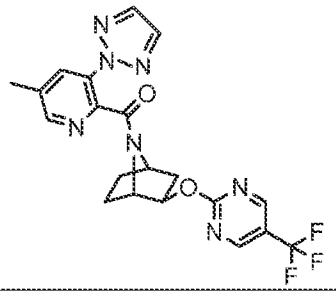
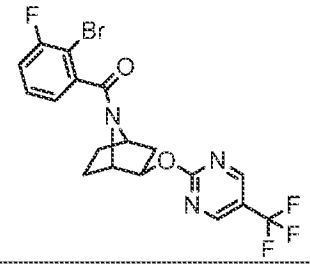
339					(3-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
340					(2-methoxy-6-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
341					(5-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
342					(4-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
343					(3-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

344					(5-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
345					(2-fluoro-6-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
346					(2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
347					(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
348					(3-methyl-2-(oxazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

349					(3-methyl-2-(pyridin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
350					(2-(5-fluoropyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
351					(2-fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
352					(5-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
353					(2-bromo-3-fluorophenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

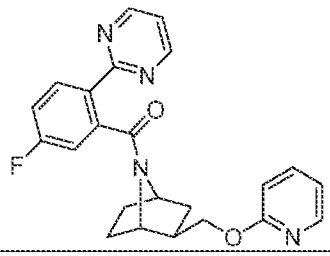
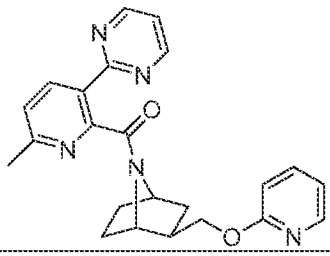
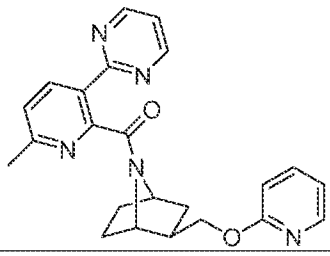
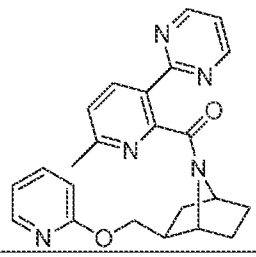
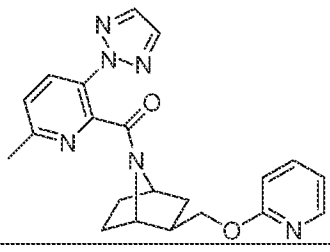
354					(2-methoxy-6-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
355					(5-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
356					(4-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
357					(3-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
358					(5-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

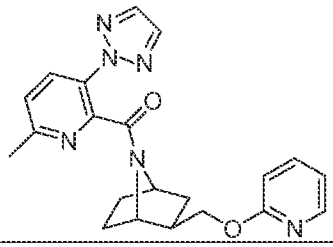
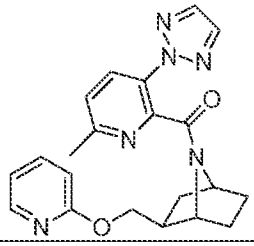
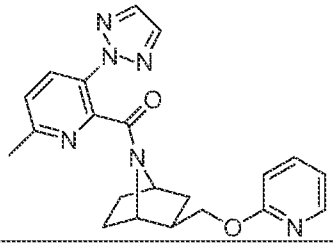
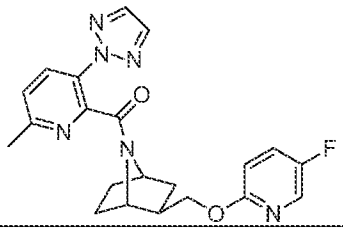
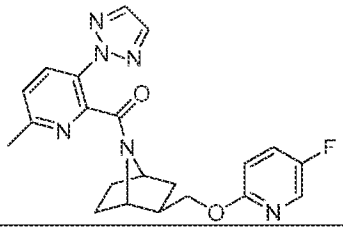
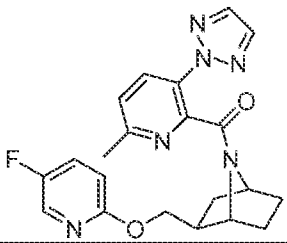
359					(2-fluoro-6-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
360					(2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
361					(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
362					(3-methyl-2-(oxazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
363					(3-methyl-2-(pyridin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

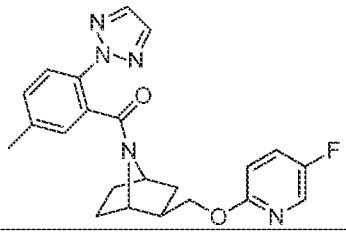
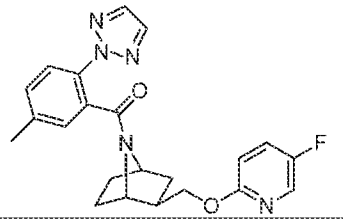
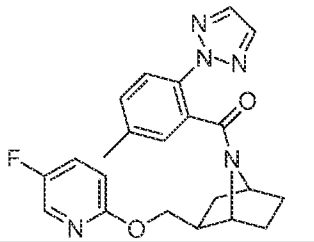
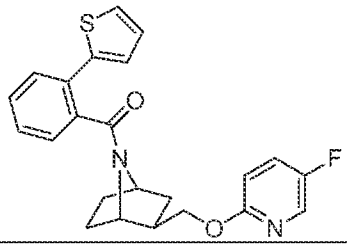
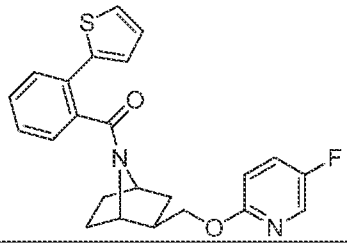
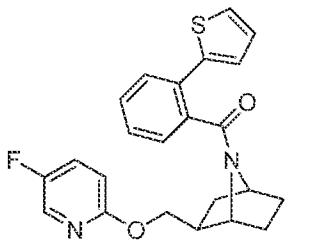
364					(2-(5-fluoropyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
365					(2-fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
366					(5-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
367					(2-bromo-3-fluorophenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

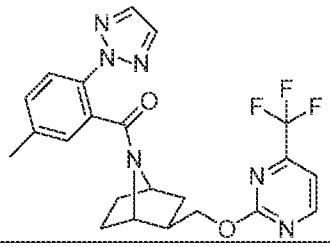
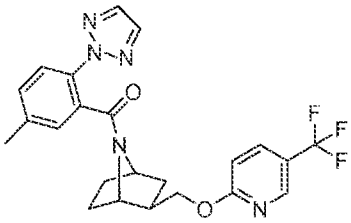
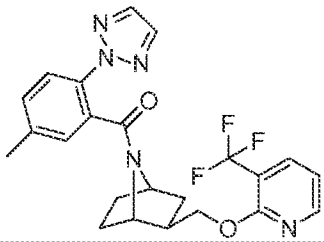
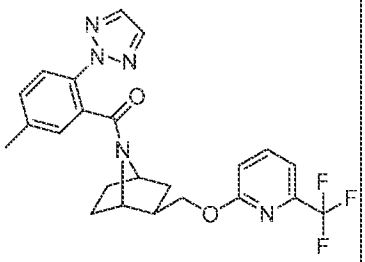
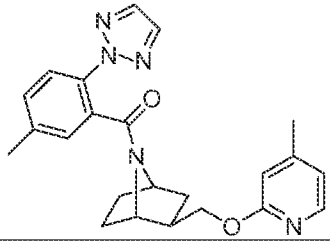
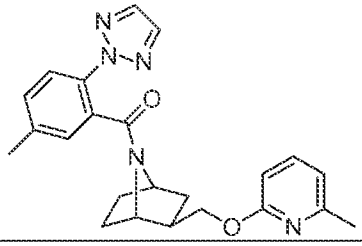
In another embodiment, preferred compounds of the invention are set forth in Table 2 below. Orexin receptor activity from further testing of certain compounds of the invention is set forth in Table 2 below.

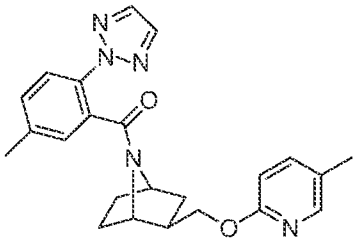
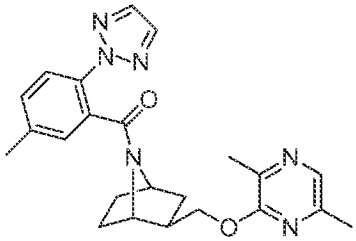
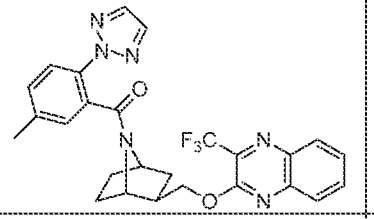
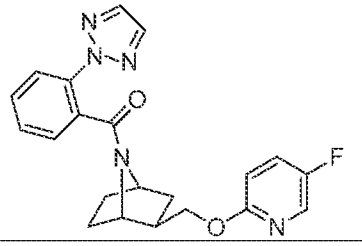
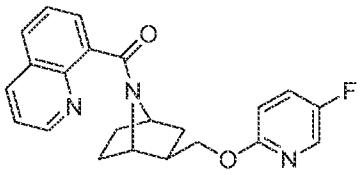
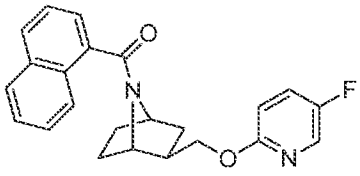
Table 2

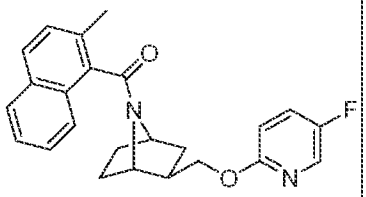
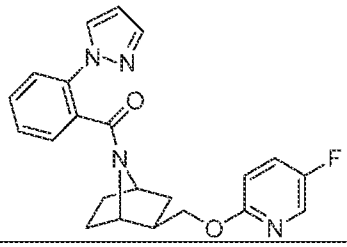
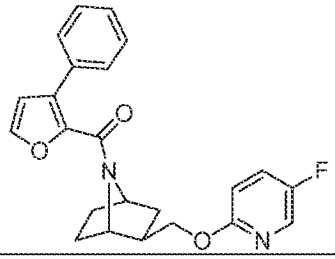
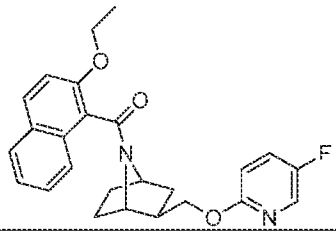
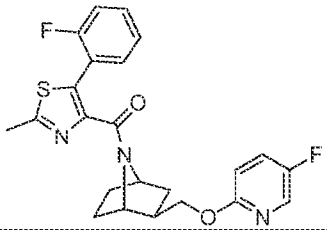
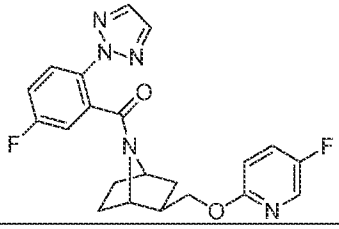
Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
1		25	41	276	(5-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
2		31	23	500	(±)-(6-methyl-3-(pyrimidin-2-yl)pyridin-2-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
3A		24	19	271	(6-methyl-3-(pyrimidin-2-yl)pyridin-2-yl)((1S*,2R*,4R*)-2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
3B		>10000		>10000	(6-methyl-3-(pyrimidin-2-yl)pyridin-2-yl)((1R*,2S*,4S*)-2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
4		36	41	927	(±)-(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

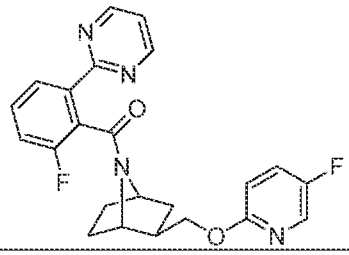
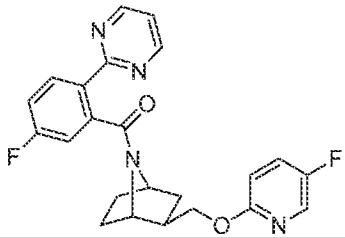
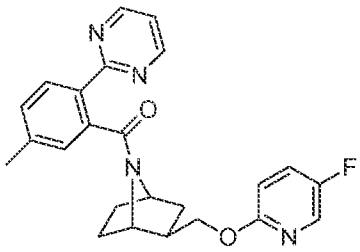
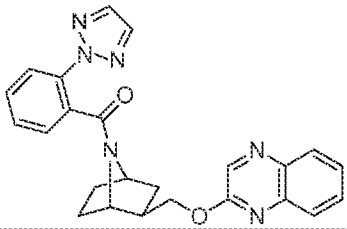
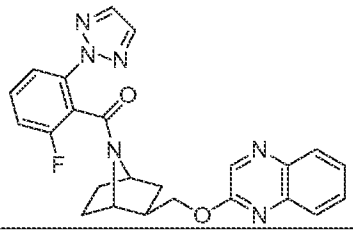
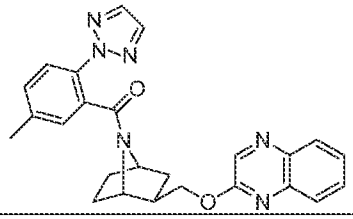
Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
5A		15	15	428	(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)((1S,2R,4R)-2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
5B		>10000		>10000	(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)((1R,2S,4S)-2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
6		15	15	428	(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)((1S,2R,4R)-2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
7		19	19	198	(±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)methanone
8A		9	14	94	((1S,2R,4R)-2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)methanone
8B		>10000		>10000	((1R,2S,4S)-2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)methanone

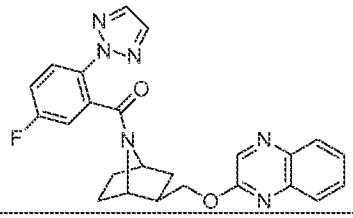
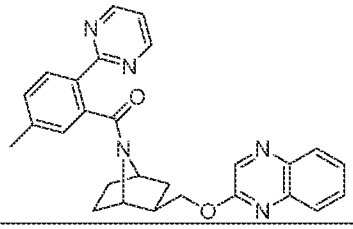
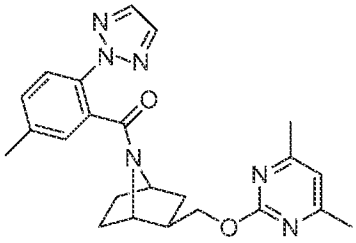
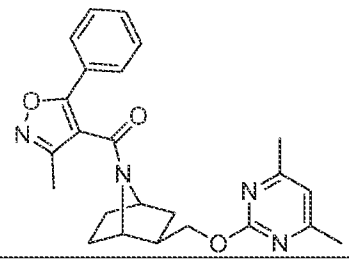
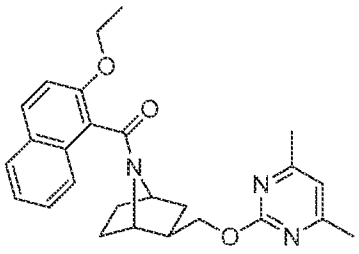
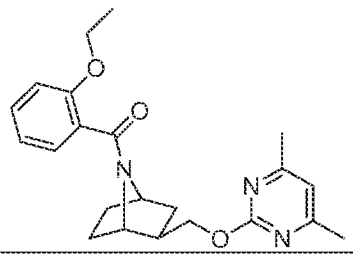
Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
9			9	60	(±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(5-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone
10A		4	3	32	((1S,2R,4R)-2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(5-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone
10B		4050	3200	5150	((1R,2S,4S)-2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(5-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone
11			10	13	(±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(2-(thiophen-2-yl)phenyl)methanone
12A			177	339	((1S*,2R*,4R*)-2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(2-(thiophen-2-yl)phenyl)methanone
12B			3	5	((1R*,2S*,4S*)-2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(2-(thiophen-2-yl)phenyl)methanone

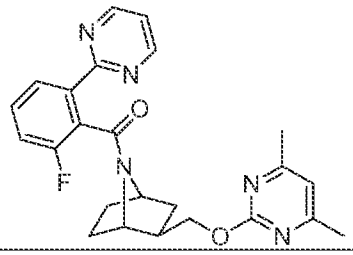
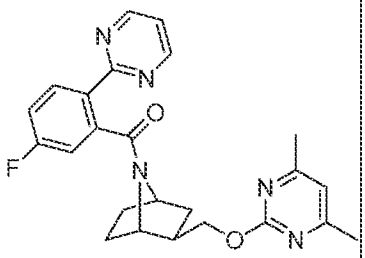
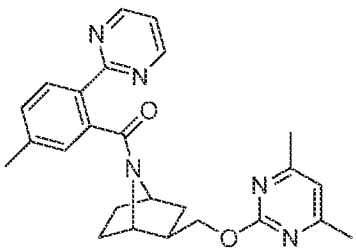
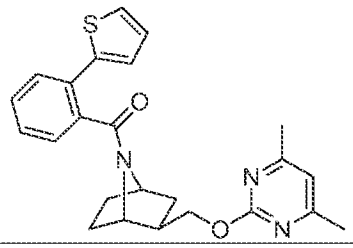
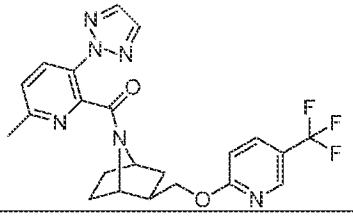
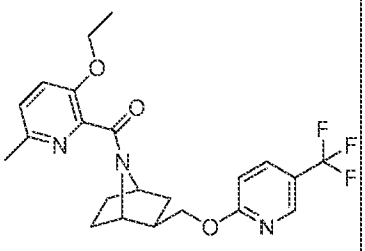
Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
13			118	109	(±)-(5-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((4-(trifluoromethyl)pyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
14			50	71	(±)-(5-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((5-(trifluoromethyl)pyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
15			56	120	(±)-(5-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((3-(trifluoromethyl)pyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
16			20	43	(±)-(5-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((6-(trifluoromethyl)pyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
17			42	69	(±)-(5-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((4-methylpyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
18			12	45	(±)-(5-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((6-methylpyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

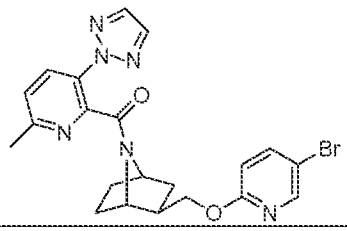
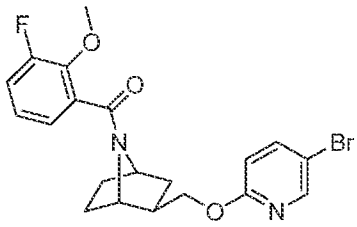
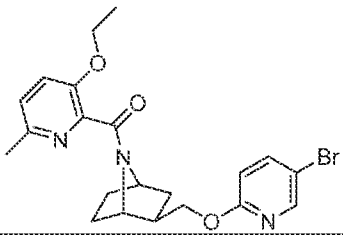
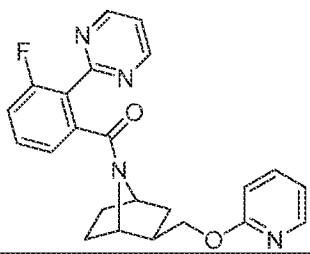
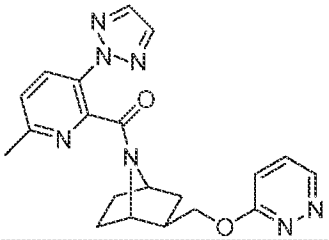
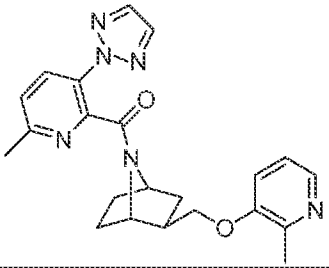
Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
19			12	45	(±)-(5-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((5-methylpyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
20			270	364	(±)-(2-(((3,6-dimethylpyrazin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(5-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone
21			300	487	(±)-(5-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((3-(trifluoromethyl)quinoxalin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
22			47	50	(±)- (2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
23			322	1500	(±)-2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(quinolin-8-yl)methanone
24			122	164	(±)-2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(naphthalen-1-yl)methanone

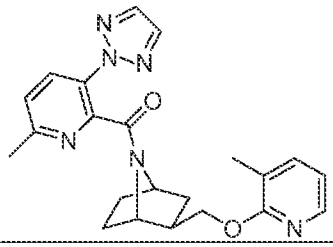
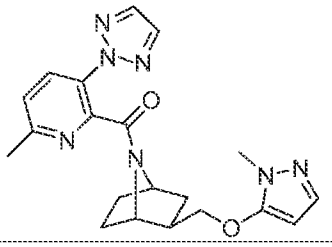
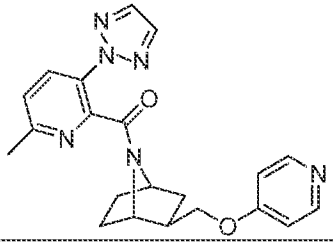
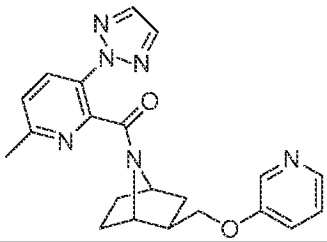
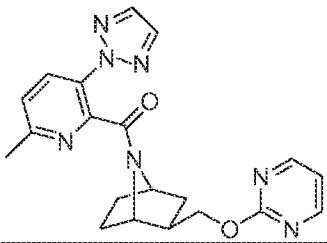
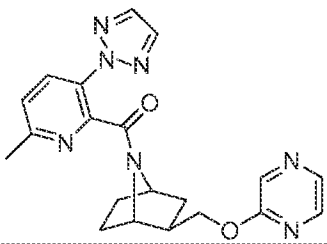
Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
25			74	160	(±)-2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(2-methylnaphthalen-1-yl)methanone
26			134	394	(±)-2-(1H-pyrazol-1-yl)phenyl)(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
27			677	380	(±)-2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(3-phenylfuran-2-yl)methanone
28			14	11	(±)-(2-ethoxynaphthalen-1-yl)(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
29			11	60	(±)-(5-(2-fluorophenyl)-2-methylthiazol-4-yl)(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
30			60	160	(±)-(5-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

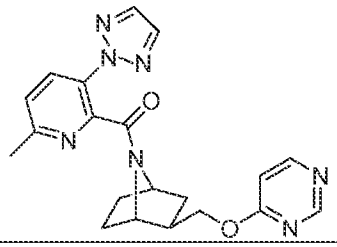
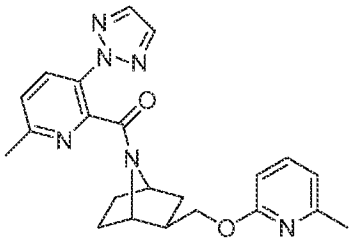
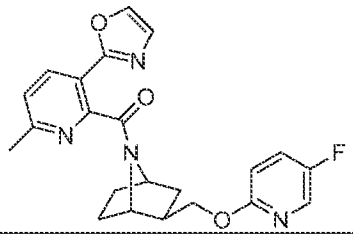
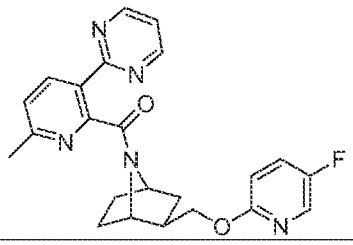
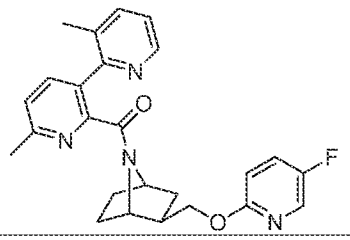
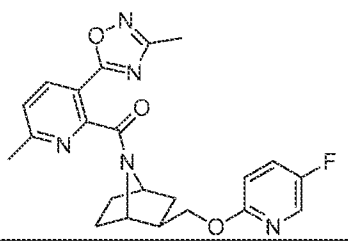
Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
31			43	125	(±)-(2-fluoro-6-(pyrimidin-2-yl)phenyl)(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
32			21	130	(±)-(5-fluoro-2-(pyrimidin-2-yl)phenyl)(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
33		15	9	40	(±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(5-methyl-2-(pyrimidin-2-yl)phenyl)methanone
34			60	467	(±)-(2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((quinoxalin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
35		69	60	708	(±)-(2-fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl)(2-((quinoxalin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
36			70	108	(±)-(5-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((quinoxalin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

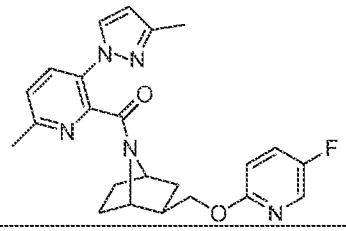
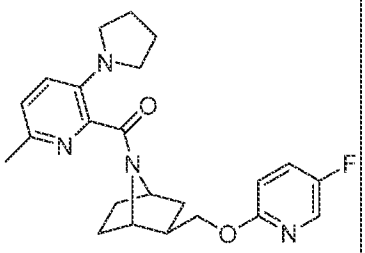
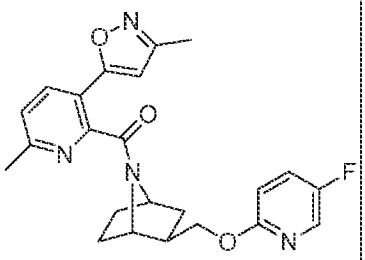
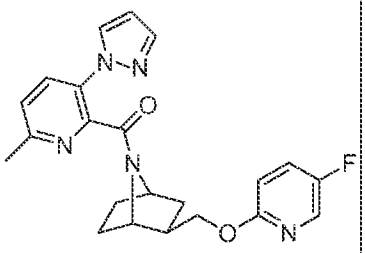
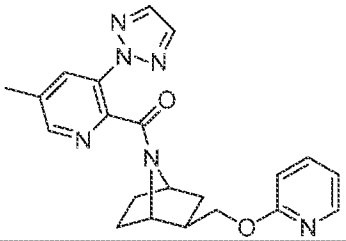
Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
37			300	487	(±)-(5-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((quinoxalin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
38			120	383	(±)-(5-methyl-2-(pyrimidin-2-yl)phenyl)(2-((quinoxalin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
39			30	28	(±)-(2-(((4,6-dimethylpyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(5-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone
40			5000	1203	(±)-2-(((4,6-dimethylpyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(3-methyl-5-phenylisoxazol-4-yl)methanone
41			35	23	(±)-(2-(((4,6-dimethylpyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(2-ethoxynaphthalen-1-yl)methanone
42			1277	253	(±)-(2-(((4,6-dimethylpyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(2-ethoxyphenyl)methanone)

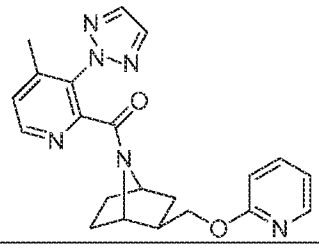
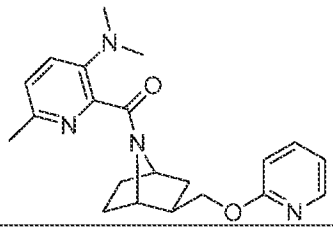
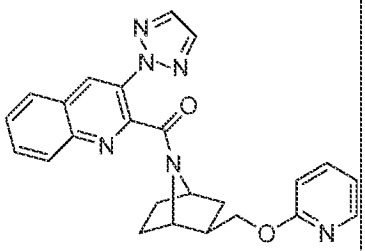
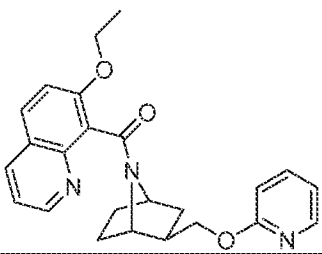
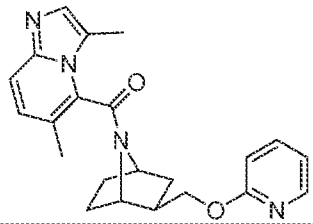
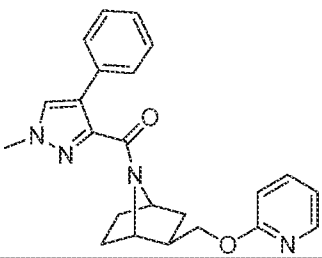
Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
43			222	92	(±)-(2-(((4,6-dimethylpyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(2-fluoro-6-(pyrimidin-2-yl)phenyl)methanone
44			400	104	(±)-(2-(((4,6-dimethylpyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(5-fluoro-2-(pyrimidin-2-yl)phenyl)methanone
45			79	59	(±)-(2-(((4,6-dimethylpyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(5-methyl-2-(pyrimidin-2-yl)phenyl)methanone
46			111	10	(±)-(2-(((4,6-dimethylpyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(2-(thiophen-2-yl)phenyl)methanone
47		460		418	(±)-(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-(((5-(trifluoromethyl)pyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
48		3900		4700	(±)-(3-ethoxy-6-methylpyridin-2-yl)(2-(((5-(trifluoromethyl)pyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

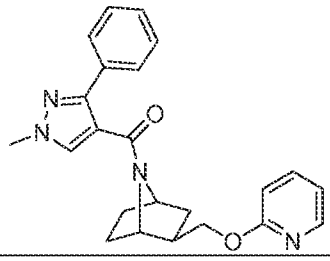
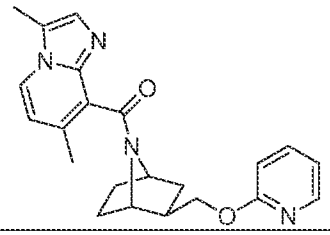
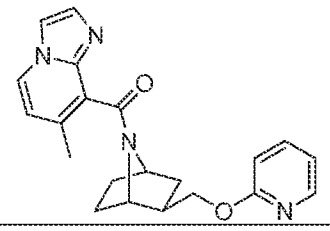
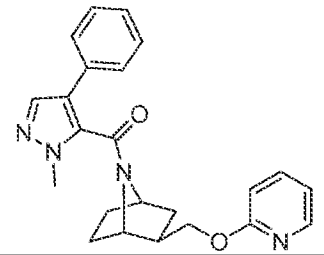
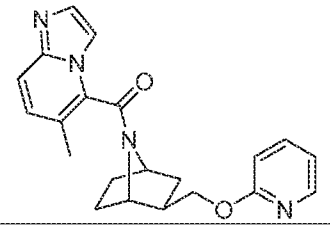
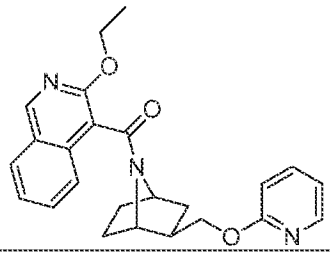
Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
49		81	69	192	(±)-(2-(((5-bromopyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)methanone
50		460		4400	(±)-(2-(((5-bromopyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-methoxyphenyl)methanone
51		974		1800	(±)-(2-(((5-bromopyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(3-ethoxy-6-methylpyridin-2-yl)methanone
52		350		2300	(±)-(3-fluoro-2-(pyrimidin-2-yl)phenyl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
53		2200		>10000	(±)-(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-((pyridazin-3-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
54		3500		2200	(±)-(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-(((2-methylpyridin-3-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

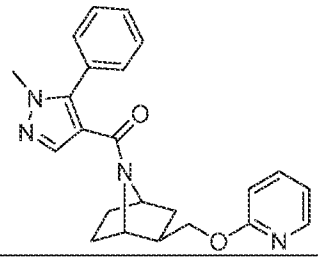
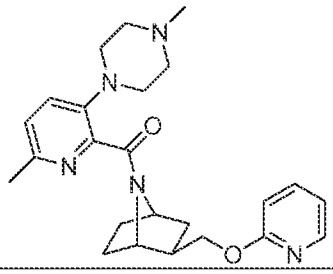
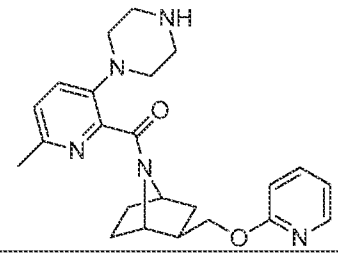
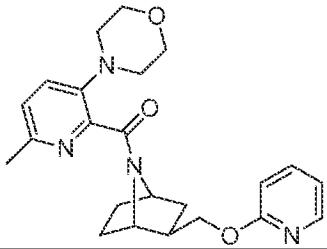
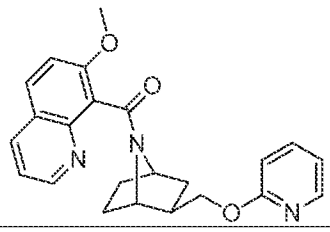
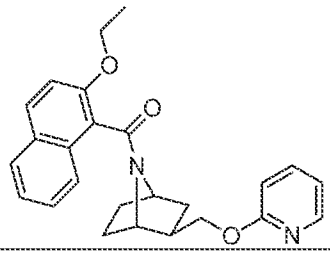
Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
55		119	150	202	(±)-(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-(((3-methylpyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
56		>10000		>10000	(±)-(2-(((1-methyl-1H-pyrazol-5-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)methanone
57		1000		7300	(±)-(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-((pyridin-4-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
58		88	117	2400	(±)-(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-((pyridin-3-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
59		2600		4900	(±)-(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-((pyrimidin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
60		7800		>10000	(±)-(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-((pyrazin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

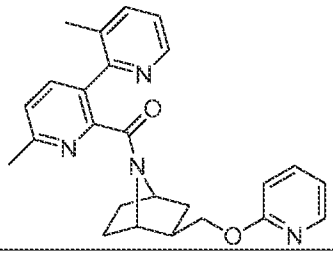
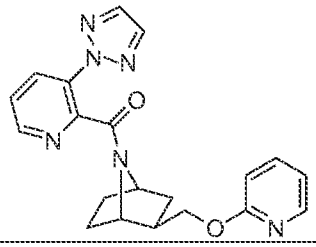
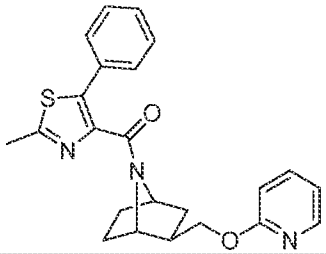
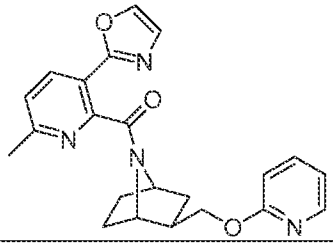
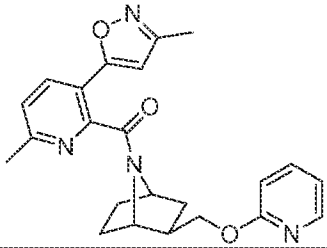
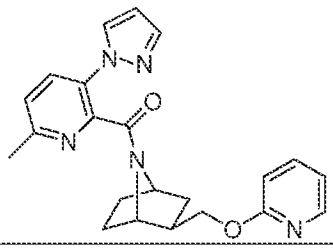
Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
61		2800		>10000	(±)-(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2- ((pyrimidin-4-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
62		74	46	188	(±)-(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-(((6-methylpyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
63		25	25	339	(±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(oxazol-2-yl)pyridin-2-yl)methanone
64		18	24	81	(±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(pyrimidin-2-yl)pyridin-2-yl)methanone
65		1440		6200	(±)-(3,6'-dimethyl-[2,3'-bipyridin]-2'-yl)(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
66		197	293	620	(±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(3-methyl-1,2,4-oxadiazol-5-yl)pyridin-2-yl)methanone

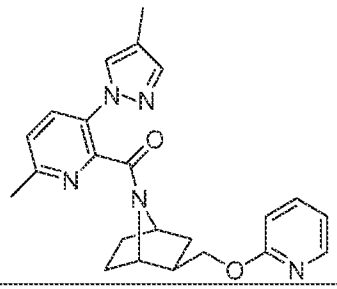
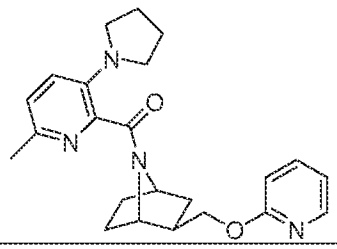
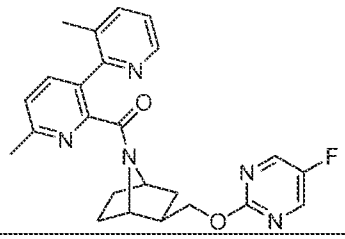
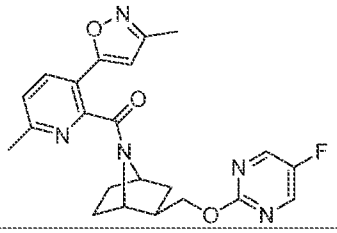
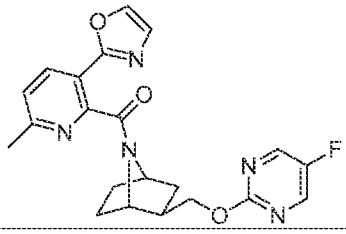
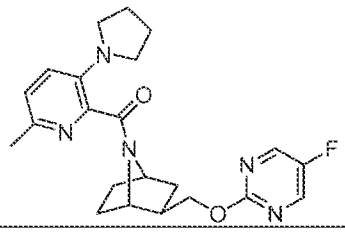
Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
67		48	69	258	(±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(3-methyl-1H-pyrazol-1-yl)pyridin-2-yl)methanone
68		27	22	576	(±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(pyrrolidin-1-yl)pyridin-2-yl)methanone
69		40	64	174	(±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(3-methylisoxazol-5-yl)pyridin-2-yl)methanone
70		88	62	624	(±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(1H-pyrazol-1-yl)pyridin-2-yl)methanone
71		1200		3700	(±)-(5-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

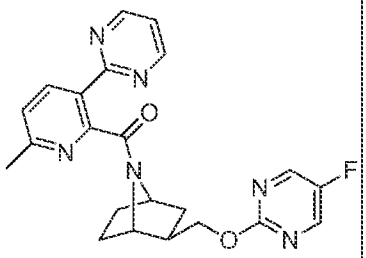
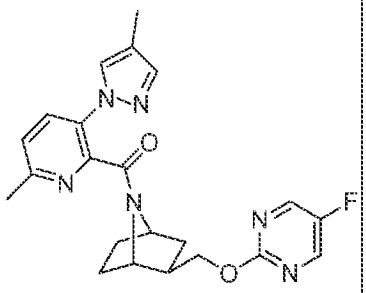
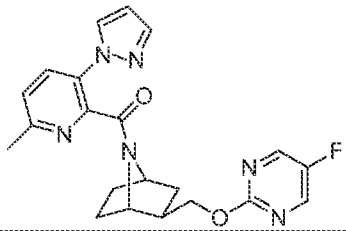
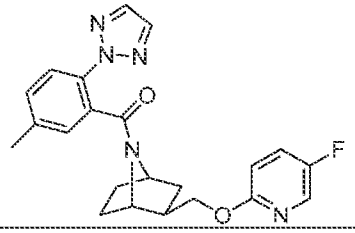
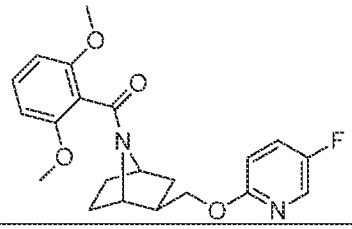
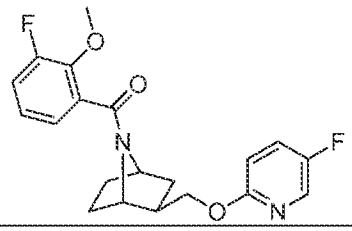
Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
72		137	162	2400	(±)- (4-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
73		278		7900	(±)-(3-(dimethylamino)-6-methylpyridin-2-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
74		359		1700	(±)-(3-(2H-1,2,3-triazol-2-yl)quinolin-2-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
75		18	7	220	(±)-(7-ethoxyquinolin-8-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
76		>10000		>10000	(±)-(3,6-dimethylimidazo[1,2-a]pyridin-5-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
77		103	66	867	(±)-(1-methyl-4-phenyl-1H-pyrazol-3-yl)((1S,2R,4R)-2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

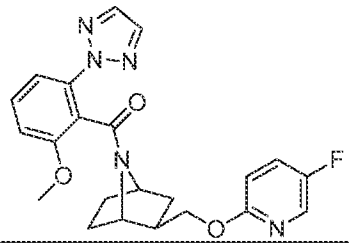
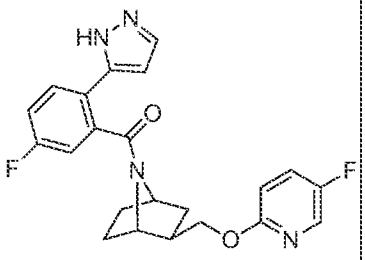
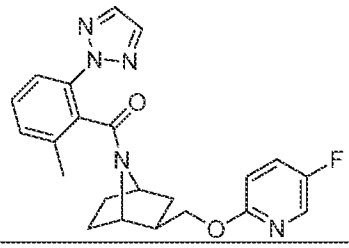
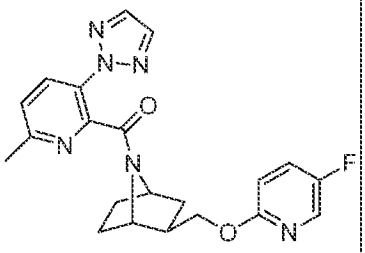
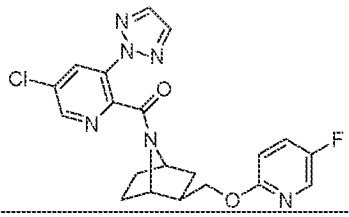
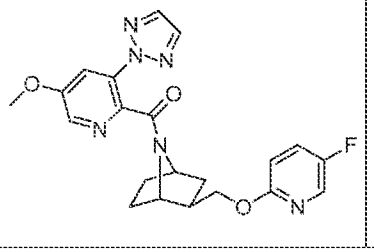
Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
78		418		3100	(±)-(1-methyl-3-phenyl-1H-pyrazol-4-yl)((1S,2R,4R)-2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
79		2400		8500	(±)-((3,7-dimethylimidazo[1,2-a]pyridin-8-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
80		1100		>10000	(±)-(7-methylimidazo[1,2-a]pyridin-8-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
81		916		2900	(±)-(1-methyl-4-phenyl-1H-pyrazol-5-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
82		>10000		>10000	(±)-((6-methylimidazo[1,2-a]pyridin-5-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
83		17	13	277	(±)-(3-ethoxyisoquinolin-4-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

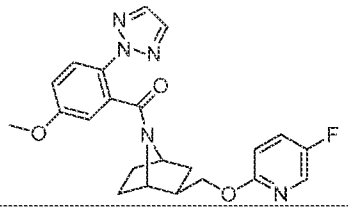
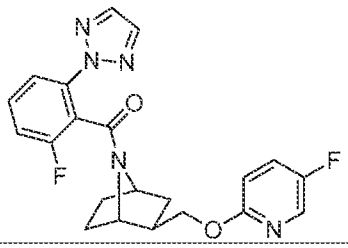
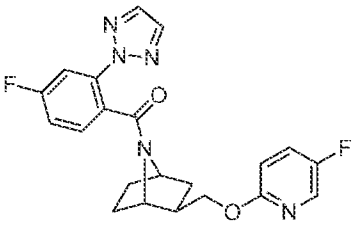
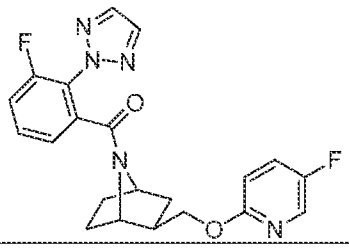
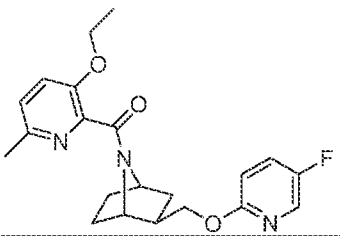
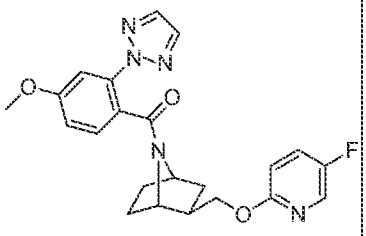
Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
84		2600		9700	(±)-(1-methyl-5-phenyl-1H-pyrazol-4-yl)(-2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
85		>10000		>10000	(±)-(6-methyl-3-(4-methylpiperazin-1-yl)pyridin-2-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
86		>10000		>10000	(±)-(6-methyl-3-(piperazin-1-yl)pyridin-2-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
87		4200		>10000	(±)-(6-methyl-3-morpholinopyridin-2-yl)((1S,2R,4R)-2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
88		47	49	690	(±)-(7-methoxyquinolin-8-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
89		11	10	38	(±)-(2-ethoxynaphthalen-1-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

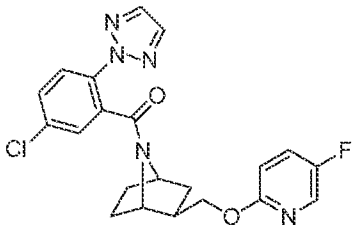
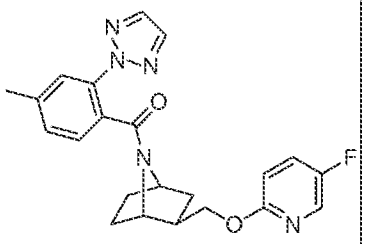
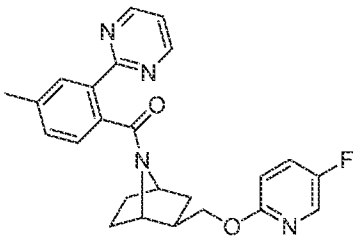
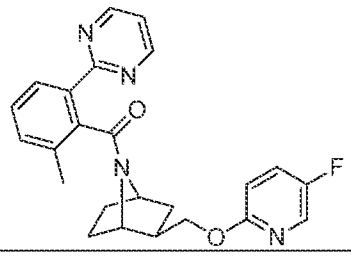
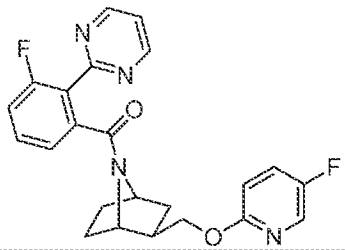
Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
90		3000		>10000	(±)-(3,6'-dimethyl-[2,3'-bipyridin]-2'-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
91		624		3300	(±)-(3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
92		20	11	218	(±)-(2-methyl-5-phenylthiazol-4-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
93		40	73	836	(±)-(6-methyl-3-(oxazol-2-yl)pyridin-2-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
94		170	200	2100	(±)-(6-methyl-3-(3-methylisoxazol-5-yl)pyridin-2-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
95		247		3700	(±)-(6-methyl-3-(1H-pyrazol-1-yl)pyridin-2-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

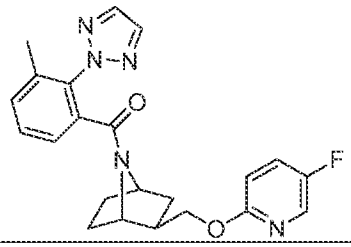
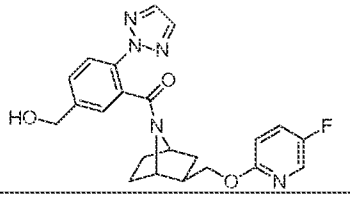
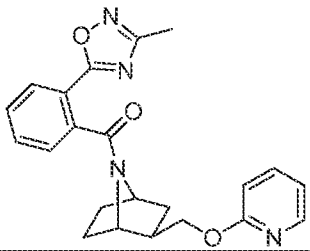
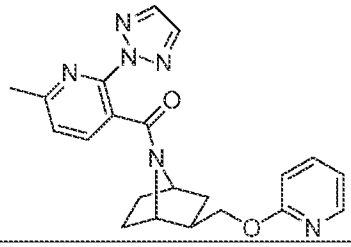
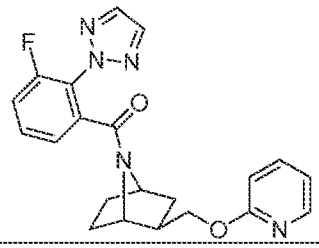
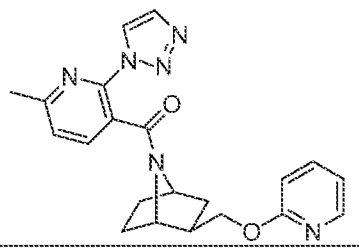
Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
96		70	76	950	(±)-(6-methyl-3-(4-methyl-1H-pyrazol-1-yl)pyridin-2-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
97		35	32	840	(±)-(6-methyl-3-(pyrrolidin-1-yl)pyridin-2-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
98		>10000		>10000	(±)-(3,6'-dimethyl-[2,3'-bipyridin]-2'-yl)(2-(((5-fluoropyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
99		1500		2900	(±)-(2-(((5-fluoropyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(3-methylisoxazol-5-yl)pyridin-2-yl)methanone
100		950		1800	(±)-(2-(((5-fluoropyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(oxazol-2-yl)pyridin-2-yl)methanone
101		650		1200	(±)-(2-(((5-fluoropyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(pyrrolidin-1-yl)pyridin-2-yl)methanone

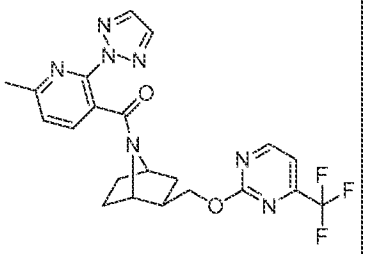
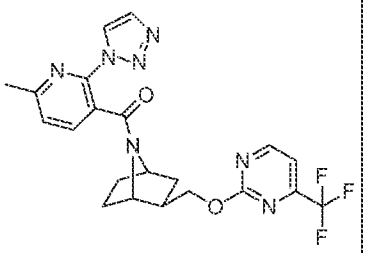
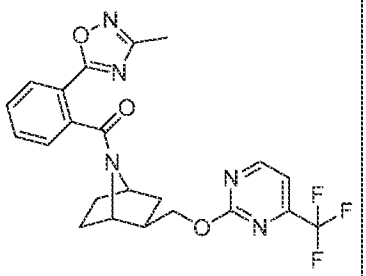
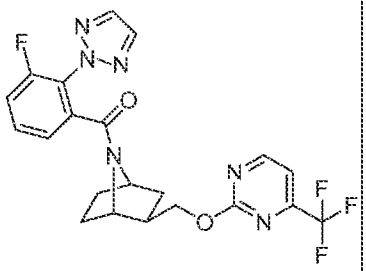
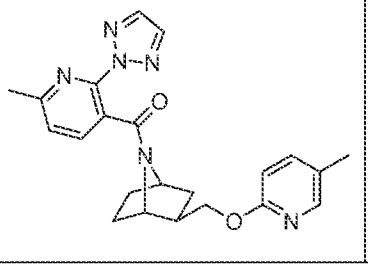
Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
102					(±)-(2-(((5-fluoropyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(pyrimidin-2-yl)pyridin-2-yl)methanone
103		1700		3600	(±)-(2-(((5-fluoropyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(4-methyl-1H-pyrazol-1-yl)pyridin-2-yl)methanone
104		1100		4600	(±)-(2-(((5-fluoropyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(1H-pyrazol-1-yl)pyridin-2-yl)methanone
105					(±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(5-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone
106		300		154	(±)-(2,6-dimethoxyphenyl)(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
107		440		2200	(±)-((3-fluoro-2-methoxyphenyl)(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

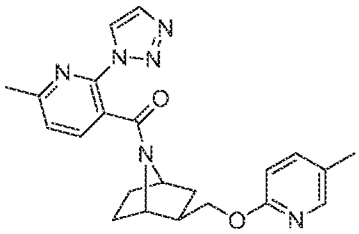
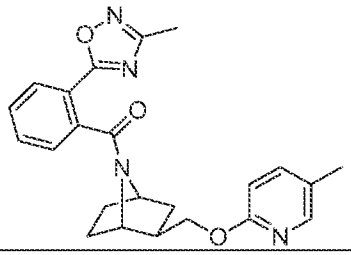
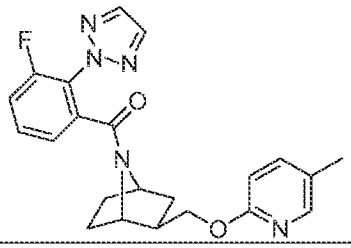
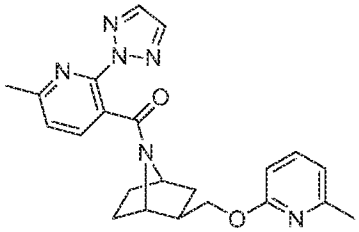
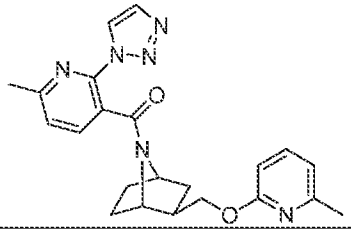
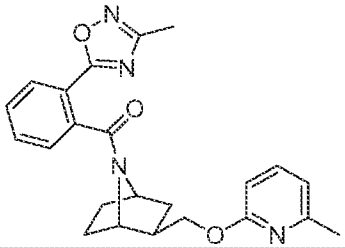
Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
108		10	12	12	(±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(2-methoxy-6-(2H-1,2,3-triazol-2-yl)phenyl)methanone
109		29	20	99	(±)-(5-fluoro-2-(1H-pyrazol-5-yl)phenyl)(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
110		54	67	94	(±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(2-methyl-6-(2H-1,2,3-triazol-2-yl)phenyl)methanone
111		19	19	198	(±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)methanone
112		480		1000	(±)-(5-chloro-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
113		3400		4800	(±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(5-methoxy-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)methanone

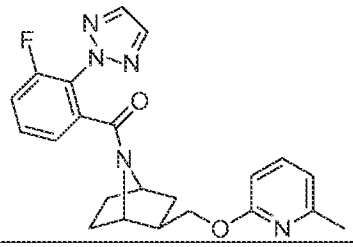
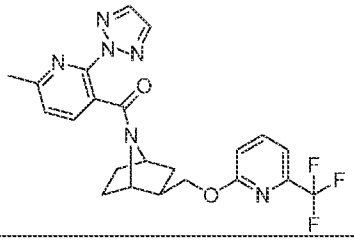
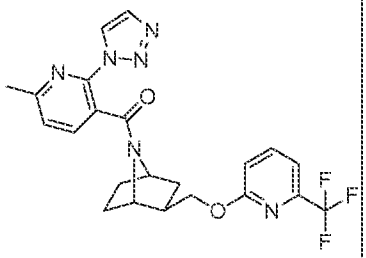
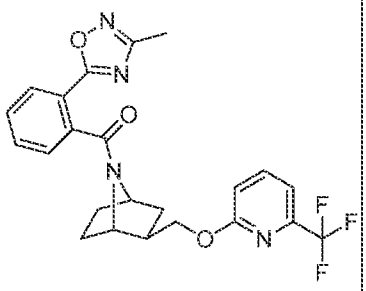
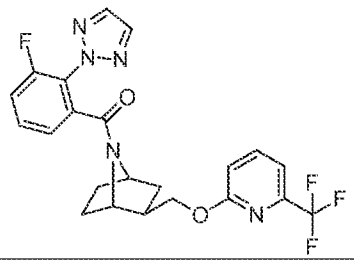
Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
114		20	48	73	(±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(5-methoxy-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone
115		57	78	108	(±)-(2-fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
116		142	250	315	(±)-(4-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
117		62	82	245	(±)-(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
118		440		2200	(±)-(3-ethoxy-6-methylpyridin-2-yl)(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
119		500		1300	(±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(4-methoxy-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone

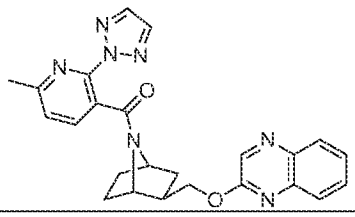
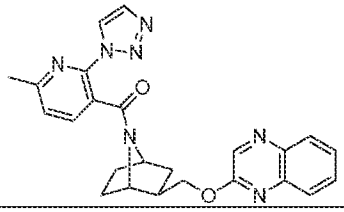
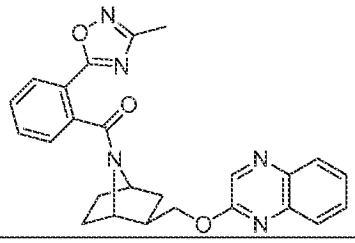
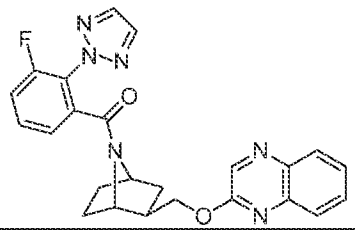
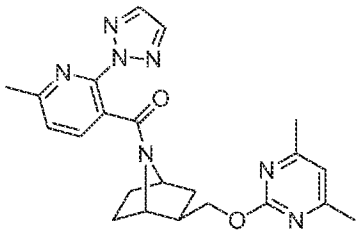
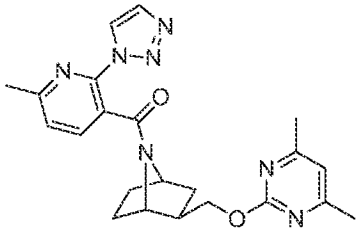
Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
120		15	14	124	(±)-(5-chloro-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
121		78	68	340	(±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(4-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone
122		118	154	1000	(±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(4-methyl-2-(pyrimidin-2-yl)phenyl)methanone
123		400		286	(±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(2-methyl-6-(pyrimidin-2-yl)phenyl)methanone
124		83	75	355	(±)-(3-fluoro-2-(pyrimidin-2-yl)phenyl)(-2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

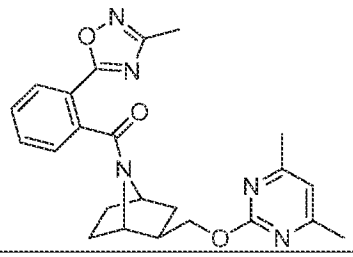
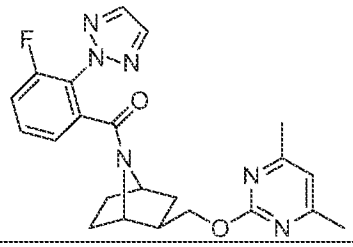
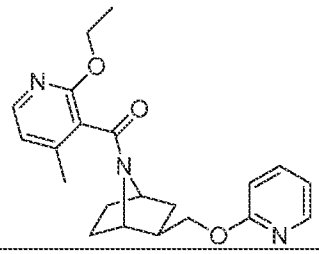
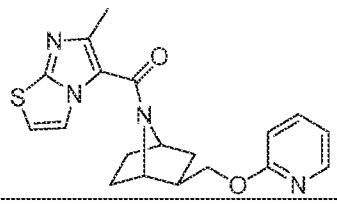
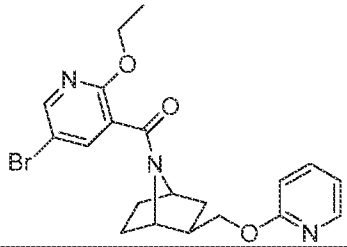
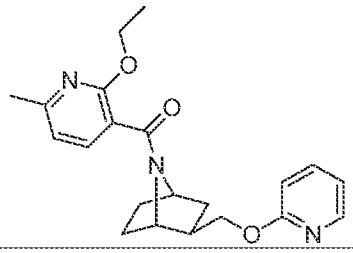
Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
125		47	29	132	(±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(3-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone
126		23	27	231	(±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(5-(hydroxymethyl)-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone
127			190	1100	(±)-(2-(3-methyl-1,2,4-oxadiazol-5-yl)phenyl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
128			5700	10000	(±)-(6-methyl-2-(2H-1,2,3-triazol-2-yl)pyridin-3-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
129			190	1000	(±)-(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
130			3700	7200	(±)-(6-methyl-2-(1H-1,2,3-triazol-1-yl)pyridin-3-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

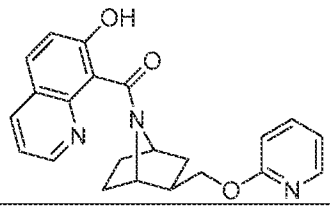
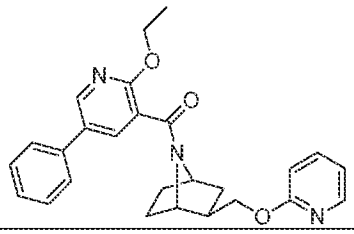
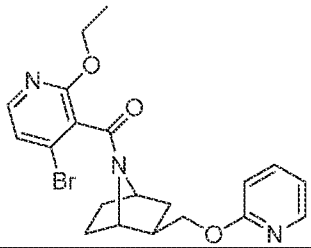
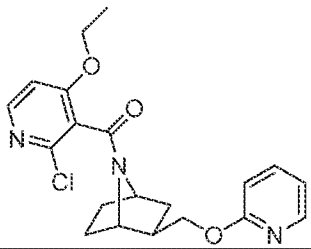
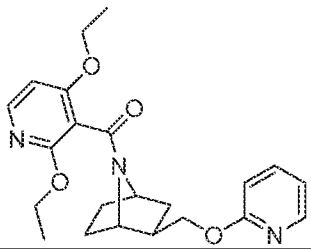
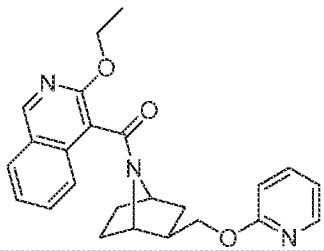
Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
131			10000	10000	(±)-(6-methyl-2-(2H-1,2,3-triazol-2-yl)pyridin-3-yl)(2-(((4-(trifluoromethyl)pyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
132			10000	7400	(±)-(6-methyl-2-(1H-1,2,3-triazol-1-yl)pyridin-3-yl)(2-(((4-(trifluoromethyl)pyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
133			1400	950	(±)-(2-(3-methyl-1,2,4-oxadiazol-5-yl)phenyl)(2-(((4-(trifluoromethyl)pyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
134			1500	690	(±)-(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((4-(trifluoromethyl)pyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
135			5400	3900	(±)-(6-methyl-2-(2H-1,2,3-triazol-2-yl)pyridin-3-yl)(2-(((5-methylpyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

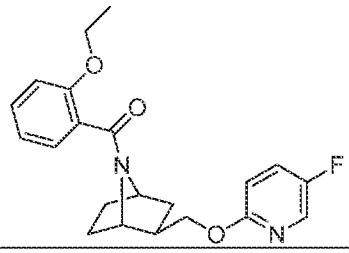
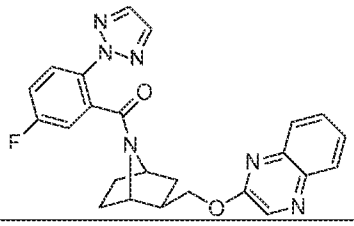
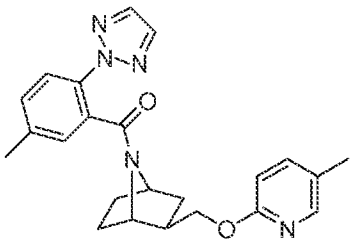
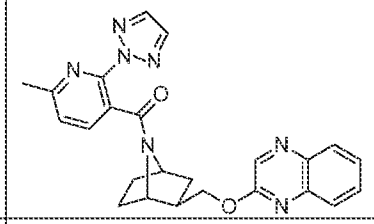
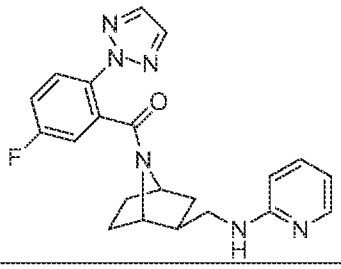
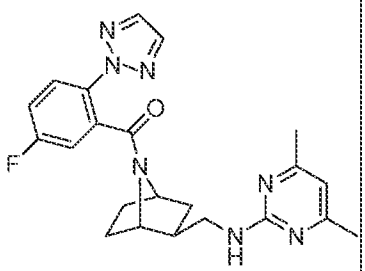
Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
136			6800	1200	(±)-(6-methyl-2-(1H-1,2,3-triazol-1-yl)pyridin-3-yl)(2-(((5-methylpyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
137			950	425	(±)-(2-(3-methyl-1,2,4-oxadiazol-5-yl)phenyl)(2-(((5-methylpyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
138			606	250	(±)-(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((5-methylpyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
139			4400	6500	(±)-(6-methyl-2-(2H-1,2,3-triazol-2-yl)pyridin-3-yl)(2-(((6-methylpyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
140			3100	2300	(±)-(6-methyl-2-(1H-1,2,3-triazol-1-yl)pyridin-3-yl)(2-(((6-methylpyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
141			280	300	(±)-(2-(3-methyl-1,2,4-oxadiazol-5-yl)phenyl)(2-(((6-methylpyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

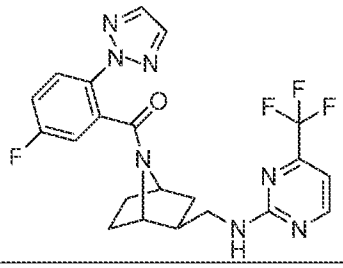
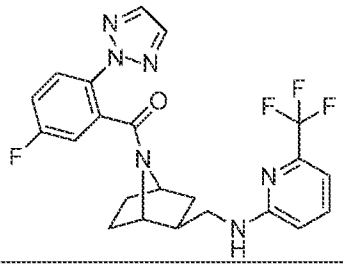
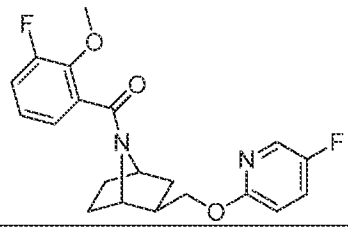
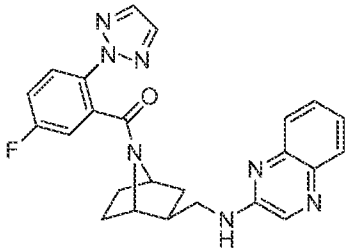
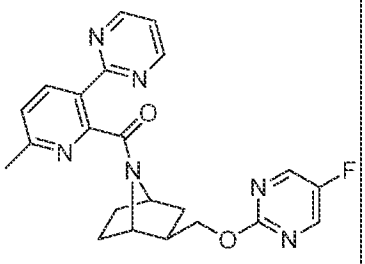
Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
142			207	300	(±)-(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((6-methylpyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
143			3900	4600	(±)-(6-methyl-2-(2H-1,2,3-triazol-2-yl)pyridin-3-yl)(2-(((6-(trifluoromethyl)pyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
144			3600	3200	(±)-(6-methyl-2-(1H-1,2,3-triazol-1-yl)pyridin-3-yl)(2-(((6-(trifluoromethyl)pyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
145			340	330	(±)-(2-(3-methyl-1,2,4-oxadiazol-5-yl)phenyl)(2-(((6-(trifluoromethyl)pyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
146			180	196	(±)-(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((6-(trifluoromethyl)pyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

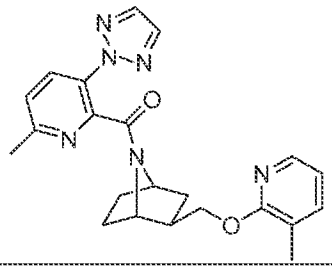
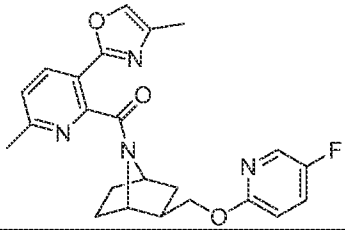
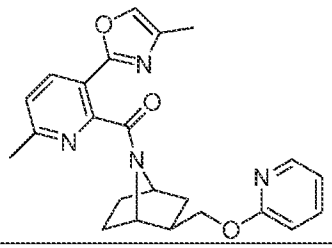
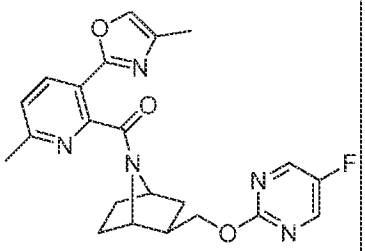
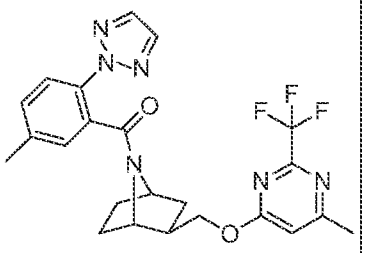
Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
147					(±)-(6-methyl-2-(2H-1,2,3-triazol-2-yl)pyridin-3-yl)(2-((quinoxalin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
148			6300	3200	(±)-(6-methyl-2-(1H-1,2,3-triazol-1-yl)pyridin-3-yl)(2-((quinoxalin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
149			220	2000	(±)-(2-(3-methyl-1,2,4-oxadiazol-5-yl)phenyl)(2-((quinoxalin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
150			180	990	(±)-(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((quinoxalin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
151			10000	10000	(±)-(2-(((4,6-dimethylpyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-2-(2H-1,2,3-triazol-2-yl)pyridin-3-yl)methanone
152			10000	5900	(±)-(2-(((4,6-dimethylpyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-2-(1H-1,2,3-triazol-1-yl)pyridin-3-yl)methanone

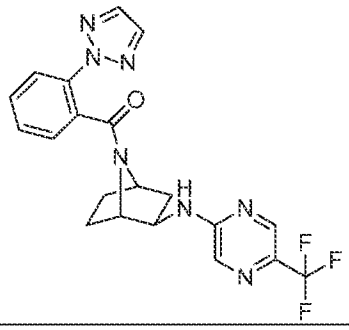
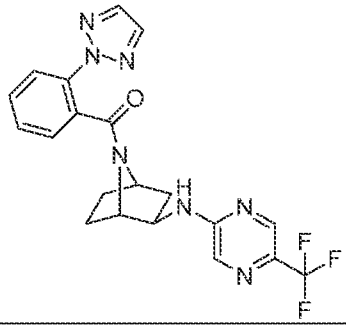
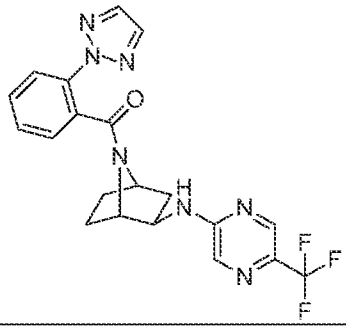
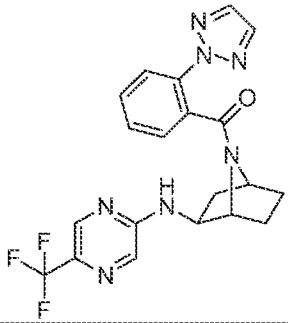
Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
153			1100	440	(±)-(2-(((4,6-dimethylpyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(2-(3-methyl-1,2,4-oxadiazol-5-yl)phenyl)methanone
154			690	300	(±)-(2-(((4,6-dimethylpyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone
155		1570		3600	(±)-(2-ethoxy-4-methylpyridin-3-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
156		>10000		>10000	(±)-(6-methylimidazo[2,1-b]thiazol-5-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
157		94	134	537	(±)-(5-bromo-2-ethoxypyridin-3-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
158		2930		1780	(±)-(2-ethoxy-6-methylpyridin-3-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

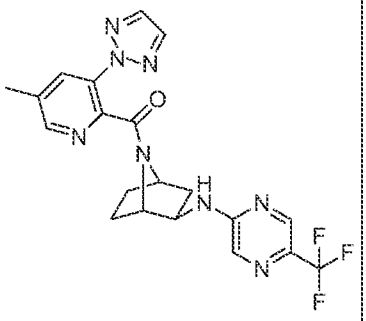
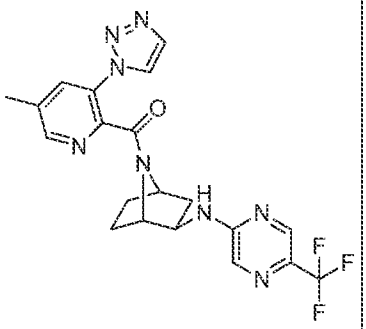
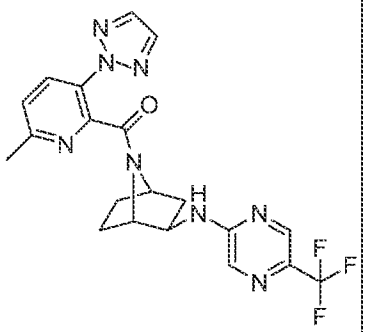
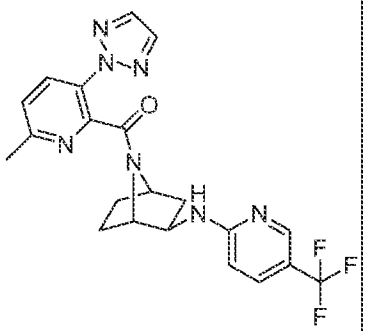
Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
159		262		786	(±)-(7-hydroxyquinolin-8-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
160		8700		>10000	(±)-(2-ethoxy-5-phenylpyridin-3-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
161		478		1450	(±)-(4-bromo-2-ethoxypyridin-3-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
162		8500		>10000	(±)-(2-chloro-4-ethoxypyridin-3-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
163		150	153	150	(±)-(2,4-diethoxypyridin-3-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
164		9	7	195	(3-ethoxyisoquinolin-4-yl)((1S,2R,4R)-2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

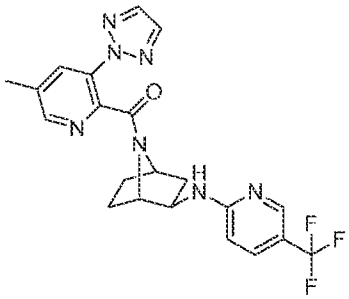
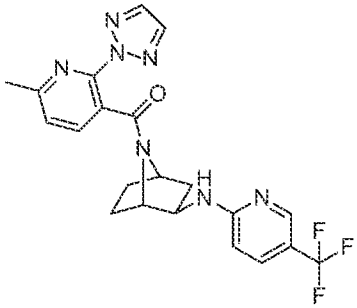
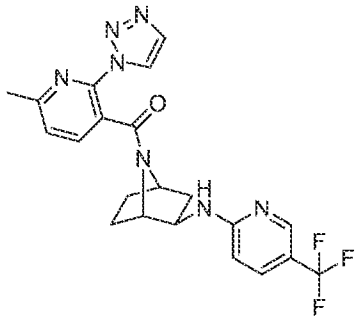
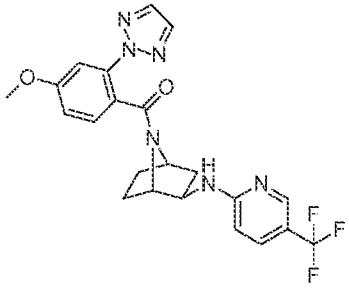
Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
165			409	550	(±)-(2-ethoxyphenyl)(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
166			107	1177	(±)-(5-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((quinoxalin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
167			9	14	(±)-5-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((5-methylpyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
168			2300	7300	(±)-(6-methyl-2-(2H-1,2,3-triazol-2-yl)pyridin-3-yl)(2-((quinoxalin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
169			9000	2526	(±)-(5-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((pyridin-2-ylamino)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
170			1965	512	(±)-(2-(((4,6-dimethylpyrimidin-2-yl)amino)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(5-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone

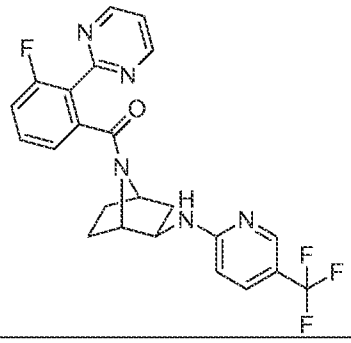
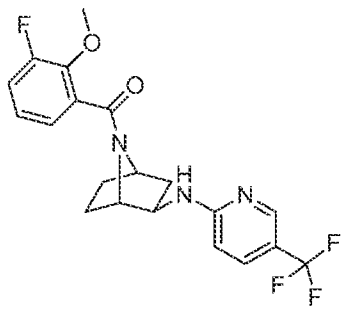
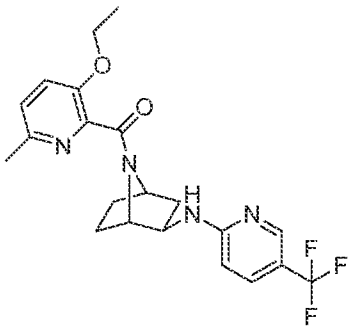
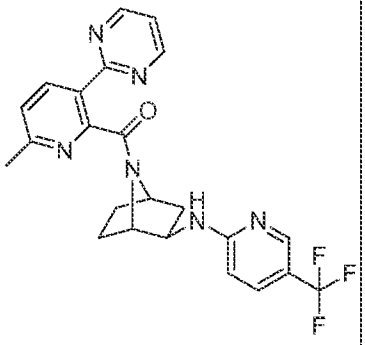
Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
171			1935		(±)-(5-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((4-(trifluoromethyl)pyrimidin-2-yl)amino)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
172			686		(±)-(5-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((6-(trifluoromethyl)pyridin-2-yl)amino)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
173		1260		3000	(±)-(3-fluoro-2-methoxyphenyl)(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
174		373		1000	(±)-(5-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((quinoxalin-2-ylamino)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
175		2500		4000	(±)-(2-(((5-fluoropyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(pyrimidin-2-yl)pyridin-2-yl)methanone

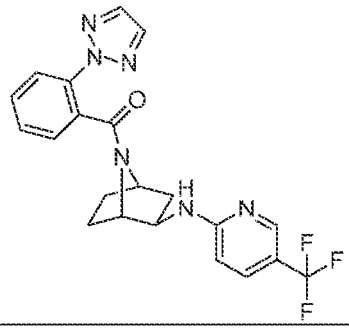
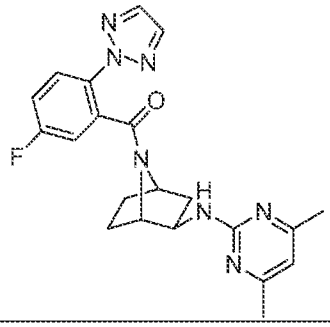
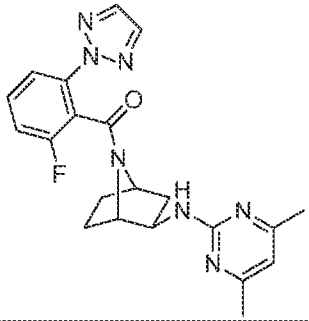
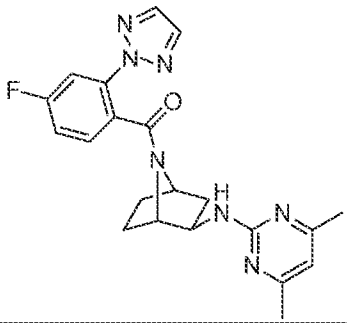
Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
176		119	150	202	(±)-(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-(((3-methylpyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
177		535		4000	(±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(4-methyloxazol-2-yl)pyridin-2-yl)methanone
178		964		>10000	(6-methyl-3-(4-methyloxazol-2-yl)pyridin-2-yl)((1S,2R,4R)-2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
179		2400		5400	((1S,2R,4R)-2-(((5-fluoropyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(4-methyloxazol-2-yl)pyridin-2-yl)methanone
180			33	32	(±)-(5-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((6-methyl-2-(trifluoromethyl)pyrimidin-4-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

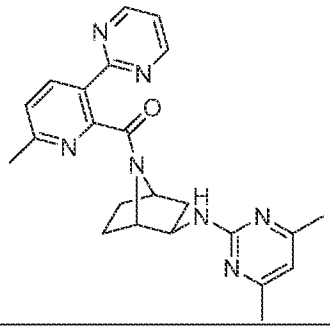
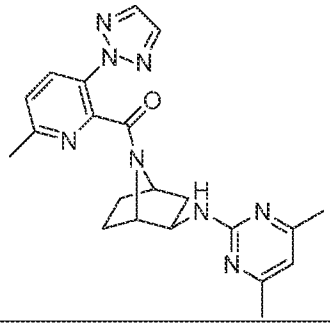
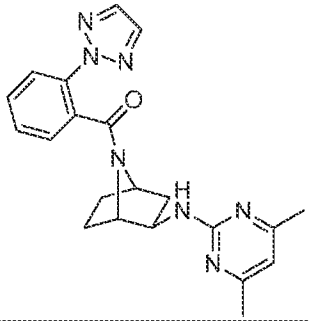
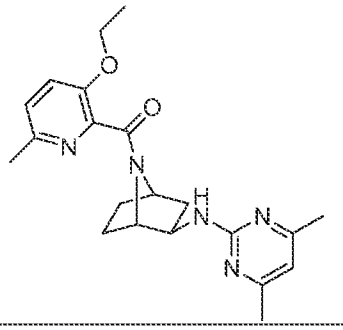
Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
181		35	28	728	(2-(2H-1,2,3-triazol-2-yl)phenyl)(1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
182		47	38	1100	(±)-((2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
183A		>10000		>10000	(2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
183B		35	28	728	(2-(2H-1,2,3-triazol-2-yl)phenyl)((1R,2S,4S)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

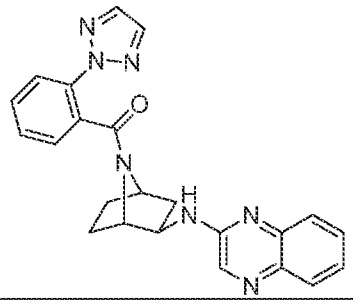
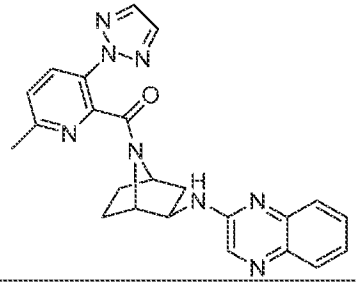
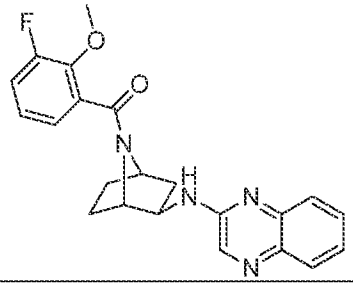
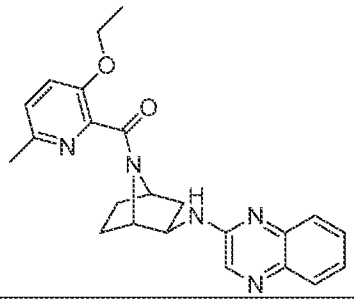
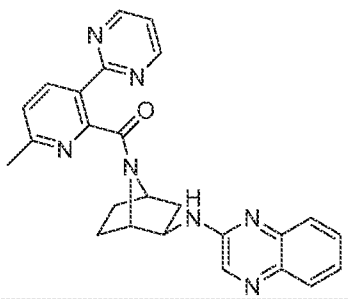
Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
184		189	349	4100	(±)-(5-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
185		1500		2700	(±)-(5-methyl-3-(1H-1,2,3-triazol-1-yl)pyridin-2-yl)(2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
186		134	164	1200	(±)-(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
187		81	48	620	(±)-(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

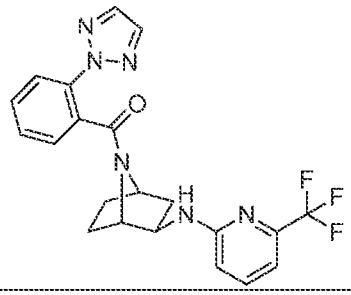
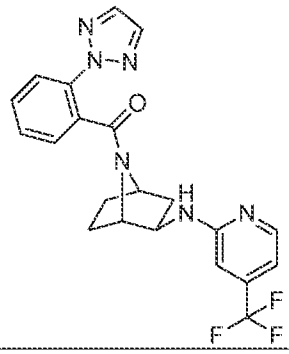
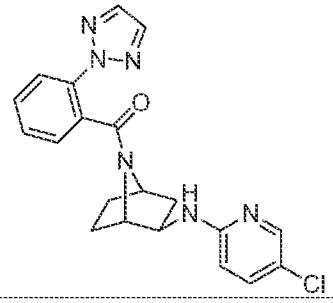
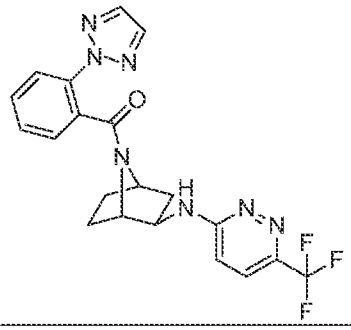
Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
188		295		1500	(±)-(5-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
189		766		1500	(±)-(6-methyl-2-(2H-1,2,3-triazol-2-yl)pyridin-3-yl)(2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
190		589		1200	(±)-(6-methyl-2-(1H-1,2,3-triazol-1-yl)pyridin-3-yl)(2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
191		257		8800	(±)-(4-methoxy-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

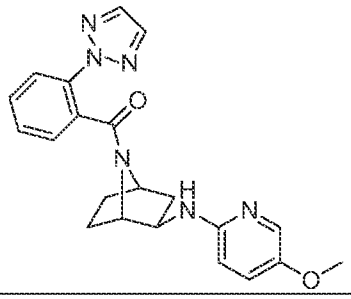
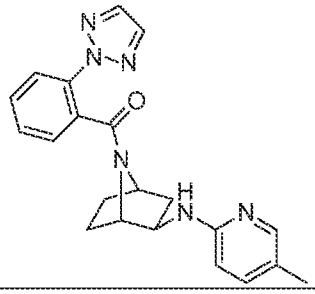
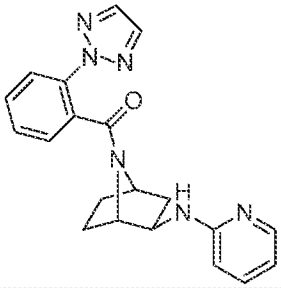
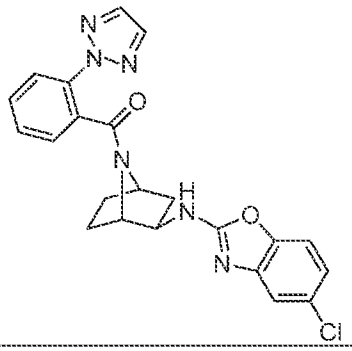
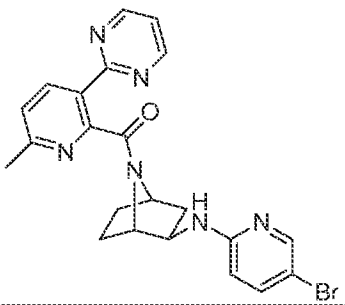
Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
192		60	52	1500	(±)-(3-fluoro-2-(pyrimidin-2-yl)phenyl)(2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
193		2900		>10000	(±)-((3-fluoro-2-methoxyphenyl)(2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
194		450		800	(±)-(3-ethoxy-6-methylpyridin-2-yl)(2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
195		57	37	325	(±)-(6-methyl-3-(pyrimidin-2-yl)pyridin-2-yl)(2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

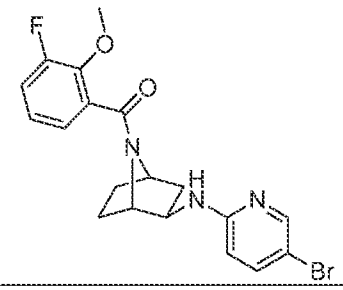
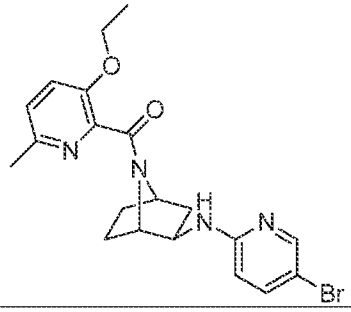
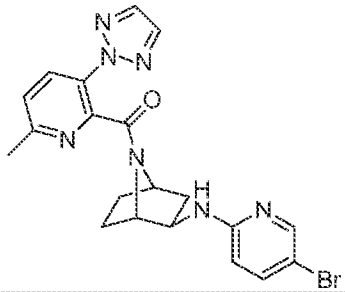
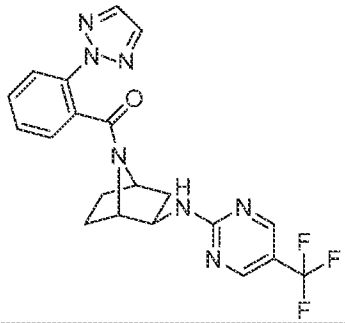
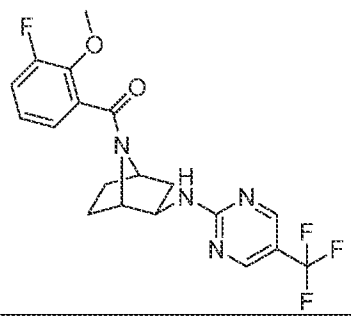
Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
196		59	61	1500	(±)-(2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
197			9000	862	(±)-(2-((4,6-dimethylpyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(5-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone
198			1411	704	(±)-(2-((4,6-dimethylpyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(2-fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl)methanone
199			1634	553	(±)-(2-((4,6-dimethylpyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(4-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone

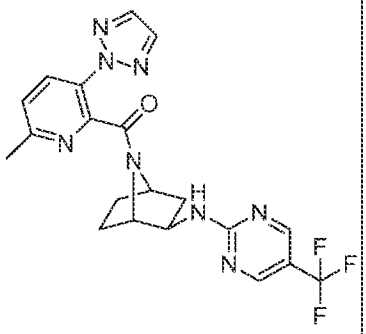
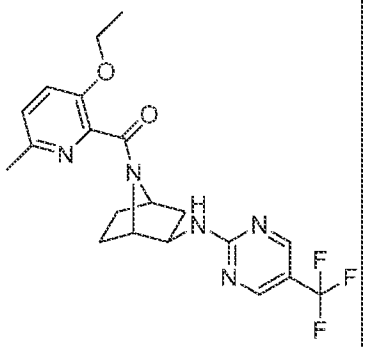
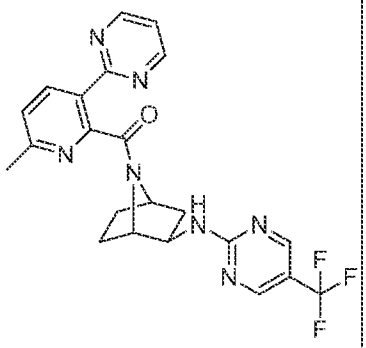
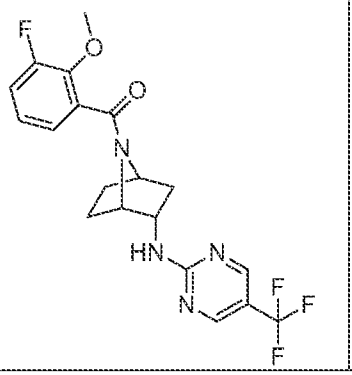
Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
200		1100		552	(±)-(2-((4,6-dimethylpyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(pyrimidin-2-yl)pyridin-2-yl)methanone
201		3700		1100	(±)-(2-((4,6-dimethylpyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)methanone
202		760		444	(±)-(2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((4,6-dimethylpyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
203		>10000		490	(±)-(2-((4,6-dimethylpyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-ethoxy-6-methylpyridin-2-yl)methanone

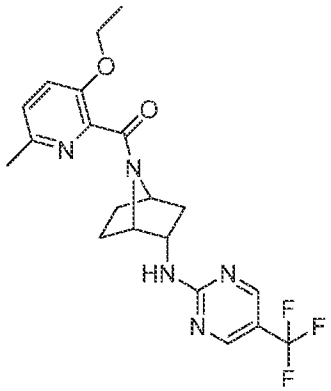
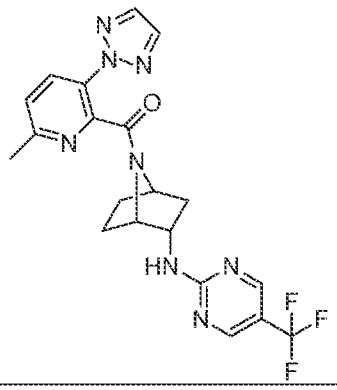
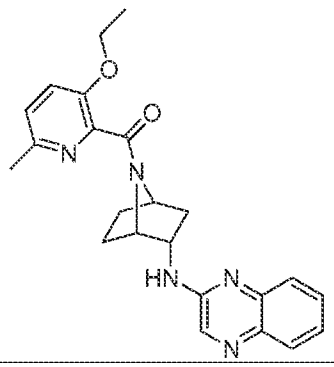
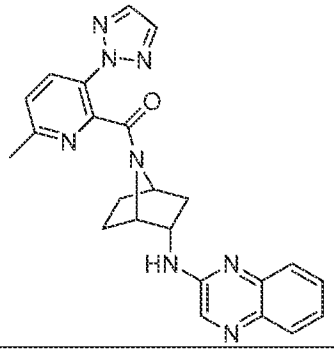
Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
204		33	25	220	(±)-(2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(quinoxalin-2-ylamino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
205		79	50	168	(±)-(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-(quinoxalin-2-ylamino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
206		1200		1500	(±)-(3-fluoro-2-methoxyphenyl)(2-(quinoxalin-2-ylamino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
207		120	95	64	(±)-(3-ethoxy-6-methylpyridin-2-yl)(2-(quinoxalin-2-ylamino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
208		26	30	90	(±)-(6-methyl-3-(pyrimidin-2-yl)pyridin-2-yl)(2-(quinoxalin-2-ylamino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

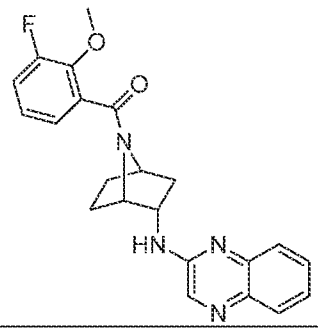
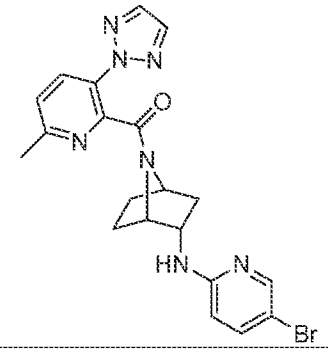
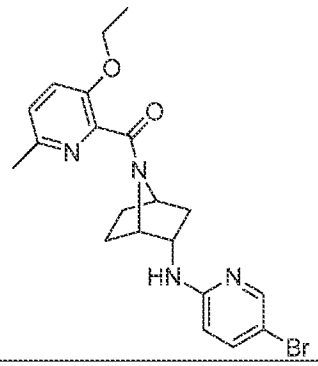
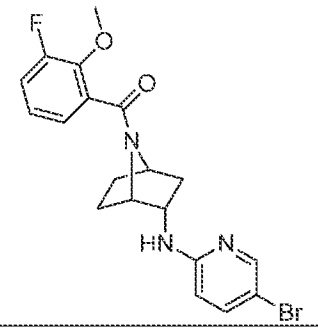
Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
209		1100		736	(±)-(2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((6-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
210		211		128	(±)-((2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((4-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
211		110	55	1800	(±)-(2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((5-chloropyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
212		734		4900	(±)-(2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((6-(trifluoromethyl)pyridazin-3-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

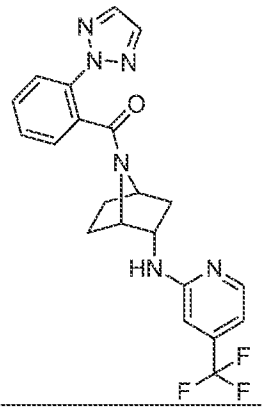
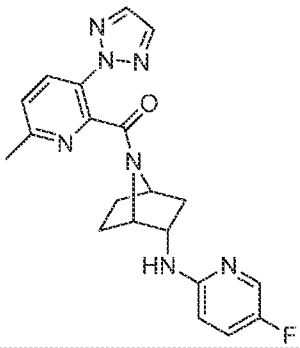
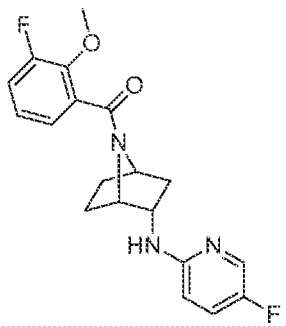
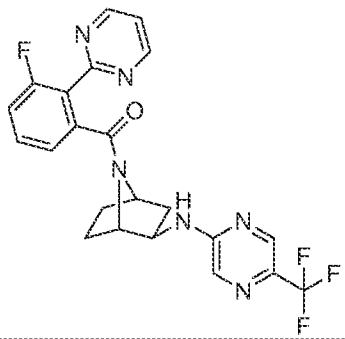
Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
213		2800		7500	(±)-(2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((5-methoxypyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
214		500		3100	(±)-(2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((5-methylpyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
215		1700		9000	(±)-(2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(pyridin-2-ylamino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
216		99	71	475	(±)-(2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((5-chlorobenzo[d]oxazol-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
217		59	40	770	(±)-(2-((5-bromopyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(pyrimidin-2-yl)pyridin-2-yl)methanone

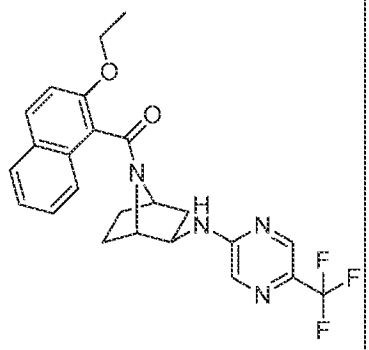
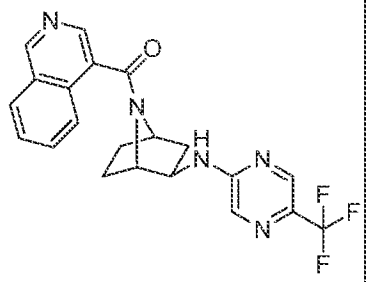
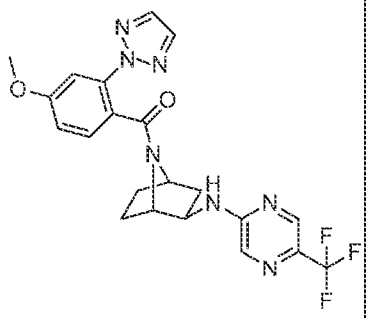
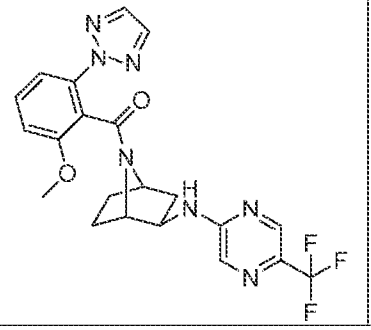
Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
218		2700		6700	(±)-(2-((5-bromopyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-methoxyphenyl)methanone
219		257		1700	(±)-(2-((5-bromopyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-ethoxy-6-methylpyridin-2-yl)methanone
220		38	26	1100	(±)-(2-((5-bromopyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)methanone
221		172	200	3300	(±)-(2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
222		4800		>10000	(±)-(3-fluoro-2-methoxyphenyl)(2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

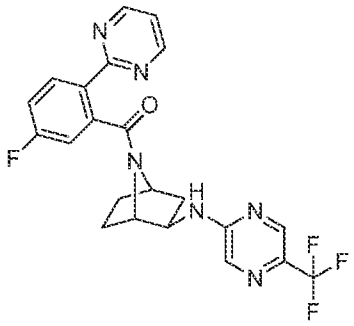
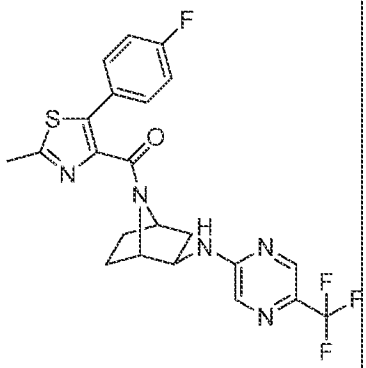
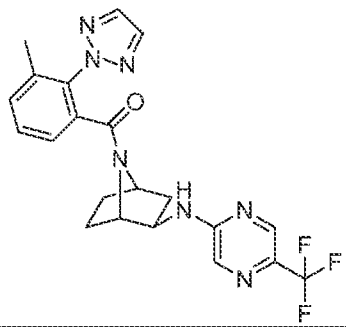
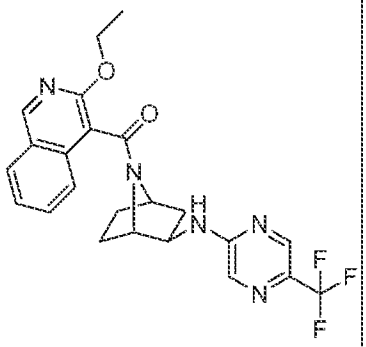
Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
223		550		4000	(±)-(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
224		2500		7400	(±)-(3-ethoxy-6-methylpyridin-2-yl)(2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
225		530		3300	(±)-(6-methyl-3-(pyrimidin-2-yl)pyridin-2-yl)(2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
226		>10000		>10000	(±)-(3-fluoro-2-methoxyphenyl)(2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

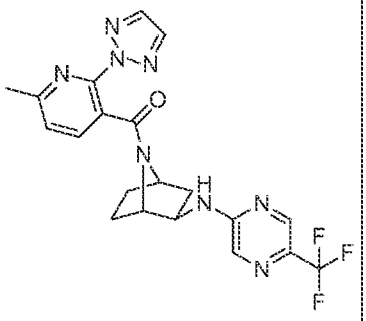
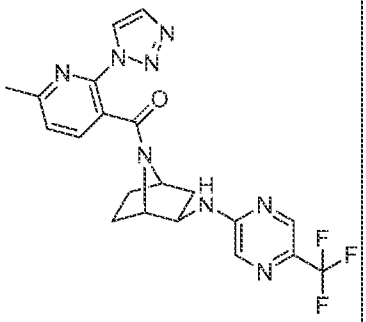
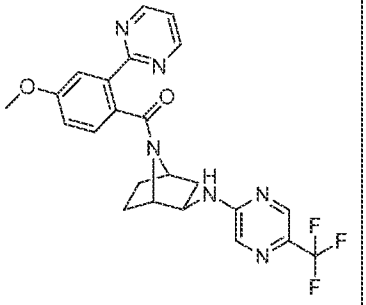
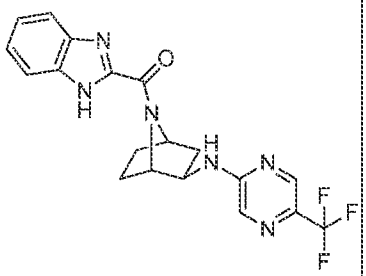
Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
227		>10000		>10000	(±)-(3-ethoxy-6-methylpyridin-2-yl)(2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
228		>10000		>10000	(±)-(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
229		>10000		>10000	(±)-(3-ethoxy-6-methylpyridin-2-yl)(2-(quinoxalin-2-ylamino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
230		>10000		>10000	(±)-(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-(quinoxalin-2-ylamino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

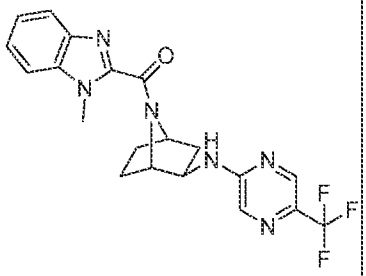
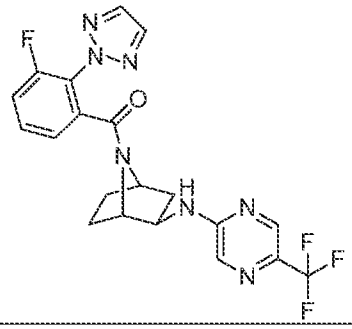
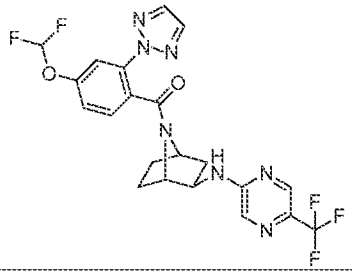
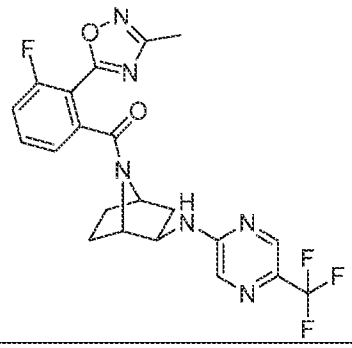
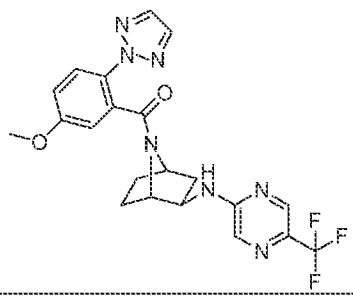
Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
231		>10000		>10000	(±)-(3-fluoro-2-methoxyphenyl)(2-(quinoxalin-2-ylamino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
232					(±)-(2-((5-bromopyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)methanone
233					(±)-(2-((5-bromopyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-ethoxy-6-methylpyridin-2-yl)methanone
234					(±)-(2-((5-bromopyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-methoxyphenyl)methanone

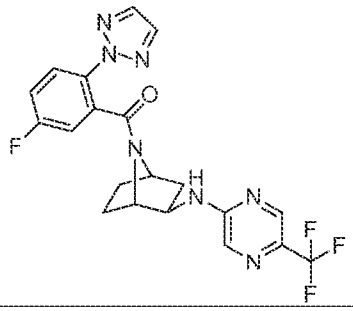
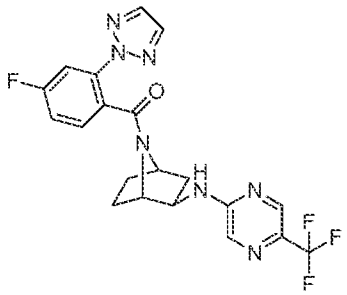
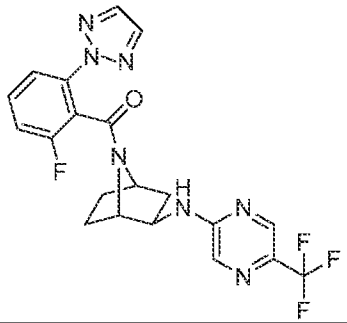
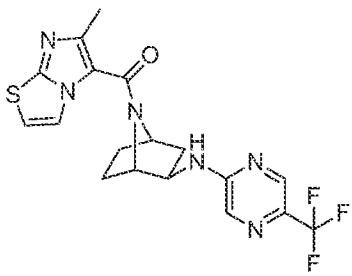
Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
235		>10000		>10000	(±)-((2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((4-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
236		>10000		>10000	(±)-(2-((5-fluoropyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)methanone
237		>10000		>10000	(±)-(3-fluoro-2-methoxyphenyl)(2-((5-fluoropyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
238		15	15	763	(3-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

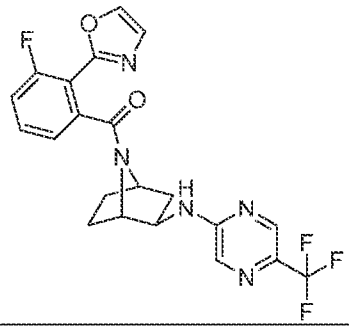
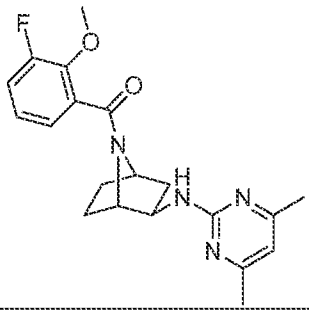
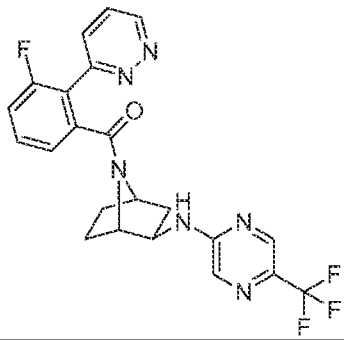
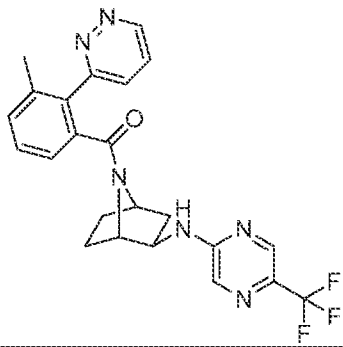
Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
239		22	19	490	(2-ethoxynaphthalen-1-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
240		400		2100	isoquinolin-4-yl((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
241		135	159	5100	(4-methoxy-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
242		31	41	239	(2-methoxy-6-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

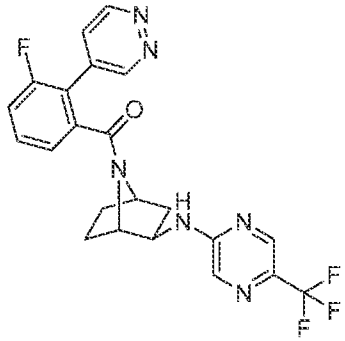
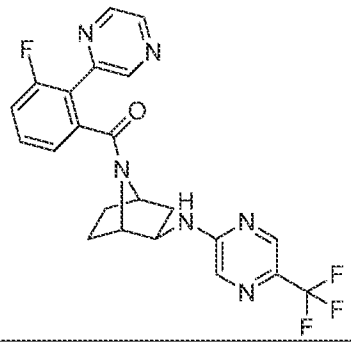
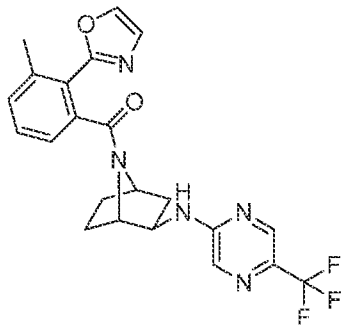
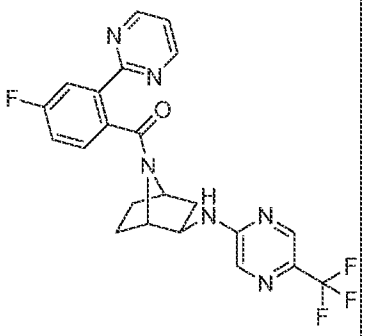
Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
243		35	45	725	(5-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
244		74	46	235	(5-(4-fluorophenyl)-2-methylthiazol-4-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
245		10	7	288	(3-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
246		30	17	1027	(3-ethoxyisoquinolin-4-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

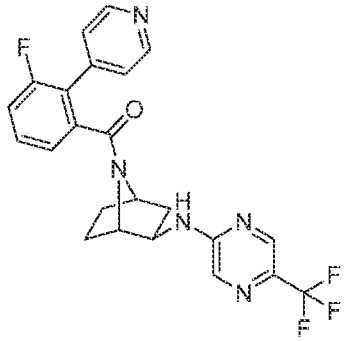
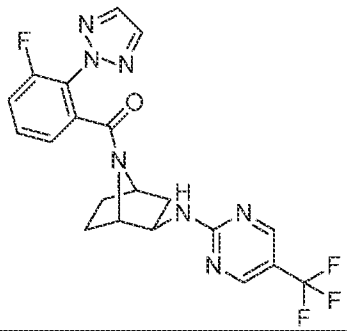
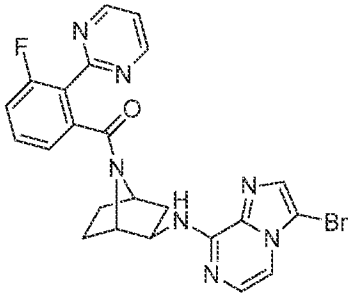
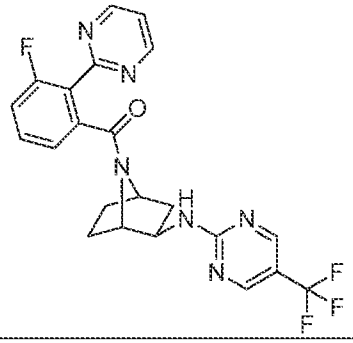
Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
247		420		1130	(6-methyl-2-(2H-1,2,3-triazol-2-yl)pyridin-3-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
248		153	119	>10000	(6-methyl-2-(1H-1,2,3-triazol-1-yl)pyridin-3-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
249		57	54	5600	(4-methoxy-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
250		5650		>10000	(1H-benzo[d]imidazol-2-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

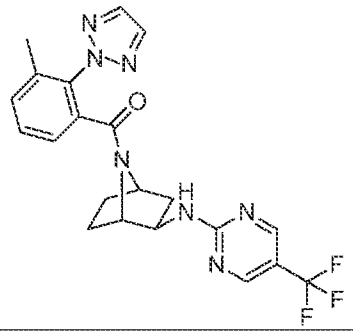
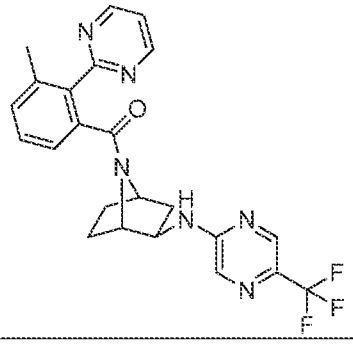
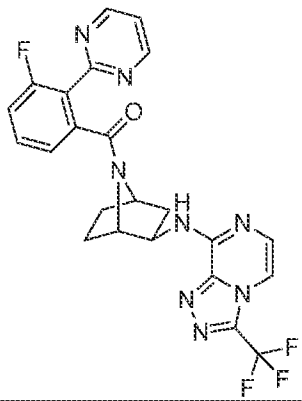
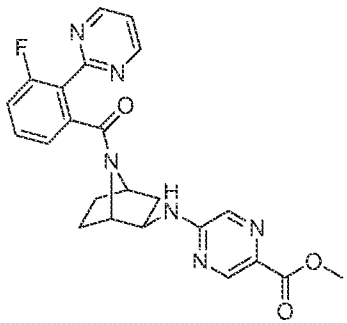
Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
251		520		5300	(1-methyl-1H-benzo[d]imidazol-2-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
252		45	27	1230	(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
253		155	152	9600	(4-(difluoromethoxy)-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
254		23	20	377	(3-fluoro-2-(3-methyl-1,2,4-oxadiazol-5-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
255		32	29	265	(5-methoxy-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

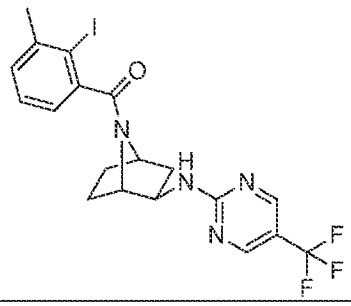
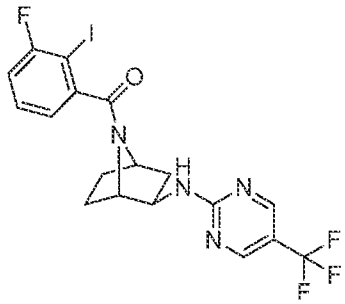
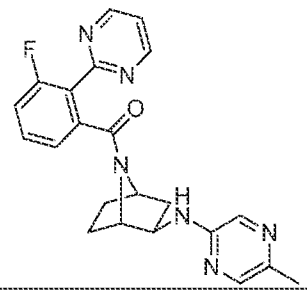
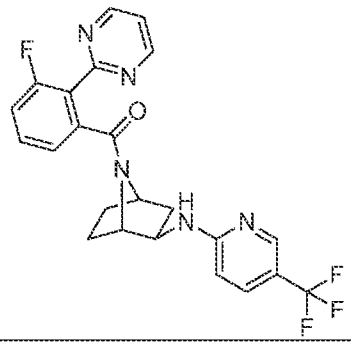
Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
256		84	60	1100	(5-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
257		85	102	3200	(4-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
258		42	48	690	(2-fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
259		>10000		>10000	(6-methylimidazo[2,1-b]thiazol-5-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

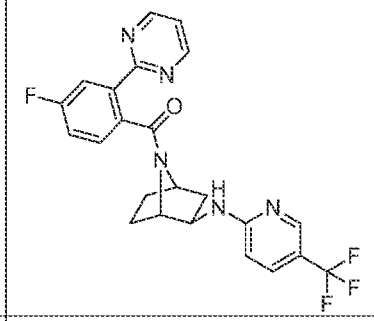
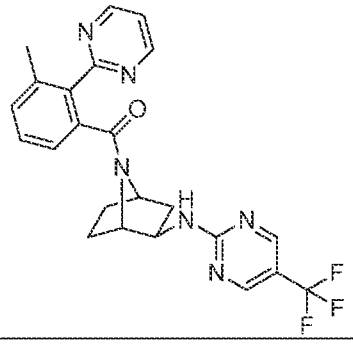
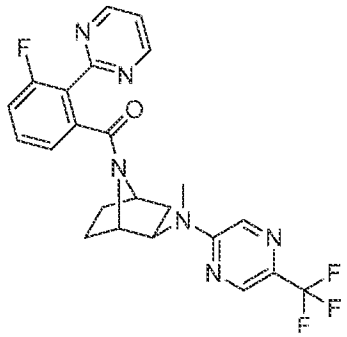
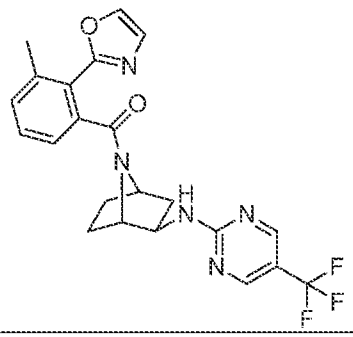
Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
260		14	10	519	(3-fluoro-2-(oxazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
261		>10000		5000	(2-((4,6-dimethylpyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-methoxyphenyl)methanone
262		106	175	4200	(3-fluoro-2-(pyridazin-3-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
263		44	41	1100	(3-methyl-2-(pyridazin-3-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

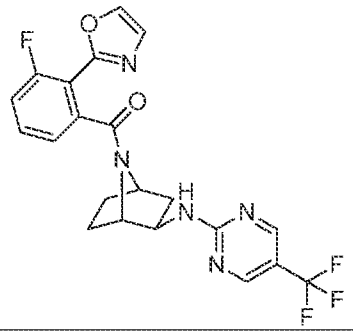
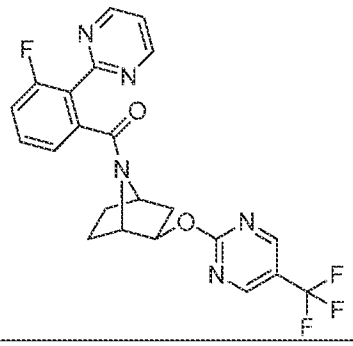
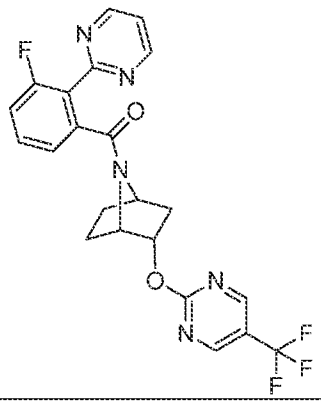
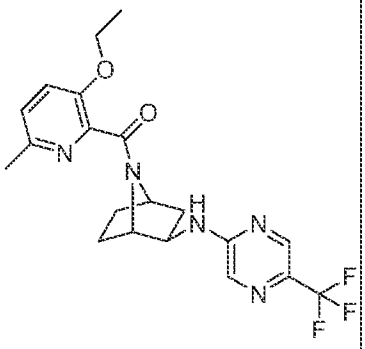
Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
264		1400		>10000	(3-fluoro-2-(pyridazin-4-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
265		20	23	188	(3-fluoro-2-(pyrazin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
266		6	7	121	(3-methyl-2-(oxazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
267		33	61	1700	(4-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

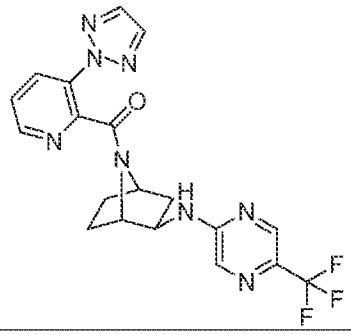
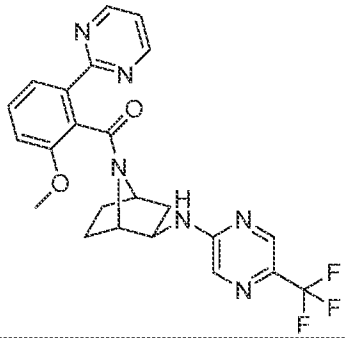
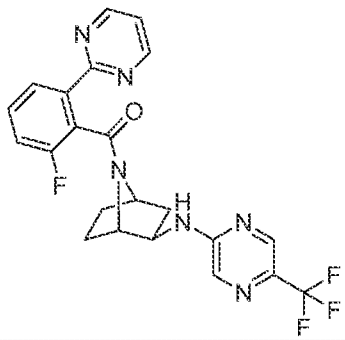
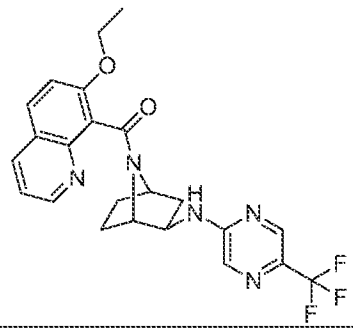
Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
268		450		3700	(3-fluoro-2-(pyridin-4-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
269		48	111	1700	(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
270		325		145	((1S,2R,4R)-2-((3-bromoimidazo[1,2-a]pyrazin-8-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-(pyrimidin-2-yl)phenyl)methanone
271		41	42	2300	(3-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

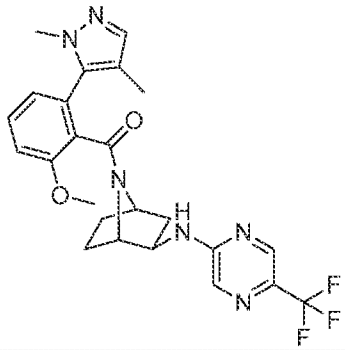
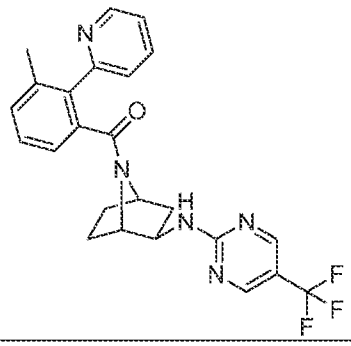
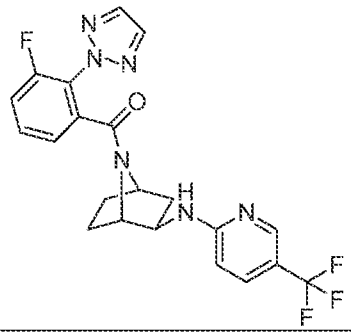
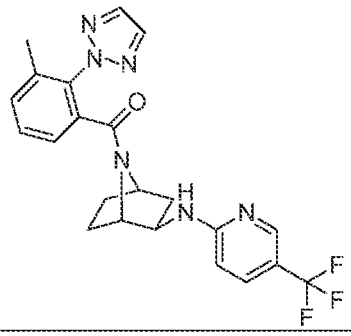
Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
272		21	26	742	(3-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
273		17	12	328	(3-methyl-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
274		>10000		2560	(3-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((3-(trifluoromethyl)-[1,2,4]triazolo[4,3-a]pyrazin-8-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
275		>10000		>10000	methyl 5-(((1S,2R,4R)-7-(3-fluoro-2-(pyrimidin-2-yl)benzoyl)-7-azabicyclo[2.2.1]heptan-2-yl)amino)pyrazine-2-carboxylate

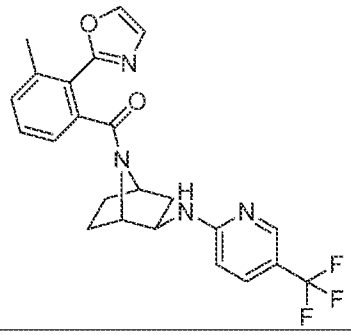
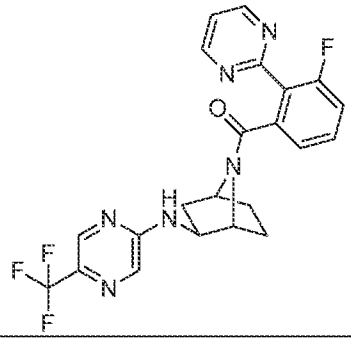
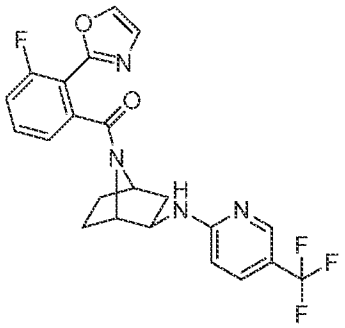
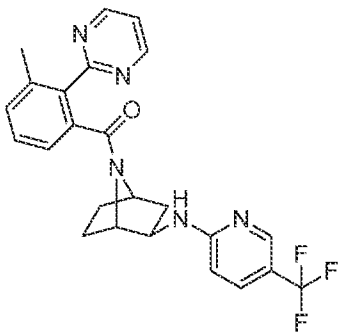
Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
276		133	97	2500	(2-iodo-3-methylphenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
277		457		7400	(3-fluoro-2-iodophenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
278		87	77	934	(3-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-methylpyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
279		18	9	990	(3-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

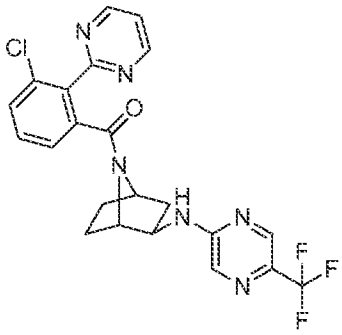
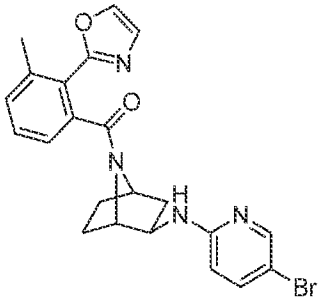
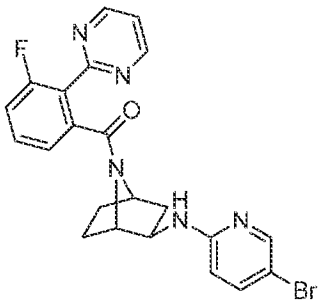
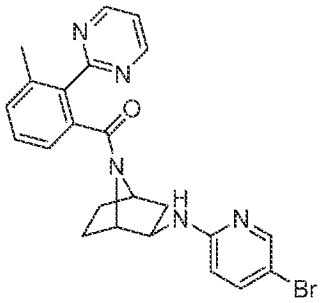
Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
280		39	37	1300	(4-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
281		21	17	1200	(3-methyl-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
282		486		>10000	(3-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-(methyl(5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
283		14	9	417	(3-methyl-2-(oxazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

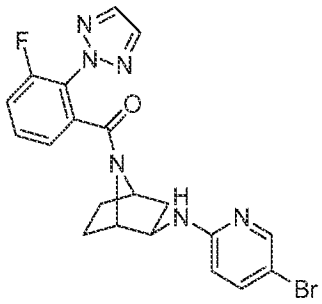
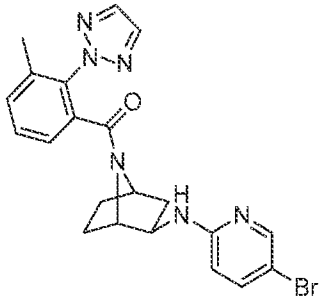
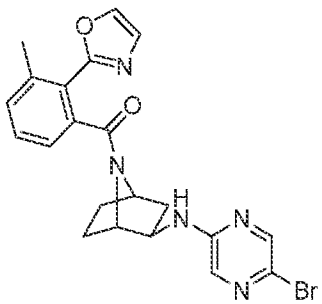
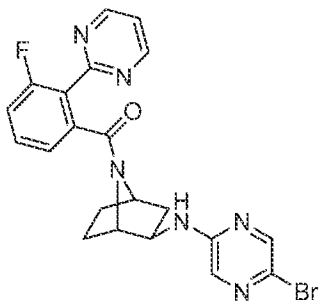
Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
284		29	27	1700	(3-fluoro-2-(oxazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
285		720		>10000	(±)-(3-fluoro-2-(pyrimidin-2-yl)phenyl)(2-((5-(trifluoromethyl)pyrimidin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
286		>10000		>10000	(±)-(3-fluoro-2-(pyrimidin-2-yl)phenyl)(2-((5-(trifluoromethyl)pyrimidin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
287		472		767	(3-ethoxy-6-methylpyridin-2-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

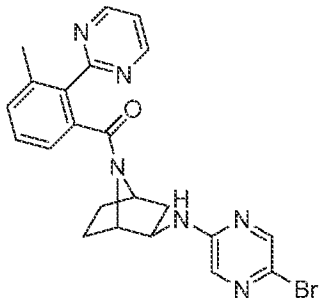
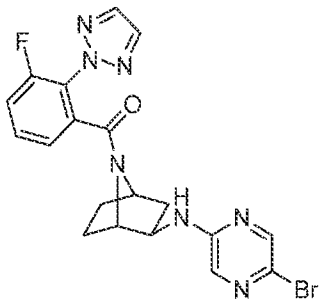
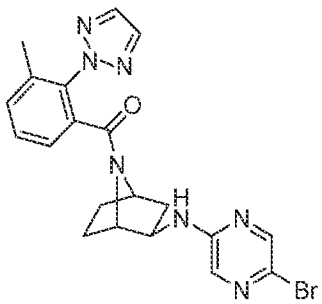
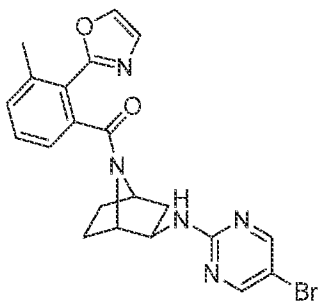
Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
288		94	128	1900	(3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
289		13	32	173	(2-methoxy-6-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
290		21	19	558	(2-fluoro-6-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
291		15	35	425	(7-ethoxyquinolin-8-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

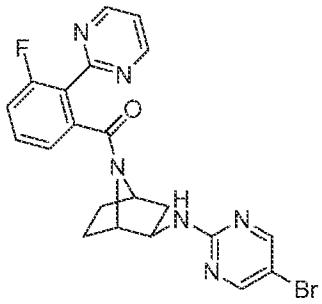
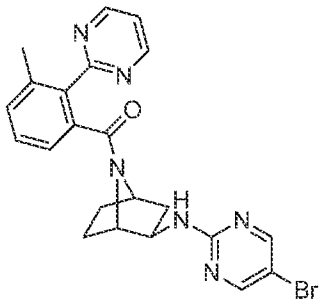
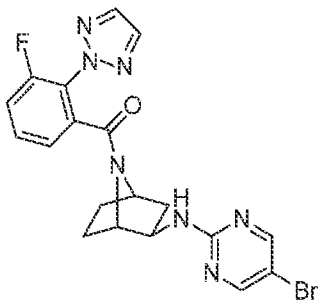
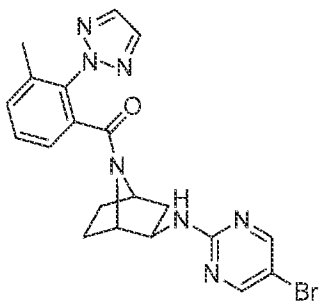
Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
292		>10000		>10000	(2-(1,4-dimethyl-1H-pyrazol-5-yl)-6-methoxyphenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
293		23	37	1100	(3-methyl-2-(pyridin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
294		21	15	1200	(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
295		9	8	257	(3-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

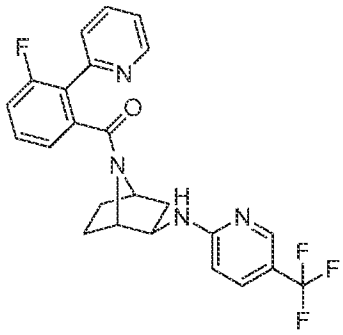
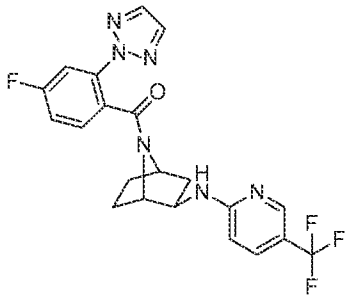
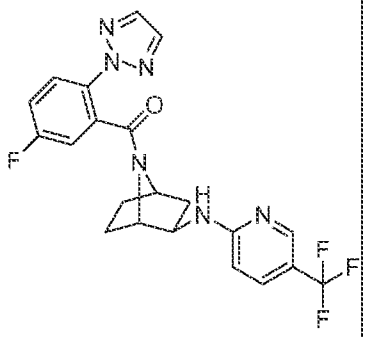
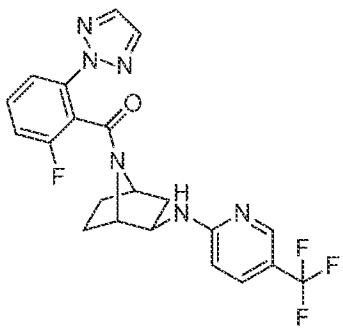
Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
296		5	6	114	(3-methyl-2-(oxazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
297		402	>10000	>10000	(3-fluoro-2-(pyrimidin-2-yl)phenyl)((1R,2S,4S)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
298		18	18	500	(3-fluoro-2-(oxazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
299		16	7	234	(3-methyl-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

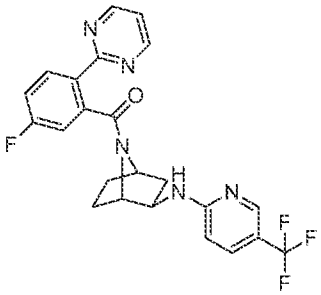
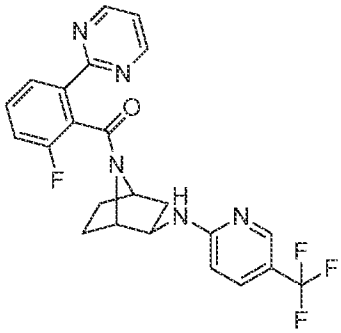
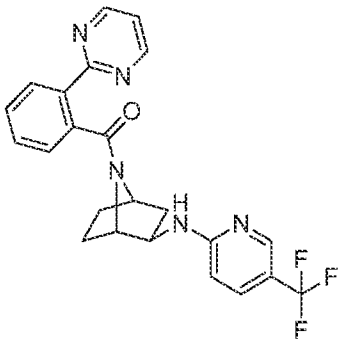
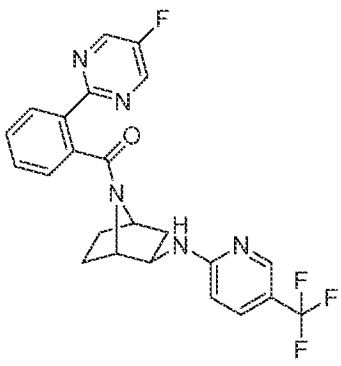
Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
300		9	9	93	(3-chloro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
302		5	5	188	((1S,2R,4R)-2-((5-bromopyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-methyl-2-(oxazol-2-yl)phenyl)methanone
303		22	16	1300	((1S,2R,4R)-2-((5-bromopyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-(pyrimidin-2-yl)phenyl)methanone
304		12	16	455	((1S,2R,4R)-2-((5-bromopyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-methyl-2-(pyrimidin-2-yl)phenyl)methanone

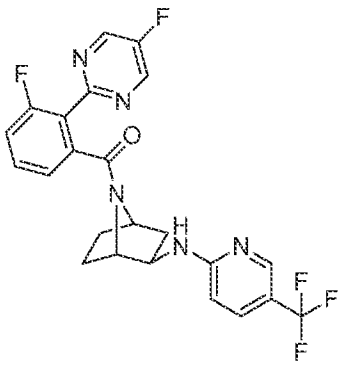
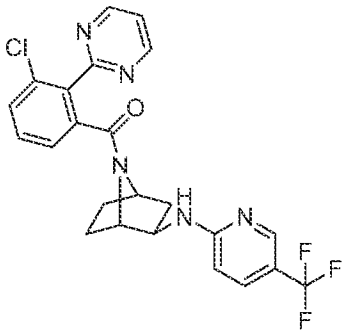
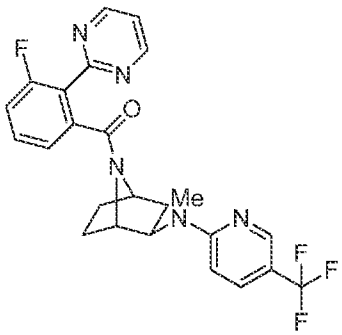
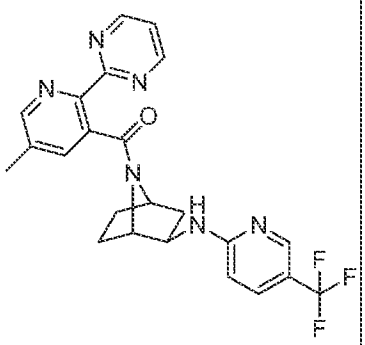
Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
305		24	12	980	((1S,2R,4R)-2-((5-bromopyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone
306		11	4	396	((1S,2R,4R)-2-((5-bromopyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone
308		6	4	173	((1S,2R,4R)-2-((5-bromopyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-methyl-2-(oxazol-2-yl)phenyl)methanone
309		19	22	1100	((1S,2R,4R)-2-((5-bromopyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-(pyrimidin-2-yl)phenyl)methanone

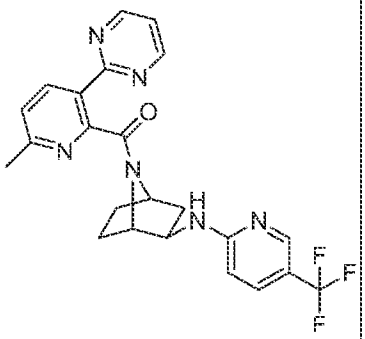
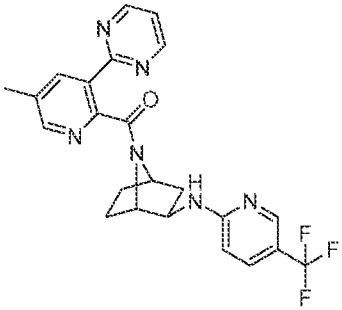
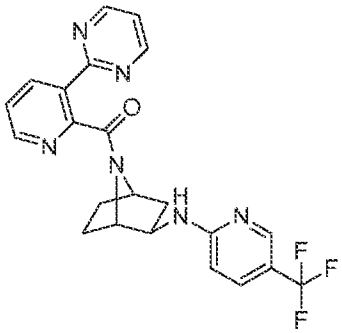
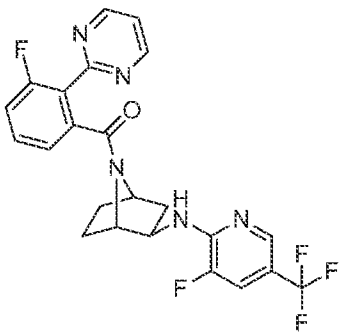
Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
310		9	7	381	((1S,2R,4R)-2-((5-bromopyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-methyl-2-(pyrimidin-2-yl)phenyl)methanone
311		17	21	1000	((1S,2R,4R)-2-((5-bromopyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone
312		6	9	360	((1S,2R,4R)-2-((5-bromopyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone
314		6	14	349	((1S,2R,4R)-2-((5-bromopyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-methyl-2-(oxazol-2-yl)phenyl)methanone

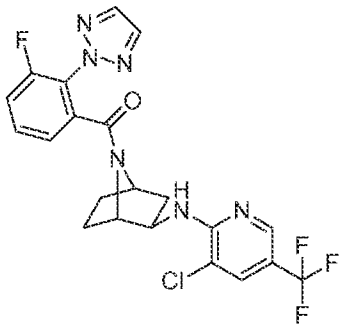
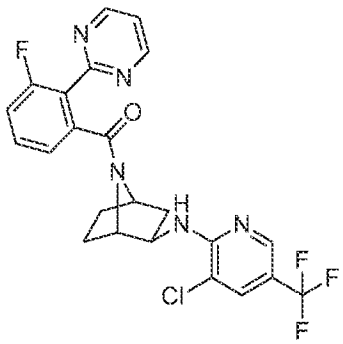
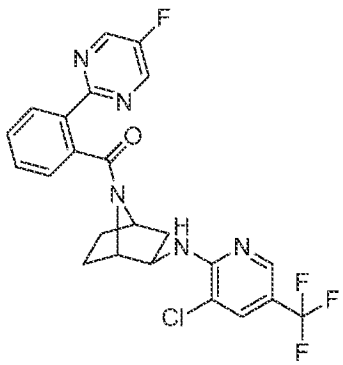
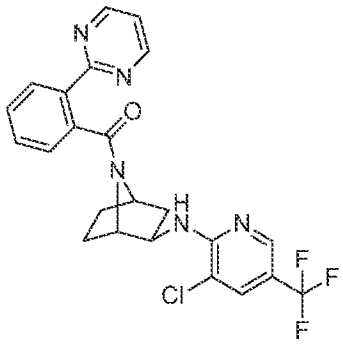
Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
315		30	52	1850	((1S,2R,4R)-2-((5-bromopyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-(pyrimidin-2-yl)phenyl)methanone
316		20	59	796	((1S,2R,4R)-2-((5-bromopyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-methyl-2-(pyrimidin-2-yl)phenyl)methanone
317		31	70	1600	((1S,2R,4R)-2-((5-bromopyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone
318		9	13	768	((1S,2R,4R)-2-((5-bromopyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone

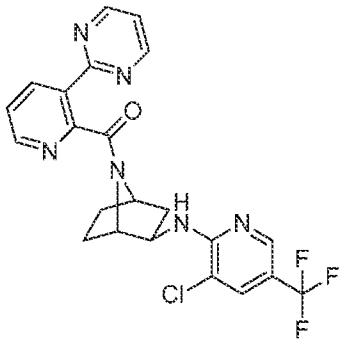
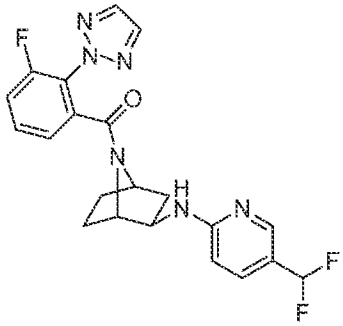
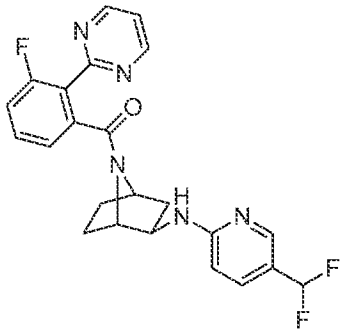
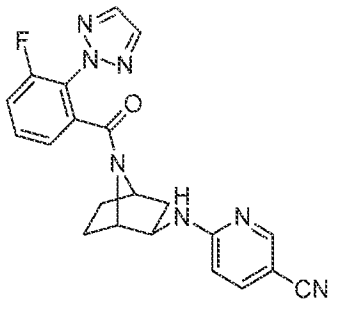
Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
320		32	14	260	(3-fluoro-2-(pyridin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
368		78	71	2600	(4-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
369		67	45	629	(5-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
370		104	142	508	(2-fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

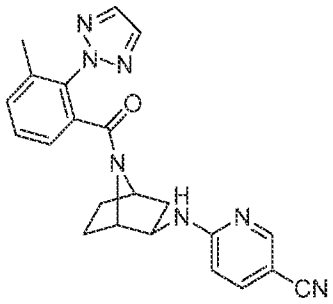
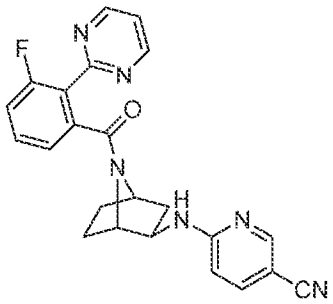
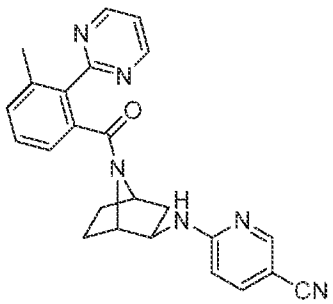
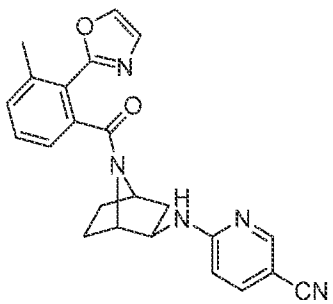
Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
371		42	27	615	(5-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
372		19	13	420	(2-fluoro-6-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
373		34	36	679	(2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
374		41	31	921	(2-(5-fluoropyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

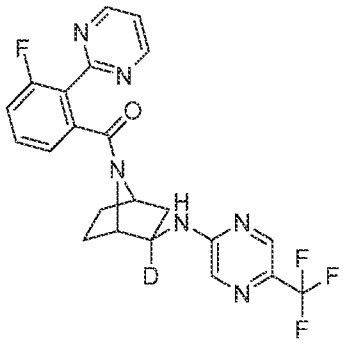
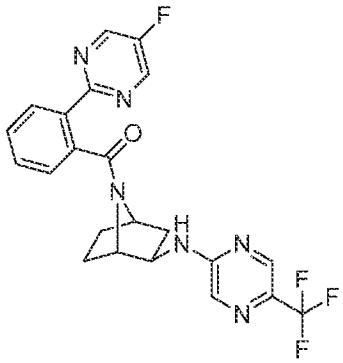
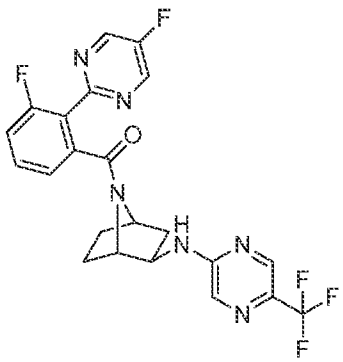
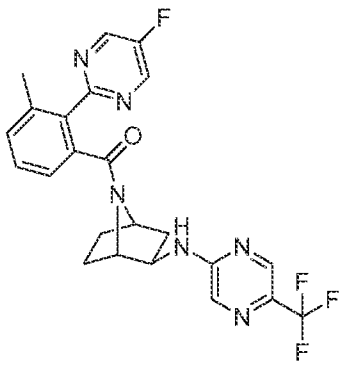
Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
375		49	89	2200	(3-fluoro-2-(5-fluoropyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
376		10	4	110	(3-chloro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
377		224	141	9000	(3-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-(methyl(5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
378		310		>10000	(5-methyl-2-(pyrimidin-2-yl)pyridin-3-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

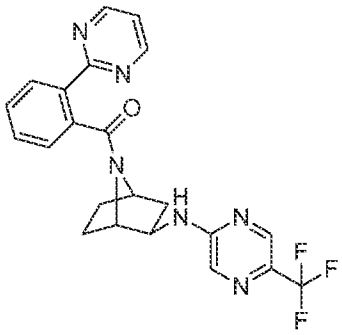
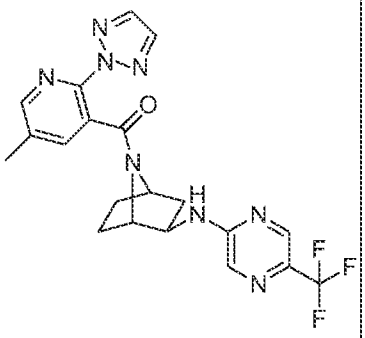
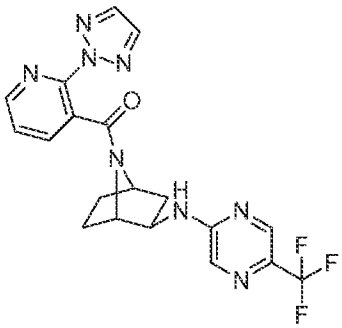
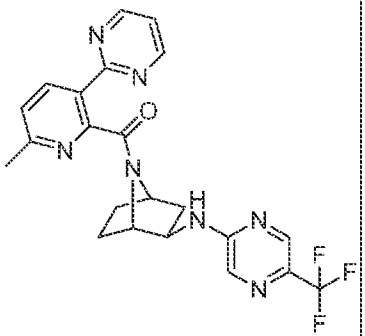
Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
379		25	24	336	(6-methyl-3-(pyrimidin-2-yl)pyridin-2-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
380		28	48	8500	(5-methyl-3-(pyrimidin-2-yl)pyridin-2-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
381		25	25	790	(3-(pyrimidin-2-yl)pyridin-2-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
382		18	15	1100	(3-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((3-fluoro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

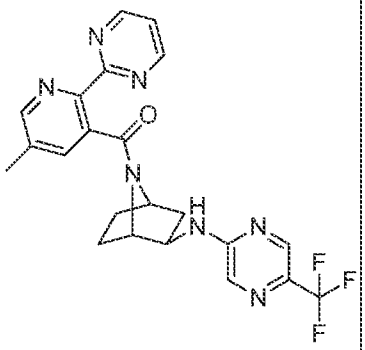
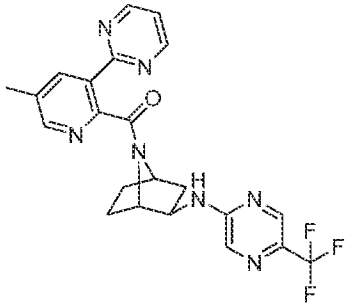
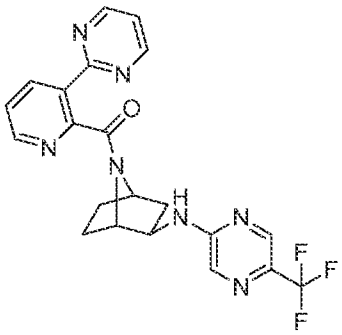
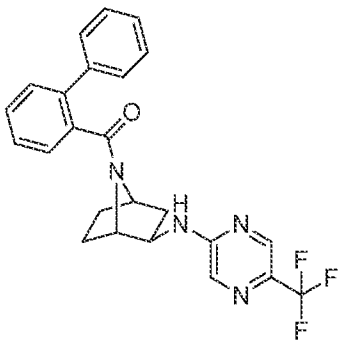
Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
383		33	16	767	((1S,2R,4R)-2-((3-chloro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone
384		15	12	612	((1S,2R,4R)-2-((3-chloro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-(pyrimidin-2-yl)phenyl)methanone
385		37	44	696	((1S,2R,4R)-2-((3-chloro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(2-(5-fluoropyrimidin-2-yl)phenyl)methanone
386		20	29	499	((1S,2R,4R)-2-((3-chloro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(2-(pyrimidin-2-yl)phenyl)methanone

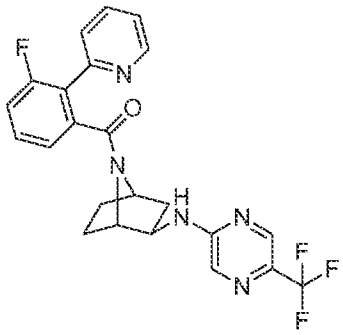
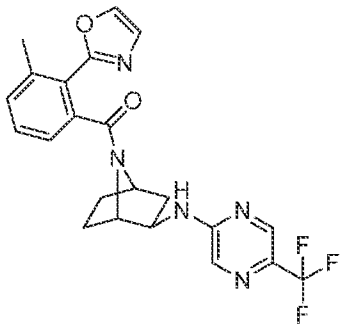
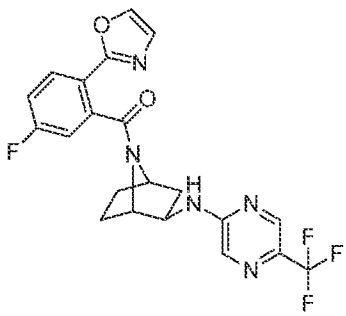
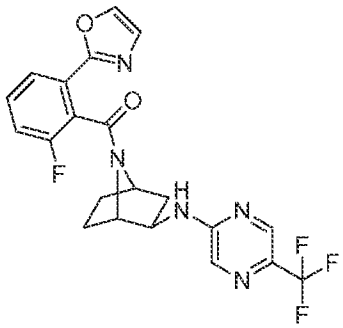
Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
387		40	33	1100	((1S,2R,4R)-2-((3-chloro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-(pyrimidin-2-yl)pyridin-2-yl)methanone
388		130	118	1100	((1S,2R,4R)-2-((5-(difluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone
389		123	168	741	((1S,2R,4R)-2-((5-(difluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-(pyrimidin-2-yl)phenyl)methanone
390		1500	1400	>10000	6-(((1S,2R,4R)-7-(3-fluoro-2-(2H-1,2,3-triazol-2-yl)benzoyl)-7-azabicyclo[2.2.1]heptan-2-yl)amino)nicotinonitrile

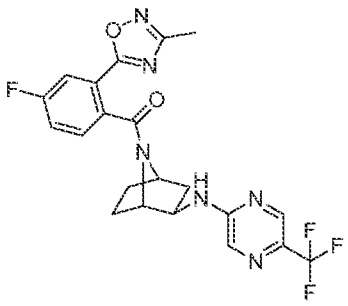
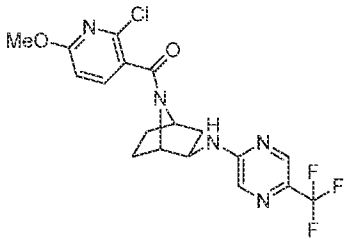
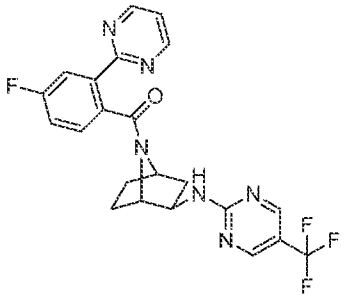
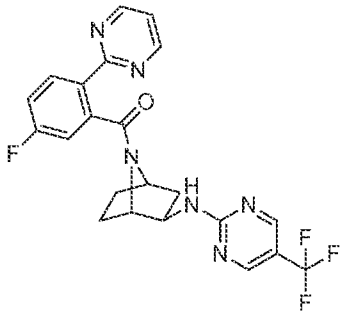
Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
391		220	315	4400	6-(((1S,2R,4R)-7-(3-methyl-2-(2H-1,2,3-triazol-2-yl)benzoyl)-7-azabicyclo[2.2.1]heptan-2-yl)amino)nicotinonitrile
392		1000	1400	>10000	6-(((1S,2R,4R)-7-(3-fluoro-2-(pyrimidin-2-yl)benzoyl)-7-azabicyclo[2.2.1]heptan-2-yl)amino)nicotinonitrile
393		500	323	8300	6-(((1S,2R,4R)-7-(3-methyl-2-(pyrimidin-2-yl)benzoyl)-7-azabicyclo[2.2.1]heptan-2-yl)amino)nicotinonitrile
394		187	250	2100	6-(((1S,2R,4R)-7-(3-methyl-2-(oxazol-2-yl)benzoyl)-7-azabicyclo[2.2.1]heptan-2-yl)amino)nicotinonitrile

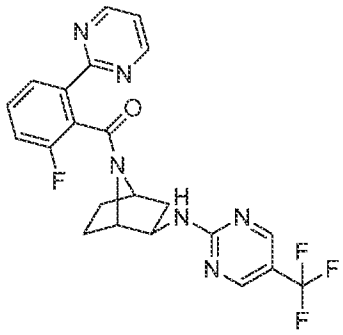
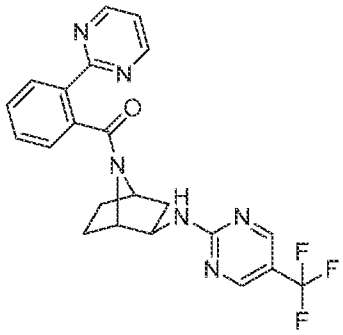
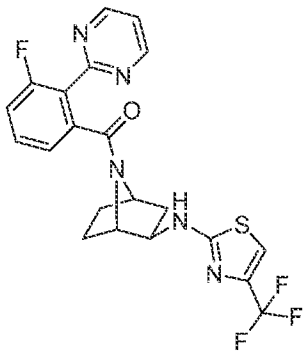
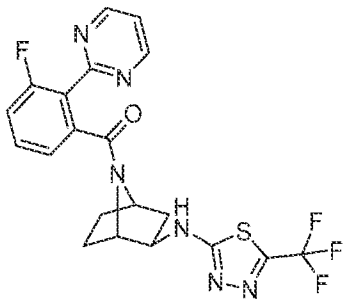
Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
395		17	14	899	(3-fluoro-2-(pyrimidin-2-yl)phenyl) ((1S,2R,4R)-(2-^{2}H)-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
397		50	24	985	(2-(5-fluoropyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
398		61	81	2100	(3-fluoro-2-(5-fluoropyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
399		10	9	300	(2-(5-fluoropyrimidin-2-yl)-3-methylphenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

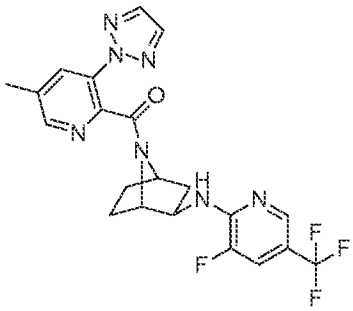
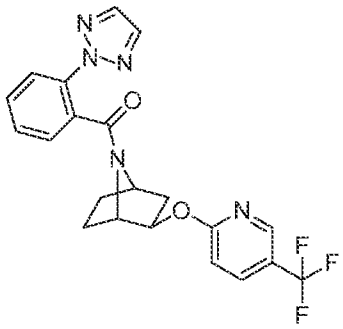
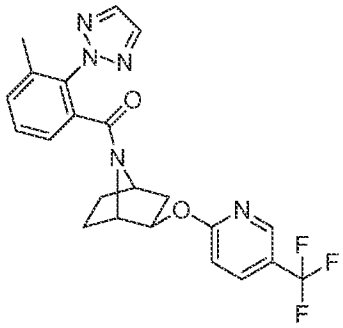
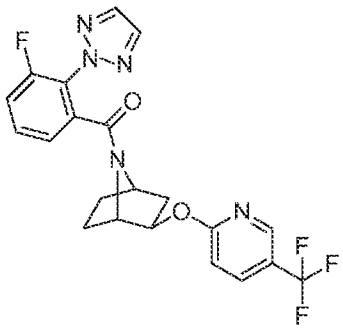
Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
400		27	19	571	(2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
401		196	394	>10000	(5-methyl-2-(2H-1,2,3-triazol-2-yl)pyridin-3-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
402		575		>10000	(2-(2H-1,2,3-triazol-2-yl)pyridin-3-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
403		88	67	431	(6-methyl-3-(pyrimidin-2-yl)pyridin-2-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

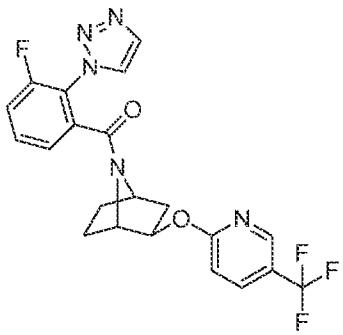
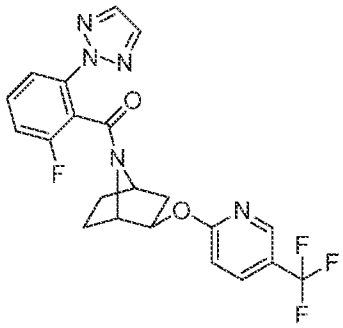
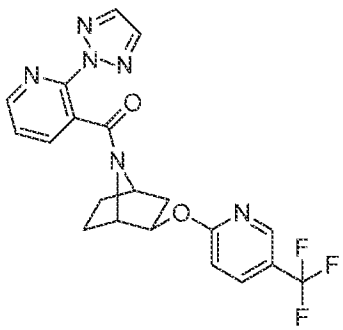
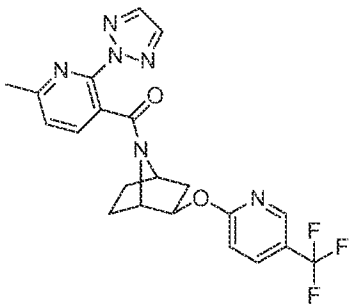
Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
404		419		>10000	(5-methyl-2-(pyrimidin-2-yl)pyridin-3-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
405		53	59	>10000	(5-methyl-3-(pyrimidin-2-yl)pyridin-2-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
406		59	44	972	(3-(pyrimidin-2-yl)pyridin-2-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
407		18	17	104	[1,1'-biphenyl]-2-yl((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

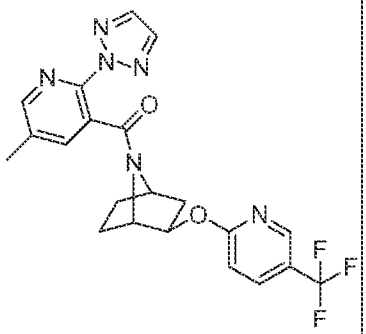
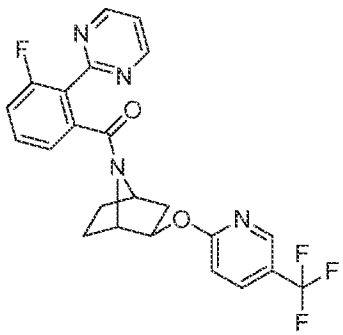
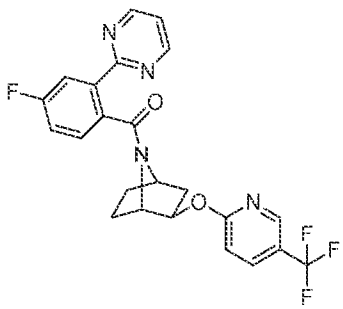
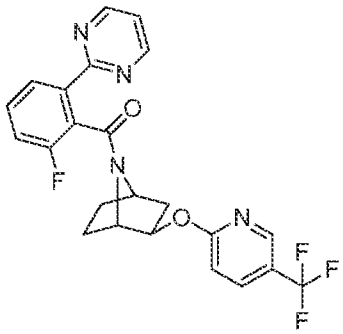
Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
408		12	19	150	(3-fluoro-2-(pyridin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
409		6	7	121	(3-methyl-2-(oxazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
410		67	90	1000	(5-fluoro-2-(oxazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
411		53	31	622	(2-fluoro-6-(oxazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

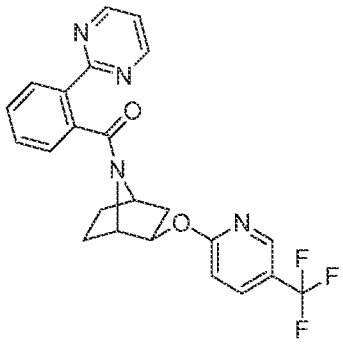
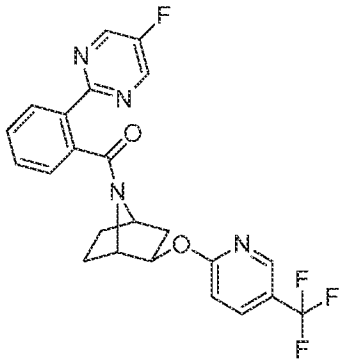
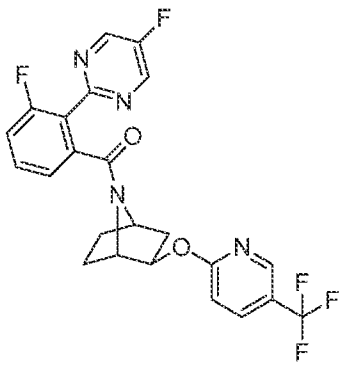
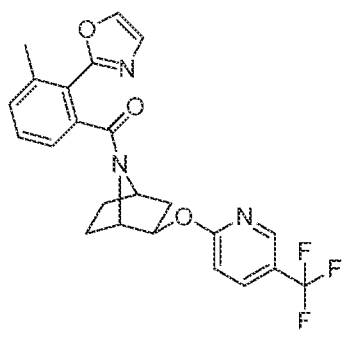
Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
412		126	329	4800	(4-fluoro-2-(3-methyl-1,2,4-oxadiazol-5-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
413		>10000		>10000	(2-chloro-6-methoxypyridin-3-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
414		160	81	5800	(4-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
415		102	70	2100	(5-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

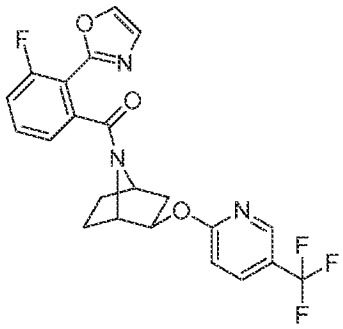
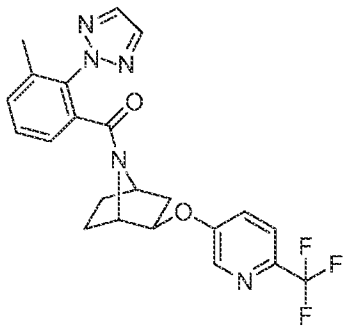
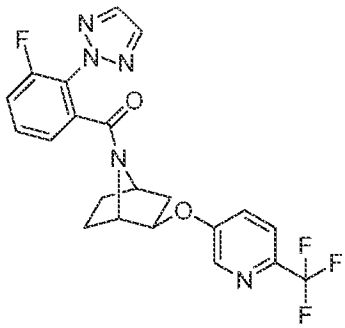
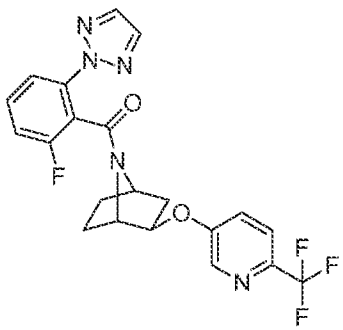
Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
416		138	85	2100	(2-fluoro-6-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
417		52	41	1900	(2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
418		459		2500	(3-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((4-(trifluoromethyl)thiazol-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
419		853		7400	(3-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)-1,3,4-thiadiazol-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

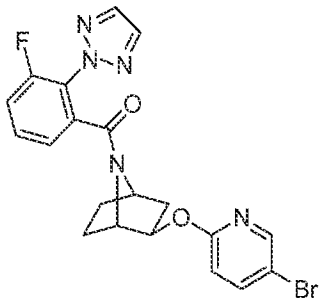
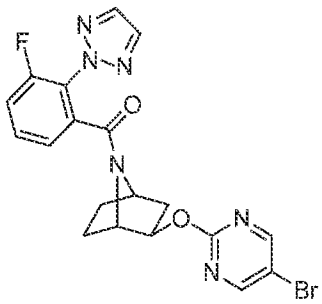
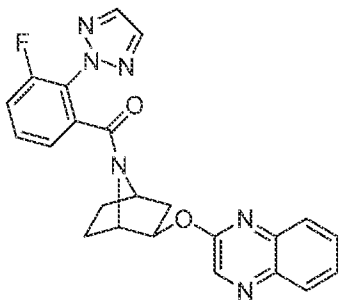
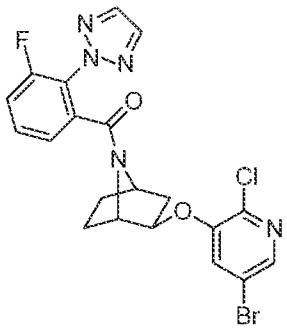
Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
420		100	114	884	((1S,2R,4R)-2-((3-fluoro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(5-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)methanone
421		205	154	4200	(R/S)-(2-(2H-1,2,3-triazol-2-yl)phenyl)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
422		91	57	2150	(R/S)-(3-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
423		202	174	4867	(R/S)-(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

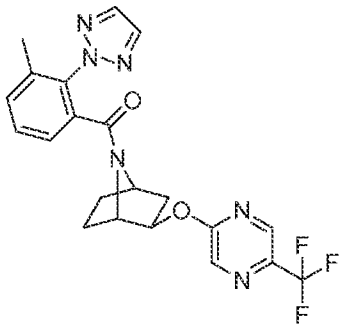
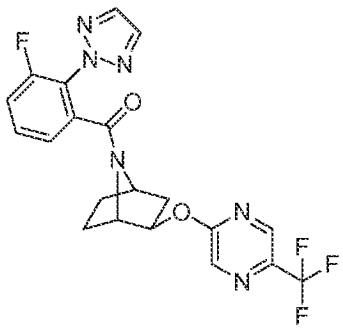
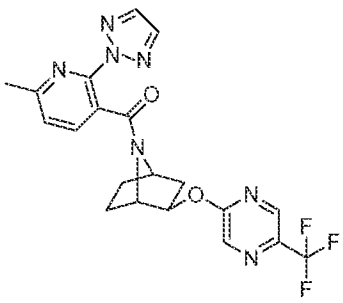
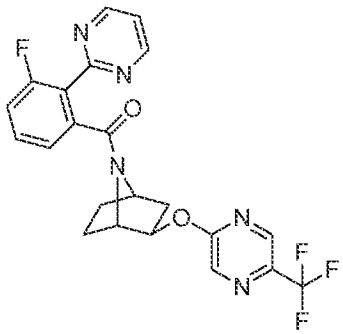
Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
424		2700		>10000	(R/S)-(3-fluoro-2-(1H-1,2,3-triazol-1-yl)phenyl)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
425		587		5100	(R/S)-(2-fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
426		5400		>10000	(R/S)-(2-(2H-1,2,3-triazol-2-yl)pyridin-3-yl)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
427		560		>10000	(R/S)-(6-methyl-2-(2H-1,2,3-triazol-2-yl)pyridin-3-yl)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

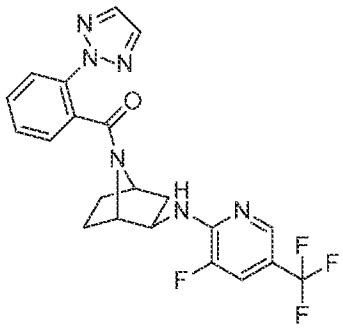
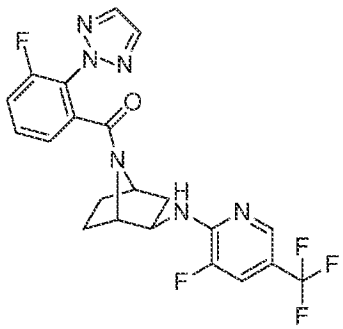
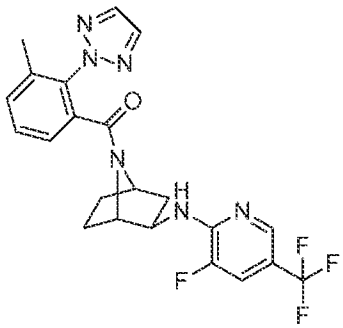
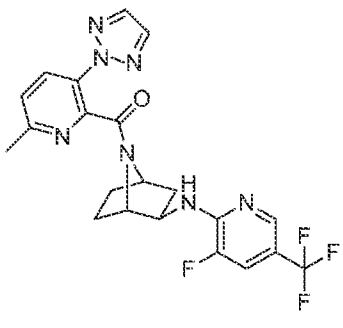
Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
428		1100		>10000	(R/S)-(5-methyl-2-(2H-1,2,3-triazol-2-yl)pyridin-3-yl)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
429		77	120	6300	(R/S)-(3-fluoro-2-(pyrimidin-2-yl)phenyl)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
430		245	300	>10000	(R/S)-(4-fluoro-2-(pyrimidin-2-yl)phenyl)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
431		143	180	5100	(R/S)-(2-fluoro-6-(pyrimidin-2-yl)phenyl)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

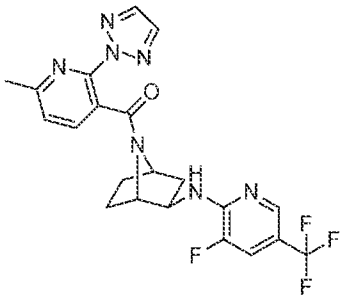
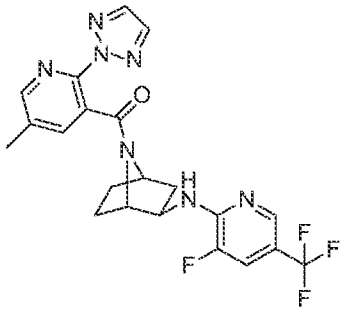
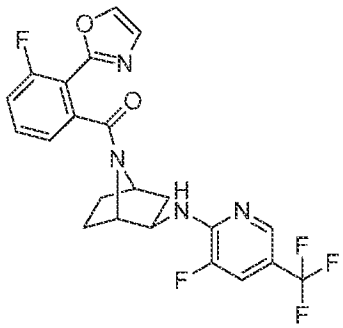
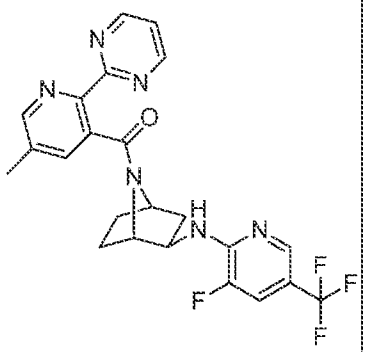
Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
432		147	307	6000	(R/S)-(2-(pyrimidin-2-yl)phenyl)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
433		107	73	2500	(R/S)-(2-(5-fluoropyrimidin-2-yl)phenyl)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
434		134	172	>10000	(R/S)- (3-fluoro-2-(5-fluoropyrimidin-2-yl)phenyl)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
435		50	29	520	(R/S)-(3-methyl-2-(oxazol-2-yl)phenyl)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

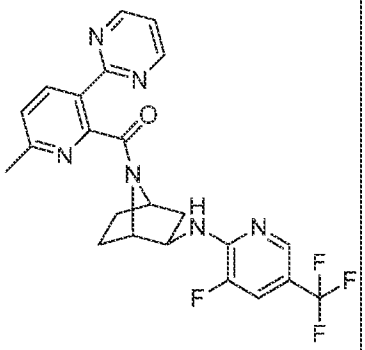
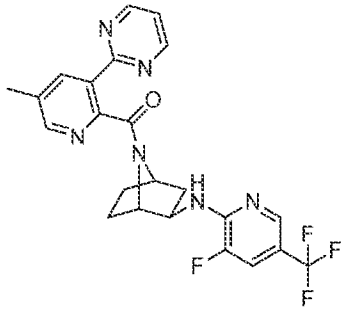
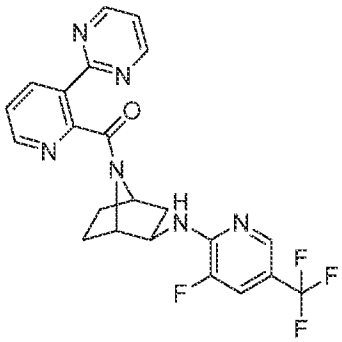
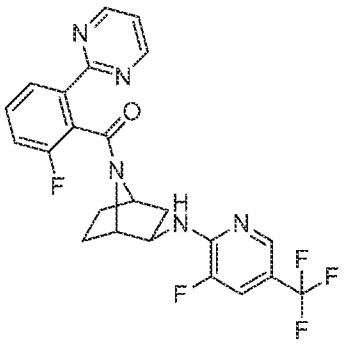
Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
436		143	116	3500	(R/S)-(3-fluoro-2-(oxazol-2-yl)phenyl)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
437		>10000		>10000	(R/S)-(3-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)-2-((6-(trifluoromethyl)pyridin-3-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
438		>10000		>10000	(R/S)-(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)-2-((6-(trifluoromethyl)pyridin-3-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
439		>10000		>10000	(R/S)- (2-fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl)-2-((6-(trifluoromethyl)pyridin-3-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

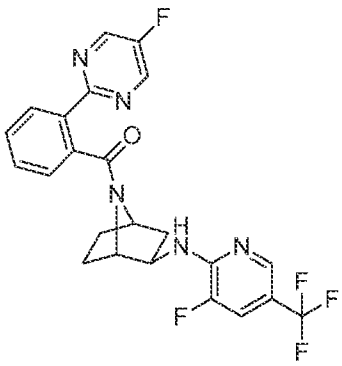
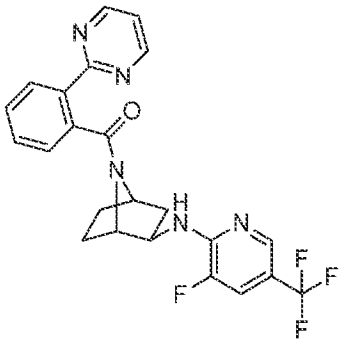
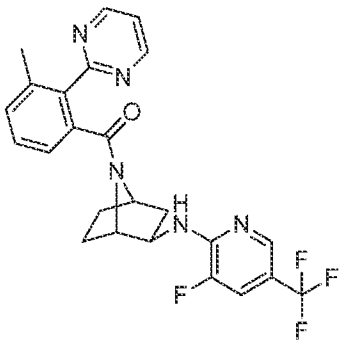
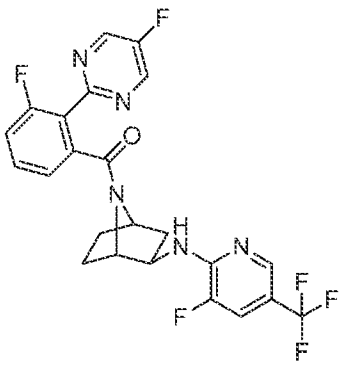
Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
440		118	100	6000	(R/S)-2-((5-bromopyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone
441		1500		>10000	(R/S)-2-((5-bromopyrimidin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone
442		349		1900	(R/S)-(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)-2-(quinoxalin-2-yloxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
443		>10000		>10000	(R/S)-2-((5-bromo-2-chloropyridin-3-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone

Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
444		165	237	4200	(R/S)-(3-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)-2-((5-(trifluoromethyl)pyrazin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
445		460		>10000	(R/S)-(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((5-(trifluoromethyl)pyrazin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
446		4700		>10000	(R/S)-(6-methyl-2-(2H-1,2,3-triazol-2-yl)pyridin-3-yl)(2-((5-(trifluoromethyl)pyrazin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
447		293		>10000	(R/S)-(3-fluoro-2-(pyrimidin-2-yl)phenyl)(2-((5-(trifluoromethyl)pyrazin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
448		41	33	666	(2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((3-fluoro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
449		34	41	873	(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((3-fluoro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
450		14	32	340	((1S,2R,4R)-2-((3-fluoro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone
451		82	84	517	((1S,2R,4R)-2-((3-fluoro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)methanone

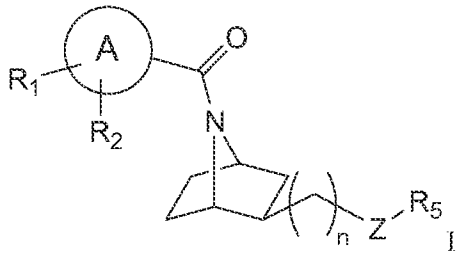
Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
452		176	223	437	((1S,2R,4R)-2-((3-fluoro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-2-(2H-1,2,3-triazol-2-yl)pyridin-3-yl)methanone
453		210	305	>10000	((1S,2R,4R)-2-((3-fluoro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(5-methyl-2-(2H-1,2,3-triazol-2-yl)pyridin-3-yl)methanone
454		18	23	590	(3-fluoro-2-(oxazol-2-yl)phenyl)((1S,2R,4R)-2-((3-fluoro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
455		464		>10000	((1S,2R,4R)-2-((3-fluoro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(5-methyl-2-(pyrimidin-2-yl)pyridin-3-yl)methanone

Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
456		68	48	454	((1S,2R,4R)-2-((3-fluoro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(pyrimidin-2-yl)pyridin-2-yl)methanone
457		55	98	9100	((1S,2R,4R)-2-((3-fluoro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(5-methyl-3-(pyrimidin-2-yl)pyridin-2-yl)methanone
458		46	45	932	((1S,2R,4R)-2-((3-fluoro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-(pyrimidin-2-yl)pyridin-2-yl)methanone
459		26	71	530	((1S,2R,4R)-2-((3-fluoro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(2-fluoro-6-(pyrimidin-2-yl)phenyl)methanone

Ex. No.	Compound	rOX1 K_i (nM)	hOX1 K_i (nM)	hOX2 K_i (nM)	Compound Name
460		52	41	1300	((1S,2R,4R)-2-((3-fluoro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(2-(5-fluoropyrimidin-2-yl)phenyl)methanone
461		30	24	760	((1S,2R,4R)-2-((3-fluoro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(2-(pyrimidin-2-yl)phenyl)methanone
462		18	31	339	((1S,2R,4R)-2-((3-fluoro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-methyl-2-(pyrimidin-2-yl)phenyl)methanone
463		53	50	1900	(3-fluoro-2-(5-fluoropyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((3-fluoro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

What is Claimed:

1. A compound of formula I:



I

or an enantiomer or diastereomer therof;

or a pharmaceutically acceptable salt thereof;

wherein

ring A is phenyl, naphthalenyl, pyridyl, quinolinyl, isoquinolinyl, imidazopyridyl, furanyl, thiazolyl, isoxazolyl, pyrazolyl, imidazothiazolyl, benzimidazolyl, or indazolyl;

R_1 is H, alkyl, alkoxy, hydroxyalkylene, OH, halo, phenyl, triazolyl, oxazolyl, isoxazolyl, pyridyl, pyrimidinyl, pyrazinyl, pyridazinyl, piperazinyl, pyrazolyl, oxadiazolyl, pyrrolidinyl, thiophenyl, morpholinyl, or dialkylamino, wherein phenyl, triazolyl, oxazolyl, isoxazolyl, pyridyl, pyrimidinyl, pyrazinyl, pyridazinyl, piperazinyl, pyrazolyl, oxadiazolyl, pyrrolidinyl, thiophenyl, or morpholinyl is optionally substituted with up to two substituents selected from halo and alkyl;

R_2 is H, alkyl, alkoxy, hydroxyalkylene, or halo;

Z is NH, N-alkyl, or O;

R_5 is pyridyl, pyrimidinyl, pyrazinyl, pyridazinyl, quinazolinyl, quinoxalinyl, pyrazolyl, thiazolyl, thiadiazolyl, benzoxazolyl, imidazopyrazinyl, or triazolopyrazinyl, optionally substituted with one or two substituents independently selected from the group consisting of alkyl, cyano, alkyl carboxylate, alkoxy, and halo; and

n is 0 or 1.

2. The compound of claim 1, wherein Z is NH.

3. The compound of claim 1, wherein Z is N-alkyl.

4. The compound of claim 3, wherein Z is N-CH_3.

5. The compound of claim 1, wherein Z is O.

6. The compound of any one of claims 1 to 5, wherein ring A is furanyl, thiazolyl, isoxazolyl, pyrazolyl, or imidazothiazolyl.

7. The compound of any one of claims 1 to 5, wherein ring A is phenyl or naphthalenyl.

8. The compound of any one of claims 1 to 5, wherein ring A is pyridyl, quinolinyl, isoquinolinyl, imidazopyridyl, benzimidazolyl, or indazolyl.

9. The compound of any one claims 1 to 8, wherein R_1 is alkyl.

10. The compound of any one of claims 1 to 8, wherein R_1 is alkoxy.

11. The compound of claim 10, wherein alkoxy is haloalkoxy.

12. The compound of any one of claims 1 to 8, wherein R_1 is hydroxyalkylene or OH.

13. The compound of any one of claims 1 to 8, wherein R_1 is halo.

14. The compound of any one of claims 1 to 8, wherein R_1 is phenyl.

15. The compound of claim 14, wherein phenyl is halo-phenyl.

16. The compound of any one of claims 1 to 8, wherein R_1 is triazolyl, oxazolyl, or isoxazolyl.

17. The compound of claim 16, wherein oxazolyl is methyl-oxazolyl.

18. The compound of claim 16, wherein isoxazolyl is methyl-isoxazolyl.

19. The compound of any one of claims 1 to 8, wherein R_1 is pyridyl.

20. The compound of claim 19, wherein pyridyl is methyl-pyridyl.

21. The compound of any one of claims 1 to 8, wherein R_1 is pyrimidinyl, pyrazinyl, or pyridazinyl.

22. The compound of any one of claims 1 to 8, wherein R_1 is piperazinyl, morpholinyl, pyrrolidinyl, or dialkyamino.

23. The compound of any one of claims 1 to 8, wherein R_1 is pyrazolyl, oxadiazolyl, or thiophenyl.

24. The compound of claim 23, wherein pyrazolyl is methyl-pyrazolyl or dimethyl-pyrazolyl.

25. The compound of claim 23, wherein oxadiazolyl is methyl-oxadiazolyl.

26. The compound of any one of claims 1 to 25, wherein R_2 is H.

27. The compound of any one of claims 1 to 25, wherein R_2 is alkyl.

28. The compound of any one of claims 1 to 25, wherein R_2 is alkoxy.

29. The compound of any one of claims 1 to 25, wherein R_2 is hydroxyalkylene.

30. The compound of any one of claims 1 to 25, wherein R_2 is halo.

31. The compound of any one of the preceding claims, wherein R_5 is pyridyl, pyrimidinyl, pyrazinyl, or pyridazinyl optionally substituted with a one or two substituents independently selected from the group consisting of alkyl, alkoxy, or halo.

32. The compound of claim 31, wherein alkyl is trihaloalkyl.

33. The compound of claim 32, wherein R_5 is pyridyl substituted with trifluoromethyl.

34. The compound of claim 32, wherein R_5 is pyrimidinyl substituted with trifluoromethyl.

35. The compound of claim 32, wherein R_5 is pyrazinyl substituted with trifluoromethyl.

36. The compound of claim 32, wherein R_5 is pyridazinyl substituted with trifluoromethyl.

37. The compound of any one of claims 1 to 30, wherein R_5 is quinazolinyl or quinoxalinyl, optionally substituted with a one or two substituents independently selected from the group consisting of alkyl, alkoxy, or halo.

38. The compound of claim 37, wherein alkyl is trihaloalkyl.

39. The compound of claim 38, wherein R_5 is quinazolinyl substituted with trifluoromethyl.

40. The compound of claim 38, wherein R_5 is quinoxalinyl substituted with trifluoromethyl.

41. The compound of any one of claims 1 to 30, wherein R_5 is pyrazolyl, benzoxazolyl, imidazopyrazinyl, or triazolopyrazinyl optionally substituted with a one or two substituents independently selected from the group consisting of alkyl, alkoxy, or halo.

42. The compound of claim 41, wherein pyrazolyl is methyl-pyrazolyl.

43. The compound of claim 41, wherein alkyl is trihaloalkyl.

44. The compound of claim 43, wherein R_5 is pyrazolyl substituted with trifluoromethyl.

45. The compound of claim 43, wherein R_5 is benzoxazolyl substituted with trifluoromethyl.

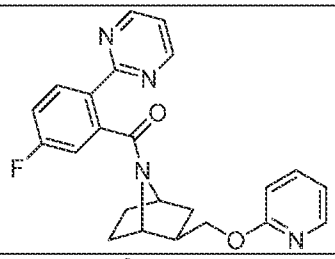
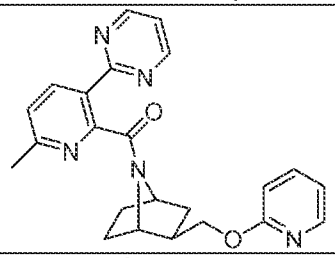
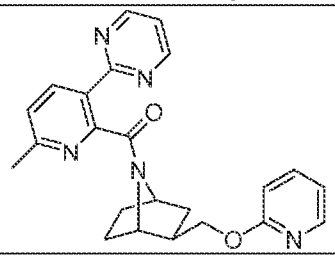
46. The compound of claim 43 wherein R_5 is imidazopyrazinyl substituted with trifluoromethyl.

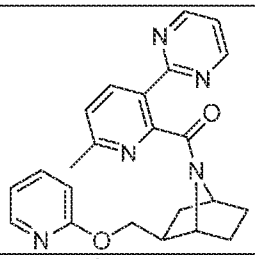
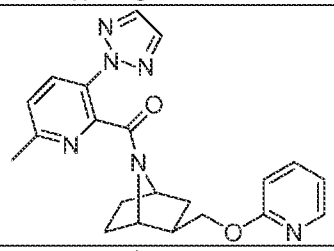
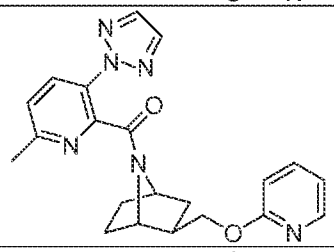
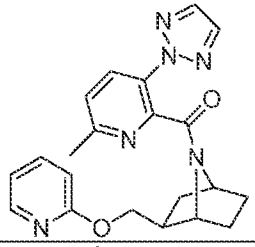
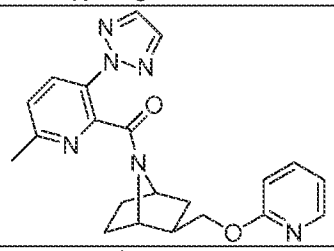
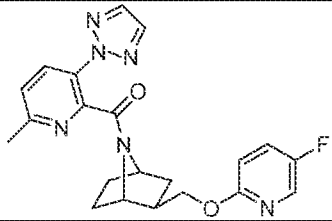
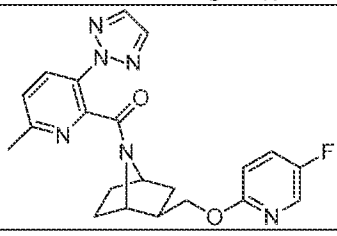
47. The compound of claim 43, wherein R_5 is triazolopyrazinyl substituted with trifluoromethyl.

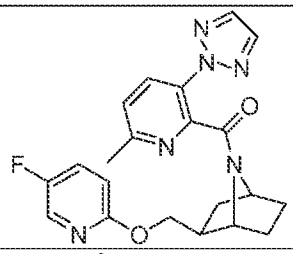
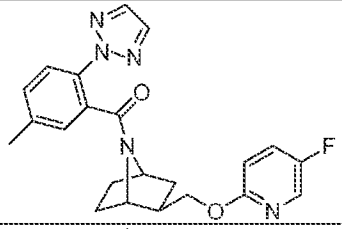
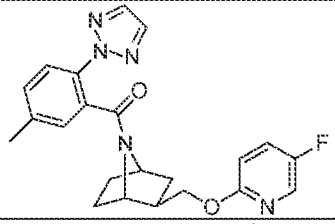
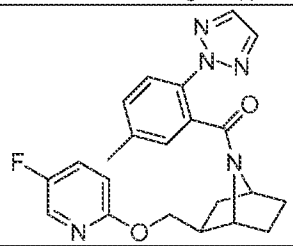
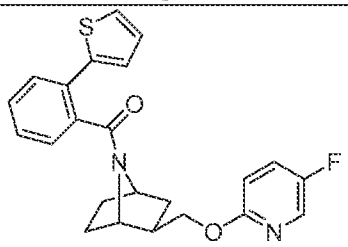
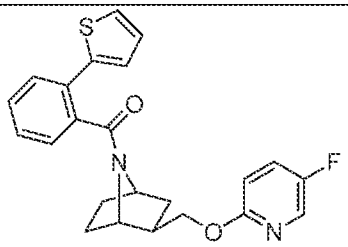
48. The compound of any one of the preceding claims, wherein n is 0.

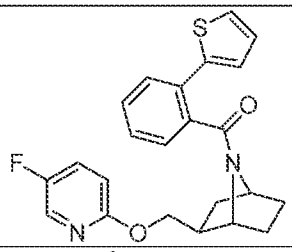
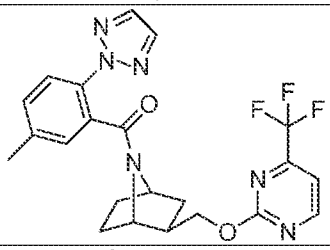
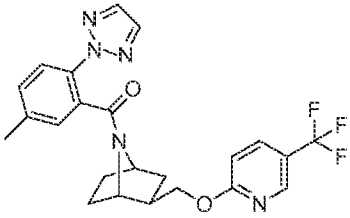
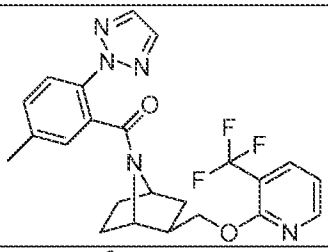
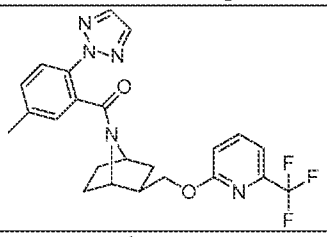
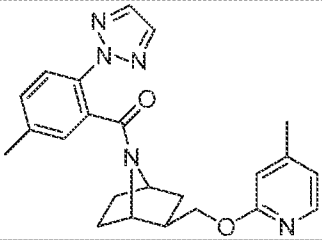
49. The compound of any one of claims 1 to 47, wherein n is 1.

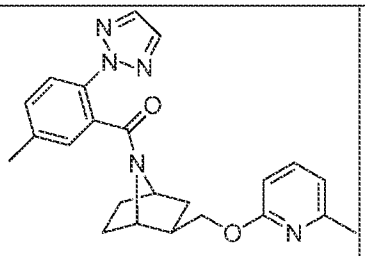
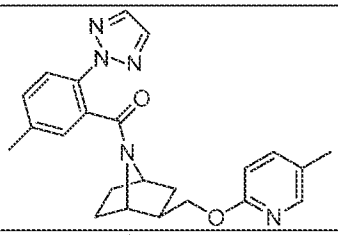
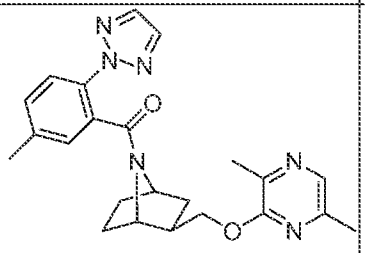
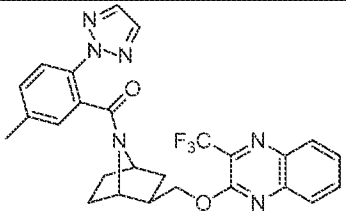
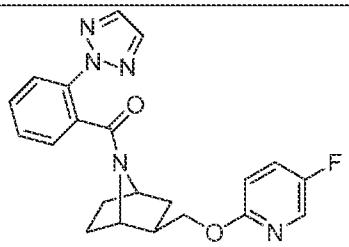
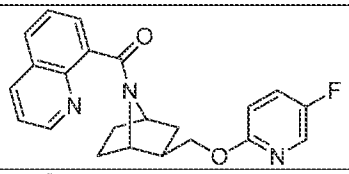
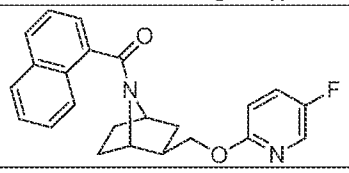
50. A compound selected from the group consisting of

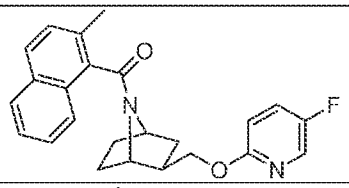
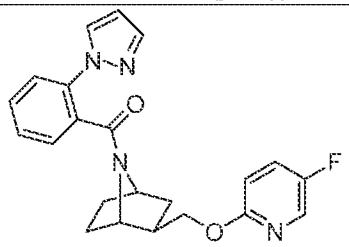
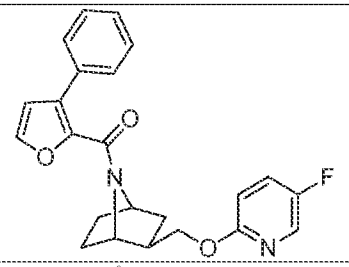
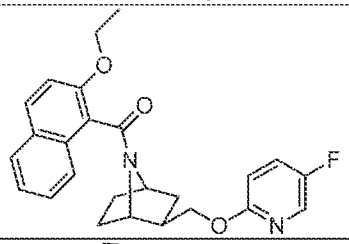
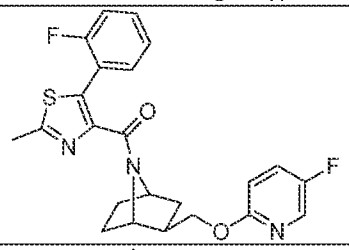
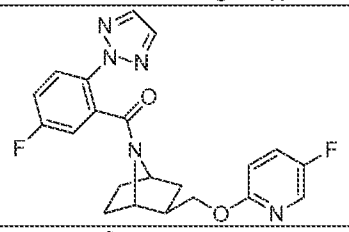
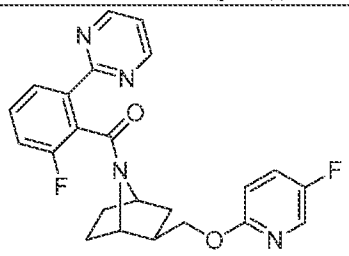
Ex. No.	Compound	Compound Name
1		(5-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
2		(±)-(6-methyl-3-(pyrimidin-2-yl)pyridin-2-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
3A		(6-methyl-3-(pyrimidin-2-yl)pyridin-2-yl)((1S*,2R*,4R*)-2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

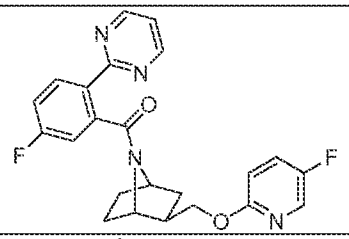
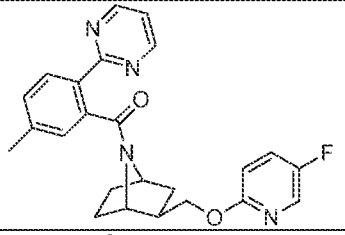
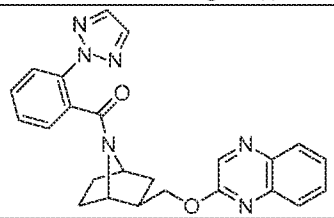
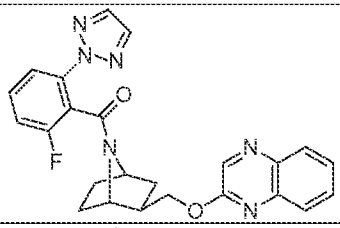
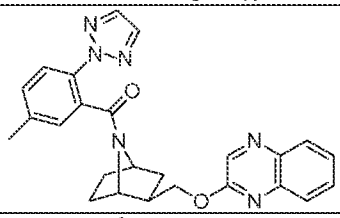
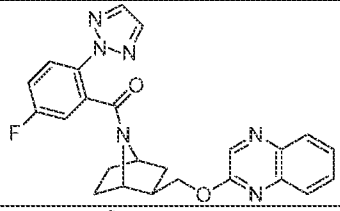
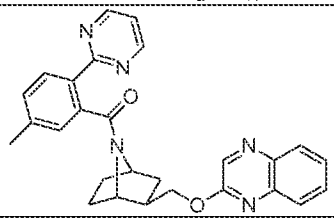
3B		(6-methyl-3-(pyrimidin-2-yl)pyridin-2-yl)((1R*,2S*,4S*)-2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
4		(±)-(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
5A		(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)((1S,2R,4R)-2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
5B		(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)((1R,2S,4S)-2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
6		(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)((1S,2R,4R)-2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
7		(±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)methanone
8A		((1S,2R,4R)-2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)methanone

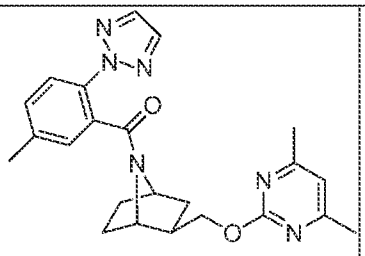
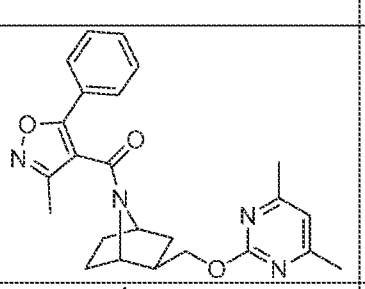
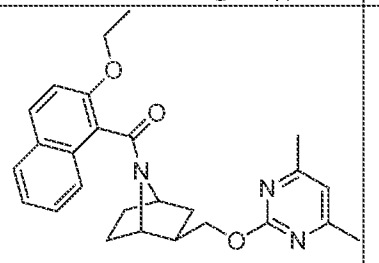
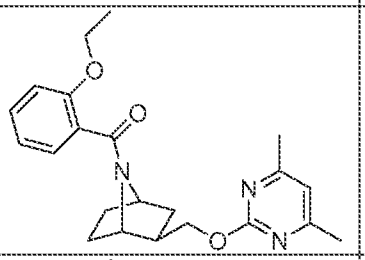
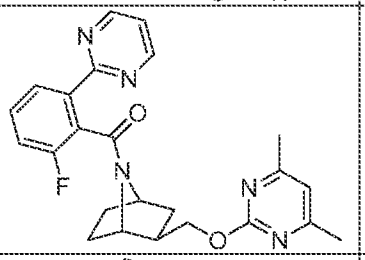
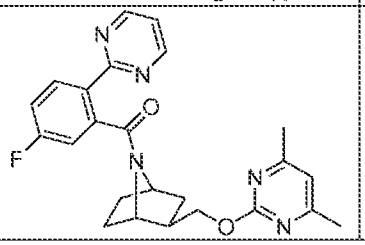
8B		((1R,2S,4S)-2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)methanone
9		(±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(5-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone
10A		((1S,2R,4R)-2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(5-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone
10B		((1R,2S,4S)-2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(5-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone
11		(±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(2-(thiophen-2-yl)phenyl)methanone
12A		((1S*,2R*,4R*)-2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(2-(thiophen-2-yl)phenyl)methanone

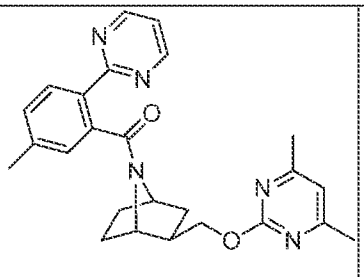
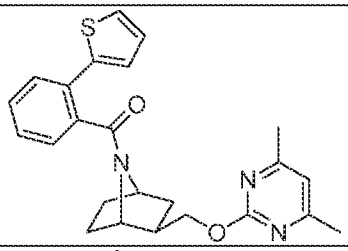
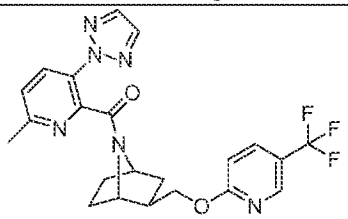
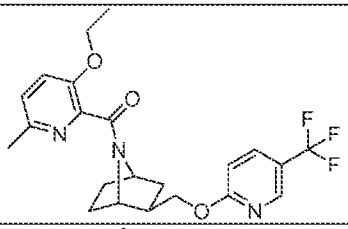
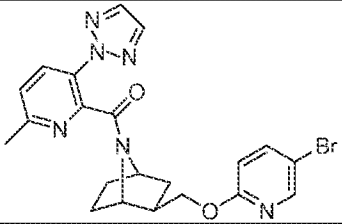
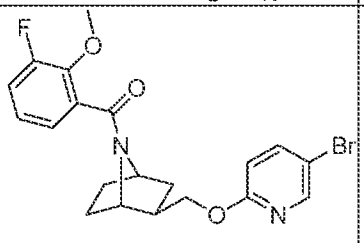
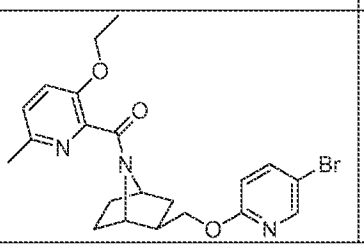
12B		((1R*,2S*,4S*)-2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(2-(thiophen-2-yl)phenyl)methanone
13		(±)-(5-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((4-(trifluoromethyl)pyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
14		(±)-(5-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((5-(trifluoromethyl)pyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
15		(±)-(5-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((3-(trifluoromethyl)pyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
16		(±)-(5-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((6-(trifluoromethyl)pyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
17		(±)-(5-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((4-methylpyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

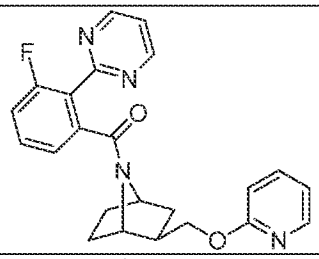
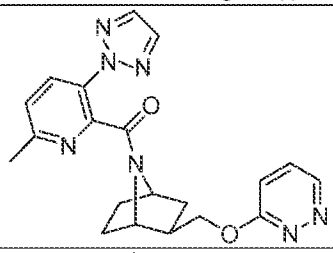
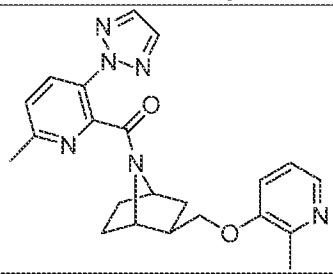
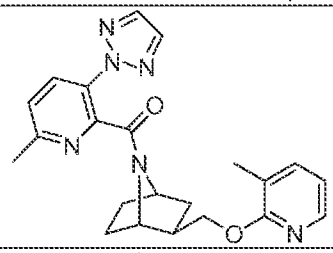
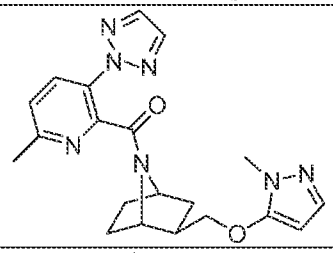
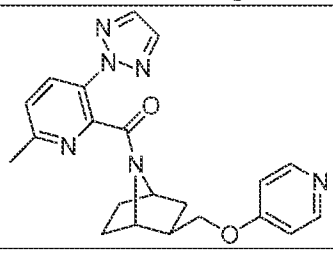
18		(±)-(5-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((6-methylpyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
19		(±)-(5-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((5-methylpyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
20		(±)-(2-(((3,6-dimethylpyrazin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(5-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone
21		(±)-(5-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((3-(trifluoromethyl)quinoxalin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
22		(±)- (2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
23		(±)-2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(quinolin-8-yl)methanone
24		(±)-2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(naphthalen-1-yl)methanone

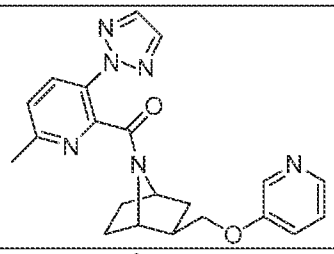
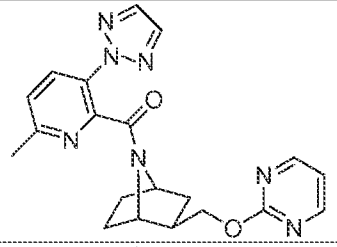
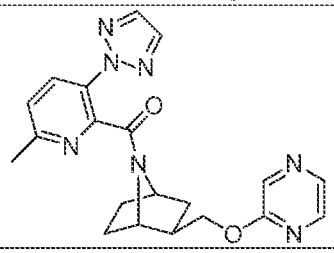
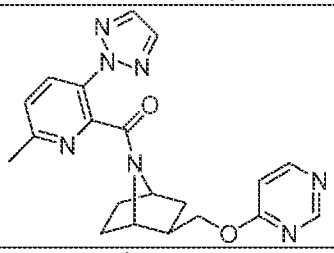
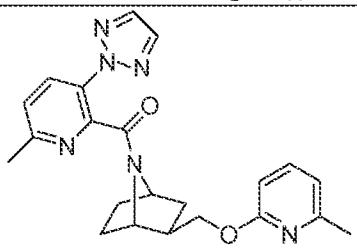
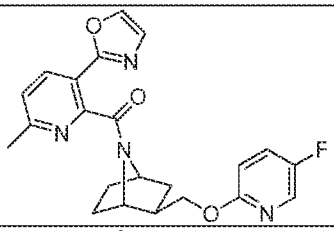
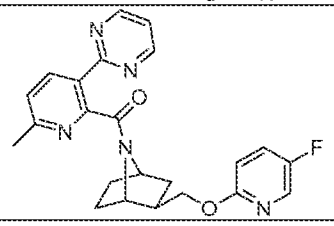
25		(±)-2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(2-methylnaphthalen-1-yl)methanone
26		(±)-2-(1H-pyrazol-1-yl)phenyl)(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
27		(±)-2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(3-phenylfuran-2-yl)methanone
28		(±)-(2-ethoxynaphthalen-1-yl)(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
29		(±)-(5-(2-fluorophenyl)-2-methylthiazol-4-yl)(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
30		(±)-(5-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
31		(±)-(2-fluoro-6-(pyrimidin-2-yl)phenyl)(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

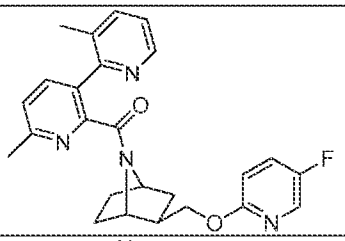
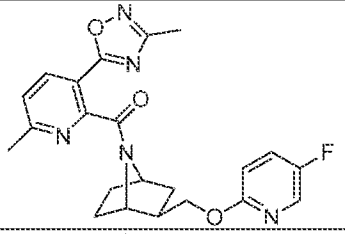
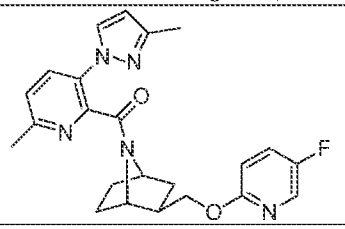
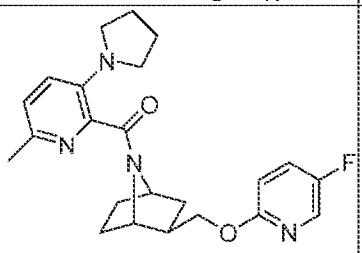
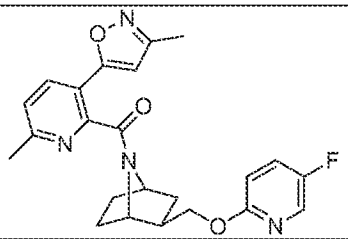
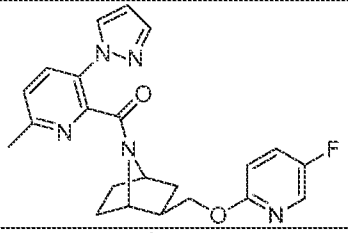
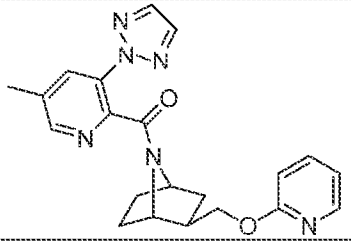
32		(±)-(5-fluoro-2-(pyrimidin-2-yl)phenyl)(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
33		(±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(5-methyl-2-(pyrimidin-2-yl)phenyl)methanone
34		(±)-(2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((quinoxalin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
35		(±)-(2-fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl)(2-((quinoxalin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
36		(±)-(5-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((quinoxalin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
37		(±)-(5-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((quinoxalin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
38		(±)-(5-methyl-2-(pyrimidin-2-yl)phenyl)(2-((quinoxalin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

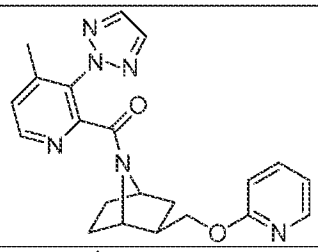
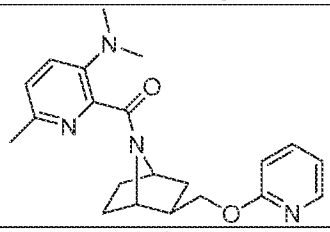
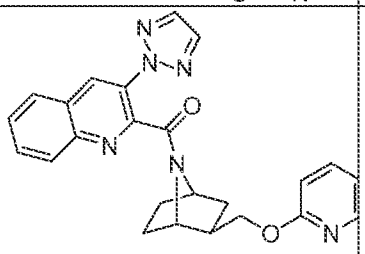
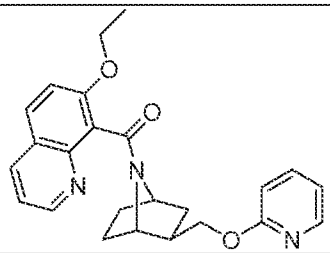
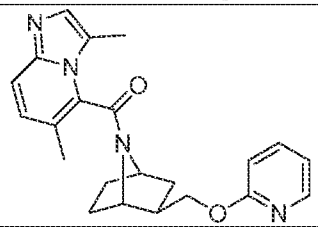
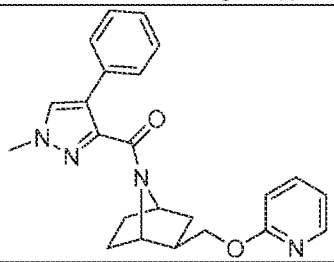
39		(±)-(2-(((4,6-dimethylpyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(5-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone
40		(±)-2-(((4,6-dimethylpyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(3-methyl-5-phenylisoxazol-4-yl)methanone
41		(±)-(2-(((4,6-dimethylpyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(2-ethoxynaphthalen-1-yl)methanone
42		(±)-(2-(((4,6-dimethylpyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(2-ethoxyphenyl)methanone)
43		(±)-(2-(((4,6-dimethylpyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(2-fluoro-6-(pyrimidin-2-yl)phenyl)methanone
44		(±)-(2-(((4,6-dimethylpyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(5-fluoro-2-(pyrimidin-2-yl)phenyl)methanone

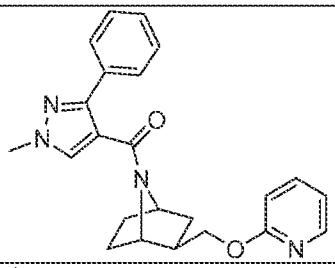
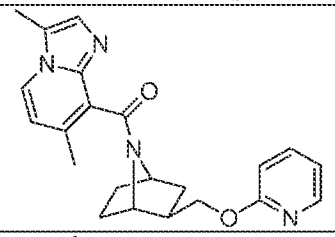
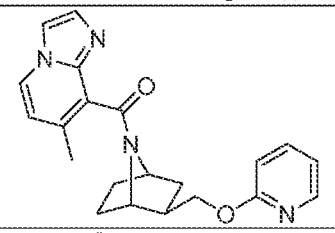
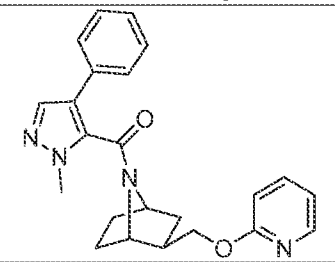
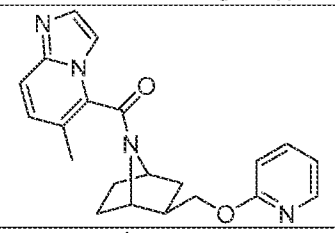
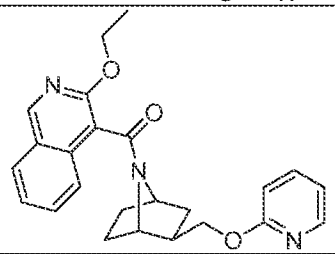
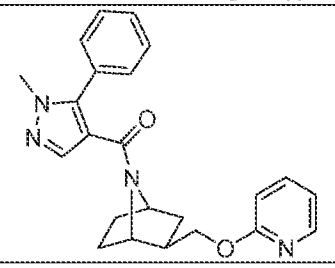
45		(±)-(2-(((4,6-dimethylpyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(5-methyl-2-(pyrimidin-2-yl)phenyl)methanone
46		(±)-(2-(((4,6-dimethylpyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(2-(thiophen-2-yl)phenyl)methanone
47		(±)-(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-(((5-(trifluoromethyl)pyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
48		(±)-(3-ethoxy-6-methylpyridin-2-yl)(2-(((5-(trifluoromethyl)pyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
49		(±)-(2-(((5-bromopyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)methanone
50		(±)-(2-(((5-bromopyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-methoxyphenyl)methanone
51		(±)-(2-(((5-bromopyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(3-ethoxy-6-methylpyridin-2-yl)methanone

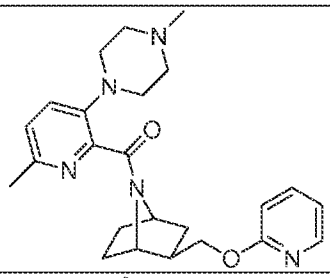
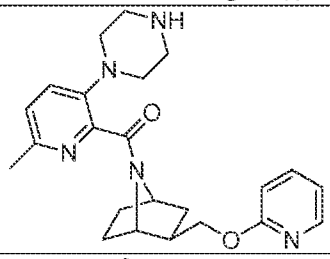
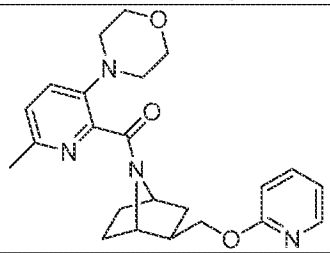
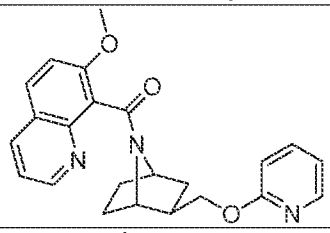
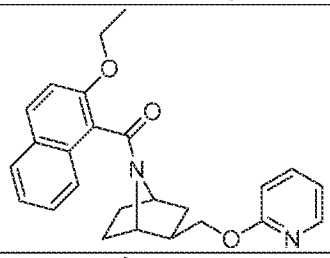
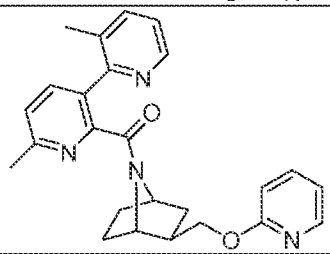
52		(±)-(3-fluoro-2-(pyrimidin-2-yl)phenyl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
53		(±)-(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-((pyridazin-3-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
54		(±)-(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-(((2-methylpyridin-3-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
55		(±)-(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-(((3-methylpyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
56		(±)-(2-(((1-methyl-1H-pyrazol-5-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)methanone
57		(±)-(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-((pyridin-4-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

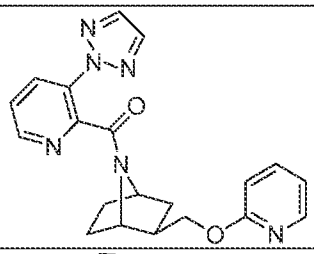
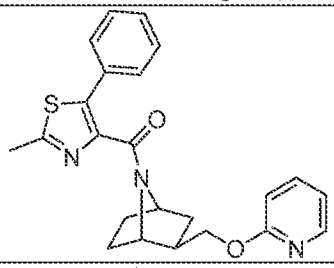
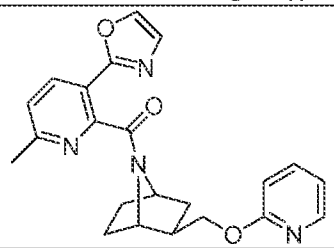
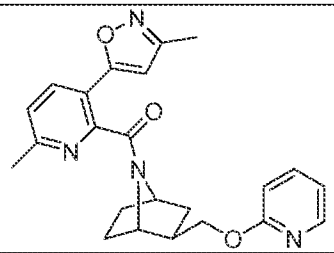
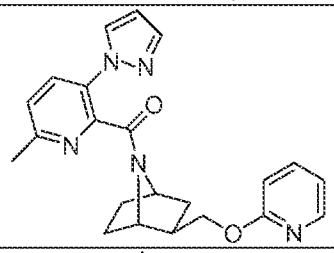
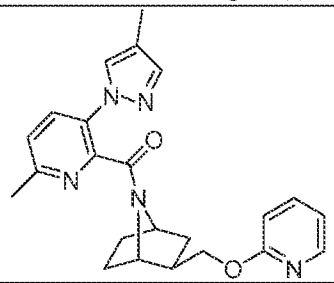
58		(±)-(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-((pyridin-3-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
59		(±)-(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-((pyrimidin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
60		(±)-(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-((pyrazin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
61		(±)-(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2- ((pyrimidin-4-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
62		(±)-(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-(((6-methylpyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
63		(±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(oxazol-2-yl)pyridin-2-yl)methanone
64		(±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(pyrimidin-2-yl)pyridin-2-yl)methanone

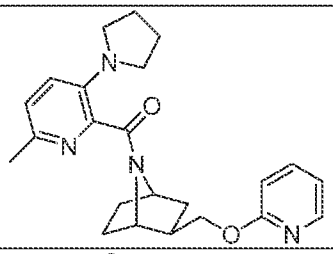
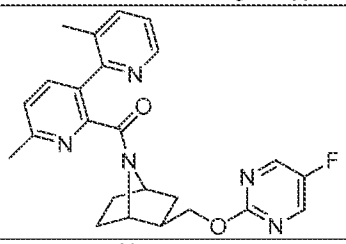
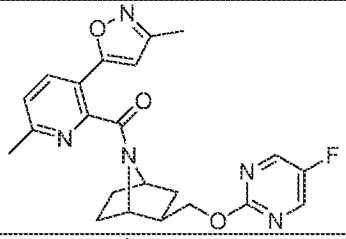
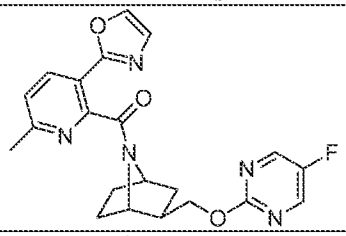
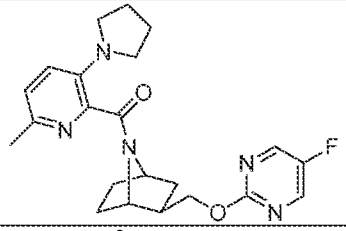
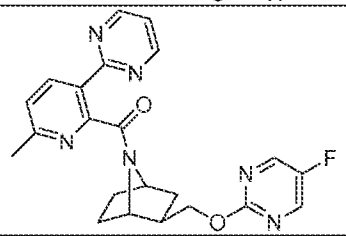
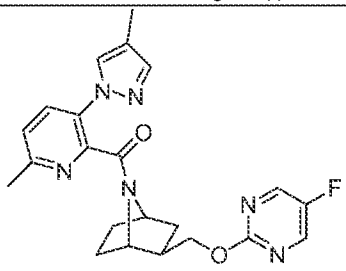
65		(±)-(3,6'-dimethyl-[2,3'-bipyridin]-2'-yl)(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
66		(±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(3-methyl-1,2,4-oxadiazol-5-yl)pyridin-2-yl)methanone
67		(±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(3-methyl-1H-pyrazol-1-yl)pyridin-2-yl)methanone
68		(±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(pyrrolidin-1-yl)pyridin-2-yl)methanone
69		(±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(3-methylisoxazol-5-yl)pyridin-2-yl)methanone
70		(±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(1H-pyrazol-1-yl)pyridin-2-yl)methanone
71		(±)-(5-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

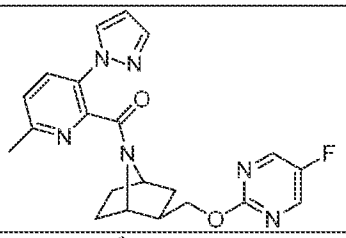
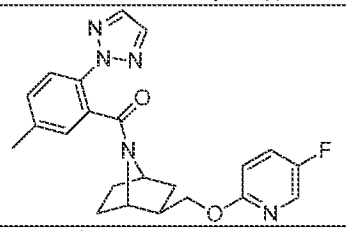
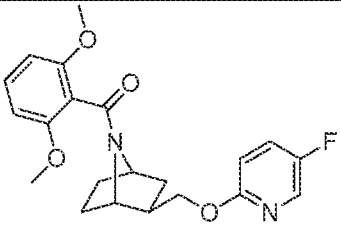
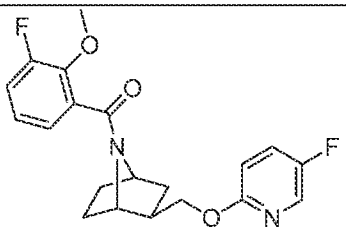
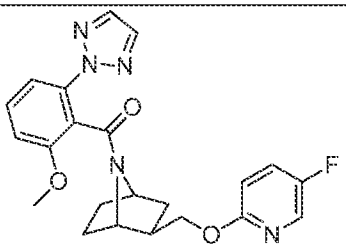
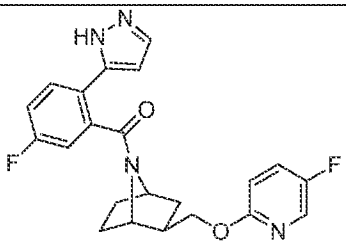
72		(±)- (4-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
73		(±)-(3-(dimethylamino)-6-methylpyridin-2-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
74		(±)-(3-(2H-1,2,3-triazol-2-yl)quinolin-2-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
75		(±)-(7-ethoxyquinolin-8-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
76		(±)-(3,6-dimethylimidazo[1,2-a]pyridin-5-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
77		(±)-(1-methyl-4-phenyl-1H-pyrazol-3-yl)((1S,2R,4R)-2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

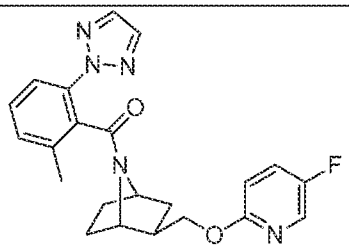
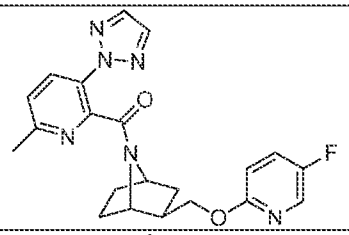
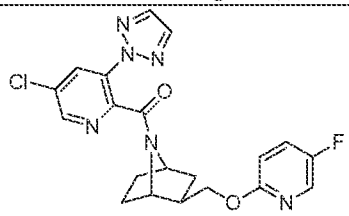
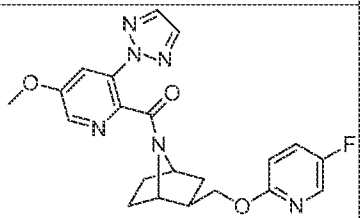
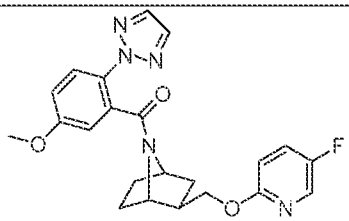
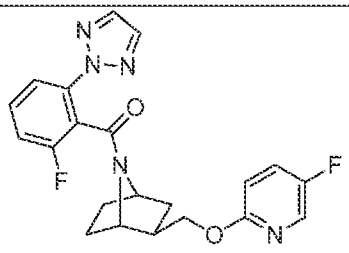
78		(±)-(1-methyl-3-phenyl-1H-pyrazol-4-yl)((1S,2R,4R)-2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
79		(±)-((3,7-dimethylimidazo[1,2-a]pyridin-8-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
80		(±)-(7-methylimidazo[1,2-a]pyridin-8-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
81		(±)-(1-methyl-4-phenyl-1H-pyrazol-5-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
82		(±)-((6-methylimidazo[1,2-a]pyridin-5-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
83		(±)-(3-ethoxyisoquinolin-4-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
84		(±)-(1-methyl-5-phenyl-1H-pyrazol-4-yl)(-2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

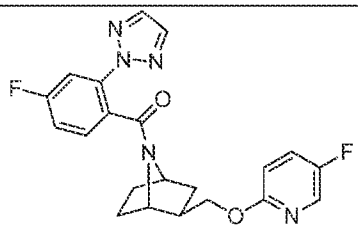
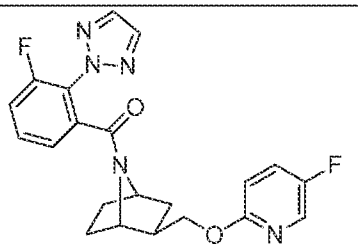
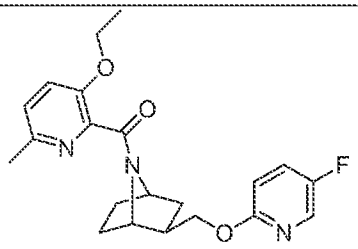
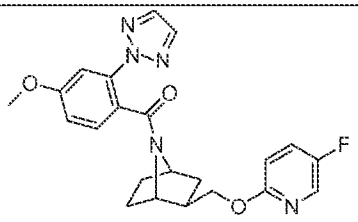
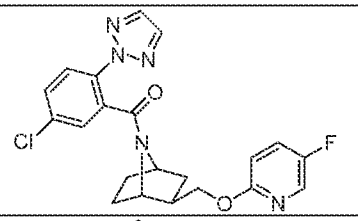
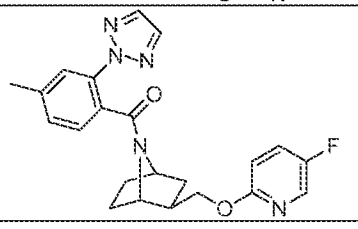
85		(±)-(6-methyl-3-(4-methylpiperazin-1-yl)pyridin-2-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
86		(±)-(6-methyl-3-(piperazin-1-yl)pyridin-2-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
87		(±)-(6-methyl-3-morpholinopyridin-2-yl)((1S,2R,4R)-2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
88		(±)-(7-methoxyquinolin-8-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
89		(±)-(2-ethoxynaphthalen-1-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
90		(±)-(3,6'-dimethyl-[2,3'-bipyridin]-2'-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

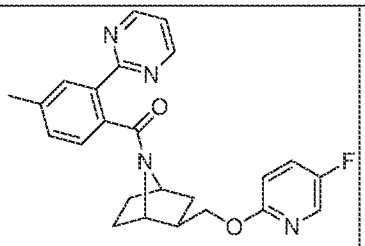
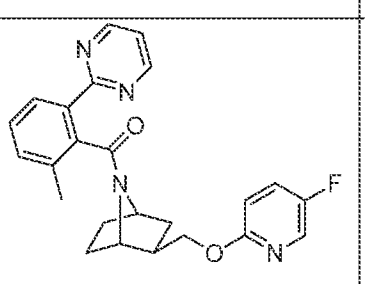
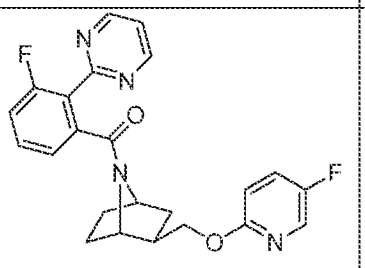
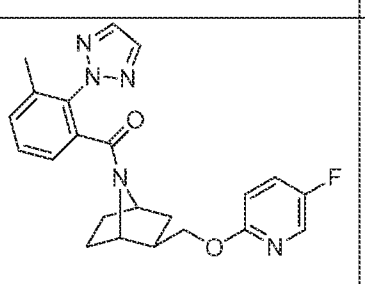
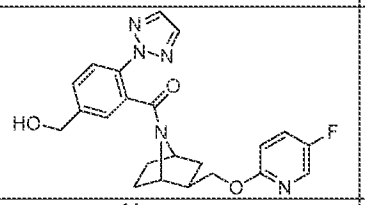
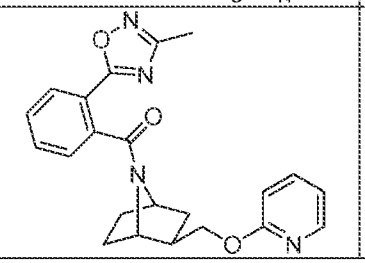
91		(±)-(3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
92		(±)-(2-methyl-5-phenylthiazol-4-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
93		(±)-(6-methyl-3-(oxazol-2-yl)pyridin-2-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
94		(±)-(6-methyl-3-(3-methylisoxazol-5-yl)pyridin-2-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
95		(±)-(6-methyl-3-(1H-pyrazol-1-yl)pyridin-2-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
96		(±)-(6-methyl-3-(4-methyl-1H-pyrazol-1-yl)pyridin-2-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

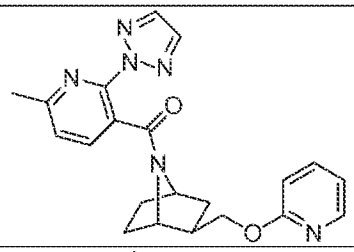
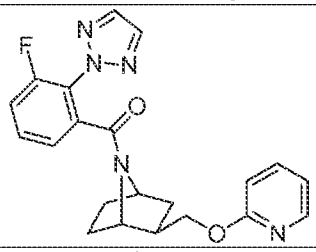
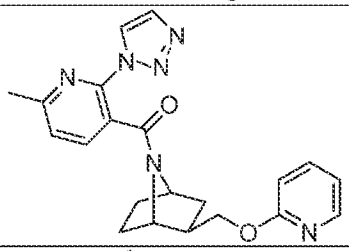
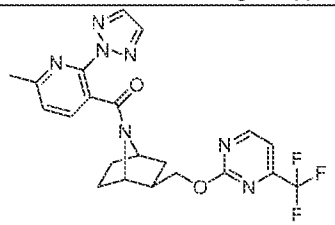
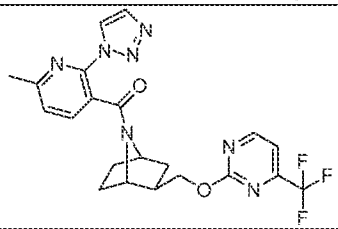
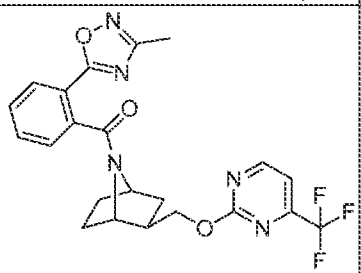
97		(±)-(6-methyl-3-(pyrrolidin-1-yl)pyridin-2-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
98		(±)-(3,6'-dimethyl-[2,3'-bipyridin]-2'-yl)(2-(((5-fluoropyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
99		(±)-(2-(((5-fluoropyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(3-methylisoxazol-5-yl)pyridin-2-yl)methanone
100		(±)-(2-(((5-fluoropyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(oxazol-2-yl)pyridin-2-yl)methanone
101		(±)-(2-(((5-fluoropyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(pyrrolidin-1-yl)pyridin-2-yl)methanone
102		(±)-(2-(((5-fluoropyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(pyrimidin-2-yl)pyridin-2-yl)methanone
103		(±)-(2-(((5-fluoropyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(4-methyl-1H-pyrazol-1-yl)pyridin-2-yl)methanone

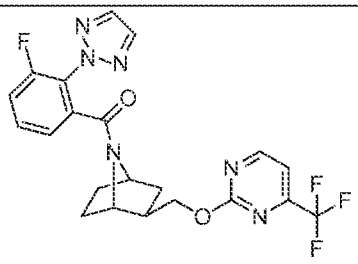
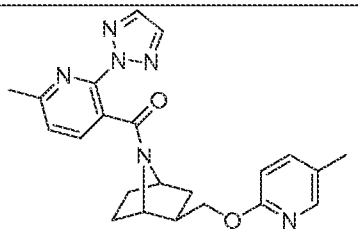
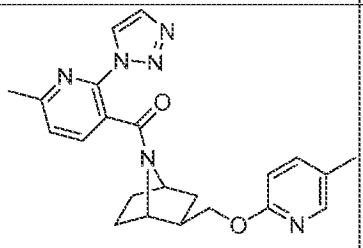
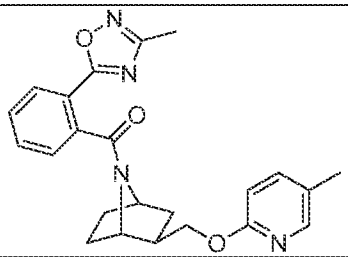
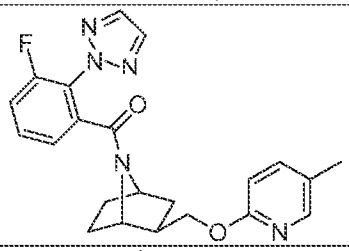
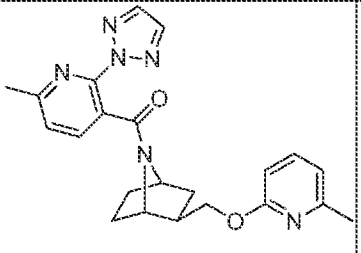
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105		(±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(5-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone
106		(±)-(2,6-dimethoxyphenyl)(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
107		(±)-((3-fluoro-2-methoxyphenyl)(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
108		(±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(2-methoxy-6-(2H-1,2,3-triazol-2-yl)phenyl)methanone
109		(±)-(5-fluoro-2-(1H-pyrazol-5-yl)phenyl)(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

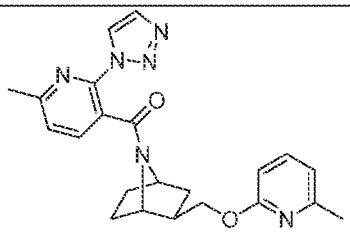
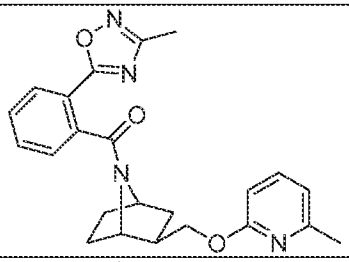
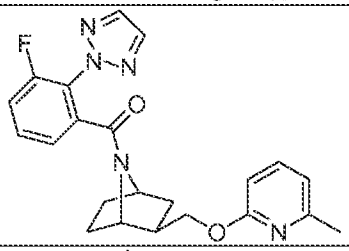
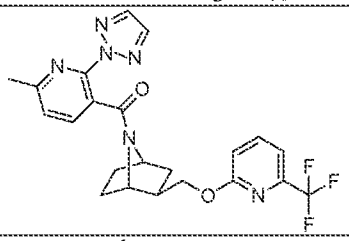
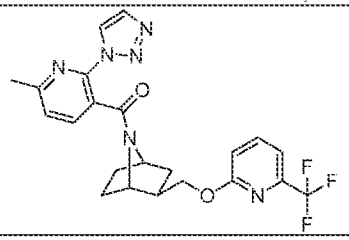
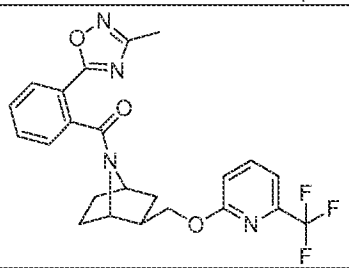
110		(±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(2-methyl-6-(2H-1,2,3-triazol-2-yl)phenyl)methanone
111		(±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)methanone
112		(±)-(5-chloro-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
113		(±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(5-methoxy-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)methanone
114		(±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(5-methoxy-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone
115		(±)-(2-fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

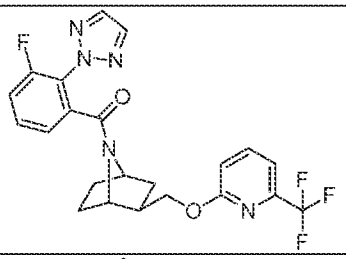
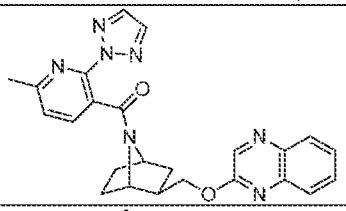
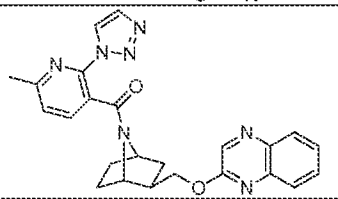
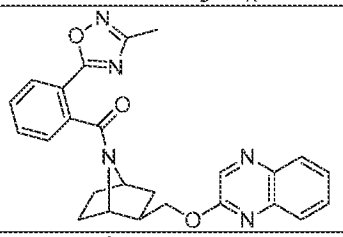
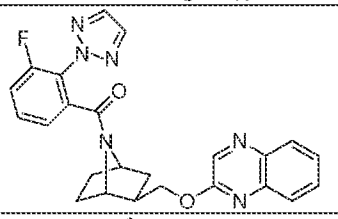
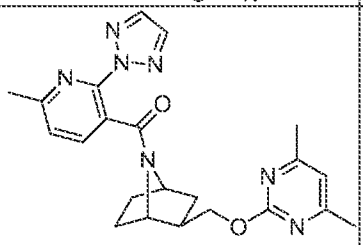
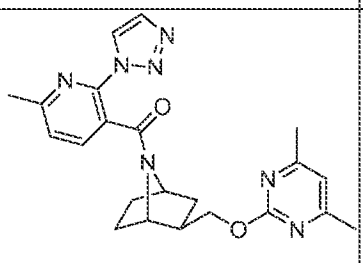
116		(±)-(4-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
117		(±)-(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
118		(±)-(3-ethoxy-6-methylpyridin-2-yl)(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
119		(±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(4-methoxy-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone
120		(±)-(5-chloro-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
121		(±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(4-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone

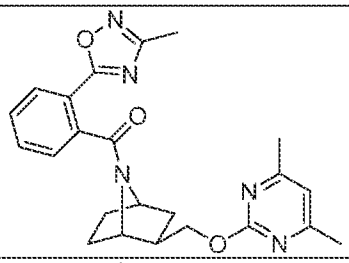
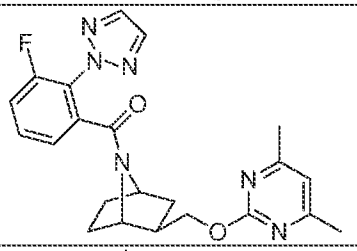
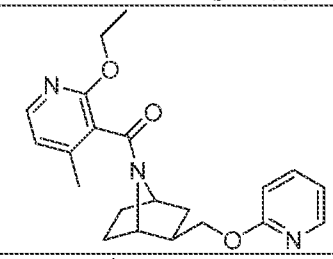
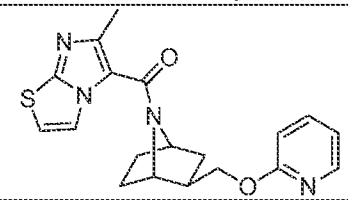
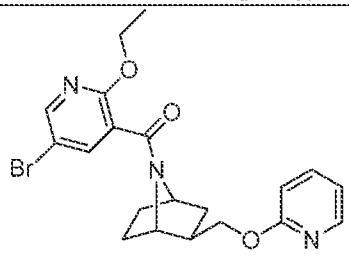
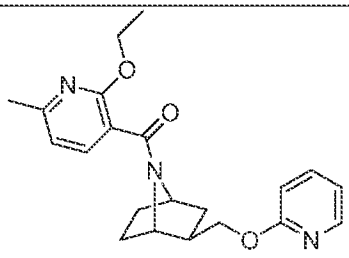
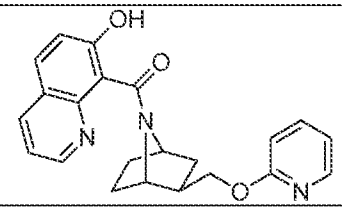
122		(±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(4-methyl-2-(pyrimidin-2-yl)phenyl)methanone
123		(±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(2-methyl-6-(pyrimidin-2-yl)phenyl)methanone
124		(±)-(3-fluoro-2-(pyrimidin-2-yl)phenyl)(-2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
125		(±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(3-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone
126		(±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(5-(hydroxymethyl)-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone
127		(±)-(2-(3-methyl-1,2,4-oxadiazol-5-yl)phenyl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

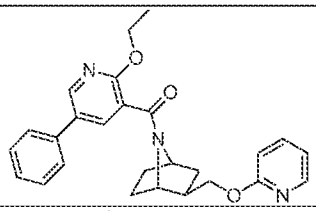
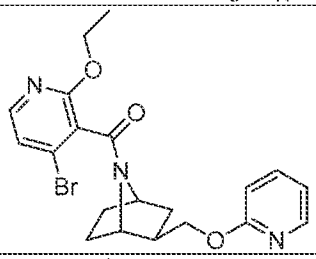
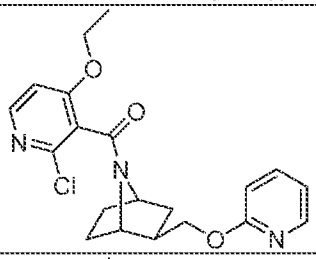
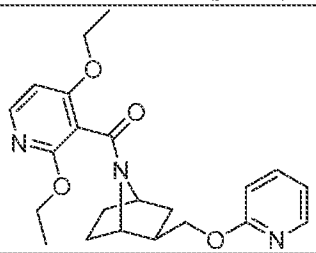
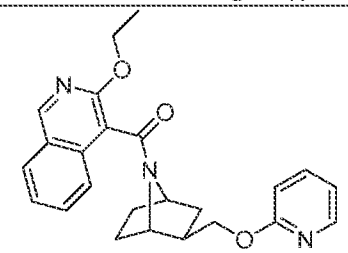
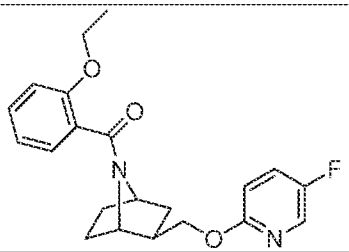
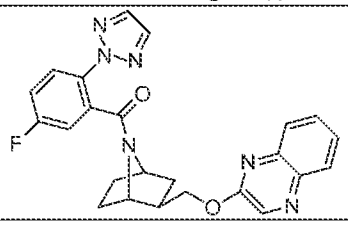
128		(±)-(6-methyl-2-(2H-1,2,3-triazol-2-yl)pyridin-3-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
129		(±)-(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
130		(±)-(6-methyl-2-(1H-1,2,3-triazol-1-yl)pyridin-3-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
131		(±)-(6-methyl-2-(2H-1,2,3-triazol-2-yl)pyridin-3-yl)(2-(((4-(trifluoromethyl)pyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
132		(±)-(6-methyl-2-(1H-1,2,3-triazol-1-yl)pyridin-3-yl)(2-(((4-(trifluoromethyl)pyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
133		(±)-(2-(3-methyl-1,2,4-oxadiazol-5-yl)phenyl)(2-(((4-(trifluoromethyl)pyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

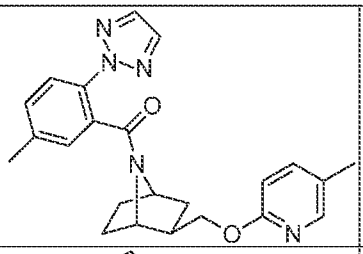
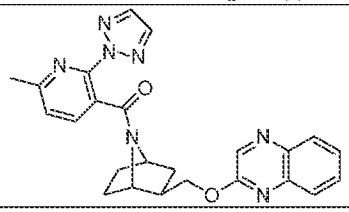
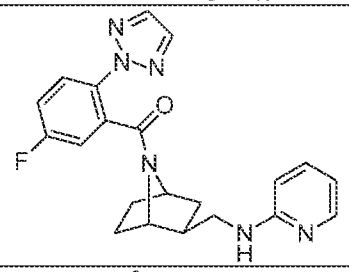
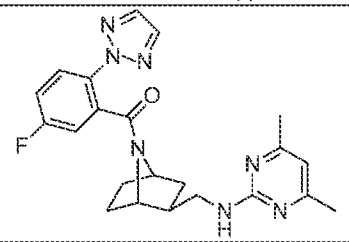
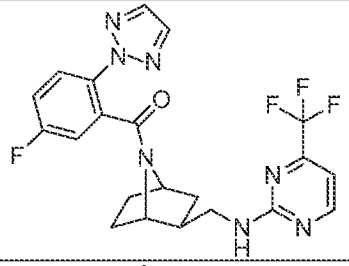
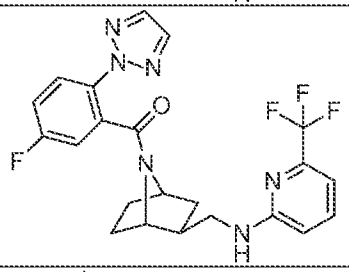
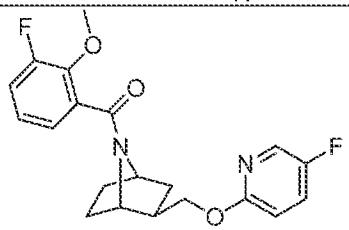
134		(±)-(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((4-(trifluoromethyl)pyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
135		(±)-(6-methyl-2-(2H-1,2,3-triazol-2-yl)pyridin-3-yl)(2-(((5-methylpyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
136		(±)-(6-methyl-2-(1H-1,2,3-triazol-1-yl)pyridin-3-yl)(2-(((5-methylpyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
137		(±)-(2-(3-methyl-1,2,4-oxadiazol-5-yl)phenyl)(2-(((5-methylpyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
138		(±)-(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((5-methylpyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
139		(±)-(6-methyl-2-(2H-1,2,3-triazol-2-yl)pyridin-3-yl)(2-(((6-methylpyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

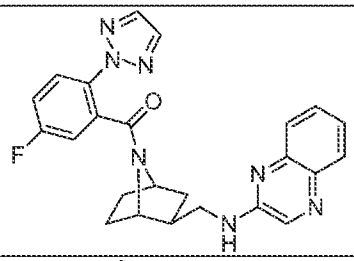
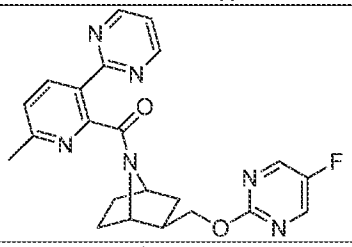
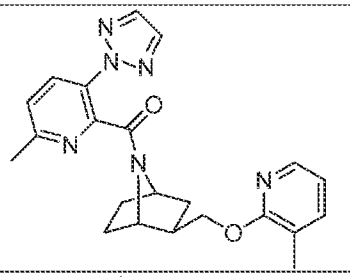
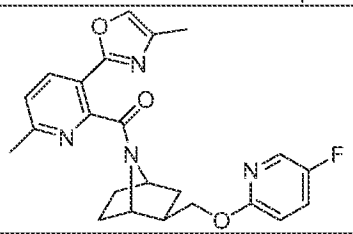
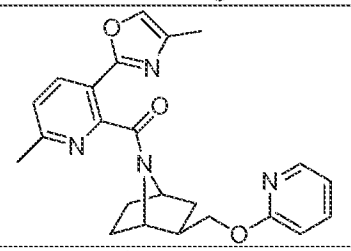
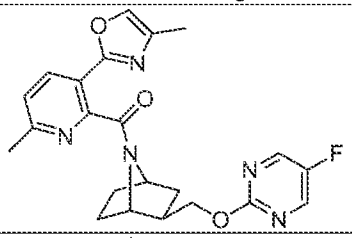
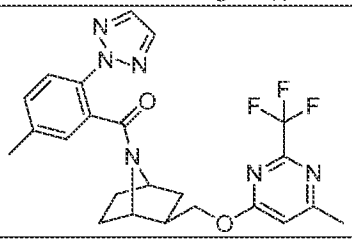
140		(±)-(6-methyl-2-(1H-1,2,3-triazol-1-yl)pyridin-3-yl)(2-(((6-methylpyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
141		(±)-(2-(3-methyl-1,2,4-oxadiazol-5-yl)phenyl)(2-(((6-methylpyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
142		(±)-(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((6-methylpyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
143		(±)-(6-methyl-2-(2H-1,2,3-triazol-2-yl)pyridin-3-yl)(2-(((6-(trifluoromethyl)pyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
144		(±)-(6-methyl-2-(1H-1,2,3-triazol-1-yl)pyridin-3-yl)(2-(((6-(trifluoromethyl)pyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
145		(±)-(2-(3-methyl-1,2,4-oxadiazol-5-yl)phenyl)(2-(((6-(trifluoromethyl)pyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

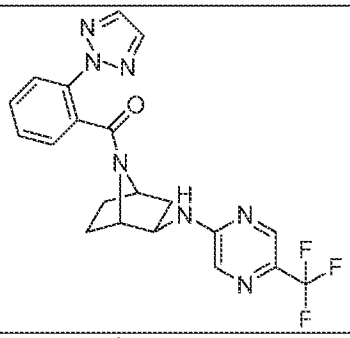
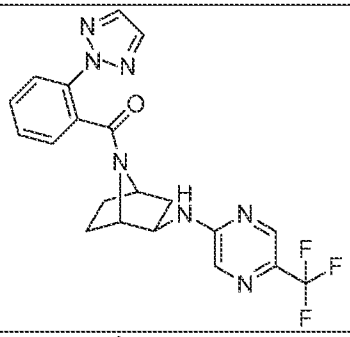
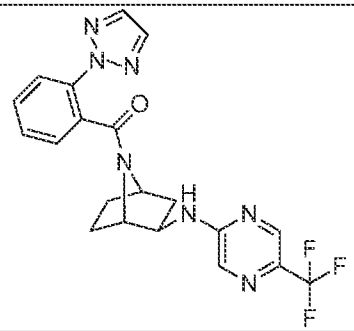
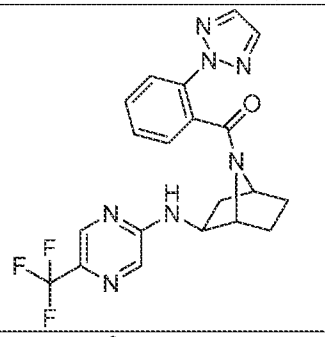
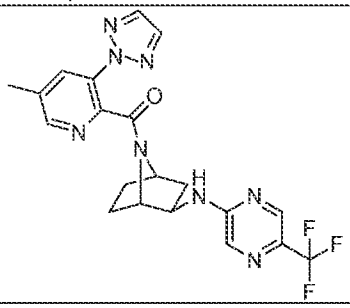
146		(±)-(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((6-(trifluoromethyl)pyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
147		(±)-(6-methyl-2-(2H-1,2,3-triazol-2-yl)pyridin-3-yl)(2-((quinoxalin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
148		(±)-(6-methyl-2-(1H-1,2,3-triazol-1-yl)pyridin-3-yl)(2-((quinoxalin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
149		(±)-(2-(3-methyl-1,2,4-oxadiazol-5-yl)phenyl)(2-((quinoxalin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
150		(±)-(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((quinoxalin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
151		(±)-(2-(((4,6-dimethylpyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-2-(2H-1,2,3-triazol-2-yl)pyridin-3-yl)methanone
152		(±)-(2-(((4,6-dimethylpyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-2-(1H-1,2,3-triazol-1-yl)pyridin-3-yl)methanone

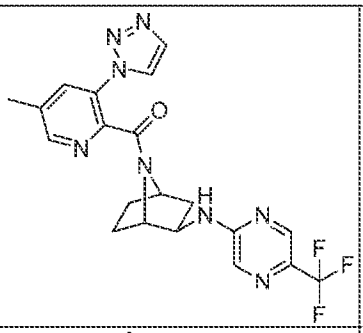
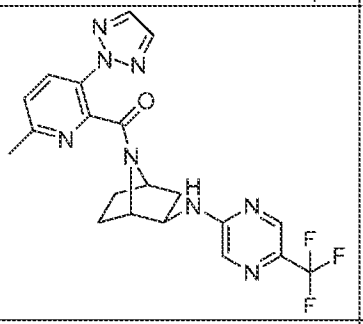
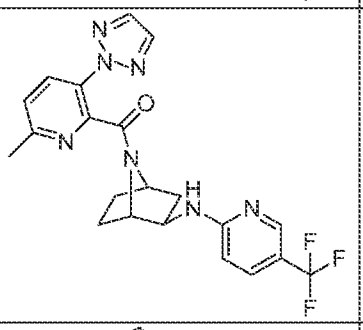
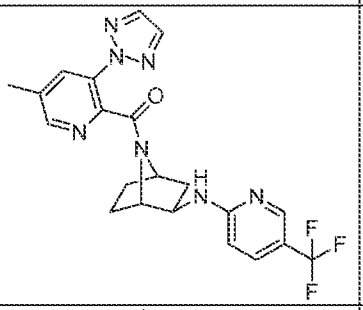
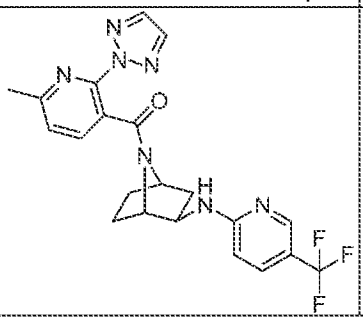
153		(±)-(2-(((4,6-dimethylpyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(2-(3-methyl-1,2,4-oxadiazol-5-yl)phenyl)methanone
154		(±)-(2-(((4,6-dimethylpyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone
155		(±)-(2-ethoxy-4-methylpyridin-3-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
156		(±)-(6-methylimidazo[2,1-b]thiazol-5-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
157		(±)-(5-bromo-2-ethoxypyridin-3-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
158		(±)-(2-ethoxy-6-methylpyridin-3-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
159		(±)-(7-hydroxyquinolin-8-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

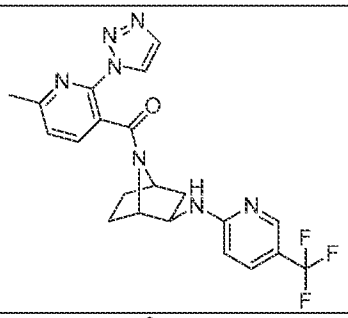
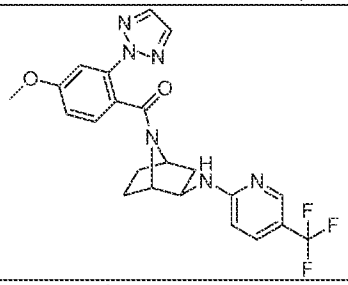
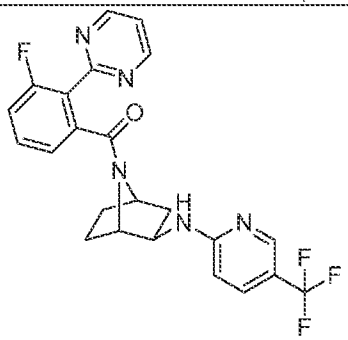
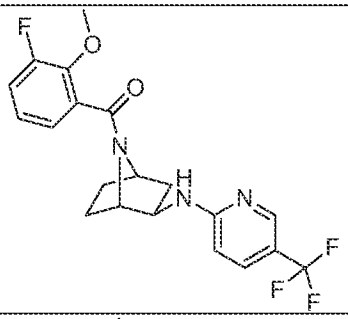
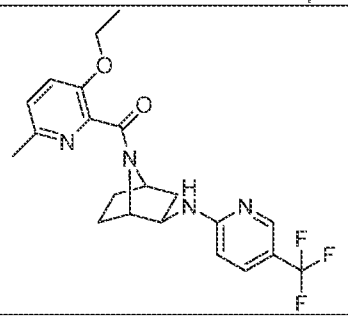
160		(±)-(2-ethoxy-5-pheuylpyridin-3-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
161		(±)-(4-bromo-2-ethoxypyridin-3-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
162		(±)-(2-chloro-4-ethoxypyridin-3-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
163		(±)-(2,4-diethoxypyridin-3-yl)(2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
164		(3-ethoxyisoquinolin-4-yl)((1S,2R,4R)-2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
165		(±)-(2-ethoxyphenyl)(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
166		(±)-(5-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((quinoxalin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

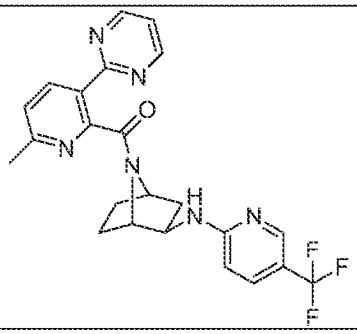
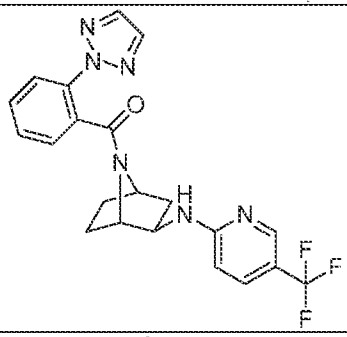
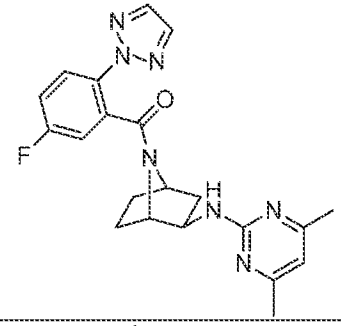
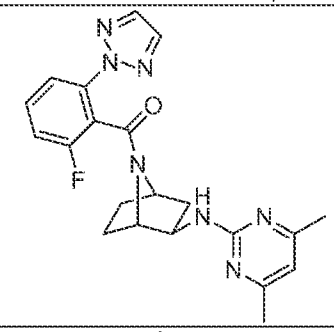
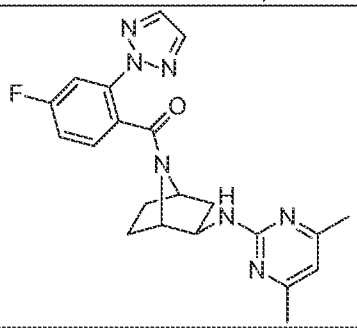
167		(±)-5-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((5-methylpyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
168		(±)-(6-methyl-2-(2H-1,2,3-triazol-2-yl)pyridin-3-yl)(2-((quinoxalin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
169		(±)-(5-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((pyridin-2-ylamino)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
170		(±)-(2-(((4,6-dimethylpyrimidin-2-yl)amino)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(5-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone
171		(±)-(5-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((4-(trifluoromethyl)pyrimidin-2-yl)amino)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
172		(±)-(5-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((6-(trifluoromethyl)pyridin-2-yl)amino)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
173		(±)-(3-fluoro-2-methoxyphenyl)(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

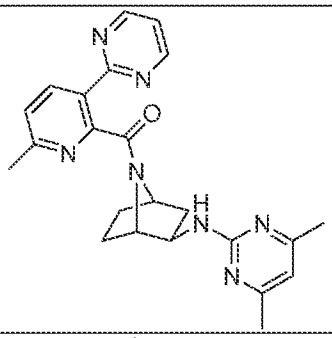
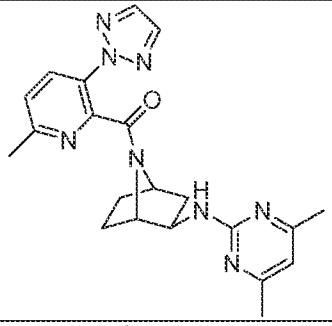
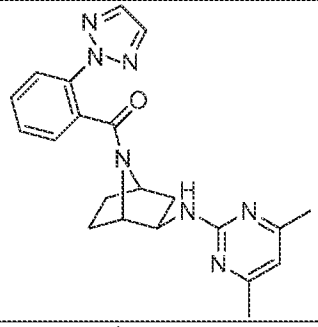
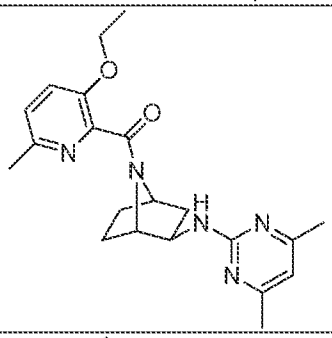
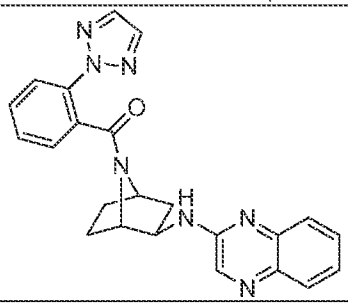
174		(±)-(5-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((quinoxalin-2-ylamino)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
175		(±)-(2-(((5-fluoropyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(pyrimidin-2-yl)pyridin-2-yl)methanone
176		(±)-(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-(((3-methylpyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
177		(±)-(2-(((5-fluoropyridin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(4-methyloxazol-2-yl)pyridin-2-yl)methanone
178		(6-methyl-3-(4-methyloxazol-2-yl)pyridin-2-yl)((1S,2R,4R)-2-((pyridin-2-yloxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
179		((1S,2R,4R)-2-(((5-fluoropyrimidin-2-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(4-methyloxazol-2-yl)pyridin-2-yl)methanone
180		(±)-(5-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(((6-methyl-2-(trifluoromethyl)pyrimidin-4-yl)oxy)methyl)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

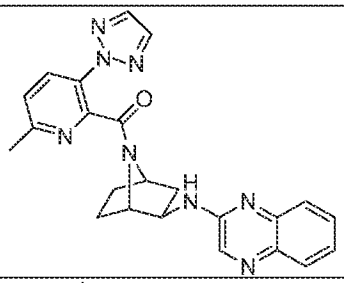
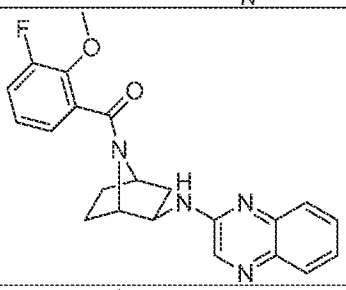
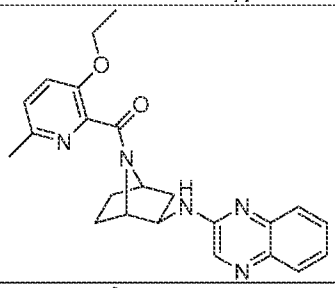
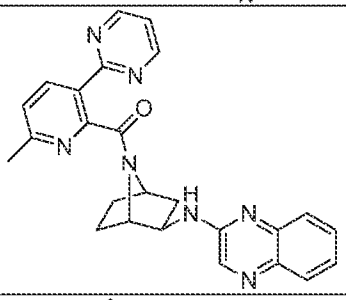
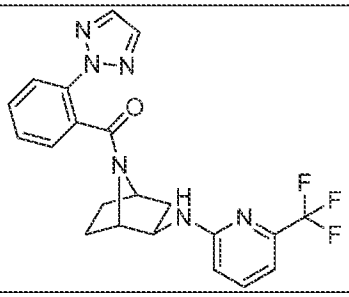
181		(2-(2H-1,2,3-triazol-2-yl)phenyl)(1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
182		(±)-((2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
183a		(2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
183b		(2-(2H-1,2,3-triazol-2-yl)phenyl)((1R,2S,4S)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
184		(±)-(5-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

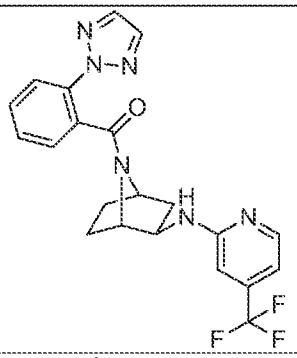
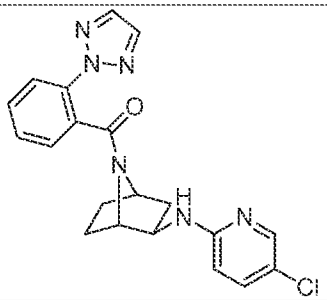
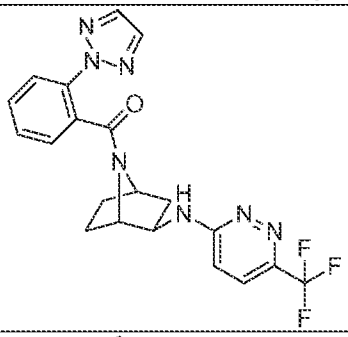
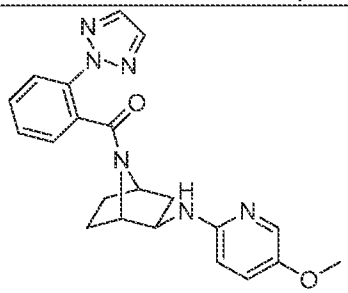
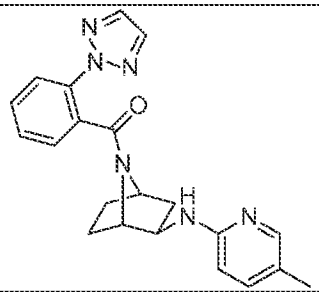
185		(±)-(5-methyl-3-(1H-1,2,3-triazol-1-yl)pyridin-2-yl)(2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
186		(±)-(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
187		(±)-(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
188		(±)-(5-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
189		(±)-(6-methyl-2-(2H-1,2,3-triazol-2-yl)pyridin-3-yl)(2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

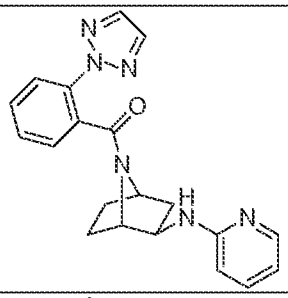
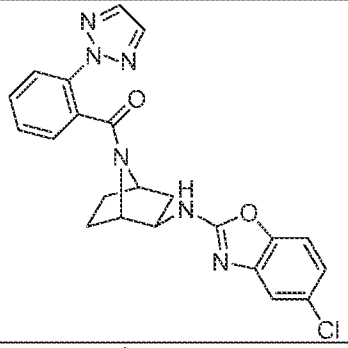
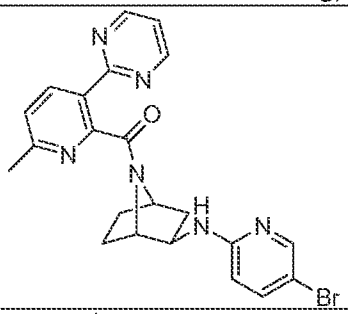
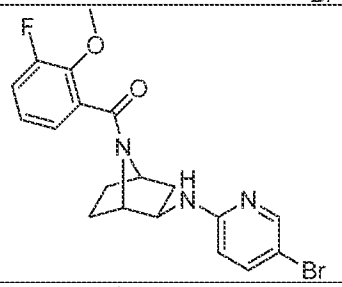
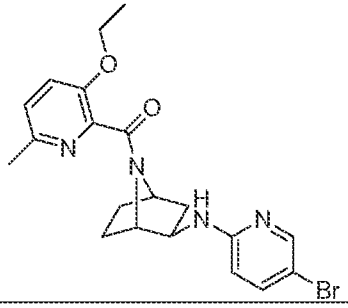
190		(±)-(6-methyl-2-(1H-1,2,3-triazol-1-yl)pyridin-3-yl)(2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
191		(±)-(4-methoxy-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
192		(±)-(3-fluoro-2-(pyrimidin-2-yl)phenyl)(2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
193		(±)-((3-fluoro-2-methoxyphenyl)(2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
194		(±)-(3-ethoxy-6-methylpyridin-2-yl)(2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

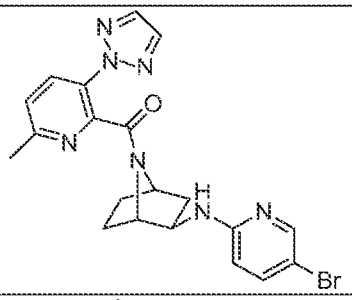
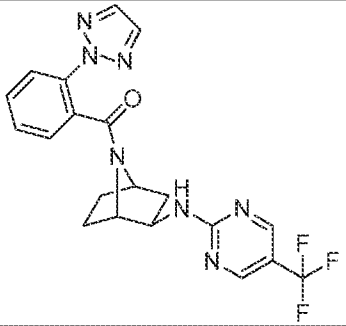
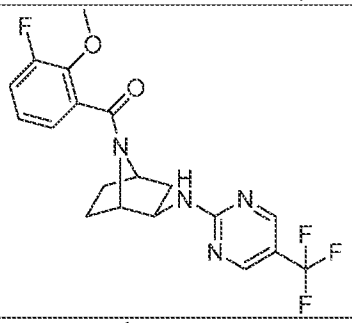
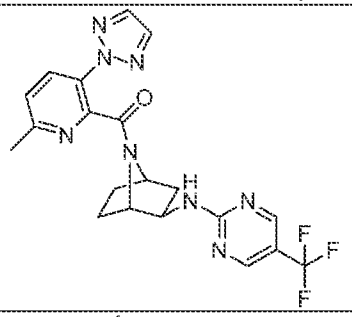
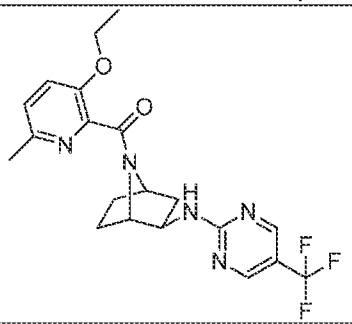
195		(±)-(6-methyl-3-(pyrimidin-2-yl)pyridin-2-yl)(2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
196		(±)-(2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
197		(±)-(2-((4,6-dimethylpyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(5-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone
198		(±)-(2-((4,6-dimethylpyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(2-fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl)methanone
199		(±)-(2-((4,6-dimethylpyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(4-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone

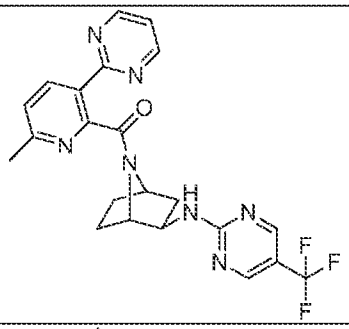
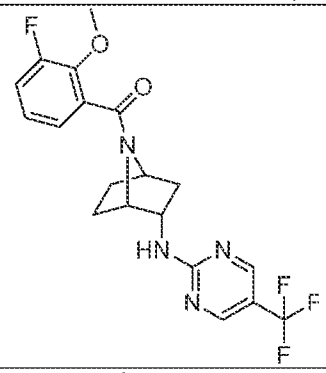
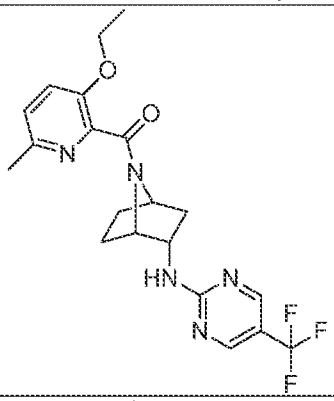
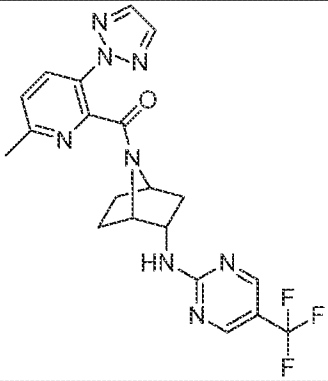
200		(±)-(2-((4,6-dimethylpyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(pyrimidin-2-yl)pyridin-2-yl)methanone
201		(±)-(2-((4,6-dimethylpyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)methanone
202		(±)-(2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((4,6-dimethylpyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
203		(±)-(2-((4,6-dimethylpyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-ethoxy-6-methylpyridin-2-yl)methanone
204		(±)-(2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(quinoxalin-2-ylamino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

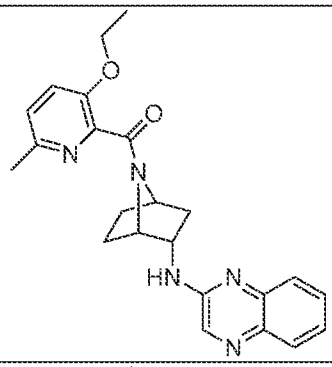
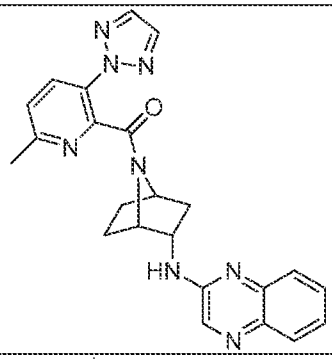
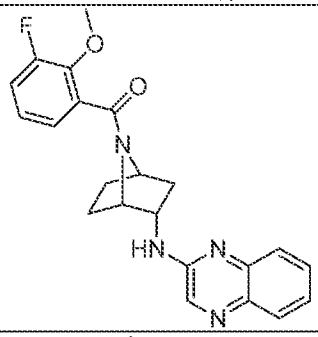
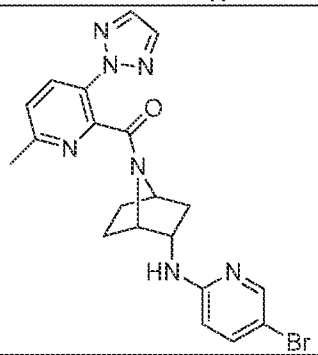
205		(±)-(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-(quinoxalin-2-ylamino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
206		(±)-(3-fluoro-2-methoxyphenyl)(2-(quinoxalin-2-ylamino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
207		(±)-(3-ethoxy-6-methylpyridin-2-yl)(2-(quinoxalin-2-ylamino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
208		(±)-(6-methyl-3-(pyrimidin-2-yl)pyridin-2-yl)(2-(quinoxalin-2-ylamino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
209		(±)-(2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((6-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

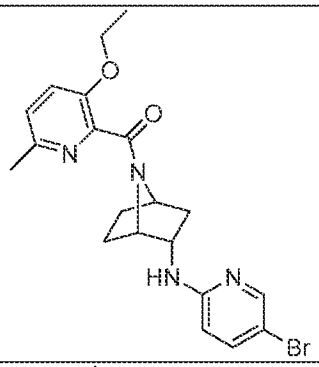
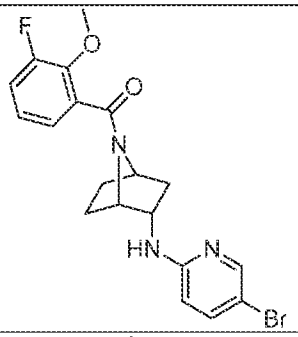
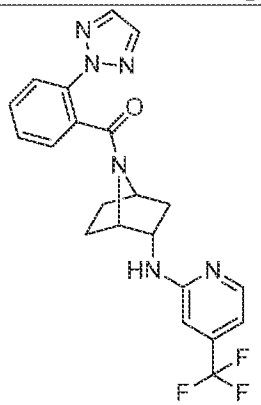
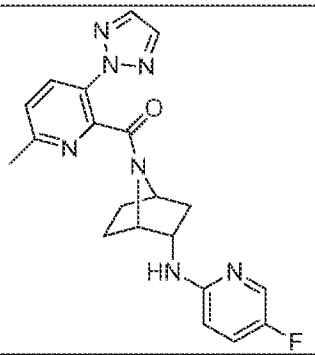
210		(±)-((2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((4-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
211		(±)-(2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((5-chloropyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
212		(±)-(2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((6-(trifluoromethyl)pyridazin-3-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
213		(±)-(2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((5-methoxypyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
214		(±)-(2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((5-methylpyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

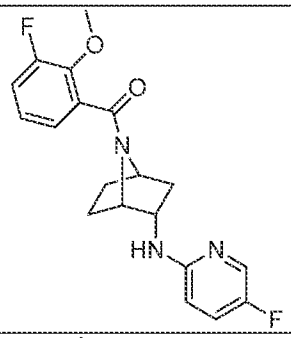
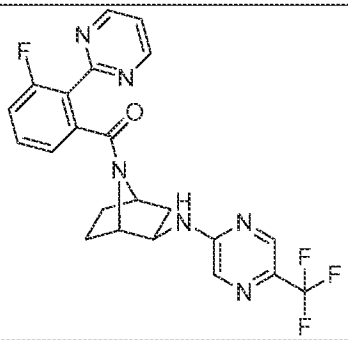
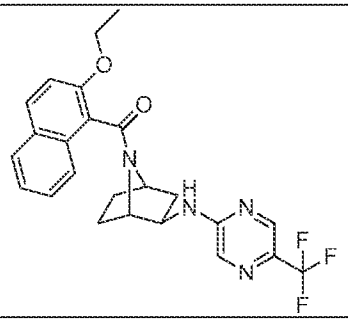
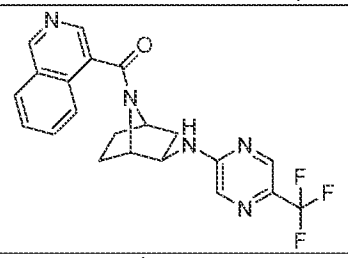
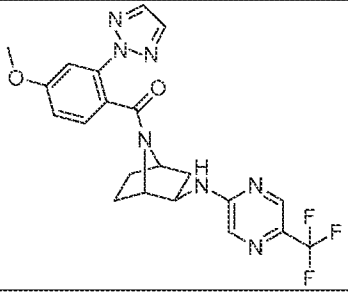
215		(±)-(2-(2H-1,2,3-triazol-2-yl)phenyl)(2-(pyridin-2-ylamino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
216		(±)-(2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((5-chlorobenzo[d]oxazol-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
217		(±)-(2-((5-bromopyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(pyrimidin-2-yl)pyridin-2-yl)methanone
218		(±)-(2-((5-bromopyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-methoxyphenyl)methanone
219		(±)-(2-((5-bromopyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-ethoxy-6-methylpyridin-2-yl)methanone

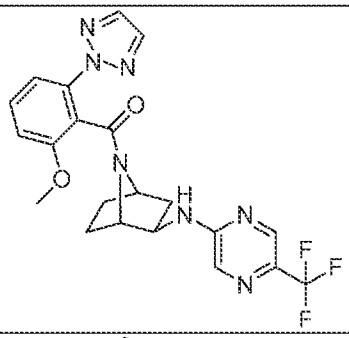
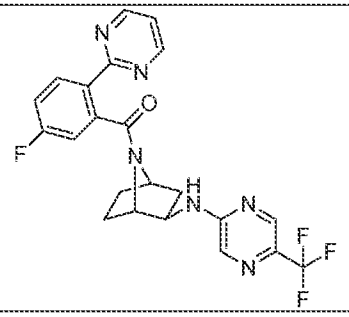
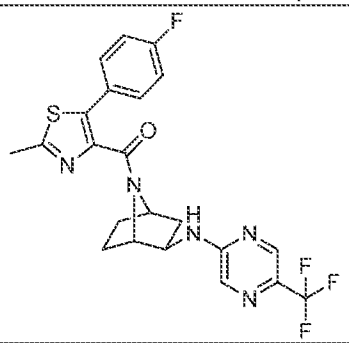
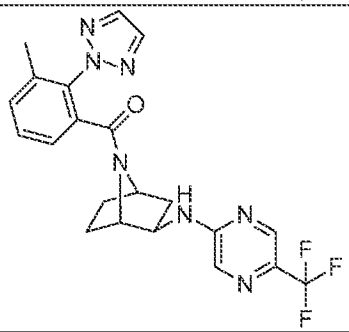
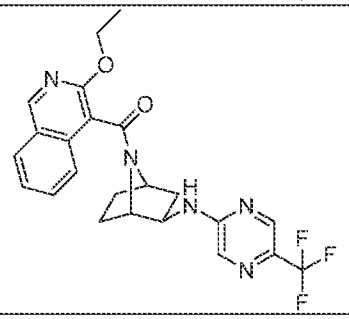
220		(±)-(2-((5-bromopyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)methanone
221		(±)-(2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
222		(±)-(3-fluoro-2-methoxyphenyl)(2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
223		(±)-(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
224		(±)-(3-ethoxy-6-methylpyridin-2-yl)(2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

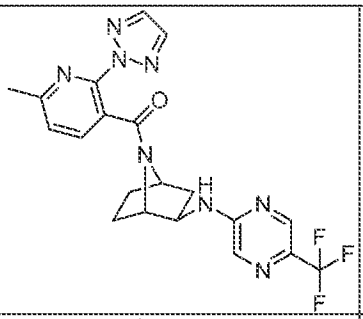
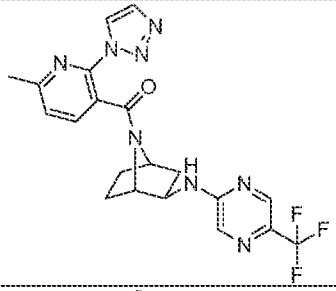
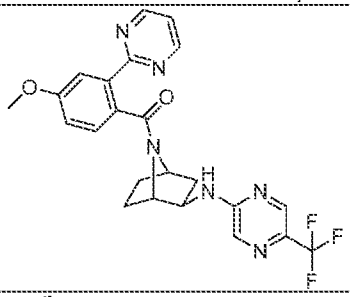
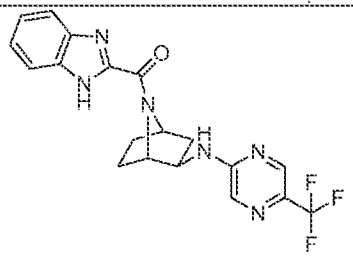
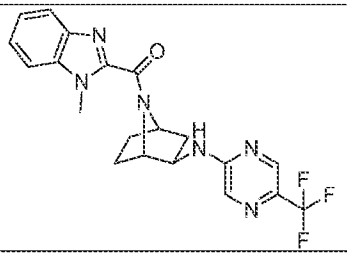
225		(±)-(6-methyl-3-(pyrimidin-2-yl)pyridin-2-yl)(2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
226		(±)-(3-fluoro-2-methoxyphenyl)(2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
227		(±)-(3-ethoxy-6-methylpyridin-2-yl)(2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
228		(±)-(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

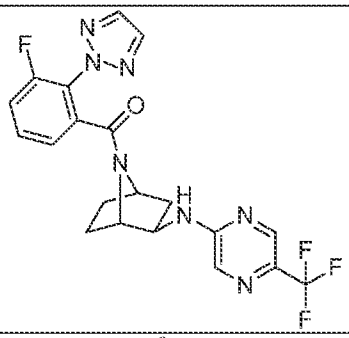
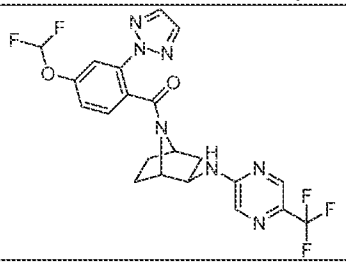
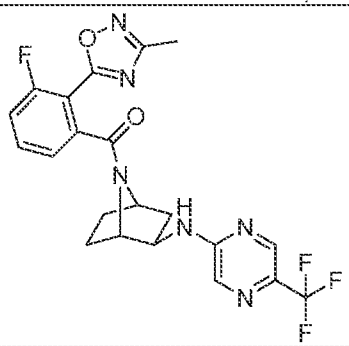
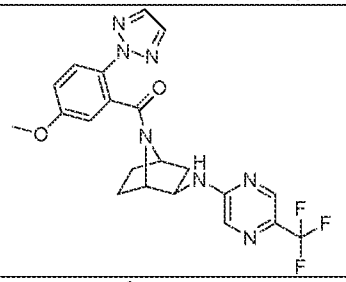
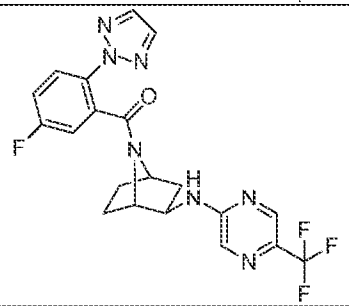
229		(±)-(3-ethoxy-6-methylpyridin-2-yl)(2-(quinoxalin-2-ylamino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
230		(±)-(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)(2-(quinoxalin-2-ylamino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
231		(±)-(3-fluoro-2-methoxyphenyl)(2-(quinoxalin-2-ylamino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
232		(±)-(2-((5-bromopyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)methanone

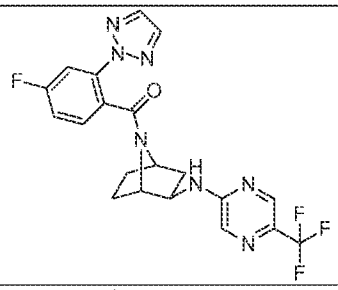
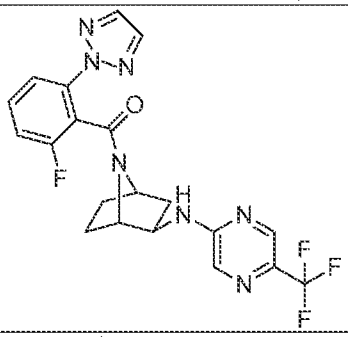
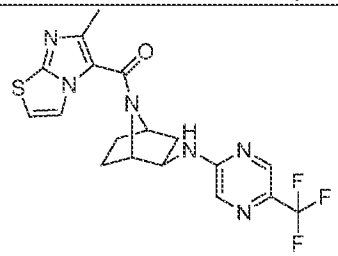
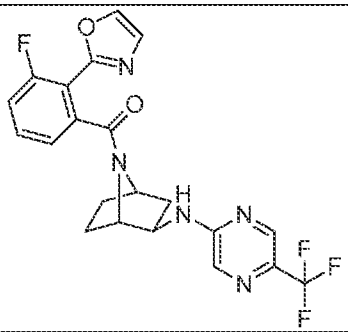
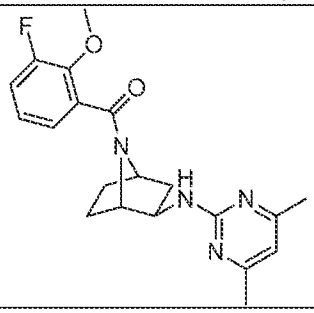
233		(±)-(2-((5-bromopyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-ethoxy-6-methylpyridin-2-yl)methanone
234		(±)-(2-((5-bromopyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-methoxyphenyl)methanone
235		(±)-((2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((4-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
236		(±)-(2-((5-fluoropyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)methanone

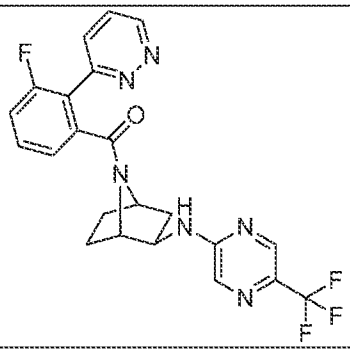
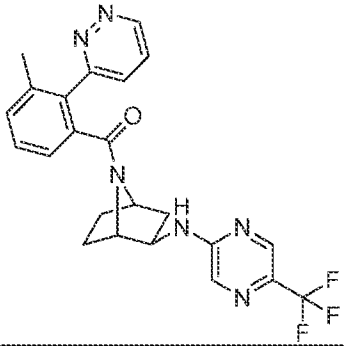
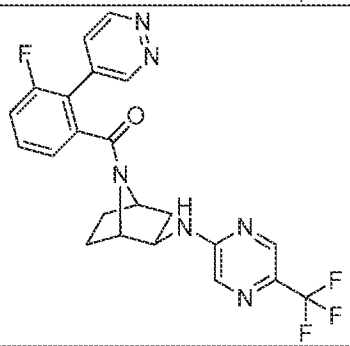
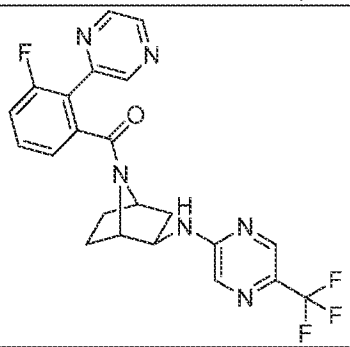
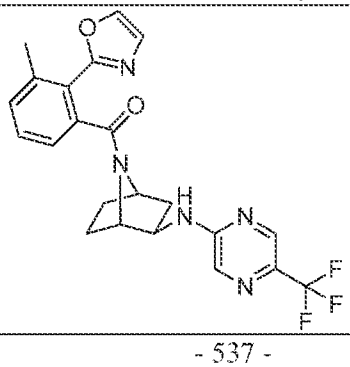
237		(±)-(3-fluoro-2-methoxyphenyl)(2-((5-fluoropyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
238		(3-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
239		(2-ethoxynaphthalen-1-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
240		isoquinolin-4-yl((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
241		(4-methoxy-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

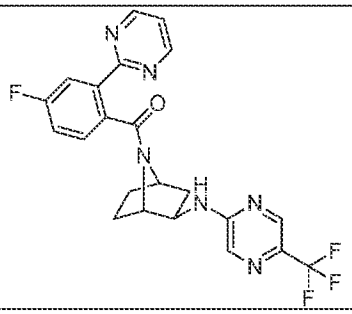
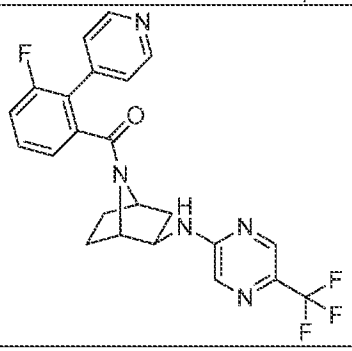
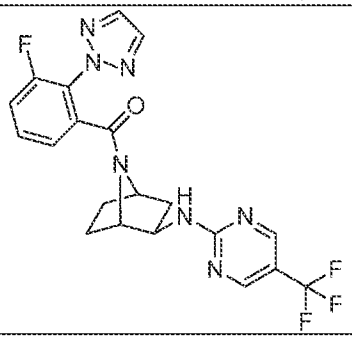
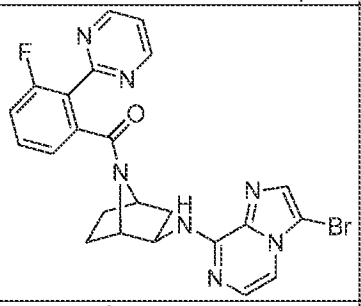
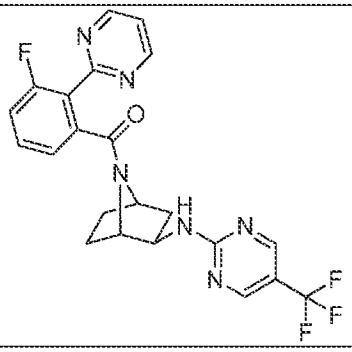
242		(2-methoxy-6-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
243		(5-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
244		(5-(4-fluorophenyl)-2-methylthiazol-4-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
245		(3-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
246		(3-ethoxyisoquinolin-4-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

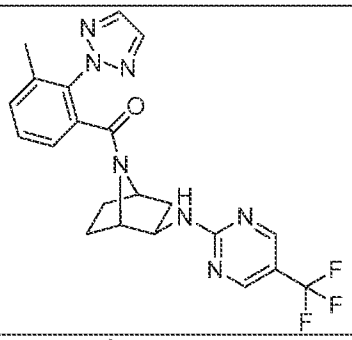
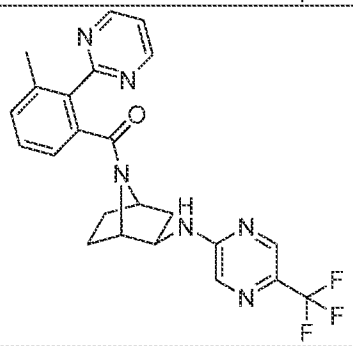
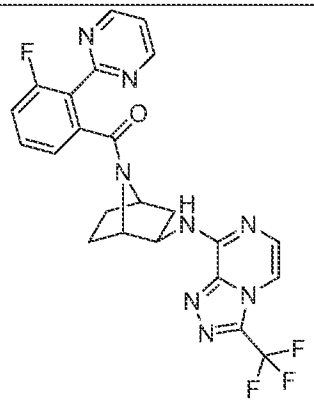
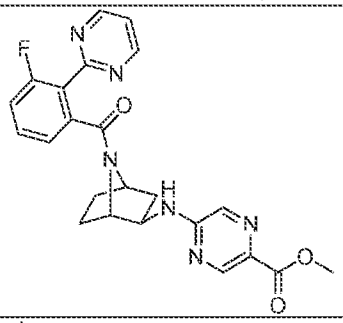
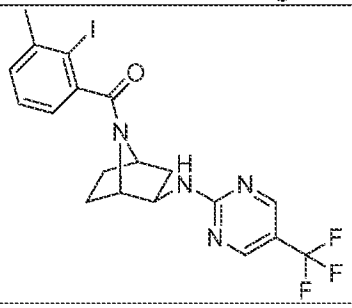
247		(6-methyl-2-(2H-1,2,3-triazol-2-yl)pyridin-3-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
248		(6-methyl-2-(1H-1,2,3-triazol-1-yl)pyridin-3-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
249		(4-methoxy-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
250		(1H-benzo[d]imidazol-2-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
251		(1-methyl-1H-benzo[d]imidazol-2-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

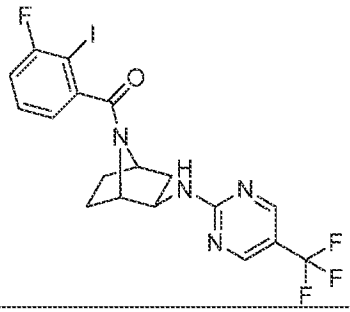
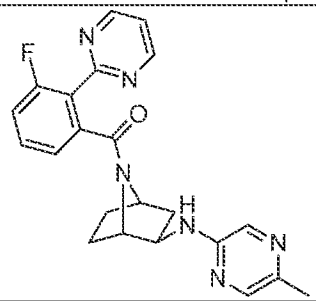
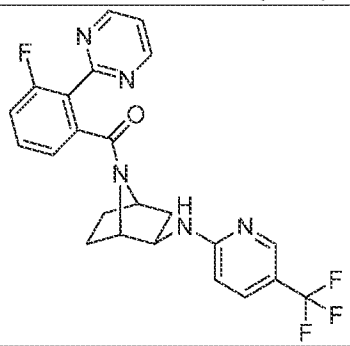
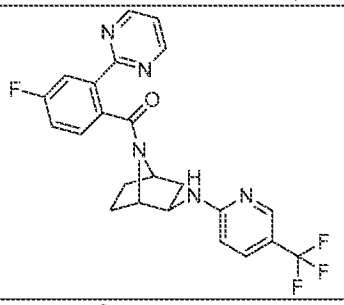
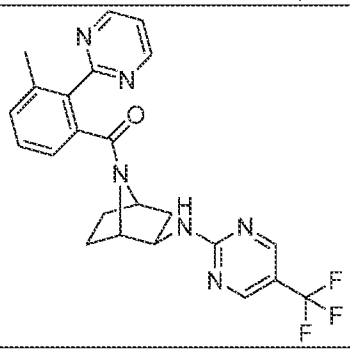
252		(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
253		(4-(difluoromethoxy)-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
254		(3-fluoro-2-(3-methyl-1,2,4-oxadiazol-5-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
255		(5-methoxy-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
256		(5-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

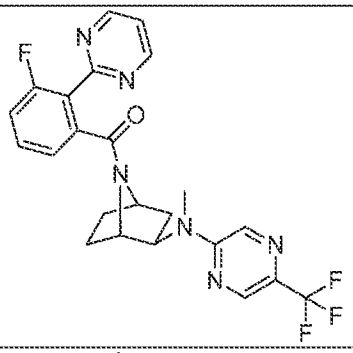
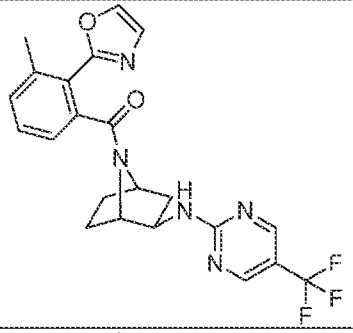
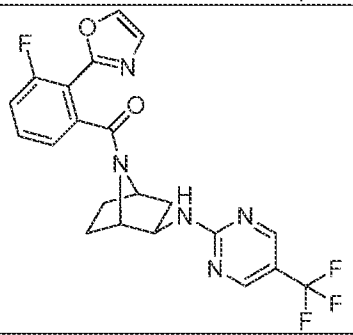
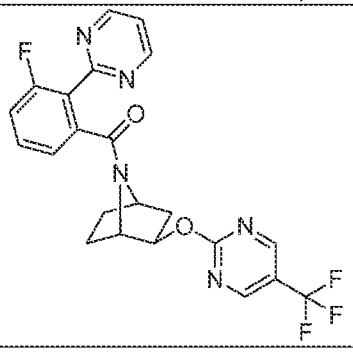
257		(4-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
258		(2-fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
259		(6-methylimidazo[2,1-b]thiazol-5-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
260		(3-fluoro-2-(oxazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
261		(2-((4,6-dimethylpyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-methoxyphenyl)methanone

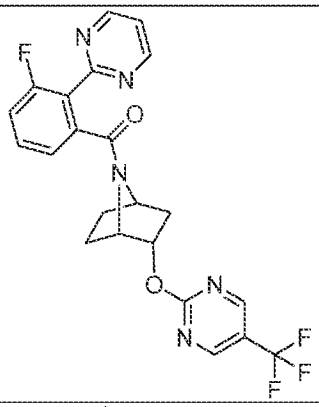
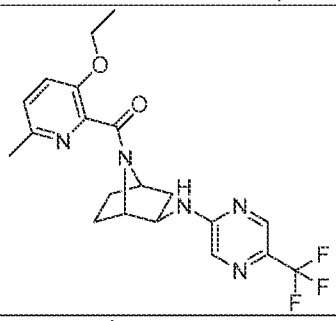
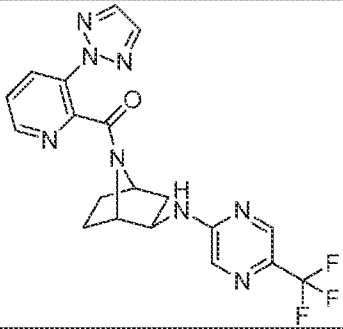
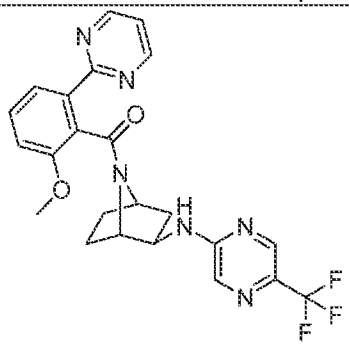
262		(3-fluoro-2-(pyridazin-3-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
263		(3-methyl-2-(pyridazin-3-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
264		(3-fluoro-2-(pyridazin-4-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
265		(3-fluoro-2-(pyrazin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
266		(3-methyl-2-(oxazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

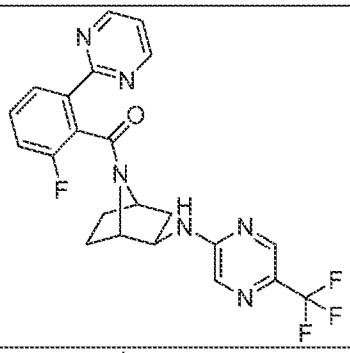
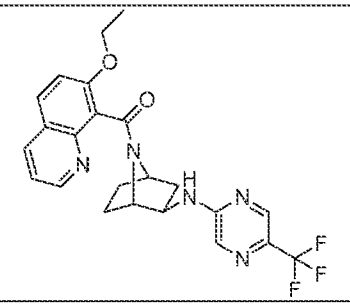
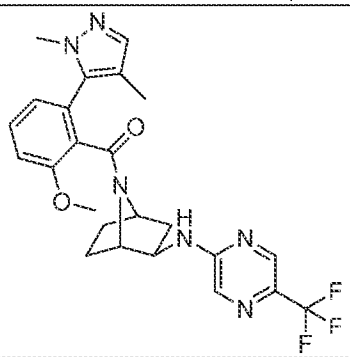
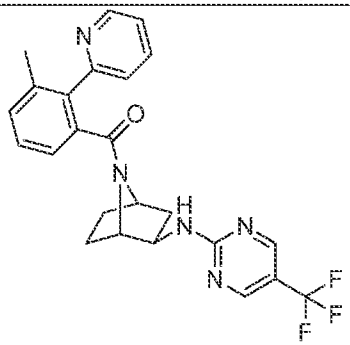
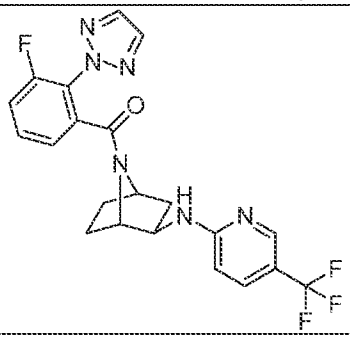
267		(4-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
268		(3-fluoro-2-(pyridin-4-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
269		(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
270		((1S,2R,4R)-2-((3-bromoimidazo[1,2-a]pyrazin-8-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-(pyrimidin-2-yl)phenyl)methanone
271		(3-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

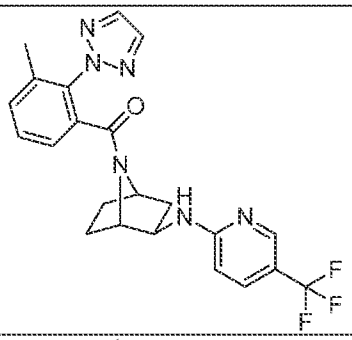
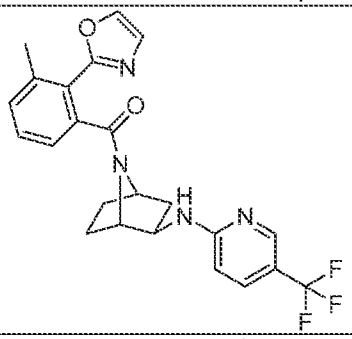
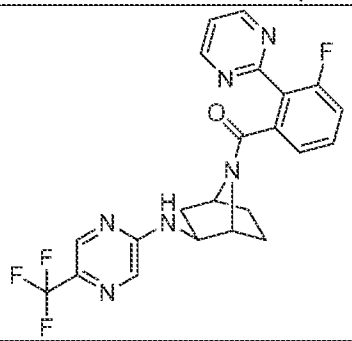
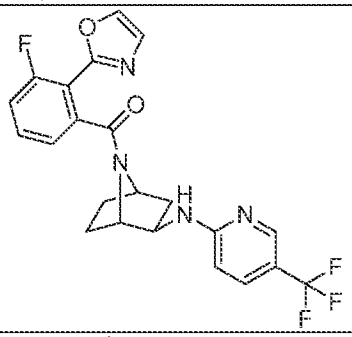
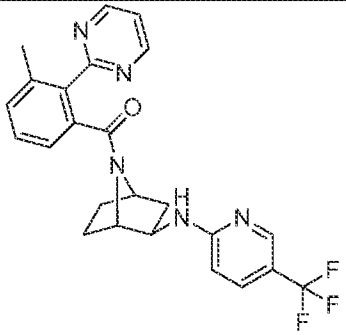
272		(3-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
273		(3-methyl-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
274		(3-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((3-(trifluoromethyl)-[1,2,4]triazolo[4,3-a]pyrazin-8-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
275		methyl 5-(((1S,2R,4R)-7-(3-fluoro-2-(pyrimidin-2-yl)benzoyl)-7-azabicyclo[2.2.1]heptan-2-yl)amino)pyrazine-2-carboxylate
276		(2-iodo-3-methylphenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

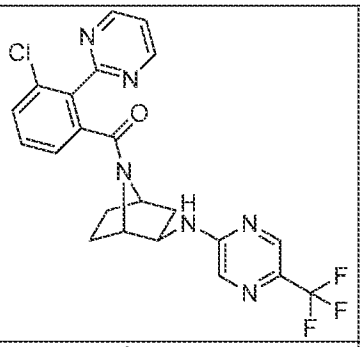
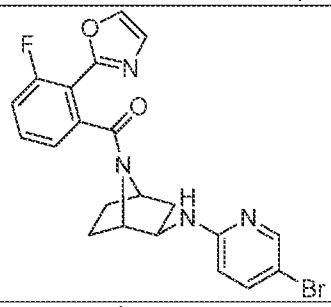
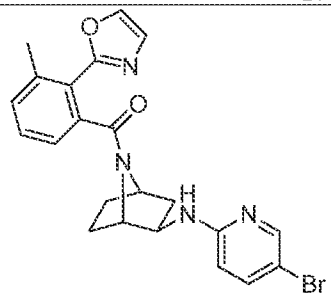
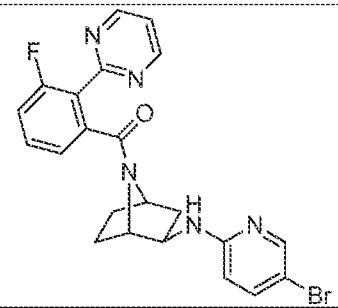
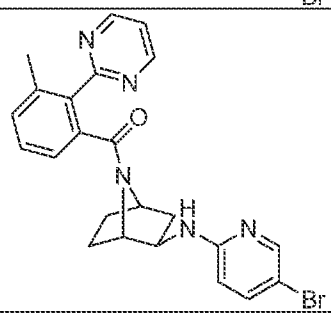
277		(3-fluoro-2-iodophenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
278		(3-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-methylpyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
279		(3-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
280		(4-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
281		(3-methyl-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

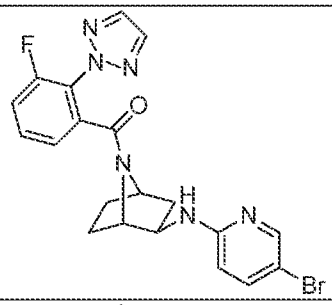
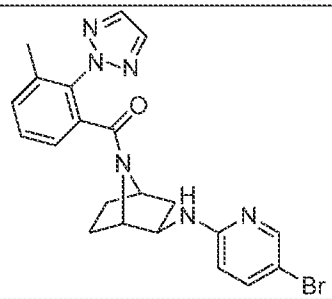
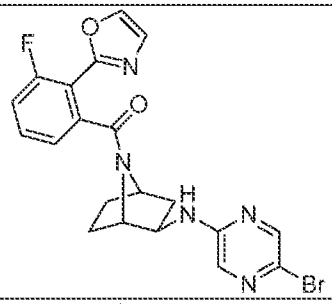
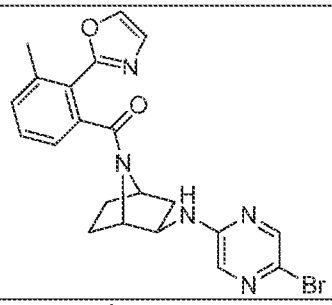
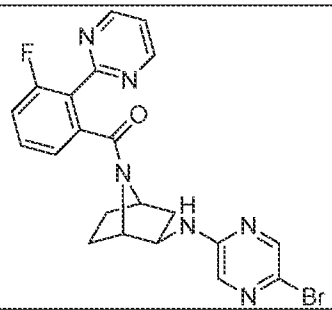
282		(3-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-(methyl(5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
283		(3-methyl-2-(oxazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
284		(3-fluoro-2-(oxazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
285		(±)-(3-fluoro-2-(pyrimidin-2-yl)phenyl)(2-((5-(trifluoromethyl)pyrimidin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

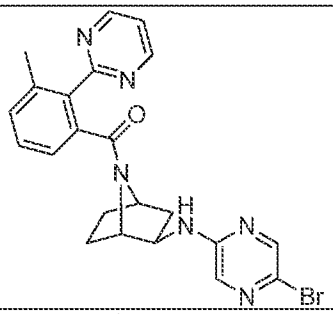
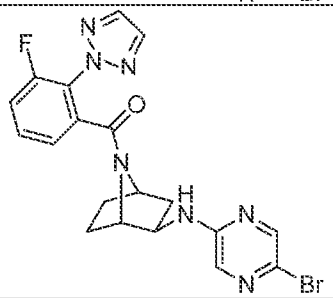
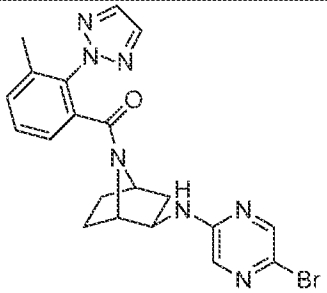
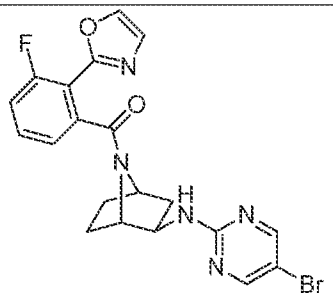
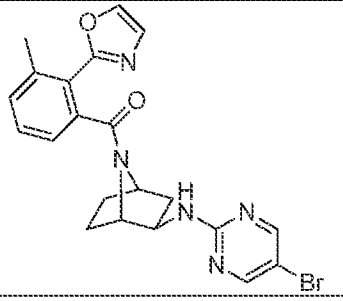
286		(±)-(3-fluoro-2-(pyrimidin-2-yl)phenyl)(2-((5-(trifluoromethyl)pyrimidin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
287		(3-ethoxy-6-methylpyridin-2-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
288		(3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
289		(2-methoxy-6-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

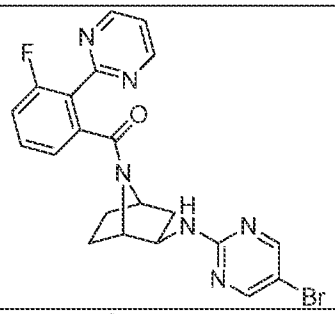
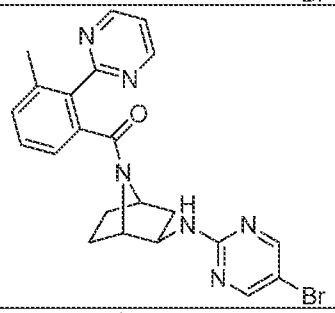
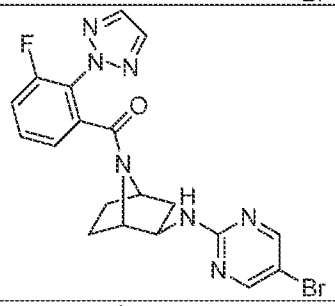
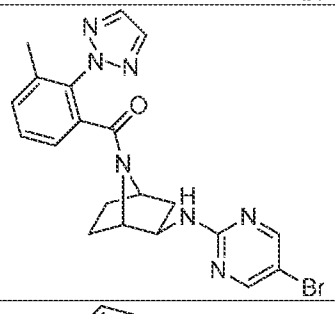
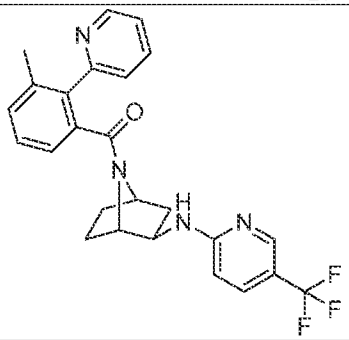
290		(2-fluoro-6-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
291		(7-ethoxyquinolin-8-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
292		(2-(1,4-dimethyl-1H-pyrazol-5-yl)-6-methoxyphenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
293		(3-methyl-2-(pyridin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
294		(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

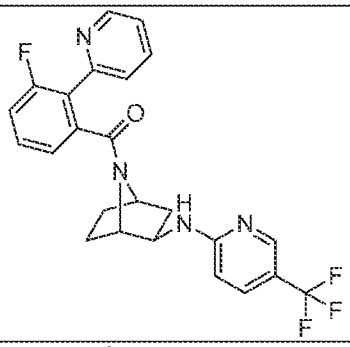
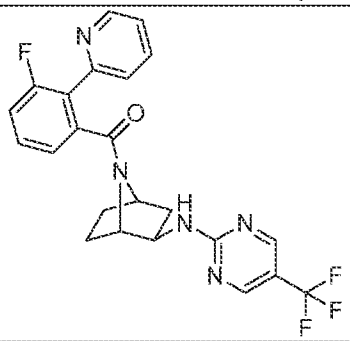
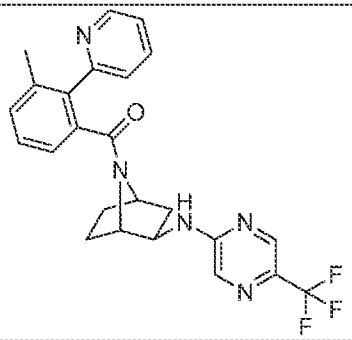
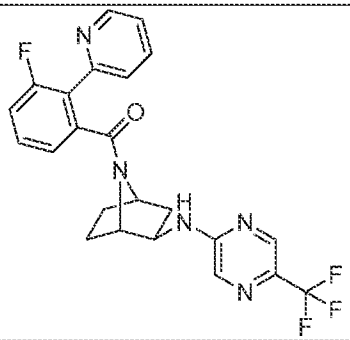
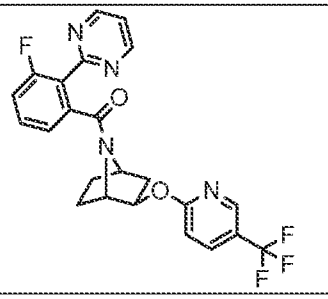
295		(3-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
296		(3-methyl-2-(oxazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
297		(3-fluoro-2-(pyrimidin-2-yl)phenyl)((1R,2S,4S)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
298		(3-fluoro-2-(oxazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
299		(3-methyl-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

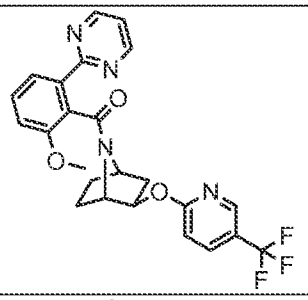
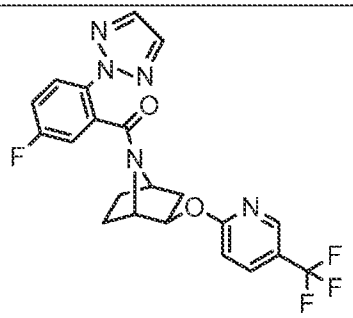
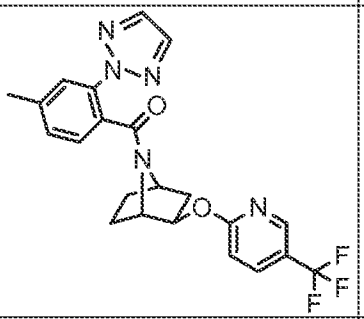
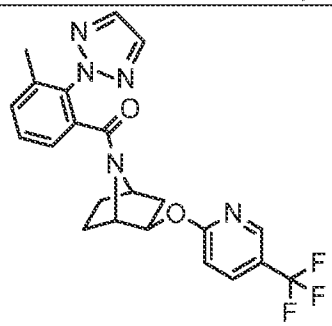
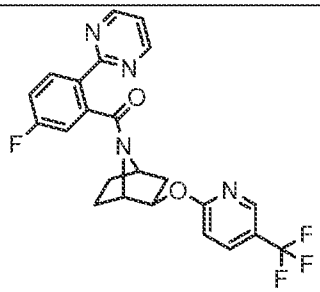
300		(3-chloro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
301		((1S,2R,4R)-2-((5-bromopyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-(oxazol-2-yl)phenyl)methanone
302		((1S,2R,4R)-2-((5-bromopyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-methyl-2-(oxazol-2-yl)phenyl)methanone
303		((1S,2R,4R)-2-((5-bromopyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-(pyrimidin-2-yl)phenyl)methanone
304		((1S,2R,4R)-2-((5-bromopyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-methyl-2-(pyrimidin-2-yl)phenyl)methanone

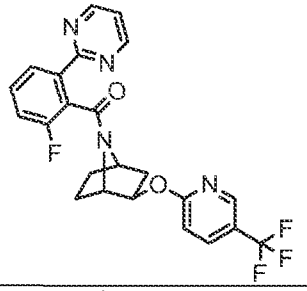
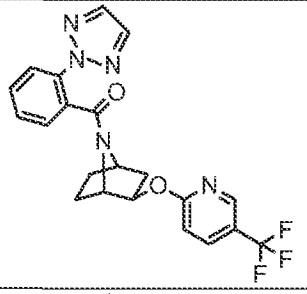
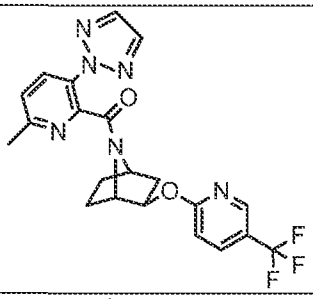
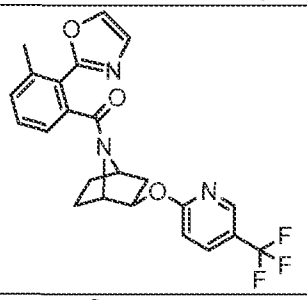
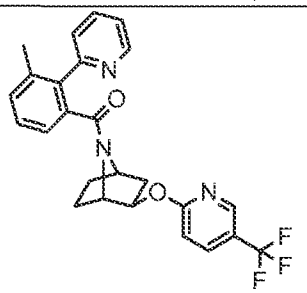
305		((1S,2R,4R)-2-((5-bromopyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone
306		((1S,2R,4R)-2-((5-bromopyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone
307		((1S,2R,4R)-2-((5-bromopyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-(oxazol-2-yl)phenyl)methanone
308		((1S,2R,4R)-2-((5-bromopyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-methyl-2-(oxazol-2-yl)phenyl)methanone
309		((1S,2R,4R)-2-((5-bromopyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-(pyrimidin-2-yl)phenyl)methanone

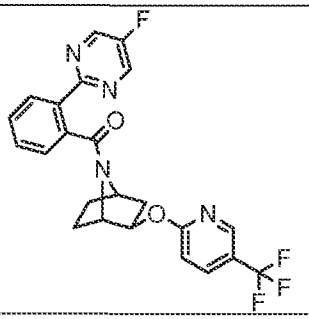
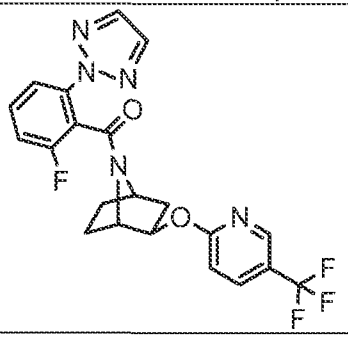
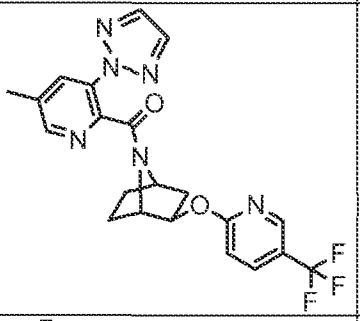
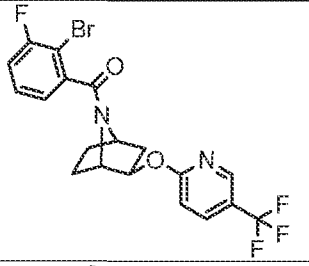
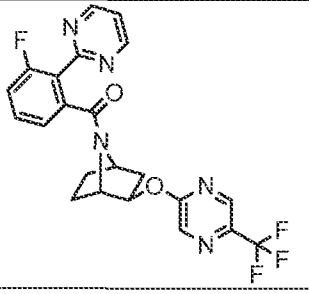
310		((1S,2R,4R)-2-((5-bromopyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-methyl-2-(pyrimidin-2-yl)phenyl)methanone
311		((1S,2R,4R)-2-((5-bromopyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone
312		((1S,2R,4R)-2-((5-bromopyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone
313		((1S,2R,4R)-2-((5-bromopyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-(oxazol-2-yl)phenyl)methanone
314		((1S,2R,4R)-2-((5-bromopyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-methyl-2-(oxazol-2-yl)phenyl)methanone

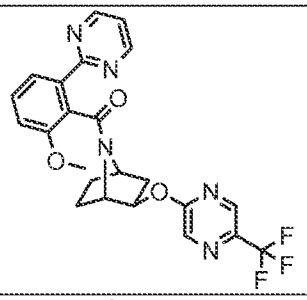
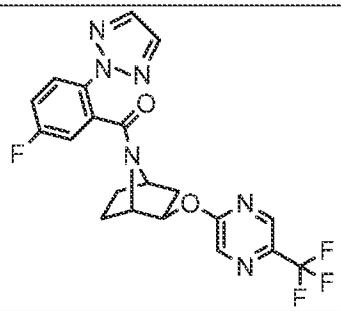
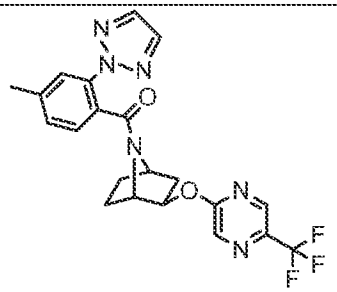
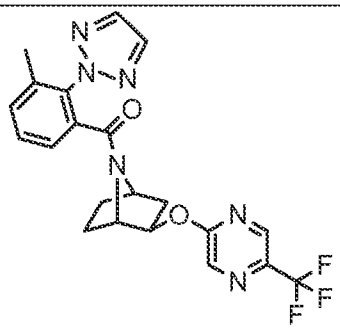
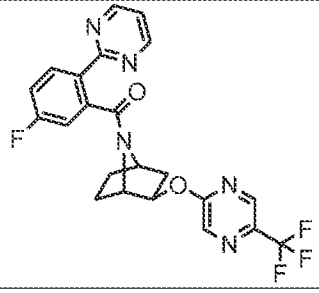
315		((1S,2R,4R)-2-((5-bromopyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-(pyrimidin-2-yl)phenyl)methanone
316		((1S,2R,4R)-2-((5-bromopyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-methyl-2-(pyrimidin-2-yl)phenyl)methanone
317		((1S,2R,4R)-2-((5-bromopyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone
318		((1S,2R,4R)-2-((5-bromopyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone
319		(3-methyl-2-(pyridin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

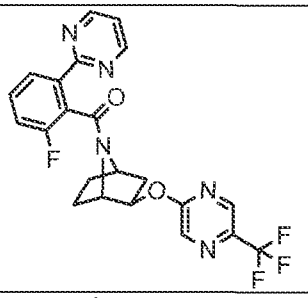
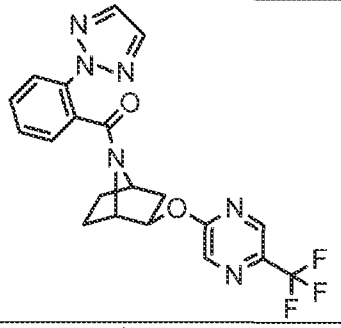
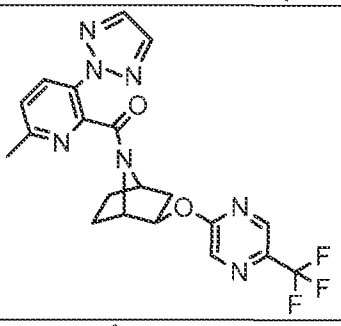
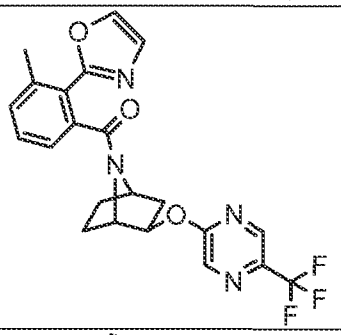
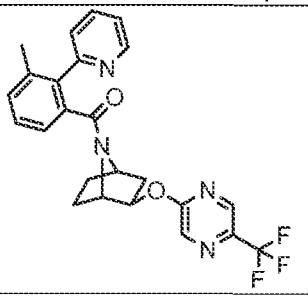
320		(3-fluoro-2-(pyridin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
321		(3-fluoro-2-(pyridin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
322		(3-methyl-2-(pyridin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
323		(3-fluoro-2-(pyridin-2-yl)phenyl)((2S)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
324		(3-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

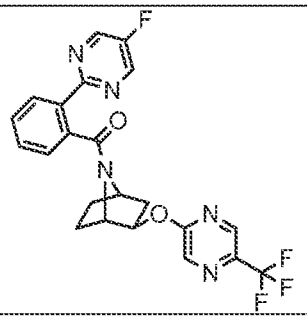
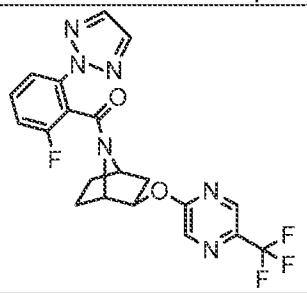
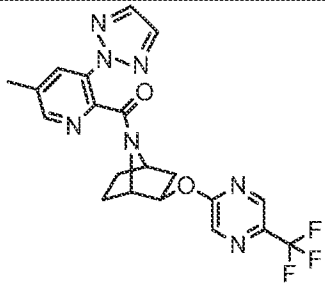
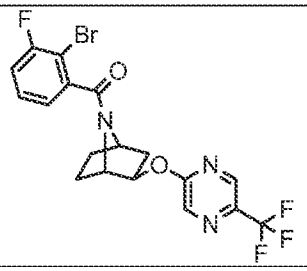
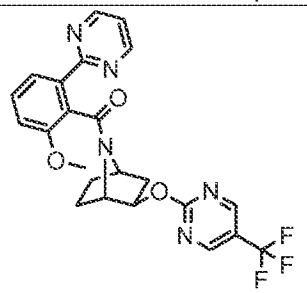
325		(2-methoxy-6-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
326		(5-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
327		(4-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
328		(3-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
329		(5-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

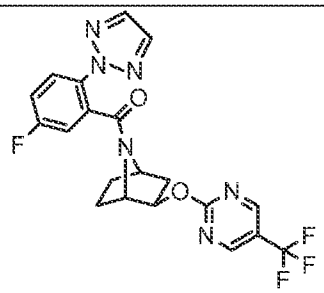
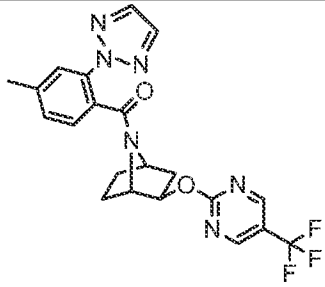
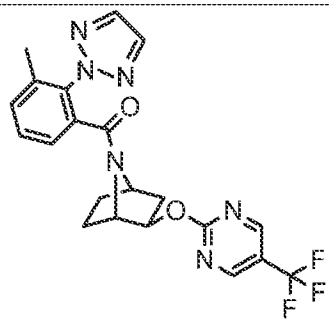
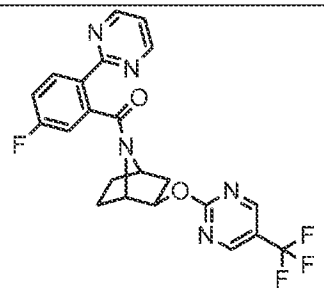
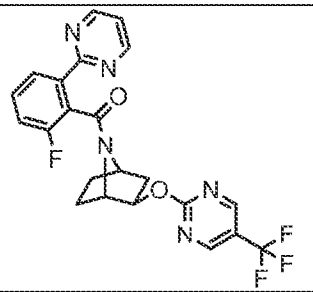
330		(2-fluoro-6-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
331		(2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
332		(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
333		(3-methyl-2-(oxazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
334		(3-methyl-2-(pyridin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

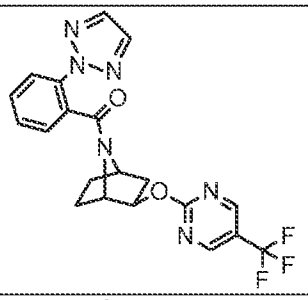
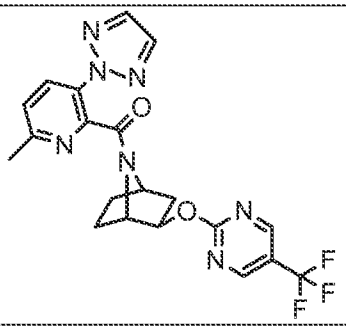
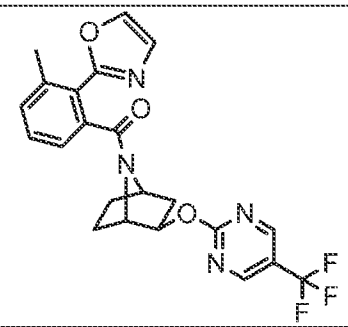
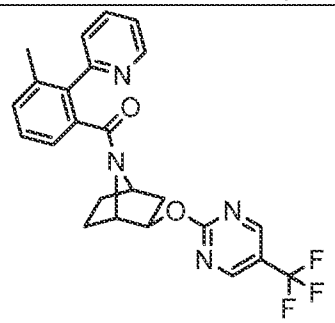
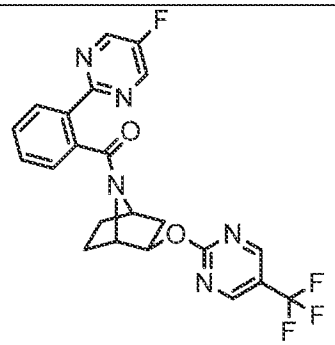
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336		(2-fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
337		(5-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
338		(2-bromo-3-fluorophenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
339		(3-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

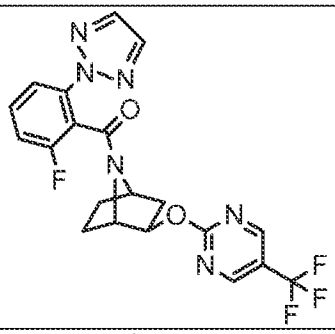
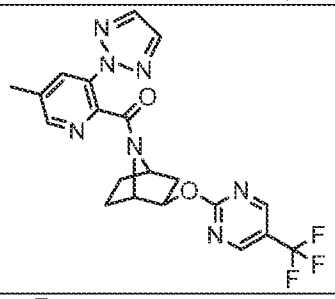
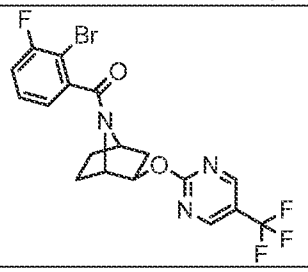
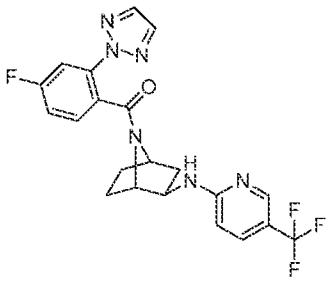
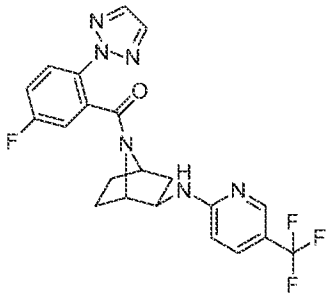
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341		(5-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
342		(4-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
343		(3-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
344		(5-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

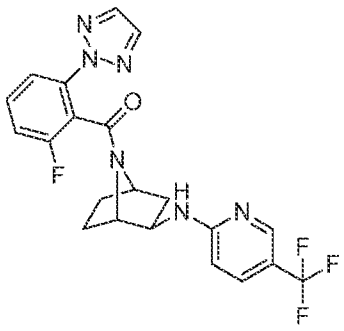
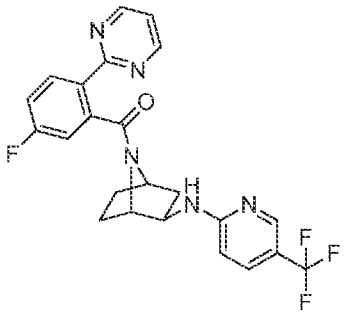
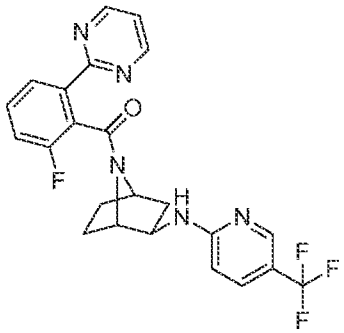
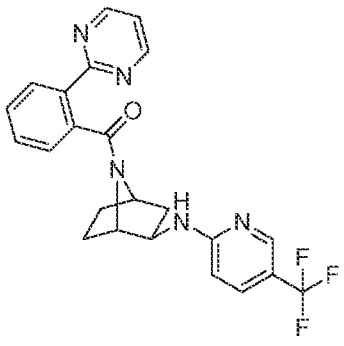
345		(2-fluoro-6-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
346		(2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
347		(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
348		(3-methyl-2-(oxazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
349		(3-methyl-2-(pyridin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

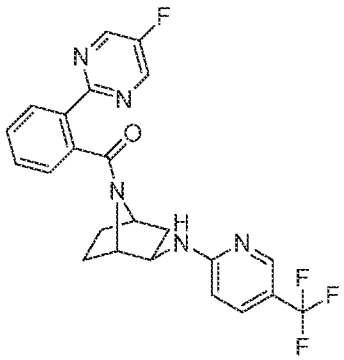
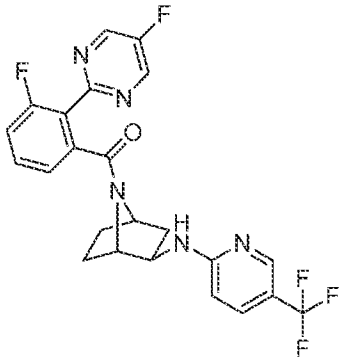
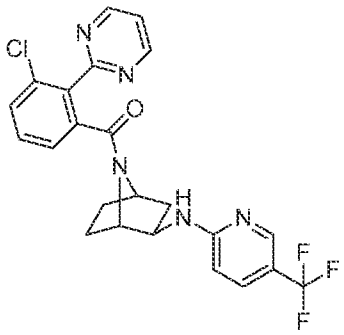
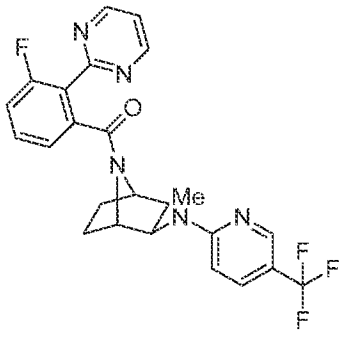
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351		(2-fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
352		(5-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
353		(2-bromo-3-fluorophenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
354		(2-methoxy-6-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

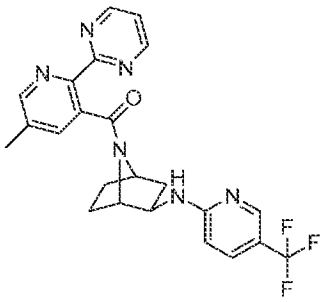
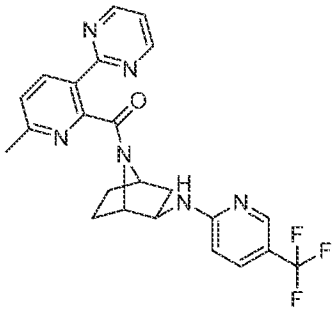
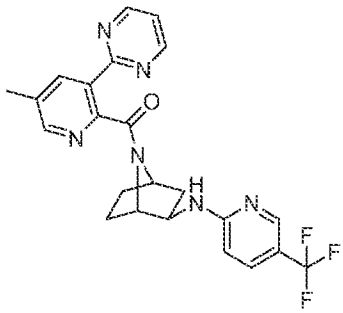
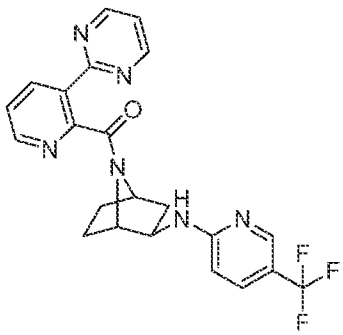
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356		(4-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
357		(3-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
358		(5-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
359		(2-fluoro-6-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

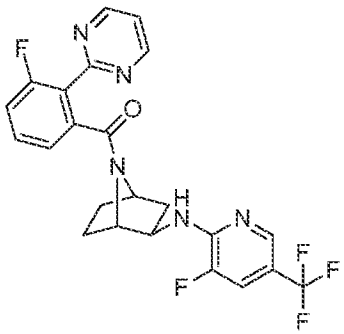
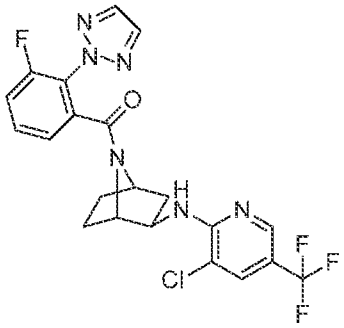
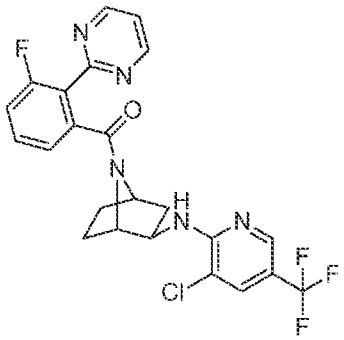
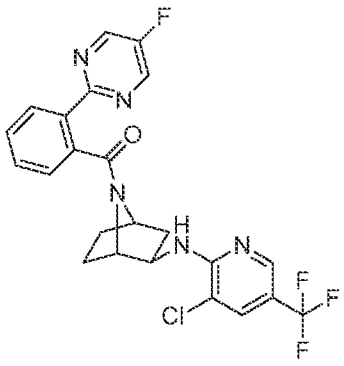
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361		(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
362		(3-methyl-2-(oxazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
363		(3-methyl-2-(pyridin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
364		(2-(5-fluoropyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

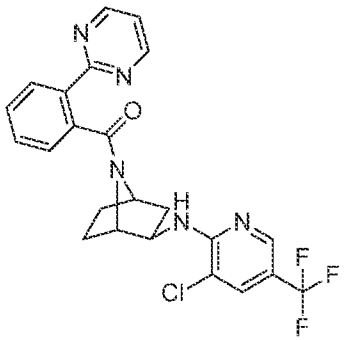
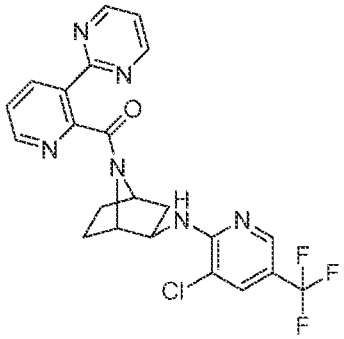
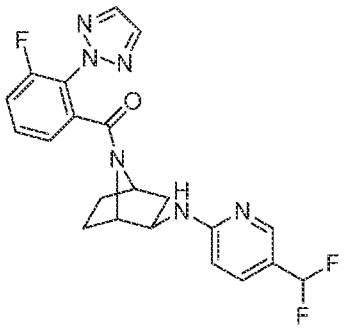
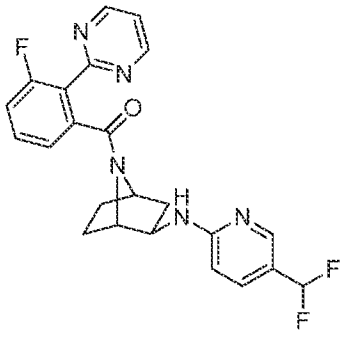
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366		(5-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
367		(2-bromo-3-fluorophenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
368		(4-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
369		(5-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

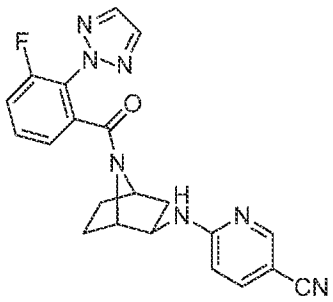
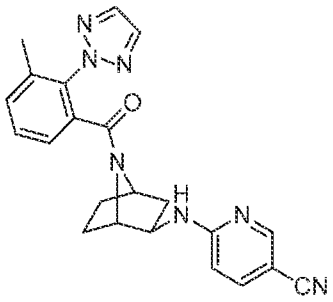
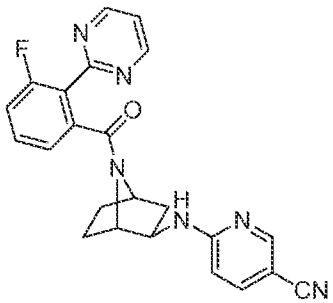
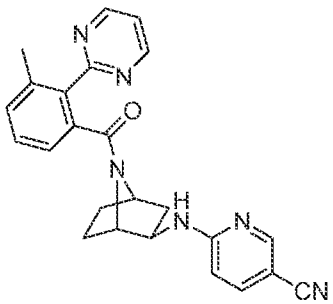
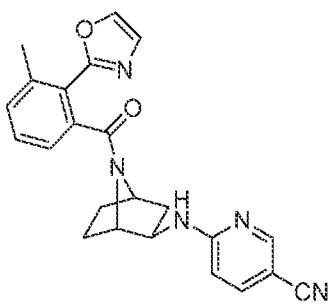
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371		(5-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
372		(2-fluoro-6-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
373		(2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

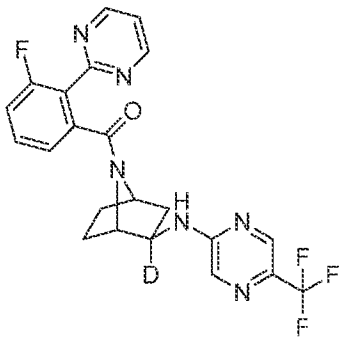
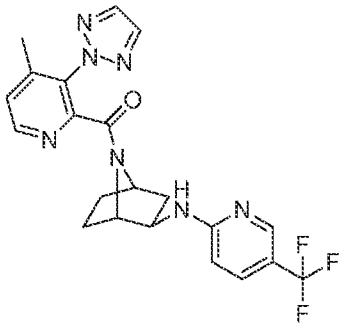
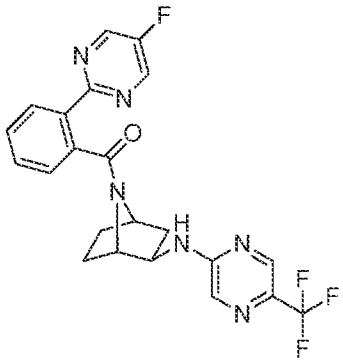
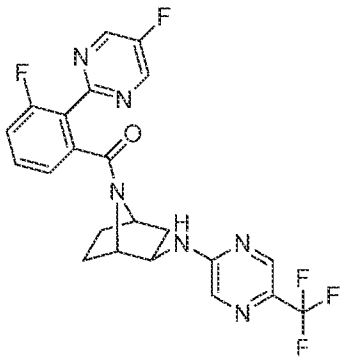
374		(2-(5-fluoropyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
375		(3-fluoro-2-(5-fluoropyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
376		(3-chloro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
377		(3-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-(methyl(5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

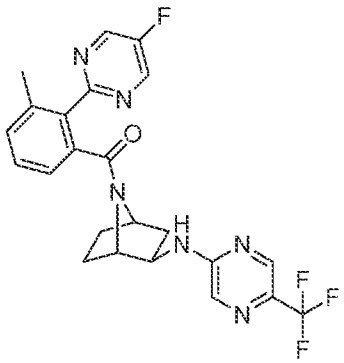
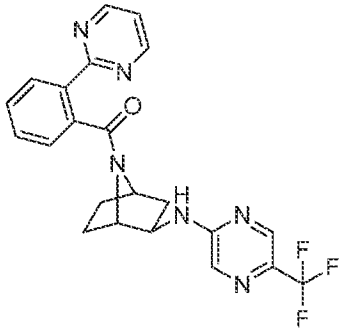
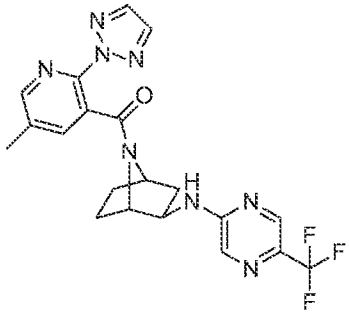
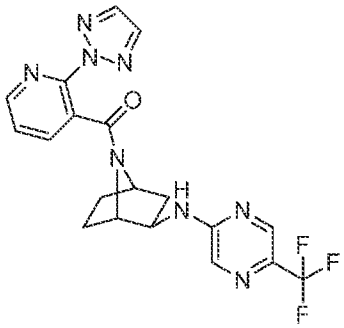
378		(5-methyl-2-(pyrimidin-2-yl)pyridin-3-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
379		(6-methyl-3-(pyrimidin-2-yl)pyridin-2-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
380		(5-methyl-3-(pyrimidin-2-yl)pyridin-2-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
381		(3-(pyrimidin-2-yl)pyridin-2-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

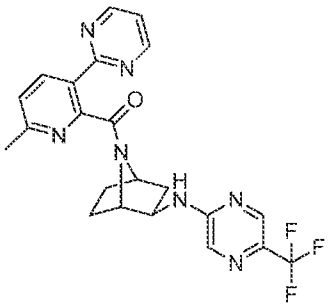
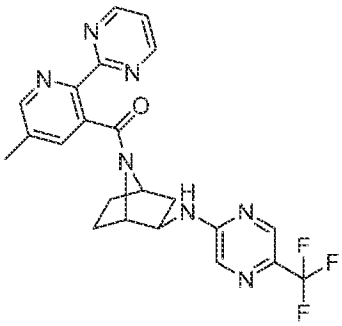
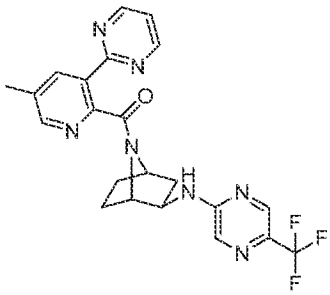
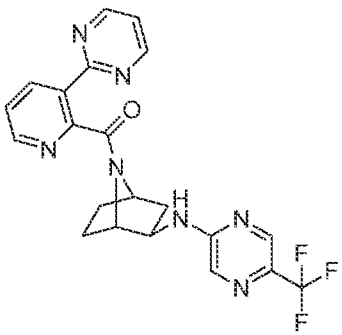
382		(3-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((3-fluoro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
383		((1S,2R,4R)-2-((3-chloro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone
384		((1S,2R,4R)-2-((3-chloro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-(pyrimidin-2-yl)phenyl)methanone
385		((1S,2R,4R)-2-((3-chloro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(2-(5-fluoropyrimidin-2-yl)phenyl)methanone

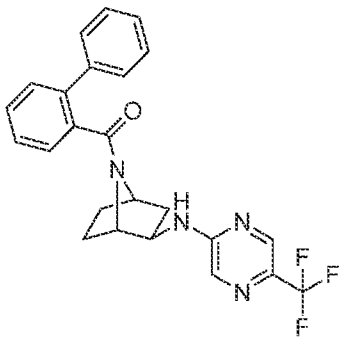
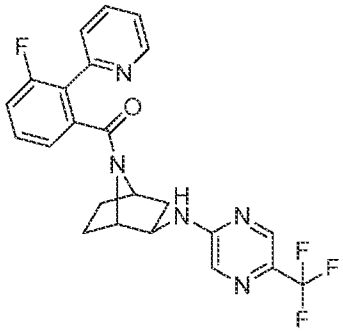
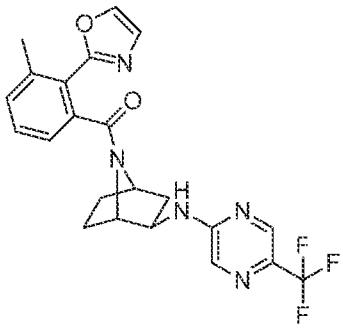
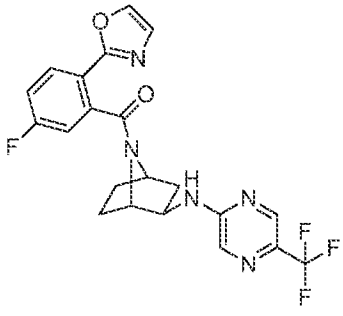
386		((1S,2R,4R)-2-((3-chloro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(2-(pyrimidin-2-yl)phenyl)methanone
387		((1S,2R,4R)-2-((3-chloro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-(pyrimidin-2-yl)pyridin-2-yl)methanone
388		((1S,2R,4R)-2-((5-(difluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone
389		((1S,2R,4R)-2-((5-(difluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-(pyrimidin-2-yl)phenyl)methanone

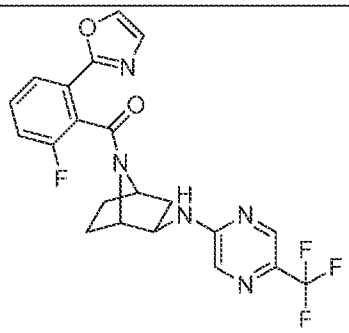
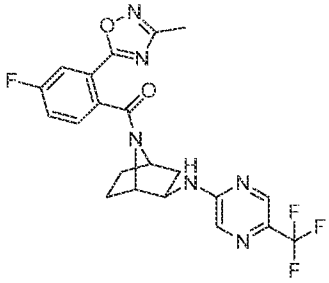
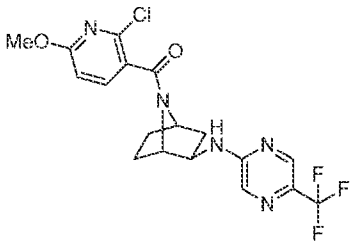
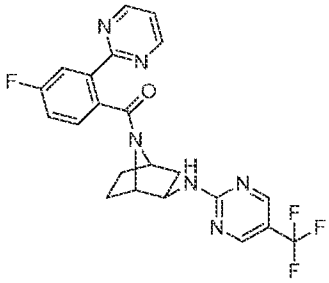
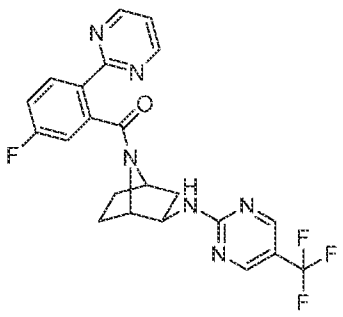
390		6-(((1S,2R,4R)-7-(3-fluoro-2-(2H-1,2,3-triazol-2-yl)benzoyl)-7-azabicyclo[2.2.1]heptan-2-yl)amino)nicotinonitrile
391		6-(((1S,2R,4R)-7-(3-methyl-2-(2H-1,2,3-triazol-2-yl)benzoyl)-7-azabicyclo[2.2.1]heptan-2-yl)amino)nicotinonitrile
392		6-(((1S,2R,4R)-7-(3-fluoro-2-(pyrimidin-2-yl)benzoyl)-7-azabicyclo[2.2.1]heptan-2-yl)amino)nicotinonitrile
393		6-(((1S,2R,4R)-7-(3-methyl-2-(pyrimidin-2-yl)benzoyl)-7-azabicyclo[2.2.1]heptan-2-yl)amino)nicotinonitrile
394		6-(((1S,2R,4R)-7-(3-methyl-2-(oxazol-2-yl)benzoyl)-7-azabicyclo[2.2.1]heptan-2-yl)amino)nicotinonitrile

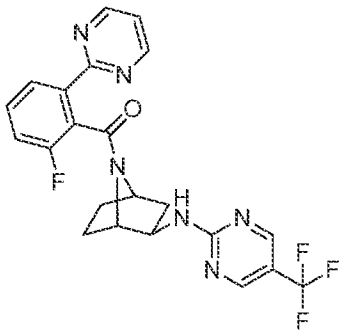
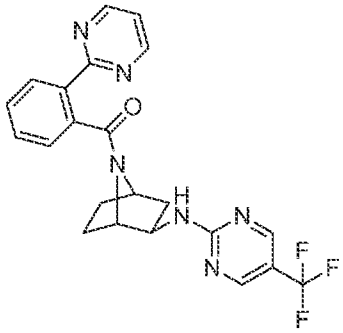
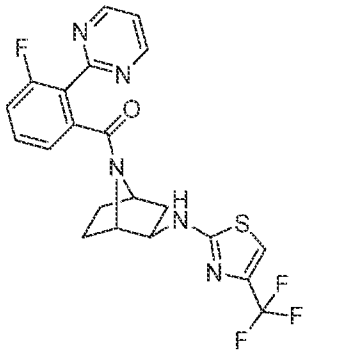
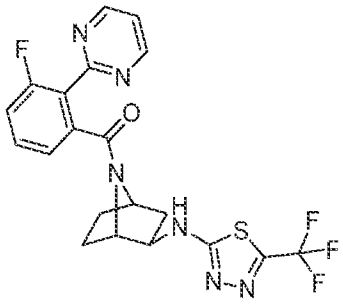
395		(3-fluoro-2-(pyrimidin-2-yl)phenyl) ((1S,2R,4R)-(2-^{2}H)-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
396		(4-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
397		(2-(5-fluoropyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
398		(3-fluoro-2-(5-fluoropyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

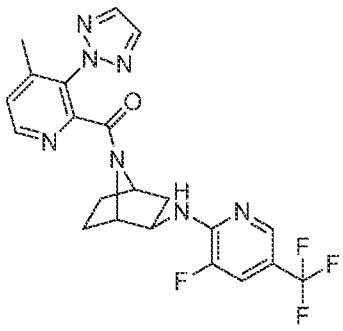
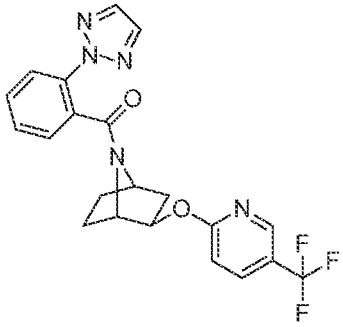
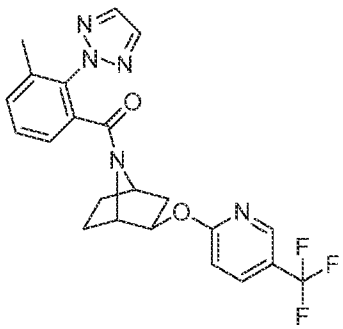
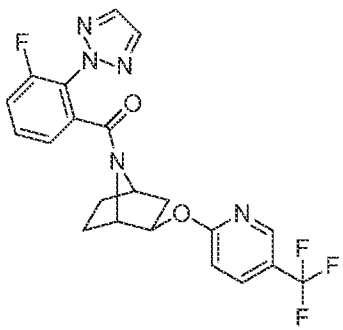
399		(2-(5-fluoropyrimidin-2-yl)-3-methylphenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
400		(2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
401		(5-methyl-2-(2H-1,2,3-triazol-2-yl)pyridin-3-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
402		(2-(2H-1,2,3-triazol-2-yl)pyridin-3-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

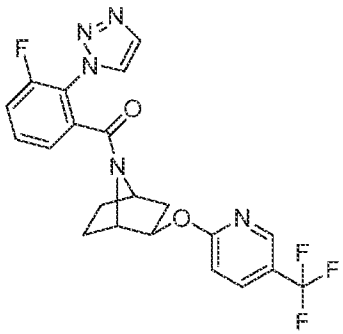
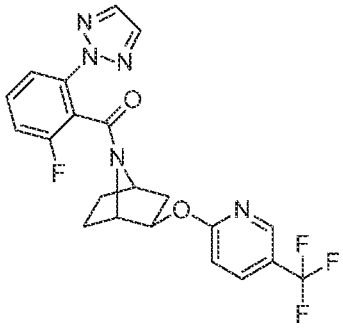
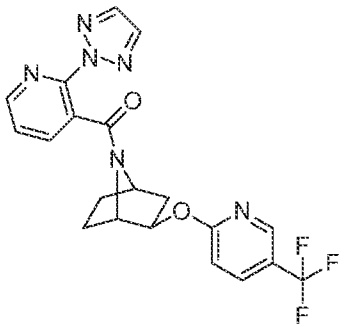
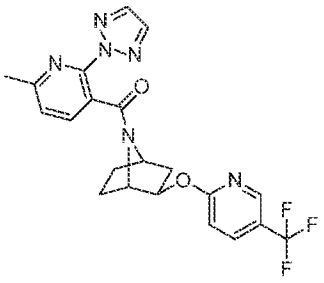
403		(6-methyl-3-(pyrimidin-2-yl)pyridin-2-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
404		(5-methyl-2-(pyrimidin-2-yl)pyridin-3-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
405		(5-methyl-3-(pyrimidin-2-yl)pyridin-2-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
406		(3-(pyrimidin-2-yl)pyridin-2-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

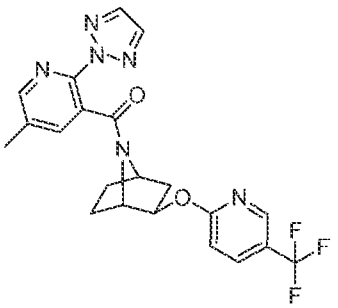
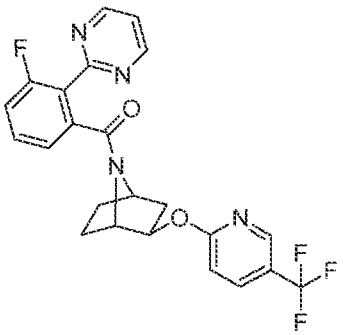
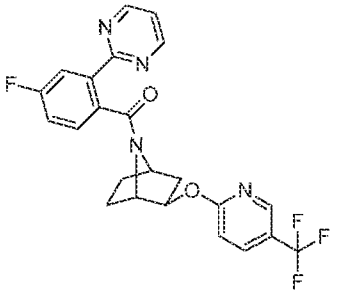
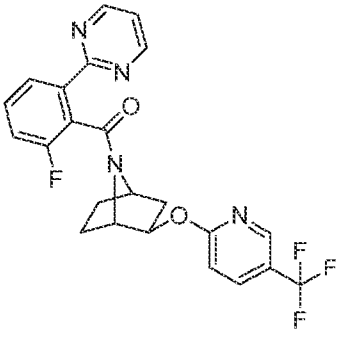
407		[1,1'-biphenyl]-2-yl((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
408		(3-fluoro-2-(pyridin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
409		(3-methyl-2-(oxazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
410		(5-fluoro-2-(oxazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
411		(2-fluoro-6-(oxazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-

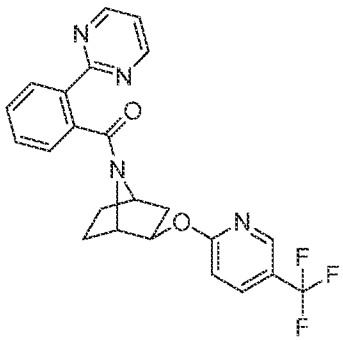
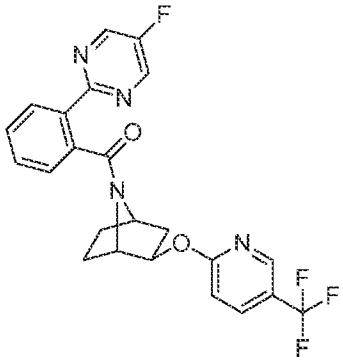
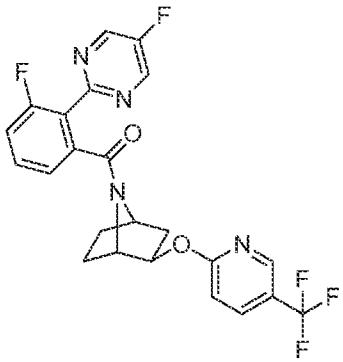
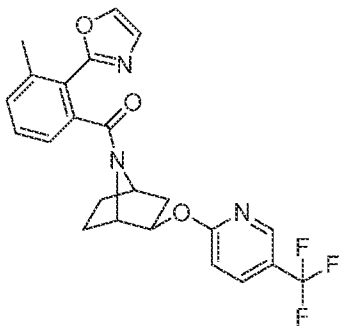
		yl)methanone
412		(4-fluoro-2-(3-methyl-1,2,4-oxadiazol-5-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
413		(2-chloro-6-methoxypyridin-3-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
414		(4-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
415		(5-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

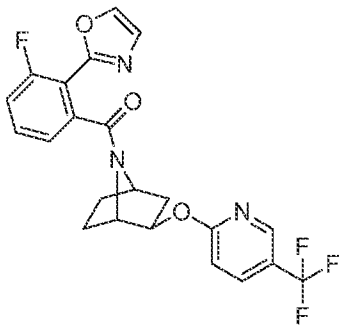
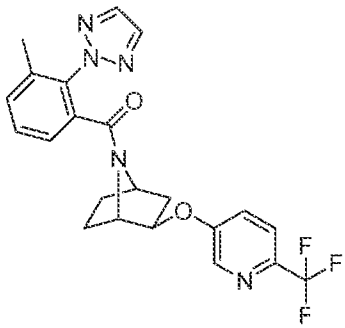
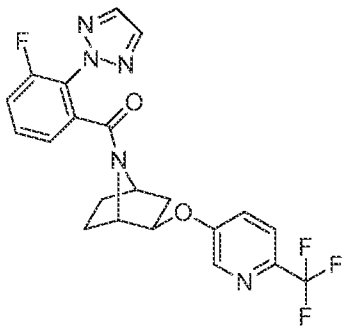
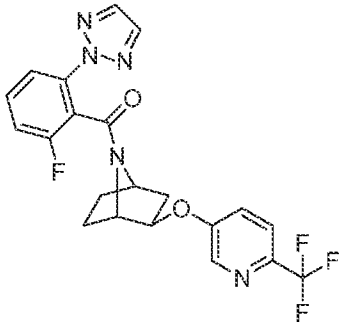
416		(2-fluoro-6-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
417		(2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
418		(3-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((4-(trifluoromethyl)thiazol-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
419		(3-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)-1,3,4-thiadiazol-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

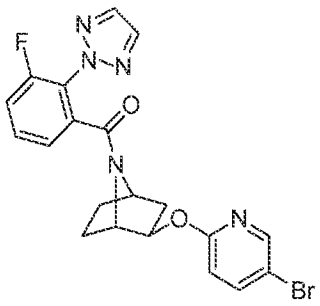
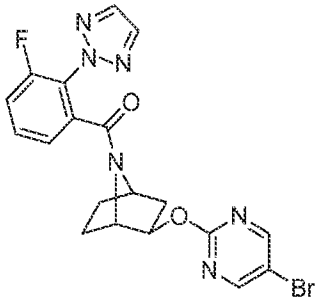
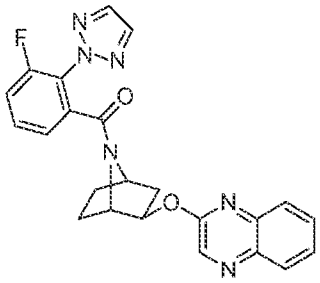
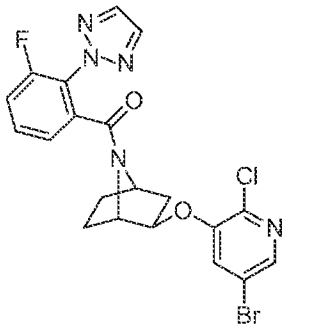
420		((1S,2R,4R)-2-((3-fluoro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(4-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)methanone
421		(R/S)-(2-(2H-1,2,3-triazol-2-yl)phenyl)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
422		(R/S)-(3-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
423		(R/S)-(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

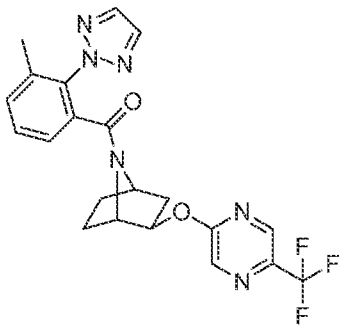
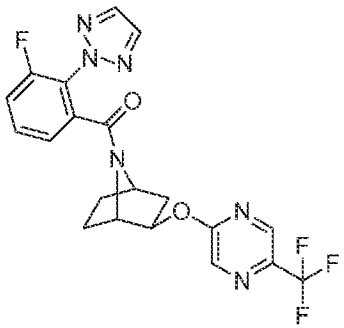
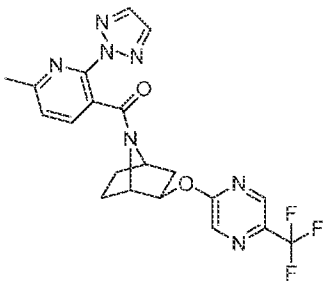
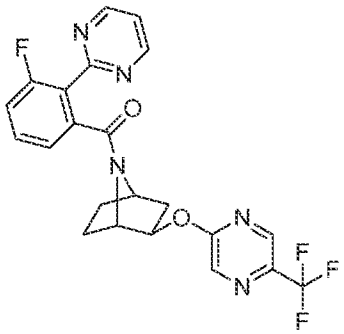
424		(R/S)-(3-fluoro-2-(1H-1,2,3-triazol-1-yl)phenyl)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
425		(R/S)-(2-fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
426		(R/S)-(2-(2H-1,2,3-triazol-2-yl)pyridin-3-yl)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
427		(R/S)-(6-methyl-2-(2H-1,2,3-triazol-2-yl)pyridin-3-yl)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

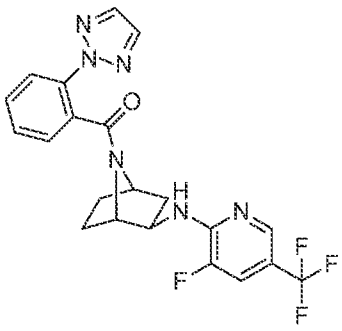
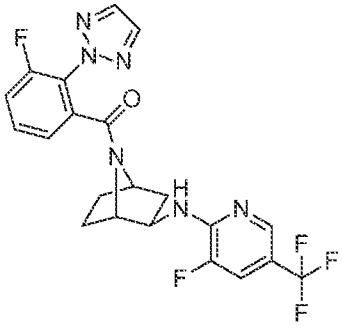
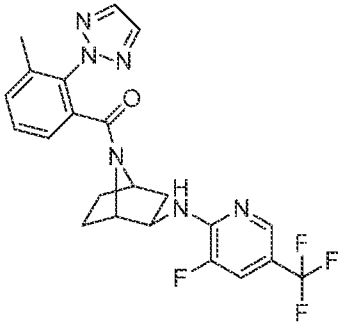
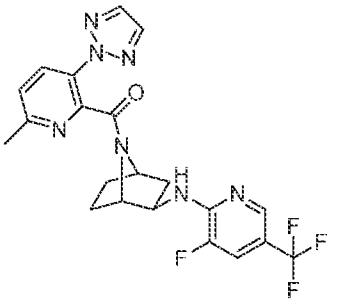
428		(R/S)-(5-methyl-2-(2H-1,2,3-triazol-2-yl)pyridin-3-yl)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
429		(R/S)-(3-fluoro-2-(pyrimidin-2-yl)phenyl)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
430		(R/S)-(4-fluoro-2-(pyrimidin-2-yl)phenyl)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
431		(R/S)-(2-fluoro-6-(pyrimidin-2-yl)phenyl)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

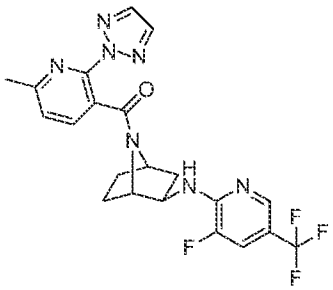
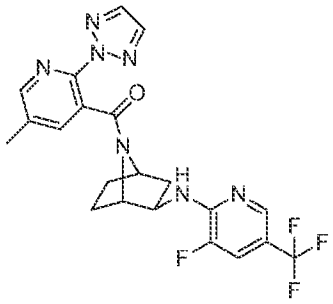
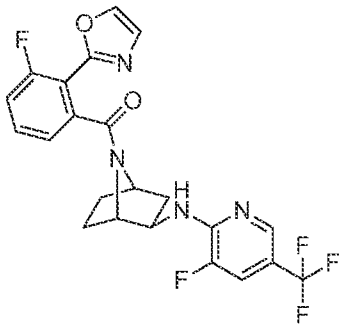
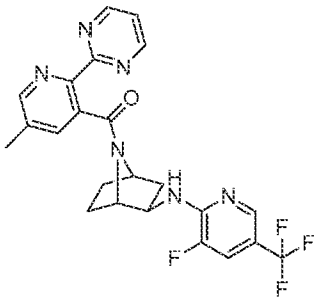
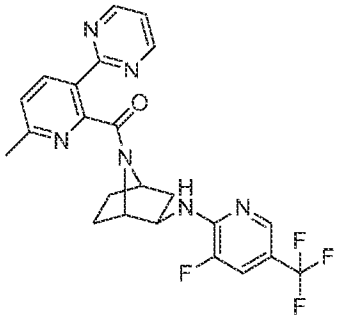
432		(R/S)-(2-(pyrimidin-2-yl)phenyl)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
433		(R/S)-(2-(5-fluoropyrimidin-2-yl)phenyl)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
434		(R/S)- (3-fluoro-2-(5-fluoropyrimidin-2-yl)phenyl)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
435		(R/S)-(3-methyl-2-(oxazol-2-yl)phenyl)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

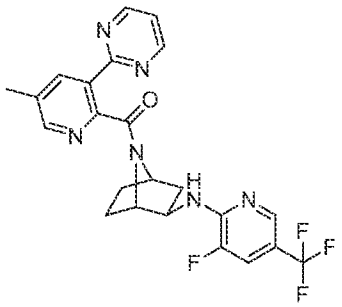
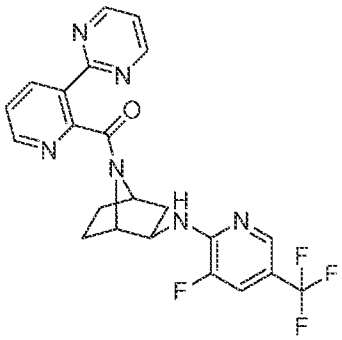
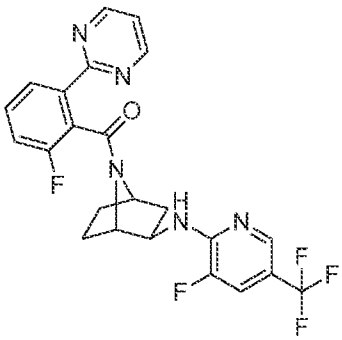
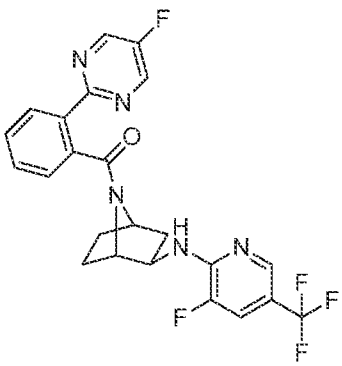
436		(R/S)-(3-fluoro-2-(oxazol-2-yl)phenyl)-2-((5-(trifluoromethyl)pyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
437		(R/S)-(3-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)-2-((6-(trifluoromethyl)pyridin-3-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
438		(R/S)-(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)-2-((6-(trifluoromethyl)pyridin-3-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
439		(R/S)- (2-fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl)-2-((6-(trifluoromethyl)pyridin-3-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

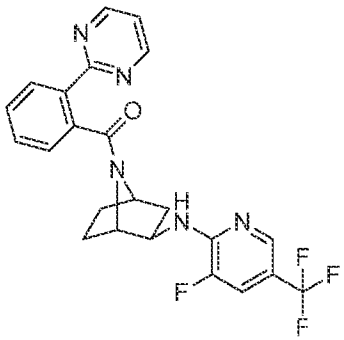
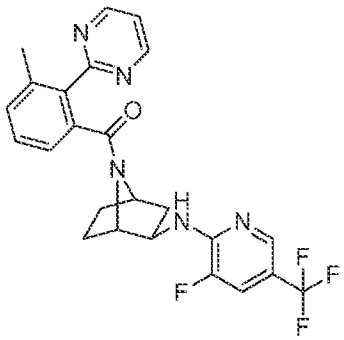
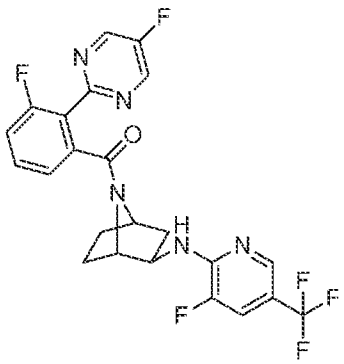
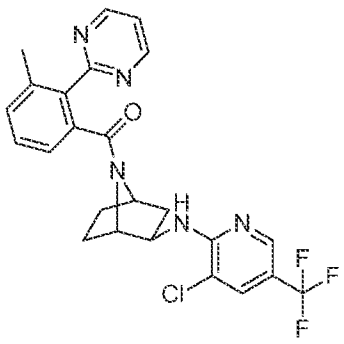
440		(R/S)-2-((5-bromopyridin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone
441		(R/S)-2-((5-bromopyrimidin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone
442		(R/S)-(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)-2-(quinoxalin-2-yloxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
443		(R/S)-2-((5-bromo-2-chloropyridin-3-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone

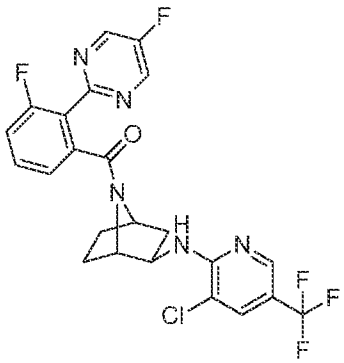
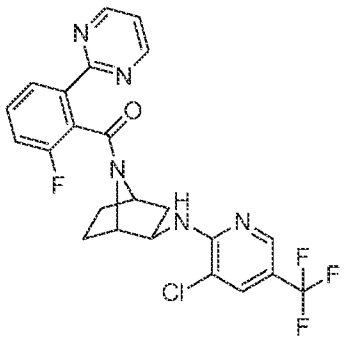
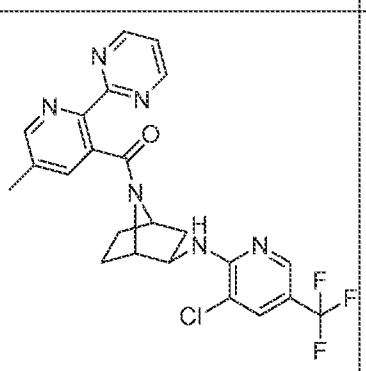
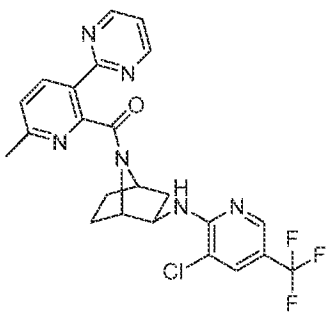
444		(R/S)-(3-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)-2-((5-(trifluoromethyl)pyrazin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
445		(R/S)-(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)(2-((5-(trifluoromethyl)pyrazin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
446		(R/S)-(6-methyl-2-(2H-1,2,3-triazol-2-yl)pyridin-3-yl)(2-((5-(trifluoromethyl)pyrazin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
447		(R/S)-(3-fluoro-2-(pyrimidin-2-yl)phenyl)(2-((5-(trifluoromethyl)pyrazin-2-yl)oxy)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

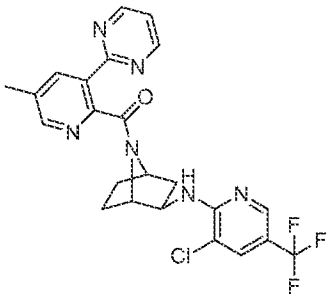
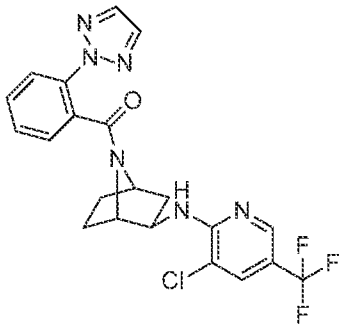
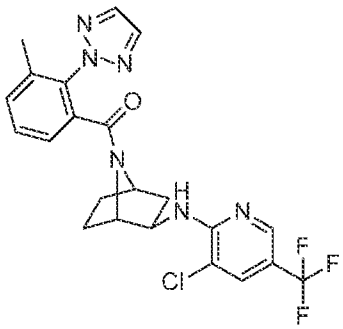
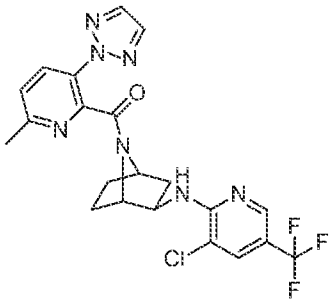
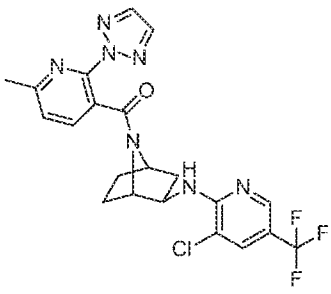
448		(2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((3-fluoro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
449		(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((3-fluoro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
450		((1S,2R,4R)-2-((3-fluoro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone
451		((1S,2R,4R)-2-((3-fluoro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)methanone

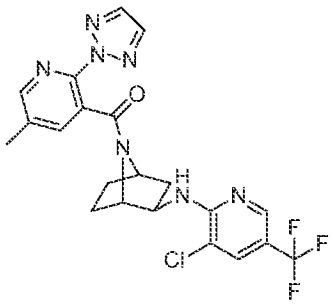
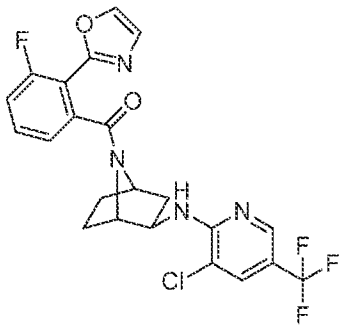
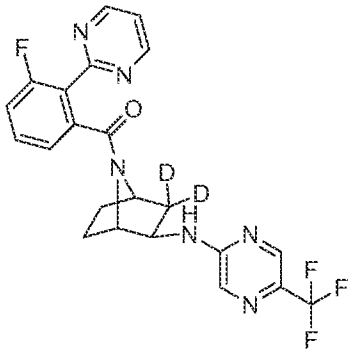
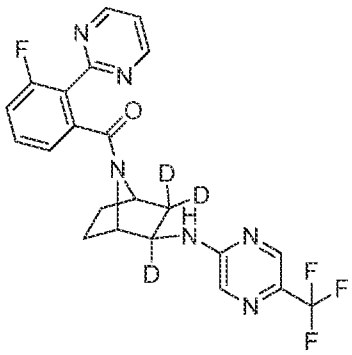
452		((1S,2R,4R)-2-((3-fluoro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-2-(2H-1,2,3-triazol-2-yl)pyridin-3-yl)methanone
453		((1S,2R,4R)-2-((3-fluoro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(5-methyl-2-(2H-1,2,3-triazol-2-yl)pyridin-3-yl)methanone
454		(3-fluoro-2-(oxazol-2-yl)phenyl)((1S,2R,4R)-2-((3-fluoro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
455		((1S,2R,4R)-2-((3-fluoro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(5-methyl-2-(pyrimidin-2-yl)pyridin-3-yl)methanone
456		((1S,2R,4R)-2-((3-fluoro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(pyrimidin-2-yl)pyridin-2-yl)methanone

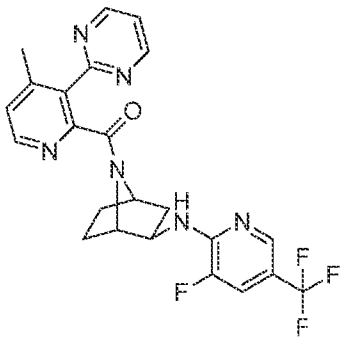
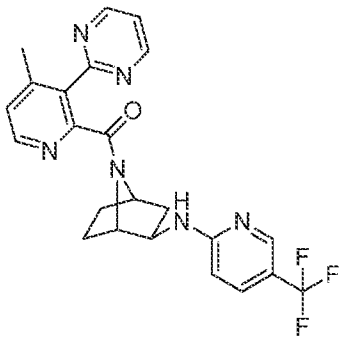
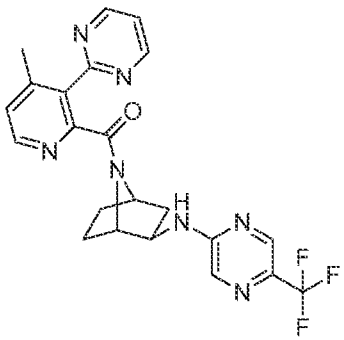
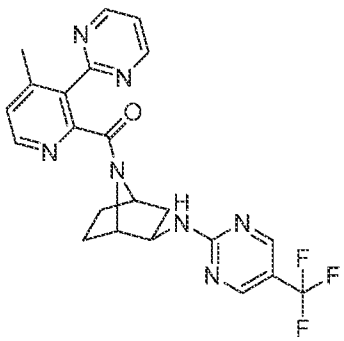
457		((1S,2R,4R)-2-((3-fluoro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(5-methyl-3-(pyrimidin-2-yl)pyridin-2-yl)methanone
458		((1S,2R,4R)-2-((3-fluoro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-(pyrimidin-2-yl)pyridin-2-yl)methanone
459		((1S,2R,4R)-2-((3-fluoro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(2-fluoro-6-(pyrimidin-2-yl)phenyl)methanone
460		((1S,2R,4R)-2-((3-fluoro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(2-(5-fluoropyrimidin-2-yl)phenyl)methanone

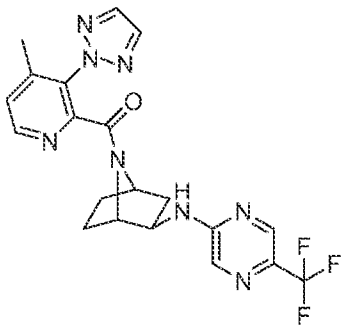
461		((1S,2R,4R)-2-((3-fluoro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(2-(pyrimidin-2-yl)phenyl)methanone
462		((1S,2R,4R)-2-((3-fluoro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-methyl-2-(pyrimidin-2-yl)phenyl)methanone
463		(3-fluoro-2-(5-fluoropyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((3-fluoro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
464		((1S,2R,4R)-2-((3-chloro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-methyl-2-(pyrimidin-2-yl)phenyl)methanone

465		((1S,2R,4R)-2-((3-chloro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-(5-fluoropyrimidin-2-yl)phenyl)methanone
466		((1S,2R,4R)-2-((3-chloro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(2-fluoro-6-(pyrimidin-2-yl)phenyl)methanone
467		((1S,2R,4R)-2-((3-chloro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(5-methyl-2-(pyrimidin-2-yl)pyridin-3-yl)methanone
468		((1S,2R,4R)-2-((3-chloro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(pyrimidin-2-yl)pyridin-2-yl)methanone

469		((1S,2R,4R)-2-((3-chloro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(5-methyl-3-(pyrimidin-2-yl)pyridin-2-yl)methanone
470		(2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((3-chloro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
471		((1S,2R,4R)-2-((3-chloro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone
472		((1S,2R,4R)-2-((3-chloro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)methanone
473		((1S,2R,4R)-2-((3-chloro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(6-methyl-2-(2H-1,2,3-triazol-2-yl)pyridin-3-yl)methanone

474		((1S,2R,4R)-2-((3-chloro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(5-methyl-2-(2H-1,2,3-triazol-2-yl)pyridin-3-yl)methanone
475		((1S,2R,4R)-2-((3-chloro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-2-(oxazol-2-yl)phenyl)methanone
476		(3-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]-(3-^{2}H,^{2}H)-heptan-7-yl)methanone
477		(3-fluoro-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-(2-^{2}H)-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]-(3-^{2}H,^{2}H)-heptan-7-yl)methanone

478		((1S,2R,4R)-2-((3-fluoro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(4-methyl-3-(pyrimidin-2-yl)pyridin-2-yl)methanone
479		(4-methyl-3-(pyrimidin-2-yl)pyridin-2-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
480		(4-methyl-3-(pyrimidin-2-yl)pyridin-2-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
481		(4-methyl-3-(pyrimidin-2-yl)pyridin-2-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrimidin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

482		(4-methyl-3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

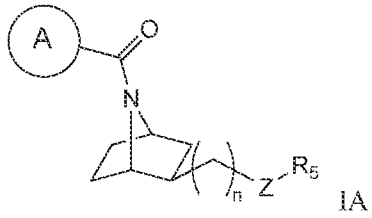
51. A pharmaceutical composition comprising a therapeutically effective amount of a compound according to any one of the preceding claims and at least one pharmaceutically acceptable excipient.

52. A method of treating a subject suffering from or diagnosed with a disease, disorder, or medical condition mediated by orexin receptor activity, comprising administering to the subject an effective amount of a compound according to any one of claims 1 to 50.

53. The method of claim 52, wherein the disease, disorder, or medical condition mediated by orexin receptor activity is a disorder of the sleep-wake cycle, insomnia, restless legs syndrome, jet-lag, disturbed sleep, a sleep disorder secondary to neurological disorders, mania, depression, manic depression, schizophrenia, a pain syndromes, fibromyalgia, neuropathic pain, catatonia, Parkinson's disease, Tourette's syndrome, anxiety, delirium, dementia, overweight, obesity or a condition related to overweight or obesity, insulin resistance, type II diabetes, hyperlipidemia, gallstones, angina, hypertension, breathlessness, tachycardia, infertility, sleep apnea, back and joint pain, varicose veins, osteoarthritis, hypertension, tachycardia, arrhythmias, angina pectoris, acute heart failure, ulcers, irritable bowel syndrome, diarrhea, gastroesophageal reflux, post-traumatic stress disorder, panic disorders, attention deficit disorders, cognitive deficiencies, or substance abuse.

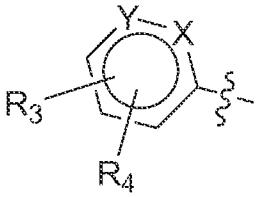
54. The method of claim 53 wherein the disease, disorder, or medical condition is mood disorders, post-traumatic stress disorder, panic disorders, attention deficit disorders, cognitive deficiencies, or substance abuse..

55. A compound of Formula IA:



IA

wherein ring A is



wherein

X is CR_6, N, or NR_6;

Y is CR_7, N, or NR_7;

R_6 is H, alkyl, alkoxy, OH, halo, triazolyl, oxazolyl, oxadiazolyl, pyridyl, pyrimidinyl, pyrazinyl, pyridazinyl, pyrazolyl, or thiophenyl, wherein triazolyl, oxazolyl, oxadiazolyl, pyridyl, pyrimidinyl, pyrazinyl, pyridazinyl, pyrazolyl, or thiophenyl is optionally substituted with up to two substituents selected from halo and alkyl;

R_7 is H, alkyl, alkoxy, or halo;

R_3 is H, alkyl, alkoxy, hydroxyalkylene, OH, halo, phenyl, triazolyl, oxazolyl, isoxazolyl, pyridyl, pyrimidinyl, pyrazinyl, pyridazinyl, piperazinyl, pyrazolyl, oxadiazolyl, pyrrolidinyl, thiophenyl, morpholinyl, or dialkylamino, wherein phenyl, triazolyl, oxazolyl, isoxazolyl, pyridyl, pyrimidinyl, pyrazinyl, pyridazinyl, piperazinyl, pyrazolyl, oxadiazolyl, pyrrolidinyl, thiophenyl, or morpholinyl is optionally substituted with up to two substituents selected from halo and alkyl;

R_4 is H, alkyl, alkoxy, or halo;

or

R_6 and R_7, together with the atoms to which they are attached, form a 5- or 6-membered heteroaryl ring optionally substituted with alkyl; or

R_3 and R_4, together with the atoms to which they are attached, form a 6-membered aryl or 6-membered heteroaryl ring; or

R_7 and R_4, together with the atoms to which they are attached, form a 6-membered aryl or 6-membered heteroaryl ring;

Z is NH, N-alkyl, or O;

R_5 is pyridyl, pyrimidinyl, pyrazinyl, pyridazinyl, quinazolinyl, quinoxalinyl, pyrazolyl, thiazolyl, thiadiazolyl, benzoxazolyl, imidazopyrazinyl, or triazolopyrazinyl, optionally substituted with one or two substituents independently selected from the group consisting of alkyl, cyano, alkyl carboxylate, alkoxy, and halo; and

n is 0 or 1.

56. The compound of claim 54, wherein X is CR_6 and Y is CR_7.

57. The compound of claim 54, wherein X is CR_6 and Y is N.

58. The compound of claim 54, wherein X is N and Y is CR_7.

59. The compound of any one of claims 55 to 57, wherein R_6 is H.

60. The compound of any one of claims 55 to 57, wherein R_6 is alkyl, alkoxy, OH, or halo.

61. The compound of any one of claims 55 to 57, wherein R_6 is triazolyl, oxazolyl, oxadiazolyl, pyrazolyl, or thiophenyl.

62. The compound of claim 61, wherein oxazolyl is methyl-oxazolyl.

63. The compound of claim 61, wherein pyrazolyl is methyl-pyrazolyl or dimethyl-pyrazolyl.

64. The compound of claim 61, wherein oxadiazolyl is methyl-oxadiazolyl.

65. The compound of any one of claims 54 to 57, wherein R_6 is pyridyl.

66. The compound of claim 65, wherein pyridyl is methyl-pyridyl.

67. The compound of any one of claims 55 to 57, wherein R_6 is pyrimidinyl, pyrazinyl, or pyridazinyl.

68. The compound of any one of claims 55, 56, or 58, wherein R_7 is H.

69. The compound of any one of claims 55, 56, or 58, wherein R_7 is alkyl, alkoxy, or halo.

70. The compound of claim 69, wherein alkoxy is haloalkoxy.

71. The compound of claim 55, wherein X is NR_6 and Y is CR_7.

72. The compound of claim 55, wherein X is CR_6 and Y is NR_7.

73. The compound of claim 47 or 48, wherein R_6 and R_7, together with the atoms to which they are attached, form a 5-membered heteroaryl ring optionally substituted with alkyl.

74. The compound of claim 71 or 72, wherein R_6 and R_7, together with the atoms to which they are attached, form a 6-membered heteroaryl ring optionally substituted with alkyl.

75. The compound of any one of claims 55, 56 or 58 to 67, wherein R_7 and R_4, together with the atoms to which they are attached, form a 6-membered aryl ring.

76. The compound of any one of claims 55, 56, or 58 to 67, wherein R_7 and R_4, together with the atoms to which they are attached, form a 6-membered heteroaryl ring.

77. The compound according to any one of claims 55 to 76, wherein R_3 is H.

78. The compound according to any one of claims 55 to 76, wherein R_3 is alkyl, alkoxy, hydroxyalkylene, OH, halo, or phenyl.

79. The compound of claim 78, wherein alkoxy is haloalkoxy.

80. The compound according to any one of claims 55 to 76, wherein R_3 is triazolyl, oxazolyl, isoxazolyl, oxadiazolyl, pyridyl, or pyrazolyl.

81. The compound of claim 80, wherein oxazolyl is methyl-oxazolyl.

82. The compound of claim 80, wherein isoxazolyl is methyl-isoxazolyl.

83. The compound of claim 80, wherein pyridyl is methyl-pyridyl.

84. The compound of claim 80, wherein pyrazolyl is methyl-pyrazolyl or dimethyl-pyrazolyl.

85. The compound of claim 80, wherein oxadiazolyl is methyl-oxadiazolyl.

86. The compound according to any one of claims 55 to 76, wherein R_3 is pyrimidinyl, pyrazinyl, or pyridazinyl.

87. The compound according to any one of claims 55 to 76, wherein R_3 is piperazinyl, pyrazolyl, pyrrolidinyl, thiophenyl, morpholinyl, or dialkylamino.

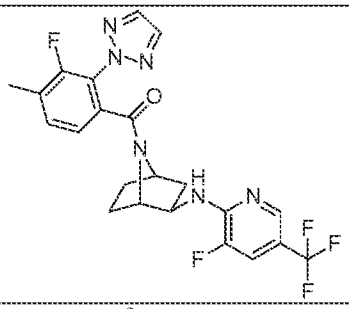
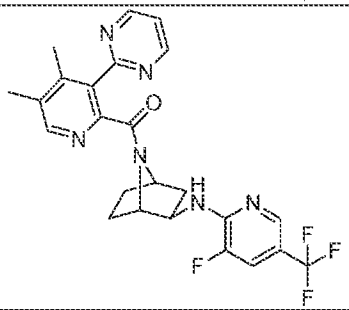
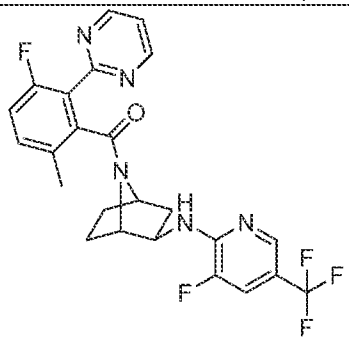
88. The compound of any one of claims 55 to 87, wherein R_4 is H.

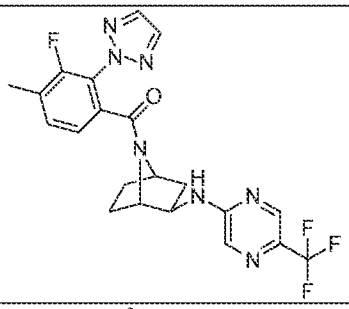
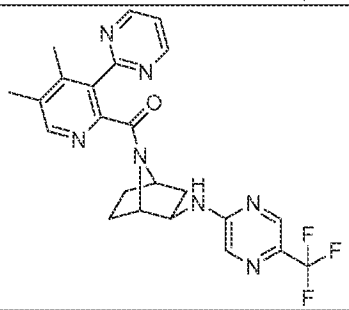
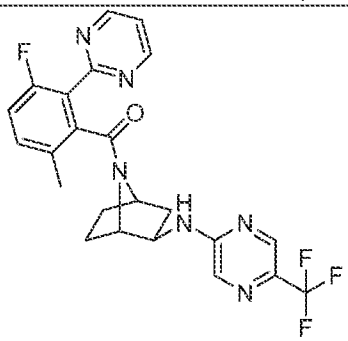
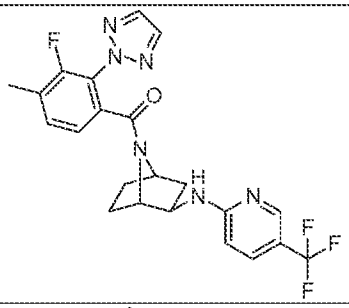
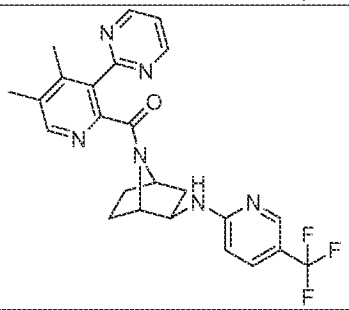
89. The compound of any one of claims 55 to 87, wherein R_4 is alkyl, alkoxy, or halo.

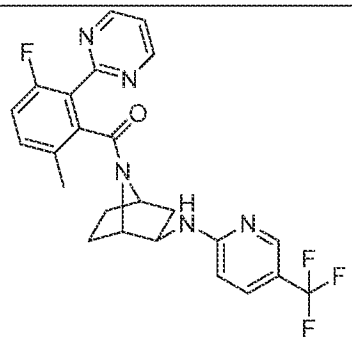
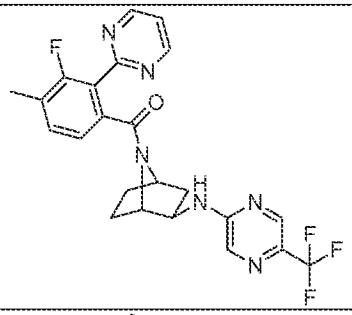
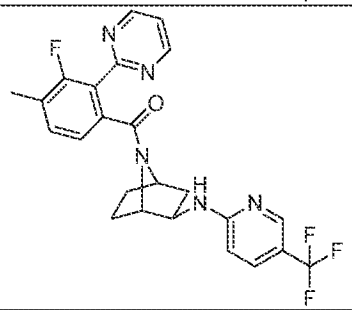
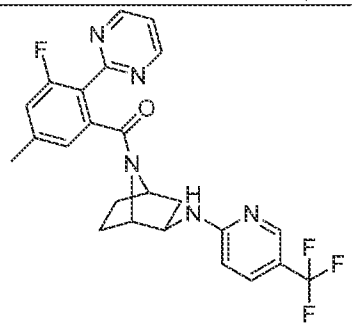
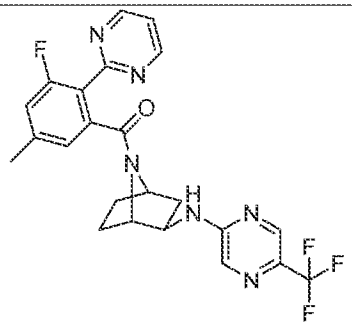
90. The compound according to any one of claims 55 to 74, wherein R_3 and R_4, together with the atoms to which they are attached, form a 6-membered aryl ring.

91. The compound according to any one of claims 55 to 74, wherein R_3 and R_4, together with the atoms to which they are attached, form a 6-membered heteroaryl ring.

92. A compound of claim 55 selected from the following

Ex. No.	Compound	Compound Name
483		(3-fluoro-4-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((3-fluoro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
484		(4,5-dimethyl-3-(pyrimidin-2-yl)pyridin-2-yl)((1S,2R,4R)-2-((3-fluoro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
485		((1S,2R,4R)-2-((3-fluoro-5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)(3-fluoro-6-methyl-2-(pyrimidin-2-yl)phenyl)methanone

486		(3-fluoro-4-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
487		(4,5-dimethyl-3-(pyrimidin-2-yl)pyridin-2-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
488		(3-fluoro-6-methyl-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
489		(3-fluoro-4-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
490		(4,5-dimethyl-3-(pyrimidin-2-yl)pyridin-2-yl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

491		(3-fluoro-6-methyl-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
492		(3-fluoro-4-methyl-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
493		(3-fluoro-4-methyl-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
494		(3-fluoro-5-methyl-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyridin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone
495		(3-fluoro-5-methyl-2-(pyrimidin-2-yl)phenyl)((1S,2R,4R)-2-((5-(trifluoromethyl)pyrazin-2-yl)amino)-7-azabicyclo[2.2.1]heptan-7-yl)methanone

93. A pharmaceutical composition comprising a therapeutically effective amount of a compound according to any one of claims 55 to 92 and at least one pharmaceutically acceptable excipient.

94. A method of treating a subject suffering from or diagnosed with a disease, disorder, or medical condition mediated by orexin receptor activity, comprising administering to the subject an effective amount of a compound according to any one of claims 55 to 92.

95. The method of claim 94, wherein the disease, disorder, or medical condition mediated by orexin receptor activity is a disorder of the sleep-wake cycle, insomnia, restless legs syndrome, jet-lag, disturbed sleep, a sleep disorder secondary to neurological disorders, mania, depression, manic depression, schizophrenia, a pain syndromes, fibromyalgia, neuropathic pain, catatonia, Parkinson's disease, Tourette's syndrome, anxiety, delirium, dementia, overweight, obesity or a condition related to overweight or obesity, insulin resistance, type II diabetes, hyperlipidemia, gallstones, angina, hypertension, breathlessness, tachycardia, infertility, sleep apnea, back and joint pain, varicose veins, osteoarthritis, hypertension, tachycardia, arrhythmias, angina pectoris, acute heart failure, ulcers, irritable bowel syndrome, diarrhea, gastroesophageal reflux, post-traumatic stress disorder, panic disorders, attention deficit disorders, cognitive deficiencies, or substance abuse.

96. The method of claim 94 wherein the disease, disorder, or medical condition is mood disorders, post-traumatic stress disorder, panic disorders, attention deficit disorders, cognitive deficiencies, or substance abuse..