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STABILIZING PHENYLALANINE
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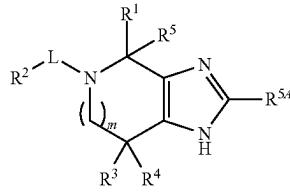
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(2) Date: Aug. 26, 2024**Related U.S. Application Data**(60) Provisional application No. 63/314,580, filed on Feb.
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519/00 (2013.01)**ABSTRACT**

The disclosure relates to compounds of Formula I or a pharmaceutically acceptable salt thereof, wherein, m, R¹-R⁵, R^{5A}, and L are defined herein. These compounds are useful in methods for stabilizing a mutant PAH protein or reducing blood phenylalanine concentration in a subject suffering from phenylketonuria. In some embodiments, the mutant PAH protein contains at least one R408W, R261Q, R243Q, Y414C, L48S, A403V, I65T, R241C, L348V, R408Q, or V388M mutation. In other embodiments, the mutant PAH protein contains at least one R408W, Y414C, I65T, F39L, R408Q, L348V, R261Q, A300S, or L48S mutation.

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A61K 31/506 (2006.01)
A61K 31/517 (2006.01)

I

COMPOUNDS AND METHODS USEFUL FOR STABILIZING PHENYLALANINE HYDROXYLASE MUTATIONS

RELATED APPLICATIONS

[0001] This application claims the benefit of priority to U.S. provisional application No. 63/314,580, filed Feb. 28, 2022, the entire contents of which are incorporated herein by reference.

TECHNICAL FIELD

[0002] This application pertains to compounds that stabilize phenylalanine hydroxylase (PAH) mutations, pharmaceutical compositions comprising those compounds, and methods of using those compounds for treating phenylketonuria.

BACKGROUND

[0003] Phenylketonuria (PKU) is an autosomal recessive disorder affecting approximately 1:10,000 people worldwide (approx. 1:15,000-1:20,000 in the U.S.). The number of patients varies globally depending on region. PKU arises in patients who have mutations in the gene encoding the phenylalanine hydroxylase (PAH) enzyme responsible for converting phenylalanine to tyrosine. PAH is a tetrameric enzyme expressed in the liver requiring BH4 cofactor for activity. Reduction or loss of PAH activity results in toxic accumulation of phenylalanine (Phe) in the blood and brain. High levels of Phe damage brain white matter and interfere with neurotransmitter production. If untreated, high levels of Phe can result in mental retardation and decreased IQ in children and neurocognitive and psychiatric issues in adults, such as executive function deficits (for example, difficulty with attention, memory, flexible thinking, and organization/time management), psychological issues (for example, depression, anxiety, and mood swings), psychiatric and/or behavioral issues (for example, attention deficit hyperactivity disorder, self-harm, schizophrenia, agoraphobia, and agitation) and neurological abnormalities (for example, spasticity, tremor, gait disturbances, and seizures).

[0004] PKU phenotypes can vary from mild hyperphenylalaninemia (HPA) to more severe phenotypes that result in untreated blood Phe concentrations exceeding 1200 μM . American medical guidelines currently recommend maintaining blood Phe concentration in the range of 120 to 360 μM in both adults and children under the age of 12 years. European medical guidelines currently recommend maintaining blood Phe concentration below 360 μM in children under the age of 12 years and in pregnant women and below 600 μM in non-pregnant patients older than 12 years.

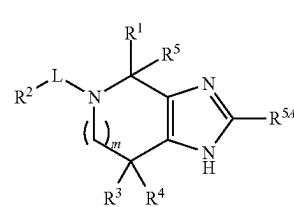
[0005] A standard of care for treating PKU is a Phe-restricted diet that severely limits the intake of natural protein. Such diets are very strict diets and challenging to adhere to. Two medications are currently approved for treating PKU, each having its own challenges. Kuvan (sapropterin dihydrochloride) is a synthetic BH4 cofactor approved in 2007 for use in infants to adults. Kuvan is not effective for all PKU patients, and the current guidelines suggest response testing in patients unless the patient is known to have two null mutations. Pegvaliase is an enzyme substitution therapy approved in 2018 for adults with a blood Phe concentration greater than 600 μM , despite prior management with available treatment options. Pegvaliase

typically involves injection of a purified PEGylated form of phenylalanine ammonia lyase that reduces Phe by converting it to ammonia and trans-cinnamic acid instead of tyrosine. One of the main complications with enzyme substitution therapy is the attainment and maintenance of therapeutically effective amounts of protein in vivo due to rapid degradation or inactivation of the infused protein. A current approach to overcome this problem is to perform numerous costly high dose injections.

[0006] Pharmaceutical agents that enable patients to increase their intake of natural protein are desired.

SUMMARY

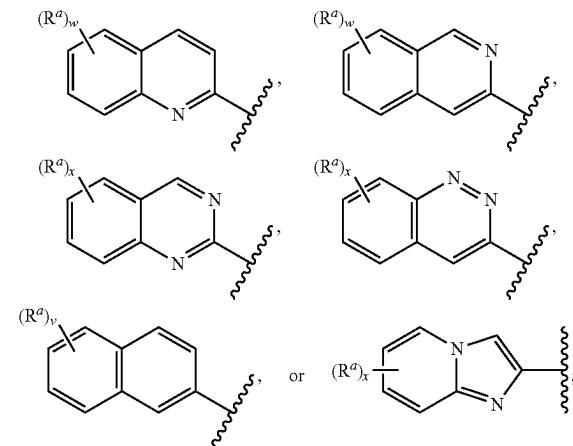
[0007] In some aspects, the disclosure provides compounds of Formula I:



[0008] or a pharmaceutically acceptable salt thereof, wherein:

[0009] m is 1 or 2;

[0010] R¹ is



[0011] v is 0 to 7;

[0012] w is 0 to 6;

[0013] x is 0 to 5;

[0014] each R^a independently is halo, C₁₋₆alkyl, C₃₋₆cycloalkyl, C₁₋₆haloalkyl, C₁₋₆alkoxy or C₁₋₆haloalkoxy;

[0015] R² is C₁₋₄alkyl, optionally substituted C₃₋₈cycloalkyl, optionally substituted heterocyclyl, optionally substituted aryl, or optionally substituted heteroaryl;

[0016] R³ is H or C₁₋₆alkyl;

[0017] R⁴ is H or C₁₋₆alkyl;

[0018] or R³ and R⁴, together with the atom to which they are attached, form a C₃₋₆cycloalkyl;

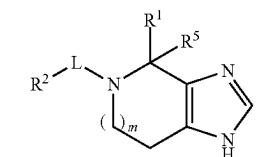
[0019] R^5 is H or D;

[0020] R^{5A} is H or D; and

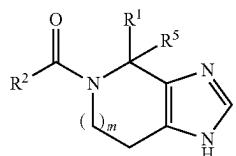
[0021] L is a bond, carbonyl, optionally substituted C_{1-6} -alkylene, optionally substituted C_{1-6} -alkylenecarbonyl, optionally substituted C_{2-6} -alkenylcarbonyl, optionally substituted C_{1-6} -haloalkylenecarbonyl, or optionally substituted $—C(O)NR^b(C_{1-6}$ -alkylene) $—$, wherein the carbon atom of the carbonyl group is connected to N in Formula I; and

[0022] R^b is H or C_{1-6} alkyl.

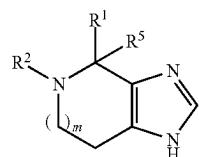
[0023] In other aspects, the disclosure provides compounds of Formula I-A, I-B, I-C, I-D, I-E, I-F, I-G, I-H, I-I, I-J, I-K, I-L, or I-M, or a pharmaceutically acceptable salt thereof:



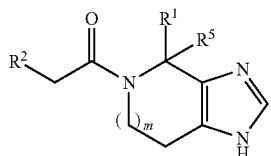
I-A



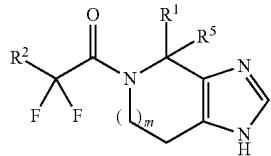
I-B



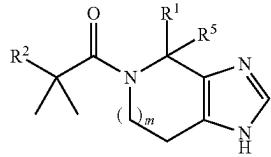
I-C



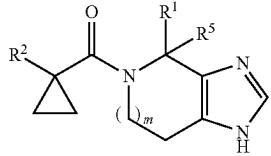
I-D



I-E



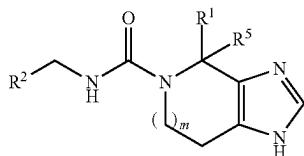
I-F



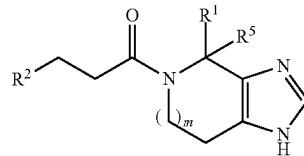
I-G

-continued

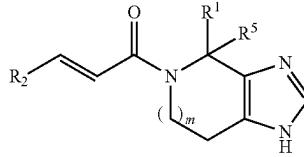
I-H



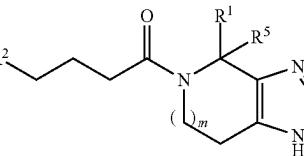
I-I



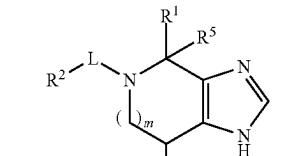
I-J



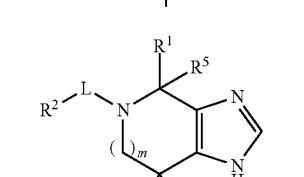
I-K



I-L



I-M



[0024] Stereoisomers and mixtures of stereoisomers of the compounds of Formula I, I-A, I-B, I-C, I-D, I-E, I-F, I-G, I-H, I-I, I-J, I-K, I-L, and I-M, and the pharmaceutical salts thereof, are also described.

[0025] In further aspects, the disclosure provides pharmaceutical compositions comprising one or more compound described herein or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient.

[0026] In yet other aspects, the disclosure provides methods for stabilizing a mutant PAH protein, comprising contacting the protein with one or more compound as described herein or a pharmaceutically acceptable salt thereof. In some embodiments, the mutant PAH protein contains at least one R408W, R261Q, R243Q, Y414C, L48S, A403V, I65T, R241C, L348V, R408Q, or V388M mutation. In other embodiments, the mutant PAH protein contains at least one R408W, Y414C, I65T, F39L, R408Q, L348V, R261Q, A300S, or L48S mutation.

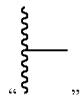
[0027] In still further aspects, the disclosure provides methods for reducing phenylalanine levels in a subject suffering from phenylketonuria comprising administering a therapeutically effective amount of one or more compound as described herein or a pharmaceutically acceptable salt thereof.

DETAILED DESCRIPTION OF ILLUSTRATIVE EMBODIMENTS

Definitions

[0028] Unless otherwise defined, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this disclosure pertains. The terminology used in the description is for describing particular embodiments only and is not intended to be limiting of the disclosure.

[0029] As used in structures herein,



indicates the point of attachment of the particular depicted structure or substituent group to the appropriate atom(s) in the remainder of the molecule.

[0030] The articles “a” and “an” as used herein and in the appended claims are used herein to refer to one or to more than one (e.g., to at least one) of the grammatical object of the article unless the context clearly indicates otherwise. By way of example, “an element” means one element or more than one element.

[0031] “Pharmaceutically acceptable” means approved or approvable by a regulatory agency of the Federal or a state government or the corresponding agency in a country other than the United States, or that is listed in the U.S. Pharmacopoeia or other generally recognized pharmacopoeia for use in animals, e.g., in humans.

[0032] “Pharmaceutically acceptable salt” refers to a salt of a compound of the disclosure that is pharmaceutically acceptable and that possesses the desired pharmacological activity of the parent compound. In particular, such salts are non-toxic and 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-ethanesulfonic acid, 2-hydroxyethanesulfonic acid, benzene-sulfonic acid, 4-chlorobenzenesulfonic acid, 2-naphthalene-sulfonic 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, fumarate, tartrate, mesylate, acetate, maleate, oxalate and the like.

[0033] 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 an agent and that is compatible therewith.

[0034] The term “alkyl,” when used alone or as part of a substituent group, refers to a straight- or branched-chain hydrocarbon group having from 1 to 12 carbon atoms (“C₁₋₁₂”), for example 1 to 6 carbons atoms (“C₁₋₆”), in the group. Examples of alkyl groups include methyl (C₁), ethyl (C₂), propyl (C₃) (e.g., n-propyl, isopropyl), butyl (C₄) (e.g., n-butyl, tert-butyl, sec-butyl, iso-butyl), pentyl (C₅) (e.g., n-pentyl, 3-pentyl, amyl, neopentyl, 3-methyl-2-butanyl, tertiary amyl), hexyl (C₆) (e.g., n-hexyl), heptyl (C₇) (e.g., n-heptyl), octyl (C₈) (e.g., n-octyl), and the like. In some embodiments, the alkyl group is a C₁₋₆alkyl; in other embodiments, it is a C₁₋₄alkyl; and in other embodiments, it is a C₁₋₃alkyl.

[0035] The term “alkylene,” when used alone or as part of a substituent group, refers to an alkyl diradical, i.e., a straight- or branched-chain hydrocarbon group that is attached to two other groups. For example, one embodiment of a C_nalkylene is the diradical —CH₂CH₂—. In some embodiments, the alkylene group is C₁₋₆alkylene; in other embodiments, it is C₁₋₄alkylene.

[0036] When a range of carbon atoms is used herein, for example, C₁₋₆, all ranges, as well as individual numbers of carbon atoms are encompassed. For example, “C₁₋₃” includes C₁₋₃, C₁₋₂, C₂₋₃, C₁, C₂, and C₃.

[0037] The term “cycloalkyl” when used alone or as part of a substituent group refers to cyclic-containing, non-aromatic hydrocarbon groups having from 3 to 10 carbon atoms (“C₃₋₁₀”), for example from 3 to 7 carbon atoms (“C₃₋₇”). Examples of cycloalkyl groups include cyclopropyl (C₃), cyclobutyl (C₄), cyclopentyl (C₅), cyclohexyl (C₆), cycloheptyl (C₇), and the like. In some embodiments, the cycloalkyl group is a C₃₋₄cycloalkyl; in other embodiments, it is a C₃₋₆cycloalkyl; and in other embodiments, it is C₃₋₈cycloalkyl. The cycloalkyl may be unsubstituted or substituted. In some embodiments, the cycloalkyl is substituted with two substituents. In further embodiments, the cycloalkyl is substituted with one substituent. In yet other embodiments, the cycloalkyl is substituted with three substituents. In still further embodiments, the cycloalkyl is unsubstituted.

[0038] The term “aryl” when used alone or as part of a substituent group also refers to a mono- or bicyclic-aromatic hydrocarbon ring structure having 6 or 10 carbon atoms in the ring, wherein one or more of the carbon atoms in the ring is optionally substituted. The term “aryl” also includes a mono- or bicyclic-aromatic hydrocarbon ring structure hav-

ing 6 or 10 carbon atoms in the ring, wherein two adjacent carbon atoms in the ring are optionally substituted such that said two adjacent carbon atoms and their respective substituents form a cycloalkyl or heterocycl ring. Examples of aryl groups include phenyl, indenyl, naphthyl, 1,2,3,4-tetrahydronaphthyl, and the like. The aryl may be unsubstituted or substituted. In other embodiments, the optionally substituted phenyl has four substituents. In further embodiments, the optionally substituted phenyl has three substituents. In yet other embodiments, the optionally substituted phenyl has two substituents. In still further embodiments, the optionally substituted phenyl has one substituent. In other embodiments, the optionally substituted phenyl is unsubstituted.

[0039] As used herein, the term “alkenyl” refers to a straight- or branched-chain group having from 2 to 12 carbon atoms (“C₂₋₁₂”) in the group, wherein the group includes at least one carbon-carbon double bond. Examples of alkenyl groups include vinyl (—CH=CH₂; C₂alkenyl), allyl (—CH₂—CH=CH₂; C₃alkenyl), propenyl (—CH=CHCH₃; C₃alkenyl), isopropenyl (—C(CH₃)=CH₂; C₃alkenyl), butenyl (—CH=CHCH₂CH₃; C₄alkenyl), sec-but enyl (—C(CH₃)=CHCH₃; C₄alkenyl), iso-but enyl (—CH=C(CH₃)₂; C₄alkenyl), 2-but enyl (—CH₂CH=CHCH₃; C₄alkenyl), pentenyl (—CH=CHCH₂CH₂CH₃; C₅alkenyl), and the like. In some embodiments, the alkenyl group is a C₂₋₆ alkenyl group; in other embodiments, it is C₂₋₄alkenyl.

[0040] As used herein, the term “alkynyl” refers to a straight- or branched-chain group having from 2 to 12 carbon atoms (“C₂₋₁₂”) in the group, and wherein the group includes at least one carbon-carbon triple bond. Examples of alkynyl groups include ethynyl (—C≡CH; C₂alkynyl), propargyl (—CH₂—C≡CH; C₃alkynyl), propynyl (—C≡CCH₃; C₃alkynyl), butynyl (—C≡CCH₂CH₃; C₄alkynyl), pentynyl (—C≡CCH₂CH₂CH₃; C₅alkynyl), and the like. In some embodiments, the alkynyl group is a C₂₋₆alkynyl group; in other embodiments, it is C₂₋₄alkynyl.

[0041] The term “carbonyl” as used by itself or as part of another group refers to C(O) or C(=O).

[0042] The term “alkylcarbonyl” as used by itself or as part of another group refers to an alkyl group as defined above wherein at least one carbon is bonded to an oxo group. For example, one embodiment of an C₃alkylcarbonyl is —CH₂C(O)CH₃. In some embodiments, the alkylcarbonyl group is a C₁₋₆alkylcarbonyl group.

[0043] The term “alkenylencarbonyl” as used by itself or as part of another group refers to an —C(O)-(alkenylene) group, where alkenylene refers to an alkylene diradical, i.e., a straight- or branched-chain hydrocarbon group containing at least one carbon-carbon double bond that is attached to two other groups. For example, one embodiment of a —C(O)—C₂alkenylene is —C(O)—CH=CH—. In some embodiments, the alkenylene group of the alkenylencarbonyl is a C₂₋₆alkenylene group; in other embodiments, the alkenylene group is C₂₋₄alkenylene.

[0044] The term “halo” or “halogen,” as used by itself or as part of another group refers to a fluorine, chlorine, bromine, or iodine atom.

[0045] As used herein, the term “haloalkyl” refers to an alkyl group wherein one or more of the hydrogen atoms has been replaced with one or more halogen atoms which may be the same or different. In some embodiments, the alkyl is substituted by at least one halogen. In other embodiments, the alkyl is substituted by one, two, or three F and/or Cl.

Examples of haloalkyl groups include fluoromethyl (CH₂F), 1-fluoroethyl (CH(CH₃)F), 2-fluoroethyl, difluoromethyl (CHF₂), trifluoromethyl (CF₃), pentafluoroethyl, 1,1-difluoroethyl (C(CH₃)F₂), 2,2-difluoroethyl (CH₂CHF₂), 2,2,2-trifluoroethyl (CH₂CF₃), 2-fluoropropan-2-yl (C(CH₃)₂F), 3,3,3-trifluoropropyl, 4,4,4-trifluorobutyl, trichloromethyl and the like. In some embodiments, the haloalkyl group is a C₁₋₆haloalkyl; in other embodiments, it is a C₁₋₄haloalkyl; and in other embodiments, it is a C₁₋₃haloalkyl.

[0046] The term “haloalkylenecarbonyl” as used by itself or as part of another group refers to a —C(O)-(haloalkylene) group, where the haloalkylene refers to a haloalkyl diradical. For example, one embodiment of a —C(O)—C₁haloalkylene is —C(O)—CF₂—. In some embodiments, the haloalkylene group is a C₁₋₆haloalkylene; in other embodiments, it is a C₁₋₄haloalkylene; and in other embodiments, it is a C₁₋₃haloalkylene.

[0047] The term “cyanoalkyl” as used by itself or as part of another group refers to an alkyl as defined herein that is substituted by one or more CN. In some embodiments, the alkyl is substituted by at least one CN. In other embodiments, the alkyl is substituted by one, two, or three CN. In further embodiments, the cyanoalkyl group is a C₁₋₆cyanoalkyl. In yet other embodiments, the cyanoalkyl is a C₁₋₄cyanoalkyl. Examples of cyanoalkyl groups include CH₂CN, CH₂CH₂CN, CH(CN)CH₃, CH₂CH₂CH₂CN, C(CH₃)₂CN, CH₂CH(CN)CH₃, CH(CN)CH₂CH₃, and the like.

[0048] The term “hydroxyalkyl” as used by itself or as part of another group refers to an alkyl group as defined herein wherein one or more of the hydrogen atoms has been replaced with one or more hydroxyl (i.e., —OH). In some embodiments, the hydroxyalkyl contains one OH. In other embodiments, the hydroxyalkyl contains two OH. In further embodiments, the hydroxyalkyl contains three OH. Examples of hydroxyalkyl groups include hydroxymethyl, hydroxyethyl (e.g., 1-hydroxyethyl, 2-hydroxyethyl), 1,2-dihydroxyethyl, hydroxypropyl (e.g., 2-hydroxypropyl, 3-hydroxypropyl), hydroxybutyl (e.g., 3-hydroxybutyl, 4-hydroxybutyl), 2-hydroxy-1-methylpropyl, 1,3-dihydroxyprop-2-yl, and the like. In some embodiments, the hydroxyalkyl group is C₁₋₆hydroxyalkyl; in other embodiments, it is C₁₋₄hydroxyalkyl; and in other embodiments, it is C₁₋₃hydroxyalkyl.

[0049] The term “cycloalkylsulfonyl” as used by itself or as part of another group refers to a cycloalkyl as defined herein that is bound to a sulfonyl, i.e., —SO₂—, and the sulfonyl group forms the point of attachment to the remainder of the molecule. In some embodiments, the cycloalkylsulfonyl is a C₃₋₈cycloalkylsulfonyl; in other embodiments, it is a C₃₋₆cycloalkylsulfonyl. Examples of cycloalkylsulfonyl groups include —SO₂-cyclopropyl, —SO₂-cyclobutyl, —SO₂-cyclopentyl, and the like.

[0050] The term “alkylsulfonyl” as used by itself or as part of another group refers to an alkyl as defined herein that is bound to a sulfonyl, i.e., —SO₂—, and the sulfonyl group forms the point of attachment to the remainder of the molecule. In some embodiments, the alkylsulfonyl is C₁₋₆alkylsulfonyl; in other embodiments, it is a C₁₋₄alkylsulfonyl. Examples of alkylsulfonyl groups include —SO₂CH₃, —SO₂CH₂CH₃, and the like.

[0051] The term “alkylsulfonyl(alkylene)” as used by itself or as part of another group refers to an alkylene group as defined herein that is bound to the sulfonyl of an alkylsulfonyl group as defined herein. Examples of

alkylsulfonyl(alkylene) groups include $—C(CH_3)_2SO_2CH_3$, $—CH_2SO_2CH_3$, $—CH(CH_3)SO_2CH_3$, and the like.

[0052] The term “alkoxy” as used by itself or as part of another group refers to an oxygen radical attached to an alkyl group by a single bond. Examples of alkoxy groups include methoxy (OCH_3), ethoxy (OCH_2CH_3), propoxy (e.g., $—O^{\prime}Pr$, $—O^{\prime}Pr$), or butoxy (e.g., $—O^{\prime}Bu$, $—O^{\prime}Bu$, $—O^{\prime\prime}Bu$, $—O^{\prime\prime}Bu$), and the like. In other embodiments, the alkoxy group is a C_{1-6} alkoxy. In further embodiments, the alkoxy group is a C_{1-4} alkoxy.

[0053] The term “alkoxy(alkylene)” as used by itself or as part of another group refers to an alkylene group as defined herein that is bound to an alkoxy group as defined herein. Examples of alkoxy(alkylene) groups include $—CH_2OCH_3$, $—CH_2CH_2OCH_3$, and the like.

[0054] The term “haloalkoxy” as used by itself or as part of another group refers to an oxygen radical attached to a haloalkyl group by a single bond, wherein haloalkyl is defined above. Examples of haloalkoxy groups include fluoromethoxy (OCH_2F), 2-fluoroethoxy, difluoromethoxy ($OCHF_2$), trifluoromethoxy (OCF_3), pentafluoroethoxy, 1,1-difluoroethoxy ($OC(CH_3)F_2$), 2,2-difluoroethoxy, 2,2,2-trifluoroethoxy (OCH_2CF_3), 3,3,3-trifluoropropoxy, 4,4,4-trifluorobutoxy, trichloromethoxy groups, and the like. In some embodiments, the haloalkoxy group is a C_{1-6} haloalkoxy; in other embodiments, it is C_{1-4} haloalkoxy; and in other embodiments, it is C_{1-3} haloalkoxy.

[0055] The term “haloalkoxy(alkylene)” as used by itself or as part of another group refers to an alkylene group as defined herein that is bound to a haloalkoxy group as defined herein. Examples of haloalkoxy(alkylene) groups include $—CH_2OCF_3$, and the like.

[0056] The term “heteroaryl” when used alone or as part of a substituent group refers to a mono- or bicyclic-aromatic ring structure including carbon atoms as well as up to four heteroatoms that are each independently nitrogen, oxygen, or sulfur. Heteroaryl rings can include a total of 5, 6, 9, or 10 ring atoms. In some embodiments, heteroaryl rings are characterized by the number of ring atoms in the heteroaryl group. For example, a 6-membered heteroaryl group refers to a heteroaryl group having 6 ring atoms in the group. Similarly, a 5-membered heteroaryl group refers to a heteroaryl group having 5 ring atoms in the group. The heteroaryl moiety can be unsubstituted, or one or more of the carbon atoms or nitrogen atoms in the ring can be substituted. Examples of heteroaryl groups include thiienyl, benzo [b]thienyl, furanyl, benzofuranyl, pyranyl, thiophenyl, isobenzofuranyl, benzoxazinyl, chromenyl, xanthenyl, 2H pyrrolyl, pyrrolyl, imidazolyl, pyrazolyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, isoindolyl, 3H-indolyl, indolyl, indazolyl, purinyl, isoquinolinyl, quinolyl, quinoxalyl, phthalazinyl, naphthyridinyl, cinnolinyl, triazolyl, tetrazolyl, thia-diazolyl, oxadiazolyl, quinazolinyl, pteridinyl, pyrimidinyl, thiazolyl, isothiazolyl, oxazolyl, isoxazolyl, furazanyl, pyrazolo[1,5-a]pyridinyl, benzoisothiazolyl, imidazol[1,5-a]pyridinyl, pyrrolo[1,2]pyridazinyl, benzo[d]thiazolyl, benzo[d]imidazolyl, benzo[d]oxazolyl, benzo[d]isoxazolyl, isothiazolyl, tetrahydropyrazolo[1,5-a]pyridinyl and the like. In some embodiments, the heteroaryl is thiienyl (e.g., thiien-2-yl and thiien-3-yl), furyl (e.g., 2-furanyl, 3-furanyl, 4-furanyl), pyrrolyl (e.g., pyrrol-2-yl, pyrrol-3-yl), imidazolyl (e.g., imidazol-2-yl, imidazol-4-yl), pyrazolyl (e.g., pyrazol-1-yl, pyrazol-3-yl, pyrazol-4-yl, pyrazol-5-yl), pyridyl (e.g., pyridin-1-yl, pyridin-2-yl, pyridin-3-yl, and

pyridin-4-yl), pyrimidinyl (e.g., pyrimidin-2-yl, pyrimidin-4-yl, and pyrimidin-5-yl), thiazolyl (e.g., thiazol-2-yl, thiazol-4-yl, and thiazol-5-yl), isothiazolyl (e.g., isothiazol-3-yl, isothiazol-4-yl, and isothiazol-5-yl), oxazolyl (e.g., oxazol-2-yl, oxazol-4-yl, and oxazol-5-yl), isoxazolyl (e.g., isoxazol-3-yl, isoxazol-4-yl, and isoxazol-5-yl), pyrazinyl (e.g., pyrazin-2-yl, pyrazin-3-yl, pyrazin-5-yl, pyrazin-6-yl), triazolyl (e.g., 1,2,4-triazol-1-yl, 1,2,4-triazol-3-yl, 1,2,4-triazol-5-yl), thiadiazolyl (e.g., 1,2,3-thiadiazolyl, 1,2,4-thiadiazolyl, 1,2,5-thiadiazolyl, 1,3,4-thiadiazolyl), oxadiazolyl (e.g., 1,2,3-oxadiazolyl, 1,2,4-oxadiazolyl, 1,2,5-oxadiazolyl, 1,3,4-oxadiazolyl), indazolyl (e.g., indazol-3-yl), pyrazolo[1,5-a]pyridinyl (e.g., pyrazolo[1,5-a]pyridin-3-yl), imidazol[1,5-a]pyridinyl (e.g., imidazol[1,5-a]pyridin-1-yl), pyrrolo[1,2]pyridazinyl (e.g., pyrrolo[1,2]pyridazin-5-yl, pyrrolo[1,2]pyridazin-6-yl), benzo[d]thiazolyl (e.g., benzo[d]thiazol-3-yl, benzo[d]thiazol-2-yl), benzo[d]imidazolyl (e.g., benzo[d]imidazol-2-yl), benzo[d]oxazolyl (e.g., benzo[d]oxazol-2-yl), benzo[d]isoxazolyl (e.g., benzo[d]isoxazol-3-yl), benzo[d]isothiazolyl (e.g., benzo[d]isothiazol-3-yl), benzo[c]isoxazolyl (e.g., benzo[c]isoxazol-3-yl), and quinolinyl (e.g., quinolin-3-yl), and pyridazinyl (e.g., pyridazin-3-yl, pyridazin-4-yl). The term “heteroaryl” also includes N-oxides. The heteroaryl may be unsubstituted or substituted. In some embodiments, the heteroaryl is substituted with two substituents. In further embodiments, the heteroaryl is substituted with one substituent. In yet other embodiments, the heteroaryl is substituted with three substituents. In still further embodiments, the heteroaryl is unsubstituted. Substitution may occur on any available carbon or heteroatom (e.g., nitrogen), or both, as permitted by substituent valency.

[0057] In some embodiments, the heteroaryl is a 5- or 6-membered heteroaryl. In some embodiments, the heteroaryl is a 5-membered heteroaryl, i.e., the heteroaryl is a monocyclic aromatic ring system having 5 ring atoms wherein at least one carbon atom of the ring is replaced with a heteroatom independently selected from nitrogen, oxygen, and sulfur. Examples of 5-membered heteroaryl groups include thiienyl, furyl, pyrrolyl, oxazolyl, pyrazolyl, imidazolyl, thiazolyl, isothiazolyl, and isoxazolyl and the like. In other embodiments, the heteroaryl is a 6-membered heteroaryl, e.g., the heteroaryl is a monocyclic aromatic ring system having 6 ring atoms wherein at least one carbon atom of the ring is replaced with a nitrogen atom. Examples of 6-membered heteroaryl groups include pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl and the like.

[0058] The term “heterocyclyl” as used by itself or as part of another group refers to non-aromatic, saturated or partially unsaturated, e.g., containing one or two double bonds, cyclic groups containing one, two, or three rings having from three to fourteen ring members, i.e., a 3-14-membered heterocyclyl, wherein at least one carbon atom of one of the rings is replaced with a heteroatom. Each heteroatom is independently selected from oxygen, sulfur, including sulfoxide and sulfone, and/or nitrogen atoms, which can be oxidized or quaternized. The term “heterocyclyl” also includes groups wherein a ring $—CH_2—$ is replaced with a $—C(O)—$. The term “heterocyclyl” also includes groups having fused optionally substituted aryl groups, e.g., indolinyl or chroman-4-yl and groups having fused optionally substituted cycloalkyl groups, e.g., 6-azaspiro[2.5]octanyl. In some embodiments, the heterocyclyl group is a C_{4-6} heterocyclyl, i.e., a 4-, 5- or 6-membered cyclic group, con-

taining one ring and one or two oxygen and/or nitrogen atoms. In other embodiments, the heterocyclyl is a C₄₋₆heterocyclyl containing one ring and one nitrogen atom. The heterocyclyl can be optionally linked to the rest of the molecule through any available carbon or heteroatom that results in a stable structure. Examples of heterocyclyl groups include azetidinyl, dioxanyl, tetrahydropyranyl, pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl, pyrrolidinyl, indolinyl, oxetanyl, tetrahydrofuranyl, tetrahydrothiophenyl, azepanyl, aziridinyl, dioxolanyl, imidazolidinyl, pyrazolidinyl, thianyl, dithianyl, thiomorpholinyl, oxazepanyl, oxiranyl, tetrahydropyranyl, and the like. In some embodiments, the heterocyclyl group includes azetidinyl, pyrrolidinyl, piperidinyl, piperazinyl, morpholinyl, and 6-azaspiro[2.5]octanyl. The heterocyclyl may be unsubstituted or substituted. In some embodiments, the heterocyclyl is substituted with two substituents. In further embodiments, the heterocyclyl is substituted with one substituent. In yet other embodiments, the heterocyclyl is substituted with three substituents. In still further embodiments, the heterocyclyl is unsubstituted.

[0059] The term “(heterocyclyl)alkylene” as used by itself or part of another group refers to an alkylene group as defined herein that is bound to a heterocyclyl group as defined herein.

[0060] The term “optionally substituted,” as used herein to describe a chemical moiety defined herein, means that the moiety may, but is not required to be, substituted with one or more suitable functional groups or other substituents as provided herein. For example, a substituent may be optionally substituted with one or more of: halo, cyano, —NO₂, —N₃, —OH, —SH, C₁₋₆alkyl, C₃₋₈cycloalkyl, C₃₋₈cycloalkenyl, C₂₋₆alkenyl, C₂₋₆alkynyl, C₁₋₆haloalkyl, C₁₋₆alkoxy, C₁₋₆alkoxy(alkylene), C₁₋₆haloalkoxy, C₁₋₆haloalkoxy(alkylene), C₁₋₆alkylcarbonyl, C₁₋₆cyanooalkyl, C₁₋₆hydroxyalkyl, C₁₋₆alkylenethio, (CR^VR^X)_pNR^VR^Z (wherein R^V and R^X are, independently, H or C₁₋₆alkyl; R^V and R^Z are independently, H, C₁₋₆alkyl, C₃₋₆cycloalkyl, C₁₋₆hydroxyalkyl, C₁₋₆haloalkyl, C₁₋₆alkoxy(alkylene), or C(O)OC₁₋₆alkyl, and p is 0, 1, 2, or 3), —C(O)NH₂, —C(O)NHC₁₋₆alkyl, —C(O)N(C₁₋₆alkyl)₂, —C(O)NHC₃₋₆cycloalkyl, —C(O)N(C₃₋₆cycloalkyl)₂, —COOH, —C₁₋₆alkyleneCOOH, —C₃₋₆cycloalkylCOOH, —C₁₋₆alkyleneCONH₂, C₃₋₆cycloalkylCONH₂, —C₁₋₆alkyleneCONHC₁₋₆alkyl, —C₁₋₆alkyleneCON(C₁₋₆alkyl)₂, —C(O)OC₁₋₆alkyl, —NHCO(C₁₋₆alkyl), —N(C₁₋₆alkyl)C(O)(C₁₋₆alkyl), —S(O)C₁₋₆alkyl, —S(O)C₃₋₆cycloalkyl, C₁₋₆alkylsulfonyl, C₃₋₈cycloalkylsulfonyl, C₁₋₆alkylsulfonyl(alkylene), oxo (O), 3-7-membered heterocyclyl, heterocyclyl(alkylene), aryl, aryl(alkylene), or heteroaryl groups. In some embodiments, the C₁₋₆alkyl group in any of the substituent groups in this paragraph is a C₁₋₄alkyl; in other embodiments it is C₁₋₃alkyl. In some embodiments, the C₁₋₆alkylene group in any of the substituent groups in this paragraph is a C₁₋₄alkylene. In some embodiments, the C₁₋₆haloalkyl substituent is a C₁₋₄haloalkyl; in other embodiments, it is C₁₋₃haloalkyl. In some embodiments, the C₃₋₆cycloalkyl substituent is a C₃₋₄cycloalkyl substituent. In some embodiments, the C₁₋₆alkoxy substituent is a C₁₋₃alkoxy; in other embodiments, it is C₁₋₄alkoxy. In some embodiments, the C₁₋₆haloalkoxy substituent is a C₁₋₃haloalkoxy; in other embodiments, it is C₁₋₄haloalkoxy.

[0061] In some embodiments, a substituent may be optionally substituted with one or more of: C₁₋₆alkyl, optionally

substituted C₂₋₆alkenyl, halo, CN, C₁₋₆cyanooalkyl, C₁₋₆haloalkyl, OH, optionally substituted C₃₋₈cycloalkyl, optionally substituted C₃₋₈cycloalkenyl, optionally substituted aryl, optionally substituted aryl(alkylene), optionally substituted heteroaryl, optionally substituted heterocyclyl, optionally substituted heterocyclyl(alkylene), C₁₋₆hydroxyalkyl, C₁₋₆haloalkoxy, C₁₋₆haloalkoxy(alkylene), C₁₋₆alkoxy, C₁₋₆alkoxy(alkylene), C₁₋₆deuteratedalkoxy(alkylene), C₁₋₆alkylcarbonyl, C₃₋₈cycloalkylsulfonyl, C₁₋₆alkylsulfonyl(alkylene), (CR^VR^X)_pNR^VR^Z (wherein R^V and R^X are, independently, H, C₁₋₆alkyl, C₃₋₆cycloalkyl, C₁₋₆hydroxyalkyl, C₁₋₆haloalkyl, C₁₋₆alkoxy(alkylene), or C(O)OC₁₋₆alkyl, and p is 0, 1, 2, or 3), and C(O)NR^{V2}R^{Z2} (wherein R^{V2} and R^{Z2} are independently, H, C₁₋₆alkyl, or C₃₋₆cycloalkyl).

[0062] The term “nitrogen protecting group” refers to a moiety that is attached to a nitrogen atom to prevent reaction at that nitrogen atom. Nitrogen protecting groups will be known by those skilled in the art and include those described in Wuts, P. G., *Greene's Protective Groups in Organic Synthesis*. Wiley; 5th edition (Oct. 27, 2014), which is incorporated by reference herein.

[0063] Recitation of ranges of values herein are intended to serve as a shorthand method of referring individually to each separate value falling within the range, unless otherwise indicated herein, and each separate value is incorporated into the specification as if it were individually recited herein. The use of any and all examples, or exemplary language (e.g., “such as”) provided herein, is intended to better illustrate the disclosure and is not a limitation on the scope of the disclosure unless otherwise claimed. No language in the specification should be construed as indicating any non-claimed element as essential to the practice of the disclosure.

[0064] The term “about” when used in combination with a numeric value or range of values means the value or range of values may deviate to an extent deemed reasonable to one of ordinary skill in the art.

[0065] Compounds described herein can comprise one or more asymmetric centers, and thus can exist in various stereoisomeric forms, e.g., enantiomers and/or diastereomers. For example, the compounds described herein can be in the form of an individual enantiomer, diastereomer or geometric isomer, or can be in the form of a mixture of stereoisomers, including racemic mixtures and mixtures enriched in one or more stereoisomer. Isomers can be isolated from mixtures by methods known to those skilled in the art, including supercritical fluid chromatography (SFC), chiral high-pressure liquid chromatography (HPLC) and the formation and crystallization of chiral salts; or preferred isomers can be prepared by asymmetric syntheses. See, for example, Jacques et al., *Enantiomers, Racemates and Resolutions* (Wiley Interscience, New York, 1981); Wilen et al., *Tetrahedron* 33:2725 (1977); Eliel, E. L. *Stereochemistry of Carbon Compounds* (McGraw-Hill, NY, 1962); and Wilen, S. H. *Tables of Resolving Agents and Optical Resolutions* p. 268 (E. L. Eliel, Ed., Univ. of Notre Dame Press, Notre Dame, IN 1972).

[0066] Exemplary compounds of the disclosure including a chiral center may be depicted herein as having particular stereochemistries, but for which absolute stereochemistry has not been obtained. Absolute configurations can be obtained using methods known in the art.

[0067] As used herein, the term "stereoisomers" refers to compounds which have identical chemical constitution and connectivity, but differ with regard to the arrangement of the atoms or groups in space, e.g., enantiomers or diastereomers.

[0068] When the stereochemical configuration at a chiral center in a compound having one or more chiral centers is depicted by its chemical name (e.g., where the configuration is indicated in the chemical name by "R" or "S") or structure (e.g., the configuration is indicated by dashed or wedge bonds), the enrichment of the indicated configuration relative to the opposite configuration is greater than 50%, 60%, 70%, 80%, 90%, 99% or 99.9%. "Enrichment of the indicated configuration relative to the opposite configuration" is a mole percent and is determined by dividing the number of compounds with the indicated stereochemical configuration at the chiral center(s) by the total number of all of the compounds with the same or opposite stereochemical configuration in a mixture.

[0069] When a disclosed compound is named or depicted by structure without indicating stereochemistry, it is understood that the name or the structure encompasses one of the possible stereoisomers or geometric isomers free of the others, or a mixture of the encompassed stereoisomers or geometric isomers.

[0070] It will be understood that certain compounds disclosed herein may exist in tautomeric forms. Such forms are included as part of the present disclosure. Thus, when a compound herein is represented by a structural formula or designated by a chemical name herein, all tautomeric forms which may exist for the compound are encompassed by the structural formula.

[0071] When the compounds described herein contain olefinic double bonds or other centers of geometric asymmetry, and unless specified otherwise, it is intended that they include both E and Z geometric isomers.

[0072] In some embodiments, the compounds described herein are isotopically enriched compound, e.g., an isotopologue. The term "isotopically enriched" refers to an atom having an isotopic composition other than the naturally abundant isotopic composition of that atom. "Isotopically enriched" may also refer to a compound containing at least one atom having an isotopic composition other than the natural isotopic composition of that atom. In an isotopologue, "isotopic enrichment" refers to the percentage of incorporation of an amount of a specific isotope of a given atom in a molecule in the place of that atom's natural isotopic composition. For example, deuterium enrichment of 1% at a given position means that 1% of the molecules in a given sample contain deuterium at the specified position. Because the naturally occurring distribution of deuterium is about 0.0156%, deuterium enrichment at any position in a compound synthesized using non-enriched starting materials is about 0.0156%. In one embodiment, one or more hydrogen atoms on a described compound may be replaced by deuterium.

[0073] Thus, as used herein, and unless otherwise indicated, the term "isotopic enrichment factor" refers to the ratio between the isotopic composition and the natural isotopic composition of a specified isotope.

[0074] With regard to the compounds provided herein, when a particular atom's position is designated as having deuterium or "D" or " ^2H ", it is understood that the abundance of deuterium at that position is substantially greater than the natural abundance of deuterium, which is about 0.015%. A position designated as having deuterium typically has a minimum isotopic enrichment factor of, in particular embodiments, at least 1000 (15% deuterium incorporation), at least 2000 (30% deuterium incorporation), at least 3000 (45% deuterium incorporation), at least 3500 (52.5% deuterium incorporation), at least 4000 (60% deuterium incorporation), at least 5500 (82.5% deuterium incorporation), at least 6000 (90% deuterium incorporation), at least 6333.3 (95% deuterium incorporation), at least 6466.7 (97% deuterium incorporation), at least 6600 (99% deuterium incorporation), or at least 6633.3 (99.5% deuterium incorporation) at each designated deuterium atom. The isotopic enrichment and isotopic enrichment factor of the compounds provided herein can be determined using conventional analytical methods known to one of ordinary skill in the art, including mass spectrometry and nuclear magnetic resonance spectroscopy.

[0075] The term "patient" or "subject" is used throughout the specification to describe an animal, preferably a human or a domesticated animal, to whom treatment, including prophylactic treatment, with the compounds or compositions according to the present disclosure is provided. For treatment of those conditions or disease states which are specific for a specific animal such as a human patient, the term patient refers to that specific animal, including a domesticated animal such as a dog or cat or a farm animal such as a horse, cow, sheep, etc. In general, in the present disclosure, the term patient refers to a human patient unless otherwise stated or implied from the context of the use of the term.

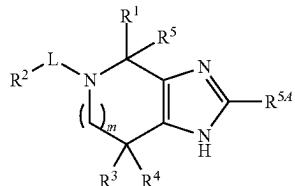
[0076] The terms "therapeutically effective amount" or "effective amount" means an amount or dose of a compound of the disclosure (or a pharmaceutically acceptable salt thereof) sufficient to generally bring about the desired therapeutic benefit in subjects in need of such treatment for the designated disease or disorder. Further, a therapeutically effective amount with respect to a compound of the disclosure means that amount of therapeutic agent alone, or in combination with other therapies, that provides a therapeutic benefit in the treatment or prevention of a disease.

[0077] "Treating" or "treatment" of any disease or disorder refers, in one embodiment, to ameliorating the disease or disorder (e.g., 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.

[0078] The terms "prevent," "preventing," and "prevention" refer to the prevention of the onset, recurrence, or spread of the disease in a subject resulting from the administration of a prophylactic or therapeutic agent.

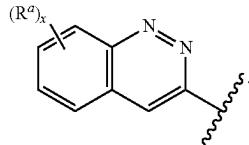
Compounds

[0079] The present disclosure provides compounds of Formula I or pharmaceutically acceptable salts thereof:

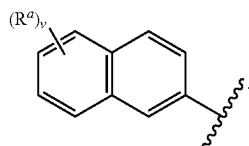


I

In yet further embodiments, R¹ is

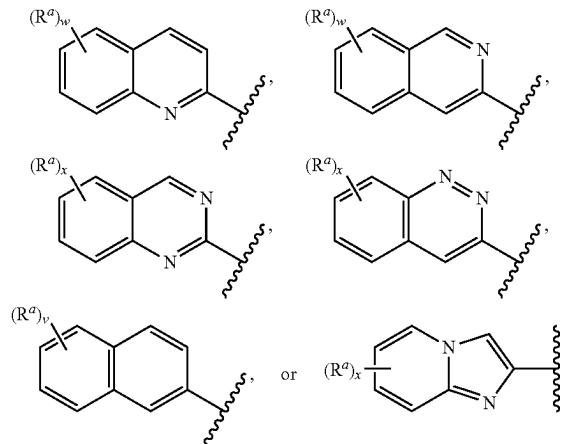


In still other embodiments, R¹ is

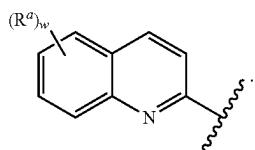


[0080] In Formula I, m is 1 or 2. In some embodiments, m is 1. In other embodiments, m is 2.

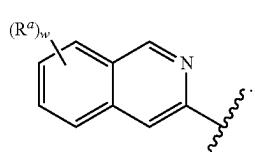
[0081] In formula I, R¹ is



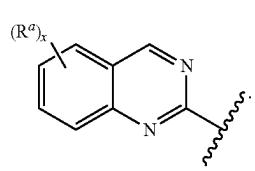
In other embodiments, R¹ is



In further embodiments, R¹ is



In still other embodiments, R¹ is

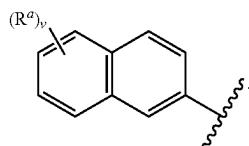


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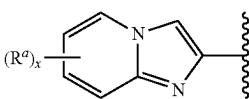
In yet further embodiments, R¹ is



In still other embodiments, R¹ is



In yet further embodiments, R¹ is

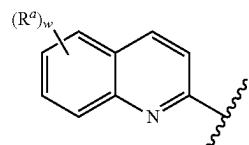


[0082] In the structures for R¹, v is 0 to 7. In some embodiments, v is 0. In other embodiments, v is 1. In further embodiments, v is 2. In yet other embodiments, v is 3. In still further embodiments, v is 4. In other embodiments, v is 5. In further embodiments, v is 6. In still further embodiments, v is 7.

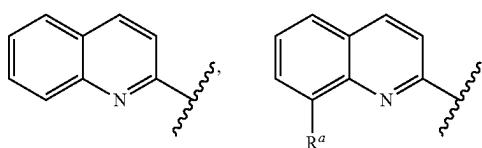
[0083] In the structures for R¹, w is 0 to 6. In some embodiments, w is 0. In other embodiments, w is 1. In further embodiments, w is 2. In yet other embodiments, w is 3. In still further embodiments, w is 4. In other embodiments, w is 5. In further embodiments, w is 6.

[0084] In the structures for R¹, x is 0 to 5. In some embodiments, x is 0. In other embodiments, x is 1. In further embodiments, x is 2. In yet other embodiments, x is 3. In still further embodiments, x is 4. In other embodiments, x is 5.

[0085] In other embodiments, R¹ is

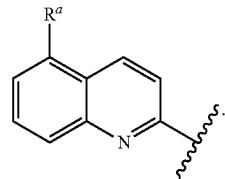
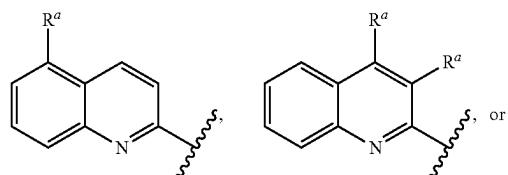
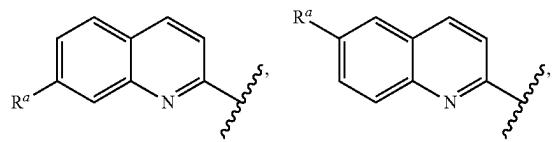


and w is 0 or 1 such as

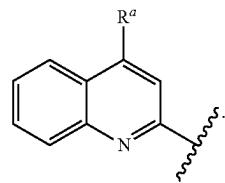


-continued

In still further embodiments, R¹ is

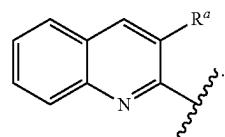
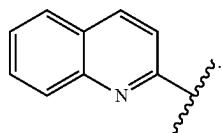


In other embodiments, R¹ is



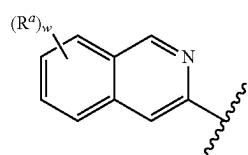
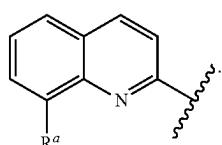
In other embodiments, R¹ is

In further embodiments, R¹ is



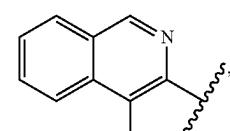
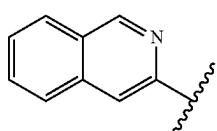
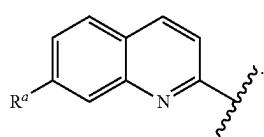
[0086] In still other embodiments, R¹ is

In other embodiments, R¹ is

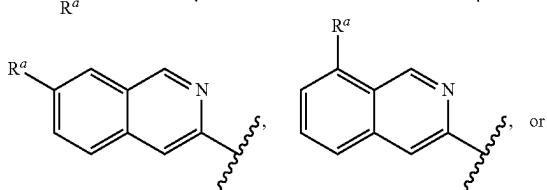
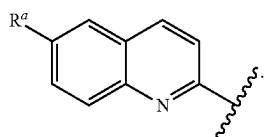


In further embodiments, R¹ is

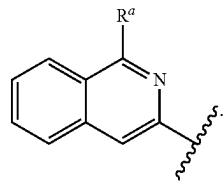
and w is 0 or 1 such as



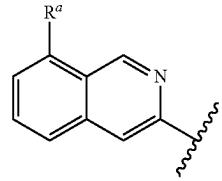
In yet other embodiments, R¹ is



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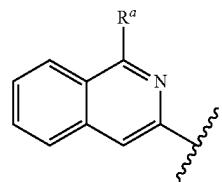
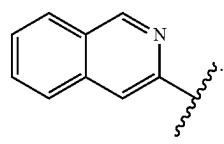


In other embodiments, R¹ is



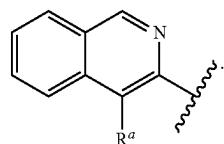
or In other embodiments, R¹ is

In further embodiments, R¹ is



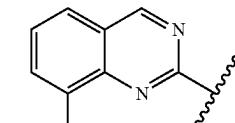
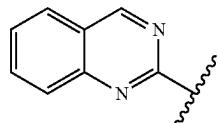
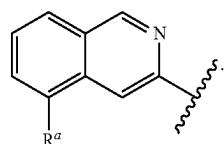
In other embodiments, R¹ is

[0087] In further embodiments, R¹ is

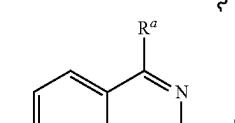
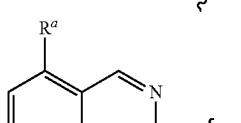
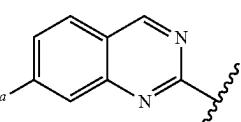
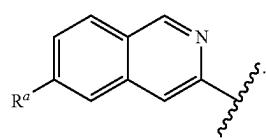


In further embodiments, R¹ is

and x is 0 or 1, such as

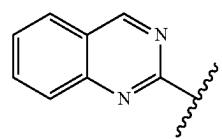
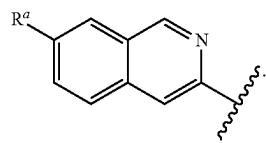


In yet other embodiments, R¹ is

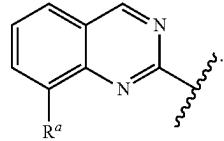


In still further embodiments, R¹ is

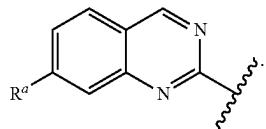
In other embodiments, R¹ is



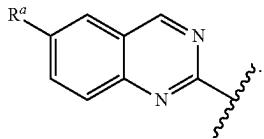
In other embodiments, R¹ is



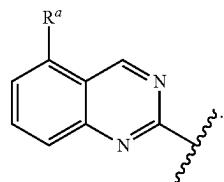
In further embodiments, R¹ is



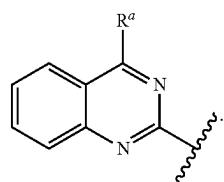
In yet other embodiments, R¹ is



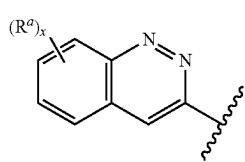
In still further embodiments, R¹ is



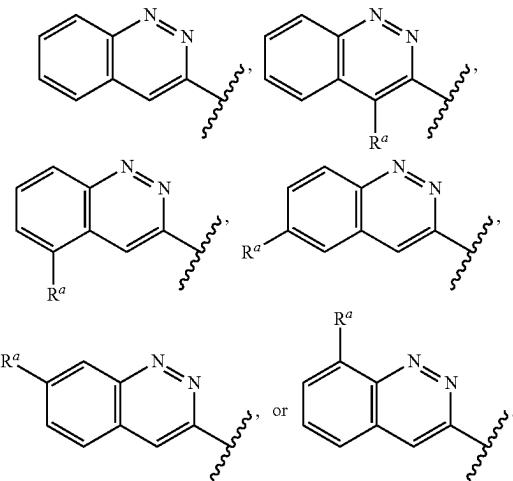
In other embodiments, R¹ is



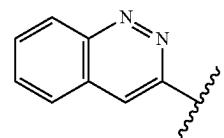
[0088] In still other embodiments, R¹ is



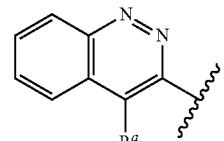
and x is 0 or 1 such as



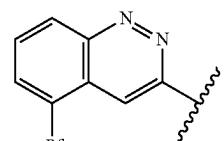
In other embodiments, R¹ is



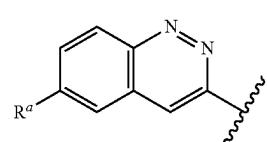
In other embodiments, R¹ is



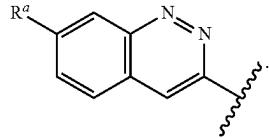
In further embodiments, R¹ is



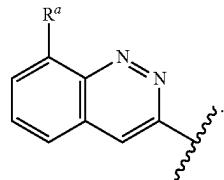
In yet other embodiments, R¹ is



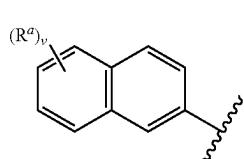
In still further embodiments, R¹ is



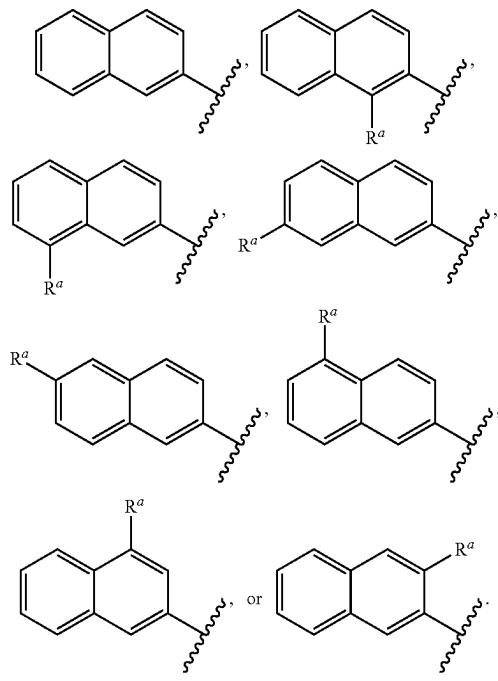
In other embodiments, R¹ is



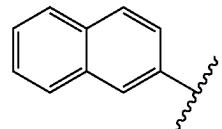
[0089] In still other embodiments, R¹ is



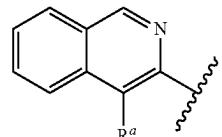
and v is 0 or 1 such as



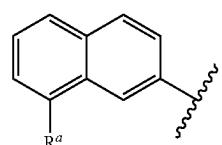
In other embodiments, R¹ is



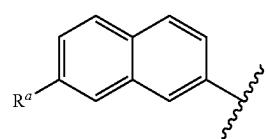
In yet other embodiments, R¹ is



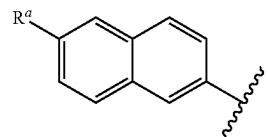
In further embodiments, R¹ is



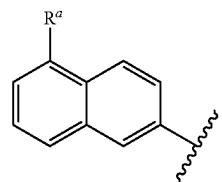
In yet other embodiments, R¹ is



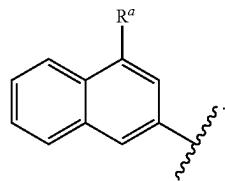
In still further embodiments, R¹ is



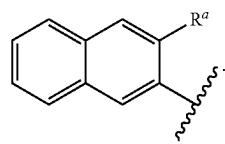
In other embodiments, R¹ is



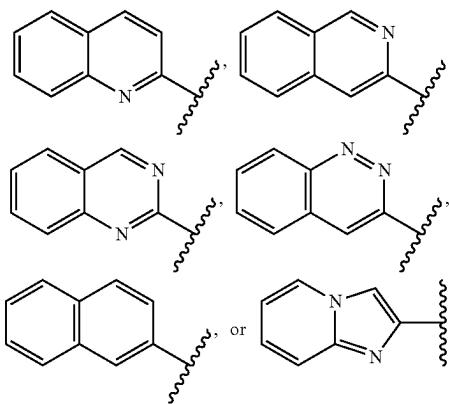
In yet other embodiments, R¹ is



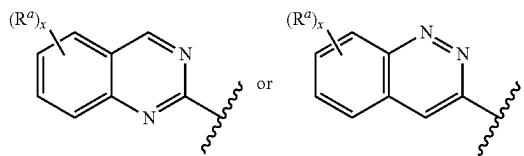
In still other embodiments, R¹ is



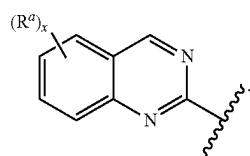
[0090] In some embodiments, R¹ is



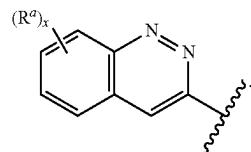
[0091] In some embodiments, the compound is a single enantiomer and the R¹ moiety is in an alpha (α) configuration. In these compounds, R¹ is



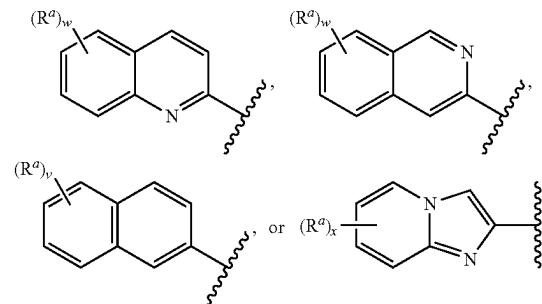
In other embodiments, the R¹ moiety is in an alpha (α) configuration and R¹ is



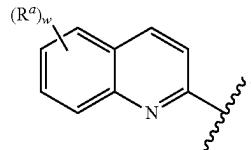
In still other embodiments, the R¹ moiety is in an alpha (α) configuration and R¹ is



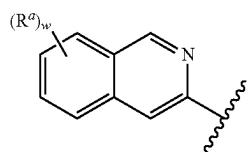
[0092] In some embodiments, the compound is a single enantiomer and the R¹ moiety is in an beta (β) configuration. In these compounds, R¹ is



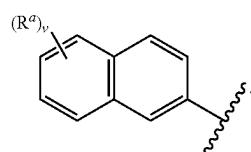
In further embodiments, the R¹ moiety is in an beta (β) configuration and R¹ is



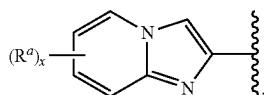
In other embodiments, the R¹ moiety is in an beta (β) configuration and R¹ is



In further embodiments, the R¹ moiety is in an beta (β) configuration and R¹ is



In still further embodiments, the R¹ moiety is in an beta (P) configuration and R¹ is



[0093] In the structures for R¹, each R^a is independently halo, C₁₋₆alkyl, C₃₋₆cycloalkyl, C₁₋₆haloalkyl, C₁₋₆alkoxy or C₁₋₆haloalkoxy. In some embodiments, R^a is halo such as F, Cl, Br or I. In other embodiments, R^a is F, Br, or Cl. In still other embodiments, R^a is F. In further embodiments, R^a is Br. In yet other embodiments, R^a is Cl. In still further embodiments, R^a is I. In other embodiments, R^a is C₁₋₆alkyl such as methyl, ethyl, propyl, butyl, pentyl, or hexyl. In yet other embodiments, R^a is methyl. In further embodiments, R^a is C₃₋₆cycloalkyl such as cyclopropyl, cyclobutyl, cyclopentyl, or cyclohexyl. In still further embodiments, R^a is cyclopropyl. In yet other embodiments, R^a is C₁₋₆haloalkyl such as CF₃, CHF₂, CH₂F, CH₂CF₃, C(CH₃)₂F, or C(CH₃)F₂. In still other embodiments, R^a is CF₃ or CHF₂. In further embodiments, R^a is C₁₋₆alkoxy such as methoxy, ethoxy, propoxy, butoxy, pentoxy, or hexoxy. In yet other embodiments, R^a is methoxy or ethoxy. In other embodiments, R^a is C₁₋₆haloalkoxy such as OCF₃ or OCH₂CF₃. In still other embodiments, one R^a is halo and the second R^a is C₁₋₆alkoxy or C₁₋₆alkyl.

[0094] In Formula I, R² is C₁₋₄alkyl, optionally substituted C₃₋₈cycloalkyl, optionally substituted heterocyclyl, optionally substituted aryl, or optionally substituted heteroaryl. In some embodiments, R² is optionally substituted C₃₋₈cycloalkyl, optionally substituted heterocyclyl, optionally substituted aryl, or optionally substituted heteroaryl. In further embodiments, R² is unsubstituted C₃₋₈cycloalkyl, unsubstituted heterocyclyl, unsubstituted aryl, or unsubstituted heteroaryl. In other embodiments, R² is substituted C₃₋₈cycloalkyl, substituted heterocyclyl, substituted aryl, or substituted heteroaryl. In some embodiments, R² is C₁₋₄alkyl such as methyl, ethyl, propyl, butyl, or tert-butyl. In other embodiments, R² is optionally substituted C₃₋₈cycloalkyl such as cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, or cyclooctyl. In further embodiments, R² is optionally substituted heterocyclyl such as azetidinyl. In still other embodiments, R² is optionally substituted aryl such as phenyl. In yet further embodiments, R² is optionally substituted heteroaryl such as pyridinyl, pyrazolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, triazolyl, oxadiazolyl, thiadiazolyl, furanyl, thiophenyl, pyrimidinyl, pyrazinyl, indazolyl, pyrazolo[1,5-a]pyridinyl, imidazol[1,5-a]pyridinyl, pyrrolo[1,2-b]pyridazinyl, benzo[d]thiazolyl, benzo[d]isothiazolyl, benzo[d]imidazolyl, benzo[d]oxazolyl, benzo[d]isoxazolyl, or benzo[d]isothiazolyl.

[0095] In Formula I, R³ is H or C₁₋₆alkyl. In some embodiments, R³ is H. In other embodiments, R³ is C₁₋₆alkyl such as methyl, ethyl, propyl, butyl, pentyl, or hexyl. In further embodiments, R³ is methyl. In yet other embodiments, R³ is ethyl. In still further embodiments, R³ is propyl. In other embodiments, R³ is butyl. In further embodiments, R³ is pentyl. In yet other embodiments, R³ is hexyl.

[0096] In Formula I, R⁴ is H or C₁₋₆alkyl. In some embodiments, R⁴ is H. In other embodiments, R⁴ is C₁₋₆alkyl such as methyl, ethyl, propyl, butyl, pentyl, or hexyl. In further embodiments, R⁴ is methyl. In yet other embodiments, R⁴ is ethyl. In still further embodiments, R⁴ is propyl. In other

embodiments, R⁴ is butyl. In further embodiments, R⁴ is pentyl. In yet other embodiments, R⁴ is hexyl.

[0097] Alternatively, R³ and R⁴, together with the atom to which they are attached, form a C₃₋₆cycloalkyl. In some embodiments, R³ and R⁴ together form a cyclopropyl. In other embodiments, R³ and R⁴ together form a cyclobutyl. In further embodiments, R³ and R⁴ together form a cyclopentyl. In yet other embodiments, R³ and R⁴ together form a cyclohexyl.

[0098] In some embodiments, both R³ and R⁴ are H. In other embodiments, R³ is methyl and R⁴ is H. In still other embodiments, both R³ and R⁴ are methyl.

[0099] In Formula I, R⁵ is H or D. In some embodiments, R⁵ is H. In further embodiments, R⁵ is D.

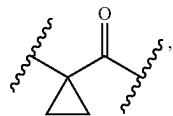
[0100] In Formula I, R^{5A} is H or D. In some embodiments, R^{5A} is H. In further embodiments, R^{5A} is D.

[0101] In Formula I, L is a bond, carbonyl, optionally substituted C₁₋₆alkylene, optionally substituted C₁₋₆alkylenecarbonyl, optionally substituted C₂₋₆alkenylidenecarbonyl, optionally substituted C₁₋₆haloalkylenecarbonyl, or optionally substituted —C(O)NR^b(C₁₋₆alkylene)-, wherein the carbon atom of the carbonyl group is connected to N in Formula I. In some embodiments, L is a bond. In other embodiments, L is carbonyl (wherein the carbon atom of the carbonyl group is connected to N in Formula I). In further embodiments, L is optionally substituted C₁₋₆alkylene such as methylene, ethylene, propylene, butylene, pentylene, or hexylene. In other embodiments, L is C₁alkylene. In still other embodiments, L is C₂alkylene. In further embodiments, L is C₃alkylene. In yet other embodiments, L is C₄alkylene. In still further embodiments, L is C₅alkylene. In other embodiments, L is C₆alkylene. In yet other embodiments, L is optionally substituted C₁₋₆alkylenecarbonyl (wherein the carbon atom of the carbonyl group is connected to N in Formula I). In further embodiments, L is —C₁alkylene-C(O)—. In other embodiments, L is —C₂alkylene-C(O)—. In further embodiments, L is —C₃alkylene-C(O)—. In yet other embodiments, L is —C₄alkylene-C(O)—. In still further embodiments, L is —C₅alkylene-C(O)—. In other embodiments, L is —C₆alkylene-C(O)—. In still further embodiments, L is optionally substituted C₂₋₆alkenylidenecarbonyl (wherein the carbon atom of the carbonyl group is connected to N in Formula I). In other embodiments, L is —C₂alkenylene-C(O)—. In further embodiments, L is —C₃alkenylene-C(O)—. In yet other embodiments, L is —C₄alkenylene-C(O)—. In still further embodiments, L is —C₅alkenylene-C(O)—. In other embodiments, L is —C₆alkenylene-C(O)—. In still further embodiments, L is optionally substituted C₁₋₆haloalkylenecarbonyl (wherein the carbon atom of the carbonyl group is connected to N in Formula I). In other embodiments, L is —C₁haloalkylene-C(O)—. In yet other embodiments, L is —C₂haloalkylene-C(O)—. In further embodiments, L is —C₃haloalkylene-C(O)—. In yet other embodiments, L is —C₄haloalkylene-C(O)—. In still further embodiments, L is —C₅haloalkylene-C(O)—. In other embodiments, L is —C₆haloalkylene-C(O)—. In further embodiments, L is —C(O)NR^b(C₁₋₆alkylene)- (wherein the carbon atom of the carbonyl group is connected to N in Formula I). In yet other embodiments, L is —C(O)NR^bC₁alkylene-. In other embodiments, L is —C(O)NR^bC₂alkylene-. In further embodiments, L is —C(O)NR^bC₃alkylene-. In yet other embodiments, L is

$-\text{C}(\text{O})\text{NR}^b\text{C}_4\text{alkylene}$. In still further embodiments, L is $-\text{C}(\text{O})\text{NR}^b\text{C}_5\text{alkylene}$. In other embodiments, L is $-\text{C}(\text{O})\text{NR}^b\text{C}_6\text{alkylene}$.

[0102] In the structures for L, R^b is H or C₁₋₆alkyl. In some embodiments, R^b is H. In other embodiments, R^b is C₁₋₆alkyl, such as methyl, ethyl, propyl, butyl, pentyl, or hexyl. In further embodiments, R^b is methyl. In yet other embodiments, R^b is ethyl. In still further embodiments, R^b is propyl. In other embodiments, R^b is butyl. In further embodiments, R^b is pentyl. In yet other embodiments, R^b is hexyl.

[0103] In some embodiments, L is a bond, $-\text{C}(\text{O})-$, $-\text{C}(\text{O})\text{CH}_2-$, $-\text{C}(\text{O})\text{CH}_2\text{CH}_2-$, $-\text{C}(\text{O})\text{CH}_2\text{CH}_2\text{CH}_2-$, $-\text{C}(\text{O})\text{CF}_2-$, $-\text{C}(\text{O})\text{CHF}-$, $-\text{C}(\text{O})\text{C}(\text{CH}_3)_2-$, $-\text{C}(\text{O})\text{CH}=\text{CH}-$,



$-\text{C}(\text{O})\text{NHCH}_2-$, $-\text{CH}_2-$, or $-\text{CH}_2\text{CH}_2-$. In yet other embodiments, L is a bond, $-\text{C}(\text{O})-$, $-\text{C}(\text{O})\text{CH}_2-$, $-\text{C}(\text{O})\text{CH}_2\text{CH}_2-$, or $-\text{C}(\text{O})\text{CF}_2-$.

[0104] In some embodiments, R² is cyclopentyl, cyclobutyl, cyclopropyl, azetidinyl, phenyl, pyrazolyl, oxazolyl, thiazolyl, triazolyl, oxadiazolyl, pyridinyl, pyrimidinyl, pyrazolo[1,5-a]pyridinyl, indazolyl, thiadiazolyl, imidazol[1,5-a]pyridinyl, pyrrolo[1,2]pyridazinyl, thiophenyl, isoxazolyl, isothiazolyl, benzo[d]thiazolyl, benzo[d]imidazolyl, benzo[d]oxazolyl, benzo[d]isoxazolyl, benzo[d]isothiazolyl, furanyl, or pyrazinyl, each of which is optionally substituted.

[0105] In further embodiments, R² is cyclopentyl, cyclobutyl, cyclopropyl, cyclohexyl, azetidinyl, phenyl, pyrazolyl, oxazolyl, thiazolyl, triazolyl, oxadiazolyl, pyridinyl, pyrimidinyl, pyrazolo[1,5-a]pyridinyl, indazolyl, thiadiazolyl, imidazol[1,5-a]pyridinyl, pyrrolo[1,2]pyridazinyl, thiophenyl, isoxazolyl, isothiazolyl, benzo[d]thiazolyl, benzo[d]imidazolyl, benzo[d]oxazolyl, benzo[d]isoxazolyl, benzo[c]isoxazolyl, benzo[d]isothiazolyl, furanyl, pyrazinyl or quinolinyl, each of which is optionally substituted.

[0106] In other embodiments, R² is cyclopentyl, cyclobutyl, cyclopropyl, azetidinyl, phenyl, pyrazolyl, oxazolyl, thiazolyl, triazolyl, oxadiazolyl, pyridinyl, pyrimidinyl, pyrazolo[1,5-a]pyridinyl, indazolyl, thiadiazolyl, imidazol[1,5-a]pyridinyl, pyrrolo[1,2]pyridazinyl, thiophenyl, isoxazolyl, isothiazolyl, benzo[d]thiazolyl, benzo[d]imidazolyl, benzo[d]oxazolyl, benzo[d]isoxazolyl, benzo[d]isothiazolyl, furanyl, or pyrazinyl, each of which is unsubstituted.

[0107] In yet other embodiments, R² is cyclopentyl, cyclobutyl, cyclopropyl, cyclohexyl, azetidinyl, phenyl, pyrazolyl, oxazolyl, thiazolyl, triazolyl, oxadiazolyl, pyridinyl, pyrimidinyl, pyrazolo[1,5-a]pyridinyl, indazolyl, thiadiazolyl, imidazol[1,5-a]pyridinyl, pyrrolo[1,2]pyridazinyl, thiophenyl, isoxazolyl, isothiazolyl, benzo[d]thiazolyl, benzo[d]imidazolyl, benzo[d]oxazolyl, benzo[d]isoxazolyl, benzo[c]isoxazolyl, benzo[d]isothiazolyl, furanyl, pyrazinyl or quinolinyl, each of which is unsubstituted.

[0108] In further embodiments, R² is optionally substituted cyclopentyl. In further embodiments, R² is optionally substituted cyclobutyl. In still other embodiments, R² is

optionally substituted cyclopropyl. In yet other embodiments, R² is optionally substituted cyclohexyl. In yet further embodiments, R² is optionally substituted azetidinyl. In other embodiments, R² is optionally substituted phenyl. In further embodiments, R² is optionally substituted pyrazolyl. In still other embodiments, R² is optionally substituted oxazolyl. In yet further embodiments, R² is optionally substituted thiazolyl. In other embodiments, R² is optionally substituted triazolyl. In further embodiments, R² is optionally substituted oxadiazolyl. In still other embodiments, R² is optionally substituted pyridinyl. In yet further embodiments, R² is optionally substituted pyrimidinyl. In other embodiments, R² is optionally substituted pyrazolo[1,5-a]pyridinyl. In further embodiments, R² is optionally substituted indazolyl. In yet other embodiments, R² is optionally substituted thiadiazolyl. In other embodiments, R² is optionally substituted imidazol[1,5-a]pyridinyl. In further embodiments, R² is optionally substituted pyrrolo[1,2]pyridazinyl. In still other embodiments, R² is optionally substituted thiophenyl. In yet further embodiments, R² is optionally substituted isoxazolyl. In further embodiments, R² is optionally substituted isothiazolyl. In other embodiments, R² is optionally substituted benzo[d]thiazolyl. In further embodiments, R² is optionally substituted benzo[d]imidazolyl. In still other embodiments, R² is optionally substituted benzo[d]oxazolyl. In yet further embodiments, R² is benzo[d]isoxazolyl. In other embodiments, R² is optionally substituted benzo[c]isoxazolyl. In still further embodiments, R² is optionally substituted benzo[d]isothiazolyl. In other embodiments, R² is optionally substituted furanyl. In yet other embodiments, R² is optionally substituted pyrazinyl. In still further embodiments, R² is optionally substituted quinolinyl.

[0109] In other embodiments, R² is azetidin-1-yl, azetidin-3-yl, pyrazol-1-yl, pyrazol-3-yl, pyrazol-4-yl, pyrazol-5-yl, 1,2,4-triazol-1-yl, 1,2,4-triazol-3-yl, 1,2,4-triazol-5-yl, 1,2,3-triazol-5-yl, 1,3,4-oxadiazol-2-yl, 1,2,4-oxadiazol-3-yl, 1,2,4-oxadiazol-5-yl, pyrazolo[1,5-a]pyridin-3-yl, indazol-3-yl, thiazol-2-yl, thiazol-4-yl, thiazol-5-yl, oxazol-2-yl, oxazol-4-yl, oxazol-5-yl, 1,3,4-thiadiazol-2-yl, pyridin-1-yl, pyridin-2-yl, pyridin-3-yl, pyridin-4-yl, pyrimidin-2-yl, imidazol[1,5-a]pyridin-1-yl, pyrrolo[1,2]pyridazin-5-yl, pyrrolo[1,2]pyridazin-6-yl, thiophen-2-yl, isoxazol-3-yl, isoxazol-4-yl, isoxazol-5-yl, benzo[d]thiazol-2-yl, benzo[d]thiazol-3-yl, benzo[d]imidazol-2-yl, benzo[d]oxazol-2-yl, benzo[d]isoxazol-3-yl, benzo[d]isothiazol-3-yl, furan-3-yl, isothiazol-3-yl, isothiazol-4-yl, isothiazol-5-yl, or pyrazin-2-yl, each of which is optionally substituted.

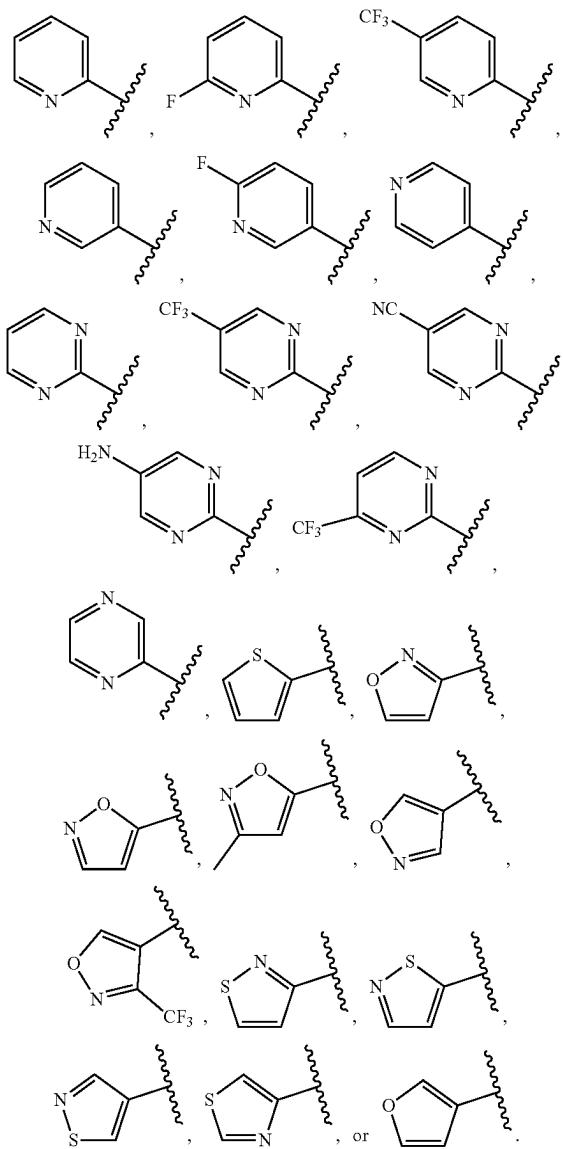
[0110] In yet other embodiments, R² is azetidin-1-yl, azetidin-3-yl, pyrazol-1-yl, pyrazol-3-yl, pyrazol-4-yl, pyrazol-5-yl, 1,2,4-triazol-1-yl, 1,2,4-triazol-3-yl, 1,2,4-triazol-5-yl, 1,2,3-triazol-5-yl, 1,3,4-oxadiazol-2-yl, 1,2,4-oxadiazol-3-yl, 1,2,4-oxadiazol-5-yl, pyrazolo[1,5-a]pyridin-3-yl, indazol-3-yl, thiazol-2-yl, thiazol-4-yl, thiazol-5-yl, oxazol-2-yl, oxazol-4-yl, oxazol-5-yl, 1,3,4-thiadiazol-2-yl, pyridin-1-yl, pyridin-2-yl, pyridin-3-yl, pyridin-4-yl, pyrimidin-2-yl, imidazol[1,5-a]pyridin-1-yl, pyrrolo[1,2]pyridazin-5-yl, pyrrolo[1,2]pyridazin-6-yl, thiophen-2-yl, isoxazol-3-yl, isoxazol-4-yl, isoxazol-5-yl, benzo[d]thiazol-2-yl, benzo[d]thiazol-3-yl, benzo[d]imidazol-2-yl, benzo[d]oxazol-2-yl, benzo[d]isoxazol-3-yl, benzo[d]isothiazol-3-yl, furan-3-yl, isothiazol-3-yl, isothiazol-4-yl, isothiazol-5-yl, pyrazin-2-yl, benzo[c]isoxazole-3-yl, or quinolin-3-yl, each of which is optionally substituted.

[0111] In further embodiments, R² is C₃₋₈cycloalkyl, heterocycl, aryl, or heteroaryl, each of which is substituted with one or more of C₁₋₆alkyl, optionally substituted C₂₋₆alkenyl, halo, CN, C₁₋₆cyanooalkyl, C₁₋₆haloalkyl, OH, optionally substituted C₃₋₈cycloalkyl, optionally substituted C₃₋₈cycloalkyl(alkylene), optionally substituted C₃₋₈cycloalkenyl, optionally substituted aryl, optionally substituted aryl(alkylene), optionally substituted heteroaryl, optionally substituted heterocycl, optionally substituted heterocycl(alkylene), C₁₋₆hydroxyalkyl, C₁₋₆haloalkoxy, C₁₋₆haloalkoxy(alkylene), C₁₋₆alkoxy, C₁₋₆alkoxy(alkylene), C₁₋₆deuteratedalkoxy(alkylene), C₁₋₆alkylcarbonyl, C₃₋₈cycloalkylsulfonyl, C₁₋₆alkylsulfonyl, C₁₋₆alkylsulfonyl(alkylene), (CR^yR^x)_pNR^yR^z (wherein R^y and R^x are, independently, H or C₁₋₆alkyl; R^y and R^z, are independently, H, C₁₋₆alkyl, C₃₋₆cycloalkyl, C₁₋₆hydroxyalkyl, C₁₋₆haloalkyl, C₁₋₆alkoxy(alkylene), or C(O)OC₁₋₆alkyl and p is 0, 1, 2, or 3), or C(O)NR^{y2}R^{z2} (wherein R^{y2} and R^{z2}, are independently, H, C₁₋₆alkyl, or C₃₋₆cycloalkyl). In other embodiments, R² is optionally substituted with C₁₋₆alkyl, such as methyl, ethyl, propyl, isopropyl, or tert-butyl. In yet further embodiments, R² is optionally substituted with C₂₋₆alkenyl such as CH=CH₂, CH=CHC(CH₃)₂OH, or CH=CH-cyclopropyl. In further embodiments, R² is optionally substituted with halo such as Br, Cl, or F. In yet other embodiments, R² is optionally substituted with CN. In still further embodiments, R² is optionally substituted with C₁₋₆cyanooalkyl such as C(CH₃)₂CN. In other embodiments, R² is optionally substituted with C₁₋₆haloalkyl, such as CF₃, CHF₂, CH₂F, CH(CH₃)F, CH₂CF₃, C(CH₃)₂F, C(CH₃)F₂, or CH₂CHF₂. In further embodiments, R² is optionally substituted with OH. In still other embodiments, R² is optionally substituted with optionally substituted C₃₋₈cycloalkyl, such as optionally substituted cyclopropyl, optionally substituted cyclobutyl, optionally substituted cyclopentyl, or optionally substituted cyclohexyl. In further embodiments, R² is optionally substituted with optionally substituted C₃₋₈cycloalkyl(alkylene) such as optionally substituted cyclopropyl(alkylene) or optionally substituted cyclobutyl(alkylene). In other embodiments, R² is optionally substituted with optionally substituted C₃₋₈cycloalkenyl, such as optionally substituted cyclohexenyl. In yet further embodiments, R² is optionally substituted with optionally substituted aryl such as optionally substituted phenyl. In further embodiments, R² is optionally substituted with optionally substituted aryl(alkylene) such as optionally substituted benzyl. In other embodiments, R² is optionally substituted with optionally substituted heteroaryl, such as optionally substituted pyrazolyl, optionally substituted imidazolyl, optionally substituted pyridinyl, optionally substituted pyrimidinyl, or optionally substituted pyrazinyl. In yet other embodiments, R² is optionally substituted with optionally substituted heteroaryl, such as optionally substituted pyrazolyl, optionally substituted imidazolyl, optionally substituted pyridinyl, optionally substituted pyrimidinyl, optionally substituted pyrazinyl, or optionally substituted pyridazinyl. In further embodiments, R² is optionally substituted with optionally substituted heterocycl such as optionally substituted azetidinyl, optionally substituted piperidinyl, optionally substituted piperazinyl, optionally substituted pyrrolidinyl, optionally substituted morpholinyl, or optionally substituted 6-azaspiro[2.5]octan-6-yl. In yet further embodiments, R² is optionally substituted with optionally substituted morpholinyl(alkylene), or optionally substituted piperidinyl(alkylene),

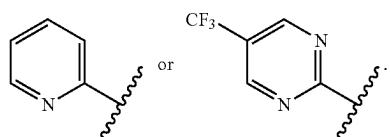
optionally substituted piperazinyl(alkylene), or optionally substituted azetidinyl(alkylene). In still other embodiments, R² is optionally substituted with C₁₋₆hydroxyalkyl such as C(CH₃)₂OH, CH(CH₃)OH, C(CH₃)₂CH₂OH, CH₂C(CH₃)₂OH, or CH(CH₂CH₃)OH. In yet further embodiments, R² is optionally substituted with C₁₋₆haloalkoxy such as OCF₃, OCH₂CF₃, or OCH₂CH₂CF₃. In still further embodiments, R² is optionally substituted with C₁₋₆haloalkoxy(alkylene) such as CH₂OCF₃. In other embodiments, R² is optionally substituted with C₁₋₆alkoxy, such as methoxy or ethoxy. In yet other embodiments, R² is optionally substituted with C₁₋₆alkoxy(alkylene), such as C(CH₃)₂OCH₃, CH₂OCH₃, or (CH₂)₂OCH₃. In further embodiments, R² is optionally substituted with C₁₋₆deuteratedalkoxy(alkylene) such as CH₂OCD₃. In further embodiments, R² is optionally substituted with C₁₋₆alkylcarbonyl, such as C(O)CH₃ or CH₂C(O)CH₃. In yet other embodiments, R² is optionally substituted with C₃₋₈cycloalkylsulfonyl such as cyclopropylsulfonyl, cyclobutylsulfonyl, or cyclopentylsulfonyl. In other embodiments, R² is optionally substituted with C₁₋₆alkylsulfonyl such as methylsulfonyl, ethylsulfonyl, or propylsulfonyl. In yet other embodiments, R² is optionally substituted with C₁₋₆alkylsulfonyl(alkylene), such as C(CH₃)₂SO₂CH₃. In still further embodiments, R² is optionally substituted with (CR^yR^x)_pNR^yR^z, wherein R^y, R^x, R^y, R^z, and p are defined above, such as NH₂, NHcyclopropyl, NHCH₃, N(CH₃)₂, CH₂N(CH₃)₂, (CH₂)₂N(CH₃)₂, CH₂N(CH₃)(CH₂CH₃), C(CH₃)₂NH(CH₃), C(CH₃)₂N(CH₃), CH₂N(CH₃)cyclobutyl, or CH₂N(CH₃)(C(O)Ottert-butyl). In some embodiments, p is 0. In other embodiments, p is 1. In further embodiments, p is 2. In still other embodiments, p is 3. In some embodiments, R^y and R^x are, independently, hydrogen or methyl. In other embodiments, R^y and R^z are, independently, hydrogen, methyl, ethyl, cyclopropyl, cyclobutyl, C(O)Omethyl, C(O)Oethyl, C(O)Opropyl, or C(O)Ottert-butyl. In other embodiments, R² is C(O)NR^{y2}R^{z2}, wherein R^{y2} and R^{z2} are defined above, such as C(O)N(CH₃)₂ or C(O)NHcyclopropyl. In yet other embodiments, R^{y2} and R^{z2} are, independently, hydrogen, methyl, or cyclopropyl. In further embodiments, R² is substituted with one or more of methyl, ethyl, propyl, isopropyl, tert-butyl, CH=CH₂, CH=CHC(CH₃)₂OH, CH=CH-cyclopropyl, Br, Cl, F, CN, C(CH₃)₂CN, CF₃, CHF₂, CH₂F, CH(CH₃)F, CH₂CF₃, C(CH₃)₂F, C(CH₃)F₂, CH₂CHF₂, OH, optionally substituted cyclopropyl, optionally substituted cyclobutyl, optionally substituted cyclopentyl, optionally substituted cyclohexyl, optionally substituted cyclohexenyl, optionally substituted cyclopropyl(alkylene), optionally substituted cyclobutyl(alkylene), optionally substituted phenyl, optionally substituted benzyl, optionally substituted pyrazolyl, optionally substituted imidazolyl, optionally substituted pyridinyl, optionally substituted pyrimidinyl, optionally substituted pyrazinyl, or optionally substituted azetidinyl, optionally substituted piperazinyl, optionally substituted pyrrolidinyl, optionally substituted morpholinyl, optionally substituted 6-azaspiro[2.5]octan-6-yl, optionally substituted morpholinyl(alkylene), optionally substituted piperidinyl(alkylene), or optionally substituted azetidinyl(alkylene), C(CH₃)₂OH, CH(CH₃)OH, C(CH₃)₂CH₂OH, CH₂C(CH₃)₂OH, CH(CH₂CH₃)OH, OCH₂CH₂CF₃, OCF₃, OCH₂CF₃, CH₂OCH₃, methoxy, ethoxy, C(CH₃)₂OCH₃, CH₂OCH₃, (CH₂)₂OCH₃, CH₂OCD₃, C(O)CH₃, CH₂C(O)CH₃, cyclopropylsulfonyl, cyclobutylsulfonyl, cyclopentylsulfonyl,

$\text{C}(\text{CH}_3)_2\text{SO}_2\text{CH}_3$, NH_2 , NHcyclopropyl , NHCH_3 , $\text{N}(\text{CH}_3)_2$, $\text{CH}_2\text{N}(\text{CH}_3)_2$, $(\text{CH}_2)_2\text{N}(\text{CH}_3)_2$, $\text{CH}_2\text{N}(\text{CH}_3)(\text{CH}_2\text{CH}_3)$, $\text{C}(\text{CH}_3)_2\text{NH}(\text{CH}_3)$, $\text{C}(\text{CH}_3)_2\text{N}(\text{CH}_3)_2$, $\text{CH}_2\text{N}(\text{CH}_3)\text{cyclobutyl}$, $\text{CH}_2\text{N}(\text{CH}_3)(\text{C}(\text{O})\text{Otert-butyl})$, $\text{C}(\text{O})\text{N}(\text{CH}_3)_2$, or $\text{C}(\text{O})\text{NHcyclopropyl}$.

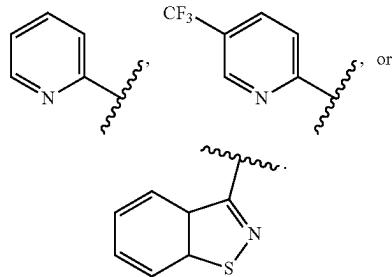
[0112] In yet further embodiments, R^2 is



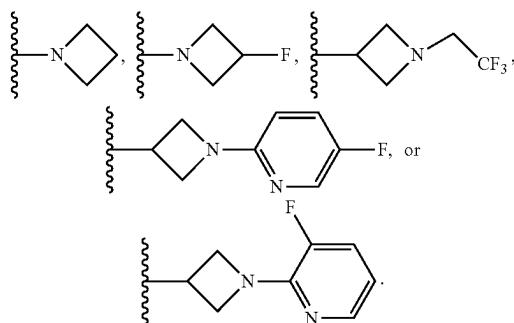
In other embodiments, R^2 is



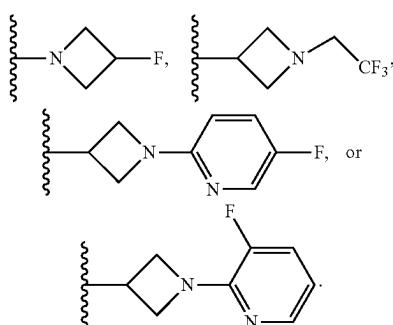
In yet other embodiments, R^2 is



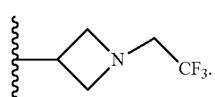
[0113] In some embodiments, R^2 is heterocyclyl, optionally substituted with one or more of halo, C_{1-6} -haloalkyl, or optionally substituted heteroaryl. In yet other embodiments, R^2 is heterocyclyl, substituted with one or more of halo, C_{1-6} -haloalkyl, or optionally substituted heteroaryl. In still other embodiments, R^2 is



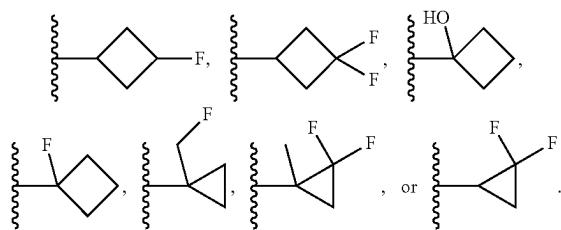
In further embodiments, R^2 is



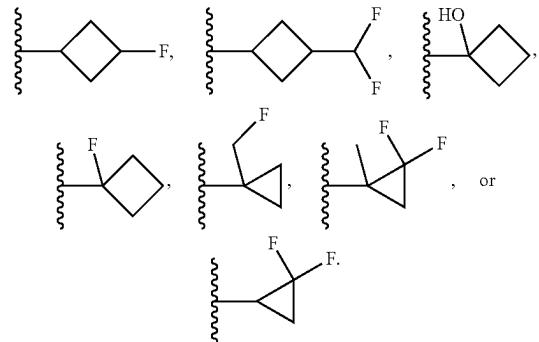
In still further embodiments, R^2 is



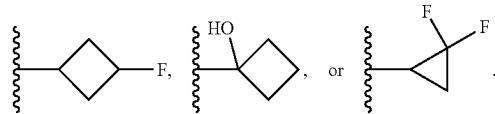
[0114] In some embodiments, R^2 is C_{3-8} cycloalkyl, optionally substituted with one or more of halo, C_{1-6} alkyl, C_{1-6} -haloalkyl, or OH. In yet other embodiments, R^2 is unsubstituted cyclopropyl, unsubstituted cyclobutyl, unsubstituted cyclopentyl, unsubstituted cyclohexyl,



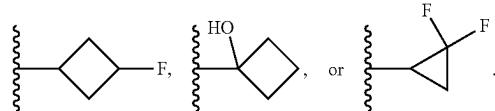
In further embodiments, R^2 is C_{3-8} cycloalkyl, substituted with one or more of halo, C_{1-6} alkyl, C_{1-6} haloalkyl, or OH. In still further embodiments, R^2 is



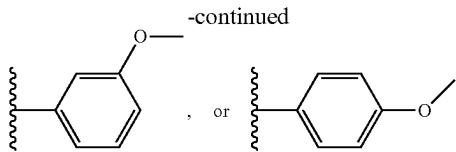
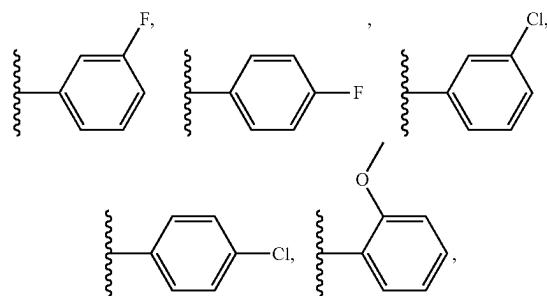
In other embodiments, R^2 is



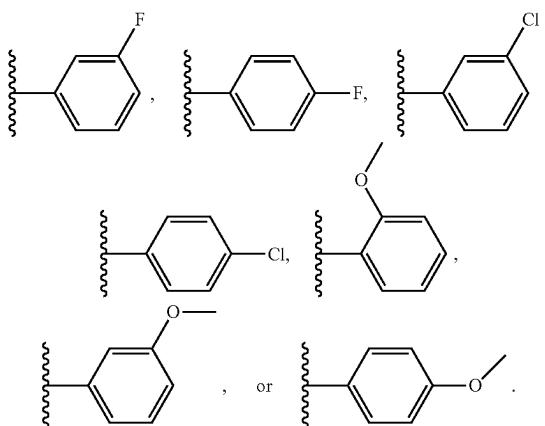
In yet other embodiments, R^2 is unsubstituted cyclopropyl,



[0115] In some embodiments, R^2 is aryl, optionally substituted with one or more of halo or C_{1-6} alkoxy. In other embodiments, R^2 is unsubstituted phenyl,



In yet other embodiments, R^2 is aryl, substituted with one or more of halo or C_{1-6} alkoxy. In further embodiments, R^2 is

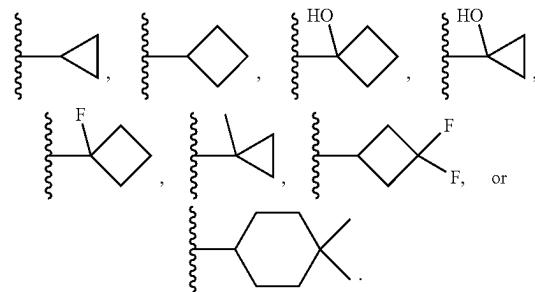


[0116] In some embodiments, R^2 is optionally substituted pyridinyl, optionally substituted pyrimidinyl, or optionally substituted pyrazinyl. In other embodiments, the pyridinyl, pyrimidinyl, or pyrazinyl group is substituted with one or more of halo, C_{1-6} haloalkyl, cyano, or NR^yR^z , wherein R^y and R^z are independently H or C_{1-6} alkyl.

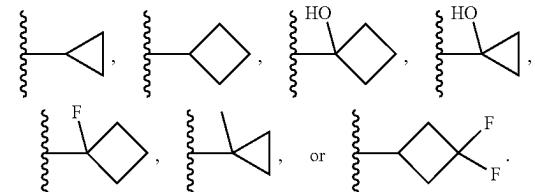
[0117] In still further embodiments, R^2 is heteroaryl, substituted with one or more of C_{1-6} alkyl, C_{1-6} cyanoalkyl, C_{1-6} haloalkyl, or C_{1-6} hydroxyalkyl. In other embodiments, R^2 is heteroaryl substituted with one or more of C_{1-6} alkyl. In yet other embodiments, R^2 is heteroaryl substituted with one or more of C_{1-6} cyanoalkyl. In further embodiments, R^2 is heteroaryl substituted with one or more of C_{1-6} haloalkyl. In still further embodiments, R^2 is heteroaryl substituted with one or more of C_{1-6} fluoroalkyl. In yet other embodiments, R^2 is heteroaryl substituted with one or more of C_{1-6} hydroxyalkyl. In other embodiments, R^2 is heteroaryl, substituted with one or more of methyl, ethyl, isopropyl, tert-butyl, $C(CH_3)_2CN$, $CH(CH_3)OH$, $C(CH_3)_2OH$, $C(CH_3)_2CH_2OH$, $CH(CH_2CH_3)OH$, $CH_2C(CH_3)_2OH$, CH_2F , CHF_2 , CF_3 , CH_2CF_3 , CH_2CHF_2 , $CH(CH_3)F$, $C(CH_3)_2F$, or $C(CH_3)_2F$. In yet other embodiments, R^2 is heteroaryl, substituted with one or more of methyl, isopropyl, tert-butyl, $C(CH_3)_2CN$, $CH(CH_3)OH$, $C(CH_3)_2OH$, CHF_2 , CF_3 , CH_2CF_3 , $CH(CH_3)F$, or $C(CH_3)_2F$. In other embodiments, R^2 is heteroaryl, substituted with methyl. In yet other embodiments, R^2 is heteroaryl, substituted with isopropyl. In other embodiments, R^2 is heteroaryl, substituted with tert-butyl. In yet other embodiments, R^2 is heteroaryl, substituted with $C(CH_3)_2CN$. In still further embodiments, R^2 is heteroaryl, substituted with $CH(CH_3)OH$. In other embodiments, R^2 is heteroaryl, substituted with $C(CH_3)_2OH$. In further embodiments, R^2 is heteroaryl, substituted with CHF_2 . In still other embodiments, R^2 is heteroaryl, substituted with CF_3 . In further embodiments, R^2 is heteroaryl,

substituted with CH_2CF_3 . In still other embodiments, R^2 is heteroaryl, substituted with $\text{CH}(\text{CH}_3)\text{F}$. In other embodiments, R^2 is heteroaryl, substituted with $\text{C}(\text{CH}_3)_2\text{F}$.

[0118] In other embodiments, R^2 is heteroaryl, substituted with $\text{C}_{3-8}\text{cycloalkyl}$, wherein the $\text{C}_{3-8}\text{cycloalkyl}$ itself is optionally substituted with one or more of halo, OH, $\text{C}_{1-6}\text{haloalkyl}$, $\text{C}_{1-6}\text{alkyl}$ or $\text{C}_{1-6}\text{alkoxy}$. In yet other embodiments, R^2 is heteroaryl, substituted with an unsubstituted $\text{C}_{3-8}\text{cycloalkyl}$, such as cyclopropyl, cyclobutyl, cyclopentyl, or cyclohexyl. In further embodiments, R^2 is heteroaryl, substituted with cyclopropyl or cyclobutyl. In yet other embodiments, R^2 is heteroaryl, substituted with $\text{C}_{3-8}\text{cycloalkyl}$, such as cyclopropyl, cyclobutyl, cyclopentyl, or cyclohexyl, wherein the $\text{C}_{3-8}\text{cycloalkyl}$ itself is substituted with one or more of halo, OH, $\text{C}_{1-6}\text{haloalkyl}$, $\text{C}_{1-6}\text{alkyl}$ or $\text{C}_{1-6}\text{alkoxy}$. In some embodiments, the substituted $\text{C}_{3-8}\text{cycloalkyl}$ is substituted with OH. In still further embodiments, the substituted $\text{C}_{3-8}\text{cycloalkyl}$ is substituted with one or more of halo, such as F, Cl, or Br. In other embodiments, the substituted $\text{C}_{3-8}\text{cycloalkyl}$ is substituted with $\text{C}_{1-6}\text{alkyl}$, such as methyl, ethyl, or propyl. In further embodiments, the substituted $\text{C}_{3-8}\text{cycloalkyl}$ is substituted with $\text{C}_{1-6}\text{haloalkyl}$, such as CF_3 , CH_2CF_3 , or CHF_2 . In still other embodiments, the substituted $\text{C}_{3-8}\text{cycloalkyl}$ is substituted with $\text{C}_{1-6}\text{alkoxy}$, such as methoxy, ethoxy, or propoxy. In further embodiments, the substituted $\text{C}_{3-8}\text{cycloalkyl}$ is cyclopropyl or cyclobutyl, each of which is substituted with one or more of F, OH, or methyl. In other embodiments, R^2 is heteroaryl, substituted with

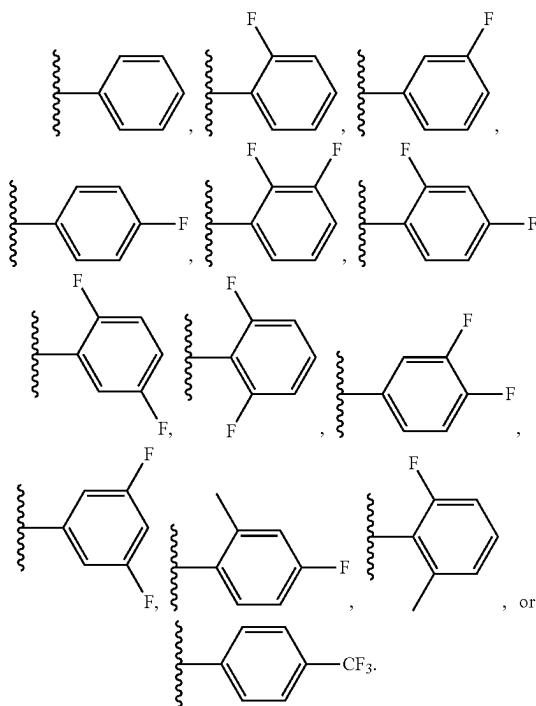


In still other embodiments, R^2 is heteroaryl, substituted with

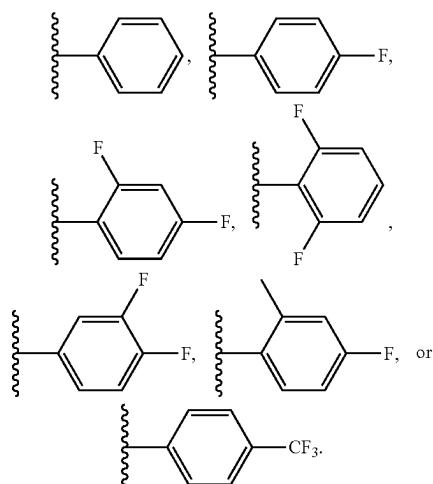


[0119] In other embodiments, R^2 is heteroaryl, substituted with aryl, wherein the aryl itself is optionally substituted with one or more of halo, $\text{C}_{1-6}\text{haloalkyl}$, $\text{C}_{1-6}\text{alkyl}$, or $\text{C}_{3-8}\text{cycloalkyl}$. In yet other embodiments, R^2 is heteroaryl, substituted with an unsubstituted phenyl. In further embodiments, R^2 is heteroaryl, substituted with aryl, such as phenyl, wherein the aryl itself is substituted with one or more of halo, $\text{C}_{1-6}\text{haloalkyl}$, $\text{C}_{1-6}\text{alkyl}$, or $\text{C}_{3-8}\text{cycloalkyl}$. In some embodiments, the substituted aryl is substituted with one or

more of halo, such as F, Cl, or Br. In yet other embodiments, the substituted aryl is substituted with $\text{C}_{1-6}\text{haloalkyl}$, such as CF_3 , CH_2CF_3 , or CHF_2 . In still further embodiments, the substituted aryl is substituted with $\text{C}_{1-6}\text{alkyl}$, such as methyl, ethyl, or propyl. In other embodiments, the substituted aryl is substituted with $\text{C}_{3-8}\text{cycloalkyl}$, such as cyclopropyl, cyclobutyl, or cyclopentyl. In yet other embodiments, the substituted aryl is phenyl that is substituted with one or more of F, methyl, or CF_3 . In further embodiments, R^2 is heteroaryl, substituted with



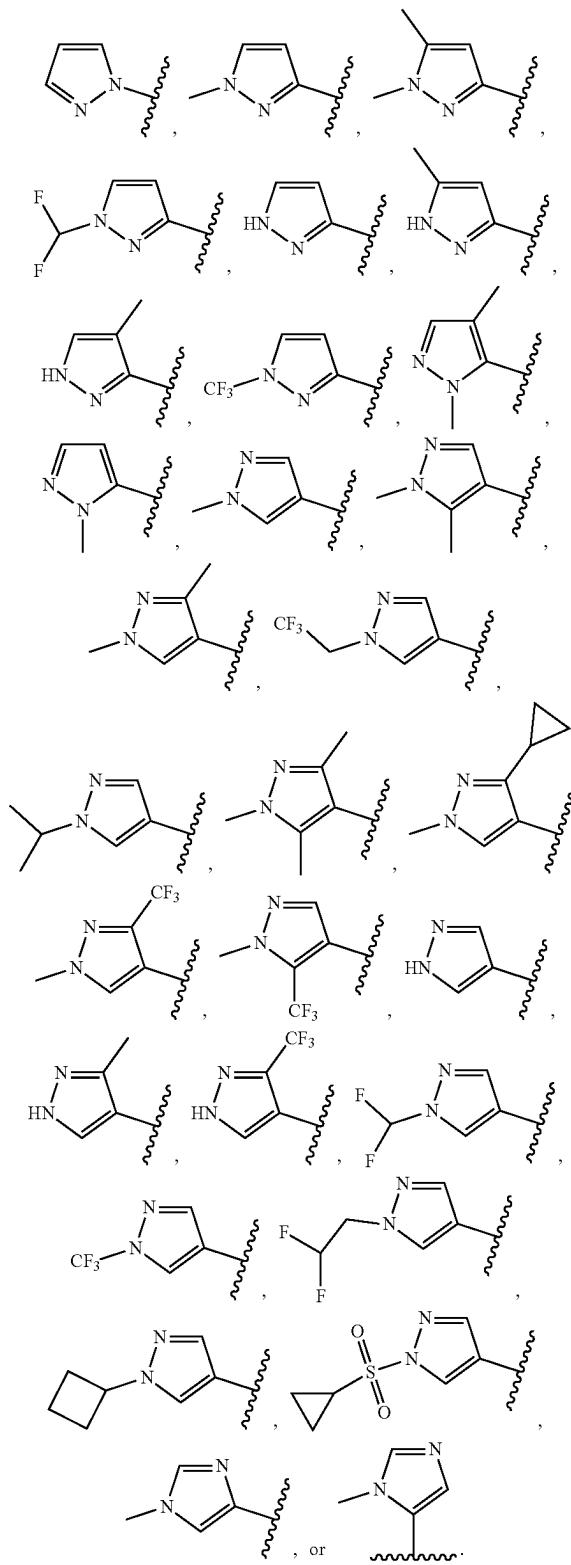
In still further embodiments, R^2 is heteroaryl, substituted with



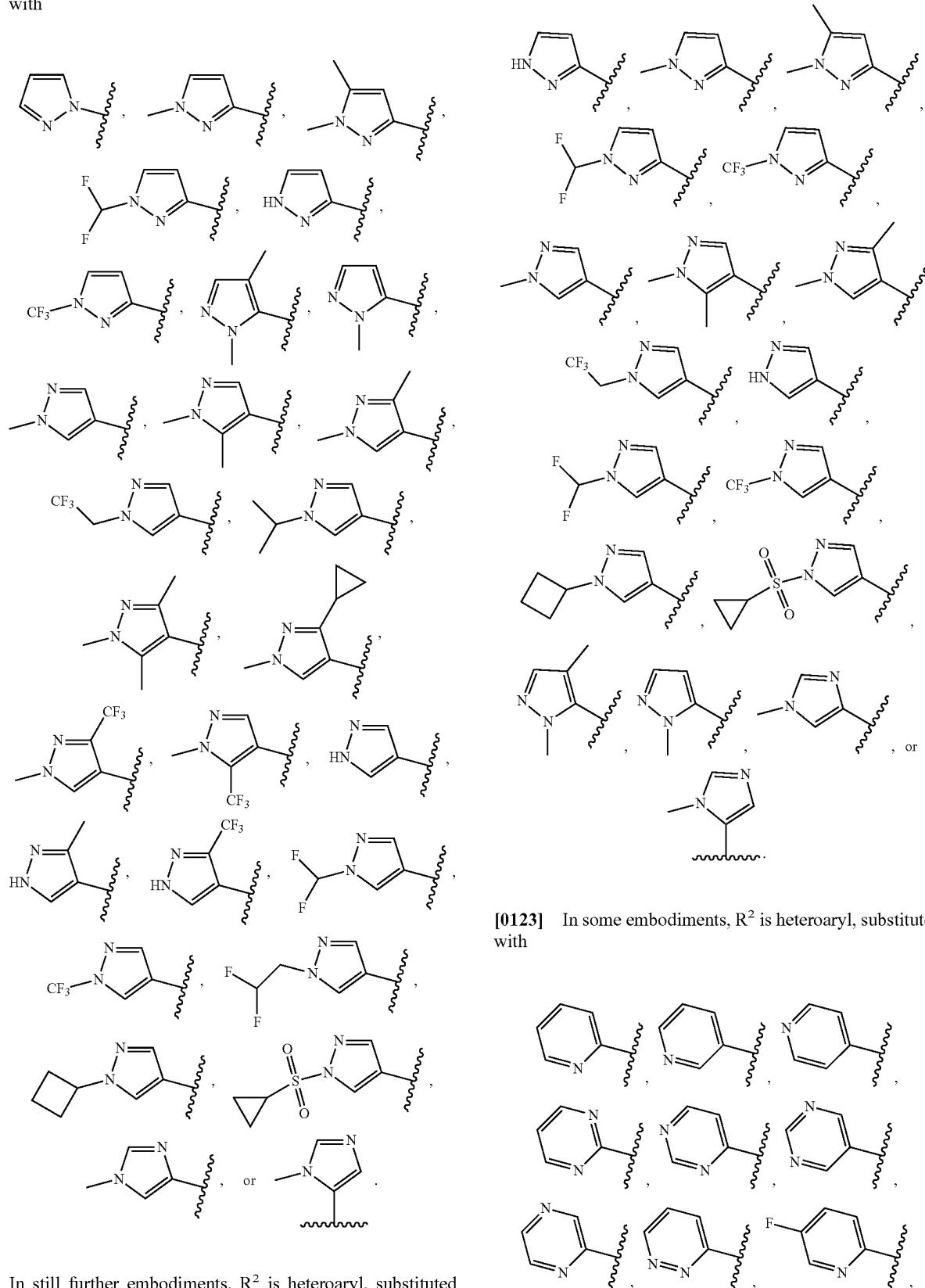
[0120] In still further embodiments, R² is heteroaryl, substituted with an optionally substituted heteroaryl. In some embodiments, the optionally substituted heteroaryl is optionally substituted pyridinyl, optionally substituted pyrazinyl, optionally substituted pyrazolyl, optionally substituted imidazolyl, or optionally substituted pyrimidinyl. In yet other embodiments, the optional substitution on the heteroaryl is one or more of halo, C₁₋₆haloalkyl, C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆haloalkoxy, C₃₋₈cycloalkyl or C₃₋₈cycloalkylsulfonyl. In other embodiments, the optionally substituted heteroaryl is substituted with one or more of halo, such as F, Cl, or Br. In still other embodiments, the optionally substituted heteroaryl is substituted with one or more of C₁₋₆haloalkyl, such as CF₃, CH₂CF₃, CH₂CHF₂, or CHF₂. In other embodiments, the optionally substituted heteroaryl is substituted with one or more of C₁₋₆alkyl, such as methyl, ethyl, propyl, or isopropyl. In still other embodiments, the optionally substituted heteroaryl is substituted with one or more of C₁₋₆alkoxy, such as methoxy, ethoxy, or propoxy. In other embodiments, the optionally substituted heteroaryl is substituted with one or more of C₁₋₆haloalkoxy, such as OCF₃. In yet other embodiments, the optionally substituted heteroaryl is substituted with one or more of C₃₋₈cycloalkyl, such as cyclopropyl, cyclobutyl, or cyclopentyl. In other embodiments, the optionally substituted heteroaryl is substituted with one or more of C₃₋₈cycloalkylsulfonyl, such as cyclopropylsulfonyl, cyclobutylsulfonyl, or cyclopentylsulfonyl. In still other embodiments, the optionally substituted heteroaryl is substituted with one or more of F, CF₃, CH₂CHF₂, CHF₂, methyl, methoxy, cyclobutyl, or cyclopropylsulfonyl.

[0121] In yet other embodiments, R² is heteroaryl, substituted with pyrazol-1-yl, pyrazol-3-yl, pyrazol-4-yl, pyrazol-5-yl, pyridin-2-yl, pyridin-3-yl, pyridin-4-yl, pyrimidin-2-yl, pyrimidin-4-yl, pyrimidin-5-yl, pyrazin-2-yl, pyrazin-3-yl, pyrazin-4-yl, pyrazin-5-yl, imidazol-4-yl, or imidazol-5-yl, each of which can be optionally substituted. In further embodiments, R² is substituted with pyrazol-1-yl, pyrazol-3-yl, pyrazol-4-yl, pyrazol-5-yl, pyridin-2-yl, pyridin-3-yl, pyridin-4-yl, pyrimidin-2-yl, pyrimidin-4-yl, pyrimidin-5-yl, pyrazin-2-yl, pyrazin-3-yl, pyrazin-4-yl, pyrazin-5-yl, imidazol-4-yl, imidazol-5-yl, pyridazin-3-yl, pyridazin-4-yl, each of which is optionally substituted. In still further embodiments, R² is substituted with optionally substituted pyrazol-1-yl. In other embodiments, R² is substituted with optionally substituted pyrazol-3-yl. In further embodiments, R² is substituted with optionally substituted pyrazol-4-yl. In yet further embodiments, R² is substituted with optionally substituted pyridin-2-yl. In other embodiments, R² is substituted with optionally substituted pyridin-3-yl. In further embodiments, R² is substituted with optionally substituted pyridin-4-yl. In further embodiments, R² is substituted with optionally substituted imidazol-4-yl. In yet other embodiments, R² is substituted with optionally substituted imidazol-5-yl. In further embodiments, R² is substituted with optionally substituted pyrimidin-2-yl. In other embodiments, R² is substituted with optionally substituted pyrimidin-4-yl. In still further embodiments, R² is substituted with optionally substituted pyrimidin-5-yl. In yet other embodiments, R² is substituted with optionally substituted pyrazin-2-yl. In other embodiments, R² is substituted with optionally substituted pyridazin-3-yl. In further embodiments, R² is substituted with optionally substituted pyridazin-4-yl.

[0122] In some embodiments, R² is heteroaryl, substituted with

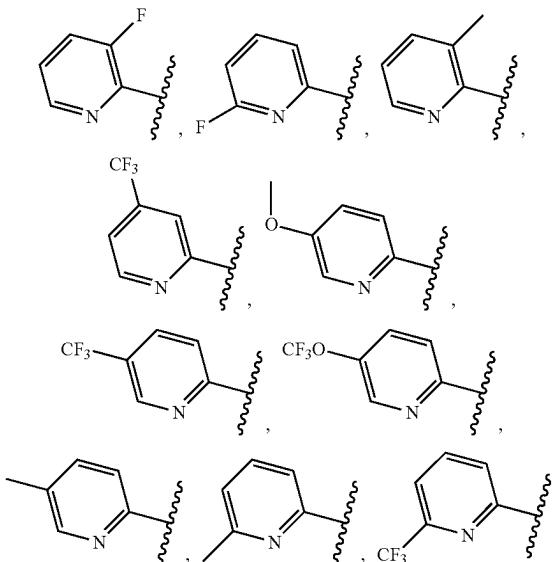


In still further embodiments, R² is heteroaryl, substituted with

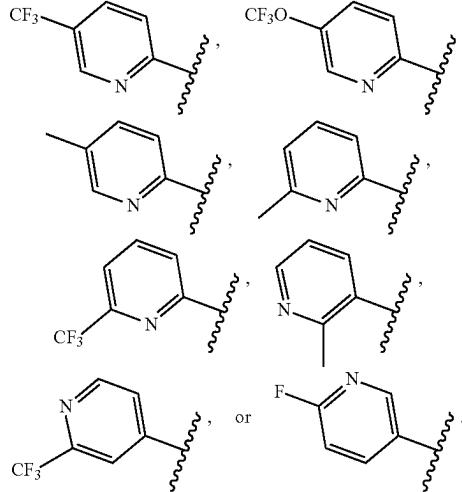
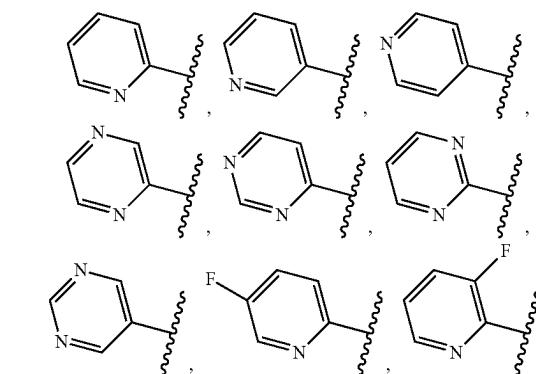
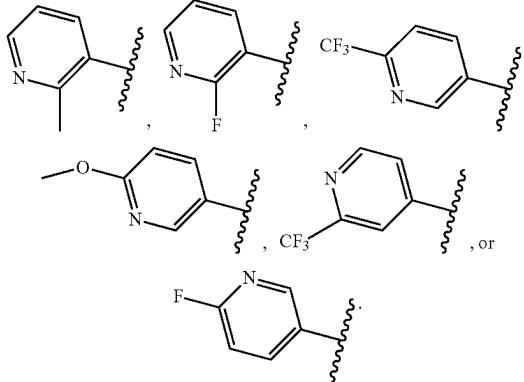
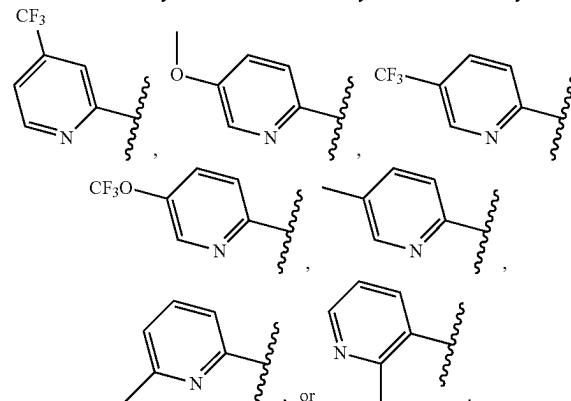
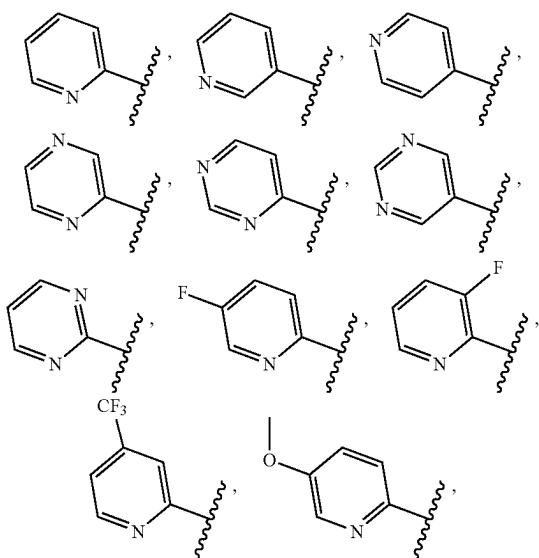


In still further embodiments, R² is heteroaryl, substituted with

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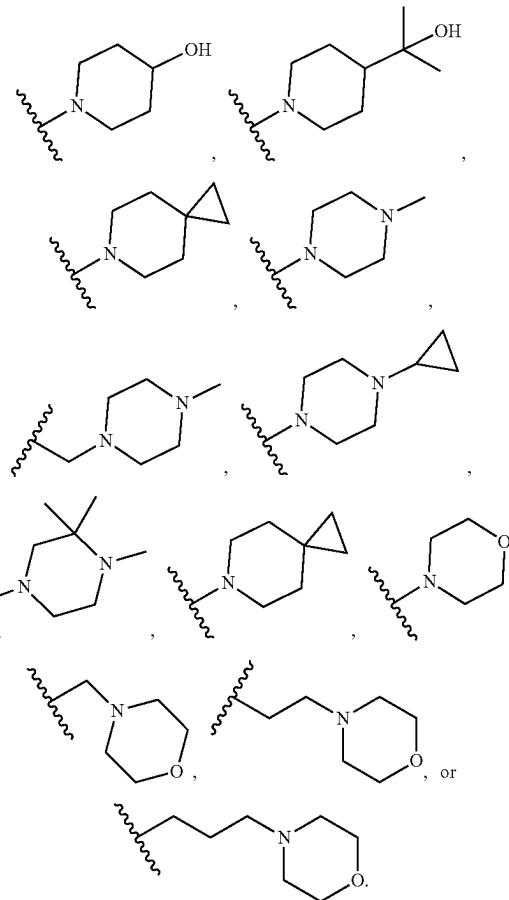
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In still other embodiments, R² is heteroaryl, substituted withIn other embodiments, R² is heteroaryl, substituted with

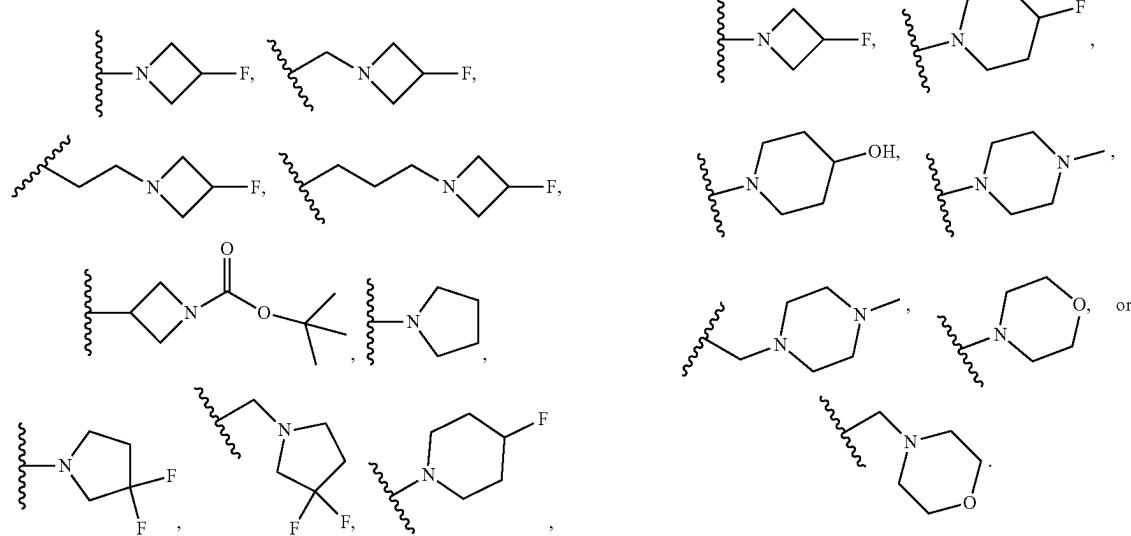
[0124] In other embodiments, R² is heteroaryl, substituted with heterocycl or heterocycl(alkylene), wherein the heterocycl and heterocycl(alkylene) groups themselves are each optionally substituted with one or more of halo, OH, C₁₋₆haloalkyl, C₁₋₆alkyl, C₁₋₆hydroxyalkyl, C₁₋₆alkoxy, C(O)O(C₁₋₆alkyl), or C₃₋₈cycloalkyl. In yet other embodiments, R² is heteroaryl, substituted with an unsubstituted heterocycl group such as azetidinyl, pyrrolidinyl, piperidinyl, piperazinyl, morpholinyl, or 6-azaspiro

[2.5]octan-6-yl, or unsubstituted heterocycl(alkylene) group, such as azetidinyl(alkylene), pyrrolidinyl(alkylene), piperidinyl(alkylene), piperazinyl(alkylene), or morpholinyl(alkylene). In further embodiments, R² is heteroaryl, substituted with heterocycl, such as azetidinyl, pyrrolidinyl, piperidinyl, piperazinyl, or morpholinyl, or heterocycl(alkylene), such as azetidinyl(alkylene), pyrrolidinyl(alkylene), piperidinyl(alkylene), piperazinyl(alkylene), or morpholinyl(alkylene), wherein the heterocycl and heterocycl(alkylene) groups themselves are each substituted with one or more of halo, OH, C₁₋₆haloalkyl, C₁₋₆alkyl, C₁₋₆hydroxalkyl, C₁₋₆alkoxy, C(O)O(C₁₋₆alkyl), or C₃₋₈cycloalkyl. In further embodiments, the substituted heterocycl or substituted heterocycl(alkylene) is substituted with one or more of halo, such as F, Cl, or Br. In yet further embodiments, the substituted heterocycl or substituted heterocycl(alkylene) is substituted with one or more of OH. In yet other embodiments, the substituted heterocycl or substituted heterocycl(alkylene) is substituted with one or more of C₁₋₆haloalkyl, such as CF₃, CH₂CF₃, or CHF₂. In still further embodiments, the substituted heterocycl or substituted heterocycl(alkylene) is substituted with one or more of C₁₋₆alkyl, such as methyl, ethyl, or propyl. In yet further embodiments, the substituted heterocycl or substituted heterocycl(alkylene) is substituted with one or more of C₁₋₆hydroxalkyl such as C(CH₃)₂OH, or CH(CH₃)OH. In other embodiments, the substituted heterocycl or substituted heterocycl(alkylene) is substituted with one or more of C₁₋₆alkoxy, such as methoxy, ethoxy, or propoxy. In yet other embodiments, the substituted heterocycl or substituted heterocycl(alkylene) is substituted with one or more of C(O)O(C₁₋₆alkyl), such as C(O)Omethyl, C(O)Oethyl, C(O)Opropyl, or C(O)Otert-butyl. In further embodiments, the substituted heterocycl or substituted heterocycl(alkylene) is substituted with one or more of C₃₋₈cycloalkyl, such as cyclopropyl, cyclobutyl, or cyclopentyl. In yet other embodiments, the substituted heterocycl or substituted heterocycl(alkylene) is substituted with one or more of F, OH, or methyl. In yet other embodiments where R² is heteroaryl, the R² is substituted with

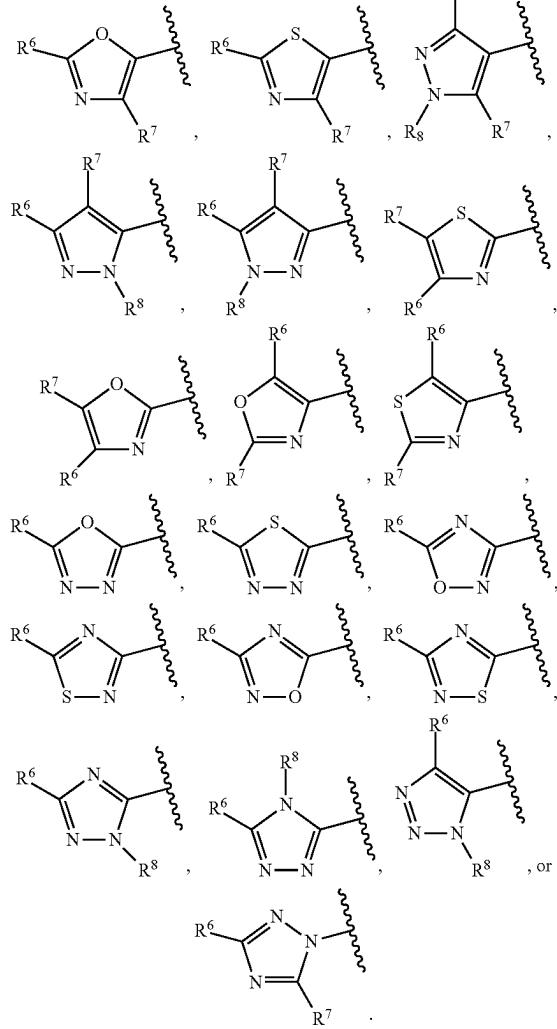
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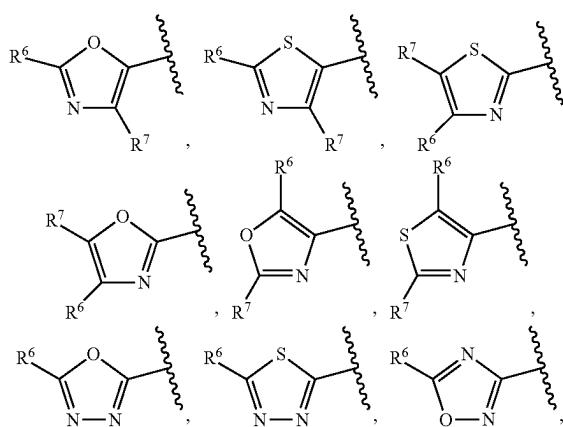
In still further embodiments where R² is heteroaryl, the R² is substituted with



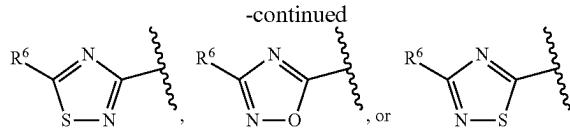
[0125] In further embodiments, R² is



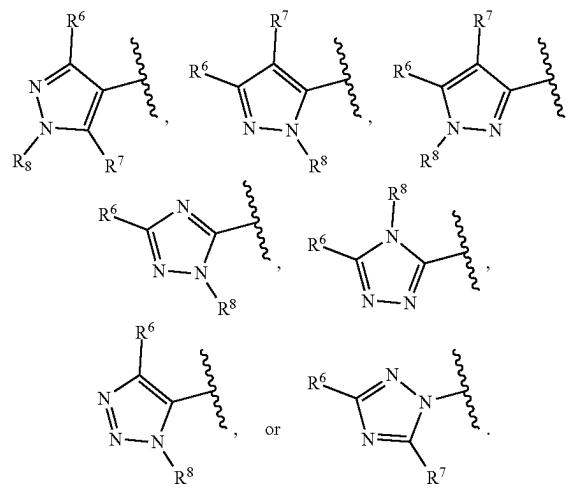
In yet further embodiments, R² is



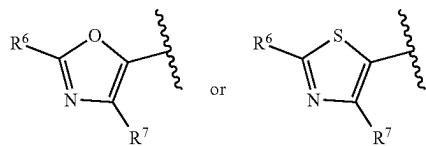
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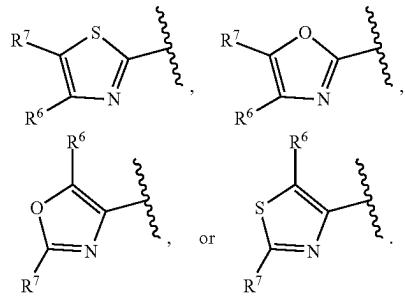
In still further embodiments, R² is,



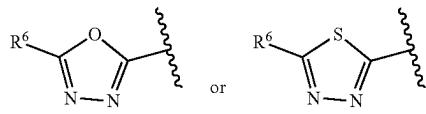
In other embodiments, R² is



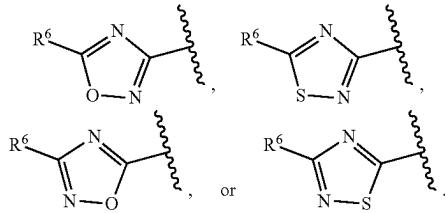
In further embodiments, R² is



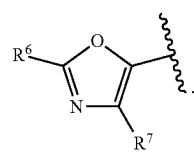
In yet further embodiments, R² is



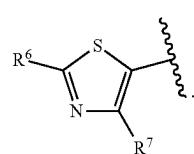
In still further embodiments, R² is



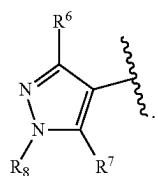
In yet other embodiments, R² is



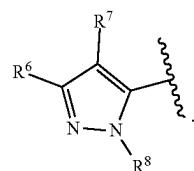
In other embodiments, R² is



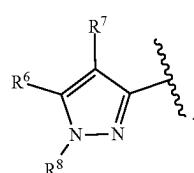
In further embodiments, R² is



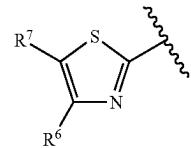
In yet other embodiments, R² is



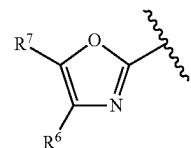
In still further embodiments, R² is



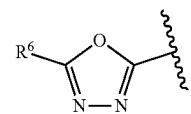
In other embodiments, R² is



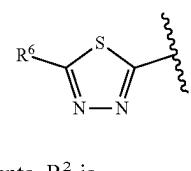
In further embodiments, R² is



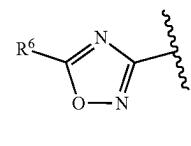
In still other embodiments, R² is



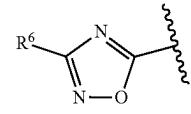
In yet further embodiments, R² is



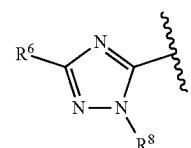
In other embodiments, R² is



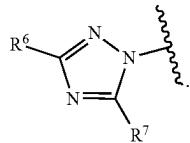
In further embodiments, R² is



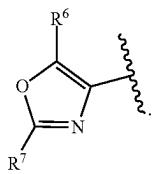
In yet other embodiments, R² is



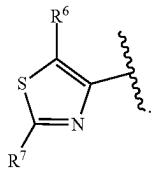
In still further embodiments, R² is



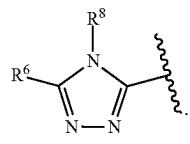
In other embodiments, R² is



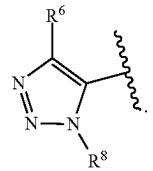
In other embodiments, R² is



In further embodiments, R² is



In yet other embodiments, R² is

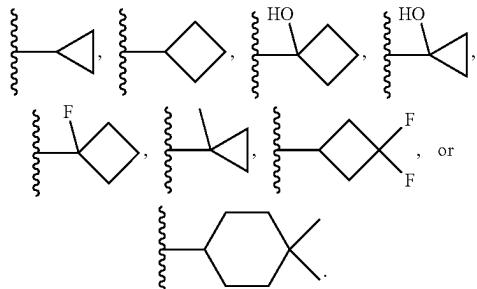


[0126] In these structures for R², R⁶ and R⁷ are each independently, H, CN, C₁₋₆alkyl, C₁₋₆haloalkyl, C₁₋₆cynoalkyl, C₁₋₆hydroxyalkyl, C₁₋₆alkoxy, C₁₋₆alkoxy(alkylene), C₁₋₆haloalkoxy, C₁₋₆haloalkoxy(alkylene), C₁₋₆deuterated-alkoxy(alkylene), halo, (CR'^vR^x)_pNR^yR^z, C(O)NR^{y2}R^{z2}, C₁₋₆alkylcarbonyl, optionally substituted C₃₋₈cycloalkyl, optionally substituted heterocycl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted C₂₋₆alkenyl, optionally substituted C₃₋₈cycloalkenyl, optionally substituted (C₃₋₈cycloalkyl)alkylene, optionally substituted (aryl)alkylene, optionally substituted (heterocycl)alkylene, or C₁₋₆alkylsulfonyl; R⁸ is H, C₁₋₆alkyl, C₁₋₆haloalkyl, C₁₋₆alkoxy(alkylene), C₁₋₆alkylcarbonyl,

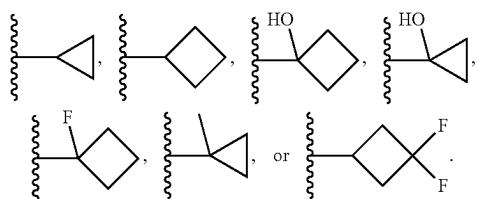
C₁₋₆hydroxyalkyl, (CR'^vR^x)_pNR^yR^z optionally substituted C₃₋₈cycloalkyl, optionally substituted aryl, optionally substituted heteroaryl, or optionally substituted (C₃₋₈cycloalkyl)alkylene; R^v and R^x are, independently, H or C₁₋₆alkyl; R^y and R^z are, independently, H, C₁₋₆alkyl, C₁₋₆alkoxy(alkylene), or C₃₋₆cycloalkyl; R^{y2} and R^{z2} are, independently, H, C₁₋₆alkyl, or C₃₋₆cycloalkyl; and p is 0, 1, 2, or 3. In some embodiments, R⁶, R⁷, and R⁸ are H.

[0127] In other embodiments, R⁶ is C₁₋₆alkyl, C₁₋₆haloalkyl, C₁₋₆cynoalkyl, or C₁₋₆hydroxyalkyl. In further embodiments, R⁶ is C₁₋₆alkyl such as methyl, ethyl, isopropyl or tert-butyl. In still further embodiments, R⁶ is C₁₋₈haloalkyl such as CF₃, CHF₂, CH₂F, CH₂CF₃, CH(CH₃)F, C(CH₃)F₂, or C(CH₃)₂F. In further embodiments, R⁶ is C₁₋₆cynoalkyl such as C(CH₃)₂CN. In other embodiments, R⁶ is C₁₋₆hydroxyalkyl such as C(CH₃)₂OH, CH(CH₃)OH, CH(CH₂CH₃)OH, CH₂C(CH₃)₂OH, or C(CH₃)₂CH₂OH. In further embodiments, R⁶ is methyl, isopropyl, tert-butyl, CF₃, CHF₂, C(CH₃)F₂, C(CH₃)₂F, C(CH₃)₂OH, or CH(CH₃)OH.

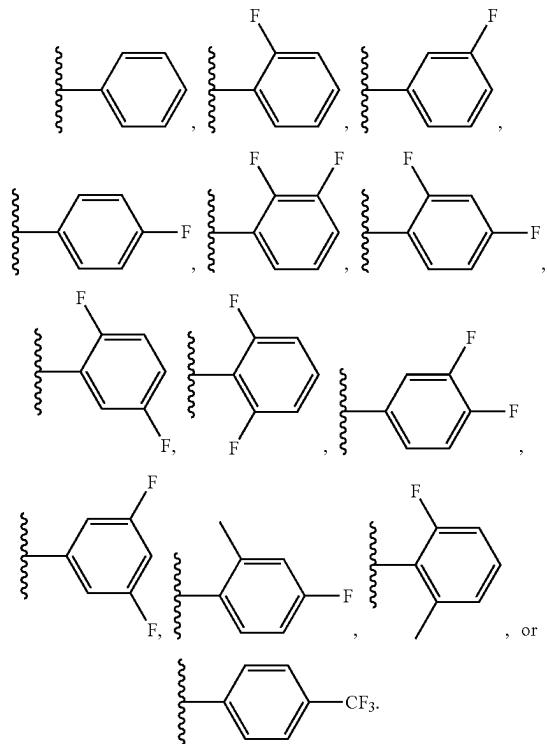
[0128] In other embodiments, R⁶ is C₃₋₆cycloalkyl optionally substituted with one or more of halo, OH, C₁₋₈haloalkyl, C₁₋₆alkyl, or C₁₋₆alkoxy. In further embodiments, R⁶ is cyclopropyl, cyclobutyl, cyclopentyl or cyclohexyl, optionally substituted with one or more of halo, OH, C₁₋₆haloalkyl, C₁₋₆alkyl, or C₁₋₆alkoxy. In still further embodiments, R⁶ is unsubstituted cyclopropyl, cyclobutyl, cyclopentyl or cyclohexyl. In other embodiments, R⁶ is C₃₋₆cycloalkyl substituted with one or more halo such as F, Cl, or Br. In yet other embodiments, R⁶ is C₃₋₆cycloalkyl substituted with one or more OH. In still further embodiments, R⁶ is C₃₋₆cycloalkyl substituted with one or more C₁₋₆haloalkyl such as CF₃, CH₂CF₃, or CHF₂. In further embodiments, R⁶ is C₃₋₆cycloalkyl substituted with one or more C₁₋₆alkyl such as methyl, ethyl, or propyl. In still further embodiments, R⁶ is C₃₋₆cycloalkyl substituted with C₁₋₆alkoxy, such as one or more methoxy, ethoxy, or propoxy. In other embodiments, R⁶ is cyclopropyl, cyclobutyl, or cyclohexyl, each of which is optionally substituted with one or more of F, OH, or methyl. In other embodiments, R⁶ is



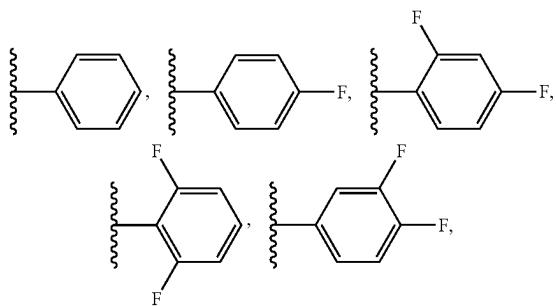
In other embodiments, R⁶ is



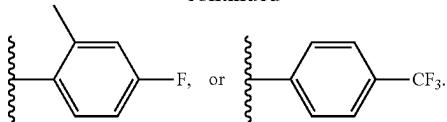
[0129] In further embodiments, R⁶ is aryl optionally substituted with one or more of halo, C₁₋₆haloalkyl, C₁₋₆alkyl or C₃₋₆cycloalkyl. In other embodiments, R⁶ is phenyl optionally substituted with one or more of halo, C₁₋₆haloalkyl, C₁₋₆alkyl or C₃₋₆cycloalkyl. In still other embodiments, R⁶ is aryl optionally substituted with one or more of halo such as F, Cl, or Br. In yet other embodiments, R⁶ is aryl optionally substituted with one or more of C₁₋₆haloalkyl such as CF₃, CH₂CF₃, or CHF₂. In other embodiments, R⁶ is aryl optionally substituted with one or more of C₁₋₆alkyl such as methyl, ethyl, or propyl. In yet other embodiments, R⁶ is aryl optionally substituted with one or more of C₃₋₆cycloalkyl such as cyclopropyl, cyclobutyl, or cyclopentyl. In other embodiments, R⁶ is aryl (e.g., phenyl) optionally substituted with F, methyl, or CF₃. In other embodiments, R⁶ is



In yet other embodiments, R⁶ is



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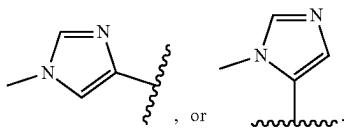


[0130] In yet other embodiments, R⁶ is heteroaryl, optionally substituted with one or more of halo, C₁₋₆haloalkyl, C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆haloalkoxy, C₃₋₆cycloalkyl, or C₃₋₆cycloalkylsulfonyl. In still other embodiments, R⁶ is pyridinyl, pyrazolyl, pyrazinyl, imidazolyl, or pyrimidinyl, each of which is optionally substituted. In still other embodiments, R⁶ is pyridinyl, pyrazolyl, pyrazinyl, pyridazinyl, imidazolyl, or pyrimidinyl, each of which is optionally substituted. In further embodiments, R⁶ is optionally substituted pyrazinyl such as pyrazin-2-yl, pyrazin-3-yl, pyrazin-4-yl, or pyrazin-5-yl. In other embodiments, R⁶ is optionally substituted pyrazolyl such as pyrazol-1-yl, pyrazol-3-yl, pyrazol-4-yl, or pyrazol-5-yl. In still further embodiments, R⁶ is optionally substituted pyridinyl such as pyridin-2-yl, pyridin-3-yl, or pyridin-4-yl. In other embodiments, R⁶ is optionally substituted pyridazinyl such as pyridazin-3-yl or pyridazin-4-yl. In yet other embodiments, R⁶ is optionally substituted imidazolyl such as imidazol-4-yl or imidazol-5-yl. In further embodiments, R⁶ is optionally substituted pyrimidinyl such as pyrimidin-2-yl, pyrimidin-4-yl, or pyrimidin-5-yl. In other embodiments, R⁶ is pyrazin-2-yl, pyrazin-3-yl, pyrazin-4-yl, pyrazin-5-yl, pyrazol-1-yl, pyrazol-3-yl, pyrazol-4-yl, pyrazol-5-yl, pyridin-2-yl, pyridin-3-yl, pyridin-4-yl, imidazol-4-yl, imidazol-5-yl, pyrimidin-2-yl, pyrimidin-4-yl, pyrimidin-5-yl, pyridazin-3-yl or pyridazin-4-yl, each of which is optionally substituted. In further embodiments, R⁶ is unsubstituted pyridin-2-yl, unsubstituted pyridin-3-yl, unsubstituted pyridin-4-yl, unsubstituted pyrimidin-2-yl, unsubstituted pyrimidin-4-yl, unsubstituted pyrimidin-5-yl, or unsubstituted pyrazin-2-yl. In further embodiments, R⁶ is unsubstituted pyridin-2-yl, unsubstituted pyridin-3-yl, unsubstituted pyridin-4-yl, unsubstituted pyrimidin-2-yl, unsubstituted pyrimidin-4-yl, unsubstituted pyrimidin-5-yl, unsubstituted pyrazin-2-yl, or unsubstituted pyridazin-3-yl. In other embodiments, R⁶ is optionally substituted with one or more halo such as F, Cl, or Br. In yet other embodiments, R⁶ is optionally substituted with one or more C₁₋₆haloalkyl such as CF₃, CH₂CF₃, or CHF₂. In other embodiments, R⁶ is optionally substituted with one or more C₁₋₆alkyl such as methyl, ethyl, propyl, or isopropyl. In still other embodiments, R⁶ is optionally substituted with one or more C₁₋₆alkoxy such as methoxy, ethoxy, or propoxy. In yet further embodiments, R⁶ is optionally substituted with one or more C₁₋₆haloalkoxy such as OCF₃. In further embodiments, R⁶ is optionally substituted with one or more C₃₋₆cycloalkyl such as cyclopropyl, cyclobutyl, or cyclopentyl. In yet further embodiments, R⁶ is optionally substituted with one or more C₃₋₆cycloalkylsulfonyl such as cyclopropylsulfonyl, cyclobutylsulfonyl, or cyclopentylsulfonyl. In yet other embodiments, R⁶ is

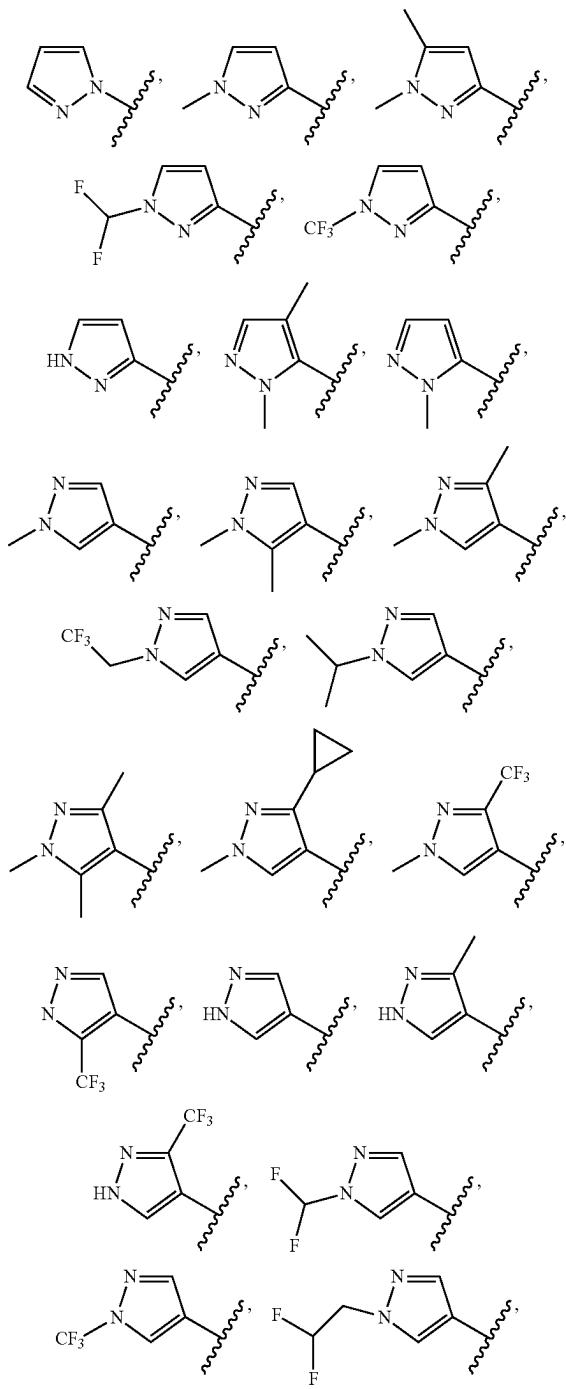
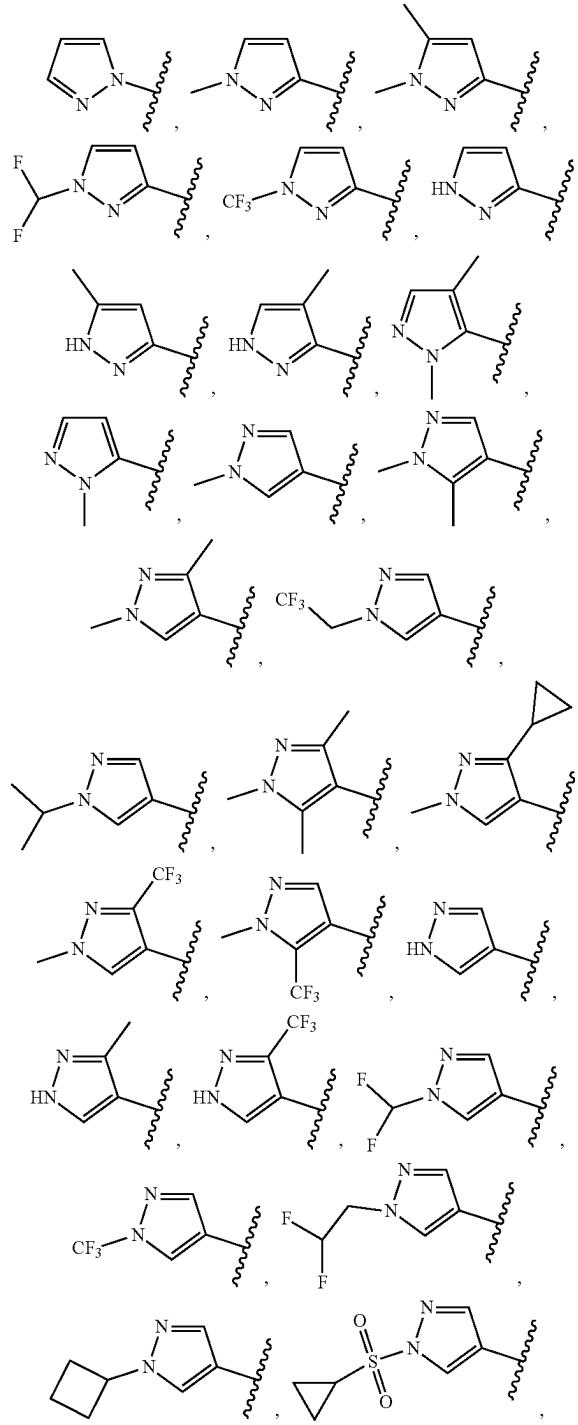
heteroaryl optionally substituted with one or more of F, CF₃, CH₂CF₃, CHF₂, methyl, methoxy, OCF₃, cyclobutyl, or cyclopropylsulfonyl.

[0131] In other embodiments, R⁶ is a five-membered heteroaryl, optionally substituted with one or more of CF₃, CH₂CF₃, CHF₂, methyl, cyclobutyl, or cyclopropylsulfonyl. In further embodiments, R⁶ is

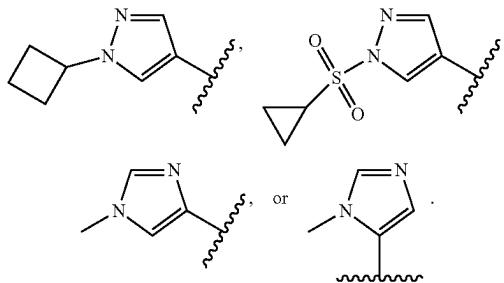
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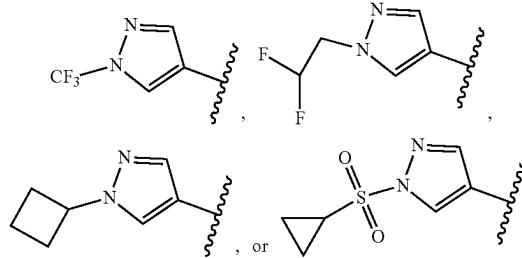
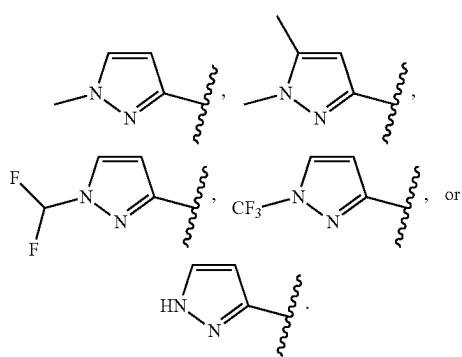
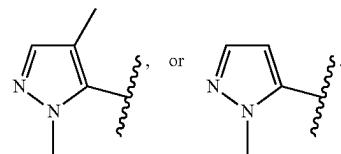
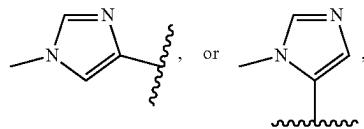
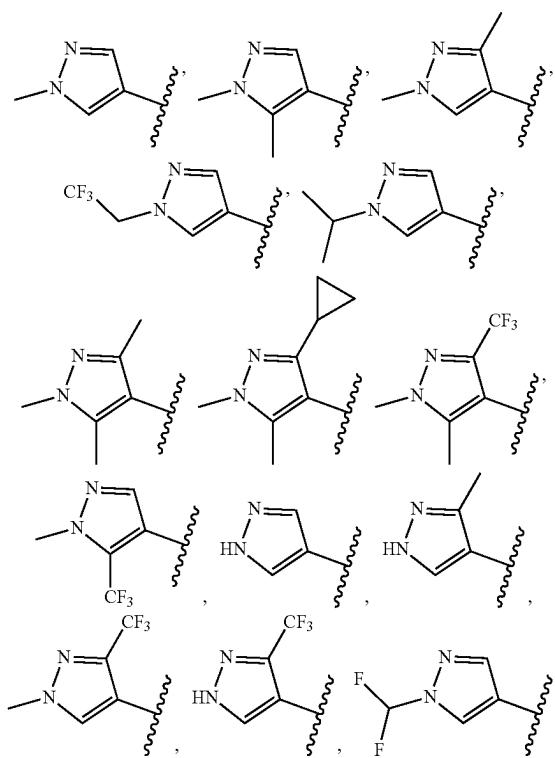
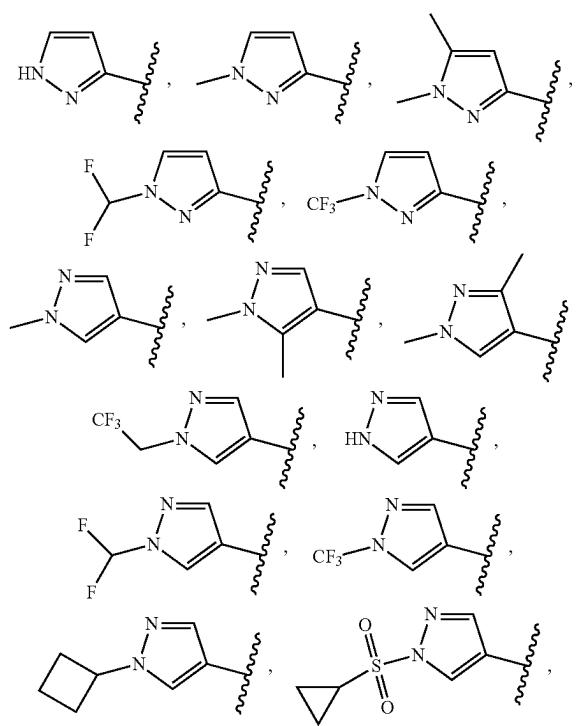
In still further embodiments, R⁶ is



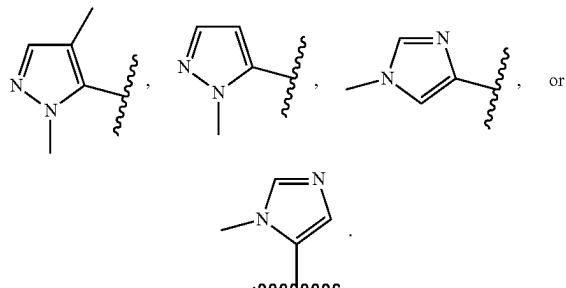
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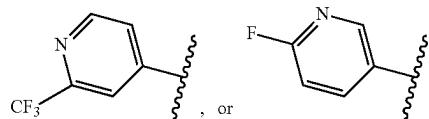
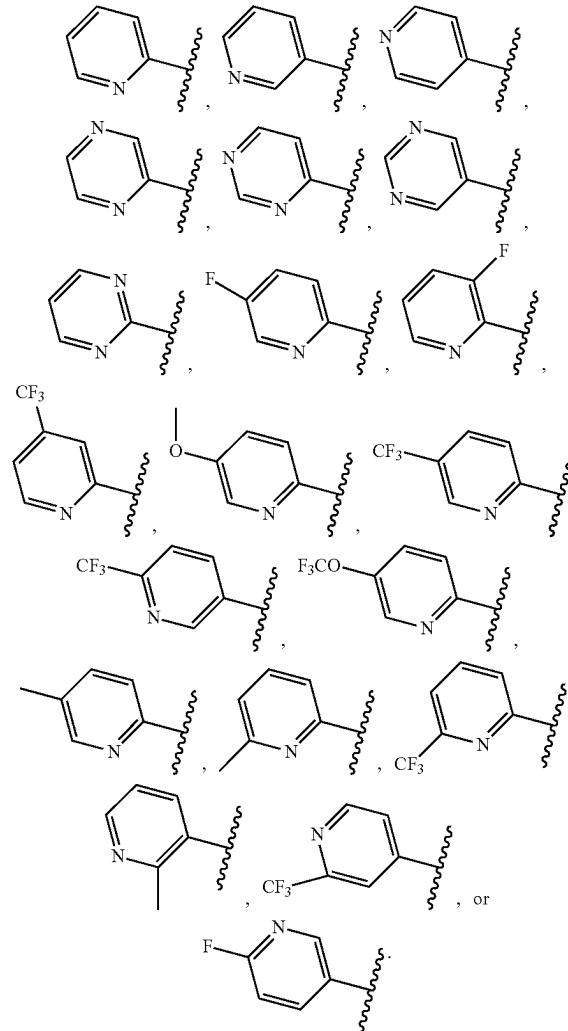
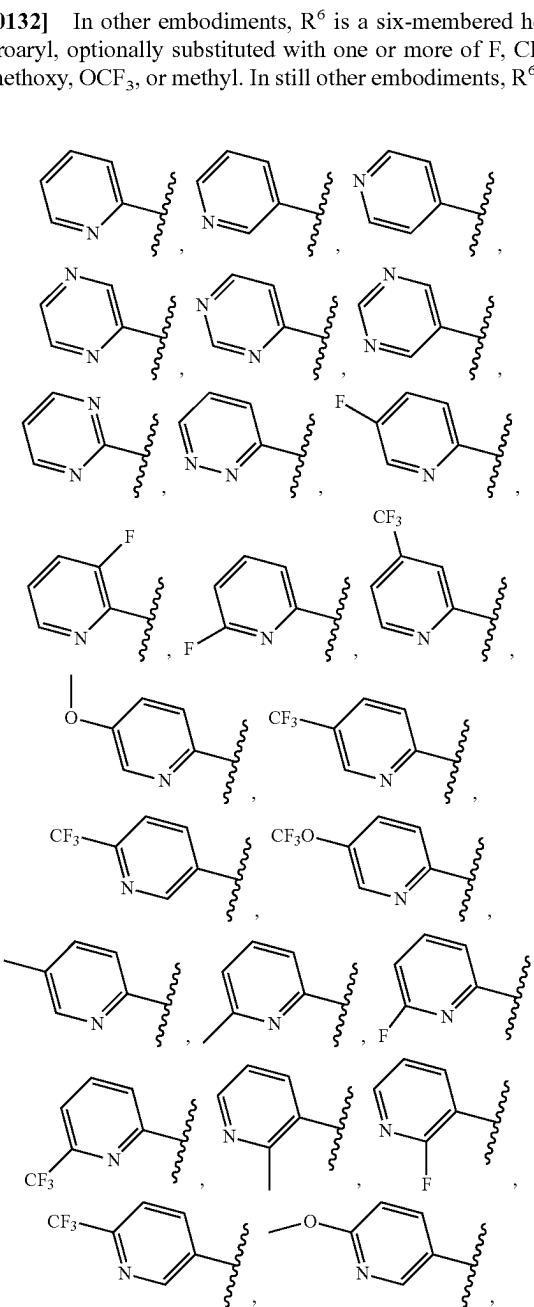
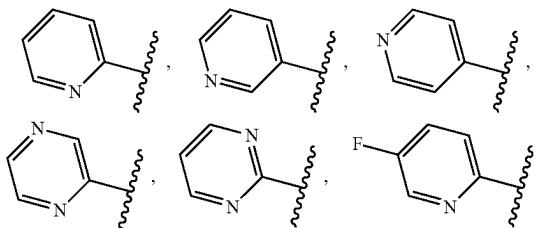
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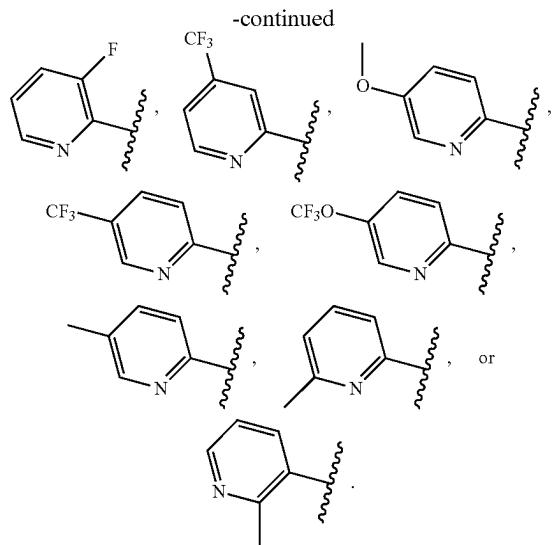
In other embodiments, R⁶ isIn yet further embodiments, R⁶ isIn further embodiments, R⁶ isIn still further embodiments, R⁶ isIn yet further embodiments, R⁶ is

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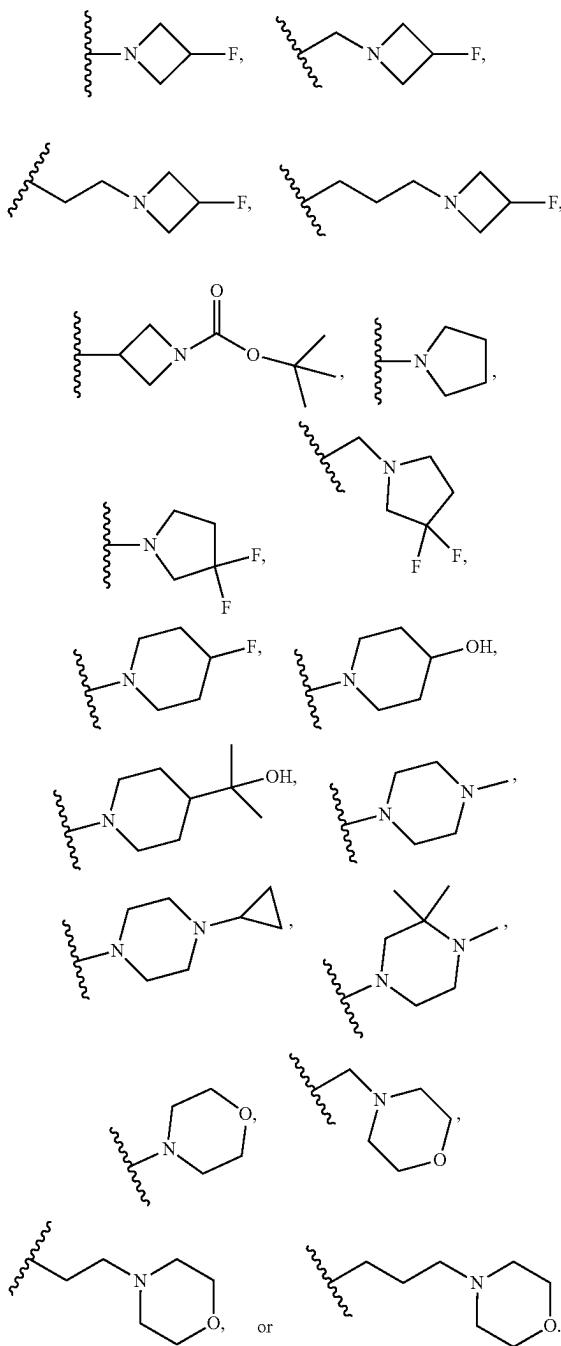
In still further embodiments, R^6 isIn yet other embodiments, R^6 is



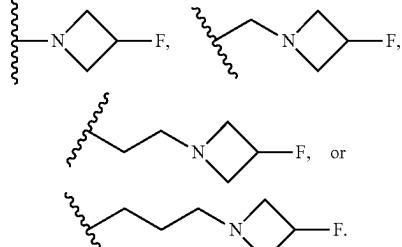
[0133] In yet other embodiments, R^6 is heterocyclyl or heterocyclyl(alkylene), each optionally substituted with one or more of halo, OH, C_{1-6} haloalkyl, C_{1-6} alkyl, C_{1-6} hydroxyalkyl, C_{1-6} alkoxy, $C(O)O(C_{1-6}$ alkyl), or C_{3-6} cycloalkyl. In further embodiments, R^6 is optionally substituted azetidinyl, optionally substituted pyrrolidinyl, optionally substituted piperidinyl, optionally substituted piperazinyl, or optionally substituted morpholinyl. In other embodiments, R^6 is optionally substituted azetidinyl. In yet other embodiments, R^6 is optionally substituted pyrrolidinyl. In further embodiments, R^6 is optionally substituted piperidinyl. In yet other embodiments, R^6 is optionally substituted piperazinyl. In still further embodiments, R^6 is optionally substituted morpholinyl. In other embodiments, R^6 is optionally substituted morpholinyl(alkylene), optionally substituted piperidinyl(alkylene), optionally substituted piperazinyl(alkylene), or optionally substituted azetidinyl(alkylene). In further embodiments, R^6 is unsubstituted azetidinyl, pyrrolidinyl, piperidinyl, piperazinyl, or morpholinyl. In other embodiments, R^6 is unsubstituted morpholinyl(alkylene), piperidinyl(alkylene), piperazinyl(alkylene), or azetidinyl(alkylene). In yet other embodiments, R^6 is unsubstituted morpholinyl or morpholinyl(alkylene). In other embodiments, the heterocyclyl and heterocyclyl(alkylene) groups are optionally substituted with one or more halo such as F, Cl, or Br. In yet other embodiments, the heterocyclyl and heterocyclyl(alkylene) groups are optionally substituted with one or more OH. In further embodiments, the heterocyclyl and heterocyclyl(alkylene) groups are optionally substituted with one or more C_{1-6} haloalkyl such as CF_3 , CH_2CF_3 , or CHF_2 . In still further embodiments, the heterocyclyl and heterocyclyl(alkylene) groups are optionally substituted with one or more C_{1-6} alkyl such as methyl, ethyl, or propyl. In further embodiments, the heterocyclyl and heterocyclyl(alkylene) groups are optionally substituted with one or more C_{1-6} hydroxyalkyl such as $C(CH_3)_2OH$. In yet further embodiments, the heterocyclyl and heterocyclyl(alkylene) groups are optionally substituted with one or more C_{1-6} alkoxy, such as methoxy, ethoxy, or propoxy. In other embodiments, the heterocyclyl and heterocyclyl(alkylene) groups are optionally substituted with one or more $C(O)O$ (C_{1-6} alkyl), such as $C(O)Omethyl$, $C(O)Oethyl$, $C(O)Opropyl$.

yl, or $C(O)Ot$ ert-butyl. In still further embodiments, the heterocyclyl and heterocyclyl(alkylene) groups are optionally substituted with one or more C_{3-6} cycloalkyl such as one or more cyclopropyl, cyclobutyl, or cyclopentyl. In yet other embodiments, R^6 is heterocyclyl and heterocyclyl(alkylene), each optionally substituted with one or more of F, OH, $C(CH_3)_2(OH)$, methyl, $C(O)O$ (tert-butyl), or cyclopropyl.

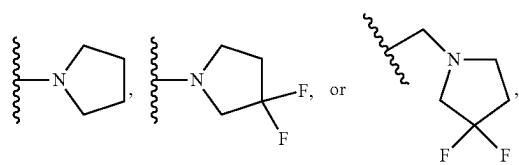
[0134] In further embodiments, R^6 is



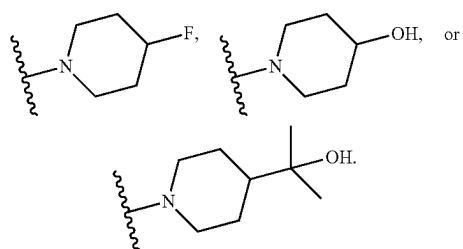
In yet other embodiments, R⁶ is



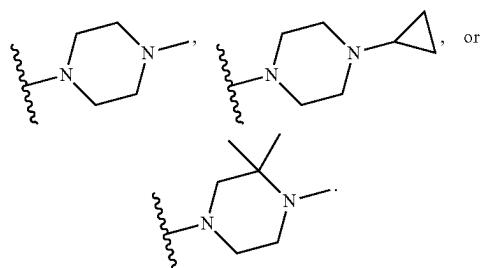
In further embodiments, R⁶ is



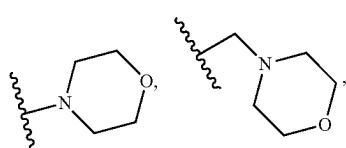
In still further embodiments, R⁶ is



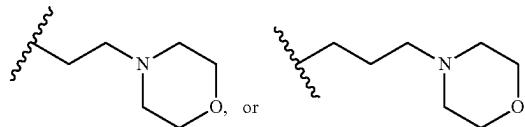
In yet other embodiments, R⁶ is



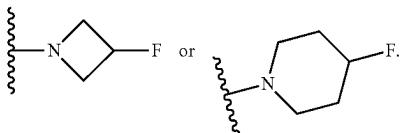
In other embodiments, R⁶ is



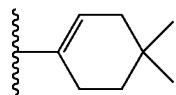
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In yet further embodiments, R⁶ is



[0135] In further embodiments, R⁶ is H, CN, C₁₋₆alkoxy, C₁₋₆alkoxy(alkylene), C₁₋₆haloalkoxy, C₁₋₆haloalkoxy(alkylene), C₁₋₆deuteratedalkoxy(alkylene), halo, (CR^vR^x)_pNR^yR^z, C(O)NR^{y2}R^{z2}, C₁₋₆alkylcarbonyl, optionally substituted C₂₋₆alkenyl, optionally substituted C₃₋₆cycloalkenyl, optionally substituted (C₃₋₆cycloalkyl)alkylene, optionally substituted (aryl)alkylene, or C₁₋₆alkylsulfonyl. In other embodiments, R⁶ is H. In further embodiments, R⁶ is CN. In still other embodiments, R⁶ is C₁₋₆alkoxy such as methoxy. In yet other embodiments, R⁶ is C₁₋₆alkoxy(alkylene) such as CH₂OCH₃, C(CH₃)₂OCH₃, or (CH₂)₂OCH₃. In still other embodiments, R⁶ is C₁₋₆haloalkoxy such as OCF₃, OCHF₂, OCH₂F, or O(CH₂)₂CF₃. In other embodiments, R⁶ is C₁₋₆haloalkoxy(alkylene) such as CH₂OCF₃. In yet other embodiments, R⁶ is C₁₋₆deuteratedalkoxy(alkylene) such as CH₂OCD₃. In further embodiments, R⁶ is halo such as F, Br, or Cl. In yet further embodiments, R⁶ is (CR^vR^x)_pNR^yR^z such as NH₂, N(CH₃)₂, NHCH₂CF₃, NHCH₂CH₂OCH₃, NH(cyclopropyl), CH₂N(CH₃)₂, (CH₂)₂N(CH₃)₂, C(CH₃)₂NHCH₃, C(CH₃)₂N(CH₃)₂, CH₂NH(cyclopropyl), or CH₂CH₂NH(cyclopropyl). In other embodiments, R⁶ is C(O)NR^{y2}R^{z2} such as C(O)N(CH₃)₂ or C(O)NH(cyclopropyl). In yet other embodiments, R⁶ is C₁₋₆alkylcarbonyl such as C(O)CH₃. In further embodiments, R⁶ is optionally substituted C₂₋₆alkenyl such as CH=CH₂, CH=CH-cyclopropyl, or CH=CHC(CH₃)₂OH. In yet other embodiments, R⁶ is optionally substituted C₃₋₆cycloalkenyl such as

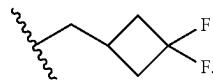


In still other embodiments, R⁶ is optionally substituted (C₃₋₆cycloalkyl)alkylene such as CH₂-cyclopropyl, CH₂CH₂-cyclopropyl or C(CH₃)OH-cyclopropyl. In further embodiments, R⁶ is optionally substituted (aryl)alkylene such as benzyl. In other embodiments, C₁₋₆alkylsulfonyl (alkylene) such as C(CH₃)₂SO₂CH₃. In yet other embodiments, R⁶ is H, CH₂OCH₃, Cl, NH(cyclopropyl), or C(O)N(CH₃)₂.

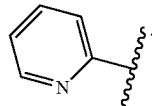
[0136] In some embodiments, R⁷ is H, CN, C₁₋₆alkyl, C₁₋₆haloalkyl, halo, C₃₋₈cycloalkyl, aryl, or heteroaryl. In yet other embodiments, R⁷ is H. In still further embodiments, R⁷ is CN. In other embodiments, R⁷ is C₁₋₆alkyl, such as methyl, ethyl, or propyl. In further embodiments, R⁷ is

methyl. In yet other embodiments, R^7 is C_{1-6} haloalkyl, such as CHF_2 , CH_2F , $\text{C}(\text{CH}_3)\text{F}_2$, CH_2CHF_2 , or CF_3 . In still further embodiments, R^7 is CHF_2 or CF_3 . In further embodiments, R^7 is halo, such as F, Br, or Cl. In yet other embodiments, R^7 is Br or Cl. In still further embodiments, R^7 is C_{3-6} cycloalkyl, such as cyclopropyl, cyclobutyl, or cyclopentyl. In other embodiments, R^7 is cyclopropyl. In further embodiments, R^7 is aryl. In yet other embodiments, R^7 is phenyl. In still further embodiments, R^7 is heteroaryl. In other embodiments, R^7 is pyridinyl. In further embodiments, R^7 is H, CN, methyl, CF_3 , CH_2F , CHF_2 , $\text{CF}_2(\text{CH}_3)$, CH_2CHF_2 , Br, Cl, cyclopropyl, phenyl, or pyridinyl. In yet other embodiments, R^7 is H, CN, methyl, CHF_2 , CF_3 , Br, Cl, cyclopropyl, phenyl, or pyridinyl.

[0137] In some embodiments of R^2 , R^8 is H. In other embodiments, R^8 is C_{1-6} alkyl such as methyl, ethyl, isopropyl, or tert-butyl. In further embodiments, R^8 is C_{1-6} haloalkyl such as CF_3 , CHF_2 , CH_2F , CH_2CF_3 , CH_2CHF_2 , $\text{C}(\text{CH}_3)_2\text{F}$, or $\text{C}(\text{CH}_3)\text{F}_2$. In still further embodiments, R^8 is C_{1-6} alkoxy(alkylene) such as $\text{CH}_2\text{CH}_2\text{OCH}_3$. In other embodiments, R^8 is C_{1-6} alkylcarbonyl such as $\text{CH}_2\text{C}(\text{O})\text{CH}_3$. In still other embodiments, R^8 is C_{1-6} hydroxyalkyl such as $\text{CH}_2\text{C}(\text{CH}_3)_2\text{OH}$. In further embodiments, R^8 is $(\text{CR}^1\text{R}^x)_p\text{NR}^y\text{R}^z$ such as $(\text{CH}_2)_2\text{N}(\text{CH}_3)_2$. In yet other embodiments, R^8 is optionally substituted C_{3-8} cycloalkyl such as optionally substituted cyclopropyl, optionally substituted cyclobutyl, optionally substituted cyclopentyl, or optionally substituted cyclohexyl. In other embodiments, R^8 is optionally substituted aryl such as optionally substituted phenyl. In further embodiments, R^8 is optionally substituted heteroaryl, such as optionally substituted pyridinyl. In still further embodiments, R^8 is optionally substituted heteroaryl such as optionally substituted pyridinyl. In yet other embodiments, R^8 is optionally substituted $(C_{3-8}$ cycloalkyl) alkylene such as



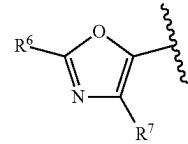
In still further embodiments, R^8 is H, methyl, isopropyl, CHF_2 , CH_2CF_3 , CF_3 , cyclopropyl, or



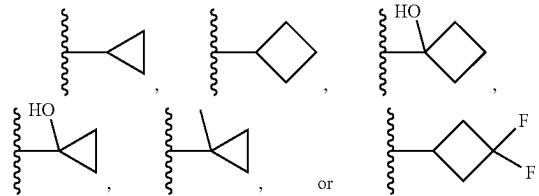
[0138] In some embodiments, one or both of R^y and R^x are H. In other embodiments, one or both of R^y and R^x are C_{1-6} alkyl such as methyl, ethyl, propyl, or butyl. In yet other embodiments, one or both of R^y and R^x are methyl. In some embodiments, one or both of R^y and R^z are H. In other embodiments, one or both of R^y and R^z are C_{1-6} alkyl such as methyl, ethyl, propyl, or butyl. In yet other embodiments, one or both of R^y and R^z are C_{1-6} alkoxy(alkylene) such as CH_2OCH_3 . In further embodiments, one or both of R^y and R^z are C_{3-6} cycloalkyl such as cyclopropyl, cyclobutyl, cyclopentyl, or cyclohexyl. In some embodiments, one or both of R^{y2} and R^{z2} are H. In other embodiments, one or both of R^{y2} and R^{z2} are C_{1-6} alkyl such as methyl, ethyl, propyl, or butyl.

In further embodiments, one or both of R^{y2} and R^{z2} are C_{3-6} cycloalkyl such as cyclopropyl, cyclobutyl, cyclopentyl, or cyclohexyl. In further embodiments, p is 0. In other embodiments, p is 1. In still further embodiments, p is 2. In yet other embodiments, p is 3.

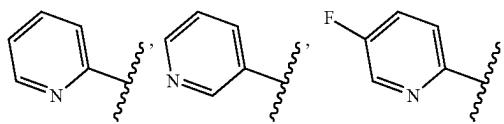
[0139] In some embodiments, R^2 is

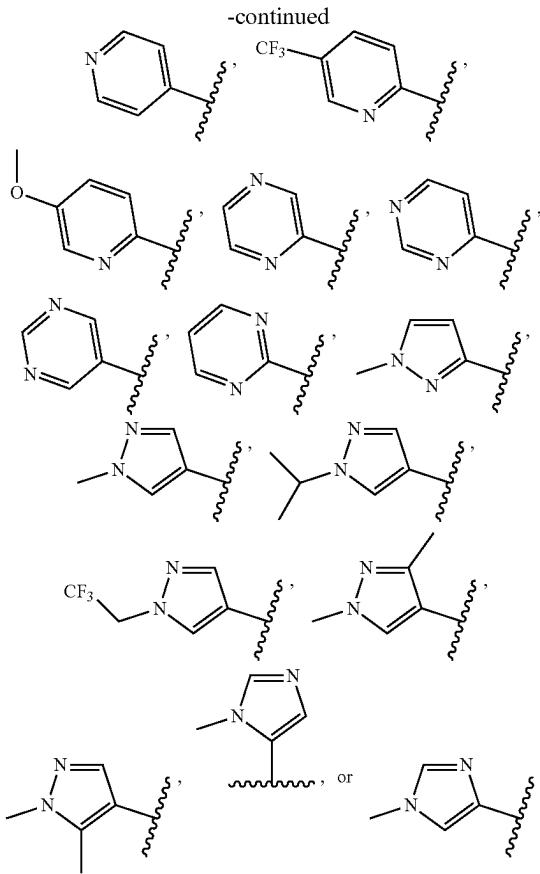


wherein: R^6 is H, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{1-6} cyanoalkyl, C_{1-6} hydroxyalkyl, C_{1-6} alkoxy, C_{1-6} alkoxy(alkylene), optionally substituted C_{3-6} cycloalkyl, or optionally substituted heteroaryl; and R^7 is H, CN, C_{1-6} alkyl, C_{1-6} haloalkyl, halo, C_{3-6} cycloalkyl, aryl, or heteroaryl. In further embodiments, R^6 is H, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{1-6} cyanoalkyl, C_{1-6} hydroxyalkyl, C_{1-6} alkoxy, C_{1-6} alkoxy(alkylene), optionally substituted C_{3-6} cycloalkyl, optionally substituted heteroaryl, or optionally substituted heterocycl; and R^7 is H, CN, C_{1-6} alkyl, C_{1-6} haloalkyl, halo, C_{3-6} cycloalkyl, aryl, or heteroaryl. In other embodiments, R^6 is H. In further embodiments, R^6 is C_{1-6} alkyl. In still further embodiments, R^6 is methyl, isopropyl, or tert-butyl. In yet other embodiments, R^6 is C_{1-6} haloalkyl. In still further embodiments, R^6 is CF_2H , $\text{C}(\text{CH}_3)_2\text{F}$, $\text{CH}(\text{CH}_3)\text{F}$, or CF_3 . In other embodiments, R^6 is C_{1-6} cyanoalkyl. In further embodiments, R^6 is $\text{C}(\text{CH}_3)_2\text{CN}$. In yet other embodiments, R^6 is C_{1-6} hydroxyalkyl. In still further embodiments, R^6 is $\text{C}(\text{CH}_3)_2\text{OH}$, $\text{CH}_2\text{C}(\text{CH}_3)_2\text{OH}$, $\text{C}(\text{CH}_3)_2(\text{CH}_2\text{OH})$, or $\text{CH}(\text{CH}_3)\text{OH}$. In other embodiments, R^6 is C_{1-6} alkoxy. In still other embodiments, R^6 is methoxy or ethoxy. In yet other embodiments, R^6 is C_{1-6} alkoxy(alkylene). In further embodiments, R^6 is CH_2OCH_3 or $(\text{CH}_2)_2\text{OCH}_3$. In other embodiments, R^6 is optionally substituted C_{3-6} cycloalkyl. In further embodiments, R^6 is

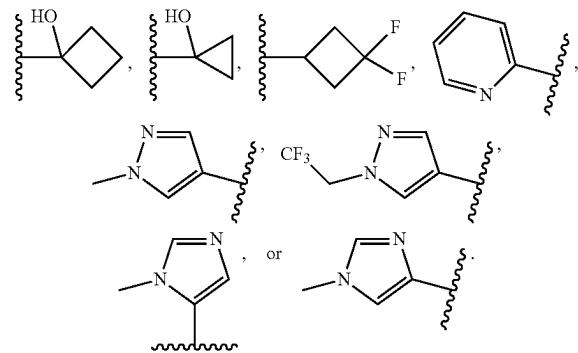


In other embodiments, R^6 is optionally substituted heteroaryl. In yet other embodiments, R is optionally substituted pyridinyl, optionally substituted pyrazolyl, optionally substituted pyrazinyl, optionally substituted pyrimidinyl, or optionally substituted imidazolyl. In further embodiments, R^6 is

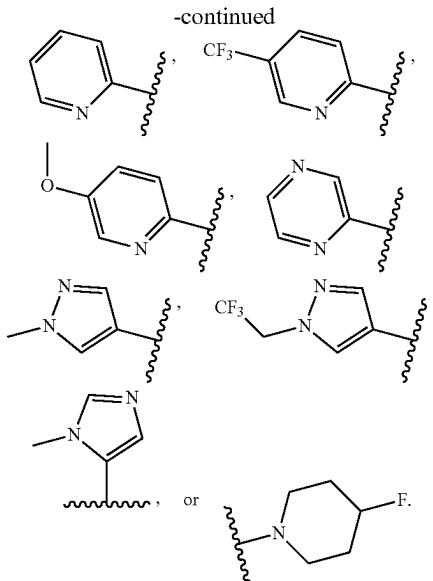
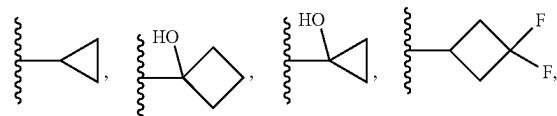




In other embodiments, R⁶ is H, methyl, tert-butyl, C(CH₃)₂F, C(CH₃)₂CN, C(CH₃)₂OH, CH(CH₃)OH, CH₂OCH₃, cyclopropyl,

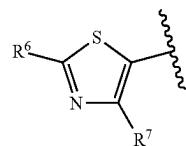


In still further embodiments, R⁶ is H, methyl, tert-butyl, C(CH₃)₂F, C(CH₃)₂CN, C(CH₃)₂OH, CH(CH₃)OH, CH₂OCH₃,

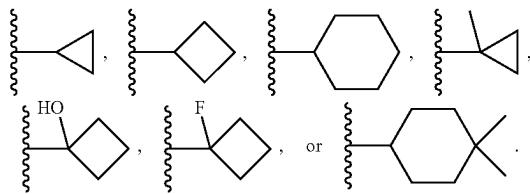


or In yet other embodiments, R⁷ is H. In still further embodiments, R⁷ is CN. In other embodiments, R⁷ is C₁₋₆alkyl. In further embodiments, R⁷ is methyl. In yet other embodiments, R⁷ is C₁₋₆haloalkyl. In still further embodiments, R⁷ is CF₂H, CHF₂, CH₂F, C(CH₃)F₂, or CF₃. In further embodiments, R⁷ is halo. In yet other embodiments, R⁷ is Br or Cl. In still further embodiments, R⁷ is C₃₋₆cycloalkyl. In other embodiments, R⁷ is cyclopropyl. In further embodiments, R⁷ is aryl. In yet other embodiments, R⁷ is phenyl. In still further embodiments, R⁷ is heteroaryl. In other embodiments, R⁷ is pyridinyl. In yet other embodiments, R⁷ is H, CN, methyl, CHF₂, CF₃, Br, Cl, cyclopropyl, phenyl, or pyridinyl.

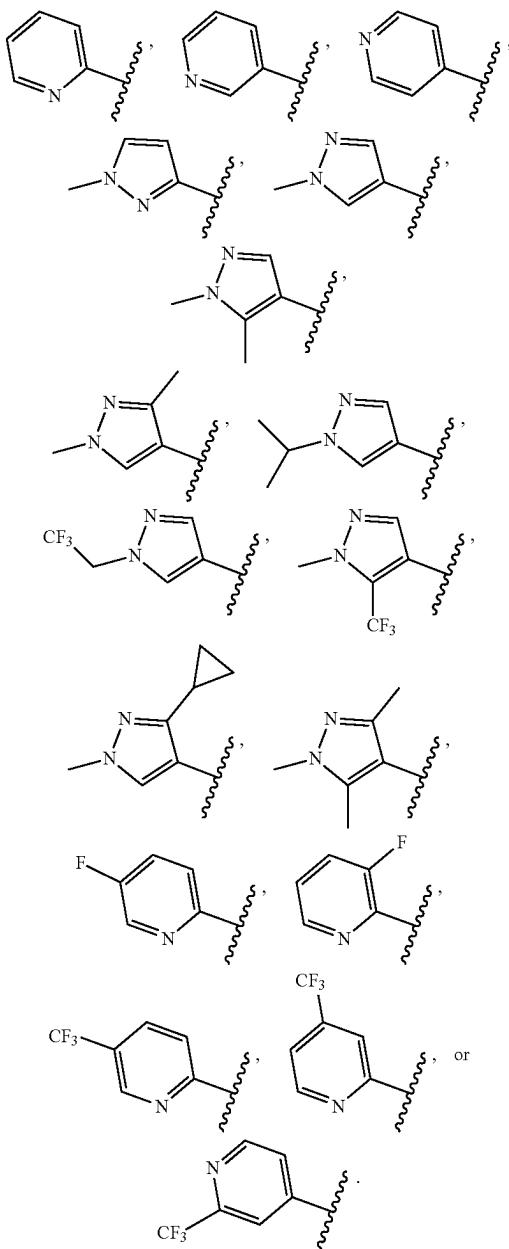
[0140] In other embodiments, R² is



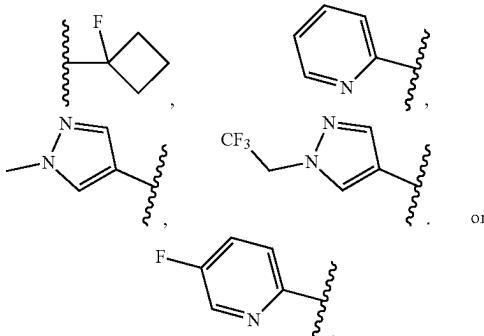
wherein: R⁶ is H, CN, C₁₋₆alkyl, C₁₋₆haloalkyl, C₁₋₆hydroxyalkyl, C₁₋₆alkoxy, C₁₋₆alkoxy(alkylene), optionally substituted C₃₋₆cycloalkyl, or optionally substituted heteroaryl; and R⁷ is H, C₁₋₆alkyl, C₁₋₆haloalkyl, halo, or C₃₋₆cycloalkyl. In further embodiments, R⁶ is H. In other embodiments, R⁶ is CN. In further embodiments, R⁶ is C₁₋₆alkyl. In still further embodiments, R⁶ is methyl, isopropyl, or tert-butyl. In yet other embodiments, R⁶ is C₁₋₆haloalkyl. In still further embodiments, R⁶ is CHF₂, C(CH₃)₂F, C(CH₃)F₂, or CF₃. In yet other embodiments, R⁶ is C₁₋₆hydroxyalkyl. In still further embodiments, R⁶ is C(CH₃)₂OH. In other embodiments, R⁶ is C₁₋₆alkoxy. In still further embodiments, R⁶ is methoxy or ethoxy. In yet other embodiments, R⁶ is C₁₋₆alkoxy(alkylene). In further embodiments, R⁶ is CH₂OCH₃. In other embodiments, R⁶ is optionally substituted C₃₋₆cycloalkyl. In yet further embodiments, R⁶ is



In other embodiments, R^6 is optionally substituted heteroaryl. In yet other embodiments, R^6 is optionally substituted pyridinyl or optionally substituted pyrazolyl. In further embodiments, R^6 is

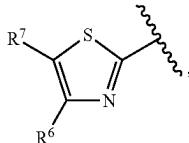


In other embodiments, R^6 is H, tert-butyl, $C(CH_3)_2F$, $C(CH_3)F_2$, $C(CH_3)_2OH$, CH_2OCH_3 ,



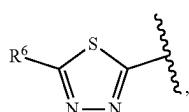
In yet other embodiments, R^7 is H. In other embodiments, R^7 is C_{1-6} alkyl. In further embodiments, R^7 is methyl. In yet other embodiments, R^7 is C_{1-6} haloalkyl. In still further embodiments, R^7 is CF_2H or CF_3 . In further embodiments, R^7 is halo. In yet other embodiments, R^7 is Br or Cl. In still further embodiments, R^7 is C_{3-6} cycloalkyl. In other embodiments, R^7 is cyclopropyl. In still further embodiments, R^7 is H, methyl, CF_2H , CF_3 , Br, Cl, or cyclopropyl.

[0141] In further embodiments, R^2 is



wherein R^6 and R^7 are independently H, C_{1-6} alkyl, C_{1-6} haloalkyl, halo, optionally substituted C_{3-6} cycloalkyl, or optionally substituted aryl. In other embodiments, R^6 and R^7 are each H. In further embodiments, one of R^6 or R^7 is C_{1-6} alkyl such as methyl. In yet other embodiments, one of R^6 or R^7 is C_{1-6} haloalkyl such as CF_3 . In still other embodiments, one of R^6 or R^7 is halo such as Br or Cl. In yet further embodiments, one of R^6 or R^7 is optionally substituted C_{3-6} cycloalkyl such as unsubstituted cyclopropyl. In other embodiments, one of R^6 or R^7 is optionally substituted aryl such as unsubstituted phenyl. In yet other embodiments, R^6 is methyl, CF_3 , Cl, cyclopropyl, or phenyl and R^7 is H. In still other embodiments, R^7 is methyl, CF_3 , Cl, cyclopropyl, or phenyl and R^6 is H.

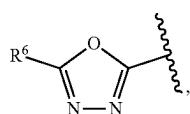
[0142] In yet further embodiments, R^2 is



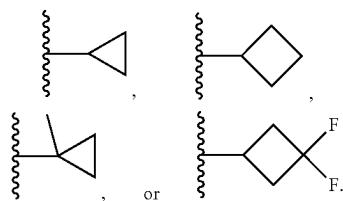
wherein R^6 is H, C_{1-6} alkyl, halo, or optionally substituted aryl. In other embodiments, R^6 is H. In further embodiments, R^6 is C_{1-6} alkyl, such as methyl, ethyl, isopropyl, or tert-butyl. In other embodiments, R^6 is methyl or ethyl. In other embodiments, R^6 is halo, such as F, Br, or Cl. In further

embodiments, R^6 is Br. In other embodiments, R^6 is optionally substituted aryl. In further embodiments, R^6 is phenyl. In yet other embodiments, R^6 is H, methyl, ethyl, Br, or phenyl. In still other embodiments, R^6 is H, methyl, or phenyl.

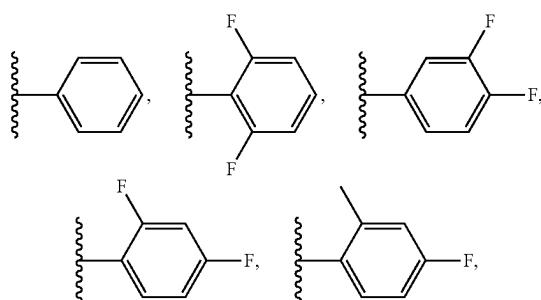
[0143] In yet other embodiments, R^2 is



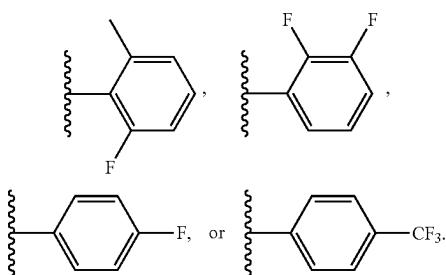
wherein R^6 is H, C_{1-6} -alkyl, C_{1-6} -haloalkyl, C_{1-6} -hydroxyalkyl, $C(O)NR^{12}R^{22}$, $(CR'NR')_pNR''R'''$, optionally substituted C_{3-6} -cycloalkyl, optionally substituted aryl, optionally substituted heterocyclyl, or optionally substituted heteroaryl; R^y and R^x are, independently, H or C_{1-6} -alkyl; R^y and R^z are, independently, H, C_{1-6} -alkyl, C_{1-6} -alkoxy(alkylene), or C_{3-6} -cycloalkyl; R^{12} and R^{22} are, independently, H, C_{1-6} -alkyl, or C_{3-6} -cycloalkyl; and p is 0, 1, 2, or 3. In some embodiments, R^6 is H. In further embodiments, R^6 is C_{1-6} -alkyl. In other embodiments, R^6 is methyl, ethyl, isopropyl, or tert-butyl. In other embodiments, R^6 is C_{1-6} -haloalkyl. In further embodiments, R^6 is CHF_2 , CF_3 , or $C(CH_3)_2F$. In yet other embodiments, R^6 is C_{1-6} -hydroxyalkyl. In still further embodiments, R^6 is $C(CH_3)_2OH$ or $CH(CH_3)_2OH$. In still other embodiments, R^6 is $C(O)NR^{12}R^{22}$. In yet further embodiments, R^6 is $C(O)N(CH_3)_2$ or $C(O)NH(cyclopropyl)$. In other embodiments, R^6 is $(CR'NR')_pNR''R'''$. In further embodiments, R^6 is NH_2 , $N(CH_3)_2$, $NHCH_2CF_3$, $NHCH_2CH_2OCH_3$, $NH(cyclopropyl)$, $CH_2N(CH_3)_2$, $CH_2NH(cyclopropyl)$, or $CH_2CH_2NH(cyclopropyl)$. In yet other embodiments, R^6 is optionally substituted C_{3-6} -cycloalkyl. In still further embodiments, R^6 is



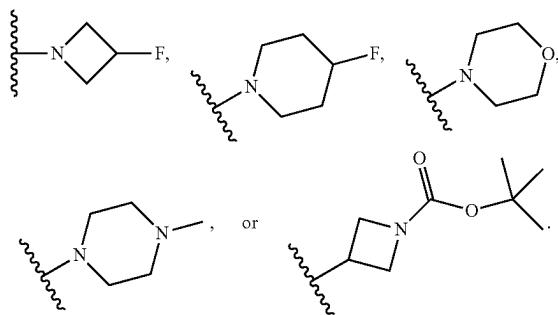
In other embodiments, R^6 is optionally substituted aryl. In further embodiments, R^6 is



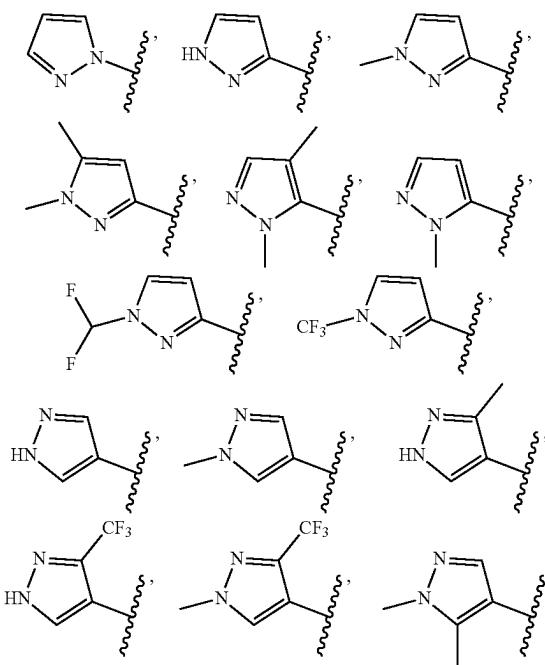
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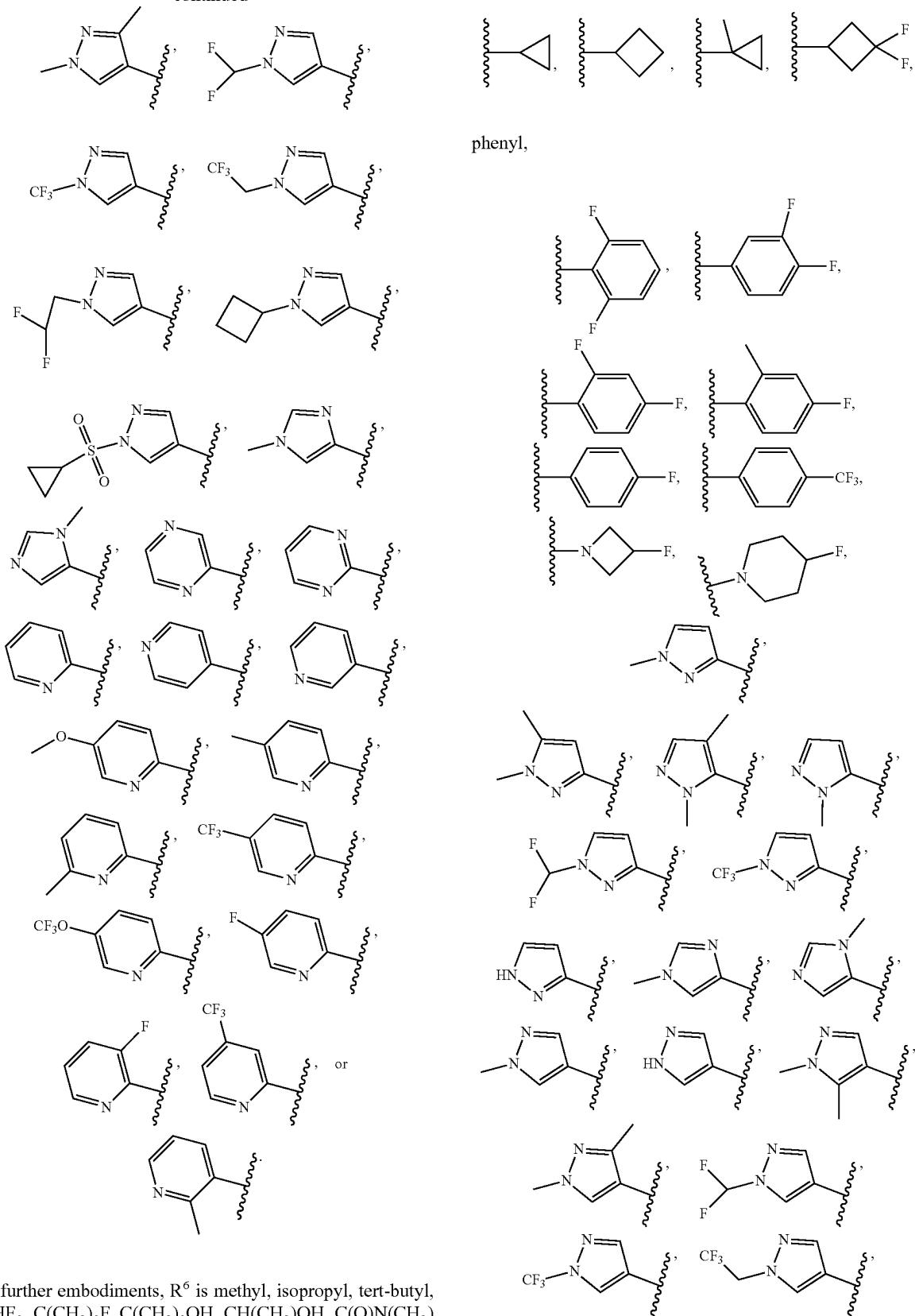
In still other embodiments, R^6 is optionally substituted heterocyclyl. In yet further embodiments, R^6 is



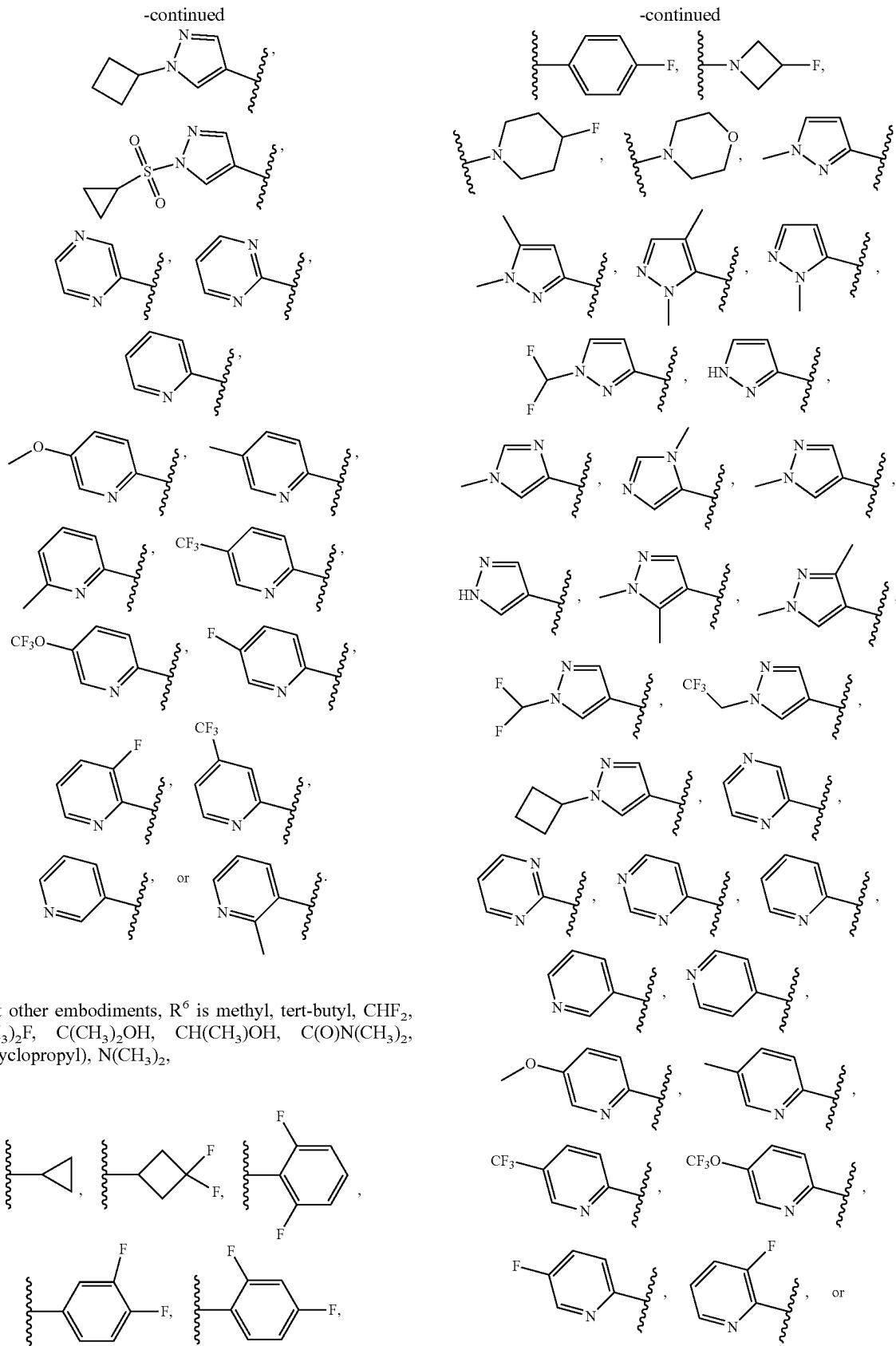
In other embodiments, R^6 is optionally substituted heteroaryl such as optionally substituted pyrazolyl, optionally substituted imidazolyl, optionally substituted pyridinyl, or optionally substituted pyrazinyl. In yet other embodiments, R^6 is



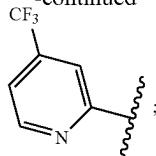
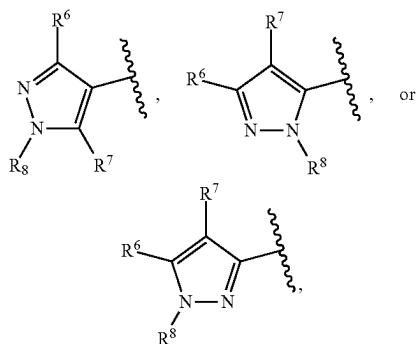
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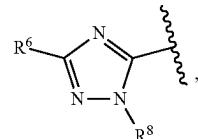
In further embodiments, R⁶ is methyl, isopropyl, tert-butyl, CHF₂, C(CH₃)₂F, C(CH₃)₂OH, CH(CH₃)OH, C(O)N(CH₃)₂, NH)cyclopropyl),



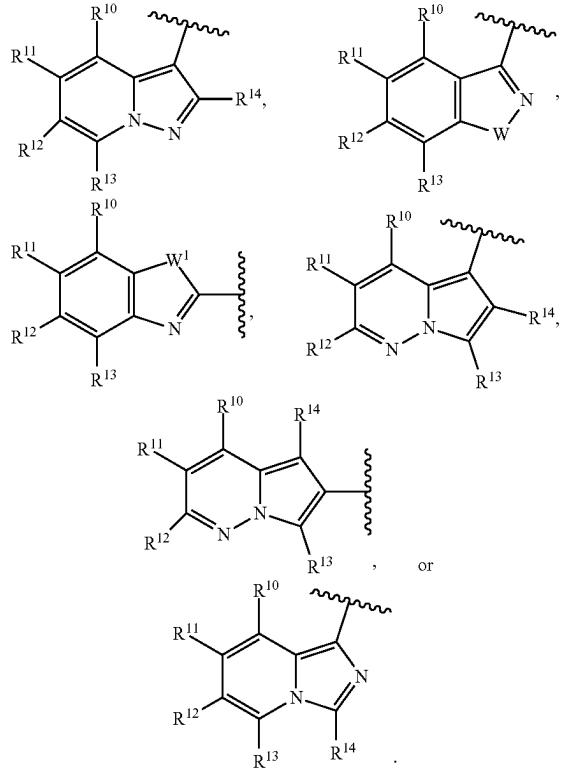
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[0144] In still further embodiments, R² is

wherein and R⁶ and R⁷ are independently H, halo, C₁₋₆alkyl, or C₁₋₆haloalkyl; and R⁸ is H, C₁₋₆alkyl, C₁₋₆haloalkyl, C₃₋₆cycloalkyl, optionally substituted aryl, or heteroaryl. In yet other embodiments, R⁶ and R⁷ are independently H, halo, C₁₋₆alkyl, C₁₋₆haloalkyl, or NR^vR^x wherein R^v and R^x are independently H or C₁₋₆alkyl; and R⁸ is H, C₁₋₆alkyl, C₁₋₆haloalkyl, or heteroaryl. In other embodiments, one or both of R⁶ and R⁷ are H. In still other embodiments, one of R⁶ or R⁷ is halo. In further embodiments, one of R⁶ or R⁷ is Cl or Br. In yet other embodiments, one of R⁶ or R⁷ is C₁₋₆alkyl. In still further embodiments, one of R⁶ or R⁷ is methyl. In other embodiments, one of R⁶ or R⁷ is C₁₋₆haloalkyl. In further embodiments, one of R⁶ or R⁷ is CHF₂, CH₂CF₃, CF₂H, or CF₃. In still further embodiments, one of R⁶ or R⁷ is NR^vR^x wherein R^v and R^x are independently H or C₁₋₆alkyl. In other embodiments, one of R⁶ or R⁷ is NH₂, NH(CH₃), or N(CH₃)₂. In yet other embodiments, one of R⁶ or R⁷ is Cl, Br, methyl, CHF₂, or CF₃. In other embodiments, one of R⁶ or R⁷ is methyl, Cl, CHF₂, or CF₃. In still other embodiments, one of R⁶ or R⁷ is Cl, CHF₂, or NH₂. In some embodiments, R⁸ is H. In other embodiments, R⁸ is C₁₋₆alkyl. In further embodiments, R⁸ is methyl, ethyl, isopropyl, or tert-butyl. In still other embodiments, R⁸ is C₁₋₈haloalkyl. In yet further embodiments, R⁸ is CHF₂, CH₂CF₃, CF₂H, CH₂CHF₂, or CF₃. In other embodiments, R⁸ is C₃₋₆cycloalkyl. In further embodiments, R⁸ is cyclopropyl. In yet other embodiments, R⁸ is optionally substituted aryl. In still further embodiments, R⁸ is phenyl or fluorophenyl. In other embodiments, R⁸ is heteroaryl. In further embodiments, R⁸ is pyridinyl. In still other embodiments, R⁸ is H, methyl, isopropyl, tert-butyl, CHF₂, CH₂CF₃, CH₂CHF₂, CH₂C(O)CH₃, CH₂C(CH₃)₂OH, (CH₂)₂N(CH₃)₂, cyclopropyl, fluoroxyphenyl, pyridinyl, CH₂-cyclopropyl or CH₂-cyclobutyl. In yet other embodiments, R⁸ is methyl, isopropyl, CHF₂, CH₂CF₃, CF₃, cyclopropyl, and pyridinyl. In still further embodiments, R⁸ is H, methyl, CHF₂, CH₂CF₃, or pyridinyl.

[0145] In further embodiments, R² is

wherein R⁶ is H, C₁₋₆alkyl, halo, C₁₋₆haloalkyl, or C₃₋₆cycloalkyl; and R⁸ is H, C₁₋₆alkyl, or C₁₋₆haloalkyl. In still further embodiments, R⁶ is H, C₁₋₆alkyl, halo, or C₁₋₆haloalkyl; and R⁸ is H, C₁₋₆alkyl, or C₁₋₆haloalkyl. In other embodiments, R⁶ is H. In still other embodiments, R⁶ is C₁₋₆alkyl, such as methyl. In yet other embodiments, R⁶ is halo such as Cl or Br. In other embodiments, R⁶ is C₁₋₆haloalkyl such as CHF₂ or CF₃. In yet other embodiments, R⁶ is C₃₋₆cycloalkyl such as cyclopropyl. In still further embodiments, R⁶ is H, methyl, Cl, CHF₂, CF₃, or cyclopropyl. In yet other embodiments, R⁶ is H, Cl, or CHF₂. In some embodiments, R⁸ is H. In other embodiments, R⁸ is C₁₋₆alkyl such as methyl, ethyl, or isopropyl. In yet other embodiments, R⁸ is C₁₋₆haloalkyl, such as CF₃ or CHF₂. In other embodiments, R⁸ is methyl.

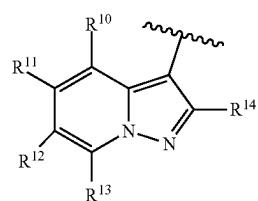
[0146] In yet other embodiments, R² is

In these structures, W is S or NR¹⁵; W¹ is S, O, or NR¹⁵; R¹⁰, R¹¹, R¹², R¹³, and R¹⁴ are each independently H, C₁₋₆alkyl, C₁₋₆haloalkyl, C₁₋₆alkoxy, C₁₋₆alkoxy(alkylene), C₁₋₆hydroxyalkyl, C₁₋₆haloalkoxy, C₁₋₆haloalkoxy(alkylene), C₂₋₆alkenyl, CN, halo, (CR^vR^x)_p, NR^vR^x, C(O)NR^vR^x, optionally substituted C₃₋₈cycloalkyl, optionally substituted heterocyclyl, optionally substituted heterocyclyl(alkylene), optionally substituted aryl, or optionally substituted het-

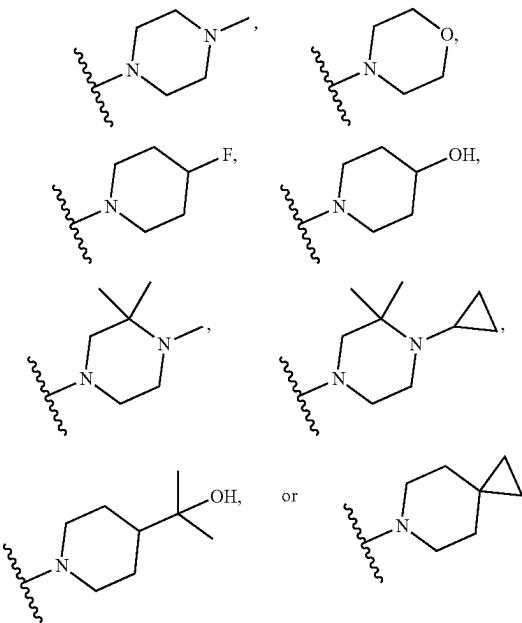
eroaryl; R^y and R^x are, independently, H or C₁₋₆alkyl; R^y and R^z are, independently, H, C₁₋₆alkyl, C₃₋₆cycloalkyl, C₁₋₆hydroxyalkyl, C₁₋₆haloalkyl, C₁₋₆alkoxy(alkylene), or C(O)OC₁₋₆alkyl; R^{y2} and R^{z2}, are independently, H, C₁₋₆alkyl, or C₃₋₆cycloalkyl; p is 0, 1, 2, or 3; and R¹⁵ is H or C₁₋₆alkyl.

[0147] In some embodiments, W is S. In other embodiments, W is NR¹⁵. In some embodiments, W¹ is S. In other embodiments, W¹ is O. In further embodiments, W¹ is NR¹⁵. In some embodiments, R¹⁰, R¹¹, R¹², R¹³, and R¹⁴ are H. In further embodiments, R¹⁰, R¹¹, R¹², and R¹³ are H. In other embodiments, at least one of R¹⁰, R¹¹, R¹², R¹³, and R¹⁴ is C₁₋₆alkyl. In further embodiments, at least one of R¹⁰, R¹¹, R¹², R¹³, and R¹⁴ is C₁₋₆haloalkyl. In yet other embodiments, at least one of R¹⁰, R¹¹, R¹², R¹³, and R¹⁴ is C₁₋₆alkoxy. In still other embodiments, at least one of R¹⁰, R¹¹, R¹², R¹³, and R¹⁴ is C₁₋₆alkoxy(alkylene). In further embodiments, at least one of R¹⁰, R¹¹, R¹², R¹³, and R¹⁴ is C₁₋₆hydroxyalkyl. In other embodiments, at least one of R¹⁰, R¹¹, R¹², R¹³, and R¹⁴ is C₁₋₆haloalkoxy. In still other embodiments, at least one of R¹⁰, R¹¹, R¹², R¹³, and R¹⁴ is C₁₋₆haloalkoxy(alkylene). In yet other embodiments, at least one of R¹⁰, R¹¹, R¹², R¹³, and R¹⁴ is C₂₋₆alkenyl. In further embodiments, at least one of R¹⁰, R¹¹, R¹², R¹³, and R¹⁴ is CN. In yet other embodiments, at least one of R¹⁰, R¹¹, R¹², R¹³, and R¹⁴ is halo. In still further embodiments, at least one of R¹⁰, R¹¹, R¹², R¹³, and R¹⁴ is (CR^yR^x)NR^{y2}R^{z2}. In other embodiments, at least one of R¹⁰, R¹¹, R¹², R¹³, and R¹⁴ is optionally substituted C₃₋₈cycloalkyl. In yet other embodiments, at least one of R¹⁰, R¹¹, R¹², R¹³, and R¹⁴ is optionally substituted heterocyclyl. In still other embodiments, at least one of R¹⁰, R¹¹, R¹², R¹³, and R¹⁴ is optionally substituted heterocyclyl(alkylene). In still further embodiments, at least one of R¹⁰, R¹¹, R¹², R¹³, and R¹⁴ is optionally substituted aryl. In other embodiments, at least one of R¹⁰, R¹¹, R¹², R¹³, and R¹⁴ is optionally substituted heteroaryl. In some embodiments, one or both of R^y and R^x are H. In other embodiments, one or both of R^y and R^x is C₁₋₆alkyl. In some embodiments, one or both of R^y and R^z is H. In other embodiments, one or both of R^y and R^z is C₁₋₆alkyl. In further embodiments, one or both of R^y and R^z is C₃₋₆cycloalkyl. In yet other embodiments, one or both of R^y and R^z is C₁₋₆hydroxyalkyl. In still further embodiments, one or both of R^y and R^z is C₁₋₆haloalkyl. In further embodiments, one or both of R^y and R^z is C(O)OC₁₋₆alkyl. In some embodiments, one or both of R^{y2} and R^{z2} is H. In other embodiments, one or both of R^{y2} and R^{z2} is C₁₋₆alkyl. In further embodiments, one or both of R^{y2} and R^{z2} is C₃₋₆cycloalkyl. In some embodiments, p is 0. In other embodiments, p is 1. In further embodiments, p is 2. In yet other embodiments, p is 3. In some embodiments, R¹⁵ is H. In other embodiments, R¹⁵ is C₁₋₆alkyl.

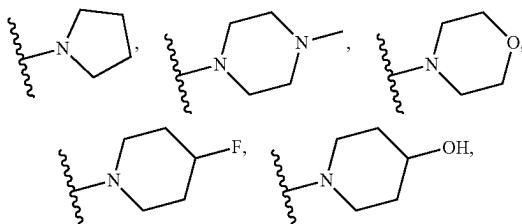
[0148] In still further embodiments, R² is



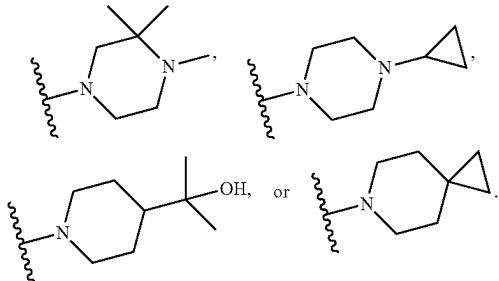
wherein R¹⁰, R¹¹, R¹², R¹³, and R¹⁴ are each independently H, C₁₋₆alkyl, C₁₋₆haloalkyl, C₃₋₆cycloalkyl, C₁₋₆alkoxy, C₁₋₆alkoxy(alkylene), halo, optionally substituted aryl, optionally substituted heterocyclyl, optionally substituted heterocyclyl(alkylene), optionally substituted heteroaryl, or (CR^yR^x)_pNR^{y2}R^{z2}. In some embodiments, R¹⁰, R¹¹, R¹², R¹³, and R¹⁴ are H. In other embodiments, at least one of R¹⁰, R¹¹, R¹², R¹³, and R¹⁴ is C₁₋₆alkyl such as methyl or ethyl. In further embodiments, at least one of R¹⁰, R¹¹, R¹², R¹³, and R¹⁴ is C₁₋₆haloalkyl such as CF₃, or C(CH₃)₂F. In yet further embodiments, at least one of R¹⁰, R¹¹, R¹², R¹³, and R¹⁴ is C₃₋₆cycloalkyl such as cyclopropyl. In yet other embodiments, at least one of R¹⁰, R¹¹, R¹², R¹³, and R¹⁴ is C₁₋₆alkoxy such as methoxy. In other embodiments, at least one of R¹⁰, R¹¹, R¹², R¹³, and R¹⁴ is C₁₋₆alkoxy(alkylene) such as CH₂OCH₃ or (CH₂)₂OCH₃. In yet other embodiments, at least one of R¹⁰, R¹¹, R¹², R¹³, and R¹⁴ is halo such as F, Br, or Cl. In still further embodiments, at least one of R¹⁰, R¹¹, R¹², R¹³, and R¹⁴ is optionally substituted aryl such as unsubstituted phenyl. In yet other embodiments, at least one of R¹⁰, R¹¹, R¹², R¹³, and R¹⁴ is optionally substituted heterocyclyl such as



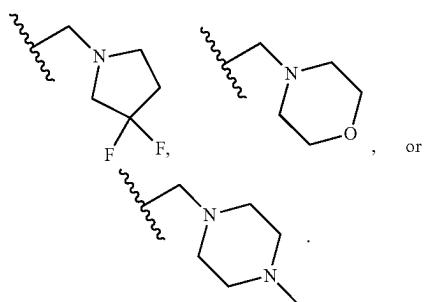
In still other embodiments, at least one of R¹⁰, R¹¹, R¹², R¹³, and R¹⁴ is optionally substituted heterocyclyl such as



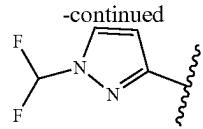
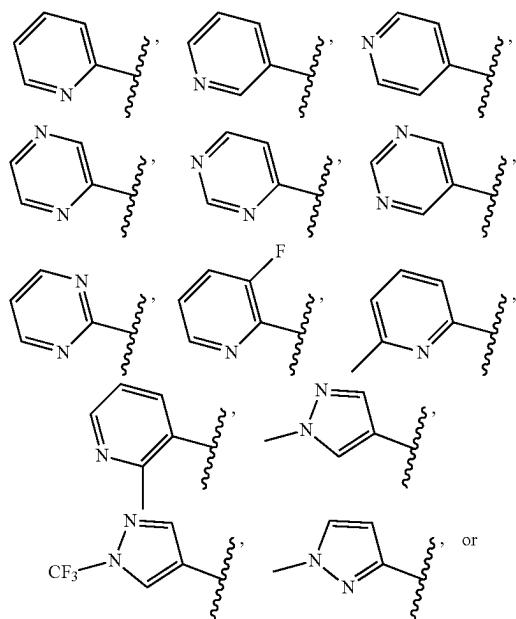
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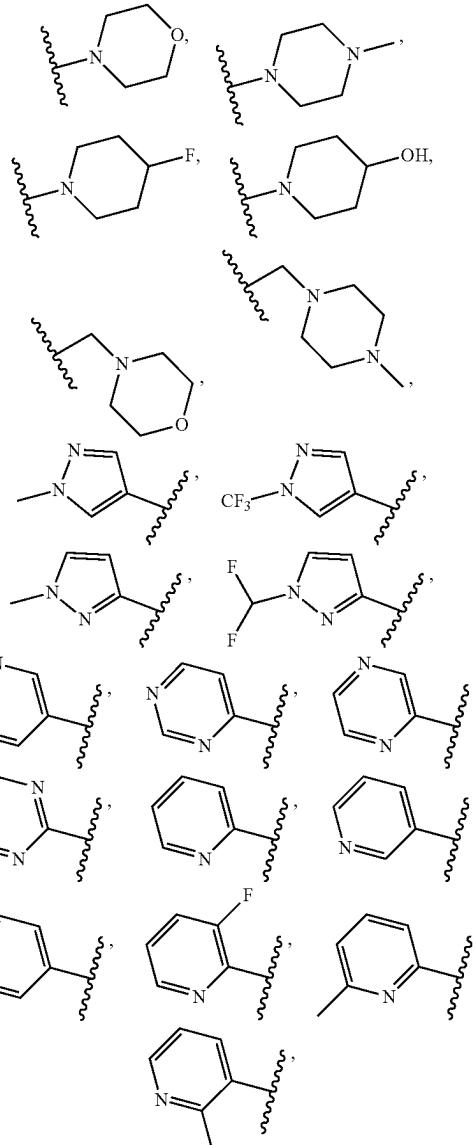
In further embodiments, at least one of R¹⁰, R¹¹, R¹², R¹³, and R¹⁴ is optionally substituted heterocycl(alkylene). In still further embodiments, at least one of R¹⁰, R¹¹, R¹², R¹³, and R¹⁴ is



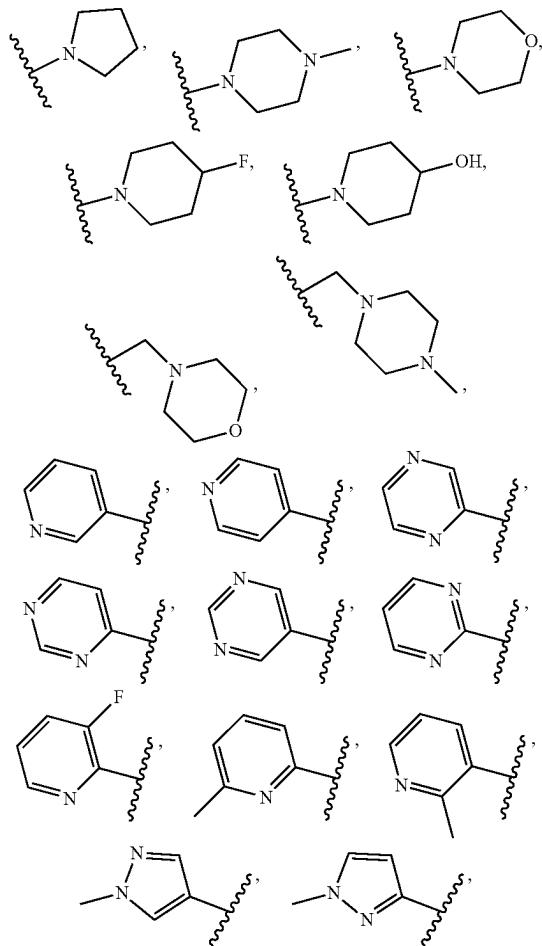
In other embodiments, at least one of R¹⁰, R¹¹, R¹², R¹³, and R¹⁴ is optionally substituted heteroaryl such as optionally substituted pyridinyl, optionally substituted pyrazinyl, optionally substituted pyrimidinyl, or optionally substituted pyrazolyl. In yet other embodiments, at least one of R¹⁰, R¹¹, R¹², R¹³, and R¹⁴ is



In still further embodiments, at least one of R¹⁰, R¹¹, R¹², R¹³, and R¹⁴ is (CR^xR^y)_pNR^yR^z such as NH₂, NH(CH₃), N(CH₃)₂, CH₂N(CH₃)₂, or CH₂CH₂N(CH₃)₂. In further embodiments, R¹⁰, R¹¹, R¹², R¹³, and R¹⁴ are each independently H, methyl, C(CH₃)₂F, cyclopropyl, methoxy, CH₂OCH₃, (CH₂)₂OCH₃, Br, F, Cl, phenyl,



N(CH₃)₂, CH₂N(CH₃)₂, or CH₂CH₂N(CH₃)₂. In yet other embodiments, R¹⁰, R¹¹, R¹², R¹³, and R¹⁴ are each independently H, methyl, C(CH₃)₂F, cyclopropyl, methoxy, CH₂OCH₃, (CH₂)₂OCH₃, Br, F, Cl, phenyl,



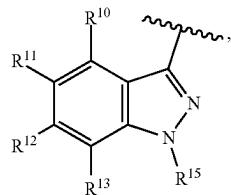
$\text{N}(\text{CH}_3)_2$, $\text{CH}_2\text{N}(\text{CH}_3)_2$, or $\text{CH}_2\text{CH}_2\text{N}(\text{CH}_3)_2$. In other embodiments, R^{10} , R^{13} , and R^{14} are each hydrogen. In further embodiments, R^{10} , R^{13} , and R^{14} are each hydrogen; and R^{11} is halo. In still further embodiments, R^{10} , R^{11} , R^{13} , and R^{14} are each hydrogen.

[0149] In further embodiments, at least one of R^{10} , R^{11} , R^{12} , R^{13} , and R^{14} is substituted heterocycl or substituted heterocycl(alkylene), substituted with one or more of halo such as F, Cl, or Br; C_{1-6} haloalkyl such as CF_3 , CH_2CF_3 , or CHF_2 ; C_{1-6} alkyl such as methyl, ethyl, or propyl; OH; C_{1-6} hydroxyalkyl such as $\text{C}(\text{CH}_3)_2\text{OH}$; C_{1-6} alkoxy such as methoxy, ethoxy, or propoxy; or C_{3-6} cycloalkyl such as cyclopropyl, cyclobutyl, or cyclopentyl. In other embodiments, the substituted heterocycl or substituted heterocycl(alkylene) is substituted with one or more methyl, OH, or F.

[0150] In further embodiments, at least one of R^{10} , R^{11} , R^{12} , R^{13} , and R^{14} is substituted heteroaryl, substituted with one or more of halo such as F, Cl, or Br; C_{1-6} haloalkyl such as CF_3 , CH_2CF_3 , or CHF_2 ; C_{1-6} alkyl such as methyl, ethyl, propyl, or isopropyl; C_{1-6} alkoxy such as methoxy, ethoxy, or propoxy; C_{1-6} haloalkoxy such as OCF_3 ; C_{3-6} cycloalkyl such as cyclopropyl, cyclobutyl, or cyclopentyl; or C_{3-6} cycloalkylsulfonyl such as cyclopropylsulfonyl, cyclobutylsulfo-

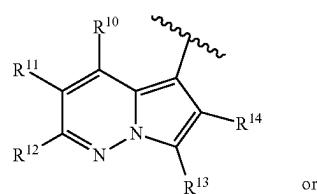
nyl, or cyclopentylsulfonyl. In yet other embodiments, the substituted heteroaryl is substituted with one or more of F, CF_3 , CHF_2 , or methyl.

[0151] In other embodiments, R^2 is

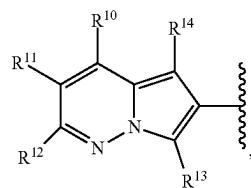


wherein R^{10} , R^{11} , R^{12} , and R^{13} are each independently H, C_{1-6} alkyl, or halo and R^{15} is H or C_{1-6} alkyl. In further embodiments, R^{10} , R^{11} , R^{12} , and R^{13} are H. In other embodiments, at least one of R^{10} , R^{11} , R^{12} , and R^{13} is C_{1-6} alkyl. In further embodiments, at least one of R^{10} , R^{11} , R^{12} , and R^{13} is halo. In yet other embodiments, at least one of R^{10} , R^{11} , R^{12} , and R^{13} is Br. In some embodiments, one of R^{10} , R^{11} , R^{12} , or R^{13} is C_{1-6} alkyl, or halo such as Br and the remainder of R^{10} , R^{11} , R^{12} , or R^{13} are each H. In some embodiments, R^{15} is H. In other embodiments, R^{15} is C_{1-6} alkyl. In further embodiments, R^{15} is methyl. In yet other embodiments, R^{15} is H or methyl.

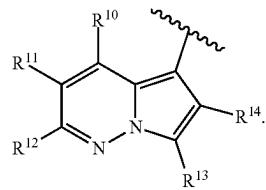
[0152] In further embodiments, R^2 is



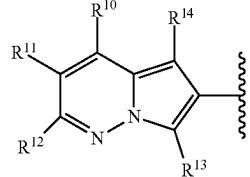
or



wherein R^{10} , R^{11} , R^{12} , R^{13} , and R^{14} are each independently H, halo, or C_{1-6} alkyl. In some embodiments, R^2 is

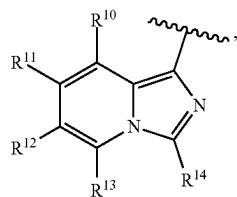


In other embodiments, R² is



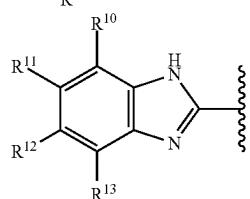
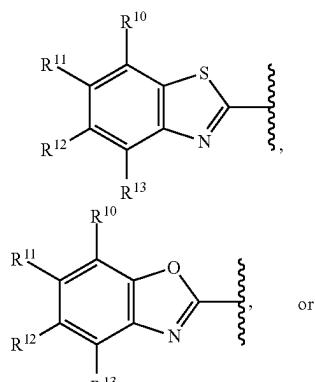
In some embodiments, R¹⁰, R¹¹, R¹², R¹³, and R¹⁴ are H. In other embodiments, at least one of R¹⁰, R¹¹, R¹², R¹³, and R¹⁴ is halo. In further embodiments, at least one of R¹⁰, R¹¹, R¹², R¹³, and R¹⁴ is C₁₋₆alkyl.

[0153] In yet other embodiments, R² is

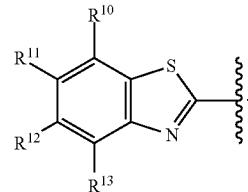


wherein R¹⁰, R¹¹, R¹², R¹³, and R¹⁴ are each independently H, halo, or C₁₋₆alkyl. In some embodiments, R¹⁰, R¹¹, R¹², R¹³, and R¹⁴ are H. In other embodiments, at least one of R¹⁰, R¹¹, R¹², R¹³, and R¹⁴ is halo. In further embodiments, at least one of R¹⁰, R¹¹, R¹², R¹³, and R¹⁴ is Br. In yet other embodiments, at least one of R¹⁰, R¹¹, R¹², R¹³, and R¹⁴ is C₁₋₆alkyl.

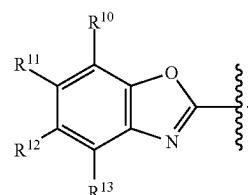
[0154] In still further embodiments, R² is



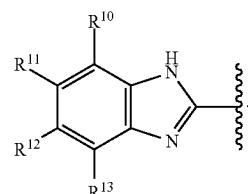
wherein R¹⁰, R¹¹, R¹², and R¹³ are each independently H, C₁₋₆alkyl, or halo. In some embodiments, R² is



In other embodiments, R² is

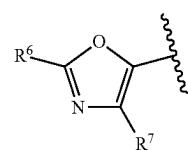


In further embodiments, R² is

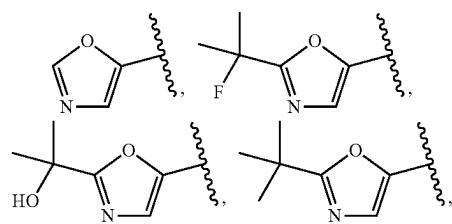


In some embodiments, R¹⁰, R¹¹, R¹², and R¹³ are H. In other embodiments, at least one of R¹⁰, R¹¹, R¹², and R¹³ is halo. In further embodiments, at least one of R¹⁰, R¹¹, R¹², and R¹³ is F. In yet other embodiments, at least one of R¹⁰, R¹¹, R¹², and R¹³ is C₁₋₆alkyl. In still further embodiments, at least one of R¹⁰, R¹¹, R¹², and R¹³ is methyl. In yet other embodiments, R¹⁰, R¹¹, R¹², and R¹³ are each independently H, methyl, or F.

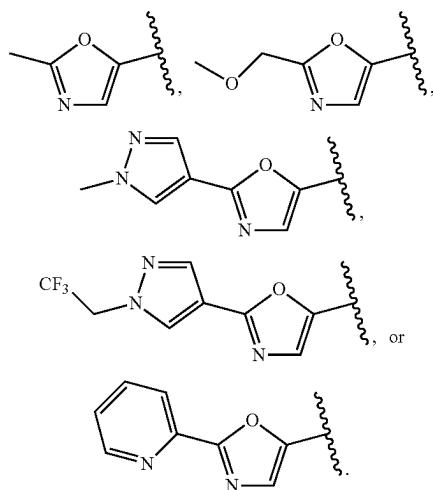
[0155] In other embodiments, R² is



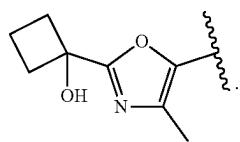
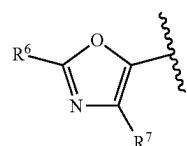
wherein R⁶ is defined herein and R⁷ is H. In yet other embodiments, R² is



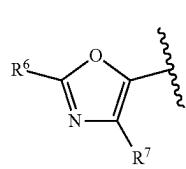
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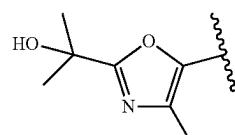
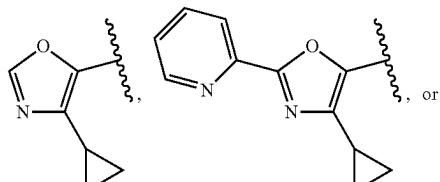
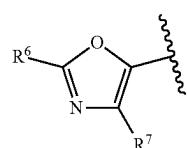
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[0157] In yet other embodiments, R² is

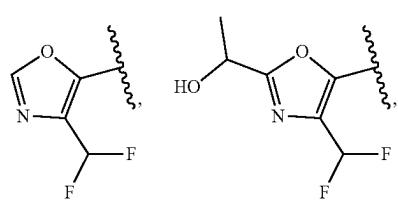
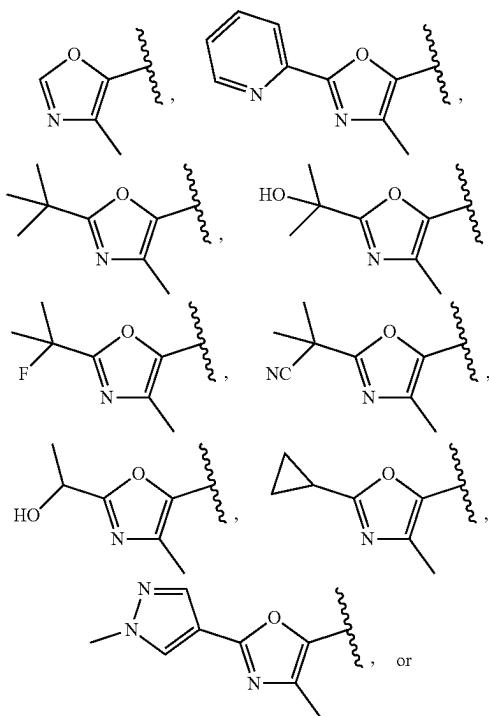
wherein R⁶ is defined herein and R⁷ is cyclopropyl. In further embodiments, R² is

[0156] In further embodiments, R² is

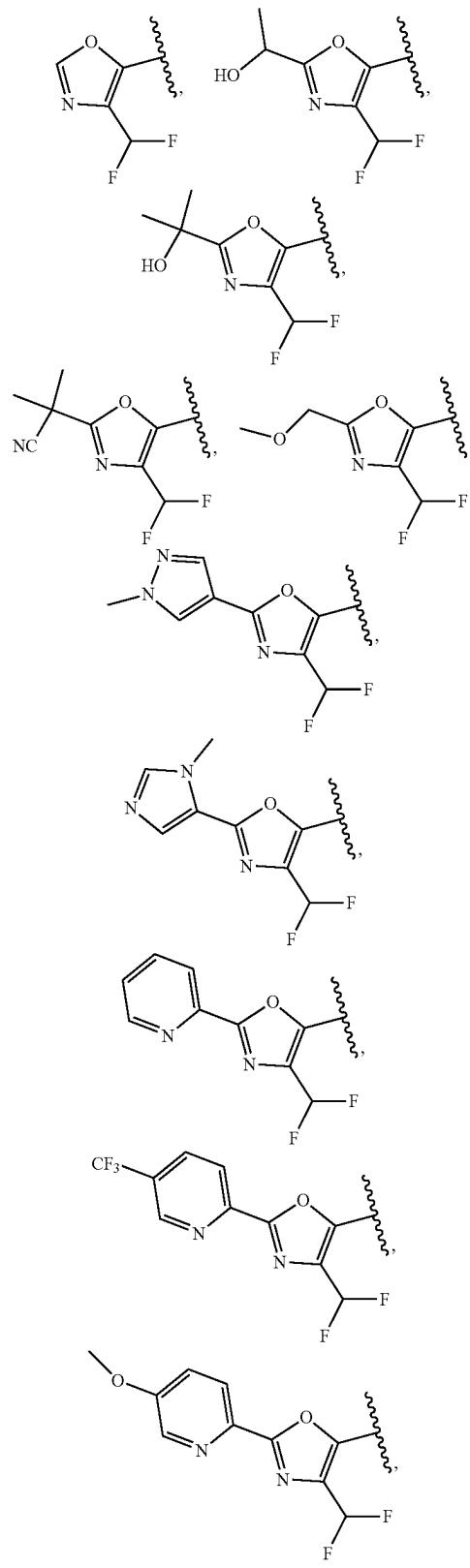
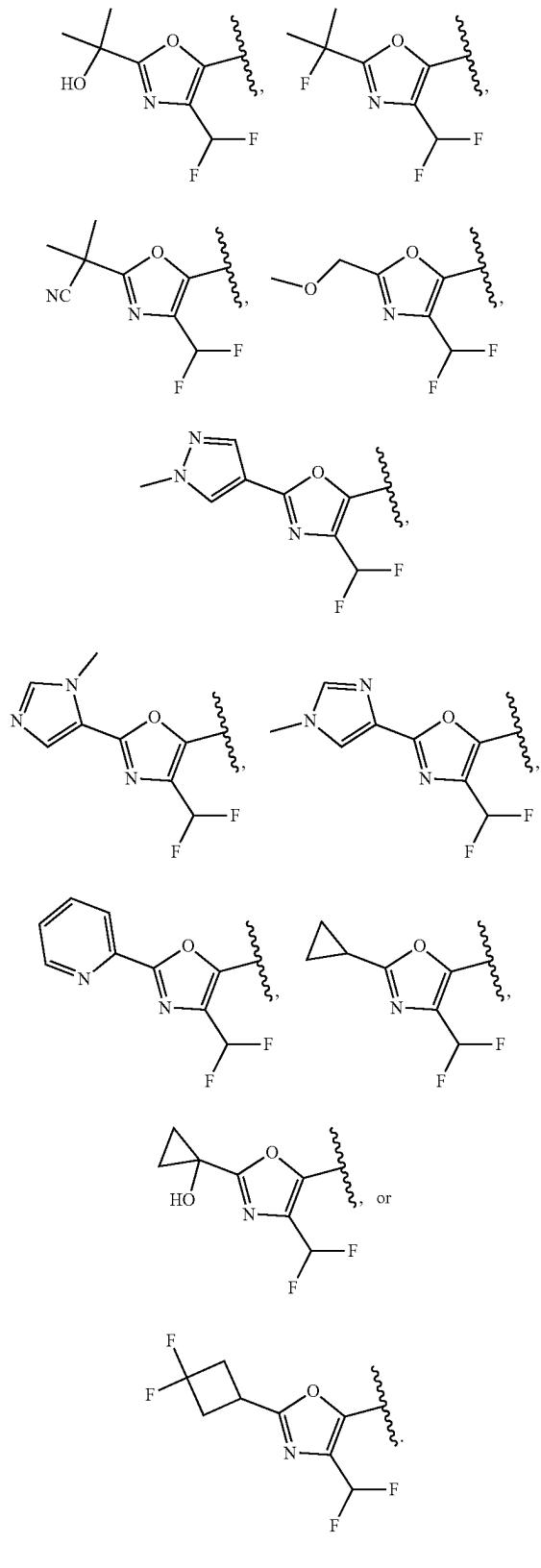
wherein R⁶ is defined herein and R⁷ is CH₃. In other embodiments, R² is

[0158] In still further embodiments, R² is

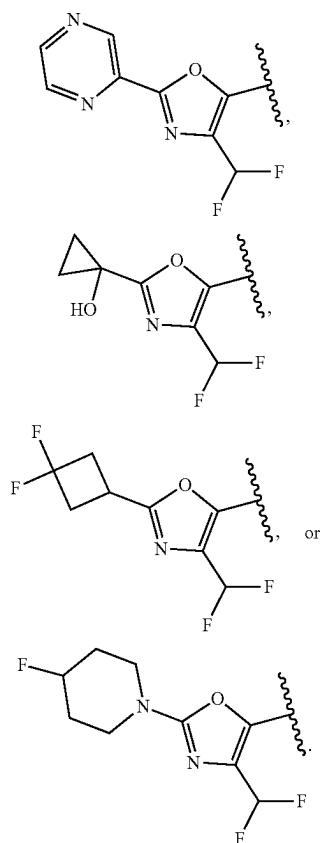
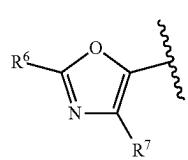
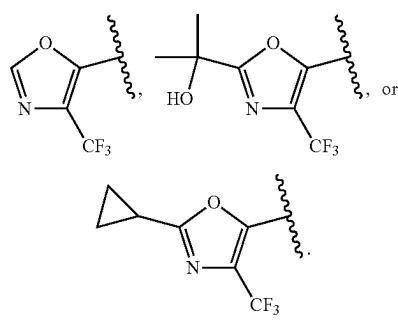
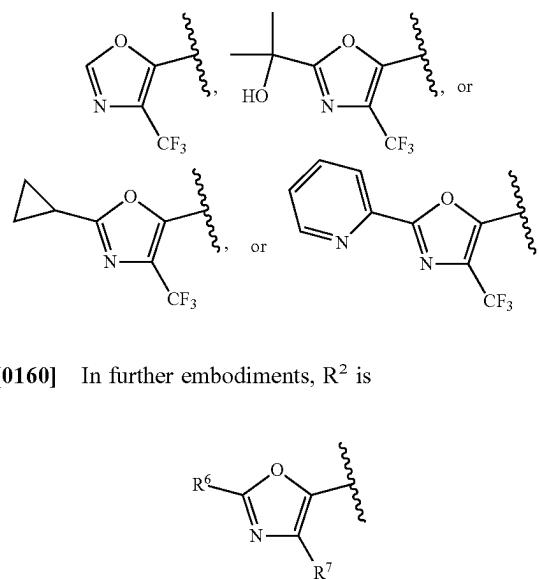
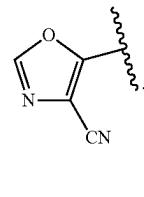
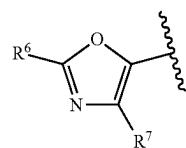
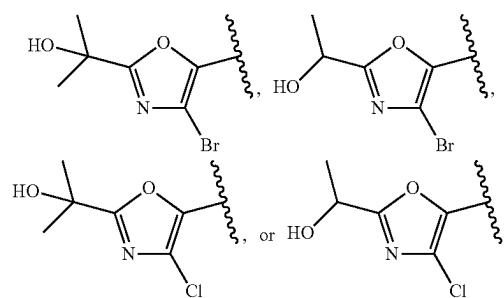
wherein R⁶ is defined herein and R⁷ is CHF₂. In other embodiments, R² is



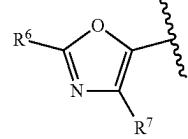
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In yet other embodiments, In other embodiments, R² is

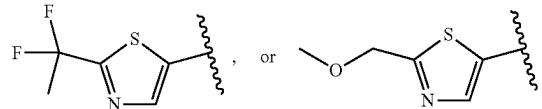
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[0159] In other embodiments, R² iswherein R⁶ is defined herein and R⁷ is CF₃. In still other embodiments, R² isIn yet other embodiments, R² iswherein R⁶ is defined herein and R⁷ is CN. In still further embodiments, R² is[0161] In yet other embodiments, R² iswherein R⁶ is defined herein and R⁷ is Br or Cl. In further embodiments, R² is

[0162] In still further embodiments, R² is

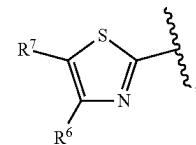
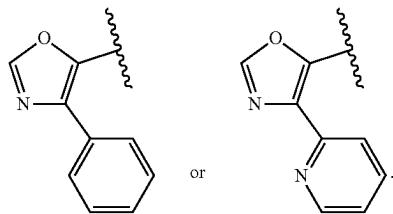


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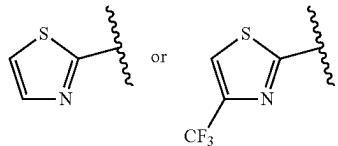
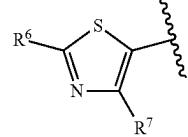
[0164] In further embodiments, R² is

wherein R⁶ is defined herein and R⁷ is phenyl or pyridinyl.
In other embodiments, R² is

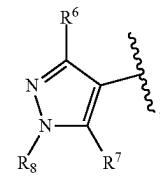
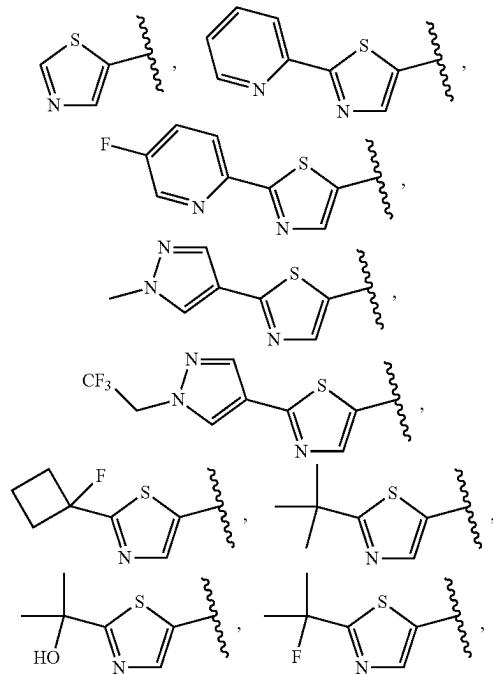


wherein R⁶ and R⁷ are defined herein. In yet other embodiments, R² is

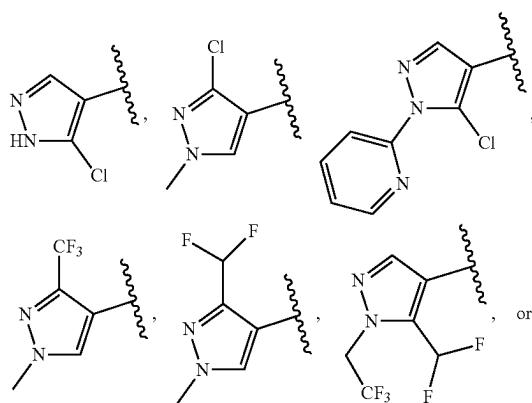
[0163] In further embodiments, R² is

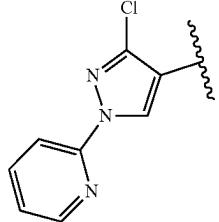
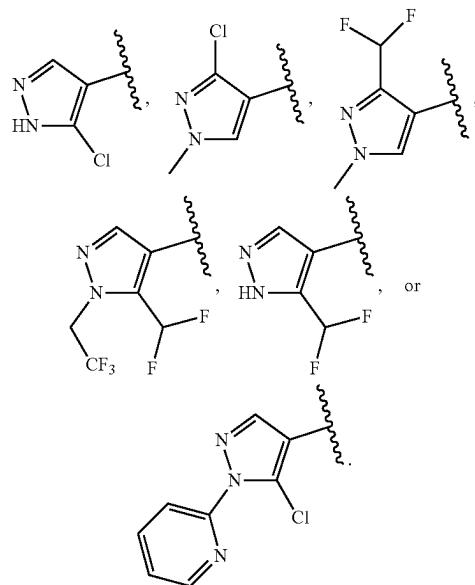
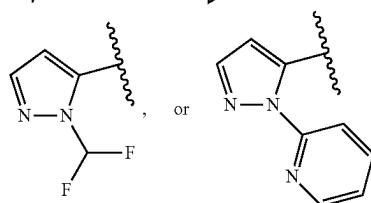
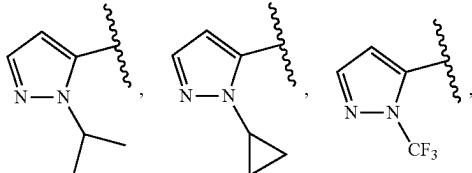
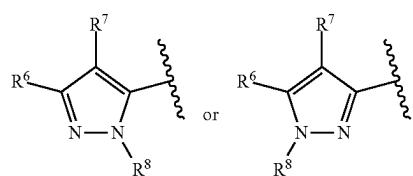
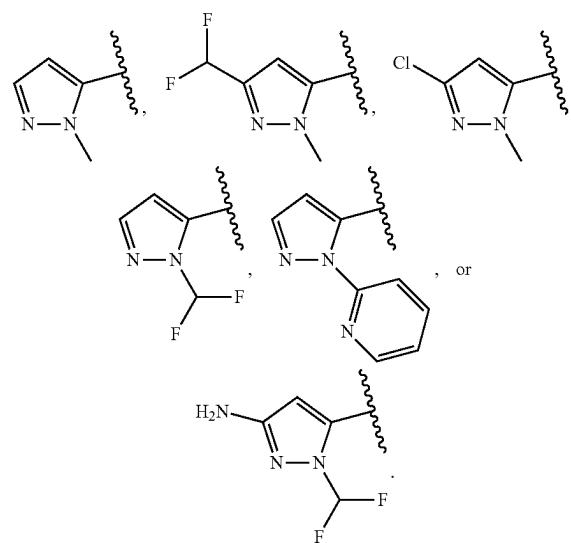
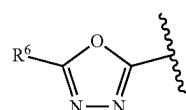
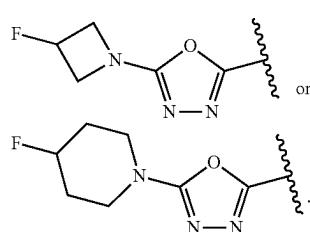
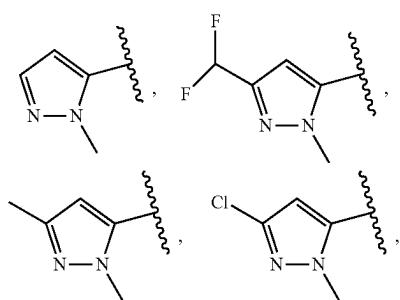


wherein R⁶ is defined herein and R⁷ is H. In yet other embodiments, R² is

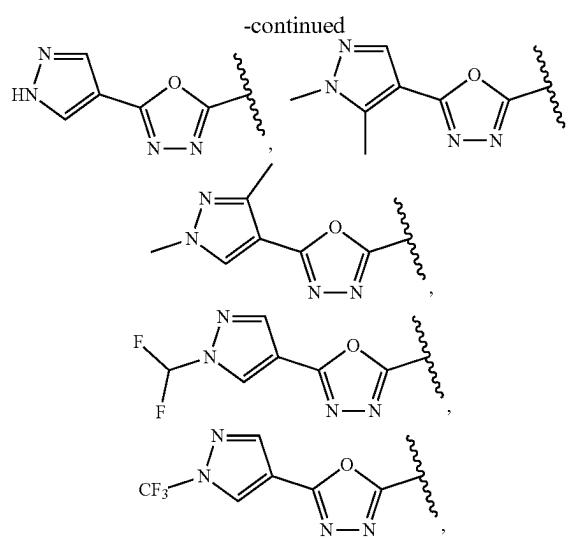
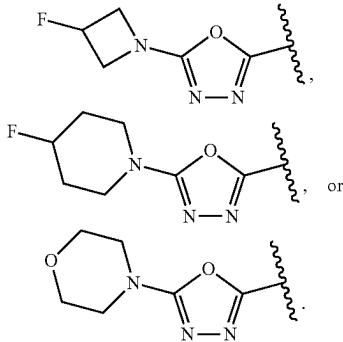


wherein R⁶-R⁸ are defined herein. In still other embodiments, R² is

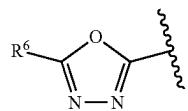


-continuedIn yet other embodiments, R² is*-continued*[0166] In further embodiments, R² iswherein R⁶-R⁸ are defined herein. In still further embodiments, R² isIn yet other embodiments, R² is[0167] In other embodiments, R² iswherein R⁶ is optionally substituted heterocycl. In yet other embodiments, R² is

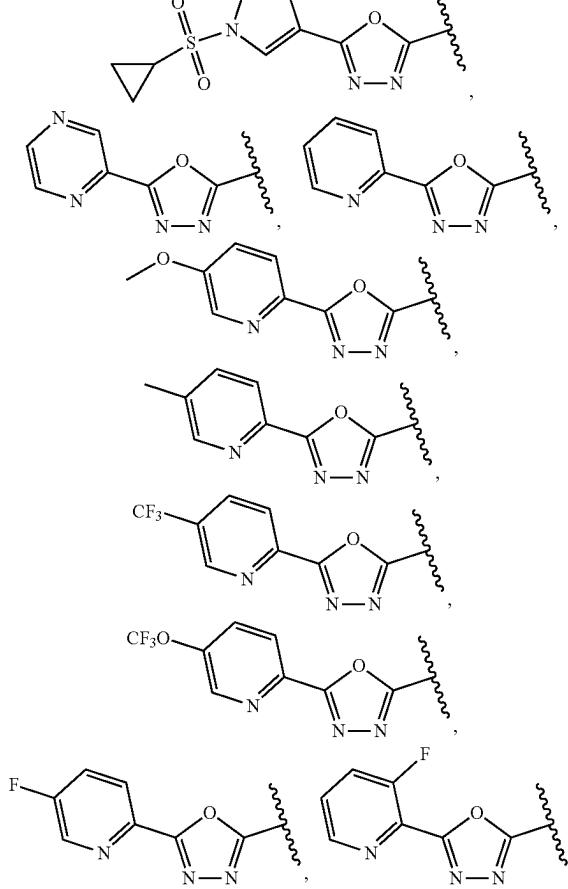
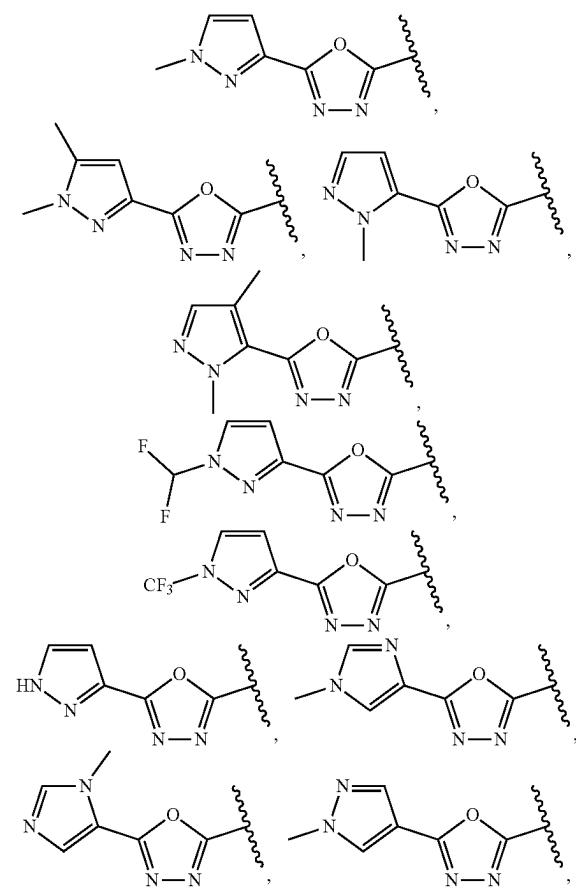
In still other embodiments, R² is



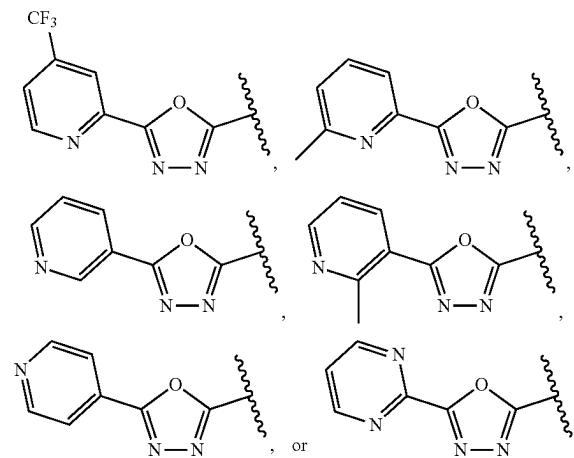
[0168] In further embodiments, R² is



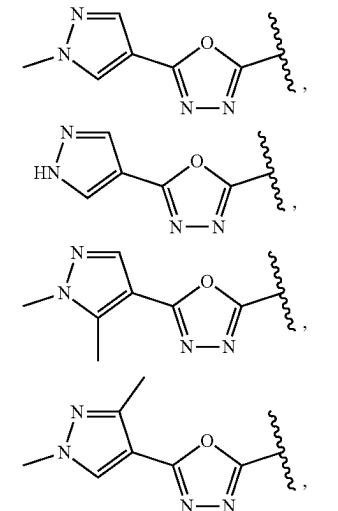
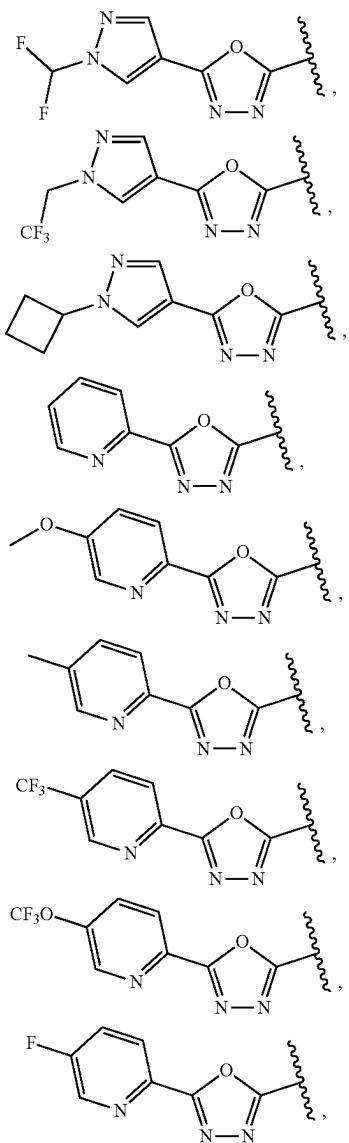
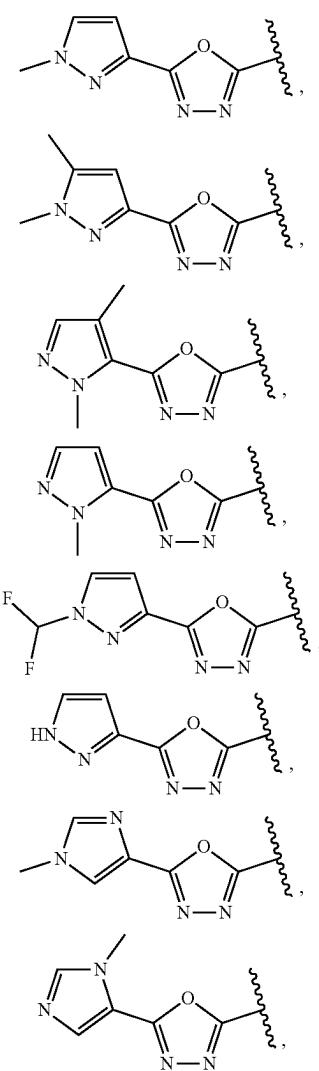
wherein R⁶ is optionally substituted heteroaryl. In still further embodiments, R² is

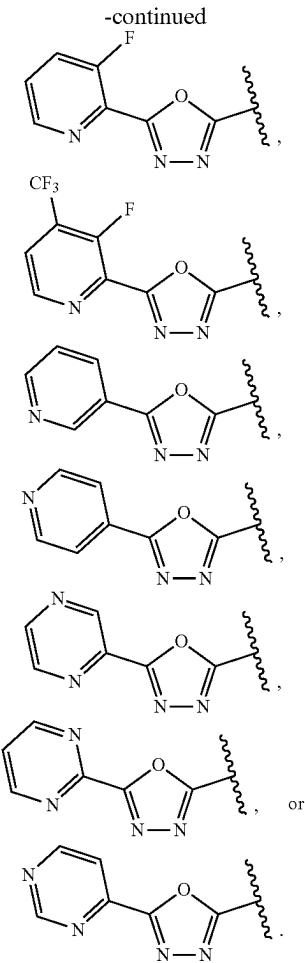


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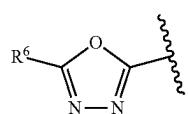


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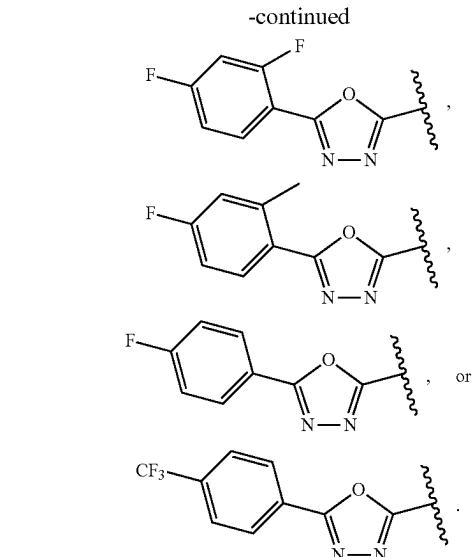
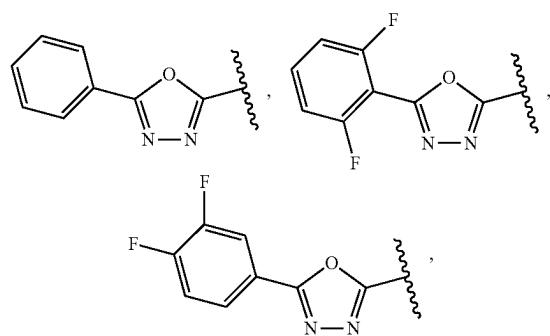
In yet other embodiments R² is



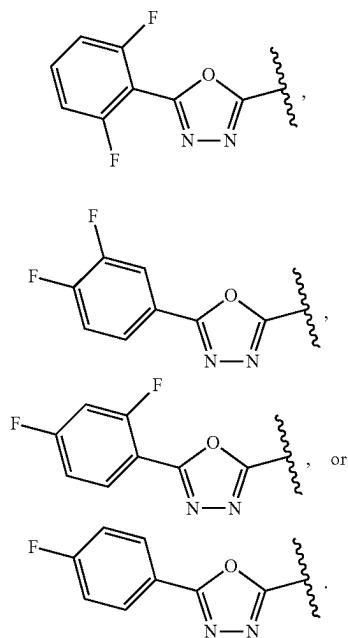
[0169] In other embodiments R² is



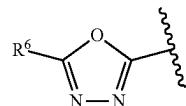
wherein R⁶ is optionally substituted aryl. In still other embodiments, R² is



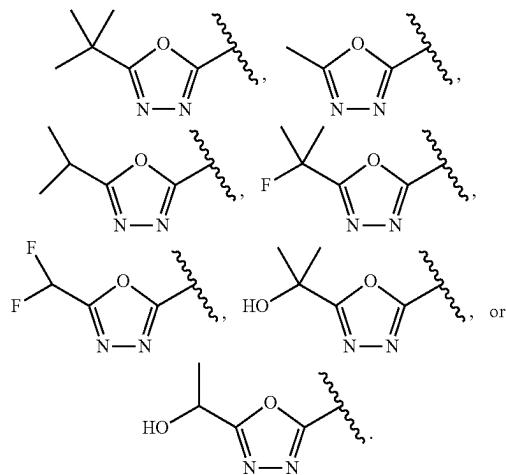
In yet other embodiments, R² is



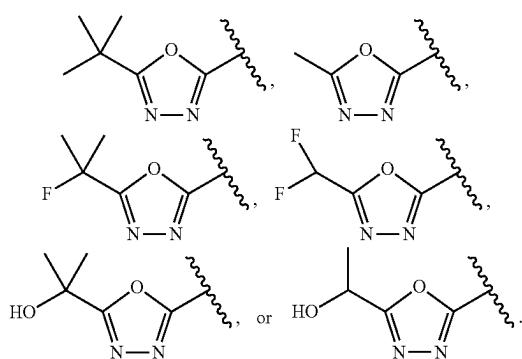
[0170] In further embodiments, R² is



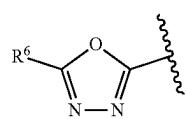
wherein R⁶ is C₁₋₆alkyl, C₁₋₆haloalkyl, or C₁₋₆hydroxyalkyl. In still further embodiments, R² is



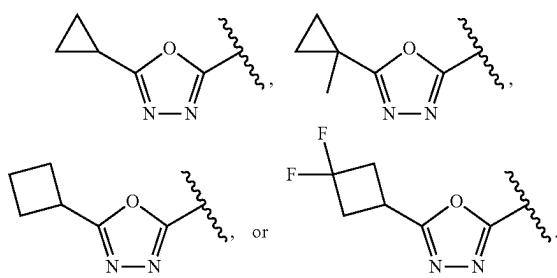
In yet other embodiments, R² is



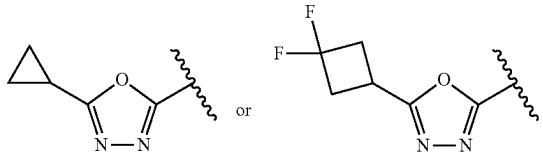
[0171] In other embodiments, R² is



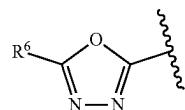
wherein R⁶ is optionally substituted C₃₋₈cycloalkyl. In yet other embodiments, R² is



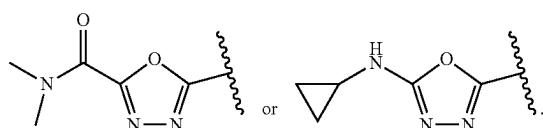
In still other embodiments, R² is



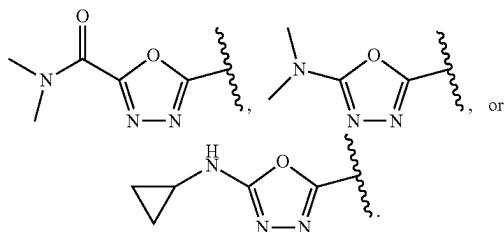
[0172] In yet other embodiments, R² is



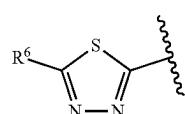
wherein R⁶ is C(O)NR^{y2}R^{z2} or (CR^vR^x)_pNR^yR^z and R^{y2}, R^{z2}, p, R^v, R^x, R^y, and R^z are defined herein. In other embodiments, R² is



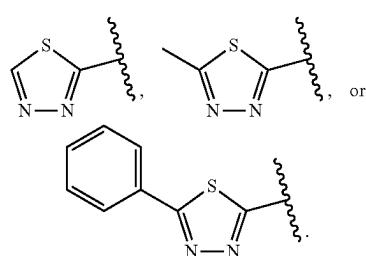
In still other embodiments, R² is



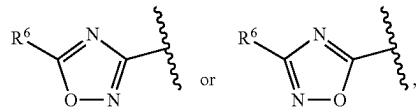
[0173] In other embodiments, R² is



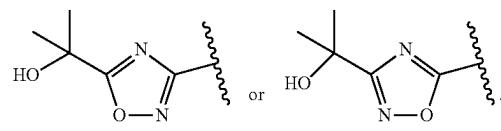
wherein R⁶ is H, C₁₋₆alkyl, or optionally substituted aryl. In still other embodiments, R² is



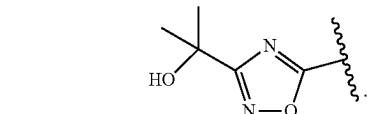
[0174] In further embodiments, R² is



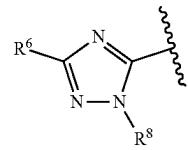
wherein R⁶ is C₁₋₆hydroxyalkyl. In yet further embodiments, R² is



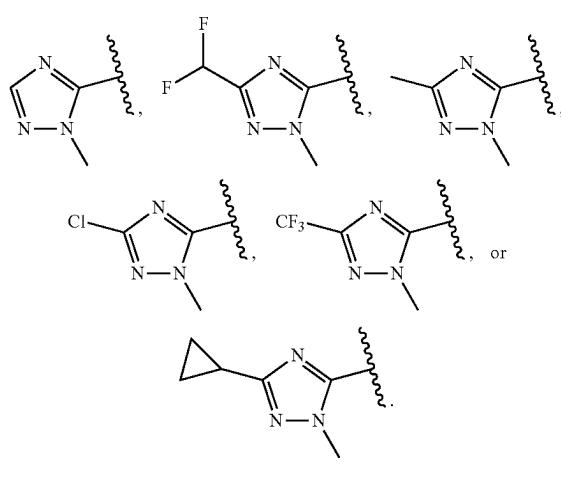
In other embodiments, R² is



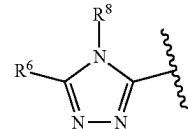
[0175] In other embodiments, R² is



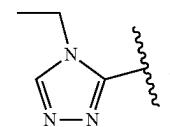
wherein R⁸ is C₁₋₆alkyl and R⁶ is defined herein. In still other embodiments, R² is



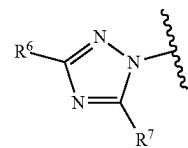
[0176] In further embodiments, R² is



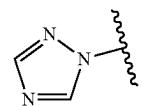
wherein R⁶ and R⁸ are defined herein. In yet other embodiments, R² is



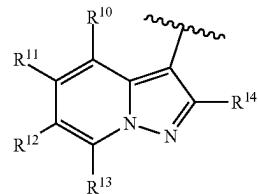
[0177] In other embodiments, R² is



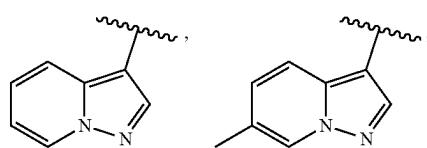
wherein R⁶ and R⁷ are defined herein. In yet other embodiments, R² is



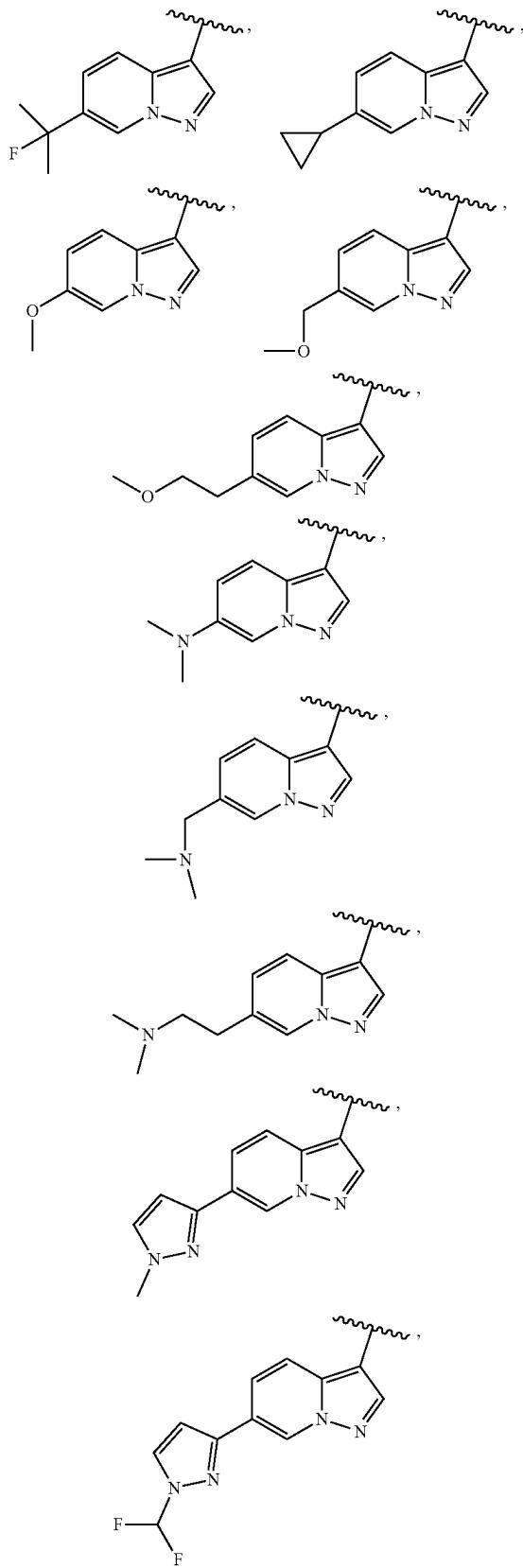
[0178] In further embodiments, R² is



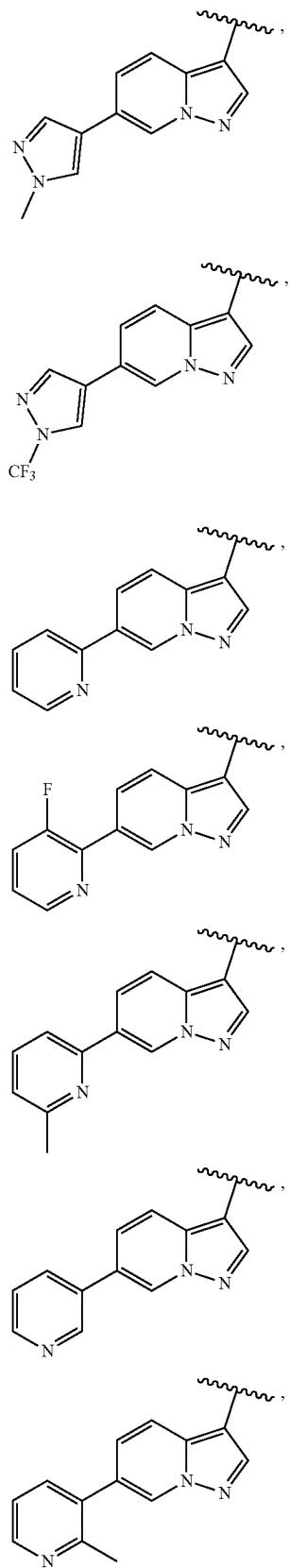
wherein R^{10-R14} are defined herein. In still further embodiments, R² is



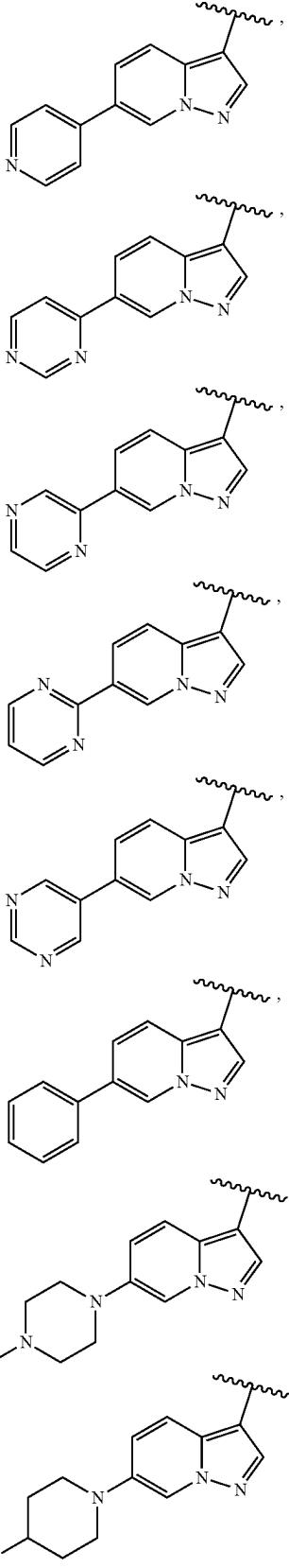
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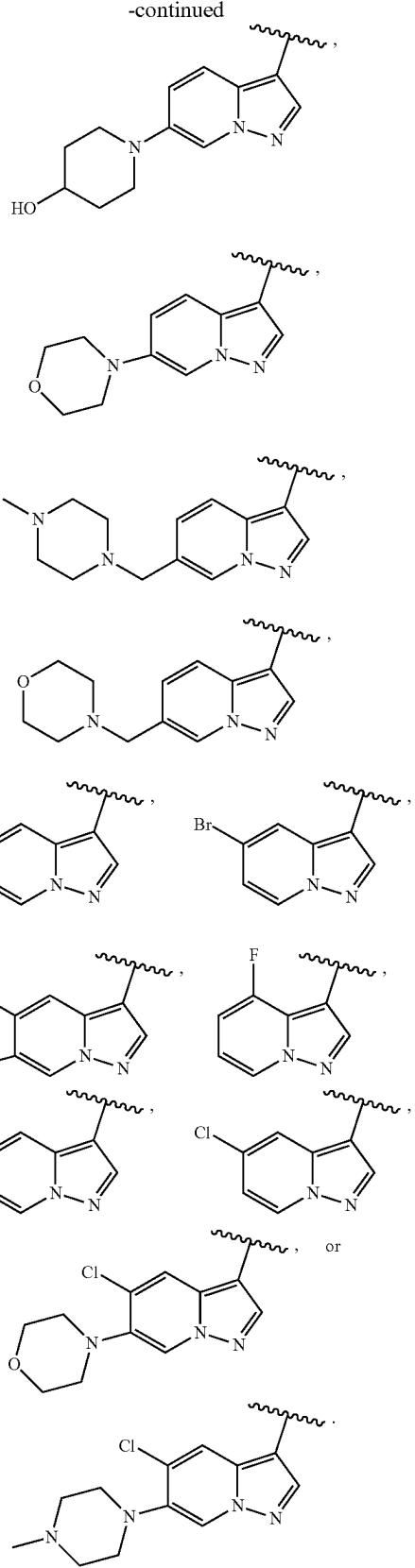
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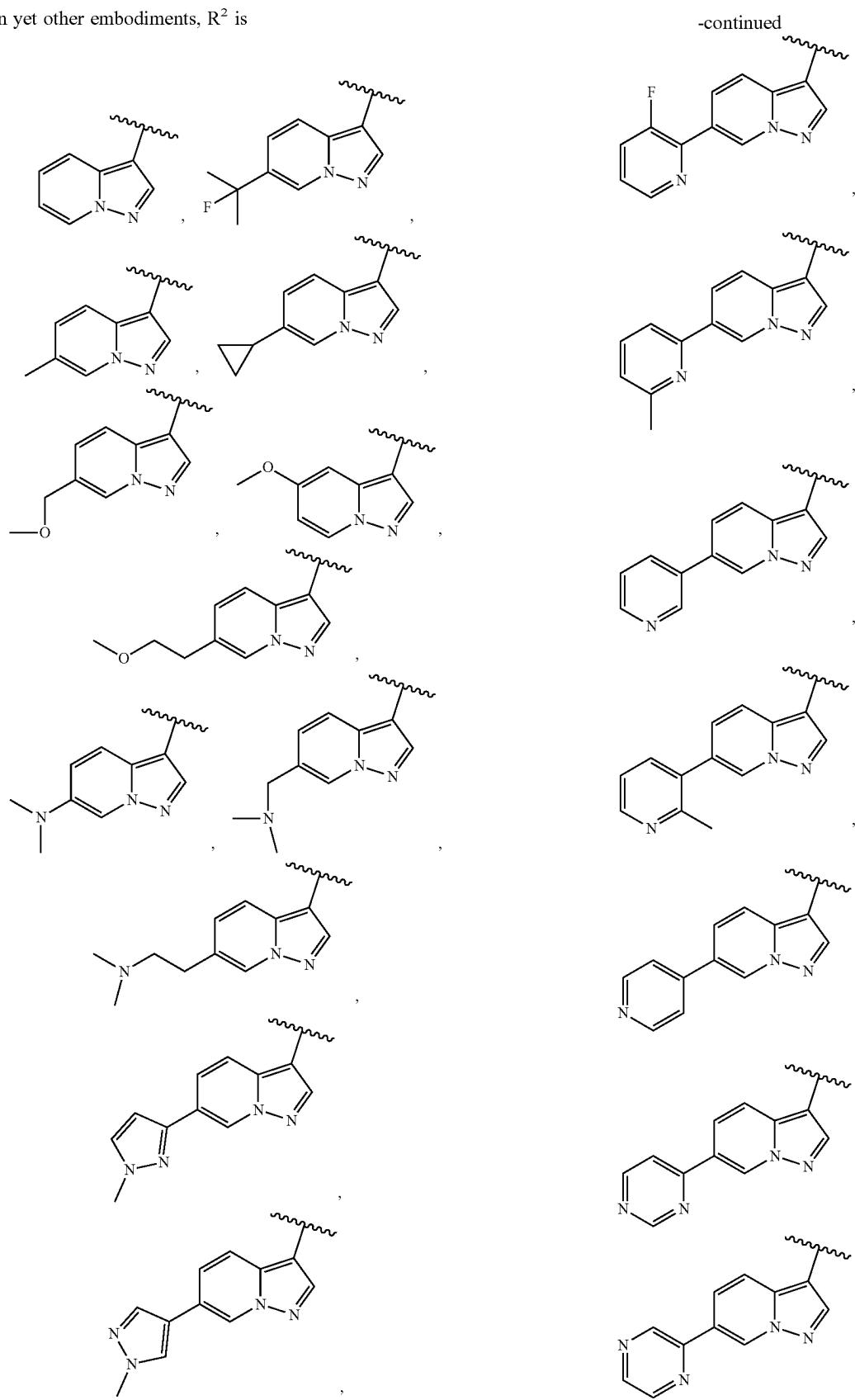
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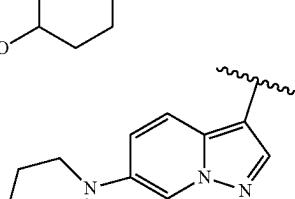
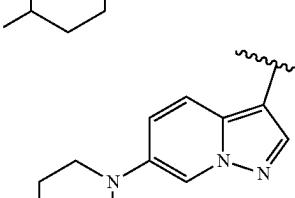
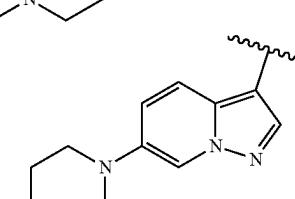
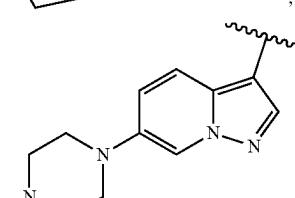
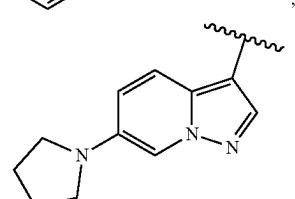
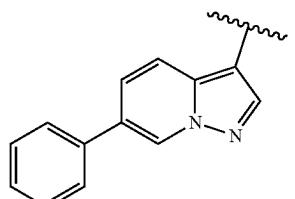
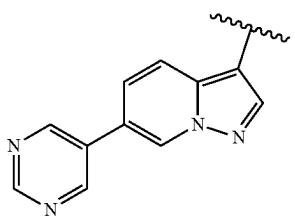
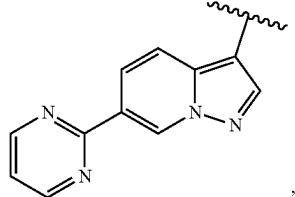
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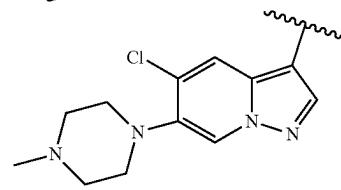
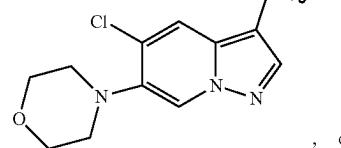
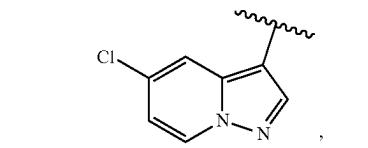
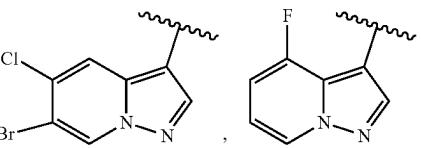
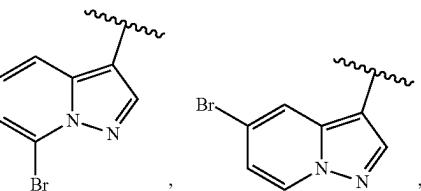
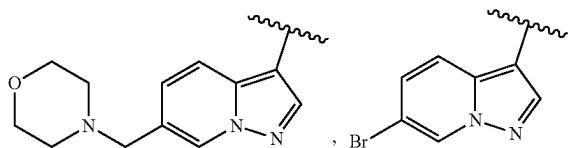
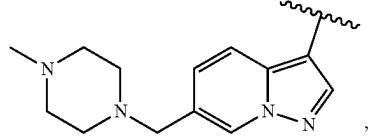
In yet other embodiments, R² is



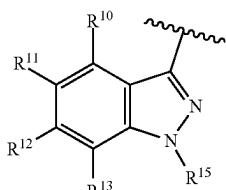
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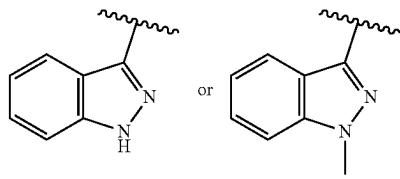
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[0179] In other embodiments, R² is

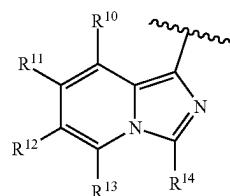


wherein R¹³ is H and R¹⁰, R¹¹, R¹², R¹⁴, and R¹⁵ are defined herein. In yet other embodiments, R² is

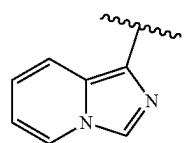


I-A-1

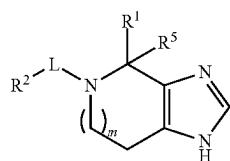
[0180] In still other embodiments, R² is



and R¹⁰-R¹⁴ are defined herein. In yet other embodiments, R² is

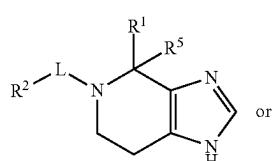


[0181] In some embodiments, the compound of Formula I is of Formula I-A or a pharmaceutically acceptable salt thereof:

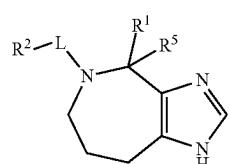


I-A

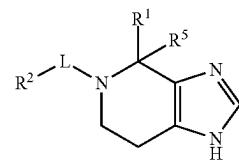
such as



I-A-1

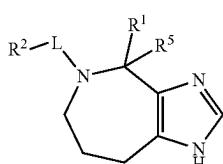


I-A-2



I-A-1

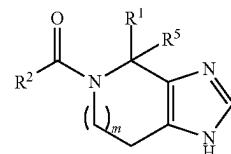
or a pharmaceutically acceptable salt thereof. In other embodiments, the compound is



I-A-2

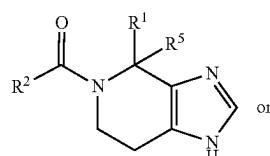
or a pharmaceutically acceptable salt thereof.

[0182] In other embodiments, the compound of Formula I is of Formula I-B or a pharmaceutically acceptable salt thereof:

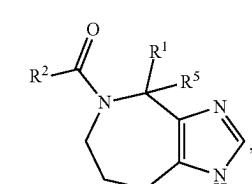


I-B

such as



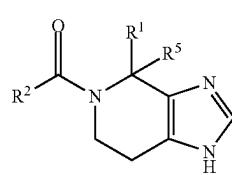
I-B-1



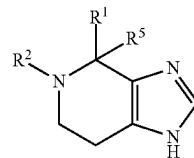
I-B-2

wherein R¹, R², R⁵, L, and m are defined herein. In other embodiments, the compound is

wherein R¹, R², R⁵, and m are defined herein. In further embodiments, the compound is

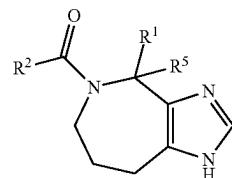


I-B-1

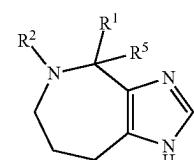


I-C-1

or a pharmaceutically acceptable salt thereof. In other embodiments, the compound is



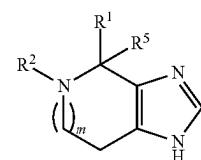
I-B-2



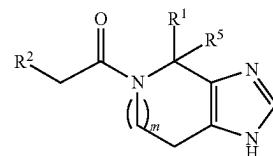
I-C-2

or a pharmaceutically acceptable salt thereof.

[0183] In further embodiments, the compound of Formula I is of Formula I-C or a pharmaceutically acceptable salt thereof:



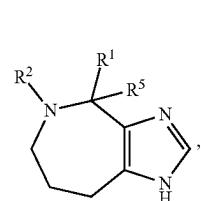
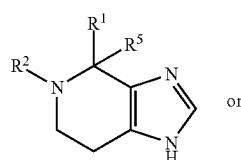
I-C



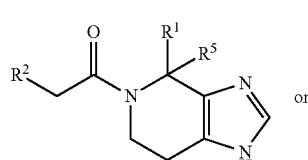
I-D

such as

such as

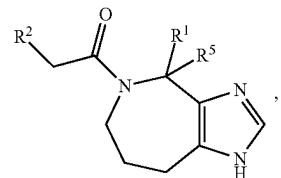


I-C-1



I-D-1

I-C-2

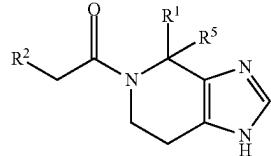


I-D-2

wherein R¹, R², R⁵, and m are defined herein. In other embodiments, the compound is

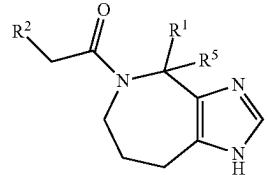
wherein R¹, R², R⁵, and m are defined herein. In some embodiments, the compound is

I-D-1



or a pharmaceutically acceptable salt thereof. In other embodiments, the compound is

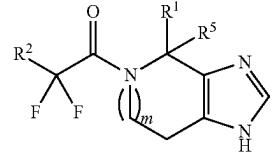
I-D-2



or a pharmaceutically acceptable salt thereof.

[0185] In still further embodiments, the compound of Formula I is of Formula I-E or a pharmaceutically acceptable salt thereof:

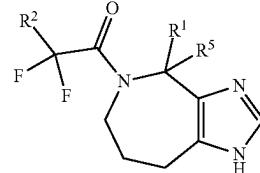
I-E



such as

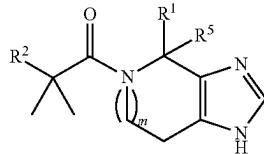
such as

I-E-2



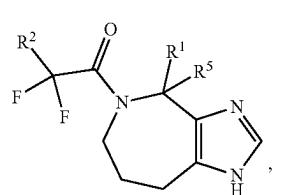
or a pharmaceutically acceptable salt thereof. In other embodiments, the compound is

I-F

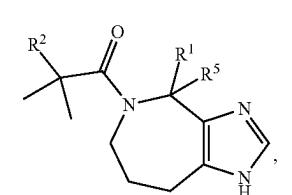


wherein R¹, R², R⁵, and m are defined herein. In other embodiments, the compound is

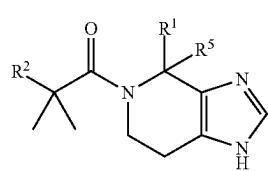
I-E-2



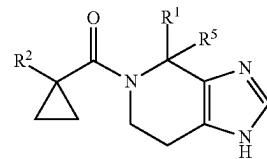
I-F-2



wherein R¹, R², R⁵, and m are defined herein. In yet other embodiments, the compound is

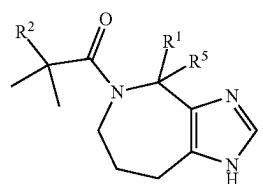


I-F-1

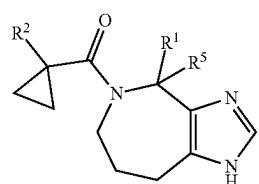


I-G-1

or a pharmaceutically acceptable salt thereof. In other embodiments, the compound is



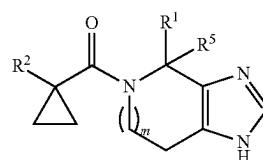
I-F-2



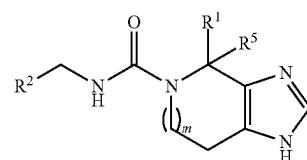
I-G-2

or a pharmaceutically acceptable salt thereof.

[0187] In further embodiments, the compound of Formula I is of Formula I-G or a pharmaceutically acceptable salt thereof:

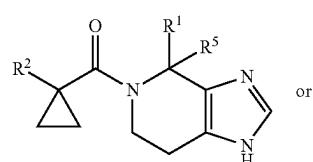


I-G

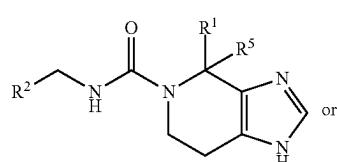


I-H

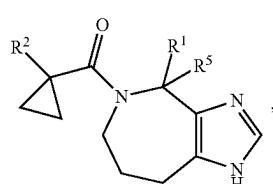
such as



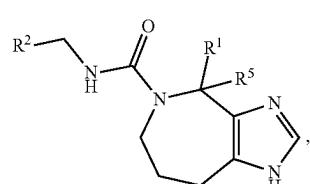
I-G-1



I-H-1



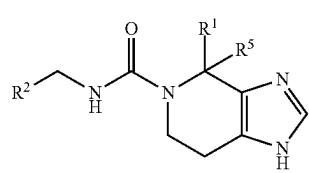
I-G-2



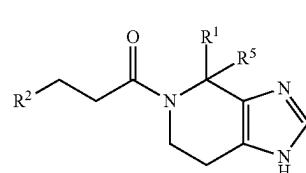
I-H-2

wherein R¹, R², R⁵, and m are defined herein. In still further embodiments, the compound is

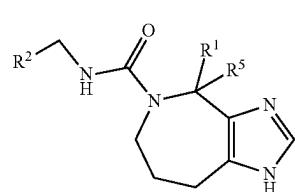
wherein R¹, R², R⁵, and m are defined herein. In other embodiments, the compound is



or a pharmaceutically acceptable salt thereof. In other embodiments, the compound is

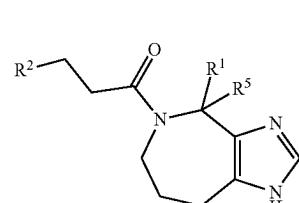


or a pharmaceutically acceptable salt thereof. In other embodiments, the compound is



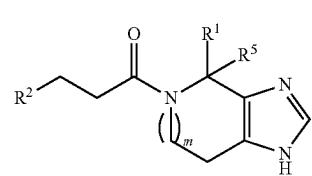
or a pharmaceutically acceptable salt thereof.

[0189] In still further embodiments, the compound of Formula I is of Formula I-I or a pharmaceutically acceptable salt thereof:

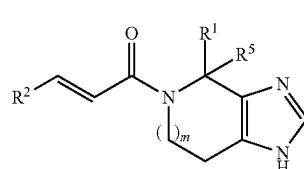


or a pharmaceutically acceptable salt thereof.

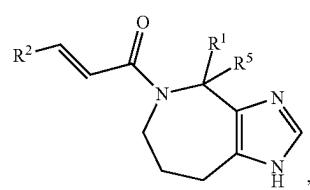
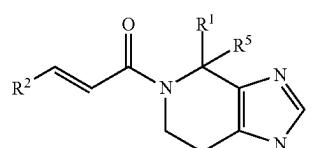
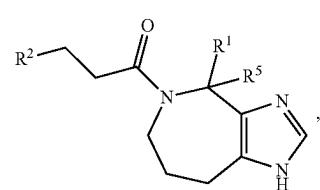
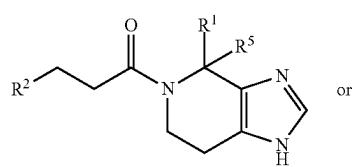
[0190] In other embodiments, the compound of Formula I is of Formula I-J or a pharmaceutically acceptable salt thereof:



such as

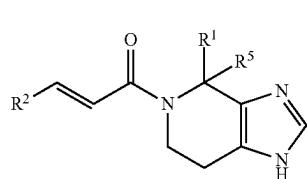


such as

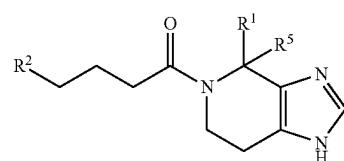


wherein R¹, R², R⁵, and m are defined herein. In other embodiments, the compound is

wherein R¹, R², R⁵, and m are defined herein. In yet other embodiments, the compound is

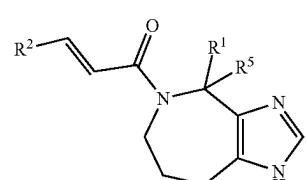


I-J-1

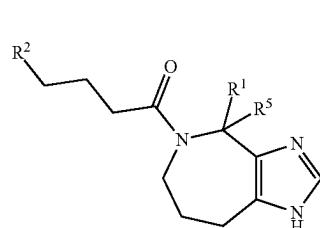


I-K-1

or a pharmaceutically acceptable salt thereof. In other embodiments, the compound is



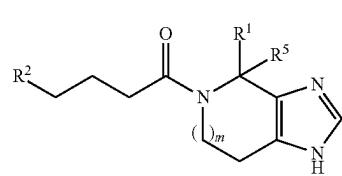
I-J-2



I-K-2

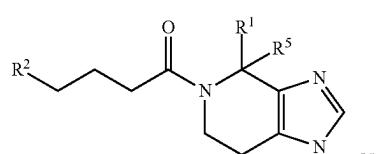
or a pharmaceutically acceptable salt thereof.

[0191] In further embodiments, the compound of Formula I is of Formula I-K or a pharmaceutically acceptable salt thereof:

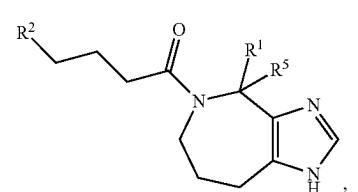


I-K

such as

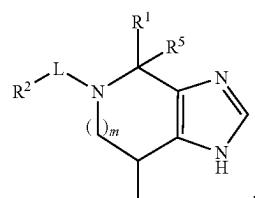


I-K-1



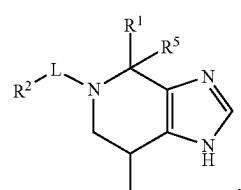
I-K-2

wherein R¹, R², R⁵, and m are defined herein. In other embodiments, the compound is



I-L

wherein R¹, R², R⁵, L, and m are defined herein. In further embodiments, the compound is

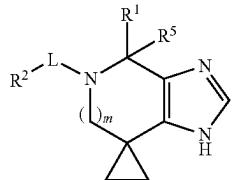


I-L-1

or a pharmaceutically acceptable salt thereof.

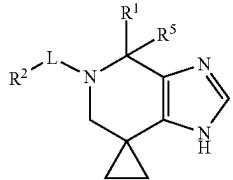
[0193] In yet further embodiments, the compound of Formula I is of Formula I-M or a pharmaceutically acceptable salt thereof:

I-M



wherein R¹, R², R⁵, L, and m are defined herein. In other embodiments, the compound is

I-M-1



or a pharmaceutically acceptable salt thereof.

[0194] In some embodiments, compounds of the disclosure are any one or more of the compounds of Tables 1-5, and their pharmaceutically acceptable salts and/or isotopologues. Compounds having the Formula I are further disclosed in the Exemplification and are included in the present disclosure. Pharmaceutically acceptable salts thereof as well as the neutral forms are included.

[0195] The disclosure further provides R-enantiomers, S-enantiomers, or racemic mixtures of any of the compounds described herein. In some embodiments, the compound is an S-enantiomer. In other embodiments, the compound is the R-enantiomer. In further embodiments, the compound is racemic.

[0196] In another embodiment, the compounds of the disclosure may be enantiomerically enriched, e.g., the enantiomeric excess or “ee” of the compound is greater than about 5% as measured by chiral HPLC. In some embodiments, the ee is greater than about 10%. In other embodiments, the ee is greater than about 20%. In further embodiments, the ee is greater than about 30%. In yet other embodiments, the ee is greater than about 40%. In still further embodiments, the ee is greater than about 50%. In other embodiments, the ee is greater than about 60%. In further embodiments, the ee is greater than about 70%. In still other embodiments, the ee is greater than about 80%. In yet further embodiments, the ee is greater than about 85%. In other embodiments, the ee is greater than about 90%. In further embodiments, the ee is greater than about 91%. In yet other embodiments, the ee is greater than about 92%. In still further embodiments, the ee is greater than about 93%. In other embodiments, the ee is greater than about 94%. In further embodiments, the ee is greater than about 95%. In still other embodiments, the ee is greater than about 96%. In yet further embodiments, the ee is greater than about 97%. In other embodiments, the ee is greater than about 98%. In further embodiments, the ee is greater than about 99%.

[0197] The present disclosure encompasses the preparation and use of salts of compounds of the disclosure. Salts of compounds of the disclosure can be prepared during the

final isolation and purification of the compounds or separately by reacting the compound with an acid or base as appropriate.

Treatment Methods

[0198] Compounds of the disclosure have several uses as described herein. In some embodiments, compounds of the disclosure are useful in methods for stabilizing mutant PAH proteins. These methods comprise contacting the protein with one or more compounds described herein or a pharmaceutically acceptable salt thereof. The compounds of the disclosure can provide for better Phe control for patients whose disease is not well-managed on diet alone and lessen the severity of a patient’s phenylketonuria. Thus, patients administered a compound of the disclosure will have a better quality of life, e.g., a more normal lifestyle and/or none or fewer dietary restrictions, as compared with phenylketonuria patients who have not been administered a compound of the disclosure. In some embodiments, patients administered a compound of the disclosure may experience increases in executive function, decreases in anxiety symptoms, and/or decreases in attention deficit hyperactivity disorder symptoms.

[0199] The term “mutant PAH gene” as used herein refers to the full DNA sequence of PAH that differs in one or more ways from the canonically accepted sequence (“the basis gene”) that is published in any one of a variety of curated databases. As one example, the sequence described by GenBank Accession number NG_008690.2 describes the basis gene.

[0200] The term “mutant PAH protein” as used herein refers to a PAH protein that contains at least one mutation in the amino acid sequence relative to that encoded by the reference. The reference human PAH protein is described by Genbank Accession number NP_000268 and contains 452 amino acids. PAH protein mutations can be identified using methods known in the art. In some embodiments, the mutant PAH protein contains at least one R408W, R261Q, R243Q, Y414C, L48S, A403V, I65T, R241C, L348V, R408Q, or V388M mutation. In other embodiments, the mutant PAH protein contains at least one R408W, Y414C, I65T, F39L, R408Q, L348V, R261Q, A300S, or L48S mutation. In still other embodiments, the mutant PAH protein contains at least one R408W, R243Q, R408Q, V388M, or L348V mutation. In yet other embodiments, the mutant PAH protein contains at least one R408W mutation. In further embodiments, the mutant PAH protein contains at least two R408W mutations. In further embodiments, the mutant PAH protein contains at least one R261Q mutation. In yet other embodiments, the mutant PAH protein contains at least one R243Q mutation. In yet other embodiments, the mutant PAH protein contains at least one Y414C mutation. In still further embodiments, the mutant PAH protein contains at least one L48S mutation. In other embodiments, the mutant PAH protein contains at least one A403V mutation. In further embodiments, the mutant PAH protein contains at least one I65T mutation. In yet further embodiments, the mutant PAH protein contains at least one R241C mutation. In yet other embodiments, the mutant PAH protein contains at least one L348V mutation. In further embodiments, the mutant PAH protein contains at least one R408Q mutation. In other embodiments, the mutant PAH protein contains at least one V388M mutation. In other embodiments, the mutant PAH protein contains at least one F39L mutation. In still further embodiments, the

mutant PAH protein contains at least one A300S mutation. In yet further embodiments, the mutant PAH protein contains at least one L48S mutation.

[0201] In other embodiments, the disclosure provides methods for stabilizing the activity of mutant phenylalanine hydroxylase (PAH) proteins as compared to wild type PAH. Such methods include contacting phenylalanine hydroxylase with one or more compounds described herein, or a pharmaceutically acceptable salt thereof. The term "stabilizing" as used herein refers to modulating the activity or quantity of a PAH enzyme so that it catalyzes hydroxylation of the aromatic side-chain of phenylalanine at a rate that is more similar to the PAH catalysis rate of a control population having wild type PAH, i.e., without a mutant PAH gene mutation, as compared to the baseline PAH catalysis rate. In some aspects, the term "stabilizing" refers to modulating the activity of a subject's PAH so that it catalyzes hydroxylation of the aromatic side-chain of phenylalanine at a flux more similar to the PAH catalytic flux of a control subject population without a mutant PAH gene mutation. In some embodiments, "stabilizing" activity of PAH includes increasing levels of the enzyme PAH as compared to baseline. By increasing the buildup of stabilized active PAH protein, a subject's toxic Phe levels can be reduced as compared to the subject's baseline levels of dietary Phe prior to administration of a compound of the disclosure or a pharmaceutical composition comprising compounds of the disclosure.

[0202] In some embodiments, the disclosure provides methods for reducing blood phenylalanine concentrations in a subject suffering from phenylketonuria to a concentration less than or equal to about 600 μM . In other embodiments, the blood Phe concentration is reduced to a concentration less than or equal to about 360 PM. In other embodiments, the disclosure provides methods for reducing blood Phe concentrations as compared to untreated baseline. In some embodiments, a subject's blood Phe concentration as compared to untreated baseline is reduced by a percentage including but not limited at least about 10%, at least about 20%, at least about 30%, at least about 40%, at least about 50%, at least about 60%, at least about 70%, at least about 80%, or at least about 90%. In other embodiments, a subject's blood Phe concentration as compared to untreated baseline is reduced by at least about 10%. In further embodiments, a subject's blood Phe concentration as compared to untreated baseline is reduced by at least about 20%. In yet other embodiments, a subject's blood Phe concentration as compared to untreated baseline is reduced by at least about 30%. In still further embodiments, a subject's blood Phe concentration as compared to untreated baseline is reduced by at least about 40%. In other embodiments, a subject's blood Phe concentration as compared to untreated baseline is reduced by at least about 50%. In further embodiments, a subject's blood Phe concentration as compared to untreated baseline is reduced by at least about 60%. In yet other embodiments, a subject's blood Phe concentration as compared to untreated baseline is reduced by at least about 70%. In still further embodiments, a subject's blood Phe concentration as compared to untreated baseline is reduced by at least about 80%. In other embodiments, a subject's blood Phe concentration as compared to untreated baseline is reduced by at least about 90%. A subject's Phe concentration can be determined by blood tests and methods for measuring such levels are known in the art. In some embodiments, the

reduction in Phe concentration achieved using compounds of the disclosure is obtained in conjunction with the subject actively managing their dietary Phe intake. In other embodiments, the reduction in Phe concentration is obtained in conjunction with the subject maintaining a Phe-restricted diet.

[0203] In some embodiments, a subject is treated with compounds of the disclosure, or a pharmaceutical composition comprising compounds of the disclosure. The compound is administered in an amount sufficient for stabilizing the PAH protein, or for reducing blood phenylalanine concentration in a subject, or combinations thereof in the subject.

[0204] In further embodiments, the subject is a human patient, such as a human adult over 18 years old in need of treatment. In yet further embodiments, the human patient is a human child less than 18 years old. In still further embodiments, the human patient is a human child between 12 years and 18 years old. In yet other embodiments, the human patient is a human child less than 12 years old. In any of the embodiments, the subject has phenylketonuria (PKU), optionally classic PKU or severe PKU. In some embodiments, the subject has a blood Phe concentration greater than about 600 μM prior to administration of a compound of the disclosure or a pharmaceutical composition comprising compounds of the disclosure. In other embodiments, the subject's blood Phe concentration prior to administration is greater than about 700 μM . In further embodiments, the subject's blood Phe concentration prior to administration is greater than about 800 μM . In still further embodiments, the subject's blood Phe concentration prior to administration is greater than about 900 μM . In yet other embodiments, the subject's blood Phe concentration prior to administration is greater than about 1000 μM . In further embodiments, the subject's blood Phe concentration prior to administration is greater than about 1100 PM. In other embodiments, the subject's blood Phe concentration prior to administration is greater than about 1200 μM .

[0205] The present methods also encompass administering an additional therapeutic agent to the subject in addition to the compounds of the disclosure. In some embodiments, the additional therapeutic agent is selected from drugs known as useful in a stabilizing mutant PAH protein and/or reducing blood Phe concentrations. The additional therapeutic agent is different from the compounds of the disclosure. In some embodiments, the additional therapeutic agent is saproterin or sepiapterin. In other embodiments, the additional therapeutic agent is a nutritional supplement. Nutritional supplements that may be used include those that contain amino acids and other nutrients. In further embodiments, the nutritional supplement contains large neutral amino acids such as leucine, tyrosine, tryptophan, methionine, histidine, isoleucine, valine, threonine. In other embodiments, the nutritional supplement contains tyrosine. In further embodiments, the nutritional supplement contains casein glycomacropeptide, i.e., a milk peptide naturally free of Phe in its pure form. In other embodiments, the additional therapeutic agent is an enzyme substrate or enzyme co-factor. In yet other embodiments, the enzyme substrate or co-factor is tetrahydrobiopterin. In other embodiments, the additional therapeutic agent is a biopterin analogue. In further embodiments, the additional therapeutic agent is a biotherapeutic, synthetic biotic, microbiota or probiotic. In yet other embodiments, the biotherapeutic, synthetic biotic, microbiota or probiotic con-

tains a genetically modified phenylalanine ammonia lyase (PAL) gene, such as, for example, *E. coli* Nissle PAL. Examples of genetically modified *E. coli* Nissle PAL biotherapeutics include SYNB1934 and SYNB1618, and the like. In still further embodiments, the additional therapeutic agent is an inhibitor of an amino acid transporter. In some embodiments, the amino acid transporter is B⁰AT1 (also referred to as SLC6A19), and the additional therapeutic agent is a SLC6A19 inhibitor. Examples of SLC6A19 inhibitors include nimesulide, benzotropine, NSC63912, NSC22789, cinromide, CB3, E62, JNT-517 and the like.

[0206] Compounds of the disclosure and the additional therapeutic agents can be administered simultaneously or sequentially to achieve the desired effect. In addition, the compounds of the disclosure and additional therapeutic agent can be administered in a single composition or two separate compositions.

[0207] The additional therapeutic agent is administered in an amount to provide its desired therapeutic effect. The effective dosage range for each additional therapeutic agent is known in the art, and the additional therapeutic agent is administered to an individual in need thereof within such established ranges.

[0208] Compounds of the disclosure and the additional therapeutic agents can be administered together as a single-unit dose or separately as multi-unit doses, wherein the compounds of the disclosure are administered before the additional therapeutic agent or vice versa. One or more doses of the compounds of the disclosure and/or one or more dose of the additional therapeutic agents can be administered.

[0209] The compounds of the disclosure may also be administered sequentially or concurrently with non-pharmacological techniques. In some embodiments, the patient uses non-pharmacological techniques to maintain lower Phe levels. In other embodiments, the non-pharmacological technique is administering a diet that is low in Phe. One skilled in the art would be able to determine what type of diet to maintain appropriate levels of Phe. In some embodiments, a phenylamine diet containing about 200 to about 500 mg/day (patients 10 years or younger) of Phe or less than about 600 mg/day (patients over 10 years of age). In other embodiments, the diet may include restricting or eliminating one or more foods that are high in Phe, such as soybeans, egg whites, shrimp, chicken breast, spirulina, watercress, fish, nuts, crayfish, lobster, tuna, turkey, legumes, and low-fat cottage cheese.

[0210] An example of a dose is in the range of from about 0.001 to about 100 mg of compound per kg of subject's body weight per day, in single or divided dosage units (e.g., BID, TID, QID). For a 70-kg human, a suitable dosage amount is from about 0.05 to about 7 g/day.

[0211] In some embodiments, the therapeutically effective amount of one or more compounds described herein is an amount that is effective in stabilizing a mutant PAH protein described herein. In other embodiments, the therapeutically effective amount of one or more compounds described herein is an amount that is effective in reducing blood phenylalanine concentrations.

[0212] Unless otherwise noted, the amounts of the compounds described herein are set forth on a free base basis. That is, the amounts indicate that amount of the compound administered, exclusive of, for example, solvent or counterions (such as in pharmaceutically acceptable salts).

Pharmaceutical Compositions

[0213] The disclosure also provides pharmaceutical compositions comprising compounds of the disclosure and a pharmaceutically acceptable carrier or excipient.

[0214] The methods of the present disclosure can be accomplished by administering compounds of the disclosure as the neat compound or as a pharmaceutical composition. Administration of a pharmaceutical composition, or neat compound of the disclosure, can be performed at any time period as determined by the attending physician. Typically, the pharmaceutical compositions contain no toxic, carcinogenic, or mutagenic compounds that would cause an adverse reaction when administered.

[0215] Pharmaceutical compositions include those wherein compounds of the disclosure are administered in an effective amount to achieve its intended purpose. The exact formulation, route of administration, and dosage is determined by an individual physician.

[0216] Compounds of the disclosure can be administered by any suitable route, e.g., by oral, buccal, inhalation, sublingual, rectal, vaginal, intracisternal or intrathecal through lumbar puncture, transurethral, nasal, percutaneous, i.e., transdermal, or parenteral (including intravenous, intramuscular, subcutaneous, intracoronary, intradermal, intramammary, intraperitoneal, intraarticular, intrathecal, retrobulbar, intrapulmonary injection and/or surgical implantation at a particular site) administration. Parenteral administration can be accomplished using a needle and syringe or using a high-pressure technique.

[0217] The above-mentioned additional therapeutically active agents, one or more of which can be used in combination with compounds of the disclosure, are prepared and administered as described in the art.

[0218] Compounds of the disclosure may be administered in admixture with pharmaceutical carriers selected with regard to the intended route of administration and standard pharmaceutical practice. Pharmaceutical compositions for use in accordance with the present disclosure are formulated in a conventional manner using one or more physiologically acceptable carriers comprising excipients and/or auxiliaries that facilitate processing of compounds of the disclosure.

[0219] Administration of the compounds or pharmaceutical compositions of the disclosure can be effected by any method that enables delivery of the compounds to the site of action. These methods include oral routes, intraduodenal routes, parenteral injection (including intravenous, intraarterial, subcutaneous, intramuscular, intravascular, intraperitoneal or infusion), topical (e.g., transdermal application), rectal administration, via local delivery by catheter or stent or through inhalation. Compounds can also be administered intraadiposally or intrathecally.

[0220] The amount of the compound administered will be dependent on the subject being treated, the severity of the disorder or condition, the rate of administration, the disposition of the compound and the discretion of the prescribing physician. The desired dose can be administered in a single dose, or as multiple doses administered at appropriate intervals, e.g., as one, two, three, four or more subdoses per day. In some embodiments, the compounds disclosed herein are effective over a wide dosage range. For example, in the treatment of adult humans, dosage forms containing from about 0.01 to 2000 mg of a compound disclosed herein per day are examples of dosage forms that may be used. The exact dosage will depend upon the route of administration,

the form in which the compound is administered, the subject to be treated, the body weight of the subject to be treated, and the preference and experience of the attending physician. In some instances, dosage levels below the lower limit of the aforesaid range may be more than adequate, while in other cases still larger doses may be employed without causing any harmful side effect, e.g., by dividing such larger doses into several small doses for administration throughout the day.

[0221] In some embodiments, a compound of the disclosure is administered in a single dose.

[0222] Typically, such administration will be by a solid oral dosage form such as tablet or capsule. However, other routes may be used as appropriate. A single dose of a compound may also be used for treatment of an acute condition.

[0223] In some embodiments, a compound of the disclosure may be administered in multiple doses. Dosing may be about once, twice, three times, four times, five times, six times, or more than six times per day. In another embodiment, a compound described herein and another therapeutic agent are administered together about once per day to about 6 times per day. Administration of the compounds disclosed herein may continue as long as necessary. In some embodiments, a compound is administered chronically on an ongoing basis, e.g., for the treatment of chronic effects.

[0224] An effective amount of a compound of the disclosure may be administered in either single or multiple doses by any of the accepted modes of administration of therapeutic agents having similar utilities, including rectal, buccal, intranasal and transdermal routes, by intra-arterial injection, intravenously, intraperitoneally, parenterally, intramuscularly, subcutaneously, orally, topically, or as an inhalant.

[0225] The pharmaceutical composition may, for example, be in a form suitable for oral administration as a tablet, capsule, pill, powder, sustained release formulations, solution, suspension, for parenteral injection as a sterile solution, suspension or emulsion, for topical administration as an ointment or cream or for rectal administration as a suppository. The pharmaceutical composition may be in unit dosage forms suitable for single administration of precise dosages. The pharmaceutical composition will include one or more conventional pharmaceutical carriers or excipients and a compound disclosed herein as an active ingredient. In addition, it may include other medicinal or pharmaceutical agents, carriers, adjuvants, etc.

[0226] Exemplary parenteral administration forms include solutions or suspensions of the compound of the disclosure in sterile aqueous solutions, for example, aqueous propylene glycol or dextrose solutions. Such dosage forms can be suitably buffered, if desired.

Pharmaceutical Compositions for Oral Administration

[0227] In some embodiments, the disclosure provides a pharmaceutical composition for oral administration containing a compound of the disclosure and pharmaceutical excipients suitable for oral administration.

[0228] In some embodiments, the disclosure provides a solid pharmaceutical composition for oral administration containing: (i) an effective amount of a compound of the disclosure; optionally (ii) an effective amount of a second therapeutic agent; and (iii) a pharmaceutical excipient suit-

able for oral administration. In some embodiments, the composition further contains: (iv) an effective amount of a third therapeutic agent.

[0229] In some embodiments, the pharmaceutical composition may be a pharmaceutical composition suitable for oral consumption. Pharmaceutical compositions containing a compound of the disclosure suitable for oral administration can be presented as discrete dosage forms, such as capsules, cachets, or tablets, or liquids or aerosol sprays each containing a predetermined amount of an active ingredient as a powder or in granules, a solution, or a suspension in an aqueous or non-aqueous liquid, an oil-in-water emulsion, or a water-in-oil liquid emulsion. Such dosage forms can be prepared by any of the methods of pharmacy, but all methods include the step of bringing the compound of the disclosure into association with the carrier, which constitutes one or more necessary ingredients. In general, the compositions are prepared by uniformly and intimately admixing the compound of the disclosure with liquid carriers or finely divided solid carriers or both, and then, if necessary, shaping the product into the desired presentation. For example, a tablet can be prepared by compression or molding, optionally with one or more accessory ingredients. Compressed tablets can be prepared by compressing in a suitable machine the active ingredient in a free-flowing form such as powder or granules, optionally mixed with an excipient such as, but not limited to, a binder, a lubricant, an inert diluent, and/or a surface active or dispersing agent. Molded tablets can be made by molding in a suitable machine a mixture of the powdered compound moistened with an inert liquid diluent.

[0230] This disclosure further encompasses anhydrous pharmaceutical compositions and dosage forms comprising an active ingredient, since water can facilitate the degradation of some compounds. For example, water may be added (e.g., 5%) in the pharmaceutical arts as a means of simulating long-term storage in order to determine characteristics such as shelf-life or the stability of formulations over time. Anhydrous pharmaceutical compositions and dosage forms containing a compound of the disclosure can be prepared using anhydrous or low moisture containing ingredients and low moisture or low humidity conditions. Pharmaceutical compositions and dosage forms containing a compound of the disclosure which contain lactose can be made anhydrous if substantial contact with moisture and/or humidity during manufacturing, packaging, and/or storage is expected. An anhydrous pharmaceutical composition may be prepared and stored such that its anhydrous nature is maintained. Accordingly, anhydrous compositions may be packaged using materials known to prevent exposure to water such that they can be included in suitable formulary kits. Examples of suitable packaging include, but are not limited to, hermetically sealed foils, plastic or the like, unit dose containers, blister packs, and strip packs.

[0231] The compound of the disclosure can be combined in an intimate admixture with a pharmaceutical carrier according to conventional pharmaceutical compounding techniques. The carrier can take a wide variety of forms depending on the form of preparation desired for administration. In preparing the compositions for an oral dosage form, any of the usual pharmaceutical media can be employed as carriers, such as, for example, water, glycols, oils, alcohols, flavoring agents, preservatives, coloring agents, and the like in the case of oral liquid preparations

(such as suspensions, solutions, and elixirs) or aerosols; or carriers such as starches, sugars, micro-crystalline cellulose, diluents, granulating agents, lubricants, binders, and disintegrating agents can be used in the case of oral solid preparations, in some embodiments without employing the use of lactose. For example, suitable carriers include powders, capsules, and tablets, with the solid oral preparations. If desired, tablets can be coated by standard aqueous or nonaqueous techniques.

[0232] Binders suitable for use in pharmaceutical compositions and dosage forms include, but are not limited to, corn starch, potato starch, or other starches, gelatin, natural and synthetic gums such as acacia, sodium alginate, alginic acid, other alginates, powdered tragacanth, guar gum, cellulose and its derivatives (e.g., ethyl cellulose, cellulose acetate, carboxymethyl cellulose calcium, sodium carboxymethyl cellulose), polyvinyl pyrrolidone, methyl cellulose, pre-gelatinized starch, hydroxypropyl methyl cellulose, micro-crystalline cellulose, colloidal silicon dioxide and mixtures thereof.

[0233] Examples of suitable fillers for use in the pharmaceutical compositions and dosage forms disclosed herein include, but are not limited to, talc, calcium carbonate (e.g., granules or powder), microcrystalline cellulose, powdered cellulose, dextrates, kaolin, mannitol, silicic acid, sorbitol, starch, pre-gelatinized starch, and mixtures thereof.

[0234] Disintegrants may be used in the compositions of the disclosure to provide tablets that disintegrate when exposed to an aqueous environment. Too much of a disintegrant may produce tablets which may disintegrate in the bottle. Too little may be insufficient for disintegration to occur and may thus alter the rate and extent of release of the active ingredient(s) from the dosage form. Thus, a sufficient amount of disintegrant that is neither too little nor too much to detrimentally alter the release of the active ingredient(s) may be used to form the dosage forms of the compounds disclosed herein. The amount of disintegrant used may vary based upon the type of formulation and mode of administration, and may be readily discernible to those of ordinary skill in the art. About 0.5 to about 15 weight percent of disintegrant, or about 1 to about 5 weight percent of disintegrant, may be used in the pharmaceutical composition. Disintegrants that can be used to form pharmaceutical compositions and dosage forms of the disclosure include, but are not limited to, agar-agar, alginic acid, calcium carbonate, microcrystalline cellulose, croscarmellose sodium, crospovidone, polacrilin potassium, sodium starch glycolate, potato or tapioca starch, other starches, pre-gelatinized starch, other starches, clays, other algin, other celluloses, gums or mixtures thereof.

[0235] Lubricants which can be used to form pharmaceutical compositions and dosage forms of the disclosure include, but are not limited to, calcium stearate, magnesium stearate, sodium stearly fumarate, mineral oil, light mineral oil, glycerin, sorbitol, mannitol, polyethylene glycol, other glycols, stearic acid, sodium lauryl sulfate, talc, hydrogenated vegetable oil (e.g., peanut oil, cottonseed oil, sunflower oil, sesame oil, olive oil, corn oil, and soybean oil), zinc stearate, ethyl oleate, ethyl laureate, agar, or mixtures thereof. Additional lubricants include, for example, a silyo silica gel, a coagulated aerosol of synthetic silica, or mixtures thereof. A lubricant can optionally be added, in an amount of less than about 2 weight percent of the pharmaceutical composition.

[0236] When aqueous suspensions and/or elixirs are desired for oral administration, the active ingredient therein may be combined with various sweetening or flavoring agents, coloring matter or dyes and, if so desired, emulsifying and/or suspending agents, together with such diluents as water, ethanol, propylene glycol, glycerin and various combinations thereof.

[0237] The tablets can be uncoated or coated by known techniques to delay disintegration and absorption in the gastrointestinal tract and thereby provide a sustained action over a longer period. For example, a time delay material such as glyceryl monostearate or glyceryl distearate can be employed. Formulations for oral use can also be presented as hard gelatin capsules wherein the active ingredient is mixed with an inert solid diluent, for example, calcium carbonate, calcium phosphate or kaolin, or as soft gelatin capsules wherein the active ingredient is mixed with water or an oil medium, for example, peanut oil, liquid paraffin or olive oil.

[0238] Surfactants which can be used to form pharmaceutical compositions and dosage forms of the disclosure include, but are not limited to, hydrophilic surfactants, lipophilic surfactants, and mixtures thereof. That is, a mixture of hydrophilic surfactants may be employed, a mixture of lipophilic surfactants may be employed, or a mixture of at least one hydrophilic surfactant and at least one lipophilic surfactant may be employed.

[0239] A suitable hydrophilic surfactant may generally have an HLB value of at least 10, while suitable lipophilic surfactants may generally have an HLB value of or less than about 10. An empirical parameter used to characterize the relative hydrophilicity and hydrophobicity of non-ionic amphiphilic compounds is the hydrophilic-lipophilic balance ("HLB" value). Surfactants with lower HLB values are more lipophilic or hydrophobic, and have greater solubility in oils, while surfactants with higher HLB values are more hydrophilic, and have greater solubility in aqueous solutions.

[0240] Hydrophilic surfactants are generally considered to be those compounds having an HLB value greater than about 10, as well as anionic, cationic, or zwitterionic compounds for which the HLB scale is not generally applicable. Similarly, lipophilic (i.e., hydrophobic) surfactants are compounds having an HLB value equal to or less than about 10. However, HLB value of a surfactant is merely a rough guide generally used to enable formulation of industrial, pharmaceutical, and cosmetic emulsions.

[0241] Hydrophilic surfactants may be either ionic or non-ionic. Suitable ionic surfactants include, but are not limited to, alkylammonium salts; fusidic acid salts; fatty acid derivatives of amino acids, oligopeptides, and polypeptides; glyceride derivatives of amino acids, oligopeptides, and polypeptides; lecithins and hydrogenated lecithins; lyssolecithins and hydrogenated lyssolecithins; phospholipids and derivatives thereof; lysophospholipids and derivatives thereof; carnitine fatty acid ester salts; salts of alkylsulfates; fatty acid salts; sodium docusate; acyl lactylates; mono- and di-acetylated tartaric acid esters of mono- and di-glycerides; succinylated mono- and di-glycerides; citric acid esters of mono- and di-glycerides; and mixtures thereof.

[0242] Within the aforementioned group, ionic surfactants include, by way of example: lecithins, lysolecithin, phospholipids, lysophospholipids and derivatives thereof; carnitine fatty acid ester salts; salts of alkylsulfates; fatty acid salts; sodium docusate; acylactylates; mono- and di-acetylated tartaric acid esters of mono- and di-glycerides; succinylated mono- and di-glycerides; citric acid esters of mono- and di-glycerides; and mixtures thereof.

[0243] Ionic surfactants may be the ionized forms of lecithin, lysolecithin, phosphatidylcholine, phosphatidylethanamine, phosphatidylglycerol, phosphatidic acid, phosphatidylserine, lysophosphatidylcholine, lysophosphatidylethanamine, lysophosphatidylglycerol, lysophosphatidic acid, lysophosphatidylserine, PEG-phosphatidylethanolamine, PVP-phosphatidylethanolamine, lactic esters of fatty acids, stearoyl-2-lactylate, stearoyl lactylate, succinylated monoglycerides, mono/diacetylated tartaric acid esters of mono/diglycerides, citric acid esters of mono/diglycerides, cholylsarcosine, caproate, caprylate, caprate, laurate, myristate, palmitate, oleate, ricinoleate, linoleate, linolenate, stearate, lauryl sulfate, teraceetyl sulfate, docosate, lauroyl carnitines, palmitoyl carnitines, myristoyl carnitines, and salts and mixtures thereof.

[0244] Hydrophilic non-ionic surfactants may include, but are not limited to, alkylglucosides; alkylmaltosides; alkyl-thioglucosides; lauryl macrogolglycerides; polyoxyalkylene alkyl ethers such as polyethylene glycol alkyl ethers; polyoxyalkylene alkylphenols such as polyethylene glycol alkyl phenols; polyoxyalkylene alkyl phenol fatty acid esters such as polyethylene glycol fatty acids monoesters and polyethylene glycol fatty acids diesters; polyethylene glycol glycerol fatty acid esters; polyglycerol fatty acid esters; polyoxyalkylene sorbitan fatty acid esters such as polyethylene glycol sorbitan fatty acid esters; hydrophilic transesterification products of a polyol with at least one member of the group consisting of glycerides, vegetable oils, hydrogenated vegetable oils, fatty acids, and sterols; polyoxyethylene sterols, derivatives, and analogues thereof; polyoxyethylated vitamins and derivatives thereof; polyoxyethylene-polyoxypropylene block copolymers; and mixtures thereof; polyethylene glycol sorbitan fatty acid esters and hydrophilic transesterification products of a polyol with at least one member of the group consisting of triglycerides, vegetable oils, and hydrogenated vegetable oils. The polyol may be glycerol, ethylene glycol, polyethylene glycol, sorbitol, propylene glycol, pentaerythritol, or a saccharide.

[0245] Other hydrophilic-non-ionic surfactants include, without limitation, PEG-10 laurate, PEG-12 laurate, PEG-20 laurate, PEG-32 laurate, PEG-32 dilaurate, PEG-12 oleate, PEG-15 oleate, PEG-20 oleate, PEG-20 dioleate, PEG-32 oleate, PEG-200 oleate, PEG-400 oleate, PEG-15 stearate, PEG-32 distearate, PEG-40 stearate, PEG-100 stearate, PEG-20 dilaurate, PEG-25 glycercyl trioleate, PEG-32 dioleate, PEG-20 glycercyl laurate, PEG-30 glycercyl laurate, PEG-20 glycercyl stearate, PEG-20 glycercyl oleate, PEG-30 glycercyl oleate, PEG-40 glycercyl laurate, PEG-40 palm kernel oil, PEG-50 hydrogenated castor oil, PEG-40 castor oil, PEG-35 castor oil, PEG-60

castor oil, PEG-40 hydrogenated castor oil, PEG-60 hydrogenated castor oil, PEG-60 corn oil, PEG-6 caprate/caprylate glycerides, PEG-8 caprate/caprylate glycerides, polyglyceryl-10 laurate, PEG-30 cholesterol, PEG-25 phytosterol, PEG-30 soya sterol, PEG-20 trioleate, PEG-40 sorbitan oleate, PEG-80 sorbitan laurate, polysorbate 20, polysorbate 80, POE-9 lauryl ether, POE-23 lauryl ether, POE-10 oleyl ether, POE-20 oleyl ether, POE-20 stearyl ether, tocopheryl PEG-1000 succinate, PEG-24 cholesterol, polyglyceryl-10-oleate, Tween 40, Tween 60, sucrose monostearate, sucrose mono laurate, sucrose monopalmitate, PEG 10-100 nonyl phenol series, PEG 15-100 octyl phenol series, and poloxamers.

[0246] Suitable lipophilic surfactants include, by way of example only: fatty alcohols; glycerol fatty acid esters; acetylated glycerol fatty acid esters; lower alcohol fatty acids esters; propylene glycol fatty acid esters; sorbitan fatty acid esters; polyethylene glycol sorbitan fatty acid esters; sterols and sterol derivatives; polyoxyethylated sterols and sterol derivatives; polyethylene glycol alkyl ethers; sugar esters; sugar ethers; lactic acid derivatives of mono- and di-glycerides; hydrophobic transesterification products of a polyol with at least one member of the group consisting of glycerides, vegetable oils, hydrogenated vegetable oils, fatty acids and sterols; oil-soluble vitamins/vitamin derivatives; and mixtures thereof. Within this group, preferred lipophilic surfactants include glycerol fatty acid esters, propylene glycol fatty acid esters, and mixtures thereof, or are hydrophobic transesterification products of a polyol with at least one member of the group consisting of vegetable oils, hydrogenated vegetable oils, and triglycerides.

[0247] In one embodiment, the composition may include a solubilizer to ensure good solubilization and/or dissolution of the compound of the disclosure and to minimize precipitation of the compound of the disclosure. This can be important for compositions for non-oral use, e.g., compositions for injection. A solubilizer may also be added to increase the solubility of the hydrophilic drug and/or other components, such as surfactants, or to maintain the composition as a stable or homogeneous solution or dispersion.

[0248] Examples of suitable solubilizers include, but are not limited to, the following: alcohols and polyols, such as ethanol, isopropanol, butanol, benzyl alcohol, ethylene glycol, propylene glycol, butanediols and isomers thereof, glycerol, pentaerythritol, sorbitol, mannitol, transcutol, dimethyl isosorbide, polyethylene glycol (PEG), polypropylene glycol, polyvinylalcohol, hydroxypropyl methylcellulose and other cellulose derivatives, cyclodextrins and cyclodextrin derivatives; ethers of polyethylene glycols having an average molecular weight of about 200 to about 6000, such as tetrahydrofurfuryl alcohol PEG ether (glycofurool) or methoxy PEG; polyethylene glycol 660 12-hydroxystearate, amides and other nitrogen-containing compounds such as 2-pyrrolidone, 2-piperidone, ϵ -caprolactam, N-alkylpyrrolidone, N-hydroxyalkylpyrrolidone, N-alkylpiperidone, N-alkylcaprolactam, dimethylacetamide and polyvinylpyrrolidone; esters such as ethyl propionate, tributylcitrate, acetyl triethylcitrate, acetyl tributyl citrate, triethylcitrate, ethyl oleate, ethyl caprylate, ethyl butyrate, triacetin, propylene

glycol monoacetate, propylene glycol diacetate, ϵ -caprolactone and isomers thereof, δ -valerolactone and isomers thereof, β -butyrolactone and isomers thereof; and other solubilizers known in the art, such as dimethyl acetamide, dimethyl isosorbide, N-methyl pyrrolidones, mono-octanoin, diethylene glycol monoethyl ether, and water.

[0249] Mixtures of solubilizers may also be used. Examples include, but not limited to, triacetin, triethylcitrate, ethyl oleate, ethyl caprylate, dimethylacetamide, N-methylpyrrolidone, N-hydroxyethylpyrrolidone, polyvinylpyrrolidone, hydroxypropyl methylcellulose, hydroxypropyl cyclodextrins, ethanol, glycofurool, transcutol, propylene glycol, and dimethyl isosorbide. Particularly preferred solubilizers include sorbitol, glycerol, triacetin, ethyl alcohol, PEG having an average molecular weight of about 100 to about 8000 g/mole, glycofurool and propylene glycol.

[0250] The amount of solubilizer that can be included is not particularly limited. The amount of a given solubilizer may be limited to a bioacceptable amount, which may be readily determined by one of skill in the art. In some circumstances, it may be advantageous to include amounts of solubilizers far in excess of bioacceptable amounts, for example to maximize the concentration of the drug, with excess solubilizer removed prior to providing the composition to a subject using conventional techniques, such as distillation or evaporation. Thus, if present, the solubilizer can be in a weight ratio of less than about 10%, less than about 25%, less than about 50%, about 100%, or up to less than about 200% by weight, based on the combined weight of the drug, and other excipients. If desired, very small amounts of solubilizer may also be used, such as less than about 5%, less than about 2%, less than about 1% or even less. Typically, the solubilizer may be present in an amount of less than about 1% to about 100%, more typically less than about 5% to less than about 25% by weight.

[0251] The composition can further include one or more pharmaceutically acceptable additives and excipients. Such additives and excipients include, without limitation, detackifiers, anti-foaming agents, buffering agents, polymers, antioxidants, preservatives, chelating agents, viscomodulators, tonicifiers, flavorants, colorants, odorants, opacifiers, suspending agents, binders, fillers, plasticizers, lubricants, and mixtures thereof.

Pharmaceutical Compositions for Injection

[0252] In some embodiments, the disclosure provides a pharmaceutical composition for injection containing a compound described herein and pharmaceutical excipients suitable for injection. Components and amounts of agents in the compositions are as described herein.

[0253] The forms in which the compositions of the disclosure may be incorporated for administration by injection include aqueous or oil suspensions or emulsions. Such compositions may comprise sesame oil, corn oil, cottonseed oil, peanut oil, elixirs containing mannitol or dextrose, sterile water, and similar pharmaceutical vehicles.

[0254] Aqueous solutions in saline are also conventionally used for injection. Ethanol, glycerol, propylene glycol, liquid polyethylene glycol, and the like (and suitable mixtures thereof), cyclodextrin derivatives, and vegetable oils may also be employed. The proper fluidity can be maintained, for example, by the use of a coating, such as lecithin, for the maintenance of the required particle size in the case of dispersion and by the use of surfactants. The prevention of the action of microorganisms can be brought about by various antibacterial and antifungal agents, for example, parabens, chlorobutanol, phenol, sorbic acid, thimerosal, and the like.

[0255] Sterile injectable solutions are prepared by incorporating the compound of the disclosure in the required amount in the appropriate solvent with various other ingredients as enumerated above, as required, followed by filtered sterilization. Generally, dispersions are prepared by incorporating the various sterilized active ingredients into a sterile vehicle which contains the basic dispersion medium and the required other ingredients from those enumerated above. In the case of sterile powders for the preparation of sterile injectable solutions, certain desirable methods of preparation are vacuum-drying and freeze-drying techniques which yield a powder of the active ingredient plus any additional desired ingredient from a previously sterile-filtered solution thereof.

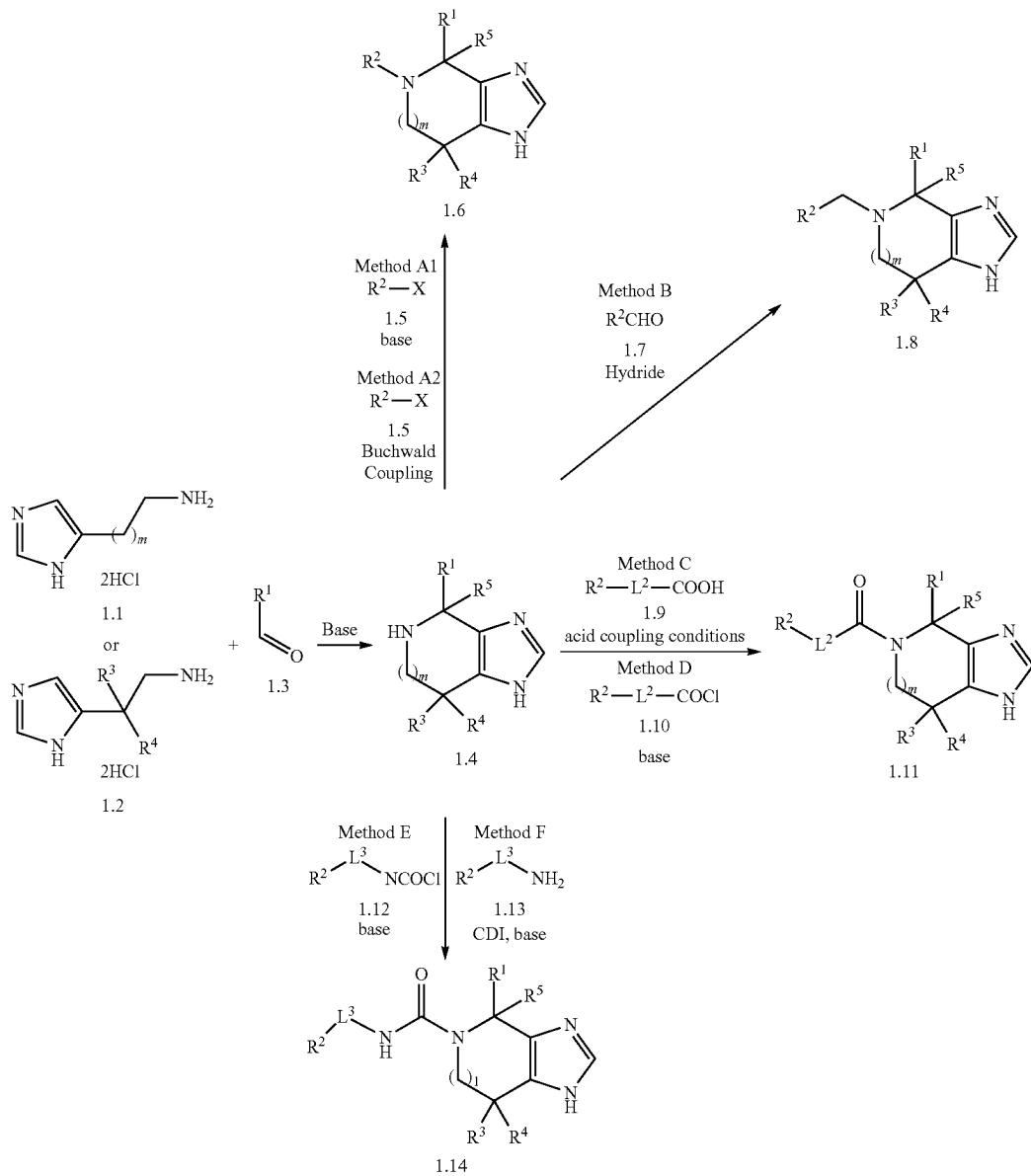
Other Pharmaceutical Compositions

[0256] Pharmaceutical compositions may also be prepared from compositions described herein and one or more pharmaceutically acceptable excipients suitable for topical, sub-lingual, buccal, rectal, intraosseous, intraocular, intranasal, epidural, or intraspinal administration. Preparations for such pharmaceutical compositions are well-known in the art. See, e.g., Anderson, Philip O.; Knoben, James E.; Troutman, William G., eds., *Handbook of Clinical Drug Data*, Tenth Edition, McGraw-Hill, 2002; Pratt and Taylor, eds., *Principles of Drug Action*, Third Edition, Churchill Livingston, New York, 1990; Katzung, ed., *Basic and Clinical Pharmacology*, Ninth Edition, McGraw Hill, 2004; Goodman and Gilman, eds., *The Pharmacological Basis of Therapeutics*, Tenth Edition, McGraw Hill, 2001; Remington's *Pharmaceutical Sciences*, 20th Ed., Lippincott Williams & Wilkins., 2000; Martindale, *The Extra Pharmacopoeia*, Thirty-Second Edition (The Pharmaceutical Press, London, 1999); all of which are incorporated by reference herein in their entirety.

Synthesis of Compounds of the Disclosure

[0257] Compounds of the disclosure can be prepared by methods described in the General Schemes, procedures, and Examples set forth within, and by related methods known in the art. For example, Compounds of Formula I can be prepared by the general methods shown in General Schemes 1-11.

General Scheme 1: Preparation of Compounds of Formula I



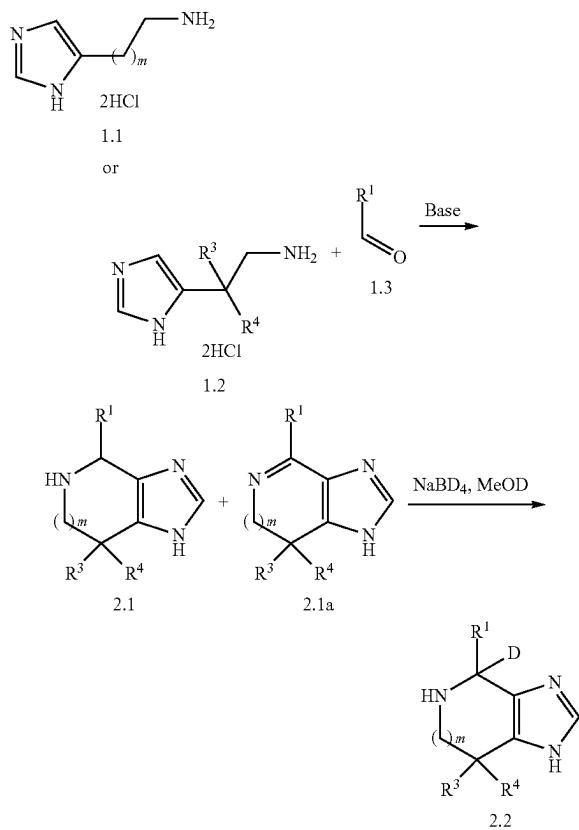
[0258] Compounds of Formula I were obtained through the reactions depicted in General Scheme 1. An amine of formulas 1.1 or 1.2 and an aldehyde of formula 1.3 were first reacted under Pictet-Spengler reaction conditions to afford the core amine of formula 1.4. To the extent that an imine by-product is formed during the Pictet-Spengler reaction, the imine by-product can be converted to the core amine of formula 1.4 by reaction with sodium borohydride in an alcoholic solvent (for example, methanol or ethanol). Various L and R² groups were then installed by using either a nucleophilic substitution reaction (Method A1), a Buchwald or other similar cross-coupling reaction (Method A2), a reductive amination reaction (Method B), or amide coupling reactions (Methods C, D, E, and F). Under Method A1, a R² aryl or heteroaryl halide of formula 1.5 (wherein X is Br, Cl, or I)

or F) is coupled to the core amine of formula 1.4 using a nucleophilic substitution reaction under basic conditions, such as DIPEA, to afford compounds of formula 1.6. Under Method A2, a R² aryl or heteroaryl halide of formula 1.5 (wherein X is Br, Cl, or I) is coupled to the core amine of formula 1.4 using Buchwald coupling or cross-coupling conditions known in the art, such as using a palladium catalyst (for example, CPhos-Pd-G3, Pd(OAc)₂, Pd(dppf) Cl₂), and a base such as Cs₂CO₃ to afford compounds of formula 1.6. Under Method B, a R² aryl or heteroaryl aldehyde of formula 1.7 is coupled to the core amine of formula 1.4 under reductive amination reaction conditions using a hydride such as sodium triacetoxyborohydride to afford compounds of formula 1.8. Under Method C, a R² carboxylic acid of formula 1.9 or a basic salt (i.e., Li, K, or

Na) thereof is coupled to core amine of formula 1.4 using acid coupling conditions known in the art, such as using one of the following reagents—HOEt, EDCI, HATU, T3P—along with a base, such as DIPEA (Hunig's base), pyridine, or TEA, to afford compounds of formula 1.11, wherein L² is a bond, optionally substituted C₁₋₆alkylene, optionally substituted C₂₋₆alkenylene, or optionally substituted C₁₋₆haloalkylene. Alternatively, under Method D, a R² acid chloride of formula 1.10 is coupled to the core amine of formula 1.4 under basic conditions to afford compounds of formula 1.11, wherein L² is a bond, optionally C₁₋₆alkylene, optionally substituted C₂₋₆alkenylene, or optionally substituted C₁₋₆haloalkylene. Under Method E, an R² acid chloride of formula 1.12 is coupled to the core amine of formula 1.4 under basic conditions to afford compounds of formula 1.14, wherein L³ is a bond or optionally substituted C₁₋₆alkylene. Under Method F, an R² amine of formula 1.13 is coupled to the core amine of formula 1.4 and carbonyldiimidazole under basic conditions to afford compounds of formula 1.14, wherein L³ is a bond or optionally substituted C₁₋₆alkylene.

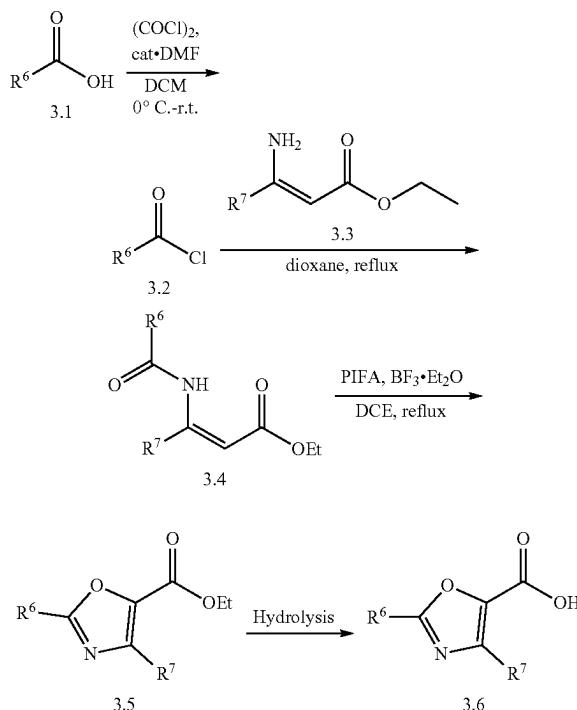
Formula 2.2

General Scheme 2: Preparation of Deuterated Core Amine Intermediates of Formula 2.2

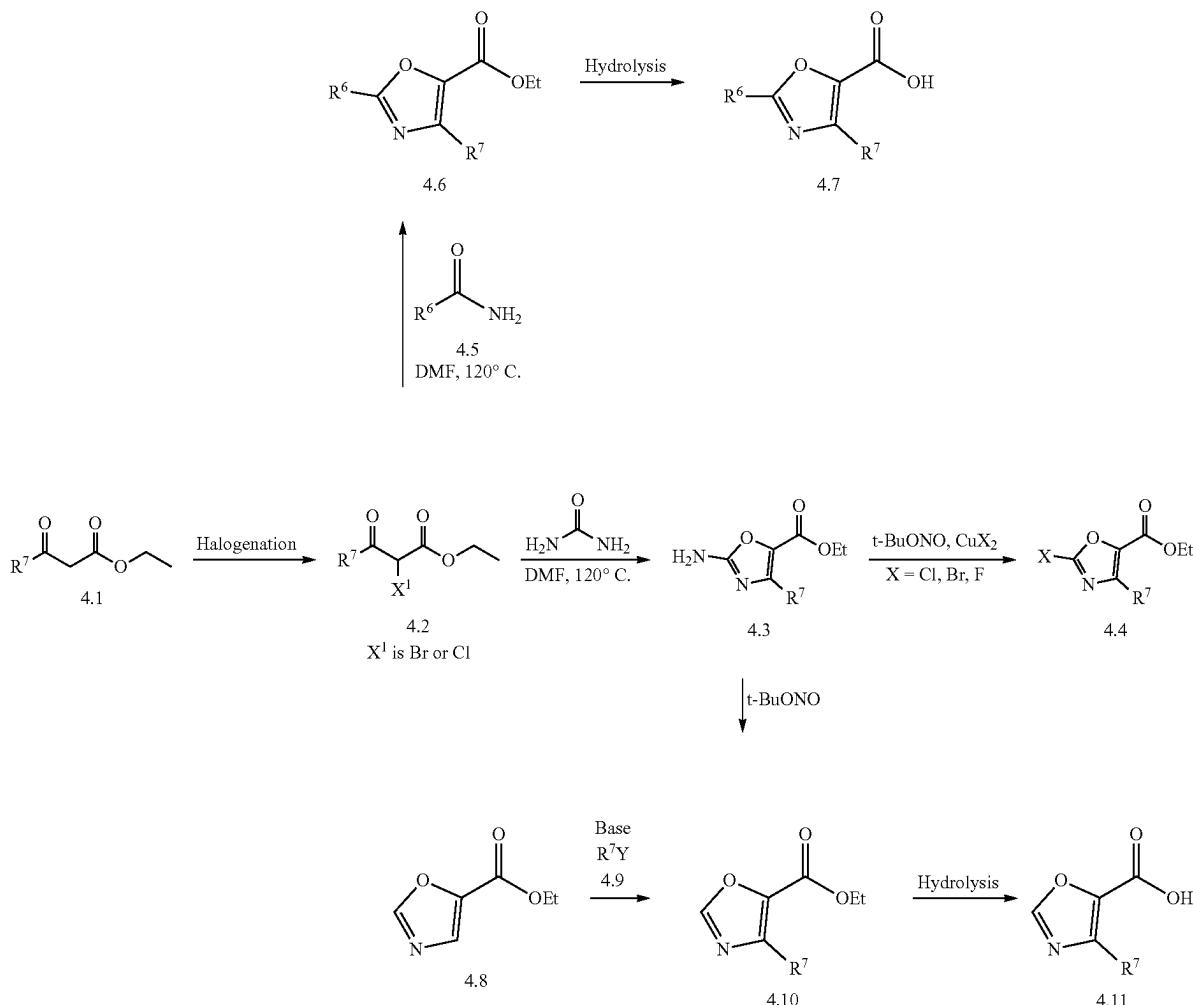


[0259] Compounds of Formula I wherein R⁵ is D are prepared in accordance with General Scheme 2. An amine of formula 1.1 or 1.2 and an aldehyde of formula 1.3 are reacted under Pictet-Spengler reaction conditions to afford compounds of formula 2.1 or mixtures of compounds of

formula 2.1 and the imine by-product of formula 2.1a. Compounds of formula 2.1 or mixtures of compounds of formulas 2.1 and 2.1a are then reacted with sodium borodeuteride in deuterated methanol to afford deuterated core amine of formula 2.2. Deuterated core amine intermediates of formula 2.2 can then be further coupled to various L and R² groups via methods A, B, C, D, E, and F as described in General Scheme 1 to afford Compounds of Formula I, wherein R⁵ is D.

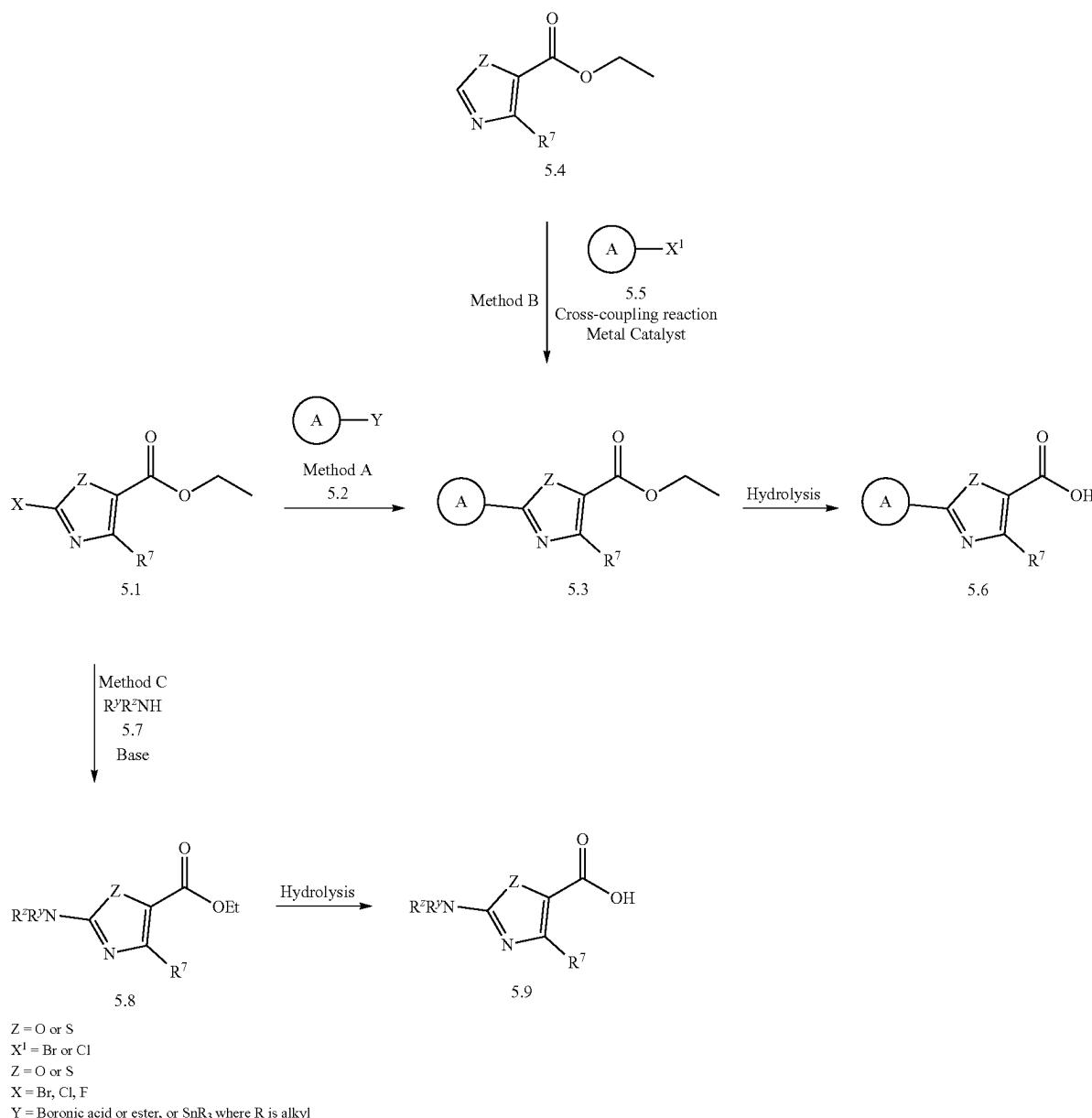
General Scheme 3: Preparation of Oxazolyl R² Acid Intermediates

[0260] Oxazolyl R² carboxylic acid intermediates containing substitutions at the R⁶ and/or R⁷ positions were prepared in accordance with General Scheme 3. A carboxylic acid of formula 3.1 was reacted with oxalyl chloride and catalytic N,N-dimethylformamide to afford acid chloride of formula 3.2. Acid chloride of formula 3.2 was then reacted with an enamine of formula 3.3 to afford an enamide of formula 3.4. An enamide of formula 3.4 then underwent hypervalent iodine-mediated cyclization after reaction with [bis(trifluoroacetoxy)iodo]benzene and boron trifluoride diethyl etherate to afford oxazole of formula 3.5. Hydrolysis of the ester of the oxazole formula 3.5 with a base such as LiOH, KOH, or NaOH in THF/water afforded compounds of formula 3.6. Alternatively, the basic salt (i.e., Li, K, or Na) of the carboxylic acid of formula 3.6 may be obtained after the hydrolysis reaction by isolating the product at a basic pH. The carboxylic acid or basic salt thereof can then be used without further purification in the coupling reactions described in General Scheme 1, Method C.

General Scheme 4: Preparation of Oxazolyl R² Acid Intermediates

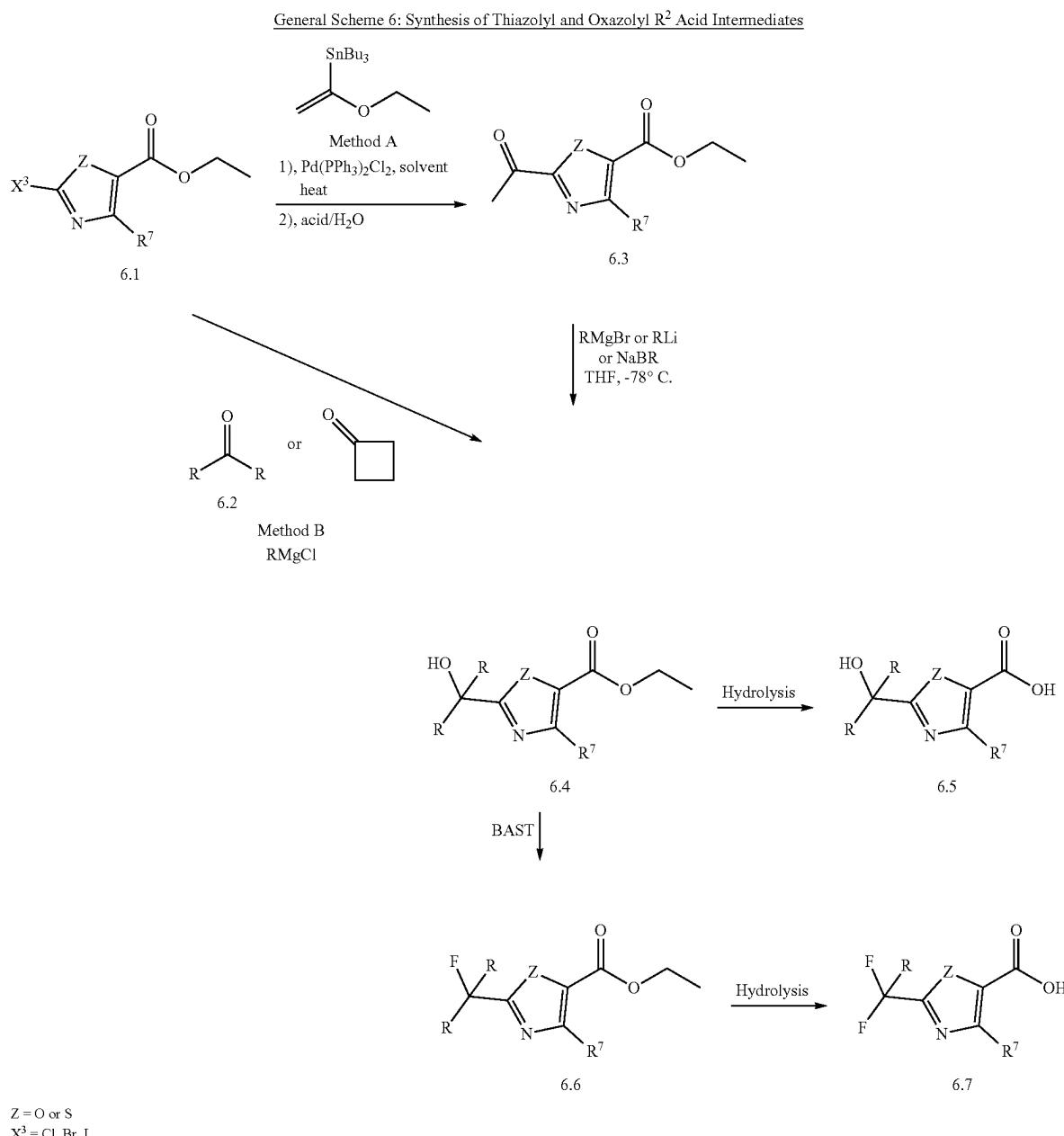
[0261] Oxazolyl R² carboxylic acid intermediates containing substitutions at the R⁶ and/or R⁷ positions were prepared in accordance with General Scheme 4. A β -keto ester of formula 4.1 was halogenated with a chlorinating agent such as SOCl₂ or brominating agent such as NBS to yield compounds of formula 4.2 (wherein X¹ is Br or Cl). Compounds of formula 4.2 were reacted with urea to afford amine oxazole compounds of formula 4.3. In addition, compounds of formula 4.2 were reacted with amides of formula 4.5 to afford oxazole compounds of formula 4.6. The amine in compounds of formula 4.3 was subjected to Sandmeyer reaction conditions to afford compounds of formula 4.4 (wherein X is Cl, Br, or F) and compounds of formula 4.10. Alternatively, compounds of formula 4.10 may be obtained

by deprotonating a compound of formula 4.8 with a base such as LiHMDS followed by reaction in a nucleophilic substitution reaction with reagents of formula 4.9 (wherein Y is a suitable leaving group such as Br, Cl, mesylate, or tosylate) to afford compounds of formula 4.10. Hydrolysis of the ester of compounds of formulas 4.6 and 4.10 with a base such as LiOH, KOH, or NaOH in THF/water affords compounds of formulas 4.7 and 4.11. Alternatively, the basic salt (i.e., Li, K, or Na) of the carboxylic acid of formulas 4.7 and 4.11 may be obtained after the hydrolysis reaction by isolating the product at a basic pH. The carboxylic acid or basic salt thereof can then be used without further purification in the coupling reactions described in General Scheme 1, Method C.

General Scheme 5: Synthesis of Thiazoyl and Oxazoyl R² Acid Intermediates

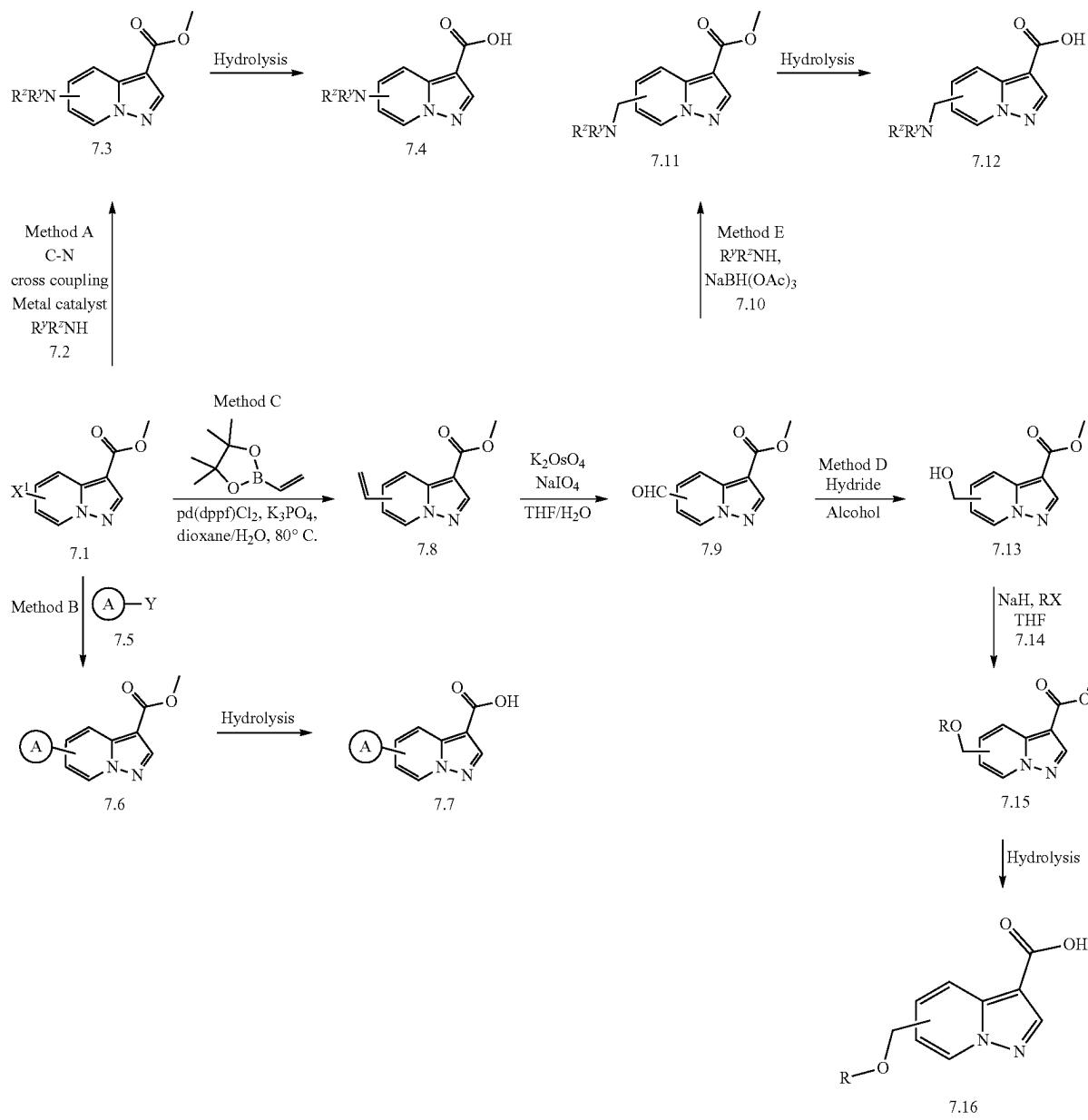
[0262] Oxazoyl and thiazoyl R² carboxylic acid intermediates containing PGP-3 substitutions at the R⁶ and/or R⁷ positions were prepared in accordance with General Scheme 5. Under Method A, a halide of formula 5.1 was reacted with a heteroaryl or aryl of formula 5.2 in either a Suzuki coupling (where Y is a boronic acid or ester) or a Stille coupling (where Y is SnR₃) to afford compounds of formula 5.3. Under Method B, compounds of formula 5.3 were obtained by reaction of a compound of formula 5.4 with a heteroaryl or aryl halide compound of formula 5.5 in a cross-coupling reaction using a metal catalyst such as a Buchwald catalyst or Ullman catalyst. Under Method C, a

halide of formula 5.1 may also be reacted with an amine of formula 5.7 or a heterocyclic amine such as piperidine, morpholine, piperazine, azetidine, and pyrrolidine, and a base such as TEA in a displacement reaction to afford compounds of formula 5.8. Hydrolysis of the ester of compounds of formulas 5.3 and 5.8 with a base such as LiOH, KOH, or NaOH in THF/water affords compounds of formulas 5.6 and 5.9. Alternatively, the basic salt (i.e., Li, K, or Na) of the carboxylic acid of formulas 5.6 and 5.9 may be obtained after the hydrolysis reaction by isolating the product at a basic pH. The carboxylic acid or basic salt thereof can then be used without further purification in the coupling reactions described in General Scheme 1, Method C.



[0263] Oxazoyl and thiazoyl R² carboxylic acid intermediates containing hydroxyalkyl and haloalkyl substitutions were prepared in accordance with General Scheme 6. Under Method A, a halide of formula 6.1 was reacted with tributyl (1-ethoxyvinyl)stannane in a Stille coupling, followed by hydrolysis with acid/water such as TFA to afford compounds of formula 6.3. An alkyl group ("R") is then added to the ketone in compounds of formula 6.3 using RMgBr or RLi or through reduction of the ketone with NaBr to afford compounds of formula 6.4. Under Method B, compounds of formula 6.4 may also be obtained starting with a compound of formula 6.1 through a Grignard addition reaction with a ketone of formula 6.2 (wherein R is an alkyl) or cyclobu-

tanone and RMgCl such as iPrMgCl. The hydroxyl substituent in compounds of formula 6.4 was converted to a fluorine substituent using a fluorinating agent such as BAST to afford compounds of formula 6.6. Hydrolysis of the ester of compounds of formulas 6.4 and 6.6 with a base such as LiOH, KOH, or NaOH in THF/water affords compounds of formulas 6.5 and 6.7. Alternatively, the basic salt (i.e., Li, K, or Na) of the carboxylic acid of formulas 6.5 and 6.7 may be obtained after the hydrolysis reaction by isolating the product at a basic pH. The carboxylic acid or basic salt thereof can then be used without further purification in the coupling reactions described in General Scheme 1, Method C.

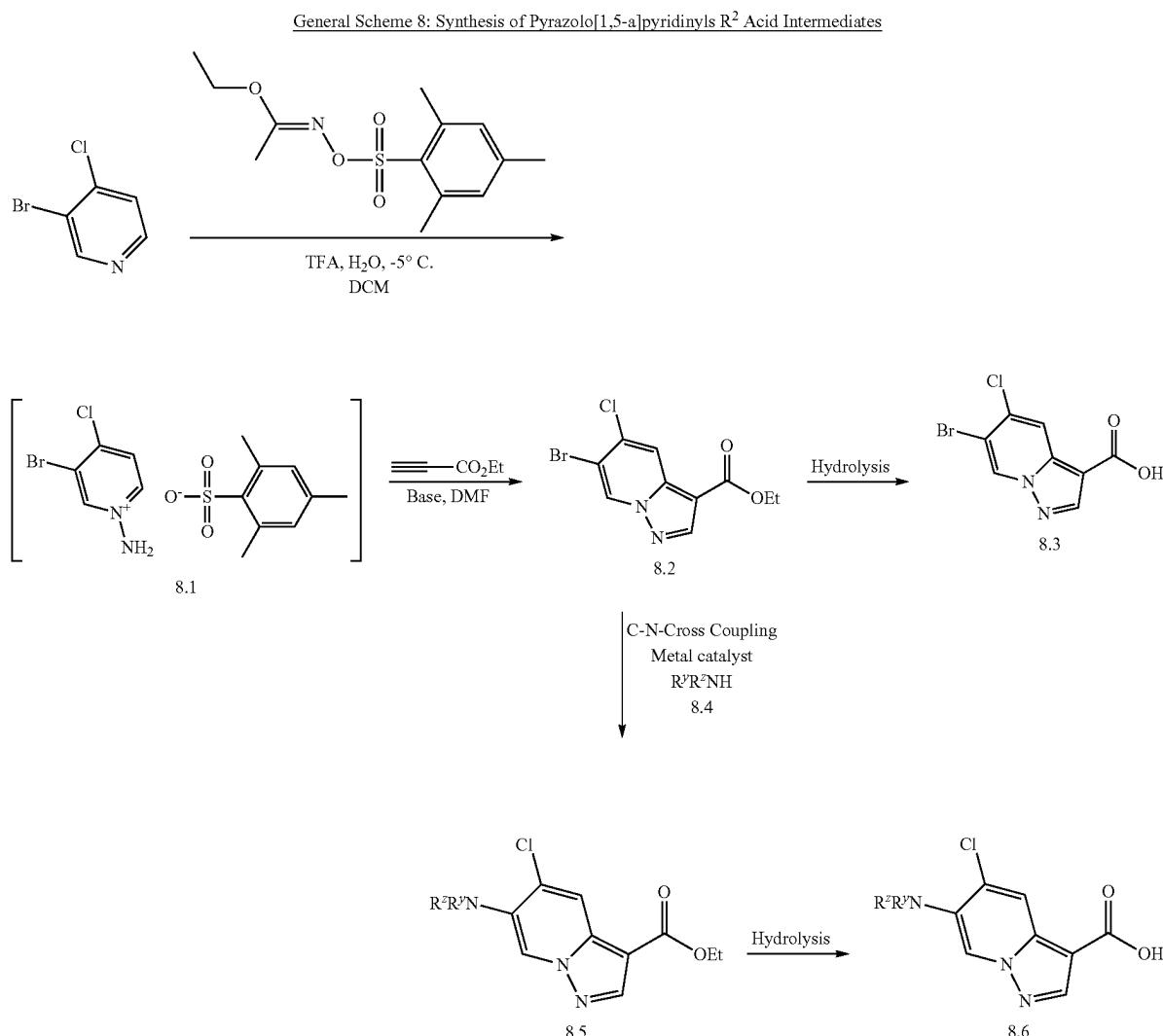
General Scheme 7: Synthesis of Pyrazolo[1,5-a]pyridinyl R² Acid Intermediates

[0264] Substituted pyrazolo[1,5-a]pyridinyl R² carboxylic acid intermediates were prepared in accordance with General Scheme 7. Under Method A, a halide of formula 7.1 (wherein X¹ is Br or Cl) was reacted in a C—N cross-coupling reaction using a metal catalyst such as a Buchwald catalyst or Ullman catalyst with an amine of formula 7.2 or a heterocyclic amine such as piperidine, morpholine, piperazine, azetidine, and pyrrolidine to afford compounds of formula 7.3. Under Method B, a halide of formula 7.1 (wherein X¹ is Br or Cl) may also be reacted with a

heteroaryl or aryl compound of formula 7.5 in either a Suzuki coupling (where Y is a boronic acid or ester) or a Stille coupling (where Y is SnR₃) to afford compounds of formula 7.6. Under Method C, a halide of formula 7.1 (wherein X¹ is Br or Cl) was reacted with 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane in a Suzuki coupling to afford compounds of formula 7.8. The olefin in compounds of formula 7.8 then underwent oxidative cleavage to an aldehyde to afford compounds of formula 7.9. Under Method D, the aldehyde in compounds of formula 7.9 was

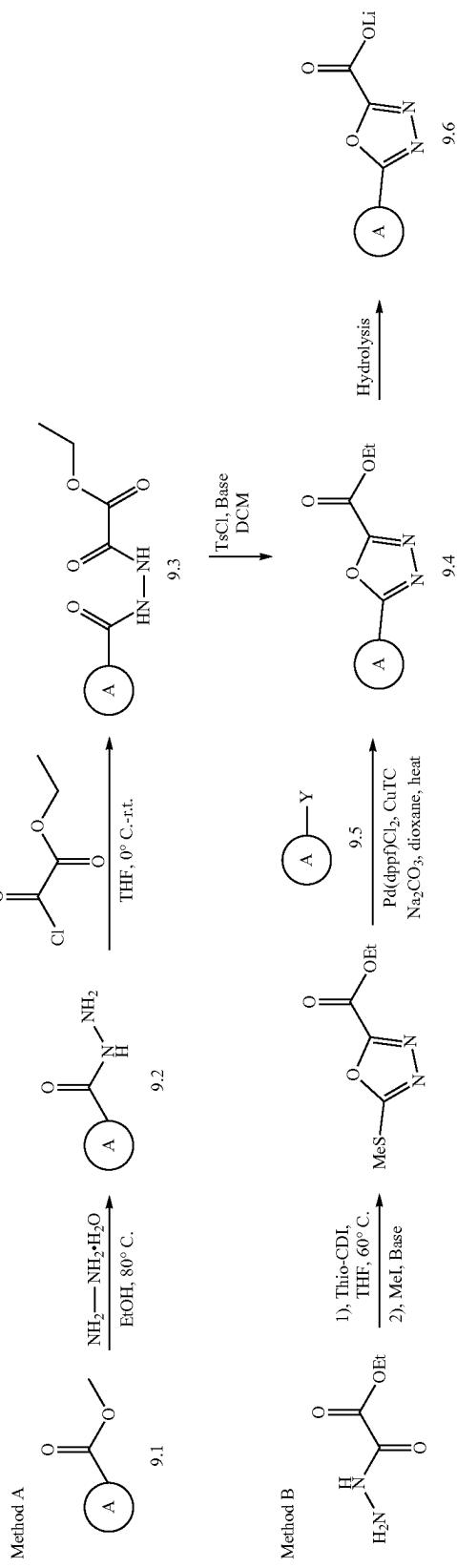
reduced to an alcohol with a hydride such as NaBH_4 in an alcoholic solvent such as methanol or ethanol to afford formula 7.13. The alcohol in compounds of formula 7.13 was alkylated with sodium hydride and an alkyl ("R") halide of formula 7.14 (wherein X is Cl, Br, or F) to afford compounds of formula 7.15. Under Method E, a compound of formula 7.9 was reacted with an amine of formula 7.10 under reductive amination conditions to afford compounds of formula 7.11. Hydrolysis of the ester of compounds of formulas 7.3, 7.6, 7.11, and 7.15 with a base such as LiOH, KOH, or NaOH in THF/water affords compounds of formulas 7.4, 7.7, 7.12, and 7.16. Alternatively, the basic salt (i.e., Li, K, or Na) of the carboxylic acid of formulas 7.4, 7.7, 7.12, and 7.16 may be obtained after the hydrolysis reaction by isolating the product at a basic pH. The carboxylic acid or basic salt thereof can then be used without further purification in the coupling reactions described in General Scheme 1, Method C.

General Scheme 8. Starting reagent 3-bromo-4-chloropyridine was reacted with ethyl (E)-N-((mesylsulfonyl)oxy)acetimidate to afford the N-aminopyridinium salt 8.1. A cycloaddition reaction of the N-aminopyridinium salt 8.1 with ethyl propiolate and base such as K_2CO_3 afforded ethyl 6-bromo-5-chloropyrazolo[1,5-a]pyridine-3-carboxylate 8.2. Compound 8.2 was reacted in a C—N cross-coupling reaction using a metal catalyst such as a Buchwald catalyst or Ullman catalyst with an amine of formula 8.4 or a heterocyclic amine such as piperidine, morpholine, piperazine, azetidine, and pyrrolidine to afford compounds of formula 8.5. Hydrolysis of the ester of compounds of formulas 8.2 and 8.5 with a base such as LiOH, KOH, or NaOH in THF/water affords compounds of formulas 8.3 and 8.6. Alternatively, the basic salt (i.e., Li, K, or Na) of the carboxylic acid of formulas 8.3 and 8.6 may be obtained after the hydrolysis reaction by isolating the product at a basic pH. The carboxylic acid or basic salt thereof can then



[0265] Di-substituted pyrazolo[1,5-a]pyridinyl R² carboxylic acid intermediates were prepared in accordance with

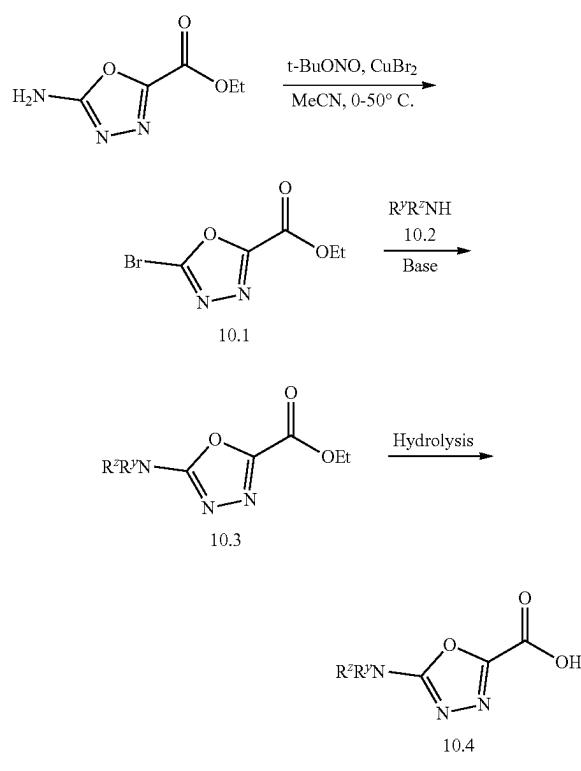
be used without further purification in the coupling reactions described in General Scheme 1, Method C.

General Scheme 9: Synthesis of 1,3,4-Oxadiazolyl R² Acid Intermediates

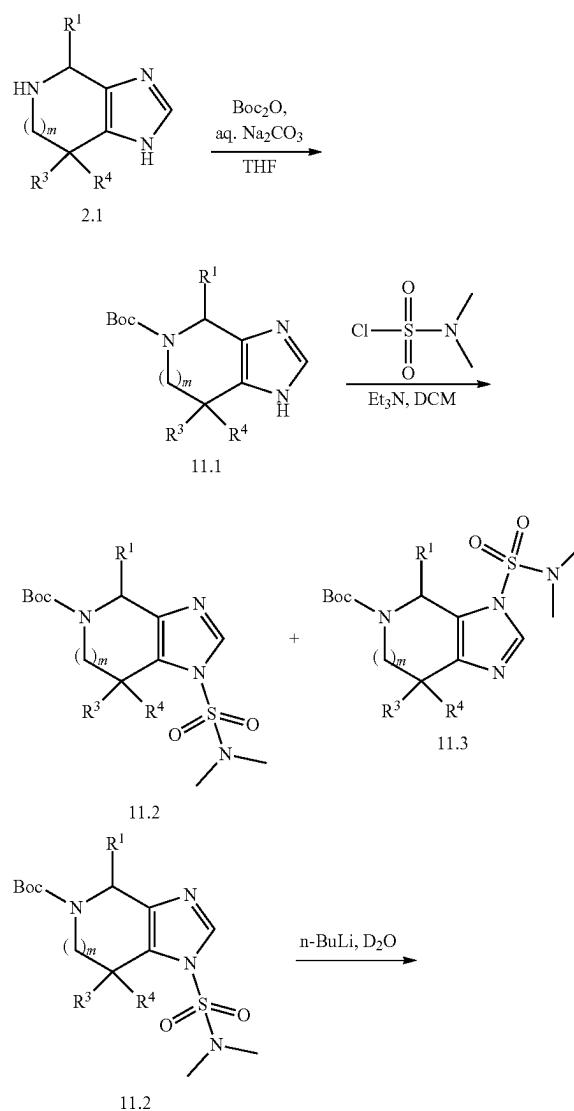
[0266] Heteroaryl and aryl-substituted oxadiazolyl R² carboxylic acid intermediates were prepared in accordance with General Scheme 9. Under Method A, heteroaryl and aryl esters of formula 9.1 were reacted with hydrazine hydrate to afford hydrazines of formula 9.2. Compounds of formula 9.2 were then reacted with ethyl-2-chloro-2-oxoacetate to afford compounds of formula 9.3, which subsequently underwent intramolecular cyclization with p-toluenesulfonyl chloride and a base such as TEA to afford the 1,3,4-oxadiazole of formula 9.4. Alternatively, compounds of formula 9.4 can be made using Method B. Under Method B, ethyl 2-hydrazinyl-2-oxoacetate was reacted with 1,1'-thiocarbonyldimidazole to form the 1,3,4-oxadiazole, which was then alkylated with methyl iodide and base such as TEA to afford ethyl 5-(methylthio)-1,3,4-oxadiazole-2-carboxylate. Ethyl 5-(methylthio)-1,3,4-oxadiazole-2-carboxylate was reacted with a heteroaryl or aryl boronic acid or ester of formula 9.5 in a desulfitative C—C cross coupling reaction (also known as Liebeskind-Srogl cross-coupling) to afford compounds of formula 9.4. Hydrolysis of the ester of compounds of formula 9.4 with a base such as LiOH, KOH, or NaOH in THF/water affords compounds of formula 9.6. Alternatively, the basic salt (i.e., Li, K, or Na) of the carboxylic acid of formula 9.6 may be obtained after the hydrolysis reaction by isolating the product at a basic pH. The carboxylic acid or basic salt thereof can then be used without further purification in the coupling reactions described in General Scheme 1, Method C.

Scheme 10. Starting reagent ethyl 5-amino-1,3,4-oxadiazole-2-carboxylate was subjected to Sandmeyer reaction conditions to afford ethyl 5-bromo-1,3,4-oxadiazole-2-carboxylate (Compound 10.1). The bromo in compound 10.1 was reacted with an amine of formula 10.2 or a heterocyclic amine such as piperidine, morpholine, piperazine, azetidine, and pyrrolidine, and a base such as TEA to afford compounds of formula 10.3. Hydrolysis of the ester of compounds of formula 10.3 with a base such as LiOH, KOH, or NaOH in THF/water afforded compounds of formula 10.4. Alternatively, the basic salt (i.e., Li, K, or Na) of the carboxylic acid of formula 10.4 may be obtained after the hydrolysis reaction by isolating the product at a basic pH. The carboxylic acid or basic salt thereof can then be used without further purification in the coupling reactions described in General Scheme 1, Method C.

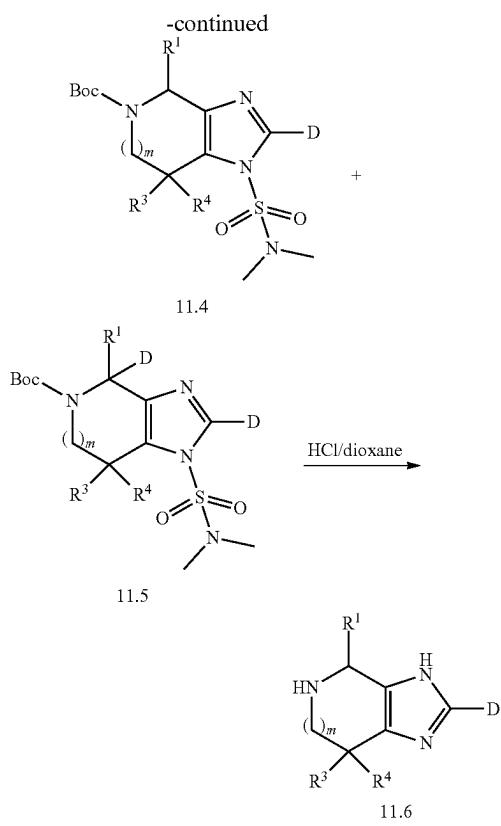
General Scheme 10: Synthesis of 1,3,4-Oxadiazolyl R² Acid Intermediates



General Scheme 11: Preparation of Deuterated Core Amine Intermediates of Formulas 11.6 and 11.7



[0267] Substituted 1,3,4-oxadiazolyl R² carboxylic acid intermediates were prepared in accordance with General



[0268] Compounds of Formula I wherein R^{5A} is D are prepared in accordance with General Scheme 11. An amine of formula 2.1, prepared according to General Scheme 2, is protected with a BOC protecting group or other suitable nitrogen protecting group to afford compounds of formula 11.1. The amine in formula 11.1 is then protected with a dimethylsulfamoyl protecting group to afford a mixture of compounds of formula 11.2 and 11.3, which are separated during purification. Deuterium is then incorporated at the R^{5A} position by deprotonating compounds of formula 11.2 with butyllithium and then adding D₂O to afford compounds of formulas 11.4 and 11.5. Deprotection of the nitrogen protecting groups with acid afforded deuterated core amine intermediates of formulas 11.6. Deuterated core amine intermediates of formulas 11.6 can be further coupled to various L and R² groups via methods A, B, C, D, E, and F as described in General Scheme 1 to afford Compounds of Formula I, wherein R^{5A} is D.

[0269] The present disclosure will be more fully understood by reference to the following examples. The examples provided herein are illustrative and should not, however, be construed as limiting the scope of the present disclosure.

EXAMPLES

[0270] In some embodiments, the disclosure provides specific examples of Formula I, and their pharmaceutically acceptable salts and/or isotopologues, as set forth in Table 1 below.

TABLE 1

Quinolines		
Ex. #	Structure	Name
1		(R)-(2-(pyridin-2-yl)thiazol-5-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
2		(S)-(2-(pyridin-2-yl)thiazol-5-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone

TABLE 1-continued

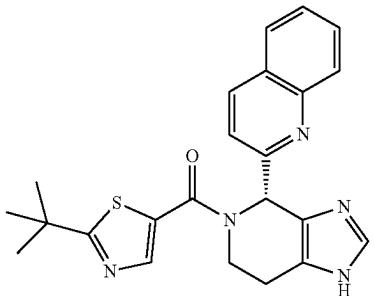
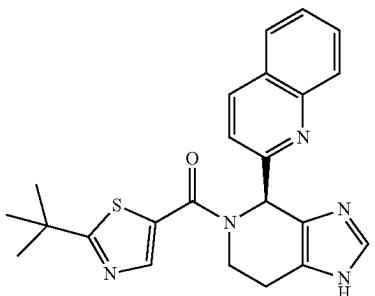
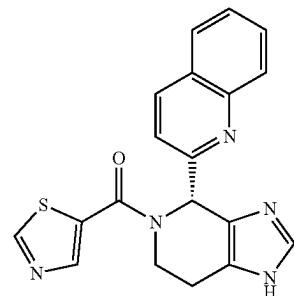
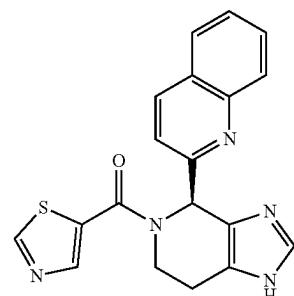
Quinolines		
Ex. #	Structure	Name
3		(R)-(2-(tert-butyl)thiazol-5-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
4		(S)-(2-(tert-butyl)thiazol-5-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
5		(R)-(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(thiazol-5-yl)methanone
6		(S)-(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(thiazol-5-yl)methanone

TABLE 1-continued

Quinolines		
Ex. #	Structure	Name
7		(R)-(2-(tert-butyl)-4-methyloxazol-5-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
8		(S)-(2-(tert-butyl)-4-methyloxazol-5-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
9		(R)-(5-cyclopropyl-1,3,4-oxadiazol-2-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
10		(S)-(5-cyclopropyl-1,3,4-oxadiazol-2-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone

TABLE 1-continued

Quinolines		
Ex. #	Structure	Name
11		(R)-(5-(4-fluorophenyl)-1,3,4-oxadiazol-2-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
12		(S)-(5-(4-fluorophenyl)-1,3,4-oxadiazol-2-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
13		(R)-(2-(2-hydroxypropan-2-yl)-4-methyloxazol-5-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
14		(S)-(2-(2-hydroxypropan-2-yl)-4-methyloxazol-5-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone

TABLE 1-continued

Quinolines		
Ex. #	Structure	Name
15		(R)-(2-(2-fluoropropan-2-yl)thiazol-5-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
16		(S)-(2-(2-fluoropropan-2-yl)thiazol-5-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
17		(R)-(2-(2-fluoropropan-2-yl)oxazol-5-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
18		(S)-(2-(2-fluoropropan-2-yl)oxazol-5-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone

TABLE 1-continued

Quinolines		
Ex. #	Structure	Name
19		(S)-2-(4-fluorophenyl)-5-(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)-1,3,4-oxadiazole
20		(R)-2-(4-fluorophenyl)-5-(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)-1,3,4-oxadiazole
21		(S)-(2-(2-fluoropropan-2-yl)-4-methyloxazol-5-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
22		(R)-(2-(2-fluoropropan-2-yl)-4-methyloxazol-5-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone

TABLE 1-continued

Quinolines		
Ex. #	Structure	Name
23		(R)-(5-(2,6-difluorophenyl)-1,3,4-oxadiazol-2-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
24		(S)-(5-(2,6-difluorophenyl)-1,3,4-oxadiazol-2-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
25		(S)-(4-methyl-2-(1-methyl-1H-pyrazol-4-yl)oxazol-5-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
26		(R)-(4-methyl-2-(1-methyl-1H-pyrazol-4-yl)oxazol-5-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone

TABLE 1-continued

Quinolines		
Ex. #	Structure	Name
27		(S)-(5-(2-hydroxypropan-2-yl)-1,3,4-oxadiazol-2-yl)(4-quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
28		(R)-(5-(2-hydroxypropan-2-yl)-1,3,4-oxadiazol-2-yl)(4-quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
29		(R)-2-(5-(trifluoromethyl)pyrimidin-2-yl)-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridin-4-yl)quinoline
30		(S)-2-(5-(trifluoromethyl)pyrimidin-2-yl)-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridin-4-yl)quinoline

TABLE 1-continued

Quinolines		
Ex. #	Structure	Name
31		(R)-(4-methyl-2-(pyridin-2-yl)oxazol-5-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
32		(S)-(4-methyl-2-(pyridin-2-yl)oxazol-5-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
33		(R)-(5-(5-fluoropyridin-2-yl)-1,3,4-oxadiazol-2-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
34		(S)-(5-(5-fluoropyridin-2-yl)-1,3,4-oxadiazol-2-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone

TABLE 1-continued

Quinolines		
Ex. #	Structure	Name
35		(R)-(2-cyclopropyl-4-methyloxazol-5-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
36		(S)-(2-cyclopropyl-4-methyloxazol-5-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
37		(R)-(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(4-(trifluoromethyl)oxazol-5-yl)methanone
38		(S)-(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(4-(trifluoromethyl)oxazol-5-yl)methanone

TABLE 1-continued

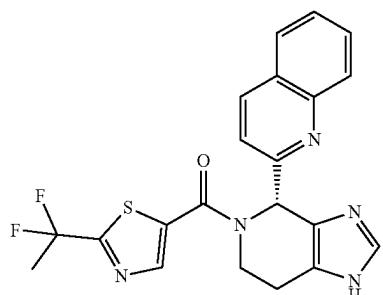
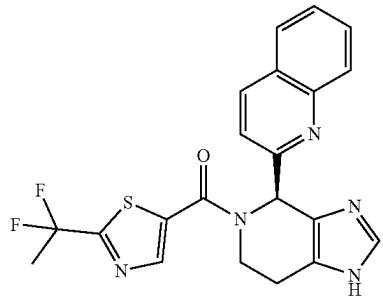
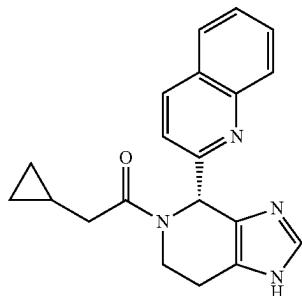
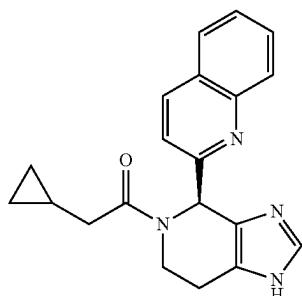
Quinolines		
Ex. #	Structure	Name
39		(R)-(2-(1,1-difluoroethyl)thiazol-5-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
40		(S)-(2-(1,1-difluoroethyl)thiazol-5-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
41		(R)-2-cyclopropyl-1-(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)ethanone
42		(S)-2-cyclopropyl-1-(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)ethanone

TABLE 1-continued

Quinolines		
Ex. #	Structure	Name
43		(R)-(4-cyclopropyl-2-(pyridin-2-yl)oxazol-5-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
44		(S)-(4-cyclopropyl-2-(pyridin-2-yl)oxazol-5-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
45		(R)-(5-(pyridin-2-yl)-1,3,4-oxadiazol-2-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
46		(S)-(5-(pyridin-2-yl)-1,3,4-oxadiazol-2-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone

TABLE 1-continued

Quinolines		
Ex. #	Structure	Name
47		(R)-(5-(1-methyl-1H-pyrazol-4-yl)-1,3,4-oxadiazol-2-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
48		(S)-(5-(1-methyl-1H-pyrazol-4-yl)-1,3,4-oxadiazol-2-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
49		((R)-2,2-difluorocyclopropyl)((R)-4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
50		((S)-2,2-difluorocyclopropyl)((S)-4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone

TABLE 1-continued

Quinolines		
Ex. #	Structure	Name
51		(R)-(4-(difluoromethyl)oxazol-5-yl)(4-(quinolin-2-yl)-6,7-dihydro-3H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
52		(S)-(4-(difluoromethyl)oxazol-5-yl)(4-(quinolin-2-yl)-6,7-dihydro-3H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
53		(R)-2-(3-fluorocyclobutyl)-1-(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)ethanone
54		(S)-2-(3-fluorocyclobutyl)-1-(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)ethanone

TABLE 1-continued

Quinolines		
Ex. #	Structure	Name
55		(R)-2,2-difluoro-2-(1-hydroxycyclobutyl)-1-(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)ethanone
56		(S)-2,2-difluoro-2-(1-hydroxycyclobutyl)-1-(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)ethanone
57		(R)-5-(4-(quinolin-2-yl)-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine-5-carbonyl)oxazole-4-carbonitrile
58		(S)-5-(4-(quinolin-2-yl)-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine-5-carbonyl)oxazole-4-carbonitrile

TABLE 1-continued

Quinolines		
Ex. #	Structure	Name
59		(R)-2-(1-hydroxycyclobutyl)-1-(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)ethanone
60		(S)-2-(1-hydroxycyclobutyl)-1-(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)ethanone
61		(R)-(2-(pyridin-2-yl)oxazol-5-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
62		(S)-(2-(pyridin-2-yl)oxazol-5-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone

TABLE 1-continued

Quinolines		
Ex. #	Structure	Name
63		(R)-(5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-1,3,4-oxadiazol-2-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
64		(S)-(5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-1,3,4-oxadiazol-2-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
65		(R)-(4-(difluoromethyl)-2-(pyridin-2-yl)oxazol-5-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
66		(S)-(4-(difluoromethyl)-2-(pyridin-2-yl)oxazol-5-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone

TABLE 1-continued

Quinolines		
Ex. #	Structure	Name
67		[(4R)-4-(2-quinolyl)-1,4,6,7-tetrahydroimidazo[4,5-c]pyridin-5-yl]-[5-[1-(2,2,2-trifluoroethyl)pyrazol-4-yl]-1,3,4-oxadiazol-2-yl]methanone
68		[(4S)-4-(2-quinolyl)-1,4,6,7-tetrahydroimidazo[4,5-c]pyridin-5-yl]-[5-[1-(2,2,2-trifluoroethyl)pyrazol-4-yl]-1,3,4-oxadiazol-2-yl]methanone
69		(R)-5-(3,4-difluorophenyl)-1,3,4-oxadiazol-2-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
70		(S)-5-(3,4-difluorophenyl)-1,3,4-oxadiazol-2-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone

TABLE 1-continued

Quinolines		
Ex. #	Structure	Name
71		(R)-(2-(3,3-difluorocyclobutyl)-4-(difluoromethyl)oxazol-5-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
72		(S)-(2-(3,3-difluorocyclobutyl)-4-(difluoromethyl)oxazol-5-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
73		(R)-(3-(difluoromethyl)-1-methyl-1H-pyrazol-5-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
74		(S)-(3-(difluoromethyl)-1-methyl-1H-pyrazol-5-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone

TABLE 1-continued

Quinolines		
Ex. #	Structure	Name
75		(R)-(5-(2,4-difluorophenyl)-1,3,4-oxadiazol-2-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
76		(S)-(5-(2,4-difluorophenyl)-1,3,4-oxadiazol-2-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
77		(R)-(4-(difluoromethyl)-2-(methoxymethyl)oxazol-5-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
78		(S)-(4-(difluoromethyl)-2-(methoxymethyl)oxazol-5-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone

TABLE 1-continued

Quinolines		
Ex. #	Structure	Name
79		(2-methyl-1,2,4-triazol-3-yl)-[(4 <i>S</i>)-4-(2-quinolyl)-1,4,6,7-tetrahydroimidazo[4,5-c]pyridin-5-yl]methanone
80		(2-methyl-1,2,4-triazol-3-yl)-[(4 <i>R</i>)-4-(2-quinolyl)-1,4,6,7-tetrahydroimidazo[4,5-c]pyridin-5-yl]methanone
81		(<i>R</i>)-(1-(difluoromethyl)-1 <i>H</i> -pyrazol-5-yl)(4-(quinolin-2-yl)-6,7-dihydro-1 <i>H</i> -imidazo[4,5-c]pyridin-5(4 <i>H</i>)-yl)methanone
82		(<i>S</i>)-(1-(difluoromethyl)-1 <i>H</i> -pyrazol-5-yl)(4-(quinolin-2-yl)-6,7-dihydro-1 <i>H</i> -imidazo[4,5-c]pyridin-5(4 <i>H</i>)-yl)methanone

TABLE 1-continued

Quinolines		
Ex. #	Structure	Name
83		(R)-(3-(difluoromethyl)-1-methyl-1H-pyrazol-4-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
84		(S)-(3-(difluoromethyl)-1-methyl-1H-pyrazol-4-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
85		(R)-(5-(1-methyl-1H-pyrazol-3-yl)-1,3,4-oxadiazol-2-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
86		(S)-(5-(1-methyl-1H-pyrazol-3-yl)-1,3,4-oxadiazol-2-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone

TABLE 1-continued

Quinolines		
Ex. #	Structure	Name
87		(S)-(3-chloro-1-methyl-1H-pyrazol-4-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
88		(R)-(3-chloro-1-methyl-1H-pyrazol-4-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
89		(R)-(5-(3-fluoropyridin-2-yl)-1,3,4-oxadiazol-2-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
90		(S)-(5-(3-fluoropyridin-2-yl)-1,3,4-oxadiazol-2-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone

TABLE 1-continued

Quinolines		
Ex. #	Structure	Name
91		(R)-(4-(difluoromethyl)-2-(2-hydroxypropan-2-yl)oxazol-5-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
92		(S)-(4-(difluoromethyl)-2-(2-hydroxypropan-2-yl)oxazol-5-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
93		(R)-(1-methyl-1H-pyrazol-5-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
94		(S)-(1-methyl-1H-pyrazol-5-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone

TABLE 1-continued

Quinolines		
Ex. #	Structure	Name
95		(S)-(5-(1-(difluoromethyl)-1H-pyrazol-3-yl)-1,3,4-oxadiazol-2-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
96		(R)-(5-(1-(difluoromethyl)-1H-pyrazol-3-yl)-1,3,4-oxadiazol-2-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
97		(R)-(4-bromo-2-(2-hydroxypropan-2-yl)oxazol-5-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
98		(S)-(4-bromo-2-(2-hydroxypropan-2-yl)oxazol-5-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone

TABLE 1-continued

Quinolines		
Ex. #	Structure	Name
99		(2-((S)-1-hydroxyethyl)-4-methyloxazol-5-yl)((R)-4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
100		(2-((S)-1-hydroxyethyl)-4-methyloxazol-5-yl)((S)-4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
101		(R)-(2-(1-hydroxycyclobutyl)-4-methyloxazol-5-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
102		(S)-(2-(1-hydroxycyclobutyl)-4-methyloxazol-5-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone

TABLE 1-continued

Quinolines		
Ex. #	Structure	Name
103		(S)-(5-(5-methylpyridin-2-yl)-1,3,4-oxadiazol-2-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
104		(R)-(5-(5-methylpyridin-2-yl)-1,3,4-oxadiazol-2-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
105		(R)-(5-(2-fluoropropan-2-yl)-1,3,4-oxadiazol-2-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
106		(S)-(5-(2-fluoropropan-2-yl)-1,3,4-oxadiazol-2-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone

TABLE 1-continued

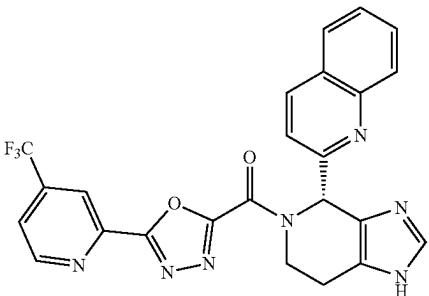
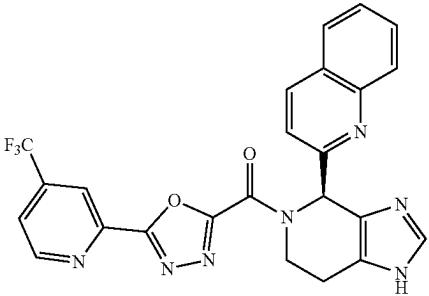
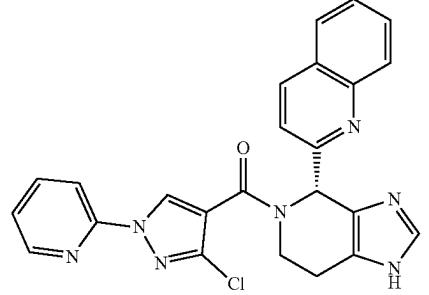
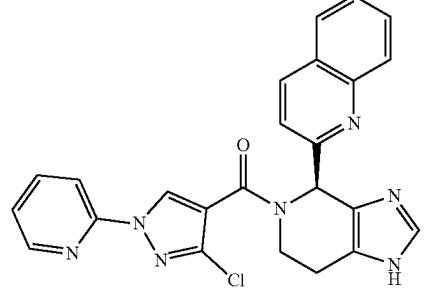
Quinolines		
Ex. #	Structure	Name
107		(R)-(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(5-(4-(trifluoromethyl)pyridin-2-yl)-1,3,4-oxadiazol-2-yl)methanone
108		(S)-(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(5-(4-(trifluoromethyl)pyridin-2-yl)-1,3,4-oxadiazol-2-yl)methanone
109		(R)-(3-chloro-1-(pyridin-2-yl)-1H-pyrazol-4-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
110		(S)-(3-chloro-1-(pyridin-2-yl)-1H-pyrazol-4-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone

TABLE 1-continued

Quinolines		
Ex. #	Structure	Name
111		(2-((R)-1-hydroxyethyl)-4-methyloxazol-5-yl)((R)-4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
112		(2-((R)-1-hydroxyethyl)-4-methyloxazol-5-yl)((S)-4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
113		(R)-(4-chloro-2-(2-hydroxypropan-2-yl)oxazol-5-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
114		(S)-(4-chloro-2-(2-hydroxypropan-2-yl)oxazol-5-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone

TABLE 1-continued

Quinolines		
Ex. #	Structure	Name
115		(R)-(5-(1H-pyrazol-3-yl)-1,3,4-oxadiazol-2-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
116		(S)-(5-(1H-pyrazol-3-yl)-1,3,4-oxadiazol-2-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
117		(S)-2-methyl-2-(4-methyl-5-(4-(quinolin-2-yl)-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine-5-carbonyl)oxazol-2-yl)propanenitrile
118		(R)-2-methyl-2-(4-methyl-5-(4-(quinolin-2-yl)-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine-5-carbonyl)oxazol-2-yl)propanenitrile

TABLE 1-continued

Quinolines		
Ex. #	Structure	Name
119		(4-(difluoromethyl)-2-((R)-1-hydroxyethyl)oxazol-5-yl)((S)-4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
120		(4-(difluoromethyl)-2-((R)-1-hydroxyethyl)oxazol-5-yl)((R)-4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
121		(4-(difluoromethyl)-2-((S)-1-hydroxyethyl)oxazol-5-yl)((S)-4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
122		(4-(difluoromethyl)-2-((S)-1-hydroxyethyl)oxazol-5-yl)((R)-4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone

TABLE 1-continued

Quinolines		
Ex. #	Structure	Name
123		(S)-(5-chloro-1H-pyrazol-4-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
124		(R)-(5-chloro-1H-pyrazol-4-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
125		(R)-(5-(difluoromethyl)-1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
126		(S)-(5-(difluoromethyl)-1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone

TABLE 1-continued

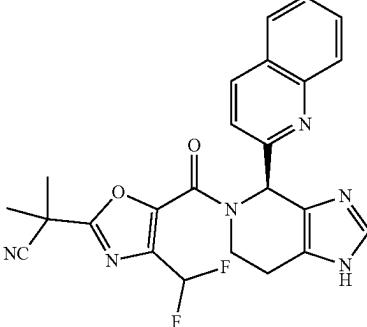
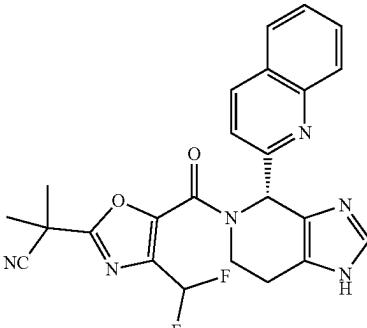
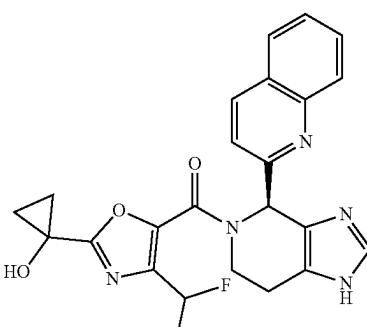
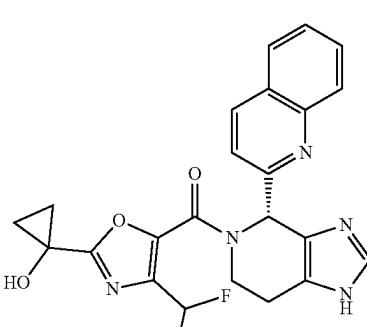
Quinolines		
Ex. #	Structure	Name
127		(S)-2-(4-(difluoromethyl)-5-(4-(quinolin-2-yl)-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine-5-carbonyl)oxazol-2-yl)-2-methylpropanenitrile
128		(R)-2-(4-(difluoromethyl)-5-(4-(quinolin-2-yl)-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine-5-carbonyl)oxazol-2-yl)-2-methylpropanenitrile
129		(S)-(4-(difluoromethyl)-2-(1-hydroxycyclopropyl)oxazol-5-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
130		(R)-(4-(difluoromethyl)-2-(1-hydroxycyclopropyl)oxazol-5-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone

TABLE 1-continued

Quinolines		
Ex. #	Structure	Name
131		(4-bromo-2-(1-hydroxyethyl)oxazol-5-yl)((S)-4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone Diastereomer #1 (Rt = 4.821 min)
132		(4-bromo-2-(1-hydroxyethyl)oxazol-5-yl)((S)-4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone Diastereomer #2 (Rt = 5.107 min)
133		(4-bromo-2-(1-hydroxyethyl)oxazol-5-yl)((R)-4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone Diastereomer #1 (Rt = 4.324 min)
134		(4-bromo-2-(1-hydroxyethyl)oxazol-5-yl)((R)-4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone Diastereomer #2 (Rt = 4.537 min)

TABLE 1-continued

Quinolines		
Ex. #	Structure	Name
135		(4-chloro-2-(1-hydroxyethyl)oxazol-5-yl)((S)-4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone Diastereomer #1 (Rt = 4.522 min)
136		(4-chloro-2-(1-hydroxyethyl)oxazol-5-yl)((S)-4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone Diastereomer #2 (Rt = 4.725 min)
137		(4-chloro-2-(1-hydroxyethyl)oxazol-5-yl)((R)-4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone Diastereomer #1 (Rt = 4.068 min)
138		(4-chloro-2-(1-hydroxyethyl)oxazol-5-yl)((R)-4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone Diastereomer #2 (Rt = 4.259 min)

TABLE 1-continued

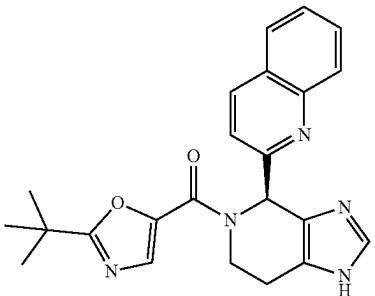
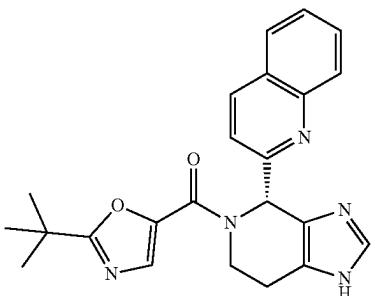
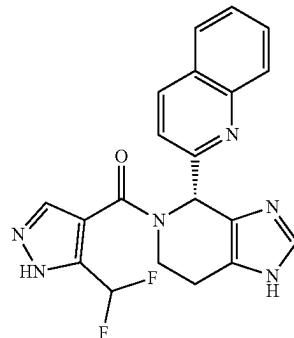
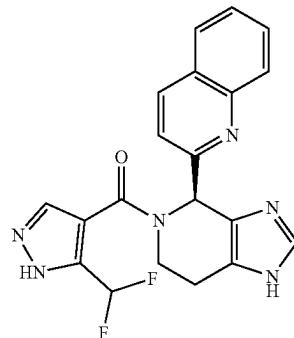
Quinolines		
Ex. #	Structure	Name
257		(S)-(2-(tert-butyl)oxazol-5-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
258		(R)-(2-(tert-butyl)oxazol-5-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
259		(R)-(5-(difluoromethyl)-1H-pyrazol-4-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
260		(S)-(5-(difluoromethyl)-1H-pyrazol-4-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone

TABLE 1-continued

Quinolines		
Ex. #	Structure	Name
261		(R)-(1-(pyridin-2-yl)-1H-pyrazol-5-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
262		(S)-(1-(pyridin-2-yl)-1H-pyrazol-5-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
263		(R)-(3-chloro-1-methyl-1H-pyrazol-5-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
264		(S)-(3-chloro-1-methyl-1H-pyrazol-5-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone

TABLE 1-continued

Quinolines		
Ex. #	Structure	Name
265		(R)-(3-chloro-1-methyl-1H-1,2,4-triazol-5-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
266		(S)-(3-chloro-1-methyl-1H-1,2,4-triazol-5-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
267		(R)-(3-amino-1-(difluoromethyl)-1H-pyrazol-5-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
268		(S)-(3-amino-1-(difluoromethyl)-1H-pyrazol-5-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone

TABLE 1-continued

Quinolines		
Ex. #	Structure	Name
269		(S)-4-ethyl-4H-1,2,4-triazol-3-yl(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
270		(R)-4-ethyl-4H-1,2,4-triazol-3-yl(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
271		(R)-1-(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)-3-(thiazol-2-yl)propan-1-one
272		(S)-1-(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)-3-(thiazol-2-yl)propan-1-one

[0271] In further embodiments, the compound of Formula I is one or more of the compounds in Table 1 that is the R-enantiomer, or a pharmaceutically acceptable salt thereof.

[0272] In yet other embodiments, the compound of Formula I is one or more of the compounds in Table 1 that is the S-enantiomer, or a pharmaceutically acceptable salt thereof.

[0273] In some embodiments, the disclosure provides specific examples of Formula I, and their pharmaceutically acceptable salts and/or isotopologues, as set forth in Table 2 below.

TABLE 2

Quinazolines and Cinnolines		
Ex. #	Structure	Name
139		(S)-(5-cyclopropyl-1,3,4-oxadiazol-2-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
140		(R)-(5-cyclopropyl-1,3,4-oxadiazol-2-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
141		(S)-(2-(2-hydroxypropan-2-yl)-4-methyloxazol-5-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone hydrochloride
142		(R)-(2-(2-hydroxypropan-2-yl)-4-methyloxazol-5-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone hydrochloride

TABLE 2-continued

Quinazolines and Cinnolines		
Ex. #	Structure	Name
143		(S)-(5-(1-methyl-1H-pyrazol-4-yl)-1,3,4-oxadiazol-2-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
144		(R)-(5-(1-methyl-1H-pyrazol-4-yl)-1,3,4-oxadiazol-2-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
145		(S)-(5-(pyridin-2-yl)-1,3,4-oxadiazol-2-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
146		(R)-(5-(pyridin-2-yl)-1,3,4-oxadiazol-2-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone

TABLE 2-continued

Quinazolines and Cinnolines		
Ex. #	Structure	Name
147		(S)-5-(4-(quinazolin-2-yl)-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine-5-carbonyl)oxazole-4-carbonitrile
148		(R)-5-(4-(quinazolin-2-yl)-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine-5-carbonyl)oxazole-4-carbonitrile
149		(S)-oxazol-5-yl(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
150		(R)-oxazol-5-yl(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone

TABLE 2-continued

Quinazolines and Cinnolines		
Ex. #	Structure	Name
151		(S)-(5-(3,3-difluorocyclobutyl)-1,3,4-oxadiazol-2-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
152		(R)-(5-(3,3-difluorocyclobutyl)-1,3,4-oxadiazol-2-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
153		(S)-(6-(methoxymethyl)pyrazolo[1,5-a]pyridin-3-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
154		(R)-(6-(methoxymethyl)pyrazolo[1,5-a]pyridin-3-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone

TABLE 2-continued

Quinazolines and Cinnolines		
Ex. #	Structure	Name
155		(S)-(6-((dimethylamino)methyl)pyrazolo[1,5-a]pyridin-3-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
156		(R)-(6-((dimethylamino)methyl)pyrazolo[1,5-a]pyridin-3-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
157		(R)-(2-(pyridin-2-yl)oxazol-5-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
158		(S)-(2-(pyridin-2-yl)oxazol-5-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone

TABLE 2-continued

Quinazolines and Cinnolines		
Ex. #	Structure	Name
159		(S)-(5-(4-fluoropiperidin-1-yl)-1,3,4-oxadiazol-2-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
160		(R)-(5-(4-fluoropiperidin-1-yl)-1,3,4-oxadiazol-2-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
161		(S)-(5-(2-fluoropropan-2-yl)-1,3,4-oxadiazol-2-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
162		(R)-(5-(2-fluoropropan-2-yl)-1,3,4-oxadiazol-2-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone

TABLE 2-continued

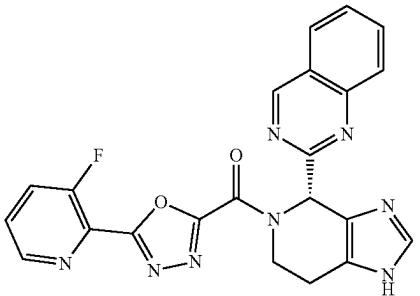
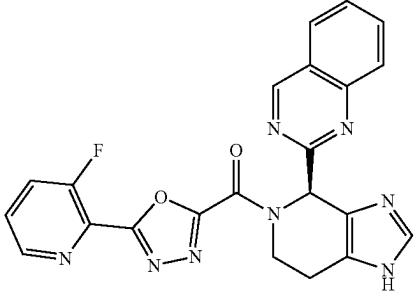
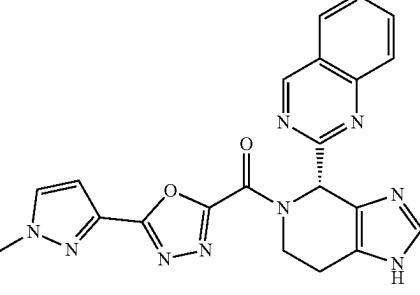
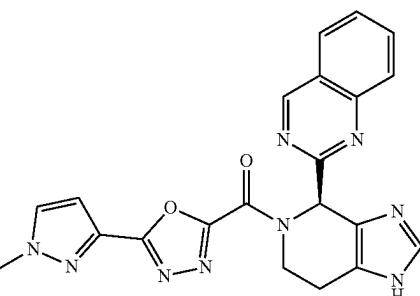
Quinazolines and Cinnolines		
Ex. #	Structure	Name
163		(S)-(5-(3-fluoropyridin-2-yl)-1,3,4-oxadiazol-2-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
164		(R)-(5-(3-fluoropyridin-2-yl)-1,3,4-oxadiazol-2-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
165		(S)-(5-(1-methyl-1H-pyrazol-3-yl)-1,3,4-oxadiazol-2-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
166		(R)-(5-(1-methyl-1H-pyrazol-3-yl)-1,3,4-oxadiazol-2-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone

TABLE 2-continued

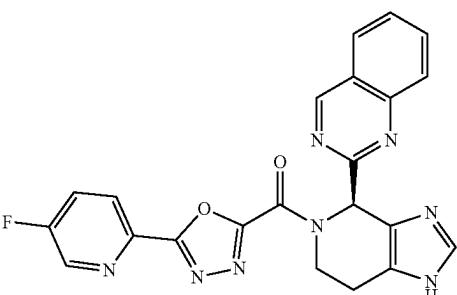
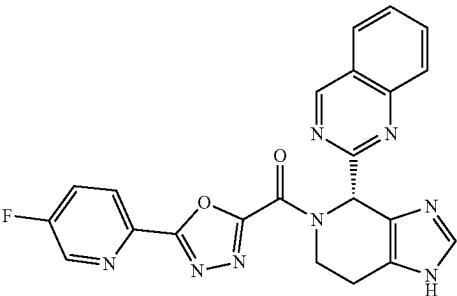
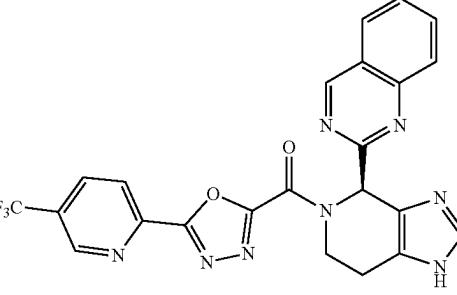
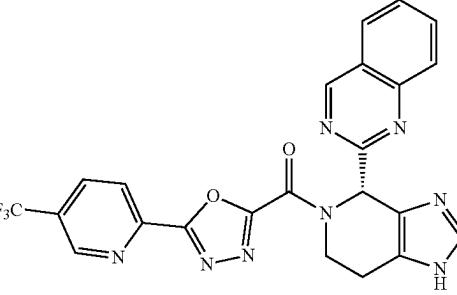
Quinazolines and Cinnolines		
Ex. #	Structure	Name
167		(R)-5-(5-fluoropyridin-2-yl)-1,3,4-oxadiazol-2-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
168		(S)-5-(5-fluoropyridin-2-yl)-1,3,4-oxadiazol-2-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
169		(R)-4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(5-(5-(trifluoromethyl)pyridin-2-yl)-1,3,4-oxadiazol-2-yl)methanone
170		(S)-4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(5-(5-(trifluoromethyl)pyridin-2-yl)-1,3,4-oxadiazol-2-yl)methanone

TABLE 2-continued

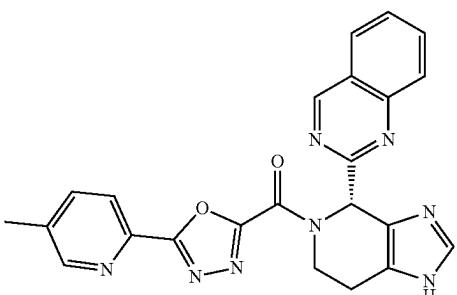
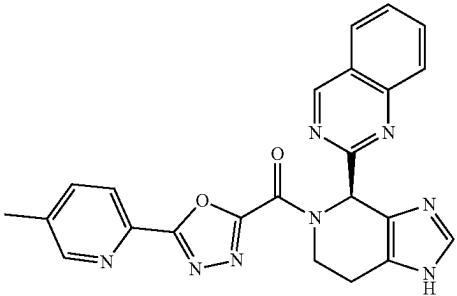
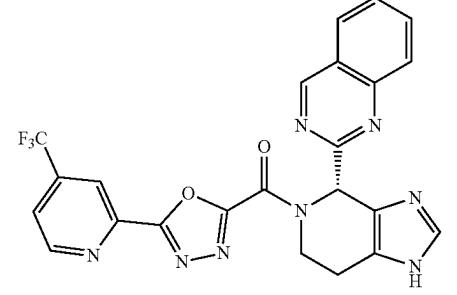
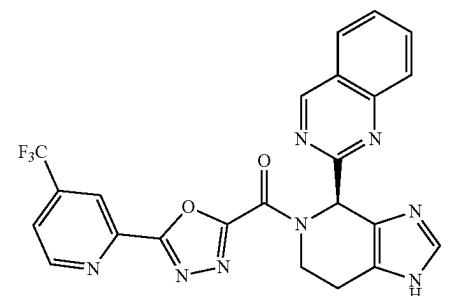
Quinazolines and Cinnolines		
Ex. #	Structure	Name
171		(S)-(5-(5-methylpyridin-2-yl)-1,3,4-oxadiazol-2-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
172		(R)-(5-(5-methylpyridin-2-yl)-1,3,4-oxadiazol-2-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
173		(S)-(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(5-(4-(trifluoromethyl)pyridin-2-yl)-1,3,4-oxadiazol-2-yl)methanone
174		(R)-(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(5-(4-(trifluoromethyl)pyridin-2-yl)-1,3,4-oxadiazol-2-yl)methanone

TABLE 2-continued

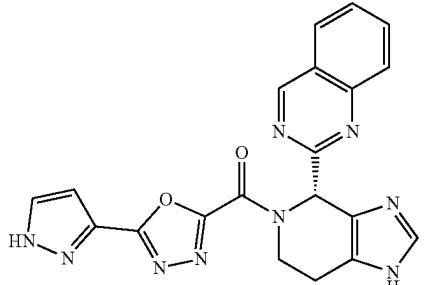
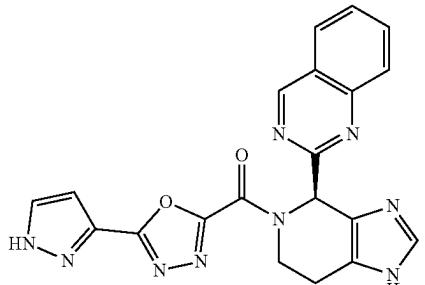
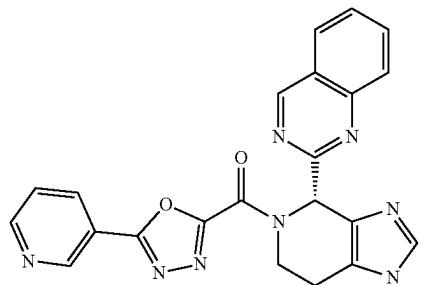
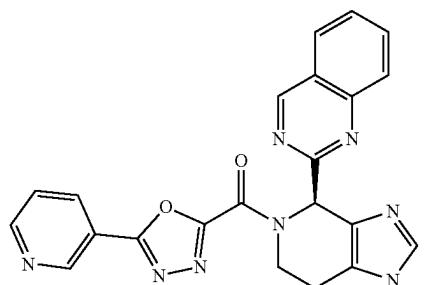
Quinazolines and Cinnolines		
Ex. #	Structure	Name
175		(S)-(5-(1H-pyrazol-3-yl)-1,3,4-oxadiazol-2-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
176		(R)-(5-(1H-pyrazol-3-yl)-1,3,4-oxadiazol-2-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
177		(S)-(5-(pyridin-3-yl)-1,3,4-oxadiazol-2-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
178		(R)-(5-(pyridin-3-yl)-1,3,4-oxadiazol-2-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone

TABLE 2-continued

Quinazolines and Cinnolines		
Ex. #	Structure	Name
179		(S)-(5-(pyridin-4-yl)-1,3,4-oxadiazol-2-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
180		(R)-(5-(pyridin-4-yl)-1,3,4-oxadiazol-2-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
181		(S)-(5-(5-methoxypyridin-2-yl)-1,3,4-oxadiazol-2-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
182		(R)-(5-(5-methoxypyridin-2-yl)-1,3,4-oxadiazol-2-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone

TABLE 2-continued

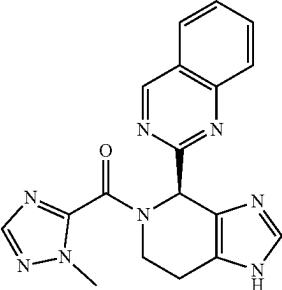
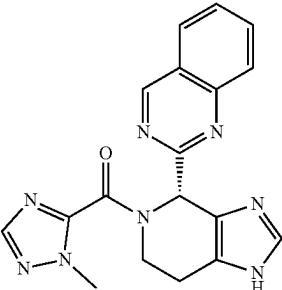
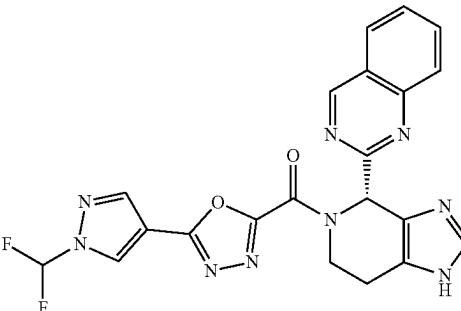
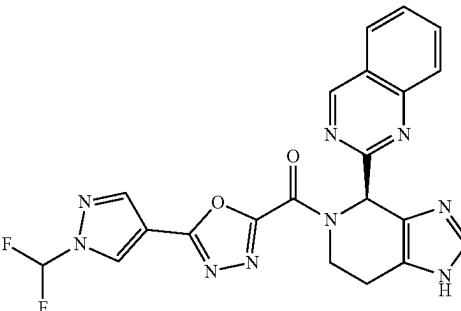
Quinazolines and Cinnolines		
Ex. #	Structure	Name
183		(R)-(1-methyl-1H-1,2,4-triazol-5-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
184		(S)-(1-methyl-1H-1,2,4-triazol-5-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
185		(S)-(5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-1,3,4-oxadiazol-2-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
186		(R)-(5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-1,3,4-oxadiazol-2-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone

TABLE 2-continued

Quinazolines and Cinnolines		
Ex. #	Structure	Name
187		(S)-(5-(1-cyclobutyl-1H-pyrazol-4-yl)-1,3,4-oxadiazol-2-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
188		(R)-(5-(1-cyclobutyl-1H-pyrazol-4-yl)-1,3,4-oxadiazol-2-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
189		(S)-(5-(1-(difluoromethyl)-1H-pyrazol-3-yl)-1,3,4-oxadiazol-2-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
190		(R)-(5-(1-(difluoromethyl)-1H-pyrazol-3-yl)-1,3,4-oxadiazol-2-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone

TABLE 2-continued

Quinazolines and Cinnolines		
Ex. #	Structure	Name
191		(R)-(5-(pyrazin-2-yl)-1,3,4-oxadiazol-2-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
192		(S)-(5-(pyrazin-2-yl)-1,3,4-oxadiazol-2-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
193		(S)-(4-methyl-2-(pyridin-2-yl)oxazol-5-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
194		(R)-(4-methyl-2-(pyridin-2-yl)oxazol-5-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone

TABLE 2-continued

Quinazolines and Cinnolines		
Ex. #	Structure	Name
195		(S)-(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(5-(5-(trifluoromethoxy)pyridin-2-yl)-1,3,4-oxadiazol-2-yl)methanone
196		(R)-(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(5-(5-(trifluoromethoxy)pyridin-2-yl)-1,3,4-oxadiazol-2-yl)methanone
197		(S)-(5-(1-methyl-1H-imidazol-4-yl)-1,3,4-oxadiazol-2-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
198		(R)-(5-(1-methyl-1H-imidazol-4-yl)-1,3,4-oxadiazol-2-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone

TABLE 2-continued

Quinazolines and Cinnolines		
Ex. #	Structure	Name
199		(R)-5-(1,3-dimethyl-1H-pyrazol-4-yl)-1,3,4-oxadiazol-2-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
200		(S)-5-(1,3-dimethyl-1H-pyrazol-4-yl)-1,3,4-oxadiazol-2-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
201		(S)-5-(tert-butyl)-1,3,4-oxadiazol-2-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
202		(R)-5-(tert-butyl)-1,3,4-oxadiazol-2-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone

TABLE 2-continued

Quinazolines and Cinnolines		
Ex. #	Structure	Name
203		(S)-(5-(1-methyl-1H-pyrazol-5-yl)-1,3,4-oxadiazol-2-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
204		(R)-(5-(1-methyl-1H-pyrazol-5-yl)-1,3,4-oxadiazol-2-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
205		(S)-(4-(cinnolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(2-(pyridin-2-yl)thiazol-5-yl)methanone
206		(R)-(4-(cinnolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(2-(pyridin-2-yl)thiazol-5-yl)methanone

TABLE 2-continued

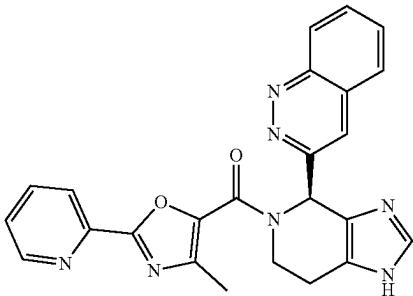
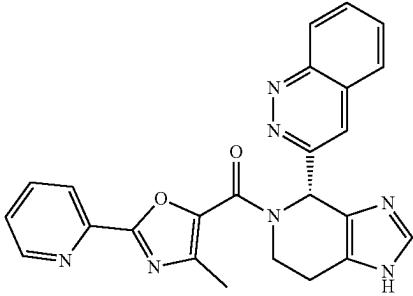
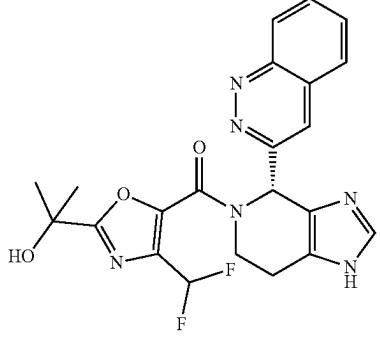
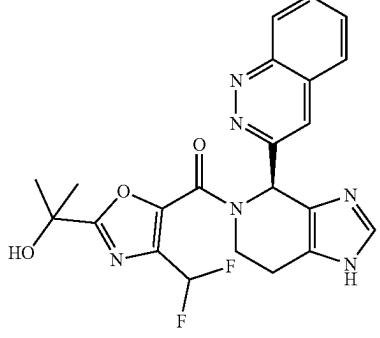
Quinazolines and Cinnolines		
Ex. #	Structure	Name
207		(R)-(4-cinnolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(4-methyl-2-(pyridin-2-yl)oxazol-5-yl)methanone
208		(S)-(4-cinnolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(4-methyl-2-(pyridin-2-yl)oxazol-5-yl)methanone
209		(S)-(4-(cinnolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(4-(difluoromethyl)-2-(2-hydroxypropan-2-yl)oxazol-5-yl)methanone
210		(R)-(4-(cinnolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(4-(difluoromethyl)-2-(2-hydroxypropan-2-yl)oxazol-5-yl)methanone

TABLE 2-continued

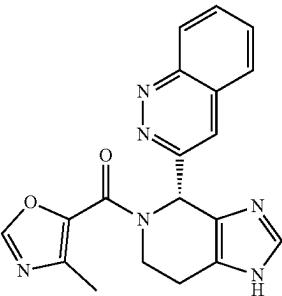
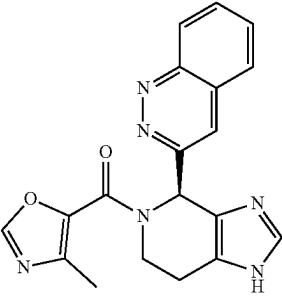
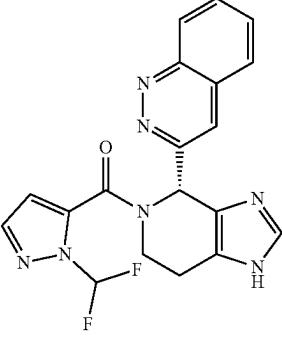
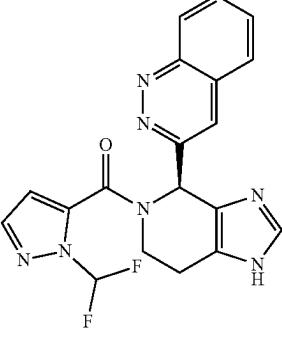
Quinazolines and Cinnolines		
Ex. #	Structure	Name
211		(S)-(4-(cinnolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(4-methyloxazol-5-yl)methanone
212		(R)-(4-(cinnolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(4-methyloxazol-5-yl)methanone
213		(S)-(4-(cinnolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(1-(difluoromethyl)-1H-pyrazol-5-yl)methanone
214		(R)-(4-(cinnolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(1-(difluoromethyl)-1H-pyrazol-5-yl)methanone

TABLE 2-continued

Quinazolines and Cinnolines		
Ex. #	Structure	Name
215		(S)-(4-(cinnolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(cyclopropyl)methanone
216		(R)-(4-(cinnolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(cyclopropyl)methanone
217		(R)-(4-(cinnolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(5-(2-fluoropropan-2-yl)-1,3,4-oxadiazol-2-yl)methanone
218		(S)-(4-(cinnolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(5-(2-fluoropropan-2-yl)-1,3,4-oxadiazol-2-yl)methanone

TABLE 2-continued

Quinazolines and Cinnolines		
Ex. #	Structure	Name
273		(S)-1-(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)-3-(thiazol-2-yl)propan-1-one
274		(R)-1-(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)-3-(thiazol-2-yl)propan-1-one
275		(R)-(3-(difluoromethyl)-1-methyl-1H-1,2,4-triazol-5-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
276		(S)-(3-(difluoromethyl)-1-methyl-1H-1,2,4-triazol-5-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone

TABLE 2-continued

Quinazolines and Cinnolines		
Ex. #	Structure	Name
277		(R)-(4-(difluoromethyl)-2-(5-(trifluoromethyl)pyridin-2-yl)oxazol-5-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
278		(S)-(4-(difluoromethyl)-2-(5-(trifluoromethyl)pyridin-2-yl)oxazol-5-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
279		(R)-(4-(difluoromethyl)-2-(4-fluoropiperidin-1-yl)oxazol-5-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
280		(S)-(4-(difluoromethyl)-2-(4-fluoropiperidin-1-yl)oxazol-5-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone

TABLE 2-continued

Quinazolines and Cinnolines

Ex. #	Structure	Name
281		(R)-(4-(difluoromethyl)-2-(1-methyl-1H-imidazol-5-yl)oxazol-5-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
282		(S)-(4-(difluoromethyl)-2-(1-methyl-1H-imidazol-5-yl)oxazol-5-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone

[0274] In further embodiments, the compound of Formula I is one or more of the compounds in Table 2 that is the S-enantiomer, or a pharmaceutically acceptable salt thereof.

[0275] In some embodiments, the disclosure provides specific examples of Formula I, and their pharmaceutically acceptable salts and/or isotopologues, as set forth in Table 3 below.

TABLE 3

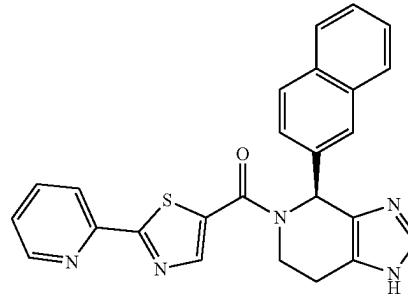
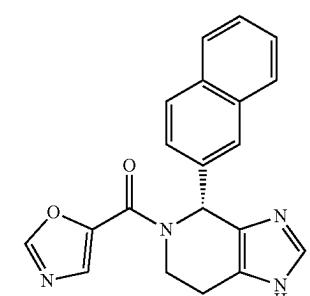
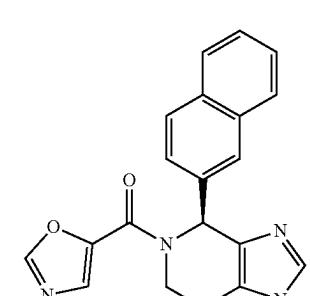
Naphthalenes

Ex. #	Structure	Name
219		(R)-1-(4-(naphthalen-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)-3-(thiazol-2-yl)propan-1-one

TABLE 3-continued

Naphthalenes			
Ex.	#	Structure	Name
220			(S)-1-(4-(naphthalen-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)-3-(thiazol-2-yl)propan-1-one
221			(R)-1-(4-(naphthalen-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)-3-(thiazol-5-yl)methanone
222			(S)-1-(4-(naphthalen-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(thiazol-5-yl)methanone
223			(R)-1-(4-(naphthalen-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(2-(pyridin-2-yl)thiazol-5-yl)methanone

TABLE 3-continued

Naphthalenes			
Ex.	#	Structure	Name
224			(S)-(4-(naphthalen-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(2-(pyridin-2-yl)thiazol-5-yl)methanone
283			(R)-(4-(naphthalen-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(oxazol-5-yl)methanone
284			(S)-(4-(naphthalen-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(oxazol-5-yl)methanone

[0276] In further embodiments, the compound of Formula I is one or more of the compounds in Table 3 that is the R-enantiomer, or a pharmaceutically acceptable salt thereof.

[0277] In some embodiments, the disclosure provides specific examples of Formula I, and their pharmaceutically acceptable salts and/or isotopologues, as set forth in Table 4 below.

TABLE 4

Imidazo[1,2-a]pyridines		
Ex. No.	Structure	Name
225		(R)-(4-(imidazo[1,2-a]pyridin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(pyrazolo[1,5-a]pyridin-3-yl)methanone
226		(S)-(4-(imidazo[1,2-a]pyridin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(pyrazolo[1,5-a]pyridin-3-yl)methanone
227		(S)-(4-(imidazo[1,2-a]pyridin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(4-methyloxazol-5-yl)methanone
228		(R)-(4-(imidazo[1,2-a]pyridin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(4-methyloxazol-5-yl)methanone

TABLE 4-continued

Imidazo[1,2-a]pyridines

Ex. No.	Structure	Name
229		(S)-2-(difluoromethyl)-5-(4-(imidazo[1,2-a]pyridin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)-1,3,4-oxadiazole
230		(R)-2-(difluoromethyl)-5-(4-(imidazo[1,2-a]pyridin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)-1,3,4-oxadiazole
231		(R)-4-(imidazo[1,2-a]pyridin-2-yl)-5-(5-(trifluoromethyl)pyrimidin-2-yl)-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine
232		(S)-4-(imidazo[1,2-a]pyridin-2-yl)-5-(5-(trifluoromethyl)pyrimidin-2-yl)-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine
233		(S)-(4-(imidazo[1,2-a]pyridin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(4-(trifluoromethyl)oxazol-5-yl)methanone

TABLE 4-continued

Imidazo[1,2-a]pyridines

Ex. No.	Structure	Name
234		(R)-(4-(imidazo[1,2-a]pyridin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(4-(trifluoromethyl)oxazol-5-yl)methanone
235		(S)-(2-(1,1-difluoroethyl)thiazol-5-yl)(4-(imidazo[1,2-a]pyridin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
236		(R)-(2-(1,1-difluoroethyl)thiazol-5-yl)(4-(imidazo[1,2-a]pyridin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
237		(S)-2-cyclopropyl-1-(4-(imidazo[1,2-a]pyridin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)ethanone
238		(R)-2-cyclopropyl-1-(4-(imidazo[1,2-a]pyridin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)ethanone

TABLE 4-continued

Imidazo[1,2-a]pyridines		
Ex. No.	Structure	Name
239		(S)-(2-cyclopropyl-4-(trifluoromethyl)oxazol-5-yl)(4-imidazo[4,5-c]pyridin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
240		(R)-(2-cyclopropyl-4-(trifluoromethyl)oxazol-5-yl)(4-imidazo[1,2-a]pyridin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
241		(S)-3-cyclopropyl-1-(4-(imidazo[1,2-a]pyridin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)propan-1-one
242		(R)-3-cyclopropyl-1-(4-(imidazo[1,2-a]pyridin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)propan-1-one

TABLE 4-continued

Imidazo[1,2-a]pyridines		
Ex. No.	Structure	Name
243		(S)-(4-cyclopropyloxazol-5-yl)(4-(imidazo[1,2-a]pyridin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
244		(R)-(4-cyclopropyloxazol-5-yl)(4-(imidazo[1,2-a]pyridin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
245		(R)-(2-(tert-butyl)thiazol-5-yl)(4-(imidazo[1,2-a]pyridin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
246		(S)-(2-(tert-butyl)thiazol-5-yl)(4-(imidazo[1,2-a]pyridin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone

TABLE 4-continued

Imidazo[1,2-a]pyridines

Ex. No.	Structure	Name
247		(S)-(2-(2-fluoropropan-2-yl)thiazol-5-yl)(4-(imidazo[1,2-a]pyridin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
248		(R)-(2-(2-fluoropropan-2-yl)thiazol-5-yl)(4-(imidazo[1,2-a]pyridin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
249		(S)-(2-(tert-butyl)oxazol-5-yl)(4-(imidazo[1,2-a]pyridin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
250		(R)-(2-(tert-butyl)oxazol-5-yl)(4-(imidazo[1,2-a]pyridin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
251		(R)-(2-(1-fluorocyclobutyl)thiazol-5-yl)(4-(imidazo[1,2-a]pyridin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone

TABLE 4-continued

Imidazo[1,2-a]pyridines		
Ex. No.	Structure	Name
252		(S)-(2-(1-fluorocyclobutyl)thiazol-5-yl)(4-(imidazo[1,2-a]pyridin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
253		(S)-2-(3-fluorocyclobutyl)-1-(4-(imidazo[1,2-a]pyridin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)ethanone
254		(R)-2-(3-fluorocyclobutyl)-1-(4-(imidazo[1,2-a]pyridin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)ethanone
255		(S)-(4-(imidazo[1,2-a]pyridin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(2-(pyridin-2-yl)-4-(trifluoromethyl)oxazol-5-yl)methanone

TABLE 4-continued

Imidazo[1,2-a]pyridines

Ex. No.	Structure	Name
256		(R)-(4-(imidazo[1,2-a]pyridin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(2-(pyridin-2-yl)-4-(trifluoromethyl)oxazol-5-yl)methanone

[0278] In further embodiments, the compound of Formula I is one or more compounds in Table 4 that is the R-enantiomer, or a pharmaceutically acceptable salt thereof.

[0279] In some embodiments, the disclosure provides specific examples of Formula I, and their pharmaceutically acceptable salts and/or isotopologues, as set forth in Table 5 below.

TABLE 5

Isoquinolines

Ex. #	Structure	Name
300		(R)-(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(2-(pyridin-2-yl)thiazol-5-yl)methanone
301		(S)-(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(2-(pyridin-2-yl)thiazol-5-yl)methanone

TABLE 5-continued

Isoquinolines			
Ex.	#	Structure	Name
302			(R)-4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(2-(1-methyl-1H-pyrazol-4-yl)thiazol-5-yl)methanone
303			(S)-4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(2-(1-methyl-1H-pyrazol-4-yl)thiazol-5-yl)methanone
304			(S)-4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(2-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)oxazol-5-yl)methanone
305			(R)-4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(2-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)oxazol-5-yl)methanone

TABLE 5-continued

Isoquinolines			
Ex.	#	Structure	Name
306			(R)-(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(2-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)thiazol-5-yl)methanone
307			(S)-(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(2-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)thiazol-5-yl)methanone
308			(R)-(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(2-(pyridin-2-yl)oxazol-5-yl)methanone
309			(S)-(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(2-(pyridin-2-yl)oxazol-5-yl)methanone

TABLE 5-continued

Isoquinolines			
Ex.	#	Structure	Name
310			(S)-(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(2-(1-methyl-1H-pyrazol-4-yl)oxazol-5-yl)methanone
311			(R)-(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(2-(1-methyl-1H-pyrazol-4-yl)oxazol-5-yl)methanone
312			(R)-(2-(5-fluoropyridin-2-yl)thiazol-5-yl)(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
313			(S)-(2-(5-fluoropyridin-2-yl)thiazol-5-yl)(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone

TABLE 5-continued

Isoquinolines			
Ex.	#	Structure	Name
314			(R)-(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(6-(methoxymethyl)pyrazolo[1,5-a]pyridin-3-yl)methanone
315			(S)-(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(6-(methoxymethyl)pyrazolo[1,5-a]pyridin-3-yl)methanone
316			(R)-(2-(tert-butyl)thiazol-5-yl)(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
317			(S)-(2-(tert-butyl)thiazol-5-yl)(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone

TABLE 5-continued

Isoquinolines			
Ex.	#	Structure	Name
318			(R)-(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(5-methyl-1,3,4-oxadiazol-2-yl)methanone
319			(S)-(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(5-methyl-1,3,4-oxadiazol-2-yl)methanone
320			(R)-(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(oxazol-5-yl)methanone
321			(S)-(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(oxazol-5-yl)methanone

TABLE 5-continued

Isoquinolines			
Ex.	#	Structure	Name
322			(R)-(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(5-(1-methyl-1H-pyrazol-4-yl)-1,3,4-oxadiazol-2-yl)methanone
323			(S)-(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(5-(1-methyl-1H-pyrazol-4-yl)-1,3,4-oxadiazol-2-yl)methanone
324			(R)-(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(5-(pyridin-2-yl)-1,3,4-oxadiazol-2-yl)methanone
325			(S)-(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(5-(pyridin-2-yl)-1,3,4-oxadiazol-2-yl)methanone

TABLE 5-continued

Isoquinolines			
Ex.	#	Structure	Name
326			(R)-(5-cyclopropyl-1,3,4-oxadiazol-2-yl)(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
327			(S)-(5-cyclopropyl-1,3,4-oxadiazol-2-yl)(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
328			(R)-(2-(2-hydroxypropan-2-yl)thiazol-5-yl)(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
329			(S)-(2-(2-hydroxypropan-2-yl)thiazol-5-yl)(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone

TABLE 5-continued

Isoquinolines			
Ex.	#	Structure	Name
330			(R)-(6-((dimethylamino)methyl)pyrazolo[1,5-a]pyridin-3-yl)(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
331			(S)-(6-((dimethylamino)methyl)pyrazolo[1,5-a]pyridin-3-yl)(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
332			(R)-(2-(2-fluoropropan-2-yl)thiazol-5-yl)(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
333			(S)-(2-(2-fluoropropan-2-yl)thiazol-5-yl)(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone

TABLE 5-continued

Isoquinolines			
Ex.	#	Structure	Name
334			(R)-5-(2,6-difluorophenyl)-1,3,4-oxadiazol-2-yl)(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
335			(S)-5-(2,6-difluorophenyl)-1,3,4-oxadiazol-2-yl)(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
336			(S)-2-(4-fluorophenyl)-5-(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)-1,3,4-oxadiazole
337			(R)-2-(4-fluorophenyl)-5-(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)-1,3,4-oxadiazole

TABLE 5-continued

Isoquinolines			
Ex.	#	Structure	Name
338			(S)-(2-(2-fluoropropan-2-yl)oxazol-5-yl)(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
339			(R)-(2-(2-fluoropropan-2-yl)oxazol-5-yl)(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
340			(R)-(5-(5-fluoropyridin-2-yl)-1,3,4-oxadiazol-2-yl)(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
341			(S)-(5-(5-fluoropyridin-2-yl)-1,3,4-oxadiazol-2-yl)(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone

TABLE 5-continued

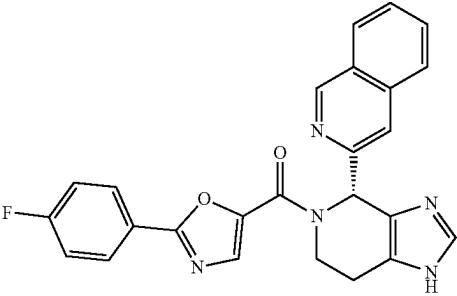
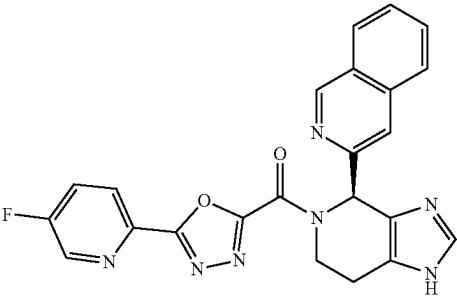
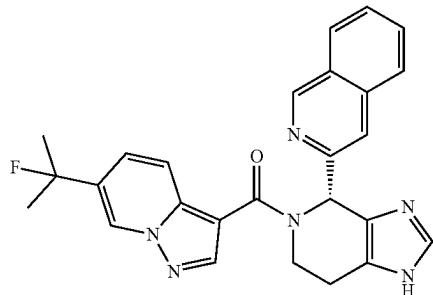
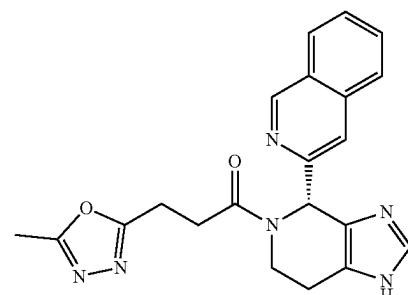
Isoquinolines			
Ex.	#	Structure	Name
342			(R)-(5-(4-fluorophenyl)-1,3,4-oxadiazol-2-yl)(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
343			(S)-(5-(4-fluorophenyl)-1,3,4-oxadiazol-2-yl)(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
344			(R)-(6-(2-fluoropropan-2-yl)pyrazolo[1,5-a]pyridin-3-yl)(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
345			(R)-1-(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)-3-(5-methyl-1,3,4-oxadiazol-2-yl)propan-1-one

TABLE 5-continued

Isoquinolines			
Ex.	#	Structure	Name
346			(R)-3-(5-(difluoromethyl)-1,3,4-oxadiazol-2-yl)-1-(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)propan-1-one
347			(R)-(5-(2-hydroxypropan-2-yl)-1,3,4-oxadiazol-2-yl)(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
348			(R)-(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(4-phenyloxazol-5-yl)methanone
349			(R)-1-(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)-2-(1,3,4-thiadiazol-2-yl)ethanone

TABLE 5-continued

Isoquinolines			
Ex.	#	Structure	Name
350			(R)-4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(1,3,4-thiadiazol-2-yl)methanone
351			(R)-1-(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)-2-(5-methyl-1,3,4-thiadiazol-2-yl)ethanone
352			(R)-(6-bromopyrazolo[1,5-a]pyridin-3-yl)(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
353			(R)-imidazo[1,5-a]pyridin-1-yl(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone

TABLE 5-continued

Isoquinolines		
Ex. #	Structure	Name
354		(R)-4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(4-(pyridin-2-yl)oxazol-5-yl)methanone
355		(R)-(7-bromopyrazolo[1,5-a]pyridin-3-yl)(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
356		(R)-(5-bromopyrazolo[1,5-a]pyridin-3-yl)(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
357		(R)-(4-fluoropyrazolo[1,5-a]pyridin-3-yl)(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone

TABLE 5-continued

Isoquinolines			
Ex.	#	Structure	Name
358			(R)-benzo[d]isothiazol-3-yl(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
359			(3a,7a-dihydro-1H-indazol-3-yl)(R)-4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
360			(R)-(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(1-methyl-1H-indazol-3-yl)methanone
361			(R)-(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(5-methyl-1,3,4-thiadiazol-2-yl)methanone

TABLE 5-continued

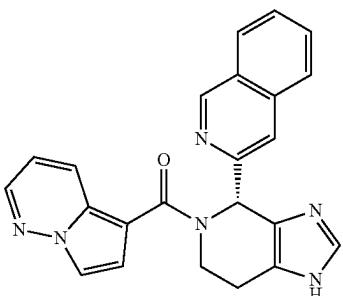
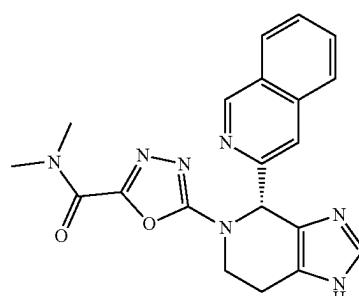
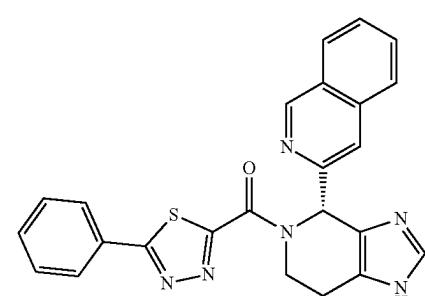
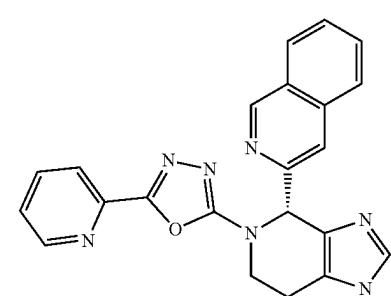
Isoquinolines			
Ex.	#	Structure	Name
362			(R)-4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(pyrrolo[1,2-b]pyridazin-5-yl)methanone
363			(R)-5-(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)-N,N-dimethyl-1,3,4-oxadiazole-2-carboxamide
364			(R)-4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(5-phenyl-1,3,4-thiadiazol-2-yl)methanone
365			(R)-2-(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)-5-(pyridin-2-yl)-1,3,4-oxadiazole

TABLE 5-continued

Isoquinolines			
Ex.	#	Structure	Name
366			(R)-(5-(dimethylamino)-1,3,4-oxadiazol-2-yl)(4-isooquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
367			(S)-(5-(dimethylamino)-1,3,4-oxadiazol-2-yl)(4-isooquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
368			(R)-1-(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)-2-(trifluoromethyl)thiazol-2-yl)ethanone
369			(R)-1-(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)-2-(1H-1,2,4-triazol-1-yl)ethanone

TABLE 5-continued

Isoquinolines			
Ex.	#	Structure	Name
370			(R)-(5-(cyclopropylamino)-1,3,4-oxadiazol-2-yl)(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
371			(S)-(5-(cyclopropylamino)-1,3,4-oxadiazol-2-yl)(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
372			(R)-1-(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)-2-(2-methyloxazol-5-yl)ethanone
373			(R)-1-(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)-2-(thiazol-5-yl)ethanone

TABLE 5-continued

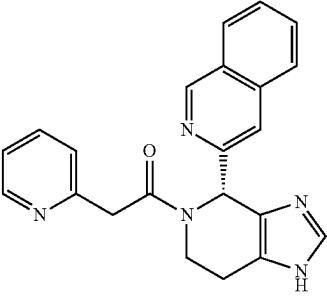
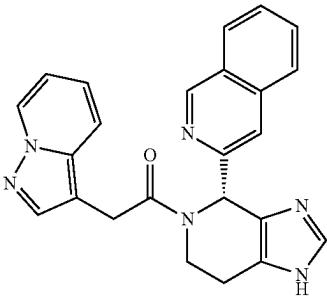
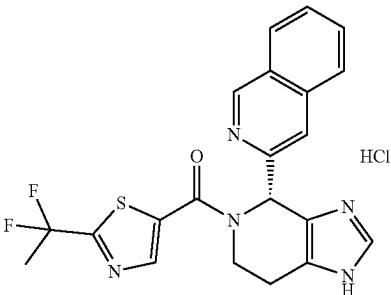
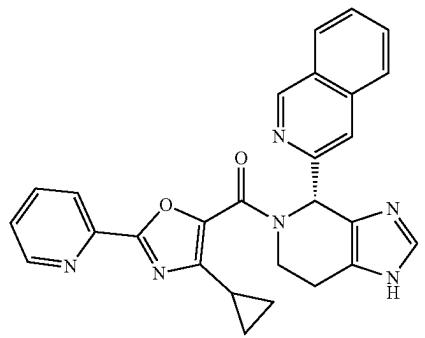
Isoquinolines			
Ex.	#	Structure	Name
374			(R)-1-(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)-2-(pyridin-2-yl)ethanone
375			(R)-1-(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)-2-(pyrazolo[1,5-a]pyridin-3-yl)ethanone
376			(R)-(2-(1,1-difluoroethyl)thiazol-5-yl)(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone hydrochloride
377			(R)-(4-cyclopropyl-2-(pyridin-2-yl)oxazol-5-yl)(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone

TABLE 5-continued

Isoquinolines			
Ex.	#	Structure	Name
378			(R)-(4-cyclopropyl-2-(2-hydroxypropan-2-yl)oxazol-5-yl)(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
379			(R)-(4-cyclopropyl-2-(pyridin-2-yl)oxazol-5-yl)(4-(isoquinolin-3-yl)-7,8-dihydroimidazo[4,5-c]azepin-5(1H,4H,6H)-yl)methanone
380			(S)-(4-cyclopropyl-2-(pyridin-2-yl)oxazol-5-yl)(4-(isoquinolin-3-yl)-7,8-dihydroimidazo[4,5-c]azepin-5(1H,4H,6H)-yl)methanone
381			((4R,7S)-4-(isoquinolin-3-yl)-7-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(2-(pyridin-2-yl)oxazol-5-yl)methanone

TABLE 5-continued

Isoquinolines			
Ex.	#	Structure	Name
382			((4S,7S)-4-(isoquinolin-3-yl)-7-methyl-6,7-dihydro-1H-imidazo[4,c]pyridin-5(4H)-yl)(2-(pyridin-2-yl)oxazol-5-yl)methanone
383			((4S,7R)-4-(isoquinolin-3-yl)-7-methyl-6,7-dihydro-1H-imidazo[4,c]pyridin-5(4H)-yl)(2-(pyridin-2-yl)oxazol-5-yl)methanone
384			((4R,7R)-4-(isoquinolin-3-yl)-7-methyl-6,7-dihydro-1H-imidazo[4,c]pyridin-5(4H)-yl)(2-(pyridin-2-yl)oxazol-5-yl)methanone
385			(4R,7S)-4-(isoquinolin-3-yl)-7-methyl-6,7-dihydro-1H-imidazo[4,c]pyridin-5(4H)-yl)(5-(pyridin-2-yl)-1,3,4-oxadiazol-2-yl)methanone

TABLE 5-continued

Isoquinolines			
Ex.	#	Structure	Name
386			((4S,7S)-4-(isoquinolin-3-yl)-7-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(5-(pyridin-2-yl)-1,3,4-oxadiazol-2-yl)methanone
387			((4S,7R)-4-(isoquinolin-3-yl)-7-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(5-(pyridin-2-yl)-1,3,4-oxadiazol-2-yl)methanone
388			((4R,7R)-4-(isoquinolin-3-yl)-7-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(5-(pyridin-2-yl)-1,3,4-oxadiazol-2-yl)methanone
389			(2-(2-hydroxypropan-2-yl)-4-methyloxazol-5-yl)((4R,7S)-4-(isoquinolin-3-yl)-7-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone

TABLE 5-continued

Isoquinolines			
Ex.	#	Structure	Name
390			(2-(2-hydroxypropan-2-yl)-4-methyloxazol-5-yl)((4S,7S)-4-(isoquinolin-3-yl)-7-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
391			(2-(2-hydroxypropan-2-yl)-4-methyloxazol-5-yl)((4S,7R)-4-(isoquinolin-3-yl)-7-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
392			(2-(2-hydroxypropan-2-yl)-4-methyloxazol-5-yl)((4R,7R)-4-(isoquinolin-3-yl)-7-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
393			(R)-(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(2-(methoxymethyl)thiazol-5-yl)methanone

TABLE 5-continued

Isoquinolines			
Ex.	#	Structure	Name
394			(R)-4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(2-(methoxymethyl)oxazol-5-yl)methanone
395			(2-(2-hydroxypropan-2-yl)oxazol-5-yl)((4R,7S)-4-(isoquinolin-3-yl)-7-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
396			(2-(2-hydroxypropan-2-yl)oxazol-5-yl)((4S,7S)-4-(isoquinolin-3-yl)-7-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
397			(2-(2-hydroxypropan-2-yl)oxazol-5-yl)((4S,7R)-4-(isoquinolin-3-yl)-7-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone

TABLE 5-continued

Isoquinolines		
Ex. #	Structure	Name
398		(2-(2-hydroxypropan-2-yl)oxazol-5-yl)((4R,7R)-4-(isoquinolin-3-yl)-7-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
399		(4-cyclopropyl-2-(2-hydroxypropan-2-yl)oxazol-5-yl)((4R,7S)-4-(isoquinolin-3-yl)-7-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
400		(4-cyclopropyl-2-(2-hydroxypropan-2-yl)oxazol-5-yl)((4S,7S)-4-(isoquinolin-3-yl)-7-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
401		(4-cyclopropyl-2-(2-hydroxypropan-2-yl)oxazol-5-yl)((4S,7R)-4-(isoquinolin-3-yl)-7-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone

TABLE 5-continued

Isoquinolines		
Ex. #	Structure	Name
402		(4-cyclopropyl-2-(2-hydroxypropan-2-yl)oxazol-5-yl)((4R,7R)-4-(isoquinolin-3-yl)-7-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
403		((4R,7S)-4-(isoquinolin-3-yl)-7-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(4-methyl-2-(pyridin-2-yl)oxazol-5-yl)methanone
404		((4S,7S)-4-(isoquinolin-3-yl)-7-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(4-methyl-2-(pyridin-2-yl)oxazol-5-yl)methanone
405		[(4S,7R)-4-(3-isooquinolyl)-7-methyl-1,4,6,7-tetrahydroimidazo[4,5-c]pyridin-5-yl]-[4-methyl-2-(2-pyridyl)oxazol-5-yl]methanone

TABLE 5-continued

Isoquinolines		
Ex. #	Structure	Name
406		[<i>(4R,7R)-4-(3-isoquinolyl)-7-methyl-1,4,6,7-tetrahydroimidazo[4,5-c]pyridin-5-yl]-[4-methyl-2-(2-pyridyl)oxazol-5-yl]methanone</i>]
407		(4-cyclopropyl-2-(pyridin-2-yl)oxazol-5-yl)(<i>(4R,7S)-4-(isoquinolin-3-yl)-7-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl</i>)methanone
408		(4-cyclopropyl-2-(pyridin-2-yl)oxazol-5-yl)(<i>(4S,7S)-4-(isoquinolin-3-yl)-7-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl</i>)methanone
409		(4-cyclopropyl-2-(pyridin-2-yl)oxazol-5-yl)(<i>(4S,7R)-4-(isoquinolin-3-yl)-7-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl</i>)methanone

TABLE 5-continued

Isoquinolines		
Ex. #	Structure	Name
410		(4-cyclopropyl-2-(pyridin-2-yl)oxazol-5-yl)((4R,7R)-4-(isoquinolin-3-yl)-7-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
411		Number not used
412		Number not used
413		Number not used
414		Number not used
415		Number not used
416		Number not used
417		Number not used
418		Number not used
419		(R)-(5-(2-fluoropropan-2-yl)-1,3,4-oxadiazol-2-yl)(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
420		(R)-(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(1-(2,2,2-trifluoroethyl)azetidin-3-yl)methanone
421		(R)-(5-(2-hydroxypropan-2-yl)-1,2,4-oxadiazol-3-yl)(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone

TABLE 5-continued

Isoquinolines			
Ex.	#	Structure	Name
422			(R)-3-(3-hydroxypropan-2-yl)-1,2,4-oxadiazol-5-yl(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
423			(R)-3-(difluoromethyl)-1-methyl-1H-1,2,4-triazol-5-yl(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
424			(R)-5-(3-fluoroazetidin-1-yl)-1,3,4-oxadiazol-2-yl(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
425			(R)-5-(4-fluoropiperidin-1-yl)-1,3,4-oxadiazol-2-yl(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone

TABLE 5-continued

Isoquinolines			
Ex.	#	Structure	Name
426			(R)-(5-(1-(difluoromethyl)-1H-pyrazol-3-yl)-1,3,4-oxadiazol-2-yl)(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
427			(5-(tert-butyl)-1,3,4-oxadiazol-2-yl)((4S,7S)-4-(isoquinolin-3-yl)-7-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
428			(5-(tert-butyl)-1,3,4-oxadiazol-2-yl)((4R,7S)-4-(isoquinolin-3-yl)-7-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
429			(5-(tert-butyl)-1,3,4-oxadiazol-2-yl)((4S,7R)-4-(isoquinolin-3-yl)-7-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone

TABLE 5-continued

Isoquinolines		
Ex. #	Structure	Name
430		(5-(tert-butyl)-1,3,4-oxadiazol-2-yl)((4R,7R)-4-(isoquinolin-3-yl)-7-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
431		(R)-(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(pyrazolo[1,5-a]pyridin-3-yl)methanone
432		(S)-(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(pyrazolo[1,5-a]pyridin-3-yl)methanone
433		(R)-(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(5-morpholino-1,3,4-oxadiazol-2-yl)methanone

TABLE 5-continued

Isoquinolines			
Ex.	#	Structure	Name
434			(S)-(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(5-morpholino-1,3,4-oxadiazol-2-yl)methanone
435			(R)-(2-(tert-butyl)oxazol-5-yl)(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
436			(S)-(2-(tert-butyl)oxazol-5-yl)(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
437			(R)-(5-(3-fluoropyridin-2-yl)-1,3,4-oxadiazol-2-yl)(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone

TABLE 5-continued

Isoquinolines			
Ex.	#	Structure	Name
438			(R)-(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(5-(5-methoxypyridin-2-yl)-1,3,4-oxadiazol-2-yl)methanone
439			(R)-(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(5-(5-methylpyridin-2-yl)-1,3,4-oxadiazol-2-yl)methanone
440			(R)-(5-(1-(difluoromethyl)-1H-pyrazol-4-yl)-1,3,4-oxadiazol-2-yl)(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
441			(R)-(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(5-(1-methyl-1H-pyrazol-3-yl)-1,3,4-oxadiazol-2-yl)methanone

TABLE 5-continued

Isoquinolines			
Ex.	#	Structure	Name
442			(R)-(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(5-(trifluoromethyl)pyridin-2-yl)-1,3,4-oxadiazol-2-yl)methanone
443			(R)-(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(5-(1-methyl-1H-imidazol-4-yl)-1,3,4-oxadiazol-2-yl)methanone
444			(R)-(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(5-(1-methyl-1H-imidazol-5-yl)-1,3,4-oxadiazol-2-yl)methanone
445			(R)-(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(5-(pyridin-3-yl)-1,3,4-oxadiazol-2-yl)methanone

TABLE 5-continued

Isoquinolines			
Ex.	#	Structure	Name
446			(R)-5-(1,5-dimethyl-1H-pyrazol-4-yl)-1,3,4-oxadiazol-2-yl)(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
447			(R)-(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(5-(1-methyl-1H-pyrazol-5-yl)-1,3,4-oxadiazol-2-yl)methanone
448			(R)-(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(5-(pyridin-4-yl)-1,3,4-oxadiazol-2-yl)methanone
449			(R)-(5-(1-cyclobutyl-1H-pyrazol-4-yl)-1,3,4-oxadiazol-2-yl)(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone

TABLE 5-continued

Isoquinolines			
Ex.	#	Structure	Name
450			(R)-5-(1,3-dimethyl-1H-pyrazol-4-yl)-1,3,4-oxadiazol-2-yl(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
451			(R)-5-(1H-pyrazol-3-yl)-1,3,4-oxadiazol-2-yl(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
452			(R)-6-cyclopropylpyrazolo[1,5-a]pyridin-3-yl(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
453			(R)-(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(6-(2-methoxyethyl)pyrazolo[1,5-a]pyridin-3-yl)methanone

TABLE 5-continued

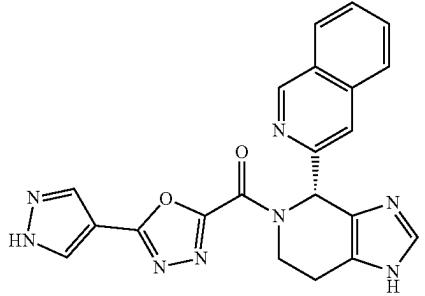
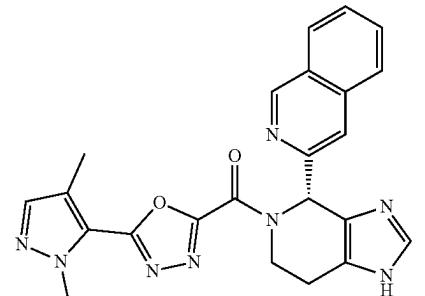
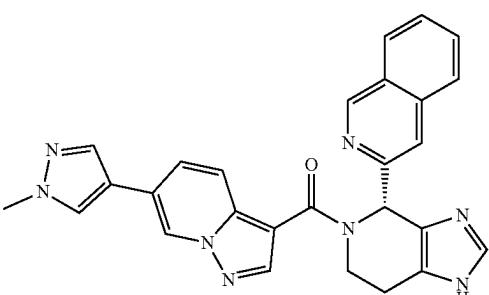
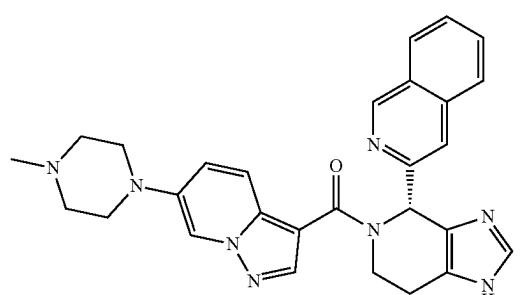
Isoquinolines			
Ex.	#	Structure	Name
454			(R)-(5-(1H-pyrazol-4-yl)-1,3,4-oxadiazol-2-yl)(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
455			(R)-(5-(1,4-dimethyl-1H-pyrazol-5-yl)-1,3,4-oxadiazol-2-yl)(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
456			(R)-(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyridin-3-yl)methanone
457			(R)-(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(6-(4-methylpiperazin-1-yl)pyrazolo[1,5-a]pyridin-3-yl)methanone

TABLE 5-continued

Isoquinolines			
Ex.	#	Structure	Name
458			(R)-(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(6-morpholinopyrazolo[1,5-a]pyridin-3-yl)methanone
459			(R)-(6-bromo-5-chloropyrazolo[1,5-a]pyridin-3-yl)(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
460			(R)-(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(6-methoxypyrazolo[1,5-a]pyridin-3-yl)methanone
461			(R)-(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(6-(pyridin-2-yl)pyrazolo[1,5-a]pyridin-3-yl)methanone

TABLE 5-continued

Isoquinolines			
Ex.	#	Structure	Name
462			(R)-5-chloropyrazolo[1,5-a]pyridin-3-yl)(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
463			(R)-5-chloro-6-morpholinopyrazolo[1,5-a]pyridin-3-yl)(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
464			(R)-5-chloro-6-(4-methylpiperazin-1-yl)pyrazolo[1,5-a]pyridin-3-yl)(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
465			(5-((R)-1-hydroxyethyl)-1,3,4-oxadiazol-2-yl)((R)-4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone

TABLE 5-continued

Isoquinolines			
Ex.	#	Structure	Name
466			(R)-(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(6-methylpyrazolo[1,5-a]pyridin-3-yl)methanone
467			(R)-(6-chloropyrazolo[1,5-a]pyridin-3-yl)(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
468			(R)-(6-(2-(dimethylamino)ethyl)pyrazolo[1,5-a]pyridin-3-yl)(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
469			(R)-(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(5-(pyrazin-2-yl)-1,3,4-oxadiazol-2-yl)methanone

TABLE 5-continued

Isoquinolines			
Ex.	#	Structure	Name
470			(R)-(6-(dimethylamino)pyrazolo[1,5-a]pyridin-3-yl)(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
471			(R)-(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(5-(pyrimidin-4-yl)-1,3,4-oxadiazol-2-yl)methanone
472			(R)-(5-(1,5-dimethyl-1H-pyrazol-3-yl)-1,3,4-oxadiazol-2-yl)(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
473			(R)-(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(5-(pyrimidin-2-yl)-1,3,4-oxadiazol-2-yl)methanone

TABLE 5-continued

Isoquinolines			
Ex.	#	Structure	Name
474			(R)-(6-(4-fluoropiperidin-1-yl)pyrazolo[1,5-a]pyridin-3-yl)(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
475			(R)-(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(6-(pyridin-3-yl)pyrazolo[1,5-a]pyridin-3-yl)methanone
476			(R)-(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(6-(pyrimidin-4-yl)pyrazolo[1,5-a]pyridin-3-yl)methanone
477			(R)-(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(6-(pyrazin-2-yl)pyrazolo[1,5-a]pyridin-3-yl)methanone

TABLE 5-continued

Isoquinolines			
Ex.	#	Structure	Name
478			(R)-(6-(4-hydroxypiperidin-1-yl)pyrazolo[1,5-a]pyridin-3-yl)(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
479			(R)-(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(6-(6-methylpyridin-2-yl)pyrazolo[1,5-a]pyridin-3-yl)methanone
480			(R)-(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(6-(2-methylpyridin-3-yl)pyrazolo[1,5-a]pyridin-3-yl)methanone
481			(R)-(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(6-(1-methyl-1H-pyrazol-3-yl)pyrazolo[1,5-a]pyridin-3-yl)methanone

TABLE 5-continued

Isoquinolines			
Ex.	#	Structure	Name
482			(R)-(6-(3-fluoropyridin-2-yl)pyrazolo[1,5-a]pyridin-3-yl)(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
483			(R)-(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(6-(pyrimidin-2-yl)pyrazolo[1,5-a]pyridin-3-yl)methanone
484			(R)-(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(6-(morpholinomethyl)pyrazolo[1,5-a]pyridin-3-yl)methanone
485			(R)-(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(6-phenylpyrazolo[1,5-a]pyridin-3-yl)methanone

TABLE 5-continued

Isoquinolines			
Ex.	#	Structure	Name
486			(R)-(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(6-(pyridin-4-yl)pyrazolo[1,5-a]pyridin-3-yl)methanone
487			(R)-(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(6-(pyrimidin-5-yl)pyrazolo[1,5-a]pyridin-3-yl)methanone
488			(R)-(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(6-((4-methylpiperazin-1-yl)methyl)pyrazolo[1,5-a]pyridin-3-yl)methanone
489			(R)-(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(6-(pyrrolidin-1-yl)pyrazolo[1,5-a]pyridin-3-yl)methanone

TABLE 5-continued

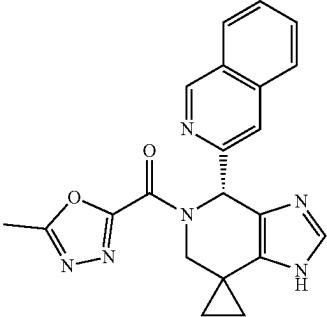
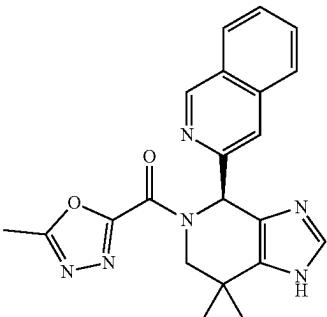
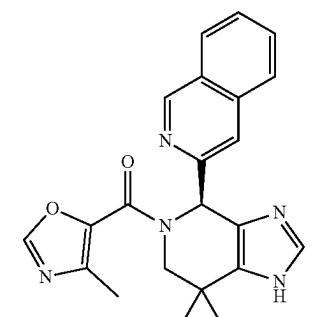
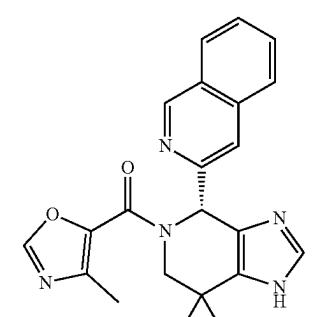
Isoquinolines		
Ex. #	Structure	Name
490		(R)-(4'-(isoquinolin-3-yl)spiro[cyclopropane-1,7'-imidazo[4,5-c]pyridin]-5'(1'H,4'H,6'H)-yl)(5-methyl-1,3,4-oxadiazol-2-yl)methanone
491		(S)-(4'-(isoquinolin-3-yl)spiro[cyclopropane-1,7'-imidazo[4,5-c]pyridin]-5'(1'H,4'H,6'H)-yl)(5-methyl-1,3,4-oxadiazol-2-yl)methanone
492		(S)-(4'-(isoquinolin-3-yl)spiro[cyclopropane-1,7'-imidazo[4,5-c]pyridin]-5'(1'H,4'H,6'H)-yl)(4-methyloxazol-5-yl)methanone
493		(R)-(4'-(isoquinolin-3-yl)spiro[cyclopropane-1,7'-imidazo[4,5-c]pyridin]-5'(1'H,4'H,6'H)-yl)(4-methyloxazol-5-yl)methanone

TABLE 5-continued

Isoquinolines			
Ex.	#	Structure	Name
494			(5-(5-fluoropyridin-2-yl)-1,3,4-oxadiazol-2-yl)((4R,7R)-4-(isoquinolin-3-yl)-7-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
495			(5-(5-fluoropyridin-2-yl)-1,3,4-oxadiazol-2-yl)((4S,7R)-4-(isoquinolin-3-yl)-7-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
496			(5-(5-fluoropyridin-2-yl)-1,3,4-oxadiazol-2-yl)((4R,7S)-4-(isoquinolin-3-yl)-7-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
497			(5-(5-fluoropyridin-2-yl)-1,3,4-oxadiazol-2-yl)((4S,7S)-4-(isoquinolin-3-yl)-7-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone

TABLE 5-continued

Isoquinolines			
Ex.	#	Structure	Name
498			(5-(2-fluoropropan-2-yl)-1,3,4-oxadiazol-2-yl)((4S,7S)-4-(isoquinolin-3-yl)-7-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
499			(5-(2-fluoropropan-2-yl)-1,3,4-oxadiazol-2-yl)((4R,7S)-4-(isoquinolin-3-yl)-7-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
500			(5-(2-fluoropropan-2-yl)-1,3,4-oxadiazol-2-yl)((4S,7R)-4-(isoquinolin-3-yl)-7-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
501			(5-(2-fluoropropan-2-yl)-1,3,4-oxadiazol-2-yl)((4R,7R)-4-(isoquinolin-3-yl)-7-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone

TABLE 5-continued

Isoquinolines			
Ex.	#	Structure	Name
502			((4S,7S)-4-(isoquinolin-3-yl)-7-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(oxazol-5-yl)methanone
503			((4R,7S)-4-(isoquinolin-3-yl)-7-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(oxazol-5-yl)methanone
504			((4S,7R)-4-(isoquinolin-3-yl)-7-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(oxazol-5-yl)methanone
505			((4R,7R)-4-(isoquinolin-3-yl)-7-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(oxazol-5-yl)methanone

TABLE 5-continued

Isoquinolines		
Ex. #	Structure	Name
506		(4-cyclopropyloxazol-5-yl)((4R,7S)-4-(isoquinolin-3-yl)-7-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
507		(4-cyclopropyloxazol-5-yl)((4S,7S)-4-(isoquinolin-3-yl)-7-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
508		(4-cyclopropyloxazol-5-yl)((4R,7R)-4-(isoquinolin-3-yl)-7-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
509		(4-cyclopropyloxazol-5-yl)((4S,7R)-4-(isoquinolin-3-yl)-7-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone

TABLE 5-continued

Isoquinolines		
Ex. #	Structure	Name
510		(5-cyclopropyl-1,3,4-oxadiazol-2-yl)((4S,7S)-4-(isoquinolin-3-yl)-7-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
511		(5-cyclopropyl-1,3,4-oxadiazol-2-yl)((4R,7S)-4-(isoquinolin-3-yl)-7-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
512		(5-cyclopropyl-1,3,4-oxadiazol-2-yl)((4S,7R)-4-(isoquinolin-3-yl)-7-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone
513		(5-cyclopropyl-1,3,4-oxadiazol-2-yl)((4R,7R)-4-(isoquinolin-3-yl)-7-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone

TABLE 5-continued

Isoquinolines			
Ex.	#	Structure	Name
514			((4S,7R)-4-(isoquinolin-3-yl)-7-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(5-(5-methoxypyridin-2-yl)-1,3,4-oxadiazol-2-yl)methanone
515			((4S,7S)-4-(isoquinolin-3-yl)-7-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(5-(5-methoxypyridin-2-yl)-1,3,4-oxadiazol-2-yl)methanone
516			((4R,7S)-4-(isoquinolin-3-yl)-7-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(5-(5-methoxypyridin-2-yl)-1,3,4-oxadiazol-2-yl)methanone
517			(R)-5-(4-(isoquinolin-3-yl)-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine-5-carbonyl)oxazole-4-carbonitrile

TABLE 5-continued

Isoquinolines		
Ex. #	Structure	Name
518		[(4R)-4-(3-isoquinolyl)-1,4,6,7-tetrahydroimidazo[4,5-c]pyridin-5-yl]-(2-methyl-1,2,4-triazol-3-yl)methanone

[0280] In further embodiments, the compound of Formula I is one or more compounds in Table 5 that is the R-enantiomer, or a pharmaceutically acceptable salt thereof.

[0281] In yet other embodiments, the compound of Formula I is one or more of the compounds in Table 5 that is the S-enantiomer, or a pharmaceutically acceptable salt thereof.

[0282] In still further embodiments, the compound of Formula I is one or more of Examples 13, 28, 47, 57, 99, 113, 145, 165, 236, 302, 308, 314, 318, 326, 330, 385, and 428, or a pharmaceutically acceptable salt thereof. In still other embodiments, the compound of Formula I is one or more of Examples 13, 47, 57, 99, 113, 145, 165, 302, 308, 314, 318, and 385, or a pharmaceutically acceptable salt thereof.

Abbreviations and Terms List:

aq	aqueous
min	minute(s)
hrs	hours
mL	milliliter
µL	microliter
mmol	millimole(s)
µmol	micromole(s)
mol	mole(s)

-continued

M	molar
eq	equivalents
LCMS	Liquid chromatography mass spectrometry
NMR	nuclear magnetic resonance
TLC	thin layer chromatography
HPLC	high-performance liquid chromatography
SFC	supercritical fluid chromatography
sat	saturated
° C.	degrees Celsius
rt	room temperature
N ₂	nitrogen gas
Hz	Hertz
δ	chemical shift
s	singlet
d	doublet
t	triplet
q	quartet
m	multiplet
br	broad
dd	doublet of doublets
ddd	doublet of doublet or doublets
td	triplet of doublets
dt	doublet of triplets
CDCl ₃	chloroform-d
CD ₃ OD	methanol-d ₄
DMSO-d ₆	dimethyl sulfoxide-d ₆

Solvents and Reagents:

DCE	1,2-dichloroethane
DCM	dichloromethane
DMAc	dimethylacetamide
DME	dimethoxyethane
DMF	dimethylformamide
EtOH	ethyl alcohol
EtOAc	ethyl acetate
i-PrOH or IPA	isopropanol
MeOH	methyl alcohol
TAAC	tert-amyl alcohol
MeCN or ACN	acetonitrile
PE	petroleum ether
TBME	tert-butyl methyl ether
H ₂ O	water
THF	tetrahydrofuran
HOAc	acetic acid
HCl	hydrochloric acid
H ₂ SO ₄	sulfuric acid
FA	formic acid
TFA	trifluoroacetic acid
TsOH	p-toluenesulfonic acid

-continued

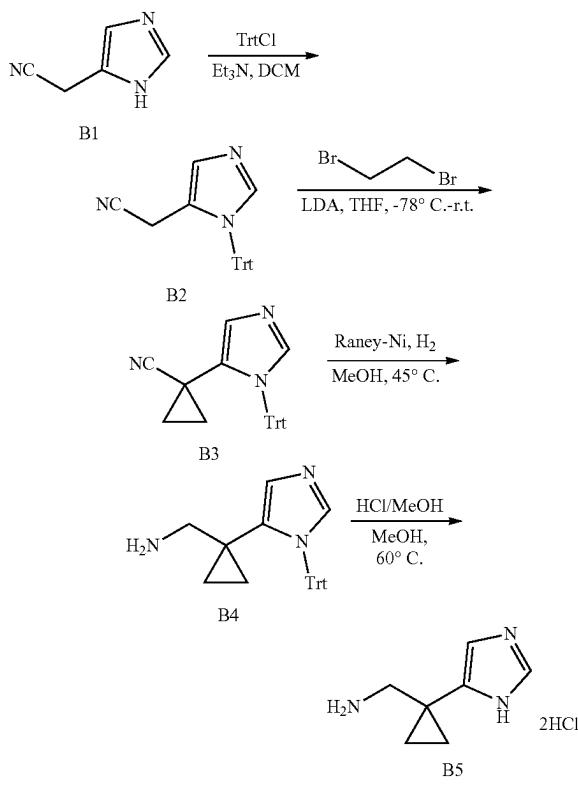
TosCl or TsCl	p-toluenesulfonyl chloride
NH ₄ Cl	ammonium chloride
KOH	Potassium hydroxide
LiOH	lithium hydroxide
K ₂ CO ₃	potassium carbonate
Na ₂ CO ₃	sodium carbonate
Cs ₂ CO ₃	cesium carbonate
Na ₂ SO ₄	sodium sulfate
NaHCO ₃	sodium bicarbonate
Na ₂ S ₂ O ₃	sodium thiosulfate
Et ₃ N or TEA	triethylamine
DIPEA	N,N-diisopropylethylamine
Py	pyridine
KOAc	potassium acetate
KF	potassium fluoride
CsF	cesium fluoride
NH ₃	ammonia
LDA	lithium diisopropylamide
LiHMDS	lithium bis(trimethylsilyl)amide
MeMgBr	methylmagnesium bromide
iPrMgCl•LiCl	isopropylmagnesium chloride lithium chloride complex
PFIB	perfluoroisobutene
BuOK	potassium t-butoxide
CAN	cerium ammonium nitrate
DIBAL-H	disobutylaluminum hydride
NaOMe	sodium methoxide
DMP	Dess-Martin periodinane
MnO ₂	manganese(IV) oxide
IBX	2-iodoxybenzoic acid
t-BuONO	tert-butyl nitrite
PIDA	(diacetoxyiodo)benzene
NFSI	N-fluorodi(benzenesulfonyl)amine
NBS	N-bromosuccinimide
NCS	N-chlorosuccinimide
MeI	methyl iodide
LiBH ₄	lithium borohydride
NaBH ₄	sodium borohydride
NaBH(OAc) ₃	Sodium triacetoxyborohydride
EDCI	1-ethyl-3-(3-dimethylaminopropyl)carbodiimide
HOBt	1-hydroxybenzotriazole
HATU	1-[Bis(dimethylamino)methylene]-1H-1,2,3-triazolo[4,5-b]pyridinium 3-oxid hexafluorophosphate
T3P	Propanephosphonic acid anhydride
CDI	carbonyldiimidazole
Thio-CDI	1,1'-Thiocarbonyldiimidazole
DPPA	diphenylphosphoryl azide
BCl ₃	boron trichloride
Boc ₂ O	di-tert-butyl dicarbonate
DHP	Dihydropyran
Pd/C	palladium on carbon
Pd(PPh ₃) ₂ Cl ₂	bis(triphenylphosphine)palladium(II) dichloride
Pd ₂ (dba) ₃	tris(dibenzylideneacetone)dipalladium
Pd(dppf)Cl ₂	(1,1'-Bis(diphenylphosphino)ferrocene)palladium(II) dichloride
Pd(OAc) ₂	palladium(II) acetate
Xantphos	4,5-Bis(diphenylphosphino)-9,9-dimethylxanthene
t-BuXPhos-Pd-	[(2-Di-tert-butylphosphino-2',4',6'-trisopropyl-1,1'-biphenyl)-2-(2'-amino-1,1'-biphenyl)] palladium(II) methanesulfonate
G3	
CPhos-Pd-G3	[(2-Dicyclohexylphosphine-2',6'-bis(N,N-dimethylamino)-1,1'-biphenyl)-2-(2'-amino-1,1'-biphenyl)] palladium(II) methanesulfonate
PPh ₃	triphenylphosphine
DEAD	diethyl azodicarboxylate
Pin ₂ B ₂	bis(pinacolato)diborane
CuI	copper iodide
CuBr ₂	copper (II) bromide
Zn(CN) ₂	zinc cyanide
H ₂	hydrogen gas
SiO ₂	silica
TFAA	Trifluoroacetic anhydride
K ₂ OsO ₄ •2H ₂ O	potassium osmate(VI) dihydrate
NaIO ₄	sodium periodate

General Experimental

[0283] In the following examples, the reagents and solvents were purchased from commercial sources (such as Alfa, Acros, AstaTech, CombiBlocks, Enamine, Sigma Aldrich, TCI, PharmaBock, Bide Pharmatech Ltd., Accela ChemBio, Aladdin, Shanghai Haohong Pharmaceutical Co., Ltd, Amkchem, Beijing Ouhe Technology Co., Ltd, Haoyuan Chemexpress Co., Ltd, Hualun, Coolpharm, Scotech, Titan and WuXi LabNetwork, and used without further purification unless otherwise specified. Flash chromatography was performed on a CombiFlashRf 150 (ISCO) via column with silica gel particles of 200-300 mesh. HPLC was performed on an Agilent 1100 Liquid Chromatography (Agilent, USA) and a Shimadzu LC 20/20A (Shimadzu, Japan). Supercritical fluid chromatography was performed on a Waters Prep SFC 150 AP/80Q/200/350 system (Waters, USA). Analytical and preparative thin layer chromatography plates (TLC) were HS_{GF} 254 (0.15-0.2 mm thickness, Shanghai Anbang Company, China). Nuclear magnetic resonance (NMR) spectra were obtained on a Bruker AV-400 NMR (Bruker, Switzerland). Chemical shifts were reported in parts per million (ppm, δ) downfield from tetramethylsilane. Mass spectra were given with electrospray ionization (ESI) from a Waters LCT TOF Mass Spectrometer (Waters, USA). LC-MS was performed on an Agilent Prime-6125B/Agilent LC1260-MS6150/Agilent LC1260-MS6125B/Agilent LC1200-MS6110 (Agilent, USA) and a Shimadzu LC20-MS2020. Microwave reactions were run on an Initiator 2.5 Microwave Synthesizer (Biotege, Sweden).

Intermediate

(1-(1H-imidazol-5-yl)cyclopropyl)methanamine hydrochloride



Step 1: Preparation of

2-(3-tritylimidazol-4-yl)acetonitrile (B2)

[0284] B2 was prepared starting with 2-(1H-imidazol-5-yl)acetonitrile (B1) in accordance with literature procedures. See, e.g., WO2008/003766 (page 19).

Step 2: Preparation of

1-(3-tritylimidazol-4-yl)cyclopropanecarbonitrile (B3)

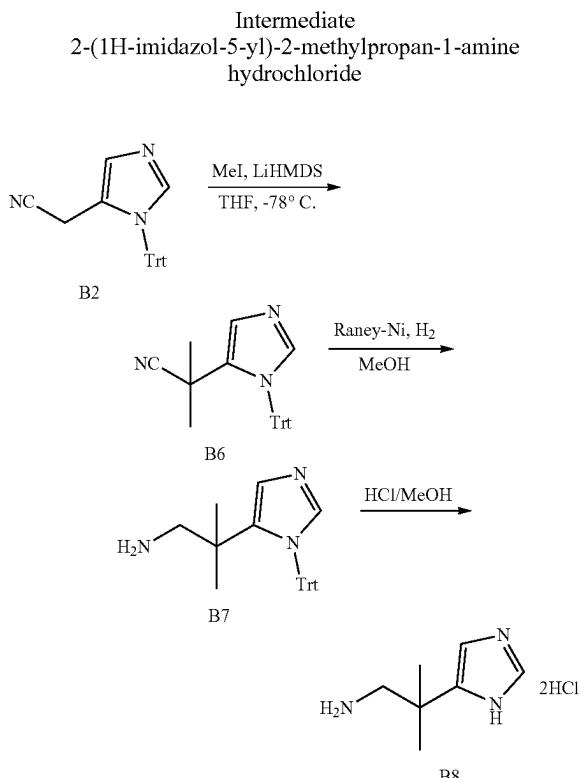
[0285] To a solution of 2-(3-tritylimidazol-4-yl)acetonitrile (B2) (10 g, 28.6 mmol) in THF (200 mL) was added LDA (2 M, 42.9 mL, 3 eq) dropwise at -78°C. After addition was complete, the reaction mixture was stirred at -20°C. to -10°C. for 1 hr. The reaction mixture was then cooled to -78°C., and 1,2-dibromoethane (10.75 g, 57.2 mmol, 4.32 mL, 2 eq) was added dropwise at -78°C. After the addition was complete, the reaction mixture was warmed to rt slowly and stirred for another 2 hrs. Reaction progress was tracked using TLC (PE:EtOAc=1:1). The reaction mixture was quenched with sat. NH₄Cl solution (200 mL) and stirred at rt for 0.5 hr. The aqueous portion was extracted with EtOAc (100 mL×3), and the combined organic layers were dried over Na₂SO₄, filtered, and concentrated to dryness. The residue (combined with two other reactions performed using 10 g of B2) was purified by flash silica gel chromatography (ISCO®; 120 g SepaFlash® Silica Flash Column, eluent of 0-40% EtOAc/PE, gradient @40 mL/min) to give B3 (23.4 g, 72% yield). ¹H NMR (400 MHz, DMSO-d₆) δ 7.30-7.52 (m, 10H), 7.09 (dd, 6H), 6.84 (d, 1H), 1.51-1.66 (m, 2H), 1.29-1.46 (m, 2H).

Step 3: Preparation of 1-(3-tritylimidazol-4-yl)cyclopropylmethanamine (B4)

[0286] A mixture of 1-(3-tritylimidazol-4-yl)cyclopropanecarbonitrile (B3) (19 g, 50.6 mmol), Raney-Ni (4.60 g, 53.7 mmol, 1.06 eq), NH₃·H₂O (591 mg, 5.06 mmol, 650 μL, 30% purity, 0.1 eq) in MeOH (200 mL) was degassed and purged with H₂ 3 times, and then the reaction mixture was stirred at 45°C. for 16 hrs under H₂ (45 psi) atmosphere. Reaction progress was tracked using TLC (DCM: MeOH=10:1). The reaction mixture was filtered, and additional Raney-Ni (4.60 g, 53.7 mmol, 1.06 eq) was added. The reaction mixture was stirred at 45°C. under H₂ (45 psi) atmosphere for another 24 hrs. The reaction mixture was filtered through a pad of Celite, and the filtrate was concentrated to dryness to give B4 (18 g), which was used without further purification. ¹H NMR (400 MHz, DMSO-d₆) δ 7.33-7.44 (m, 9H), 7.18-7.25 (m, 1H), 7.04-7.13 (m, 6H), 6.64-6.71 (m, 1H), 3.17 (br s, 2H), 2.58-2.74 (m, 2H), 0.60-0.82 (m, 4H).

Step 4: Preparation of [1-(1H-imidazol-5-yl)cyclopropyl]methanamine hydrochloride (B5)

[0287] To a solution of [1-(3-tritylimidazol-4-yl)cyclopropyl]methanamine (B4) (18 g, 47.4 mmol) in MeOH (100 mL) was added HCl/MeOH (4 M, 100 mL, 8.4 eq). The reaction mixture was stirred at 60°C. for 16 hrs. Reaction progress was tracked using LC-MS. The reaction mixture was concentrated to dryness, and the residue was triturated with EtOAc(40 mL) and stirred for 15 min. The precipitate was collected by filtration and then dried in vacuo to give B5 (8.5 g, 2HCl salt). ¹H NMR (400 MHz, DMSO-d₆) δ 14.73 (br s, 1H), 9.04 (s, 1H), 8.27 (br s, 2H), 7.51 (s, 1H), 2.98-3.22 (m, 2H), 0.90-1.23 (m, 4H).



Step 1: Preparation of (2-methyl-2-(3-tritylimidazol-4-yl)propanenitrile (B6)

[0288] To a solution of 2-(3-tritylimidazol-4-yl)acetonitrile (B2) (12 g, 34.3 mmol) in THF (400 mL) was drop-wise added LiHMDS (1 M, 96.2 mL, 2.8 eq) at -78° C. The reaction mixture was stirred at -78° C. for 15 min, and then Mel was added (14.62 g, 103 mmol, 6.41 mL, 3 eq). The reaction mixture was stirred at -78° C. for 1 hr, and then warmed to rt for 18 hrs. Reaction progress was tracked using TLC (PE:EtOAc=1:1). The reaction mixture was cooled to 0° C., quenched by the addition of sat. NH₄Cl solution (15 mL) and then H₂O (60 mL) was added. The aqueous portion was extracted with EtOAc (60 mL×3). The combined organic layers were washed with brine (60 mL), dried over Na₂SO₄, and concentrated to dryness. The residue (combined with the residue from another reaction performed using 2 g of B2) was purified by flash silica gel chromatography (ISCO®; 80 g SepaFlash® Silica Flash Column, eluent of 0-80% EtOAc/PE, gradient @60 mL/min) to give B6 (14 g, 92% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.41 (d, 1H), 7.32-7.39 (m, 9H), 7.08-7.16 (m, 6H), 6.81 (d, 1H), 1.69 (s, 6H).

Step 2: Preparation of (2-methyl-2-(3-tritylimidazol-4-yl)propan-1-amine (B7)

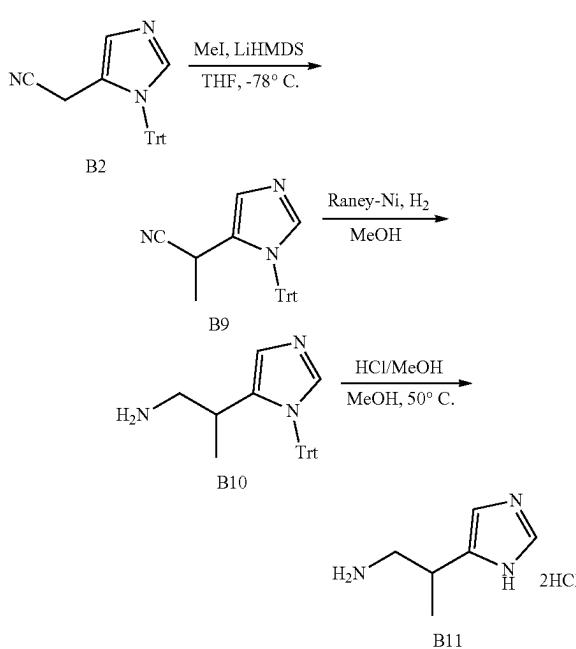
[0289] To a solution of 2-methyl-2-(3-tritylimidazol-4-yl)propanenitrile (B6) (14 g, 37.1 mmol) in MeOH (350 mL) was added Raney-Ni (2 g, 23.3 mmol, 0.63 eq) under N₂. The reaction mixture was degassed under vacuum and purged with H₂ several times. The reaction mixture was stirred under H₂ (50 psi) at 40° C. for 36 hrs. Reaction progress was tracked using TLC (PE:EtOAc=1:1). The

reaction mixture was filtered through a pad of celite, and the filtrate was concentrated to dryness to afford B7 (12 g, 85% yield). ^1H NMR (400 MHz, CDCl_3) δ 7.38 (s, 1H), 7.29–7.36 (m, 9H), 7.10–7.18 (m, 6H), 6.55 (s, 1H), 3.49 (br s, 1H), 2.74 (s, 2H), 1.20 (s, 6H); LCMS: m/z 382.2 [M+H] $^{+}$.

Step 3: Preparation of (2-(1H-imidazol-5-yl)-2-methyl-propan-1-amine (B8)

[0290] To a solution of 2-methyl-2-(3-tritylimidazol-4-yl)propan-1-amine (B7) (14 g, 36.7 mmol) in MeOH (150 mL) was added HCl/MeOH (4 M, 150 mL, 16.4 eq), and the reaction mixture was stirred at 50° C. for 18 hrs. Reaction progress was tracked using TLC (EtOAc). The reaction mixture was concentrated to dryness, and 200 mL of EtOAc was added. The mixture was stirred at 60° C. for 1 hr. The precipitate was collected by filtration and rinsed with EtOAc, and then dried in vacuo to give B8 (7.0 g, 90% yield, 2HCl salt). ^1H NMR (400 MHz, CD₃OD) δ 8.96 (s, 1H), 7.52 (s, 1H), 3.20–3.27 (m, 2H), 1.49 (s, 6H).

Intermediate 2-(1H-imidazol-5-yl)propan-1-amine hydrochloride



Step 1: Preparation of 2-(3-tritylimidazol-4-yl)propanenitrile (B9)

[0291] To a solution of 2-(3-tritylimidazol-4-yl)acetonitrile (B2) (15 g, 42.9 mmol) in THF (120 mL) was added LiHMDS (1 M, 51.5 mL, 1.2 eq) dropwise at -78°C. After addition, the reaction mixture was stirred for 0.5 hr, and then MeI (10.97 g, 77.3 mmol, 4.81 mL, 1.8 eq) was added dropwise at -78°C. The reaction mixture was stirred at -78°C. for 2 hrs. Reaction progress was tracked using TLC (PE:EtOAc=2:1). The reaction mixture was quenched by the addition of sat. NH₄Cl solution (120 mL) and stirred for 15 min. The aqueous portion was extracted with EtOAc (4000 mL), and the organic layer washed by water (100 mL) and

brine (60 mL), dried over Na_2SO_4 , filtered, and concentrated to dryness. The residue (combined with the residue from another reaction performed using 15 g of B2) was purified by column chromatography on silica gel (PE:EtOAc=20:1 to 2:1) to give B9 (33.5 g, 75% yield). ^1H NMR (400 MHz, DMSO-d_6) δ 7.38-7.45 (m, 10H), 7.06-7.13 (m, 6H), 6.82-6.92 (m, 1H), 4.12-4.23 (m, 1H), 1.48 (d, 3H).

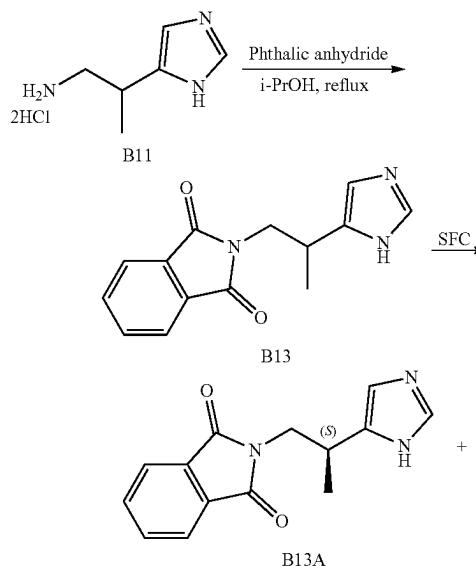
**Step 2: Preparation of
2-(3-tritylimidazol-4-yl)propan-1-amine (B10)**

[0292] A mixture of 2-(3-tritylimidazol-4-yl)propanenitrile (B9) (16.5 g, 45.4 mmol), Raney-Ni (4.08 g, 47.7 mmol, 1.05 eq), $\text{NH}_3\text{-H}_2\text{O}$ (910 mg, 7.79 mmol, 1 mL, 30% purity) in MeOH (300 mL) was degassed under vacuum and purged with H_2 3 times. The reaction mixture was stirred at 45° C. for 16 hrs under H_2 (45 psi) atmosphere. Reaction progress was tracked using TLC (PE:EtOAc=2:1). The reaction mixture was filtered through a pad of Celite and the filtrate was concentrated to dryness to afford B10 (33 g), which was used without further purification. ^1H NMR (400 MHz, CD_3OD) δ 7.36-7.44 (m, 10H), 7.13-7.20 (m, 6H), 6.72 (br s, 1H), 2.57-2.92 (m, 3H), 1.21 (br d, 3H).

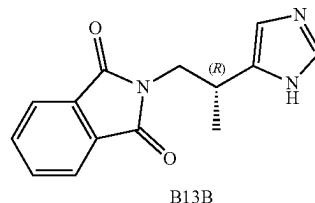
**Step 3: Preparation of
2-(1H-imidazol-5-yl)propan-1-amine (B11)**

[0293] To a solution of 2-(3-tritylimidazol-4-yl)propan-1-amine (B10) (23 g, 62.6 mmol) in MeOH (100 mL) was added HCl/MeOH (4 M, 100 mL). The mixture was stirred at rt for 12 hrs. Reaction progress was tracked using TLC (EtOAc). The reaction mixture (combined with the reaction mixture from another reaction performed using 23 g of B10) was concentrated to dryness. H_2O (40 mL) was added to the residue, and the aqueous layer washed with EtOAc (50 mL). The aqueous layer was lyophilized to give B11 (21 g, 2HCl). ^1H NMR (400 MHz, CD_3OD) δ 8.96 (d, 1H), 7.56 (s, 1H), 3.43-3.51 (m, 1H), 3.17-3.32 (m, 2H), 1.29-1.53 (m, 3H).

Intermediate 2-[(2R)-2-(1H-imidazol-5-yl)propyl]isoindoline-1,3-dione and 2-[(2S)-2-(1H-imidazol-5-yl)propyl]isoindoline-1,3-dione



-continued



Step 1: Preparation of 2-[2-(1H-imidazol-5-yl)propyl]isoindoline-1,3-dione (B13)

[0294] To a solution of 2-(1H-imidazol-5-yl)propan-1-amine (B11) (10 g, 50.5 mmol, 2HCl) and phthalic anhydride (7.85 g, 53.0 mmol, 1.05 eq) in i-PrOH (400 mL) was added Et_3N (15.32 g, 151 mmol, 21.1 mL, 3 eq). The reaction mixture was stirred at 100° C. for 18 hrs under N_2 atmosphere. After cooling, the reaction mixture was concentrated to dryness. Water (200 mL) was then added, and the mixture was stirred at rt for 10 mins. The precipitate was collected by filtration, rinsed with water (100 mL), and dried in vacuo to afford B13 (13 g), which was used without further purification. ^1H NMR (400 MHz, DMSO-d_6) δ 7.71-7.89 (m, 4H), 7.49 (s, 1H), 6.79 (s, 1H), 3.70-3.76 (m, 1H), 3.60-3.65 (m, 1H), 3.15-3.23 (m, 1H), 1.16 (d, 3H).

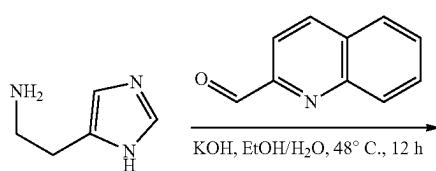
Step 2: SFC Separation

[0295] Compound 2-[2-(1H-imidazol-5-yl)propyl]isoindoline-1,3-dione (13 g) was separated by SFC separation (column: DAICEL CHIRALPAK AD(250 mm*50 mm, 10 um); mobile phase: [0.1% $\text{NH}_3\text{-H}_2\text{O}$ ETOH]; B %: 40%-40%, min) to afford Enantiomer 1 (4.8 g, 37% yield, $R_t=3.953$ min) and Enantiomer 2 (5.2 g, 40% yield, $R_t=4.652$ min).

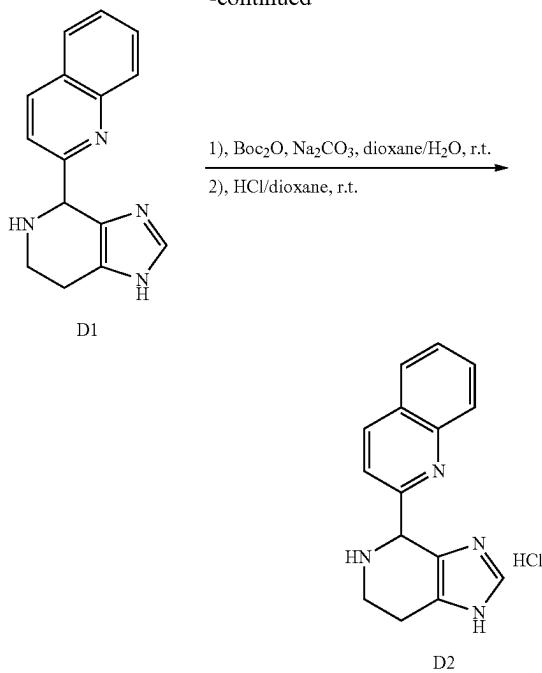
[0296] Enantiomer 1: 2-[(2R)-2-(1H-imidazol-5-yl)propyl]isoindoline-1,3-dione (B13A). ^1H NMR (400 MHz, CD_3OD) δ 7.73-7.89 (m, 4H), 7.56 (d, 1H), 6.82 (s, 1H), 3.84-3.93 (m, 1H), 3.70-3.82 (m, 1H), 3.36-3.39 (m, 1H), 1.31 (d, 3H); SFC: 98.4% ee.

[0297] Enantiomer 2: 2-[(2S)-2-(1H-imidazol-5-yl)propyl]isoindoline-1,3-dione (B13B). ^1H NMR (400 MHz, CD_3OD) δ 7.77-7.88 (m, 4H), 7.55 (d, 1H), 6.82 (s, 1H), 3.84-3.97 (m, 1H), 3.72-3.82 (m, 1H), 3.36-3.42 (m, 1H), 1.31 (d, 3H); SFC: 99.1% ee.

Intermediate 2-(4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridin-4-yl)quinoline hydrochloride according to General Scheme 1



-continued



Step 1: Preparation of 2-(4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridin-4-yl)quinoline (D1)

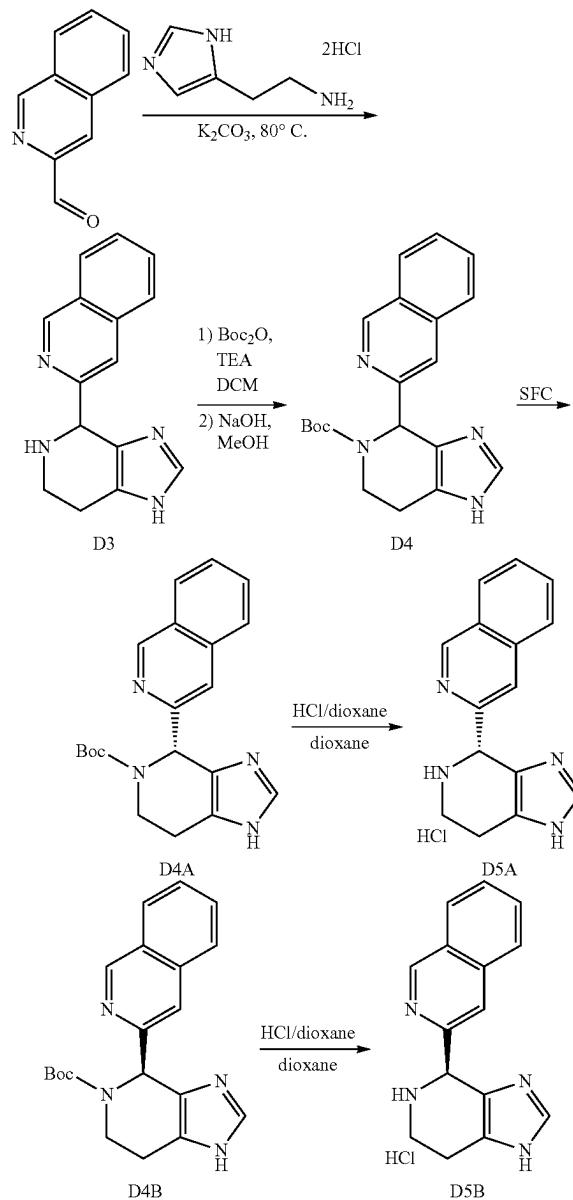
[0298] To a solution of quinoline-2-carbaldehyde (5 g, 31.8 mmol) and 2-(1H-imidazol-5-yl)ethanamine (6.44 g, 35.0 mmol, 1.1 eq, 2HCl) in EtOH (40 mL) and H₂O (10 mL) was added KOH (8.92 g, 159 mmol, 5 eq). The mixture was stirred at 48° C. for 12 hrs. Reaction progress was tracked using LCMS. The reaction mixture was combined with another reaction performed using 5 g of the aldehyde and filtered. H₂O (50 mL) was added to the filtrate, and the aqueous portion extracted with DCM (3×150 mL). The combined organic layer was washed with brine (100 mL), dried over Na₂SO₄, filtered, and concentrated to dryness to afford D1 (14 g), which was used without further purification.

Step 2: Preparation of 2-(4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridin-4-yl)quinoline hydrochloride (D2)

[0299] To a solution of D1 (14 g, 55.9 mmol) in dioxane (120 mL) and H₂O (30 mL) was added Na₂CO₃ (13.04 g, 123 mmol, 2.2 eq) and Boc₂O (26.86 g, 123 mmol, 28.3 mL, 2.2 eq). The mixture was stirred at rt for 12 hrs. Reaction progress was tracked using LCMS. EtOAc (300 mL) was added to the reaction mixture, and the organic portion washed with water (100 mL) and brine (100 mL), Na₂SO₄, filtered and concentrated to dryness. The residue was purified by column chromatography on silica gel (PE:EtOAc=20:1 to 1:1) to give a mixture (15 g of mono-/di-Boc product), which was dissolved in dioxane (100 mL) and treated with HCl/dioxane (4 M, 50 mL, 6.0 eq). The mixture was stirred at rt for 12 hrs. Reaction progress was tracked using LCMS. The reaction mixture was concentrated to dryness to give D2 (12.5 g, 2HCl). ¹H NMR (400 MHz, CD₃OD) δ 8.93-9.25 (m, 1H), 8.62 (dd, 1H), 8.10 (br dd,

2H), 7.84-7.95 (m, 2H), 7.68-7.78 (m, 1H), 6.33 (dd, 1H), 3.94-4.04 (m, 1H), 3.79-3.91 (m, 1H), 3.33-3.38 (m, 2H).

Intermediates 3-[(4R)-4,5,6,7-tetrahydro-1H-imidazo [4,5-c]pyridin-4-yl]isoquinoline and 3-[(4S)-4,5,6,7-tetrahydro-1H-imidazo [4,5-c]pyridin-4-yl]isoquinoline, according to General Scheme 1



Step 1: Preparation of 3-(4,5,6,7-tetrahydro-1H-imidazo [4,5-c]pyridin-4-yl)isoquinoline (D3)

[0300] To a solution of isoquinoline-3-carbaldehyde (10.5 g, 66.8 mmol) in EtOH (160 mL) was added 2-(1H-imidazol-5-yl)ethanamine (28.73 g, 73.5 mmol, 1.1 eq, 2HCl) and K₂CO₃ (36.93 g, 267 mmol, 4 eq) at rt, and the reaction mixture was stirred at 80° C. for 12 hrs under N₂ atmo-

sphere. Reaction progress was tracked using LCMS. The reaction mixture was cooled, filtered, and the filtrate was concentrated to dryness. The residue was purified by flash silica gel chromatography (ISCO®; 120 g SepaFlash® Silica Flash Column, eluent of 0-10% DCM/MeOH ether gradient @35 mL/min) to give D3 (18 g). ¹H NMR (400 MHz, CD₃OD) δ 9.25 (s, 1H), 8.09 (d, 1H), 7.89 (d, 1H), 7.77 (td, 1H), 7.51-7.72 (m, 3H), 5.26 (s, 1H), 3.14-3.26 (m, 1H), 3.00-3.12 (m, 1H), 2.70-2.88 (m, 2H); LCMS: m/z 251.1 [M+H]⁺.

Step 2: Preparation of tert-butyl 4-(3-isoquinolyl)-1,4,6,7-tetrahydroimidazo[4,5-c]pyridine-5-carboxylate (D4)

[0301] To a solution of 3-(4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridin-4-yl) isoquinoline (D3) (18 g, 71.9 mmol) in DCM (300 mL) was added TEA (21.83 g, 216 mmol, 30.0 mL, 3 eq), and then followed by (Boc)₂O (47.09 g, 216 mmol, 49.6 mL, 3 eq) dropwise at rt. The reaction mixture was stirred at rt for 12 hrs. Reaction progress was tracked using TLC (PE:EtOAc=1:1). DCM (200 mL) was added to the reaction mixture, and the organic portion washed with water (100 mL) and brine (100 mL×2), dried over Na₂SO₄, filtered, and concentrated to give a residue (23 g). The residue was then dissolved in MeOH (150 mL) and 1 M NaOH (60 mL) was added. The reaction mixture was stirred for 30 mins. Reaction progress was tracked using TLC (DCM:MeOH=20:1). Water (100 mL) was added, and the aqueous portion extracted with DCM (80 mL×3). The combined organic layer was washed with brine (60 mL), dried over Na₂SO₄, filtered, and concentrated to dryness. The residue was purified by flash silica gel chromatography (ISCO®; 330 g SepaFlash® Silica Flash Column, eluent of 0-8% DCM/MeOH gradient @30 mL/min) to give D4 (16 g, 89% yield). ¹H NMR (400 MHz, CD₃OD) δ 9.19 (s, 1H), 8.05 (d, 1H), 7.90 (d, 1H), 7.70-7.81 (m, 2H), 7.52-7.70 (m, 2H), 6.04-6.50 (m, 1H), 4.38 (br d, 1H), 3.41-3.68 (m, 1H), 2.55-2.95 (m, 2H), 1.46 (br s, 9H); LCMS: m/z 351.2 [M+H]⁺.

Step 3: SFC Separation

[0302] Compound tert-butyl 4-(3-isoquinolyl)-1,4,6,7-tetrahydroimidazo[4,5-c]pyridine-5-carboxylate (D4) (20 g) was separated by SFC (column: DAICEL CHIRALPAK IC(250 mm*50 mm, 10 μm); mobile phase: [0.1% NH₃H₂O ETOH]; B %: 60%-60%, min) to afford Enantiomer 1 (9.4 g, 47% yield, Rt=1.000 min) and Enantiomer 2 (9.2 g, 46% yield, Rt=2.795 min).

[0303] Enantiomer 1: tert-butyl (4R)-4-(3-isoquinolyl)-1,4,6,7-tetrahydroimidazo[4,5-c]pyridine-5-carboxylate (D4A). ¹H NMR (400 MHz, CD₃OD) δ 9.15 (s, 1H), 8.01 (d, 1H), 7.86 (d, 1H), 7.67-7.77 (m, 2H), 7.51-7.65 (m, 2H), 6.01-6.48 (m, 1H), 4.14-4.63 (m, 1H), 3.37-3.54 (m, 1H), 2.48-2.97 (m, 2H), 1.42 (br s, 9H); LCMS: m/z 351.1 [M+H]⁺; SFC: 99.3% ee.

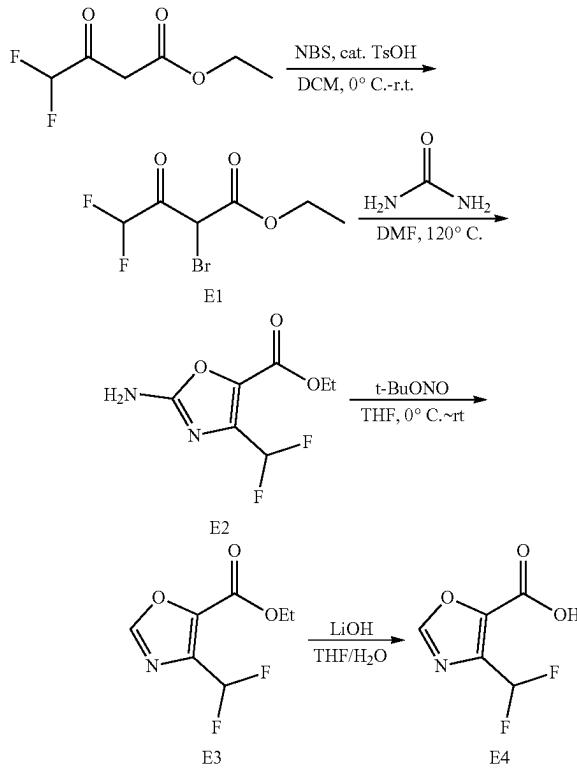
[0304] Enantiomer 2: tert-butyl (4S)-4-(3-isoquinolyl)-1,4,6,7-tetrahydroimidazo[4,5-c]pyridine-5-carboxylate (D4B). ¹H NMR (400 MHz, CD₃OD) δ 9.15 (s, 1H), 8.01 (d, 1H), 7.86 (d, 1H), 7.67-7.78 (m, 2H), 7.50-7.65 (m, 2H), 6.03-6.50 (m, 1H), 4.16-4.63 (m, 1H), 3.36-3.53 (m, 1H), 2.52-2.93 (m, 2H), 1.42 (br s, 9H); LCMS: m/z 351.1 [M+H]⁺; SFC: 99.0% ee.

Step 4: Preparation of 3-[(4R)-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridin-4-yl]isoquinoline (D5A)

[0305] A mixture of tert-butyl (4R)-4-(3-isoquinolyl)-1,4,6,7-tetrahydroimidazo[4,5-c]pyridine-5-carboxylate (D4A) (9.4 g, 26.8 mmol) in HCl/dioxane (100 mL, 4 M) was stirred at rt for 1 hr. Reaction progress was tracked using LCMS. The reaction mixture was concentrated to dryness, and the residue was triturated with MTBE (200 mL) and stirred for 30 min. The resulting precipitate was collected by filtration and then dried in vacuo to give D5A (8.3 g, 96% yield, 2HCl). ¹H NMR (400 MHz, CD₃OD) δ 9.40 (s, 1H), 9.00 (s, 1H), 8.17-8.27 (m, 2H), 8.11 (d, 1H), 7.80-7.99 (m, 2H), 6.22 (s, 1H), 3.86-3.99 (m, 1H), 3.71-3.84 (m, 1H), 3.32-3.34 (m, 1H), 3.25-3.30 (m, 1H); LCMS: m/z 251.1 [M+H]⁺.

[0306] 3-[(4S)-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridin-4-yl]isoquinoline (D5B) can be prepared using the same procedure, starting with D4B.

Intermediate 4-(difluoromethyl)oxazole-5-carboxylic acid according to General Scheme 4



Step 1: Preparation of ethyl 4,4-difluoro-3-oxo-butanoate (E1)

[0307] To a solution of ethyl 4,4-difluoro-3-oxo-butanoate (20 g, 120 mmol) in DCM (240 mL) was added TsOH (4.15 g, 24.1 mmol, 0.2 eq) and NBS (22.50 g, 126 mmol, 1.05 eq) in portions at 0°C. After addition was complete, the reaction mixture was stirred at rt for 1 hr. The reaction progress was checked using TLC (PE:EtOAc=5:1). DCM was added (100 mL), and the organic portion was washed with sat. Na₂CO₃

solution (100 mL) and brine (150 mL), dried over Na_2SO_4 , filtered, and concentrated to dryness to afford E1 (34 g), which was used without further purification. ^1H NMR (400 MHz, DMSO-d₆) δ 5.81-6.16 (m, 1H), 4.34-4.41 (m, 1H), 4.12-4.20 (m, 2H), 1.17-1.23 (m, 3H).

Step 2: Preparation of ethyl 2-amino-4-(difluoromethyl) oxazole-5-carboxylate (E2)

[0308] A mixture of E1 (37 g, 151 mmol) and urea (45.34 g, 755 mmol, 40.5 mL, 5 eq) in DMF (30 mL) was stirred at 120° C. for 12 hrs. The reaction progress was checked using LC-MS. The reaction mixture was cooled to rt and poured into 100 mL of water. The reaction mixture was stirred for 15 min at 0° C., and the precipitate was collected by filtration, rinsed with water (50 mL), dried in vacuo to give E2 (15.5 g, 63% yield for steps 1 and 2). LC-MS: m/z 207.2 (M+H)⁺; ^1H NMR (400 MHz, DMSO-d₆) δ 7.86 (s, 2H), 6.84-7.44 (m, 1H), 4.27 (q, 2H), 1.28 (t, 3H).

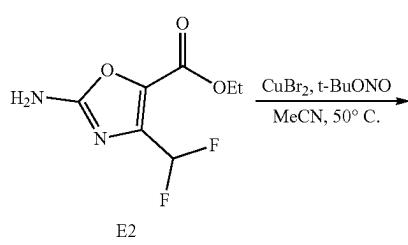
Step 3: Preparation of ethyl 4-(difluoromethyl)oxazole-5-carboxylate (E3)

[0309] To a solution of ethyl 2-amino-4-(difluoromethyl) oxazole-5-carboxylate (20 g, 97.0 mmol) in THF (300 mL) was added t-BuONO (30.01 g, 291 mmol, 34.6 mL, 3 eq) dropwise at 0° C., the reaction mixture was stirred at rt for 12 hrs. DCM (300 mL) was added, and the organic portion was washed with water (200 mL) and brine (200 mL), dried over Na_2SO_4 , filtered, and concentrated to dryness. The residue was purified by column chromatography (SiO₂, PE/EtOAc=1/10 to 1/10) to give E3 (12.7 g, 69% yield). ^1H NMR (400 MHz, CDCl₃) δ 8.05 (s, 1H), 6.93-7.27 (m, 1H), 4.44 (q, 2H), 1.40 (t, 3H).

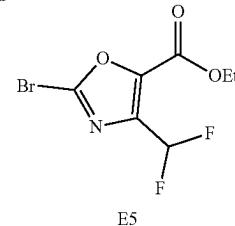
Step 5: Preparation of 4-(difluoromethyl)oxazole-5-carboxylic acid (E4)

[0310] To a solution of ethyl 4-(difluoromethyl)oxazole-5-carboxylate (12.7 g, 66.5 mmol) in THF (100 mL) and H₂O (20 mL) was added LiOH·H₂O (3.07 g, 73.1 mmol, 1.1 eq). The reaction mixture was stirred at rt for 1 hr and then concentrated in vacuo to remove THF. Water (80 mL) was added, and the aqueous portion extracted with TBME (50 mL). The aqueous layer was then adjusted to pH-6 by the addition of 0.5 M HCl. The aqueous layer was concentrated to dryness to give E4 (11 g), which was used without further purification. ^1H NMR (400 MHz, DMSO-d₆) δ 8.30 (s, 1H), 7.34-7.76 (m, 1H).

Intermediate ethyl 2-bromo-4-(difluoromethyl)oxazole-5-carboxylate according to General Scheme 4



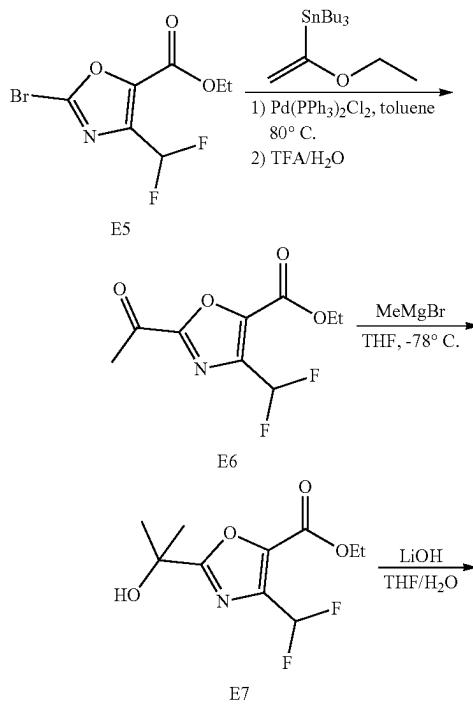
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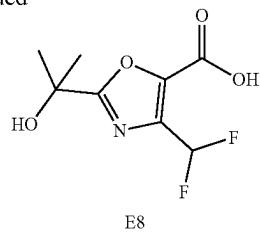
Preparation of ethyl 2-bromo-4-(difluoromethyl)oxazole-5-carboxylate (E5)

[0311] To a solution of ethyl 2-amino-4-(difluoromethyl) oxazole-5-carboxylate (E2) (25 g, 121 mmol) in MeCN (200 mL) was added CuBr₂ (40.63 g, 182 mmol, 8.5 mL, 1.5 eq) at 0° C. The mixture turned dark green and further stirred for 15 min at rt. t-BuONO (18.76 g, 182 mmol, 21.6 mL, 1.5 eq) was added at 0° C. The reaction was stirred at rt for 2 hrs, and then was heated to 50° C. and stirred for 12 hrs. Reaction progress was tracked using TLC (EtOAc:PE=5:1). The reaction mixture was filtered. DCM (200 mL) was added to the filtrate, and the organic layer was washed by water (100 mL) and brine (100 mL), dried over Na_2SO_4 , filtered, and concentrated to dryness. The residue was purified by flash silica gel chromatography (ISCO®; 120 g SepaFlash® Silica Flash Column, Eluent of 0-20% EtOAc/PE gradient @100 mL/min) to afford E5 (19 g, 58% yield). ^1H NMR (400 MHz, CDCl₃) δ 7.02 (t, 1H), 4.39 (q, 2H), 1.35 (t, 3H).

Intermediate 4-(difluoromethyl)-2-(1-hydroxy-1-methyl-ethyl)oxazole-5-carboxylic acid according to General Scheme 6, Method A



-continued



Step 1: Preparation of ethyl 2-acetyl-4-(difluoromethyl)oxazole-5-carboxylate (E6)

[0312] To a solution of ethyl 2-bromo-4-(difluoromethyl)oxazole-5-carboxylate (E5) (10 g, 37.0 mmol) in toluene (150 mL) was added Pd(PPh₃)₂Cl₂ (2.60 g, 3.70 mmol, 0.1 eq) and tributyl(1-ethoxyvinyl)stannane (17.39 g, 48.1 mmol, 16.3 mL, 1.3 eq). The mixture was stirred at 85° C. for 12 hrs under N₂ atmosphere. The reaction progress was checked using TLC (PE:EtOAc). EtOAc (100 mL) was added to the reaction mixture, and the organic portion washed with sat. KF solution (150 mL) and brine (100 mL), dried over Na₂SO₄, filtered, and concentrated to dryness. The residue was dissolved in THF (60 mL) and treated with HCl (4 M, 60 mL), and then was stirred at 40° C. for 12 hrs. The reaction progress was checked by TLC (Petroleum ether:EtOAc=10:1). EtOAc (100 mL) was added to the reaction mixture, and the organic portion washed with water (50 mL) and brine (50 mL), dried over Na₂SO₄, filtered, and concentrated to dryness. The residue was purified by flash silica gel chromatography (ISCO®; 40 g SepaFlash® Silica Flash Column, eluent of 0-20% EtOAc/PE gradient @40 mL/min) to give E6 (7.1 g, 82% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.00-7.36 (m, 1H), 4.48 (q, 2H), 2.66-2.86 (m, 3H), 1.43 (t, 3H).

Step 2: Preparation of ethyl 4-(difluoromethyl)-2-(1-hydroxy-1-methyl-ethyl)oxazole-5-carboxylate (E7)

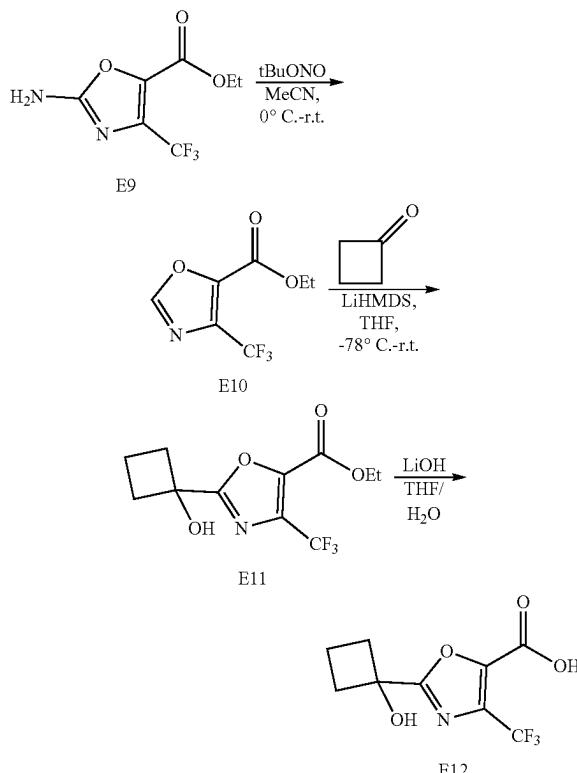
[0313] To a solution of E6 (2.5 g, 10.7 mmol) in THF (120 mL) was added MeMgBr (3 M, 7.15 mL, 2 eq) at -78° C. The mixture was stirred at -78° C. for 1 hr. The reaction progress was checked by TLC (PE:EtOAc=2:1). The reaction mixture was quenched by addition of sat. NH₄Cl solution (50 mL) and then water (100 mL) was added. The aqueous portion was extracted with EtOAc (100 mL×3). The combined organic layers were dried over Na₂SO₄, filtered, and concentrated to dryness. The residue was purified by flash silica gel chromatography (ISCO®; 40 g SepaFlash® Silica Flash Column, eluent of 0-12% EtOAc/PE gradient @40 mL/min) to give E7 (3.2 g, 60% yield). ¹H NMR (400 MHz, CDCl₃) δ 6.94-7.29 (m, 1H), 4.46 (q, 2H), 2.86 (s, 1H), 1.72 (s, 6H), 1.44 (t, 3H). The starting material E6 (300 mg) was also recovered.

Step 3: Preparation of 4-(difluoromethyl)-2-(1-hydroxy-1-methyl-ethyl)oxazole-5-carboxylic acid (E8)

[0314] To a solution of E7 (3.9 g, 15.7 mmol) in THF (40 mL) and H₂O (40 mL) was added LiOH·H₂O (690 mg, 16.4 mmol, 1.05 eq). The mixture was stirred at rt for 1 hr. The

reaction progress was checked using TLC (PE:EtOAc=5:1). The reaction mixture was concentrated to remove THF. The aqueous mixture was then adjusted to pH-3 by the addition of 1M HCl, and then lyophilized in vacuo to give E8 (4 g), which was used without further purification. ¹H NMR (400 MHz, DMSO-d₆) δ 7.35-7.71 (m, 1H), 5.68 (br s, 1H), 1.50 (s, 6H).

Intermediate 2-(1-hydroxycyclobutyl)-4-(trifluoromethyl)oxazole-5-carboxylic acid



Step 1: Preparation of ethyl 4-(trifluoromethyl)oxazole-5-carboxylate (E10)

[0315] To a solution of ethyl 2-amino-4-(trifluoromethyl)oxazole-5-carboxylate (2.00 g, 8.92 mmol) in THF (60 mL) was added t-BuONO (1.84 g, 17.9 mmol, 2.12 mL, 2 eq). The reaction mixture was stirred at 55° C. for 24 hrs. EtOAc (120 mL) was added to the reaction mixture, and the organic portion washed with water (100 mL) and brine (100 mL), dried over Na₂SO₄, filtered, and concentrated to dryness. The residue was purified by column chromatography (SiO₂, PE/EtOAc=1/0 to 8/1) to give E10 (1.2 g, 64% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.96 (s, 1H), 4.39 (q, 2H), 1.34 (t, 3H).

Step 2: Preparation of ethyl 2-(1-hydroxycyclobutyl)-4-(trifluoromethyl)oxazole-5-carboxylate (E11)

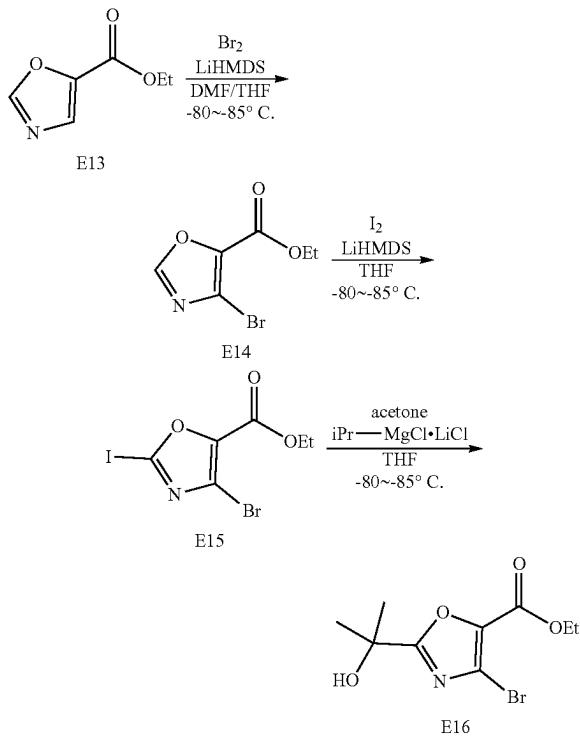
[0316] To a solution of ethyl 4-(trifluoromethyl)oxazole-5-carboxylate (1.2 g, 5.74 mmol) in THF (30 mL) was added LiHMDS (1 M, 8.61 mL, 1.5 eq) at -78° C., and the reaction

mixture was stirred at -78° C. for 0.5 hr. Cyclobutanone (1.21 g, 17.2 mmol, 1.29 mL, 3 eq) in THF (5 mL) was added to the reaction mixture, and the mixture was stirred at -78° C. for 2 hrs under N₂ atmosphere. The reaction mixture was quenched by the addition of sat. NH₄Cl solution (30 mL), and the aqueous portion extracted with EtOAc (100 mL). The organic layer washed by water (70 mL) and brine (70 mL), dried over Na₂SO₄, filtered, and concentrated to dryness. The residue was purified by column chromatography (SiO₂, PE/EtOAc=1/0 to 10/1) to give E11 (600 mg, 37% yield). ¹H NMR (400 MHz, CDCl₃) δ 4.29 (q, 2H), 2.78-2.94 (m, 1H), 2.52-2.65 (m, 2H), 2.24-2.38 (m, 2H), 1.78-1.98 (m, 3H), 1.26 (t, 3H).

Step 3: Preparation of 2-(1-hydroxycyclobutyl)-4-(trifluoromethyl)oxazole-5-carboxylic acid (E12)

[0317] To a solution of ethyl 2-(1-hydroxycyclobutyl)-4-(trifluoromethyl)oxazole-5-carboxylate (600 mg, 2.15 mmol) in H₂O (2 mL) and THF (10 mL) was added LiOH·H₂O (99.2 mg, 2.36 mmol, 1.1 eq) at 0° C. The reaction mixture was stirred at rt for 2 hrs and concentrated in vacuo to remove THF. Water (10 mL) was added, and the aqueous portion extracted with TBME (30 mL). The aqueous layer was then adjusted to pH-6 by the addition of 0.5 M HCl and concentrated to dryness to give E12 (540 mg), which was used without further purification. ¹H NMR (400 MHz, CD₃OD) δ 2.54-2.67 (m, 2H), 2.19-2.34 (m, 2H), 1.81-1.95 (m, 1H), 1.66-1.80 (m, 1H).

Intermediate ethyl 4-bromo-2-(2-hydroxypropan-2-yl)oxazole-5-carboxylate according to General Scheme 6



Step 1: Preparation of Ethyl 4-bromooxazole-5-carboxylate (E14)

[0318] Ethyl oxazole-5-carboxylate (E13) (500 mg, 3.54 mmol) was added in THF (2.50 mL) and DMF (2.50 mL) at approximately 10° C. The reaction mixture was cooled to -80° C. and LiHMDS (1 M, 4.61 mL, 1.30 eq) was added dropwise at approximately -80° C. The reaction mixture was stirred at approximately -80° C. for 0.5 hr. Br₂ (736 mg, 4.61 mmol, 1.3 eq) was then added dropwise at approximately -80° C. The reaction mixture was stirred at approximately -80° C. for 0.5 hr. The reaction progress was checked using LC-MS. The reaction mixture was combined with 19 other reactions performed using 500 mg of E13. The combined reaction mixture was poured into sat. citric acid at approximately -10° C. The aqueous portion was extracted with EtOAc (50 mL×3). The combined organic layer was washed with brine (50 mL), dried with Na₂SO₄, filtered, and concentrated to dryness. The residue was purified by column chromatography (SiO₂, PE/EtOAc=1/0 to 0/1) to give E14 (3.00 g, 19% yield). ¹H NMR (400 MHz, DMSO-d₆) δ 8.70 (s, 1H), 4.29-4.34 (m, 2H), 1.29 (t, 3H); LC-MS: m/z 219.9 & 221.9 (M+H)⁺.

Step 2: Preparation of Ethyl 4-bromo-2-iodooxazole-5-carboxylate (E15)

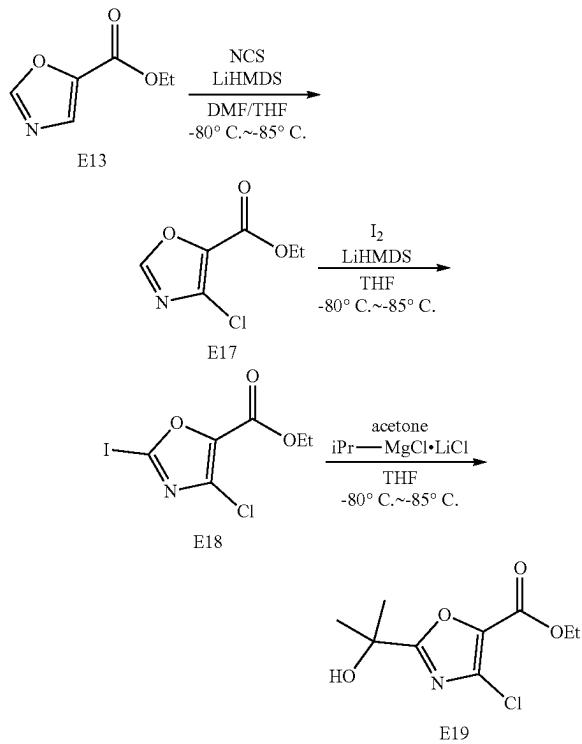
[0319] Ethyl 4-bromooxazole-5-carboxylate (E14) (3.15 g, 14.3 mmol, 1.00 eq) was added in THF (15.0 mL) at rt. LiHMDS (1 M, 17.2 mL, 1.20 eq) was added dropwise at approximately -80° C. I₂ (5.45 g, 21.5 mmol, 1.50 eq) in THF (15.0 mL) was then added dropwise at approximately -80° C. The reaction mixture was stirred at approximately -80° C. for 1 hr. The reaction progress was checked using TLC (PE/EtOAc). The reaction mixture was poured into saturated citric acid (30 mL) at approximately -10° C. The aqueous phase was extracted with ethyl acetate (30 mL×3). The combined organic layer was washed with brine (30 mL), dried with Na₂SO₄, filtered, and concentrated to dryness. The residue was purified by column chromatography (SiO₂, PE/EtOAc=1/0 to 0/1) to afford E15 (1.10 g, 22% yield). ¹H NMR (400 MHz, DMSO-d₆) δ: 4.29-4.35 (m, 2H), 1.30 (t, 3H). LC-MS: m/z 345.8 & 347.9 (M+H)⁺.

Step 3: Preparation of Ethyl 4-bromo-2-(2-hydroxypropan-2-yl)oxazole-5-carboxylate (E16)

[0320] Ethyl 4-bromo-2-iodooxazole-5-carboxylate (E15) (1.10 g, 3.18 mmol) was added in THF (10 mL) at approximately 10° C. under N₂. The reaction mixture was degassed under vacuum and purged with N₂ three times. The mixture was cooled to -80° C., and iPr-MgCl·LiCl (1.3 M, 2.45 mL, 1 eq) was added dropwise at approximately -80° C. The reaction mixture was stirred at approximately -80° C. for 0.5 hr, and then acetone (222 mg, 3.82 mmol, 1.20 eq) was added dropwise at approximately -80° C. The mixture was stirred at approximately -80° C. for 0.5 hr. The reaction progress was checked using TLC (PE/EtOAc=5/1). The reaction mixture was poured into sat. citric acid solution (5 mL) at approximately -10° C. The aqueous portion was extracted with ethyl acetate (5 mL×3). The combined organic layer was washed with brine (5 mL), dried with Na₂SO₄, filtered, and concentrated to dryness. The residue was purified by column chromatography (SiO₂, PE/EtOAc=1/0 to 0/1) and further purified by prep-HPLC (column: Phenomenex luna C18 80×40 mm×3 um; mobile

phase: [water (0.04% HCl)-ACN]; B %: 18%-45%, 7 min to afford E16 (140 mg, 16% yield). ^1H NMR (400 MHz, DMSO-d₆) δ : 5.93 (s, 1H), 4.30-4.37 (m, 2H), 1.50 (s, 6H), 1.32 (t, 3H). LC-MS: m/z 277.9 & 279.9 (M+H)⁺.

Intermediate ethyl 4-chloro-2-(2-hydroxypropan-2-yl)oxazole-5-carboxylate according to General Scheme 6



Step 1: Preparation of Ethyl 4-chlorooxazole-5-carboxylate (E17)

[0321] Ethyl oxazole-5-carboxylate (E13) (10.0 g, 70.9 mmol) was added in DMF (50 mL) at approximately 10°C. The reaction mixture was cooled to -80°C, and LiHMDS (1 M, 92.1 mL, 1.3 eq) was added dropwise at approximately -80°C. The reaction mixture was stirred at approximately -80°C for 0.5 hr, and NCS (12.3 g, 92.1 mmol, 1.3 eq) in THF (50 mL) was then added dropwise at approximately -80°C. The mixture was stirred at approximately -80°C for 0.5 hr. The reaction progress was checked using TLC (PE/EtOAc=5/1). The reaction mixture was combined for workup with seven other reactions each performed using 10 g of E13. The combined reaction mixture was poured into sat. citric acid solution (100 mL) at approximately -10°C. The aqueous portion was extracted with ethyl acetate (100 mL×3). The combined organic layer was washed with brine (50 mL), dried with Na₂SO₄, filtered, and concentrated to dryness. The residue was purified by column chromatography (SiO₂, PE/EtOAc=1/0 to 0/1) to afford E17 (18.0 g, 18% yield). ^1H NMR (400 MHz, CDCl₃) δ : 7.94 (s, 1H), 4.44 (q, 2H), 1.42 (t, 3H); LC-MS: m/z 176.0 (M+H)⁺.

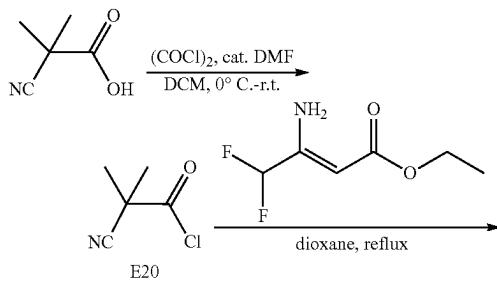
Step 2: Preparation of Ethyl 4-chloro-2-iodooxazole-5-carboxylate (E18)

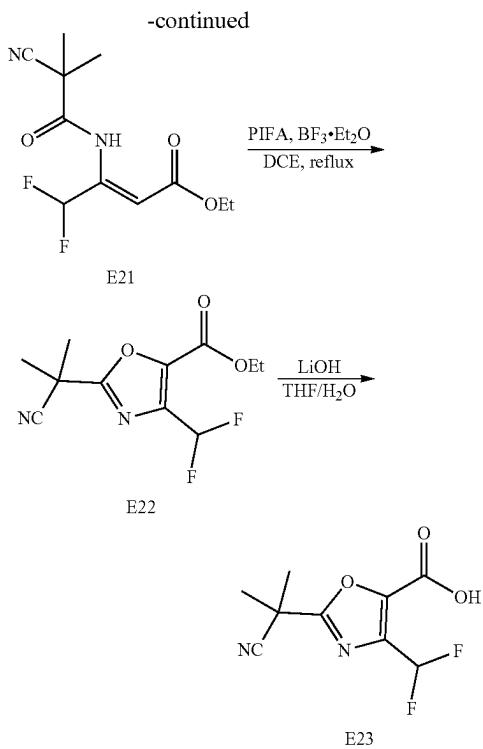
[0322] Three reactions were carried out in parallel. Ethyl 4-chlorooxazole-5-carboxylate (E17) (6.00 g, 34.2 mmol) was dissolved in THF (30 mL) at rt. LiHMDS (1 M, 41.0 mL, 1.2 eq) was added dropwise at approximately -80°C, followed by the dropwise addition of 12 (13.0 g, 51.3 mmol, 1.5 eq) in THF (30 mL) at approximately -80°C. The reaction mixture was stirred at approximately -80°C for 1 hr. The reaction progress was checked using TLC (PE/EtOAc=5/1). The three parallel reactions were combined together for workup. The combined reaction mixture was poured into sat. citric acid solution (100 mL) at approximately -5°C. The aqueous portion was extracted with ethyl acetate (100 mL×3). The combined organic layer was washed with brine (50 mL), dried with Na₂SO₄, filtered, and concentrated to dryness. The residue was purified by column chromatography (SiO₂, PE/EtOAc=1/0 to 0/1) to afford E18 (10.0 g, 32% yield). ^1H NMR (400 MHz, DMSO-d₆) δ : 4.20-4.27 (m, 2H), 1.21 (t, 3H); LC-MS: m/z 301.9 (M+H)⁺.

Step 3: Preparation of Ethyl 4-chloro-2-(2-hydroxypropan-2-yl)oxazole-5-carboxylate (E19)

[0323] Two reactions were carried out in parallel. Compound E18 (5.00 g, 16.6 mmol) was added in THF (50 mL) at approximately 10°C under N₂. The suspension was degassed under vacuum and purged with N₂ three times. The mixture was cooled to -80°C, and iPr-MgCl·LiCl (1.3 M, 12.8 mL, 1 eq) was added dropwise at approximately -80°C. The mixture was stirred at approximately -80°C for 0.5 hr, and acetone (1.16 g, 19.9 mmol, 1.2 eq) was then added dropwise at approximately -80°C. The mixture was stirred at approximately -80°C for 0.5 hr. The reaction progress was checked using TLC (PE/EtOAc=5/1). The two parallel reactions were combined together for workup. The combined reaction mixture was poured into sat. citric acid solution (50 mL) at approximately ~10°C. The aqueous portion was extracted with ethyl acetate (50 mL×3). The combined organic layer was washed with brine (50 mL), dried with Na₂SO₄, filtered, and concentrated to dryness. The residue was purified by column chromatography (SiO₂, PE/EtOAc=1/0 to 0/1) and further purified by prep-HPLC (column: Phenomenex luna C18 (250×70 mm, 15 μm); mobile phase: [water (0.05% HCl)-ACN]; B %: 20%-50%, 23 min) to afford E19 (1.80 g, 23% yield). ^1H NMR (400 MHz, DMSO-d₆) δ : 5.92 (s, 1H), 4.32-4.37 (m, 2H), 1.51 (s, 6H), 1.31 (t, 3H); LC-MS: m/z 234.0 (M+H)⁺.

Intermediate 4-(difluoromethyl)-2-(2-cyanopropan-2-yl)oxazole-5-carboxylic acid





Step 1: Preparation of 2-cyano-2-methyl-propanoyl chloride (E20)

[0324] To a solution of 2-cyano-2-methyl-propanoic acid (2 g, 17.7 mmol) and DMF (129 mg, 1.77 mmol, 136 μL , 0.1 eq) in DCM (20 mL) was added oxalyl chloride (2.69 g, 21.2 mmol, 1.86 mL, 1.2 eq) dropwise at 0° C., and then the reaction mixture was stirred at rt for 1 hr. The reaction mixture was concentrated to dryness to afford E20 (2.5 g), which was used without further purification.

Step 2: Preparation of ethyl (Z)-3-[(2-cyano-2-methyl-propanoyl)amino]-4,4-difluoro-but-2-enoate (E21)

[0325] To a solution of ethyl (Z)-3-amino-4,4-difluoro-but-2-enoate (2 g, 12.1 mmol) in dioxane (20 mL) was added a solution of 2-cyano-2-methyl-propanoyl chloride (E20) (2.39 g, 18.2 mmol, 1.5 eq) in dioxane (20 mL) at rt. The reaction mixture was stirred at 110° C. for 12 hrs. The reaction progress was checked using TLC (PE/Ethyl acetate=5/1). The reaction mixture was concentrated to dryness, and the residue was purified by flash silica gel chromatography (ISCO®; 40 g SepaFlash® Silica Flash Column, eluent of 0-7% EtOAc/PE gradient @40 mL/min) to give E21 (2.4 g, 76% yield). ^1H NMR (400 MHz, DMSO- d_6) δ 10.90 (s, 1H), 6.95-7.27 (m, 1H), 5.81 (s, 1H), 4.12-4.29 (m, 2H), 1.51-1.69 (m, 6H), 1.20 (t, 3H); LCMS: m/z 259.1 [M+H] $^+$.

Step 3: Preparation of ethyl 2-(1-cyano-1-methyl-ethyl)-4-(difluoromethyl)oxazole-5-carboxylate (E22)

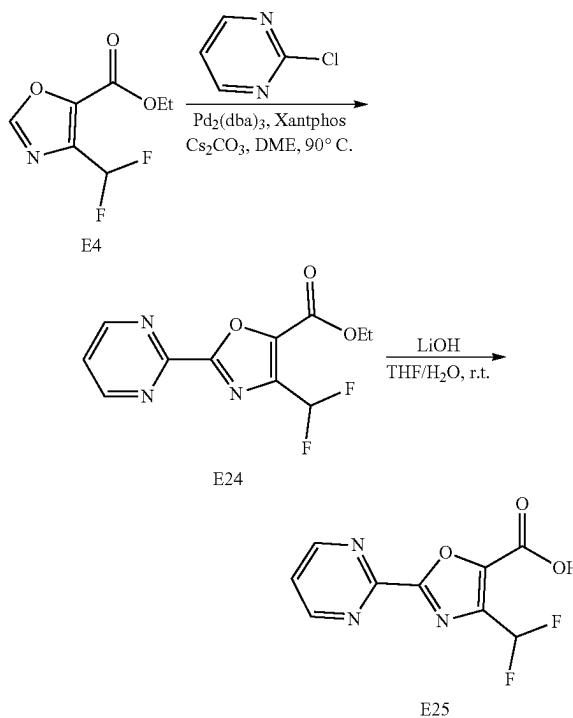
[0326] To a solution of ethyl (Z)-3-[(2-cyano-2-methyl-propanoyl)amino]-4,4-difluoro-but-2-enoate (E21) (2.4 g,

9.22 mmol) in DCE (20 mL) was added $\text{BF}_3 \cdot \text{Et}_2\text{O}$ (2.62 g, 18.4 mmol, 2.28 mL, 2 eq) and PIDA (4.16 g, 12.9 mmol, 1.4 eq) at rt. The mixture was stirred at 90° C. for 18 hrs. The reaction progress was checked by TLC (PE/EtOAc). The reaction mixture was concentrated to dryness. DCM (100 mL) was added to the residue, and the organic layer washed with sat. Na_2CO_3 solution (10 mL) and brine (50 mL), dried over Na_2SO_4 , filtered, and concentrated to dryness. The residue was purified by flash silica gel chromatography (ISCO®; 12 g SepaFlash® Silica Flash Column, eluent of 0-7% EtOAc/PE gradient @30 mL/min) to give E22 (0.25 g, 11% yield). ^1H NMR (400 MHz, DMSO- d_6) δ 7.03-7.55 (m, 1H), 4.35 (q, 2H), 1.77 (s, 6H), 1.29 (t, 3H).

Step 4: Preparation of 2-(1-cyano-1-methyl-ethyl)-4-(difluoromethyl)oxazole-5-carboxylic acid (E23)

[0327] To a solution of ethyl 2-(1-cyano-1-methyl-ethyl)-4-(difluoromethyl)oxazole-5-carboxylate (E22) (0.25 g, 968 μmol) in THF (3 mL) and H_2O (1 mL) was added LiOH- H_2O (48.8 mg, 1.16 mmol, 1.2 eq). The mixture was stirred at rt for 18 hrs. Reaction completeness was checked using TLC (PE:EtOAc=5:1). The reaction mixture was concentrated under reduced pressure to remove THF. The aqueous portion was adjusted with 2 M HCl to pH ~7, and then lyophilized under vacuo to give E23 (0.22 g, 99% yield). ^1H NMR (400 MHz, DMSO- d_6) δ 7.23-7.74 (m, 1H), 1.73 (s, 6H).

Intermediate 4-(difluoromethyl)-2-(pyrimidin-2-yl)oxazole-5-carboxylic acid according to General Scheme 5, Method B



Step 1: Preparation of ethyl 4-(difluoromethyl)-2-(pyrimidin-2-yl)oxazole-5-carboxylate (E24)

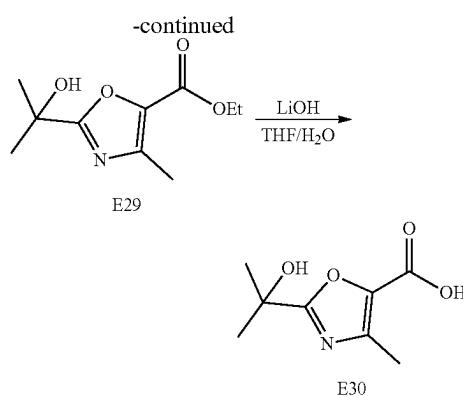
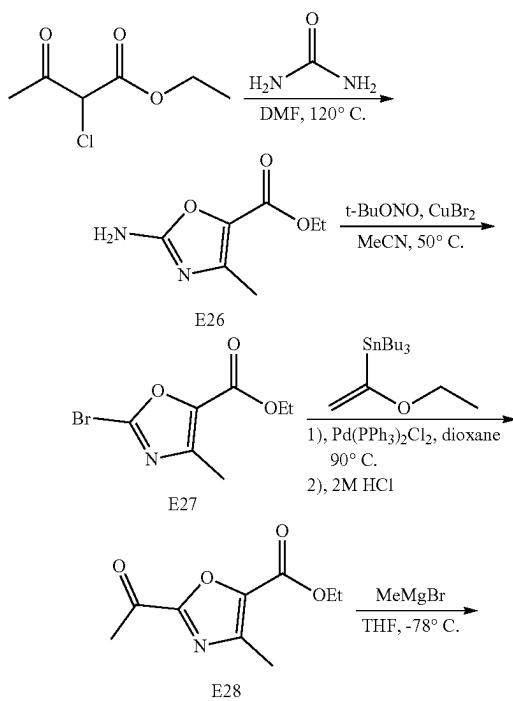
[0328] To a solution of ethyl 4-(difluoromethyl)oxazole-5-carboxylate (E4) (1 g, 5.23 mmol), $\text{Pd}_2(\text{dba})_3$ (240 mg,

262 μmol , 0.05 eq), (5-diphenylphosphanyl-9,9-dimethyl-xanthen-4-yl)-diphenyl-phosphane (151 mg, 262 μmol , 0.05 eq) and Cs_2CO_3 (3.41 g, 10.5 mmol, 2 eq) in 1,2-dimethoxyethane (3 mL) was added 2-chloropyrimidine (599 mg, 5.23 mmol) under N_2 atmosphere. The reaction mixture was stirred at 90° C. for 12 hrs. DCM (50 mL) was added to the reaction mixture, and the organic portion washed by water (40 mL) and brine (40 mL), dried over Na_2SO_4 , filtered, and concentrated to dryness. The residue was purified by column chromatography (SiO_2 , PE/EtOAc=1/0 to 1/1) to give E24 (400 mg, 25% yield). ^1H NMR (400 MHz, CDCl_3) δ 9.02 (br d, 2H), 7.52 (t, 1H), 7.38 (s, 1H), 7.24 (s, 1H), 7.11 (s, 1H), 4.54 (q, 2H), 1.48 (t, 3H).

Step 2: Preparation of 4-(difluoromethyl)-2-pyrimidin-2-yl-oxazole-5-carboxylic acid (E25)

[0329] To a solution of ethyl 4-(difluoromethyl)-2-pyrimidin-2-yl-oxazole-5-carboxylate (E24) (450 mg, 1.67 mmol) in THF (2 mL) and H_2O (2 mL) was added LiOH· H_2O (77.2 mg, 1.84 mmol, 1.1 eq). The reaction mixture was stirred at rt for 1 hr. The reaction mixture was concentrated to remove THF, and H_2O (10 mL) was added. The aqueous layer was extracted with TBME (30 mL). The aqueous layer was then adjusted to pH-6 with 0.5 M HCl and extracted with DCM/MeOH (30/3 mL) 3 times. The combined DCM/MeOH organic layer was dried over Na_2SO_4 , filtered, and concentrated to dryness to afford E25 (350 mg), which was used without further purification. ^1H NMR (400 MHz, DMSO-d_6) δ 9.06 (d, 2H), 7.75 (t, 1H), 7.20-7.57 (m, 1H).

Intermediate 2-(1-hydroxy-1-methyl-ethyl)-4-methyl-oxazole-5-carboxylic acid according to General Scheme 4 and General Scheme 6, Method A



Step 1: Preparation of ethyl 2-amino-4-methyl-oxazole-5-carboxylate (E26)

[0330] A mixture of ethyl 2-chloro-3-oxo-butanoate (55 g, 334 mmol, 46.2 mL) and urea (100.34 g, 1.67 mol, 89.6 mL, 5 eq) in DMF (100 mL) was stirred at 120° C. for 12 hours. Reaction progress was checked using TLC (PE:EtOAc=5:1). The reaction mixture was cooled to rt, poured into H_2O (400 mL), and stirred at 0° C. for 30 min. The precipitate was collected by filtration, rinsed with water (30 mL), and then dried in vacuo to give E26 (22.2 g, 39% yield). ^1H NMR (400 MHz, CD_3OD) δ 4.29 (q, 2H), 2.32 (s, 3H), 1.35 (t, 3H).

Step 2: Preparation of ethyl 2-bromo-4-methyl-oxazole-5-carboxylate (E27)

[0331] To a solution of E26 (11.1 g, 65.2 mmol) in MeCN (120 mL) was added CuBr_2 (21.85 g, 97.9 mmol, 4.58 mL, 1.5 eq) at 0° C. The mixture turned dark green and was further stirred for 15 min at rt. t-BuONO (10.09 g, 97.9 mmol, 11.6 mL, 1.5 eq) was added. The reaction was stirred at rt for 2 hrs and then heated at 50° C. for 4 hrs. Reaction progress was checked using TLC (Petroleum ether: EtOAc=3:1). The reaction mixture was concentrated to dryness. The residue was purified by flash silica gel chromatography (ISCO®; 120 g SepaFlash® Silica Flash Column, eluent of 0-5% EtOAc/PE gradient @100 mL/min) to give E27 (8.5 g, 56% yield). ^1H NMR (400 MHz, CDCl_3) δ 4.25-4.35 (m, 2H), 2.45 (s, 3H), 1.32 (t, 3H).

Step 3: Preparation of ethyl 2-acetyl-4-methyloxazole-5-carboxylate (E28)

[0332] A mixture of E27 (9.5 g, 40.6 mmol), tributyl(1-ethoxyvinyl) stannane (17.59 g, 48.7 mmol, 16.4 mL, 1.2 eq) and $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$ (2.85 g, 4.06 mmol, 0.1 eq) in toluene (200 mL) was stirred at 90° C. for 12 hrs under N_2 atmosphere. Reaction progress was checked using TLC (Petroleum ether:EtOAc=5:1). EtOAc (300 mL) was added, followed by sat. KF solution (500 mL). The resulting mixture was stirred at rt for 40 min, the mixture filtered, and the filtrate separated. The organic layer was washed with brine (100 mL), dried over Na_2SO_4 , filtered, and concentrated to dryness. The residue was dissolved in THF (300 mL), and 4 N HCl (300 mL) was added. The mixture was stirred at rt for 12 hrs. LCMS indicated the desired mass was detected. The reaction mixture was extracted with DCM (100 mL×3). The combined organic layer was dried over Na_2SO_4 , filtered, and

concentrated to dryness. The residue was purified by flash silica gel chromatography (ISCO®, 24 g SepaFlash® Silica Flash Column, eluent of 0-10% EtOAc/PE gradient @35 mL/min) to give E28 (6.8 g, 85% yield). ¹H NMR (400 MHz, CDCl₃) δ 4.35 (q, 2H), 2.62 (s, 3H), 2.48 (s, 3H), 1.34 (t, 3H); LCMS: m/z 198.1 [M+H]⁺.

Step 4: Preparation of ethyl 2-(2-hydroxypropan-2-yl)-4-methyloxazole-5-carboxylate (E29)

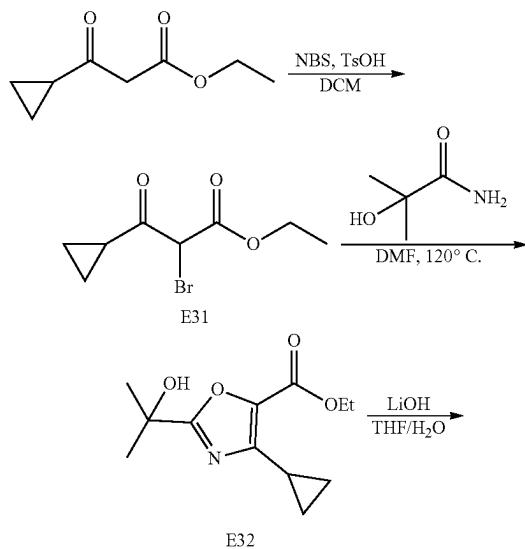
[0333] To a solution of E28 (2.5 g, 12.7 mmol) in THF (25 mL) was added MeMgBr (3 M, 12.7 mL, 3 eq) dropwise under N₂ at -78° C. The reaction was stirred at -78° C. for 1.5 hr. Reaction progress was checked using TLC (Petroleum ether:EtOAc=5:1, by UV). The reaction was quenched by the addition of sat. NH₄Cl solution (30 mL) slowly and then the organic portion extracted with EtOAc (30 mL×3). The combined organic phase was washed with brine (30 mL), dried over Na₂SO₄, filtered, and concentrated to dryness. The residue was purified by column chromatography (SiO₂, Petroleum ether/EtOAc=1/0 to 1/1) to give E29 (1.7 g, 63% yield). ¹H NMR (400 MHz, CDCl₃) δ 4.39 (q, 2H), 2.47 (s, 3H), 1.67 (s, 6H), 1.40 (t, 3H).

[0334] Alternatively, E29 can be prepared by reacting 2-hydroxy-2-methylpropanamide with ethyl 2-chloro-3-oxo-butanoate in a neat reaction at 150° C. for 6 hrs.

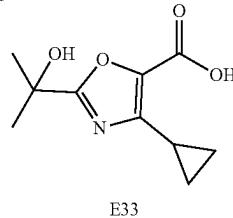
Step 5: Preparation of ethyl 2-(2-hydroxypropan-2-yl)-4-methyloxazole-5-carboxylic acid (E30)

[0335] To a solution of E29 (3.4 g, 16.0 mmol) in THF (30 mL) and H₂O (15 mL) was added LiOH·H₂O (803 mg, 19.1 mmol, 1.2 eq). The reaction was stirred at rt for 1.5 hr. Reaction progress was tracked using LCMS. The reaction mixture was adjusted to pH 7 with HCl (1 M) and concentrated to dryness to afford E30 (4 g), which was used without further purification. ¹H NMR (400 MHz, DMSO-d₆) δ 5.67 (s, 1H), 2.30 (s, 2H), 1.44 (s, 6H); LCMS: m/z 186.1 [M+H]⁺.

Intermediate 4-cyclopropyl-2-(2-hydroxypropan-2-yl)oxazole-5-carboxylic acid according to General Scheme 4



-continued



Step 1: Preparation of ethyl 2-bromo-3-cyclopropyl-3-oxo-propanoate (E31)

[0336] To a solution of ethyl 3-cyclopropyl-3-oxo-propanoate (8 g, 51.2 mmol) in DCM (100 mL) was added NBS (9.12 g, 51.2 mmol) and TsOH-H₂O (1.95 g, 10.2 mmol, 0.2 eq). The reaction mixture was stirred at rt for 2 hrs. Reaction progress was tracked using TLC (PE:EtOAc=10:1). The reaction mixture was concentrated to dryness. EtOAc (120 mL) was added to the residue, and the mixture filtered. The filtrate was washed with sat. NaHCO₃ solution (2×100 mL) and water (100 mL), dried over Na₂SO₄, filtered, and concentrated to dryness. The residue was purified by column chromatography (SiO₂, PE/EtOAc=1:0 to 10:1) to give E31 (12 g, 100% yield). ¹H NMR (400 MHz, DMSO-d₆) δ 5.71 (s, 1H), 4.18 (q, 2H), 2.14-2.28 (m, 1H), 1.18 (t, 3H), 1.01-1.08 (m, 2H), 0.89-0.96 (m, 2H); LCMS: m/z 235.0 [M+H]⁺.

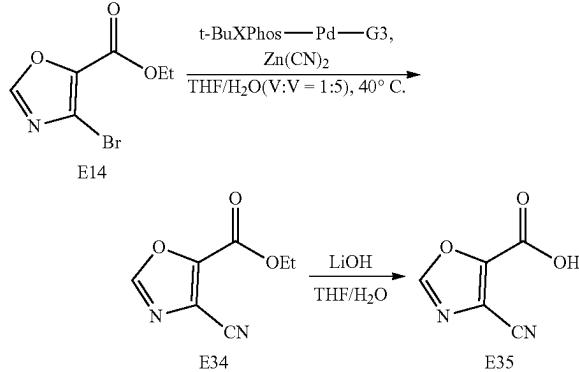
Step 2: Preparation of ethyl 4-cyclopropyl-2-(1-hydroxy-1-methyl-ethyl)oxazole-5-carboxylate (E32)

[0337] To a solution of ethyl 2-bromo-3-cyclopropyl-3-oxo-propanoate (E31) (1 g, 4.25 mmol) in DMF (2 mL) was added 2-hydroxy-2-methylpropanamide (2.19 g, 21.3 mmol, 5 eq). The mixture was stirred at 110° C. for 40 hrs. Reaction progress was tracked using LC-MS. The reaction mixture was adjusted to pH-8 by addition of sat. aq. NaHCO₃ at 0° C. H₂O (50 mL) was added, and the aqueous portion extracted with EtOAc (3×50 mL). The combined organic layers were dried over Na₂SO₄, filtered, and concentrated to dryness. The residue was purified by column chromatography (SiO₂, PE/EtOAc=1:0 to 2:1) to give E32 (0.15 g, 14% yield). ¹H NMR (400 MHz, DMSO-d₆) δ 5.70 (s, 1H), 4.29 (q, 2H), 2.40-2.45 (m, 1H), 1.43 (s, 6H), 1.27 (t, 3H), 0.94-1.04 (m, 2H), 0.79-0.92 (m, 2H); LCMS: m/z 240.0 [M+H]⁺.

Step 3: Preparation of 4-cyclopropyl-2-(1-hydroxy-1-methyl-ethyl)oxazole-5-carboxylic acid (E33)

[0338] To a solution of ethyl 4-cyclopropyl-2-(1-hydroxy-1-methyl-ethyl)oxazole-5-carboxylate (E32) (590 mg, 2.47 mmol) in THF (4 mL) and H₂O (4 mL) was added LiOH·H₂O (114 mg, 2.71 mmol, 1.1 eq). The reaction mixture was stirred at rt for 16 hrs. Reaction progress was tracked using LC-MS. The reaction mixture was concentrated to remove THF. The aqueous portion was adjusted to pH-7 by the addition of HCl (1 M) and then lyophilized to give E33 (550 mg, 90% yield). ¹H NMR (400 MHz, DMSO-d₆) δ 2.70-2.84 (m, 1H), 1.39 (s, 6H), 0.62-0.81 (m, 4H); LCMS: m/z 212.0 [M+H]⁺.

Intermediate 4-cyanooxazole-5-carboxylic acid



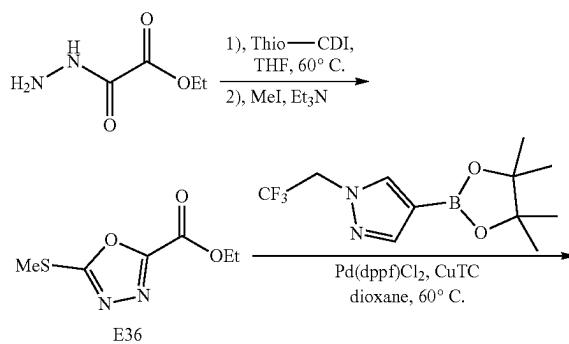
Step 1: Preparation of ethyl 4-cyanooxazole-5-carboxylate (E34)

[0339] To a solution of ethyl 4-bromooxazole-5-carboxylate (E14) (10 g, 45.5 mmol) in THF (30 mL) and H₂O (150 mL) was added Zn(CN)₂ (3.74 g, 31.8 mmol, 2.02 mL, 0.7 eq) and t-BuXPhos-Pd-G3 (1.81 g, 2.27 mmol, 0.05 eq). The reaction mixture was degassed under vacuum and purged with N₂ 3 times, and then the mixture was stirred at 40°C for 16 hrs under N₂. Reaction progress was tracked using TLC (PE:EtOAc=5:1). EtOAc (300 mL) was added to the reaction mixture, and the organic layer washed with H₂O (50 mL) and brine (50 mL), dried over Na₂SO₄, filtered, and concentrated to dryness. The residue was purified by column chromatography (SiO₂, PE/EtOAc=100/1 to 10/1) to give E34 (7.5 g, 99% yield). ¹H NMR (400 MHz, DMSO-d₆) δ 8.89 (s, 1H), 4.37 (q, 2H), 1.30 (t, 3H).

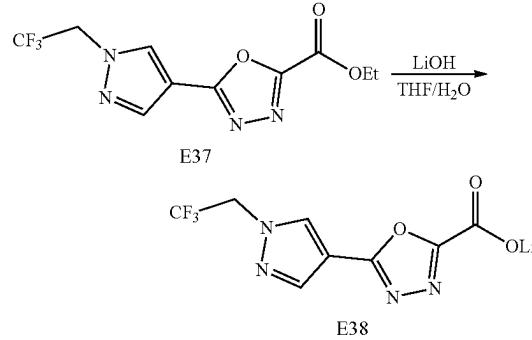
Step 2: Preparation of (4-cyanooxazole-5-carbonyl)oxylithium (E35)

[0340] To a solution of E34 (5 g, 30.1 mmol) in THF (40 mL) and H₂O (80 mL) was added LiOH·H₂O (1.33 g, 31.6 mmol, 1.05 eq). The mixture was stirred at rt for 2 hrs. Reaction progress was tracked using TLC (PE:EtOAc=5:1). The reaction mixture was concentrated in vacuo to remove most of the THF and then lyophilized in vacuo to give E35 (4.5 g), which was used without further purification. ¹H NMR (400 MHz, DMSO-d₆) δ 8.47 (s, 1H).

Intermediate [5-[1-(2,2,2-trifluoroethyl)pyrazol-4-yl]-1,3,4-oxadiazole-2-carbonyl]oxylithium according to General Scheme 9



-continued



Step 1: Preparation of ethyl 5-methylsulfanyl-1,3,4-oxadiazole-2-carboxylate (E36)

[0341] A mixture of ethyl 2-hydrazino-2-oxo-acetate (16 g, 121 mmol) and di(1H-imidazol-1-yl)methanethione (25.90 g, 145 mmol, 1.2 eq) in THF (300 mL) was stirred at rt for 12 hrs, and then heated to 75°C for 4 hrs. After cooling to rt, K₂CO₃ (50.21 g, 363 mmol, 3 eq) and CH₃I (85.95 g, 606 mmol, 37.7 mL, 5 eq) were added. The resulting mixture was stirred at rt for 2 hrs. Reaction progress was tracked using TLC (PE:EtOAc=1:1). The reaction mixture was combined with another reaction performed with 8.5 g of ethyl 2-hydrazino-2-oxo-acetate and quenched by the addition of H₂O (100 mL). DCM (500 mL) was added, and the organic layer was separated and washed with brine (2×100 mL), dried over Na₂SO₄, filtered, and concentrated to dryness. The residue was purified by flash silica gel chromatography (Eluent of 0-25% PE:EtOAc @40 mL/min) to give E36 (25 g). ¹H NMR (400 MHz, CDCl₃) δ 4.43 (q, 2H), 2.72 (s, 3H), 1.38 (t, 3H).

Step 2: Preparation of ethyl 5-[1-(2,2,2-trifluoroethyl)pyrazol-4-yl]-1,3,4-oxadiazole-2-carboxylate (E37)

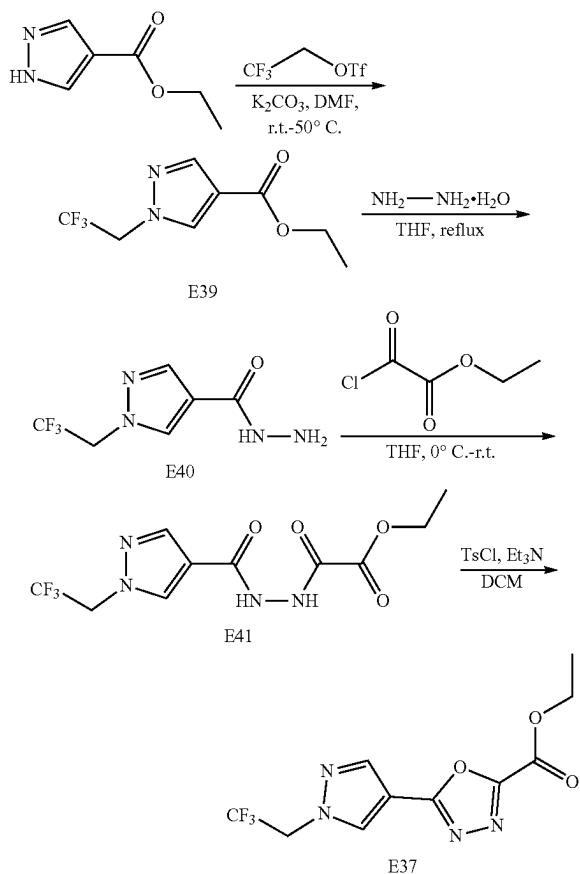
[0342] A mixture of E36 (233 mg, 1.24 mmol), 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-(2,2,2-trifluoroethyl)pyrazole (410 mg, 1.49 mmol, 1.2 eq), Na₂CO₃ (394 mg, 3.71 mmol, 3 eq), thiophene-2-carbonyloxy copper (472 mg, 2.48 mmol, 2 eq) and Pd(dppf)Cl₂ (181 mg, 248 μmol, 0.2 eq) in dioxane (9 mL) was degassed and purged with N₂ 3 times, and then the reaction mixture was stirred at 75°C for 16 hrs under N₂. Reaction progress was tracked using TLC (PE:EtOAc=2:1). EtOAc (100 mL) was added to the reaction mixture, and the organic layer washed with water (30 mL) and brine (30 mL), dried over Na₂SO₄, filtered, and concentrated to dryness. The residue was purified by column chromatography (SiO₂, PE/EtOAc=1/0 to 2/1) to give E37 (140 mg, 39% yield). ¹H NMR (400 MHz, CD₃OD) δ 8.61 (s, 1H), 8.22 (s, 1H), 5.12 (q, 2H), 4.51 (q, 2H), 1.44 (t, 3H); LCMS: m/z 291.1 (M+H)⁺.

Step 3: Preparation of [5-[1-(2,2,2-trifluoroethyl)pyrazol-4-yl]-1,3,4-oxadiazole-2-carbonyl]oxylithium (E38)

[0343] To a solution of E37 (140 mg, 482 μmol) in THF (1.5 mL) was added LiOH·H₂O (22.3 mg, 531 μmol, 1.1 eq)

in H_2O (3 mL). The reaction mixture was stirred at rt for 2 hrs. Reaction progress was tracked using TLC (DCM: MeOH). The reaction mixture was concentrated in vacuo to remove most of the THF and then lyophilized in vacuo to give E38 (115 mg), which was used without further purification. ^1H NMR (400 MHz, DMSO- d_6) δ 8.58 (s, 1H), 8.14 (s, 1H), 5.27 (q, 2H).

[0344] Alternatively, ethyl 5-[1-(2,2,2-trifluoroethyl)pyrazol-4-yl]-1,3,4-oxadiazole-2-carboxylate (E37) can be prepared accordingly to the following scheme.



Step A: Preparation of ethyl 1-(2,2,2-trifluoroethyl)pyrazole-4-carboxylate (E39)

[0345] To a solution of ethyl 1H-pyrazole-4-carboxylate (10 g, 71.4 mmol) and K_2CO_3 (19.72 g, 142 mmol, 2 eq) in DMF (45 mL) was added 2,2,2-trifluoroethyl trifluoromethanesulfonate (21.53 g, 92.8 mmol, 1.3 eq) dropwise, and then the resulting mixture was stirred at 50°C. for 6 hrs. Reaction progress was tracked using TLC (PE:EtOAc=1:1). EtOAc (300 mL) was added to the reaction mixture, and the organic layer washed with H_2O (100 mL) and brine (2×100 mL), dried over Na_2SO_4 , filtered, and concentrated to dryness. The residue was purified by flash silica gel chromatography (ISCO®; 40 g SepaFlash® Silica Flash Column, eluent of 0-12% PE/EtOAc @60 mL/min) to give E39 (16 g). ^1H NMR (400 MHz, CDCl_3) δ 8.01 (d, 2H), 4.73 (q, 2H), 4.32 (q, 2H), 1.36 (t, 3H).

Step B: Preparation of 1-(2,2,2-trifluoroethyl)pyrazole-4-carbohydrazide (E40)

[0346] To a solution of E39 (16 g, 72.0 mmol) in THF (100 mL) was added $\text{NH}_2\text{NH}_2\cdot\text{H}_2\text{O}$ (7.73 g, 151 mmol, 7.5 mL, 98% purity, 2.1 eq), and then the reaction mixture was stirred at 80°C. for 15 hrs. Reaction progress was tracked using TLC (PE:EtOAc=1:1). The reaction mixture was concentrated to dryness. The residue was triturated with TBME (50 mL) and stirred for 15 min. The precipitate was collected by filtration, and then dried in vacuo to give E40 (13 g). ^1H NMR (400 MHz, CD_3OD) δ 8.19 (s, 1H), 7.93 (s, 1H), 4.98 (q, 2H).

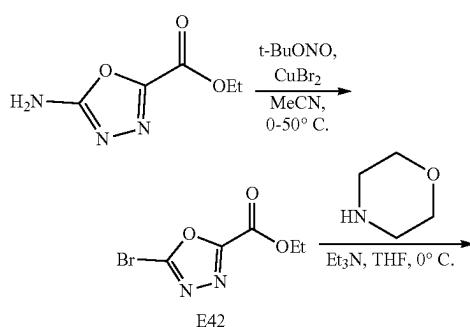
Step C: Preparation of ethyl N-[1-(2,2,2-trifluoroethyl)pyrazole-4-carboxyl]carbamate (E41)

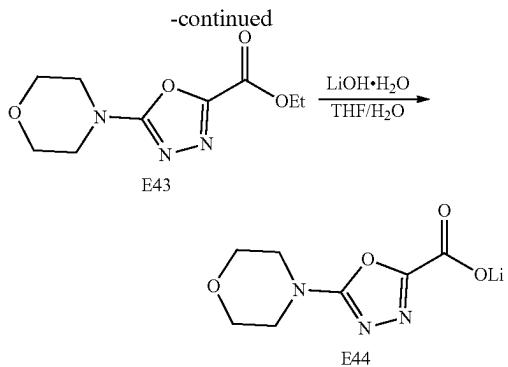
[0347] To a solution of E40 (3 g, 14.4 mmol) in THF (70 mL) was added ethyl 2-chloro-2-oxo-acetate (2.36 g, 17.3 mmol, 1.9 mL, 1.2 eq) dropwise at 0°C., and then the reaction mixture was stirred at rt for 3 hrs. The precipitate was collected by filtration and rinsed with TBME (30 mL), and then dried in vacuo to give E41 (1.5 g, 37% yield). ^1H NMR (400 MHz, CDCl_3) δ 9.75 (br s, 1H), 9.06 (br s, 1H), 8.25 (s, 1H), 7.99 (s, 1H), 4.76 (q, 2H), 4.42 (q, 2H), 1.42 (t, 3H).

Step D: Preparation of ethyl 5-[1-(2,2,2-trifluoroethyl)pyrazol-4-yl]-1,3,4-oxadiazole-2-carboxylate (E37)

[0348] To a solution of E41 (1.5 g, 5.35 mmol) and Et_3N (271 mg, 2.68 mmol, 373 μL , 0.5 eq) in DCM (30 mL) was added TsCl (491 mg, 6.96 mmol, 1.3 eq) in portions at 0°C., and then the resulting mixture was stirred at rt for 18 hrs. Reaction progress was tracked using TLC (PE:EtOAc=1:1). DCM (100 mL) was added to the reaction mixture, and the organic layer washed with sat. Na_2CO_3 solution (60 mL) and brine (60 mL), dried over Na_2SO_4 , filtered, and concentrated to dryness. The residue was purified by flash silica gel chromatography (ISCO®; 40 g SepaFlash® Silica Flash Column, Eluent of 0-16% PE/EtOAc @40 mL/min) to give E37 (0.65 g, 42% yield). ^1H NMR (400 MHz, CDCl_3) δ 8.16-8.29 (m, 2H), 4.80 (q, 2H), 4.53 (q, 2H), 1.47 (t, 3H).

Intermediate lithium
5-morpholino-1,3,4-oxadiazole-2-carboxylate
according to General Scheme 10





Step 1: Preparation of ethyl 5-bromo-1, 3, 4-oxadiazole-2-carboxylate (E42)

[0349] To a solution of ethyl 5-amino-1,3,4-oxadiazole-2-carboxylate (5 g, 31.8 mmol) in MeCN (60 mL) was added CuBr₂ (10.66 g, 47.7 mmol, 2.2 mL, 1.5 eq) at 0° C. The reaction mixture turned dark green and was stirred for 15 min at rt. t-BuONO (4.92 g, 47.7 mmol, 5.7 mL, 1.5 eq) was added at 0° C., and the reaction mixture was stirred at rt for 2 hrs, then heated at 50° C. for another 12 hrs. The reaction progress was checked using TLC (PE/EtOAc=1/1). The reaction mixture was filtered and concentrated to dryness. The residue was purified by flash silica gel chromatography (ISCO®; 40 g SepaFlash® Silica Flash Column, eluent of 0-50% EtOAc/PE gradient @40 mL/min) to give E42 (4.5 g, 64% yield). ¹H NMR (400 MHz, CDCl₃) δ 4.52 (q, 2H), 1.45 (t, 3H).

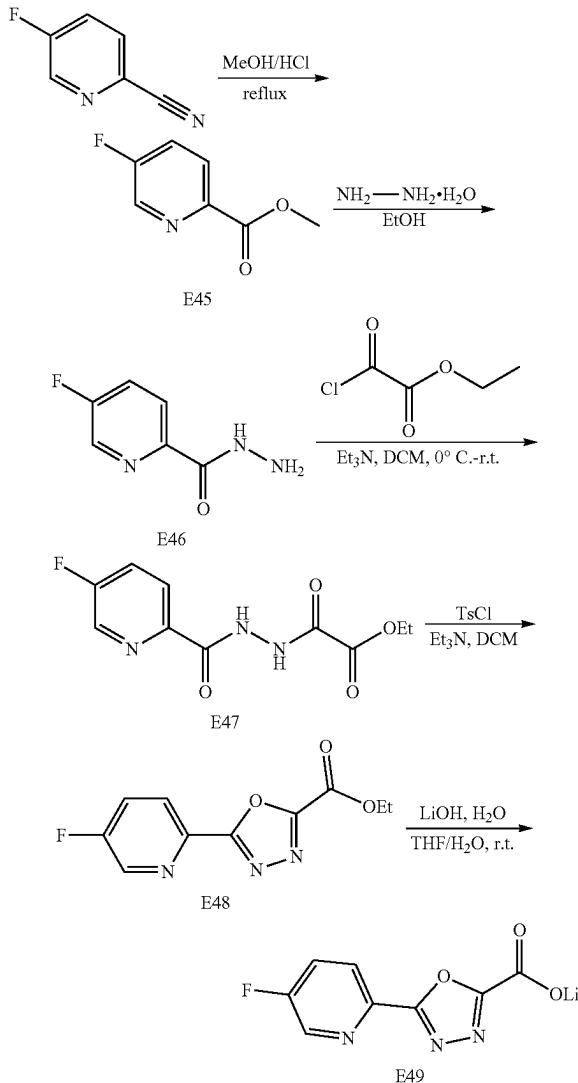
Step 2: Preparation of ethyl 5-morpholino-1,3,4-oxadiazole-2-carboxylate (E43)

[0350] To a solution of ethyl 5-bromo-1,3,4-oxadiazole-2-carboxylate (E42) (1 g, 4.52 mmol) and morpholine (473 mg, 5.43 mmol, 478 μL, 1.2 eq) in THF (40 mL) was added DIPEA (1.17 g, 9.05 mmol, 1.6 mL, 2 eq) at 0° C. The mixture was stirred at rt for 1 hr. The reaction progress was checked using TLC (PE/EtOAc=1/1). EtOAc (100 mL) was added to the reaction mixture, and the organic portion washed with water (30 mL) and brine (30 mL×2), dried over Na₂SO₄, filtered, and concentrated to dryness. The residue was purified by flash silica gel chromatography (ISCO®; 12 g SepaFlash® Silica Flash Column, Eluent of 0-30% EtOAc/PE gradient @35 mL/min) to give E43 (800 mg, 78% yield). ¹H NMR (400 MHz, DMSO-d₆) δ 4.37 (q, 2H), 3.68-3.74 (m, 4H), 3.48-3.52 (m, 4H), 1.31 (t, 3H).

Step 3: Preparation of (5-morpholino-1, 3, 4-oxadiazole-2-carboxylate) oxylithium (E44)

[0351] To a solution of ethyl 5-morpholino-1, 3, 4-oxadiazole-2-carboxylate (E43) (800 mg, 3.52 mmol) in THF (8 mL) and H₂O (12 mL) was added LiOH·H₂O (162 mg, 3.87 mmol, 1.1 eq). The reaction mixture was stirred at rt for 12 hrs. The reaction progress was checked using TLC (PE/EtOAc=1/1). The reaction mixture was concentrated to dryness to afford E44 (600 mg), which was used without further purification. ¹H NMR (400 MHz, DMSO-d₆) δ 3.62-3.74 (m, 4H), 3.36 (br d, 4H).

Intermediate [5-(5-fluoro-2-pyridyl)-1,3,4-oxadiazole-2-carboxyl]oxylithium according to General Scheme 9, Method A



Step 1: Preparation of methyl 5-fluoropyridine-2-carboxylate (E45)

[0352] A solution of 5-fluoropyridine-2-carbonitrile (15 g, 123 mmol) in HCl/MeOH (4 M, 180 mL, 5.9 eq) was stirred at 60° C. for 12 hrs. The reaction mixture was concentrated in vacuo, and the residue was dissolved in EtOAc (150 mL), washed with sat. NaHCO₃ solution (50 mL) and brine (20 mL). The organic layer was dried over Na₂SO₄, filtered, and concentrated to dryness. The residue was purified by flash silica gel chromatography (ISCO®; 80 g SepaFlash® Silica Flash Column, Eluent of 0-25% EtOAc/PE gradient @60 mL/min) to give E45 (15.24 g, 80% yield). ¹H NMR (400 MHz, CDCl₃) δ 8.58 (d, 1H), 8.20 (dd, 1H), 7.53 (ddd, 1H), 4.00 (s, 3H).

Step 2: Preparation of
5-fluoropyridine-2-carbohydrazide (E46)

[0353] A mixture of methyl 5-fluoropyridine-2-carboxylate (E45) (16 g, 103 mmol), $\text{NH}_2\text{NH}_2\cdot\text{H}_2\text{O}$ (11.06 g, 217 mmol, 10.7 mL, 98% purity, 2.1 eq) in EtOH (70 mL) was degassed and purged with N_2 for 3 times, and then the reaction mixture was stirred at rt for 3 hrs under N_2 atmosphere. The reaction mixture was concentrated to dryness to give E46 (15 g, 94% yield). ^1H NMR (400 MHz, DMSO-d_6) δ 9.89 (br s, 1H), 8.61 (d, 1H), 8.07 (dd, 1H), 7.88 (td, 1H), 4.57 (br s, 2H).

Step 3: Preparation of ethyl 2-[2-(5-fluoropyridine-2-carbonyl)hydrazino]-2-oxo-acetate (E47)

[0354] To a mixture of 5-fluoropyridine-2-carbohydrazide (E46) (13.5 g, 87.0 mmol) and TEA (17.61 g, 174 mmol, 24.2 mL, 2 eq) in DCM (500 mL) was added ethyl 2-chloro-2-oxo-acetate (15.45 g, 113 mmol, 12.7 mL, 1.3 eq) over a period of 10 min at 0° C. The reaction mixture was stirred for 2 hrs at rt. H_2O (100 mL) was added to the reaction mixture, and the aqueous portion extracted with DCM (300 mL×3). The combined organic layer was washed with brine (100 mL), dried over Na_2SO_4 , filtered, and concentrated to dryness. The residue was purified by flash silica gel chromatography (ISCO®; 80 g SepaFlash® Silica Flash Column, Eluent of 0-2.5% EtOAc/PE gradient @60 mL/min) to give E47 (16 g, 53% yield). ^1H NMR (400 MHz, CDCl_3) δ 10.03-10.15 (m, 1H), 9.65 (br d, 1H), 8.35-8.42 (m, 1H), 8.11-8.18 (m, 1H), 7.51 (td, 2H), 4.35 (q, 1H), 1.34 (t, 3H); LCMS: m/z 256.2 [M+H]⁺.

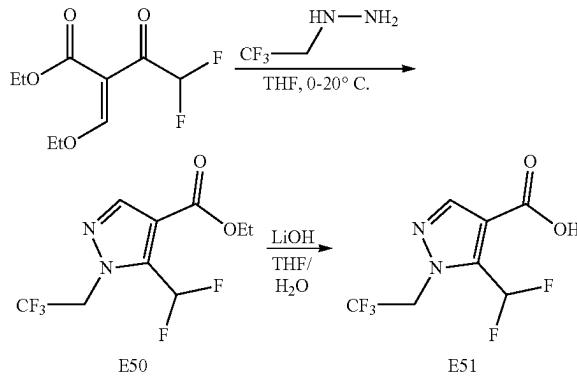
Step 4: Preparation of ethyl 5-(5-fluoro-2-pyridyl)-1,3,4-oxadiazole-2-carboxylate (E48)

[0355] To a solution of ethyl 2-[2-(5-fluoropyridine-2-carbonyl)hydrazino]-2-oxo-acetate (E47) (16 g, 62.7 mmol) in DCM (350 mL) was added TEA (8.25 g, 81.5 mmol, 11.3 mL, 1.3 eq) and TosCl (5.98 g, 31.4 mmol, 0.5 eq) in 3 portions at 0° C. The mixture was stirred at rt for 3 hrs. Sat. NaHCO_3 solution (200 mL) was added, and the aqueous portion extracted with DCM (400 mL×3). The combined organic layer was washed with brine (200 mL), dried over Na_2SO_4 , filtered, and concentrated to dryness. The residue was purified by flash silica gel chromatography (ISCO®; 120 g SepaFlash® Silica Flash Column, Eluent of 0-2.5% MeOH/DCM@85 mL/min) to give E48 (8.2 g, 49% yield). ^1H NMR (400 MHz, CDCl_3) δ 8.71 (d, 1H), 8.39 (dd, 1H), 7.66 (ddd, 1H), 4.59 (q, 2H), 1.51 (t, 3H); LCMS: m/z 238.2 [M+H]⁺.

Step 5: Preparation of [5-(5-fluoro-2-pyridyl)-1,3,4-oxadiazole-2-carbonyl]oxylithium (E49)

[0356] To a solution of ethyl 5-(5-fluoro-2-pyridyl)-1,3,4-oxadiazole-2-carboxylate (E48) (12 g, 50.6 mmol) in THF (140 mL) and H_2O (180 mL) was added $\text{LiOH}\cdot\text{H}_2\text{O}$ (2.23 g, 53.1 mmol, 1.05 eq). The mixture was stirred at rt for 2 hrs. The reaction mixture was concentrated in vacuo to remove most of THF, and the aqueous portion was lyophilized in vacuo to give E49 (11.5 g), which was used without further purification. ^1H NMR (400 MHz, DMSO-d_6) δ 8.79 (d, 1H), 8.24 (dd, 1H), 7.99 (td, 1H).

Intermediate 5-(difluoromethyl)-1-(2,2,2-trifluoroethyl)pyrazole-4-carboxylic acid



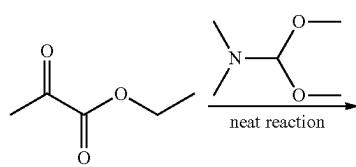
Step 1: Preparation of ethyl 5-(difluoromethyl)-1-(2,2,2-trifluoroethyl)pyrazole-4-carboxylate (E50)

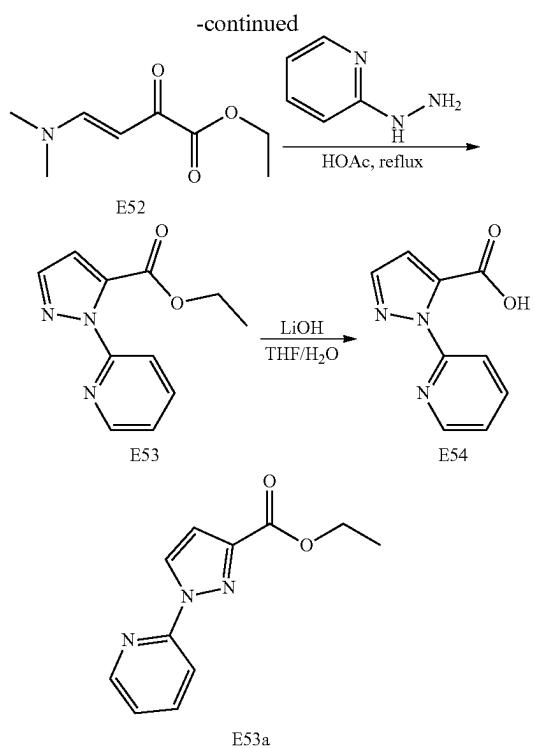
[0357] To a solution of (Z)-ethyl 2-(ethoxymethylene)-4,4-difluoro-3-oxobutanoate (1 g, 4.52 mmol) in THF (8 mL) was added 2,2,2-trifluoroethylhydrazine (670 mg, 5.88 mmol, 1.3 eq) dropwise at 0° C. The reaction mixture was stirred at 0° C. for 1 hr, and then stirred at rt for 16 hrs. Reaction progress was checked using LCMS. The reaction mixture was concentrated to dryness, and the residue was purified by flash silica gel chromatography (Eluent: 0-5% EtOAc/PE gradient) to give E50 (850 mg, 69% yield). ^1H NMR (400 MHz, CDCl_3) δ 8.02 (s, 1H), 7.38-7.75 (m, 1H), 4.95 (q, 2H), 4.37 (q, 2H), 1.40 (t, 3H); LCMS: m/z 273.1 [M+H]⁺.

Step 2: Preparation of 5-(difluoromethyl)-1-(2,2,2-trifluoroethyl)pyrazole-4-carboxylic acid (E51)

[0358] To a solution of ethyl 5-(difluoromethyl)-1-(2,2,2-trifluoroethyl)pyrazole-4-carboxylate (E50) (910 mg, 3.34 mmol) in THF (5 mL) and H_2O (5 mL) was added $\text{LiOH}\cdot\text{H}_2\text{O}$ (224 mg, 5.35 mmol, 1.6 eq). The mixture was stirred at rt for 2 hrs. The reaction progress was checked using TLC (PE:EtOAc=2:1). The reaction mixture was concentrated to remove THF. The aqueous portion was adjusted to pH-6 by the addition of HCl (1 M). The resulting precipitate was collected by filtration and then dried in vacuo to give E51 (816 mg, 100% yield). ^1H NMR (400 MHz, DMSO-d_6) δ 8.08 (s, 1H), 7.45-7.78 (m, 1H), 5.30 (q, 2H).

Intermediate ethyl 2-(2-pyridyl)pyrazole-3-carboxylate





Step 1: Preparation of ethyl (E)-4-(dimethylamino)-2-oxo-but-3-enoate (E52)

[0359] Ethyl 2-oxopropanoate (2 g, 17.2 mmol, 1.9 mL) and 1,1-dimethoxy-N,N-dimethyl-methanamine (2.09 g, 17.6 mmol, 2.3 mL, 1.02 eq) were stirred at rt for 12 hrs. The reaction progress was checked using TLC (PE:EtOAc=10:1). The reaction mixture was concentrated to dryness to give E52 (2.4 g), which was used without further purification.

Step 2: Preparation of ethyl 2-(2-pyridyl)pyrazole-3-carboxylate (E53)

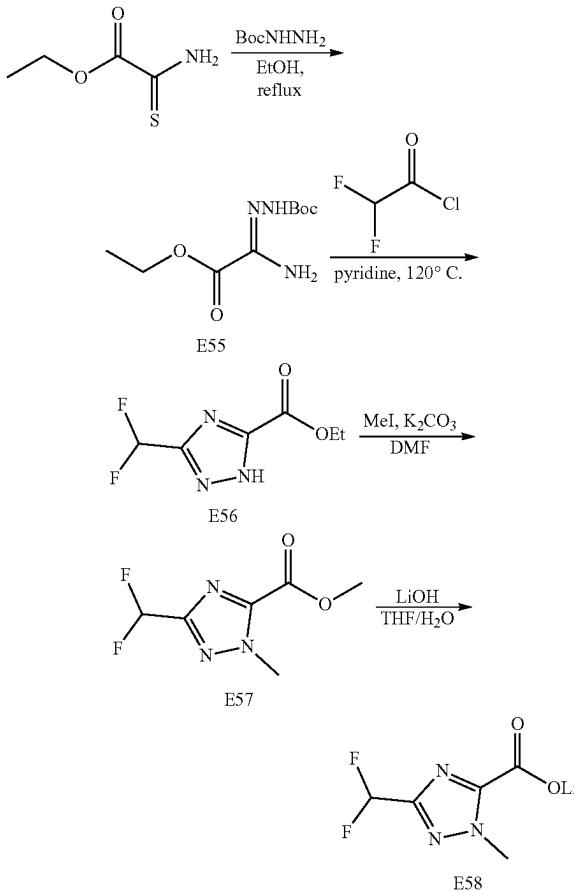
[0360] A mixture of ethyl (E)-4-(dimethylamino)-2-oxo-but-3-enoate (E52) (2.4 g, 14.0 mmol) and 2-pyridylhydrazine (1.53 g, 14.0 mmol) in HOAc (100 mL) was stirred at 110° C. for 12 hrs. The reaction progress was checked using TLC (PE:EtOAc=10:1). The reaction mixture was adjusted to pH ~9 by the addition of sat. Na_2CO_3 solution. The aqueous portion was extracted with EtOAc (300 mL). The organic layer was dried over Na_2SO_4 , filtered, and concentrated to dryness. The residue was purified by column chromatography (SiO_2 , PE:EtOAc=100/1 to 50/1) to give E53 (1.03 g, 34% yield). ^1H NMR (400 MHz, DMSO- d_6) δ 8.48 (dt, 1H), 8.05 (td, 1H), 7.83-7.96 (m, 1H), 7.76 (d, 1H), 7.49 (ddd, 1H), 6.96-7.05 (m, 1H), 4.21 (q, 2H), 1.05-1.23 (m, 3H); LCMS: m/z 218.1 [M+H]⁺.

[0361] Ethyl 1-(2-pyridyl)pyrazole-3-carboxylate (E53a) was also obtained (190 mg, 6% yield). ^1H NMR (400 MHz, DMSO- d_6) δ 8.70-8.81 (m, 1H), 8.54 (dd, 1H), 7.92-8.13 (m, 2H), 7.47 (ddd, 1H), 7.02 (d, 1H), 4.35 (q, 2H), 1.34 (t, 3H). The regiochemistry of E53 and E53a were confirmed by HSQC and HMBC NMR analysis.

Step 3: Preparation of 2-(2-pyridyl)pyrazole-3-carboxylic acid (E54)

[0362] To a solution of ethyl 2-(2-pyridyl)pyrazole-3-carboxylate (E53) (1 g, 4.60 mmol) in THF (10 mL) and H_2O (10 mL) was added LiOH- H_2O (386 mg, 9.21 mmol, 2 eq), and the reaction mixture was stirred at rt for 12 hrs. The reaction progress was checked using TLC (PE/EtOAc=1/1). The reaction mixture was concentrated under reduced pressure to remove THF. The aqueous portion was adjusted to pH-7 by the addition of 2 M HCl and lyophilized in vacuo to give (E54) (1.2 g), which was used without further purification. ^1H NMR (400 MHz, DMSO- d_6) δ 8.36-8.44 (m, 1H), 7.88 (td, 1H), 7.44-7.53 (m, 2H), 7.35 (ddd, 1H), 6.44 (d, 1H).

Intermediate [5-(difluoromethyl)-2-methyl-1,2,4-triazole-3-carbonyl]oxylithium



Step 1: Preparation of tert-butyl (Z)-2-(1-amino-2-ethoxy-2-oxoethylidene)hydrazine-1-carboxylate (E55)

[0363] Tert-butyl (Z)-2-(1-amino-2-ethoxy-2-oxoethylidene)hydrazine-1-carboxylate was prepared from ethyl 2-amino-2-thioxoacetate following the procedure in Bioorg. Med. Chem., 26 (2016) 3223-3225. The reaction was heated to reflux.

Step 2: Preparation of ethyl
3-(difluoromethyl)-1H-1,2,4-triazole-5-carboxylate
(E56)

[0364] Reagent 2,2-difluoroacetyl chloride was prepared by adding oxalyl dichloride (18.90 g, 149 mmol, 13.0 mL, 1.1 eq) dropwise at 0° C. to a solution of 2,2-difluoroacetic acid (13 g, 135 mmol, 8.5 mL) and DMF (989 mg, 13.5 mmol, 1.0 mL, 0.1 eq) in DCM (80 mL). The reaction mixture was stirred at rt for 1 hr, and the solution was used without further purification.

[0365] To a solution of tert-butyl (Z)-2-(1-amino-2-ethoxy-2-oxoethylidene)hydrazine-1-carboxylate (E55) (13 g, 56.2 mmol) in pyridine (90 mL) was added 2,2-difluoroacetyl chloride (15.47 g, 135 mmol, 2.4 eq). The reaction mixture was heated to 120° C. and stirred for 12 hrs. Reaction progress was checked using LCMS. The reaction mixture was concentrated to dryness. DCM (200 mL) was added to the residue, and the organic portion washed with 1 M HCl (30 mL) and brine (60 mL), dried over Na₂SO₄, filtered, and concentrated to dryness. The residue was purified by column chromatography on silica gel (PE: EtOAc=20:1 to 2:1) to give E56 (8.87 g, 83% yield). ¹H NMR (400 MHz, DMSO-d₆) δ 7.01-7.32 (m, 1H), 4.36 (q, 2H), 1.30 (t, 3H); LCMS: m/z 192.0 [M+H]⁺.

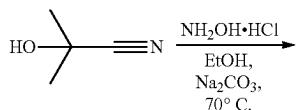
Step 3: Preparation of ethyl 5-(difluoromethyl)-2-methyl-1,2,4-triazole-3-carboxylate (E57)

[0366] To a solution of ethyl 3-(difluoromethyl)-1H-1,2,4-triazole-5-carboxylate (E56) (10 g, 52.3 mmol) in DMF (80 mL) was added Mel (22.28 g, 157 mmol, 9.8 mL, 3 eq) and K₂CO₃ (21.69 g, 157 mmol, 3 eq). The mixture was stirred at rt for 12 hrs. Reaction progress was checked using TLC (PE:EtOAc=1:1). The reaction mixture was filtered, and the precipitate was rinsed with EtOAc (150 mL). The filtrate was washed with water (30 mL) and brine (30 mL), dried over Na₂SO₄, filtered, and concentrated to dryness. The residue was purified by column chromatography on silica gel (PE:EtOAc=20:1 to 1:1) to give E57 (4.46 g, 42% yield). ¹H NMR (400 MHz, DMSO-d₆) δ 6.99-7.34 (m, 1H), 4.39 (q, 2H), 4.11-4.22 (m, 3H), 1.35 (t, 3H).

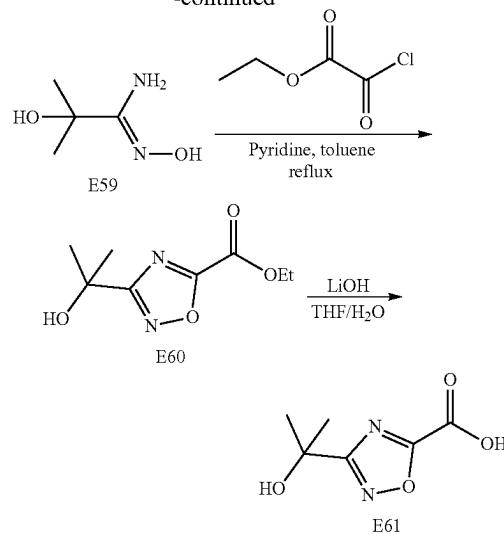
Step 4: Preparation of [5-(difluoromethyl)-2-methyl-1,2,4-triazole-3-carboxyl]oxylithium (E58)

[0367] To a solution of ethyl 5-(difluoromethyl)-2-methyl-1,2,4-triazole-3-carboxylate (E57) (2.35 g, 11.5 mmol) in THF (40 mL) and H₂O (10 mL) was added LiOH·H₂O (505 mg, 12.0 mmol, 1.05 eq). The reaction mixture was stirred at rt for 1 hr. Reaction progress was checked using TLC (PE:EtOAc=2:1). The reaction mixture was concentrated in vacuo to remove THF. H₂O (20 mL) was added, and the aqueous portion extracted with TBME (20 mL), and then lyophilized in vacuo to give E58 (2.15 g), which was used without further purification. ¹H NMR (400 MHz, DMSO-d₆) δ 6.75-7.21 (m, 1H), 4.09 (s, 3H).

Intermediate ethyl 3-(1-hydroxy-1-methyl-ethyl)-1,2,4-oxadiazole-5-carboxylate



-continued



Step 1: Preparation of
N',2-dihydroxy-2-methyl-propanamidine (E59)

[0368] To a solution of 2-hydroxy-2-methyl-propanenitrile (2.14 g, 25.2 mmol, 2.3 mL) in EtOH (20 mL) was added hydroxylamino hydrochloride (3.49 g, 50.3 mmol, 2 eq) and Na₂CO₃ (5.33 g, 50.3 mmol, 2 eq), and then the reaction was stirred at 70° C. for 16 hrs. The reaction mixture was concentrated to dryness. EtOAc (200 mL) was added to the residue, and the organic portion washed twice with water (50 mL) and brine (50 mL), dried over Na₂SO₄, filtered, and concentrated to dryness to afford E59 (1 g), which was used without further purification. ¹H NMR (400 MHz, DMSO-d₆) δ 10.11 (s, 1H), 8.86 (s, 1H), 5.03 (br s, 1H), 1.70 (s, 3H), 1.66 (s, 3H).

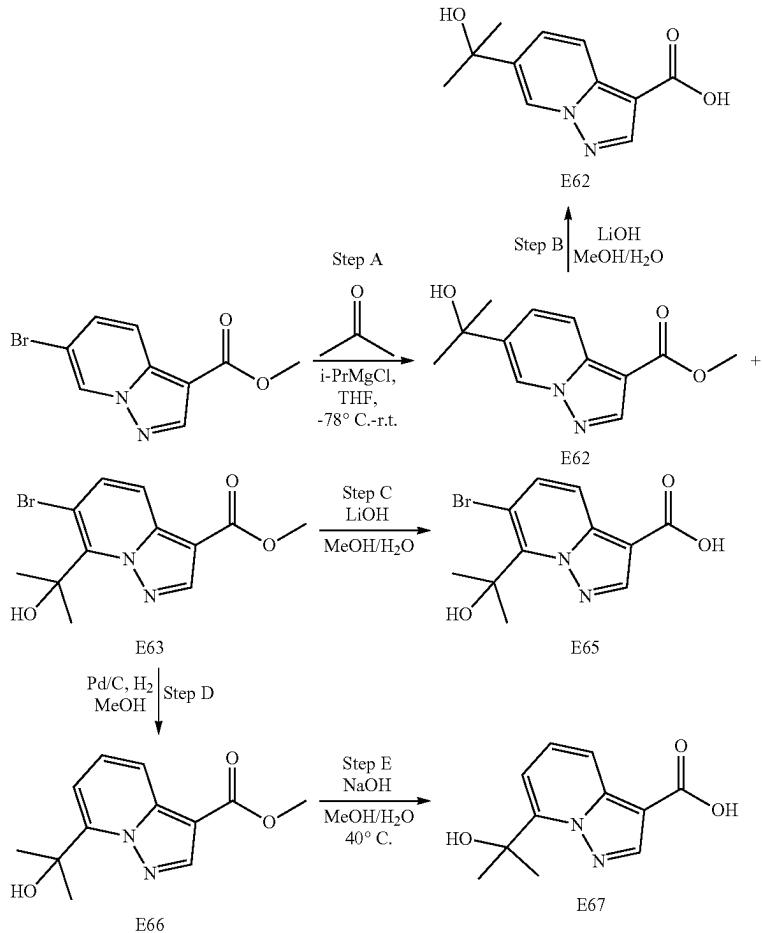
Step 2: Preparation of ethyl 3-(1-hydroxy-1-methyl-ethyl)-1,2,4-oxadiazole-5-carboxylate (E60)

[0369] To a solution of N',2-dihydroxy-2-methyl-propanamidine (E59) (520 mg, 4.40 mmol) and pyridine (696 mg, 8.80 mmol, 711 μL, 2 eq) in toluene (15 mL) was added ethyl 2-chloro-2-oxo-acetate (601 mg, 4.40 mmol, 493 μL) at 0° C. The reaction mixture was stirred at rt for 1 hr, and then stirred at 100° C. for 15 hrs. Reaction progress was checked using LCMS. The reaction mixture was concentrated to dryness. The residue was purified by column chromatography (SiO₂, PE/EtOAc=1/0 to 2/1) and further purified by prep-HPLC (column: Boston Uni C18 40*150*5 um; mobile phase: [water(0.225% FA)-ACN]; B %: 16%-46%, 7.7 min) to give E60 (250 mg, 28% yield). ¹H NMR (400 MHz, CDCl₃) δ 4.52 (q, 2H), 2.65 (br s, 1H), 1.67 (s, 6H), 1.45 (t, 3H); LCMS: m/z 201.1 [M+H]⁺.

Step 3: Preparation of ethyl 3-(1-hydroxy-1-methyl-ethyl)-1,2,4-oxadiazole-5-carboxylate (E61)

[0370] To a solution of ethyl 3-(1-hydroxy-1-methyl-ethyl)-1,2,4-oxadiazole-5-carboxylate (E60) (200 mg, 999 μmol) in THF (5 mL) and H₂O (5 mL) was added LiOH·H₂O (41.9 mg, 999 μmol), and then the reaction mixture was stirred at rt for 1 hr. The solvent was removed in vacuo, and the aqueous portion was lyophilized in vacuo to give E61 (170 mg), which was used without further purification.

Intermediates E62, E63, E64, E65, E66, and E67



Step A: Preparation of methyl 6-(2-hydroxypropan-2-yl)pyrazolo[1,5-a]pyridine-3-carboxylate (E62) and methyl 6-bromo-7-(2-hydroxypropan-2-yl)pyrazolo[1,5-a]pyridine-3-carboxylate (E63)

[0371] To a solution of methyl 6-bromopyrazolo[1,5-a]pyridine-3-carboxylate (1 g, 3.92 mmol) in THF (10 mL) was added i-PrMgCl-LiCl (1.3 M, 6.03 mL, 2 eq) at -78° C. The reaction mixture was stirred at -78° C. for 15 min, then acetone (1.37 g, 23.5 mmol, 1.7 mL, 6 eq) was added dropwise to the reaction mixture. The reaction mixture was stirred at -78° C. for 1 hr. Reaction progress was checked using LCMS. The reaction mixture was dropwise added to 10 mL of aq. NH₄Cl solution. Water (30 mL) was added, and the aqueous portion extracted with EtOAc (25 mL×2). The combined organic layers were washed with brine (20 mL), dried over Na₂SO₄, filtered, and concentrated to dryness. The residue was purified by column chromatography (SiO₂, PE/EtOAc=1/0 to 20:1) to give E62 (320 mg, 34% yield) and E63 (300 mg, 23% yield).

[0372] E62: ¹H NMR (400 MHz, CD₃OD) δ 8.40-8.54 (m, 1H), 8.14 (dd, 1H), 7.57 (dd, 1H), 7.27 (dd, 1H), 3.88-4.03 (m, 3H), 1.77-1.92 (m, 6H); LCMS: m/z 235.2 [M+H]⁺.

[0373] E63: ¹H NMR (400 MHz, CD₃OD) δ 8.46 (s, 1H), 8.02 (d, 1H), 7.76 (d, 1H), 3.93 (s, 3H), 1.95 (s, 6H); LCMS: m/z 313.0 [M+H]⁺.

Step B: Preparation of 6-(2-hydroxypropan-2-yl)pyrazolo[1,5-a]pyridine-3-carboxylic acid (E64)

[0374] To a solution of methyl 6-(2-hydroxypropan-2-yl)pyrazolo[1,5-a]pyridine-3-carboxylate (E62) (500 mg, 2.13 mmol) in MeOH (3 mL) and H₂O (1 mL) was added LiOH-H₂O (116 mg, 2.77 mmol, 1.3 eq). The reaction mixture was stirred at 40° C. for 12 hrs. Reaction progress was checked using LCMS. The reaction mixture was concentrated in vacuo to remove MeOH, and water (50 mL) was added. The aqueous portion was extracted with TBME (30 mL), and the aqueous layer was then adjusted to pH ~6 by the addition of 0.5 M HCl. The resulting suspension was extracted with DCM/MeOH (100/10 mL) 3 times. The combined DCM/MeOH organic layer was dried over Na₂SO₄, filtered, and concentrated to dryness to afford E64 (420 mg, 89% yield). LCMS: m/z 221.1 [M+H]⁺.

Step C: Preparation of 6-bromo-7-(2-hydroxypropan-2-yl)pyrazolo[1,5-a]pyridine-3-carboxylic acid (E65)

[0375] To a solution of methyl 6-bromo-7-(2-hydroxypropan-2-yl)pyrazolo[1,5-a]pyridine-3-carboxylate (E63) (120

mg, 383 μmol) in MeOH (2 mL) and H₂O (1 mL) was added LiOH·H₂O (17.69 mg, 422 μmol , 1.1 eq), the mixture was stirred at 40° C. for 12 hr. Reaction progress was checked using LCMS. The reaction mixture was concentrated in vacuo to remove MeOH, and water (10 mL) was added. The aqueous portion was extracted with TBME (30 mL) and was then adjusted to pH ~6 by the addition of 0.5 M HCl. The resulting suspension was extracted with DCM/MeOH (30/3 mL) 3 times. The combined DCM/MeOH organic layer was dried over Na₂SO₄, filtered, and concentrated to dryness to afford E65 (100 mg, 87% yield). ¹H NMR (400 MHz, CD₃OD) δ 8.44 (s, 1H), 8.07 (d, 1H), 7.74 (d, 1H), 1.96 (s, 6H); LCMS: m/z 301.1 [M+H]⁺.

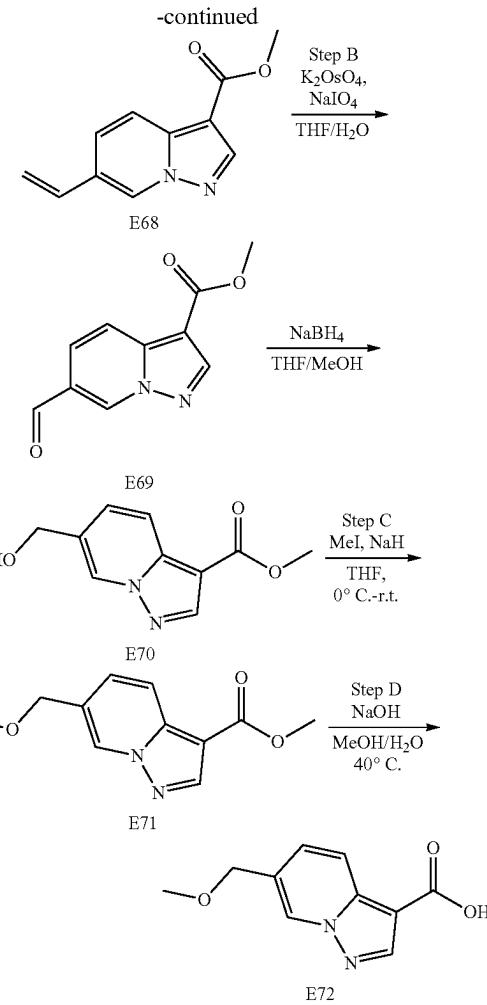
Step D: Preparation of methyl 7-(2-hydroxypropan-2-yl)pyrazolo[1,5-a]pyridine-3-carboxylate (E66)

[0376] To a solution of methyl 6-bromo-7-(2-hydroxypropan-2-yl)pyrazolo[1,5-a]pyridine-3-carboxylate (E63) (450 mg, 1.44 mmol) in MeOH (10 mL) was added Pd/C (100 mg, 10% purity) under N₂. The resulting mixture was degassed under vacuum and purged with H₂ 3 times, and then the mixture was stirred at rt for 1 hr under H₂ (15 psi). Reaction progress was checked using LCMS. The reaction mixture was filtered through a pad of Celite, and the filtrate was concentrated in vacuo to afford E66 (350 mg), which was used without further purification. LCMS: m/z 234.9 [M+H]⁺.

Step E: Preparation of 7-(2-hydroxypropan-2-yl)pyrazolo[1,5-a]pyridine-3-carboxylic acid (E67)

[0377] To a solution of methyl 7-(2-hydroxypropan-2-yl)pyrazolo[1,5-a]pyridine-3-carboxylate (E66) (350 mg, 1.49 mmol) in MeOH (5 mL) and H₂O (1 mL) was added NaOH (89.64 mg, 2.24 mmol, 1.5 eq), the mixture was stirred at 40° C. for 12 hrs. Reaction progress was checked using LCMS. The reaction mixture was concentrated in vacuo to remove MeOH, and water (10 mL) was added. The aqueous portion was extracted with TBME (30 mL), and then adjusted to pH ~6 by the addition of 0.5 M HCl. The resulting suspension was extracted with DCM/MeOH (30/3 mL) 3 times. The combined DCM/MeOH organic layer was dried over Na₂SO₄, filtered, and concentrated to dryness to afford E67 (320 mg), which was used without further purification. LCMS: m/z 220.9 [M+H]⁺.

**Intermediate E72 According to General Scheme 7,
Methods C and D**

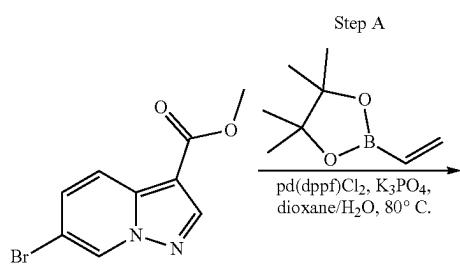


Step A: Preparation of methyl 6-vinylpyrazolo[1,5-a]pyridine-3-carboxylate (E68)

[0378] A mixture of 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane (8.15 g, 52.9 mmol, 8.98 mL), methyl 6-bromopyrazolo[1,5-a]pyridine-3-carboxylate (9 g, 35.3 mmol), K₃PO₄ (22.47 g, 106 mmol) and Pd(dppf)Cl₂ (1.29 g, 1.76 mmol) in dioxane (80 mL) and H₂O (40 mL) was stirred at 80° C. for 12 hrs under N₂. Reaction progress was checked using LCMS. The reaction mixture was combined with another 1 g batch reaction, and DCM (200 mL) was added. The organic layer was washed with brine (2×80 mL), dried over Na₂SO₄, filtered, and concentrated to dryness. The residue was purified by column chromatography (SiO₂, PE/EtOAc=1/0 to 4/1) to give E68 (6.4 g, 80.2% yield). ¹H NMR (400 MHz, CDCl₃) δ 8.37 (s, 1H), 8.30 (s, 1H), 8.03 (d, 1H), 7.52 (dd, 1H), 6.61 (dd, 1H), 5.76 (d, 1H), 5.34 (d, 1H), 3.84 (s, 3H); LCMS: m/z 203.1 [M+H]⁺.

Step B: Preparation of methyl 6-formylpyrazolo[1,5-a]pyridine-3-carboxylate (E69)

[0379] To a solution of methyl 6-vinylpyrazolo[1,5-a]pyridine-3-carboxylate (E68) (6.4 g, 31.7 mmol) in THF (80 mL) and H₂O (80 mL) was added K₂OsO₄·2H₂O (583



mg, 1.58 mmol) and NaIO₄ (16.92 g, 79.1 mmol, 4.38 mL) at 0° C., and then the reaction mixture was stirred at rt for 12 hrs. Reaction progress was checked using LCMS. DCM (200 mL) was added to the reaction mixture, and the organic layer was washed with brine (2×80 mL), dried over Na₂SO₄, filtered, and concentrated to dryness. The residue was purified by column chromatography (SiO₂, DCM/EtOAc=1/0 to 6/1) to give E69 (5.9 g, 91.3% yield). ¹H NMR (400 MHz, CDCl₃) δ 9.94 (s, 1H), 8.90-8.98 (m, 1H), 8.48 (s, 1H), 8.18 (d, 1H), 7.80 (dd, 1H), 3.88 (s, 3H); LCMS: m/z 204.9 [M+H]⁺.

Step C: Preparation of methyl 6-(hydroxymethyl)pyrazolo[1,5-a]pyridine-3-carboxylate (E70)

[0380] To a solution of methyl 6-formylpyrazolo[1,5-a]pyridine-3-carboxylate (E69) (2.4 g, 11.8 mmol) in THF (30 mL) and MeOH (30 mL) was added NaBH₄ (1.78 g, 47.0 mmol) at 0° C., and then the reaction mixture was stirred at rt for 1 hr. Reaction progress was checked using LCMS. The reaction mixture was quenched by the addition of sat. aq. NH₄Cl (50 mL), and the aqueous portion extracted with EtOAc (100 mL). The organic layer was washed with water (50 mL) and brine (40 mL), dried over Na₂SO₄, filtered, and concentrated to dryness to give E70 (2.3 g, 94.9% yield). ¹H NMR (400 MHz, CDCl₃) δ 8.54 (s, 1H), 8.38 (s, 1H), 8.11 (d, 1H), 7.41 (dd, 1H), 4.78 (s, 2H), 3.93 (s, 3H); LCMS: m/z 207.0 [M+H]⁺.

Step D: Preparation of methyl 6-(methoxymethyl)pyrazolo[1,5-a]pyridine-3-carboxylate (E71)

[0381] To a solution of methyl 6-(hydroxymethyl)pyrazolo[1,5-a]pyridine-3-carboxylate (E70) (2.2 g, 10.7 mmol) in THF (50 mL) was added NaH (512 mg, 12.8 mmol, 60% purity) at 0° C. The reaction mixture was stirred at 0° C. for 15 min, and then Mel (1.82 g, 12.8 mmol, 797 μL) was added to the reaction mixture. The reaction mixture was stirred at rt for 1 hr, and reaction progress was checked using LCMS. The reaction mixture was quenched by the addition of sat. aq. NH₄Cl (40 mL), and the aqueous portion extracted with DCM (2×60 mL). The combined organic layer was washed by water (30 mL) and brine (30 mL), dried over Na₂SO₄, filtered, and concentrated to dryness. The residue was purified by column chromatography (SiO₂, PE/EtOAc=1/0 to 5/1) to give E71 (1.8 g, 76.6% yield). ¹H NMR (400 MHz, CDCl₃) δ 8.52 (s, 1H), 8.41 (s, 1H), 8.16 (d, 1H), 7.42 (dd, 1H), 4.53 (s, 2H), 3.94 (s, 3H), 3.46 (s, 3H); LCMS: m/z 221.1 [M+H]⁺.

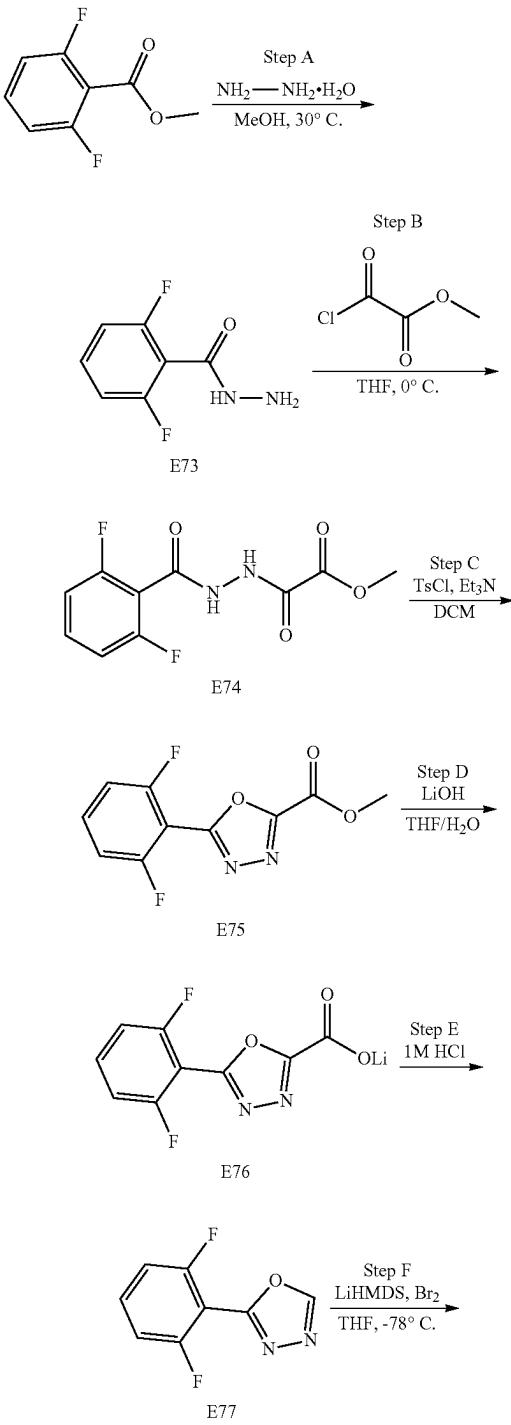
Step E: Preparation of 6-(methoxymethyl)pyrazolo[1,5-a]pyridine-3-carboxylic acid (E72)

[0382] To a solution of methyl 6-(methoxymethyl)pyrazolo[1,5-a]pyridine-3-carboxylate (E71) (1.8 g, 8.17 mmol) in MeOH (40 mL) and H₂O (40 mL) was added NaOH (719 mg, 18.0 mmol), and the reaction mixture was stirred at 40° C. for 12 hrs. Reaction progress was checked using LCMS. The reaction mixture was concentrated to remove MeOH, and then H₂O (10 mL) was added. The pH of the aqueous mixture was adjusted to

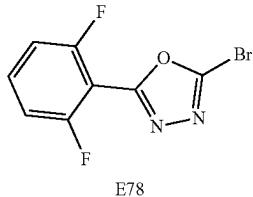
[0383] 6 by the addition of 0.5 M HCl, and the aqueous mixture was filtered. The precipitate was dried in vacuo to give E72 (1.6 g, 94.9% yield). ¹H NMR (400 MHz,

CDCl₃) δ 8.57 (s, 1H), 8.45-8.51 (m, 1H), 8.21 (d, 1H), 7.48 (dd, 1H), 4.55 (s, 2H), 3.48 (s, 3H); LCMS: m/z 206.7 [M+H]⁺.

Intermediate E78 According to General Scheme 9,
Method A



-continued



Step A: Preparation of 2,6-difluorobenzohydrazide (E73)

[0384] To a solution of methyl 2,6-difluorobenzoate (25 g, 145 mmol) in MeOH (250 mL) was added $\text{NH}_2\text{NH}_2\cdot\text{H}_2\text{O}$ (18.18 g, 363 mmol, 17.7 mL), and the reaction mixture was stirred at 60° C. for 12 hrs. Reaction progress was checked using TLC. Additional $\text{NH}_2\text{NH}_2\cdot\text{H}_2\text{O}$ (7.27 g, 145 mmol, 7.05 mL) was added, and the reaction mixture was stirred at 60° C. for another 3 hrs. The reaction mixture was concentrated in vacuo to give E73 (25 g), which was used without further purification. ^1H NMR (400 MHz, CDCl_3) δ 7.37 (s, 1H), 6.93 (t, 2H), 3.45-3.89 (m, 2H).

Step B: Preparation of methyl 2-[2-(2,6-difluorobenzoyl)hydrazino]-2-oxo-acetate (E74)

[0385] To a solution of 2,6-difluorobenzohydrazide (E73) (25 g, 145 mmol) in THF (250 mL) was added methyl 2-chloro-2-oxo-acetate (19.57 g, 160 mmol, 14.7 mL) at 0° C., and the reaction mixture was stirred at 0° C. for 1 hr. Reaction progress was checked using TLC. The reaction mixture was filtered. The precipitate was washed with MTBE (800 mL), and then dried in vacuo to give E74 (37 g). ^1H NMR (400 MHz, DMSO-d_6) δ 7.59 (ddd, 2H), 7.21 (t, 1H), 3.83 (s, 2H).

Step C: Preparation of methyl 5-(2,6-difluorophenyl)-1,3,4-oxadiazole-2-carboxylate (E75)

[0386] To a solution of methyl 2-[2-(2,6-difluorobenzoyl)hydrazino]-2-oxo-acetate (E74) (15 g, 58.1 mmol) in DCM (250 mL) was added Et_3N (23.52 g, 232 mmol, 32.4 mL) and TosCl (14.40 g, 75.5 mmol) in portions at 0° C. The reaction mixture was allowed to warm to rt and stirred at rt for 12 hrs. Reaction progress was checked using TLC. DCM (100 mL) was added to the reaction mixture, and the organic layer was washed with sat. aq. NaHCO_3 (100 mL) and water (100 mL), dried over Na_2SO_4 , filtered, and concentrated to dryness. The residue was purified by column chromatography (SiO_2 , PE/EtOAc=1/0 to 1/1) to give E75 (4.3 g, 30.8% yield). ^1H NMR (400 MHz, CDCl_3) δ 7.61 (tt, 1H), 7.14 (t, 2H), 4.10 (s, 3H).

Step D: Preparation of 5-(2,6-difluorophenyl)-1,3,4-oxadiazole-2-carboxylic acid (E76)

[0387] To a solution of methyl 5-(2,6-difluorophenyl)-1,3,4-oxadiazole-2-carboxylate (E75) (300 mg, 1.25 mmol) in H_2O (2 mL) and THF (4 mL) was added $\text{LiOH}\cdot\text{H}_2\text{O}$ (52.4 mg, 1.25 mmol). The reaction mixture was stirred at rt for 1 hr. Reaction progress was checked using LCMS. The reac-

tion mixture was concentrated in vacuo to give E76 (300 mg), which was used without further purification. LCMS: m/z 226.8 [M+H]⁺

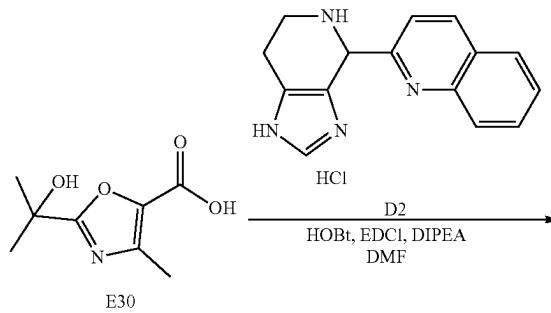
Step E: Preparation of 2-(2,6-difluorophenyl)-1,3,4-oxadiazole (E77)

[0388] To a solution of 5-(2,6-difluorophenyl)-1,3,4-oxadiazole-2-carboxylic acid (E76) (4 g, 17.7 mmol) in H_2O (20 mL) was added HCl (1 M, 35.4 mL), and the reaction mixture was stirred at rt for 1 hr. Reaction progress was checked using LCMS and TLC. DCM (60 mL) was added to the reaction mixture, and the organic layer washed by water (20 mL), dried over Na_2SO_4 , filtered, and concentrated to dryness. The residue was purified by column chromatography (SiO_2 , PE/EtOAc=1/0 to 1/1) to give E77 (1.5 g, 46.6% yield). ^1H NMR (400 MHz, CDCl_3) δ 8.63 (s, 1H), 7.57 (tt, 1H), 7.12 (t, 2H); LCMS: m/z 182.8 [M+H]⁺.

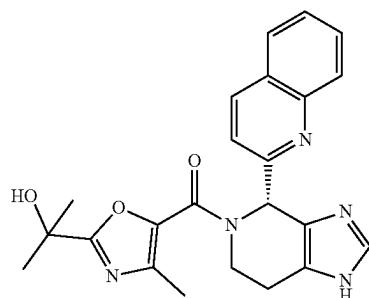
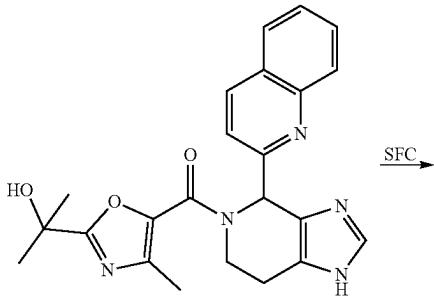
Step F: Preparation of 2-bromo-5-(2,6-difluorophenyl)-1,3,4-oxadiazole (E78)

[0389] To a solution of 2-(2,6-difluorophenyl)-1,3,4-oxadiazole (E77) (1.5 g, 8.24 mmol) in THF (50 mL) was added LiHMDS (1 M, 16.5 mL) dropwise at -78° C. The reaction mixture was stirred at -78° C. for 30 min, then Br_2 (2.63 g, 16.5 mmol, 849 μL) was added to the reaction mixture at -78° C. dropwise. The reaction mixture was stirred at -78° C. for 2 hrs. Reaction progress was checked using TLC. Sat. aq. NH_4Cl (100 mL) was added to the reaction mixture, and the aqueous portion extracted with DCM (3 \times 50 mL). The combined organic layer was washed with brine (40 mL), dried over Na_2SO_4 , filtered and concentrated to dryness. The residue was purified by column chromatography (SiO_2 , PE/EtOAc=1/0 to 3/1) to give E78 (1.6 g, 54.2% yield). ^1H NMR (400 MHz, DMSO-d_6) δ 7.79 (tt, 1H), 7.41 (t, 2H); LCMS: m/z 341.2 [M+H]⁺.

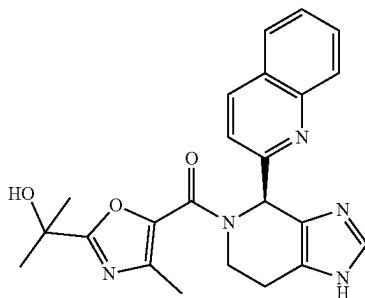
Preparation of Examples 13 and 14 According to General Scheme 1, Method C



-continued



Example 13



Example 14

Step 1: Preparation of 2-(2-hydroxypropan-2-yl)-4-methyloxazol-5-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone

[0390] To a solution of E30 (3 g, 16.2 mmol) in DMF (100 mL) was added 2-(4,5,6,7-tetrahydro-1H-imidazo[4,5-c]

pyridin-4-yl)quinoline hydrochloride (5.24 g, 16.2 mmol, 2HCl salt), EDCI (4.66 g, 24.3 mmol, 1.5 eq), HOt (3.28 g, 24.3 mmol, 1.5 eq) and DIPEA (6.28 g, 48.6 mmol, 8.5 mL, 3 eq). The reaction mixture was stirred at rt for 1.5 hrs. Reaction progress was checked using LCMS. Water (500 mL) was added, and the aqueous portion extracted with EtOAc (300 mL×5). The combined organic layer was washed with brine (300 mL), dried over Na₂SO₄, filtered, and concentrated to dryness. The residue was purified by column chromatography (SiO₂, DCM:MeOH=1/0 to 10/1) to give 2-(2-hydroxypropan-2-yl)-4-methyloxazol-5-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone (2.8 g). LC-MS: m/z 418.1 (M+H)⁺.

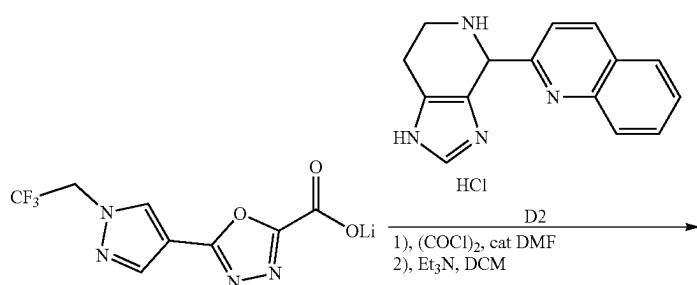
Step 2: SFC Separation

[0391] 2-(2-hydroxypropan-2-yl)-4-methyloxazol-5-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone (3.3 g) was separated by SFC (column: DAICEL CHIRALPAK AD(250 mm*30 mm, 10 μm); mobile phase: [0.1% NH₃H₂O IPA]; B %: 50%-50%, min) to afford Enantiomer 1 (1.21 g, Rt=1.836 min) and Enantiomer 2 (1.23 g, Rt=2.495 min).

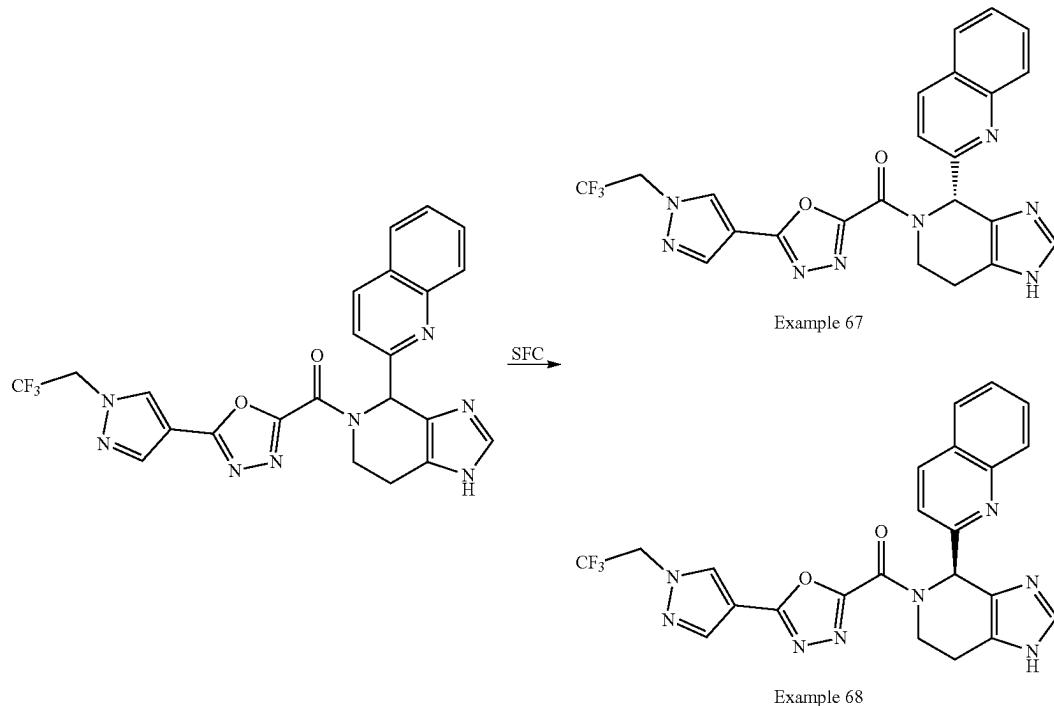
[0392] Enantiomer 1 (Example 13): (R)-(2-(2-hydroxypropan-2-yl)-4-methyloxazol-5-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone. ¹H NMR (400 MHz, CD₃OD) δ 8.30 (br d, 1H), 7.99 (br d, 1H), 7.89 (d, 1H), 7.62-7.82 (m, 3H), 7.49-7.59 (m, 1H), 6.37-6.83 (m, 1H), 4.40 (br s, 0.5H), 3.96 (br s, 0.5H), 3.47 (br s, 1H), 3.12 (br s, 1H), 2.80 (br d, 1H), 2.33 (br s, 3H), 1.21-1.76 (m, 6H); LCMS: m/z 418.2 (M+H)⁺; SFC: 96.7% ee.

[0393] Enantiomer 2 (Example 14): (S)-(2-(2-hydroxypropan-2-yl)-4-methyloxazol-5-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone. ¹H NMR (400 MHz, CD₃OD) δ 8.33 (d, 1H), 8.03 (d, 1H), 7.92 (d, 1H), 7.65-7.86 (m, 3H), 7.51-7.63 (m, 1H), 6.42-6.86 (m, 1H), 4.45 (br s, 0.5H), 4.01 (br s, 0.5H), 3.35-3.67 (m, 1H), 3.15 (br s, 1H), 2.83 (br d, 1H), 2.37 (br s, 3H), 1.29-1.77 (m, 6H); LCMS: m/z 418.1 (M+H)⁺; SFC: 98.0% ee.

Preparation of Examples 67 and 68 According to General Scheme 1, Method D



-continued



Step 1: Preparation of [4-(2-quinolyl)-1,4,6,7-tetrahydroimidazo[4,5-c]pyridin-5-yl]-[5-[1-(2,2,2-trifluoroethyl)pyrazol-4-yl]-1,3,4-oxadiazol-2-yl]methanone

[0394] To a solution of [5-[1-(2,2,2-trifluoroethyl)pyrazol-4-yl]-1,3,4-oxadiazole-2-carbonyl]oxylithium (E38) (300 mg, 1.12 mmol) and DMF (8.18 mg, 112 μ mol, 8.6 μ L, 0.1 eq) in DCM (6 mL) was added oxalyl chloride (568 mg, 4.48 mmol, 392 μ L, 4 eq) dropwise at 0° C., and then the reaction mixture was stirred at rt for 1 hr. The reaction mixture was concentrated to dryness to give a residue (410 mg), which was used without further purification.

[0395] To a solution of 2-(4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine-4-yl)quinoline (D2) (300 mg, 928 μ mol, 2HCl salt) in DCM (10 mL) was added Et₃N (470 mg, 4.64 mmol, 646 μ L, 5 eq), followed by 5-[1-(2,2,2-trifluoroethyl)pyrazol-4-yl]-1,3,4-oxadiazole-2-carbonyl chloride (391 mg, 1.39 mmol, 1.5 eq) at 0° C. The reaction mixture was stirred at rt for 2 hrs. Reaction progress was checked using LCMS. The reaction mixture was concentrated to dryness, and the residue was purified with prep-HPLC (column: Agela DuraShell C18 150*40 mm*5 μ m; mobile phase: [water (0.05% ammonia hydroxide v/v)-ACN]; B %: 22%-62%, 9 min) to give [4-(2-quinolyl)-1,4,6,7-tetrahydroimidazo[4,5-c]pyridin-5-yl]-[5-[1-(2,2,2-trifluoroethyl)pyrazol-4-yl]-1,3,4-oxadiazol-2-yl]methanone (110 mg, 24% yield). LC-MS: m/z 495.3 (M+H)⁺.

Step 2: SFC Separation

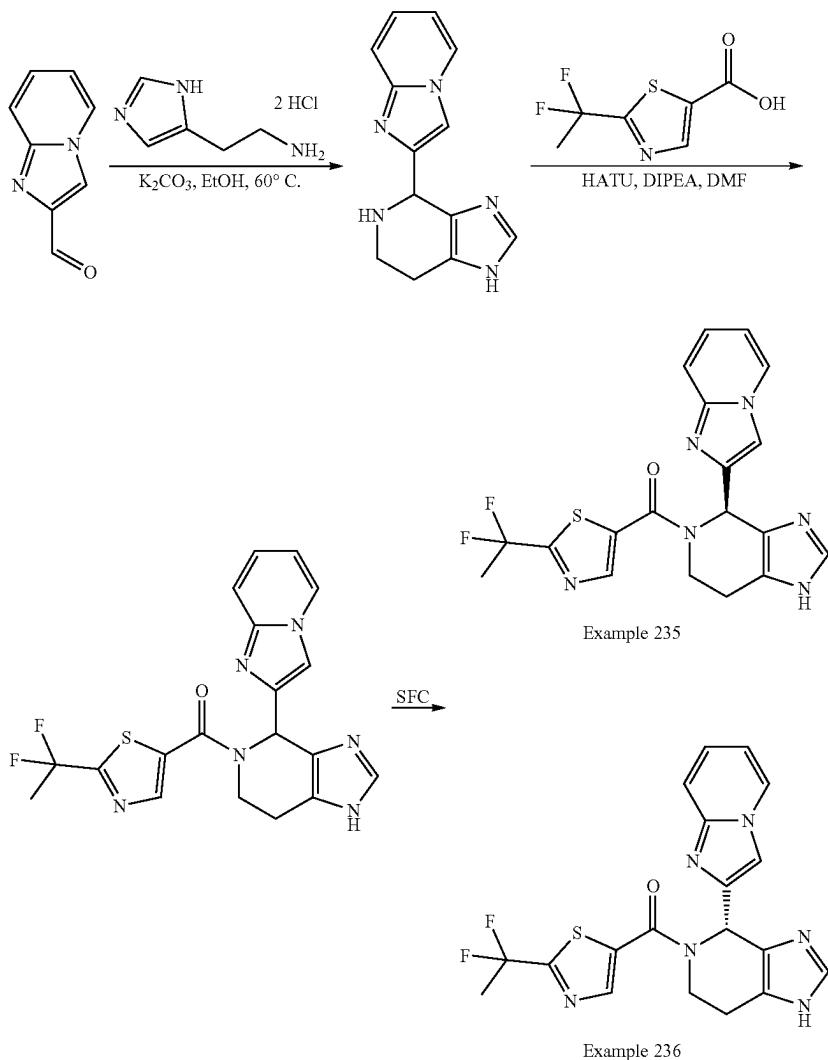
[0396] [4-(2-quinolyl)-1,4,6,7-tetrahydroimidazo[4,5-c]pyridin-5-yl]-[5-[1-(2,2,2-trifluoroethyl)pyrazol-4-yl]-1,3,4-oxadiazol-2-yl]methanone (100 mg) was separated by SFC (column DAICEL CHIRALPAK IC(250 mm*30 mm, 10 μ m); mobile phase: [0.1% NH₃H₂O MEOH]; B %: 40%-40%, min) to afford Enantiomer 1 (41.2 mg, 40% yield, Rt=2.402 min) and Enantiomer 2 (43 mg, 43% yield, Rt=3.496 min).

[0397] Enantiomer 1 (Example 67): [(4R)-4-(2-quinolyl)-1,4,6,7-tetrahydroimidazo[4,5-c]pyridin-5-yl]-[5-[1-(2,2,2-trifluoroethyl)pyrazol-4-yl]-1,3,4-oxadiazol-2-yl]methanone. ¹H NMR (400 MHz, CD₃OD) δ 8.51-8.62 (m, 1H), 8.24-8.39 (m, 1H), 8.12-8.24 (m, 1H), 8.01 (d, 0.7H), 7.89 (br dd, 2H), 7.62-7.77 (m, 2.4H), 7.49-7.60 (m, 1H), 7.40 (s, 0.3H), 6.88 (br s, 0.6H), 5.06-5.20 (m, 2.7H), 4.99-5.06 (m, 0.3H), 4.05 (br s, 0.6H), 3.41 (td, 0.4H), 3.11-3.24 (m, 0.7H), 2.94-3.08 (m, 0.3H), 2.78-2.92 (m, 1H); LC-MS: 495.2 (M+H)⁺; SFC: 99.7% ee.

[0398] Enantiomer 2 (Example 68): [(4S)-4-(2-quinolyl)-1,4,6,7-tetrahydroimidazo[4,5-c]pyridin-5-yl]-[5-[1-(2,2,2-trifluoroethyl)pyrazol-4-yl]-1,3,4-oxadiazol-2-yl]methanone. ¹H NMR (400 MHz, CD₃OD) δ 8.53-8.62 (m, 1H), 8.24-8.39 (m, 1H), 8.12-8.24 (m, 1H), 8.01 (d, 0.6H), 7.87 (td, 2H), 7.61-7.78 (m, 2.4H), 7.48-7.61 (m, 1H), 7.40 (s, 0.4H), 6.88 (s, 0.6H), 5.06-5.22 (m, 2.7H), 5.01 (br dd, 0.3H), 3.97-4.12 (m, 0.6H), 3.40 (td, 0.4H), 3.13-3.26 (m, 0.6H), 2.94-3.08 (m, 0.4H), 2.78-2.93 (m, 1H); LC-MS: 495.3 (M+H)⁺; SFC: 98.6% ee.

Preparation of Examples 235 and 236 According to General Scheme 1, Method C

7.12-7.16 (m, 1H), 6.78-6.81 (m, 1H), 4.99 (s, 1H), 2.85-3.02 (m, 2H), 2.44-2.50 (m, 2H); LCMS: m/z 240.2 [M+H]⁺.



Step 1: Preparation of 4-imidazo[1,2-a]pyridin-2-yl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine

[0399] A mixture of imidazo[1,2-a]pyridine-2-carbaldehyde (2 g, 13.7 mmol), 2-(1H-imidazol-5-yl)ethanamine (2.13 g, 19.2 mmol, 1.4 eq) and K₂CO₃ (3.78 g, 27.4 mmol, 2 eq) in EtOH (30 mL) was degassed and purged with N₂ for 3 times, and then the reaction mixture was stirred at 80° C. for 16 hrs under N₂ atmosphere. The reaction mixture was filtered, and the filtrate was concentrated to dryness. The residue was purified by flash silica gel chromatography (ISCO®; 20 g SepaFlash® Silica Flash Column, Eluent of 0-20% DCM/MeOH @40 mL/min) to give compound 4-imidazo[1,2-a]pyridin-2-yl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine (2.3 g, 70% yield). ¹H NMR (400 MHz, DMSO-d₆) δ 8.44 (d, 1H), 7.61 (s, 1H), 7.38-7.46 (m, 2H),

Step 2: Preparation of [2-(1,1-difluoroethyl)thiazol-5-yl]-[4-imidazo[1,2-a]pyridin-2-yl-1,4,6,7-tetrahydroimidazo[4,5-c]pyridin-5-yl]methanone

[0400] To a solution of 4-imidazo[1,2-a]pyridin-2-yl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine (3.5 g, 14.6 mmol) and 2-(1,1-difluoroethyl)thiazole-5-carboxylic acid (2.83 g, 14.6 mmol) in DMF (40 mL) was added HATU (6.67 g, 17.6 mmol, 1.2 eq) and DIPEA (2.27 g, 17.6 mmol, 3.1 mL, 1.2 eq). The reaction mixture was stirred at rt for 10 hrs. The reaction mixture was combined with another 500 mg batch reaction, and DCM (200 mL) was added. The organic layer was washed with sat. NaHCO₃ solution (50 mL×3) and brine (100 mL), dried over Na₂SO₄, filtered, and concentrated to dryness. The residue was purified by flash silica gel chromatography (ISCO®; 40 g SepaFlash® Silica Flash Column, Eluent of 0-10% DCM/MeOH@50 mL/min) to give compound [2-(1,1-difluoroethyl)thiazol-5-yl]-[4-

imidazo[1,2-a]pyridin-2-yl-1,4,6,7-tetrahydroimidazo[4,5-c]pyridin-5-yl)methanone (3.9 g, 56% yield). LCMS: m/z 415.1 [M+H]⁺.

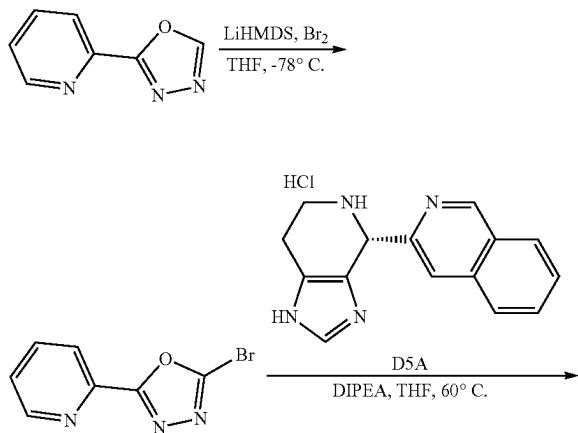
Step 3: SFC Separation

[0401] [2-(1,1-difluoroethyl)thiazol-5-yl]-4(imidazo[1,2-a]pyridin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone (3.9 g) was separated by SFC (column: DAI-CEL CHIRALPAK AD(250 mm*30 mm, 10 μ m); mobile phase: [0.1% NH₃H₂O ETOH]:B %: 40%-40%, min) to afford Enantiomer 1 (Rt=1.586 min, 1.53 g, 78% yield) and Enantiomer 2 (Rt=2.332 min, 1.31 g, 66% yield).

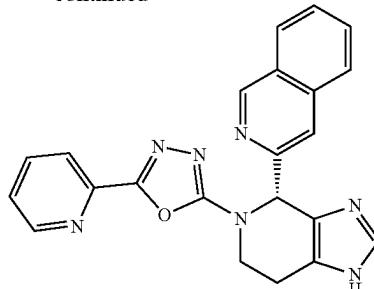
[0402] Enantiomer 1 (Example 235): (S)-(2-(1,1-difluoroethyl)thiazol-5-yl)(4-(imidazo[1,2-a]pyridin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone. ¹H NMR (400 MHz, CD₃OD) δ 8.02-8.93 (m, 2H), 7.43-7.89 (m, 3H), 7.31 (br t, 1H), 6.71-7.01 (m, 1.6H), 6.19-6.55 (m, 0.4H), 4.70 (br s, 1H), 4.22 (br s, 0.5H), 3.79 (br s, 0.5H), 2.98-3.10 (m, 1H), 2.62-2.92 (m, 1H), 2.12 (t, 3H); LCMS: m/z 415.1 [M+H]⁺; SFC: 98.2% ee.

[0403] Enantiomer 2 (Example 236): (R)-(2-(1,1-difluoroethyl)thiazol-5-yl)(4-(imidazo[1,2-a]pyridin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone. ¹H NMR (400 MHz, CD₃OD) δ 8.09-8.97 (m, 2H), 7.92 (br s, 2H), 7.55 (br d, 1H), 7.20-7.41 (m, 1H), 6.36-7.02 (m, 2H), 4.10-4.55 (m, 1H), 3.77 (br s, 1H), 2.99-3.16 (m, 1H), 2.70-2.91 (m, 1H), 2.12 (t, 3H); LCMS: m/z 415.1 [M+H]⁺; SFC: 96.5% ee.

Preparation of Example 365 According to General Scheme 1, Method A1



-continued



Example 365

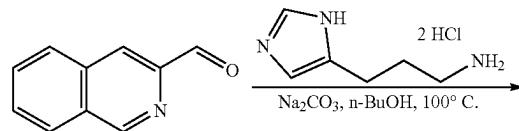
Step 1: Preparation of 2-bromo-5-(pyridin-2-yl)-1,3,4-oxadiazole

[0404] To a solution of 2-(2-pyridyl)-1,3,4-oxadiazole (450 mg, 3.06 mmol) in THF (15 mL) was added LiHMDS (1 M, 6.1 mL, 2 eq) dropwise at -78° C. After stirring for 1 hr, Br₂ (978 mg, 6.12 mmol, 315 μ L, 2 eq) was added and the reaction mixture was stirred at -78° C. for 2 hrs. Reaction progress was tracked by LCMS. Water (15 mL) was added, and the aqueous portion extracted with DCM (50 mL×3). The combined organic layer was washed with brine (20 mL), dried over Na₂SO₄, filtered, and concentrated to dryness. The residue was purified by flash silica gel chromatography (ISCO®; 4 g Sepa Flash® Silica Flash Column, Eluent of 0-20% EtOAc/PE gradient @25 mL/min) to give 2-bromo-5-(2-pyridyl)-1,3,4-oxadiazole (400 mg, 58% yield). ¹H NMR (400 MHz, DMSO-d₆) δ 8.75 (br d, 1H), 8.13 (d, 1H), 8.03 (br t, 1H), 7.57-7.67 (m, 1H); LCMS: m/z 228.1 [M+H]⁺.

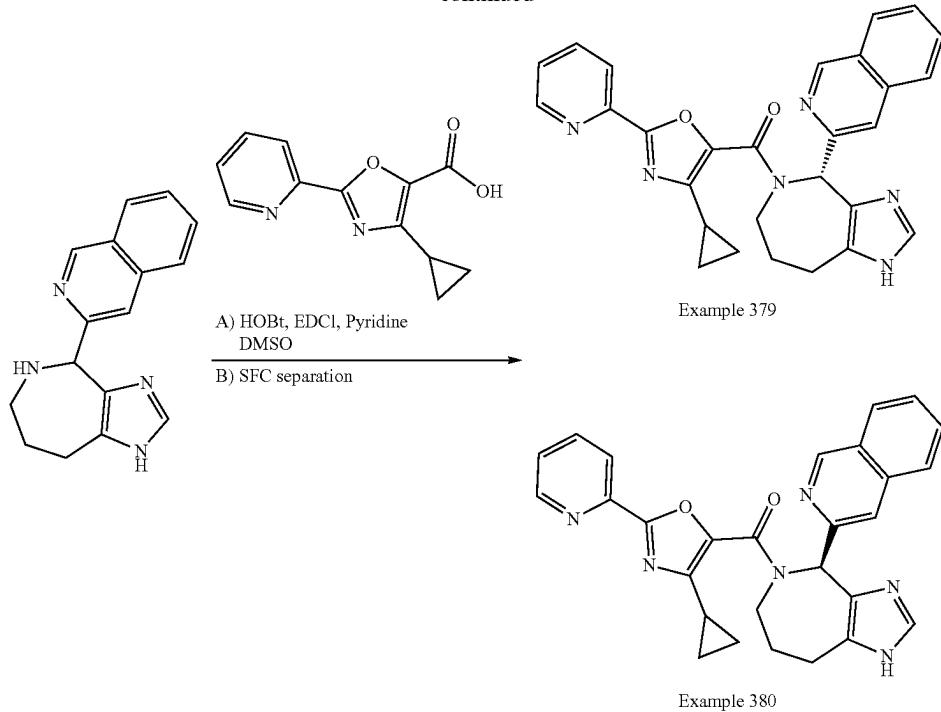
Step 2: Preparation of (R)-2-(4-(isoquinolin-3-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)-5-(pyridin-2-yl)-1,3,4-oxadiazole (Example 365)

[0405] To a solution of 3-[(4R)-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridin-4-yl]isoquinoline (D5A) (70 mg, 217 μ mol, 2HCl) and 2-bromo-5-(2-pyridyl)-1,3,4-oxadiazole (58.7 mg, 260 μ mol, 1.2 eq) in DMF (1 mL) was added DIPEA (140 mg, 1.08 mmol, 189 μ L, 5 eq). The reaction mixture was stirred at 40° C. for 12 hrs. Reaction progress was checked using LCMS. Water (30 mL) was added, and the aqueous portion was extracted with DCM (40 mL×3). The combined organic layer was washed with brine (30 mL), dried over Na₂SO₄, filtered, and concentrated to dryness. The residue was purified by prep_HPLC(column: Phenomenex Gemini-NX C18 75*30 mm*3 μ m; mobile phase: [water(0.04% NH₃H₂O+10 mM NH₄HCO₃)-ACN]:B %: 18%-48%, 8 min) to give Example 365 (33.9 mg, 38% yield). ¹H NMR (400 MHz, CD₃OD) δ 9.22 (s, 1H), 8.70 (d, 1H), 8.13 (d, 1H), 8.08 (d, 1H), 8.01 (td, 1H), 7.91-7.97 (m, 2H), 7.75-7.82 (m, 1H), 7.65-7.73 (m, 2H), 7.55 (ddd, 1H), 6.48 (s, 1H), 4.47 (br dd, 1H), 3.90-4.01 (m, 1H), 3.07-3.19 (m, 1H), 2.89 (br dd, 1H); LCMS: m/z 396.1 [M+H]⁺; SFC: 97.2% ee.

Preparation of Examples 379 and 380 According to General Scheme 1, Method C



-continued



Step 1: Preparation of 4-(isoquinolin-3-yl)-1,4,5,6,7,8-hexahydroimidazo[4,5-c]azepine

[0406] To a solution of isoquinoline-3-carbaldehyde (200 mg, 1.27 mmol) and 3-(1H-imidazol-5-yl)propan-1-amine (252 mg, 1.27 mmol, 2HCl) in n-BuOH (8 mL) was added Na₂CO₃ (405 mg, 3.82 mmol, 3 eq). The reaction mixture was stirred at 100° C. for 12 hrs. Reaction progress was checked using LCMS. The reaction mixture (combined with another reaction using 50 mg aldehyde) was filtered, and the filtrate was concentrated to dryness. The residue was submitted to prep HPLC (column: Boston Prime C18 150*30 mm*5 um; mobile phase: [water(0.04% NH₃H₂O+10 mM NH₄HCO₃)-ACN];B %: 10%-40%, 7 min) to give compound [4-cyclopropyl-2-(2-pyridyl)oxazol-5-yl]-[4-(3-isoquinolyl)-1,4,5,6,7,8-hexahydroimidazo[4,5-c]azepine (300 mg, 71% yield). ¹H NMR (400 MHz, CD₃OD) δ 9.30 (s, 1H), 8.12 (d, 1H), 7.84-7.89 (m, 1H), 7.77 (t, 1H), 7.65-7.72 (m, 1H), 7.48 (s, 1H), 7.38 (s, 1H), 5.37 (s, 1H), 2.99-3.07 (m, 1H), 2.80-2.98 (m, 3H), 1.83-1.99 (m, 2H); LCMS: m/z 265.2 [M+H]⁺.

Step 2A: Preparation of [4-cyclopropyl-2-(2-pyridyl)oxazol-5-yl]-[4-(3-isoquinolyl)-4,6,7,8-tetrahydro-1H-imidazo[4,5-c]azepin-5-yl]methanone

[0407] To a solution of 4-(3-isoquinolyl)-1,4,5,6,7,8-hexahydroimidazo[4,5-c]azepine (100 mg, 378 μmol) and 4-cyclopropyl-2-(2-pyridyl)oxazole-5-carboxylic acid (95.8 mg, 416 μmol, 1.1 eq) in DMSO (2 mL) was added EDCI (94.3 mg, 492 μmol, 1.3 eq), pyridine (120 mg, 1.51 mmol, 122 μL, 4 eq) and HOBT (66.5 mg, 492 μmol, 1.3 eq). The reaction mixture was stirred at rt for 12 hrs. Reaction progress was checked using LCMS. Water (15 mL) was added, and the aqueous portion extracted with DCM (40 mL×3). The combined organic layer was washed with brine

(20 mL), dried over Na₂SO₄, filtered, and concentrated to dryness. The residue was purified by prep HPLC (column: Boston Prime C18 150*30 mm*5 um; mobile phase: [water (0.04% NH₃H₂O+10 mM NH₄HCO₃)-ACN];B %: 20%-50%, 7 min) to give compound [4-cyclopropyl-2-(2-pyridyl)oxazol-5-yl]-[4-(3-isoquinolyl)-4,6,7,8-tetrahydro-1H-imidazo[4,5-c]azepin-5-yl]methanone (120 mg, 66% yield). LCMS: m/z 477.3 [M+H]⁺.

Step 2B: SFC Separation

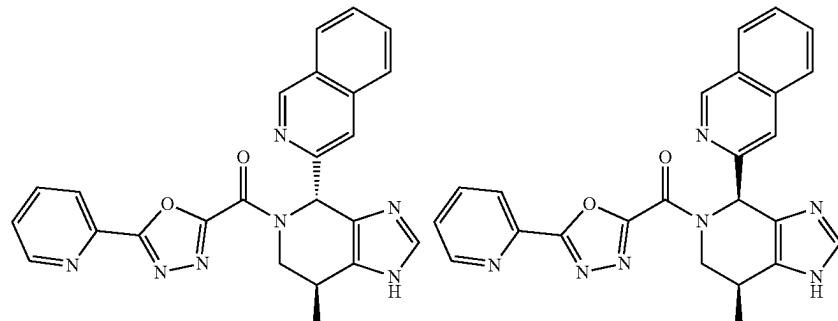
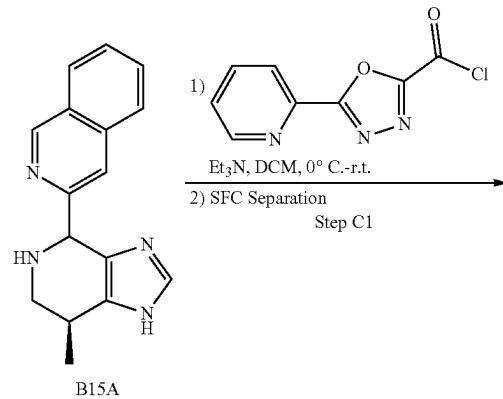
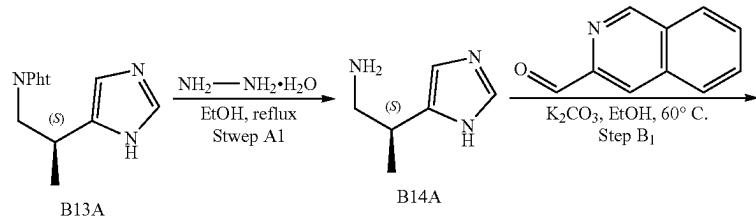
[0408] [4-cyclopropyl-2-(2-pyridyl)oxazol-5-yl]-[4-(3-isoquinolyl)-4,6,7,8-tetrahydro-1H-imidazo[4,5-c]azepin-5-yl]methanone (100 mg) was separated by SFC (column: DAICEL CHIRALPAK AD-H(250 mm*30 mm, 5 um); mobile phase: [0.1% NH₃H₂O ETOH];B %: 45%-45%, min) to afford Enantiomer 1 (47 mg, Rt=0.474 min, 47% yield) and Enantiomer 2 (46.4 mg, Rt=0.861 min, 47% yield).

[0409] Enantiomer 1 (Example 379): (R)-(4-cyclopropyl-2-(pyridin-2-yl)oxazol-5-yl)(4-(isoquinolin-3-yl)-7,8-dihydroimidazo[4,5-c]azepin-5(1H,4H,6H)-yl)methanone. ¹H NMR (400 MHz, CD₃OD) δ 9.30 (d, 1H), 8.68 (d, 1H), 8.09-8.19 (m, 2H), 7.91-8.06 (m, 1H), 7.83-7.90 (m, 1H), 7.79 (br t, 1H), 7.65-7.74 (m, 2H), 7.50-7.58 (m, 1H), 7.43 (br s, 1.5H), 6.92 (s, 0.5H), 4.28-4.56 (m, 1H), 2.84-3.04 (m, 3H), 2.38-2.68 (m, 1H), 1.96-2.21 (m, 2H), 0.78-1.27 (m, 4H); LCMS: m/z 477.2 [M+H]⁺; SFC: 100% ee.

[0410] Enantiomer 2 (Example 380): (S)-(4-cyclopropyl-2-(pyridin-2-yl)oxazol-5-yl)(4-(isoquinolin-3-yl)-7,8-dihydroimidazo[4,5-c]azepin-5(1H,4H,6H)-yl)methanone. ¹H NMR (400 MHz, CD₃OD) δ 9.30 (d, 1H), 8.68 (d, 1H), 8.09-8.20 (m, 2H), 7.93-8.03 (m, 1H), 7.83-7.90 (m, 1H), 7.79 (br t, 1H), 7.65-7.74 (m, 2H), 7.51-7.58 (m, 1H), 7.43 (br s, 1.5H), 6.92 (s, 0.5H), 4.28-4.54 (m, 1H), 2.85-3.03 (m,

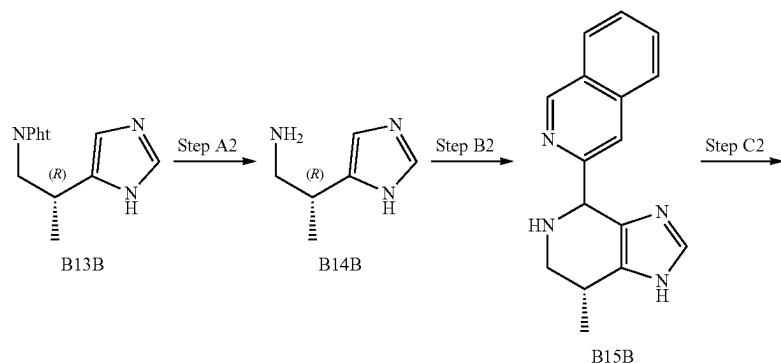
3H), 2.39-2.69 (m, 1H), 2.00-2.22 (m, 2H), 0.88-1.24 (m, 4H); LCMS: m/z 477.2 [M+H]⁺; SFC: 99.7% ee.

Preparation of Examples 385, 386, 387, and 388,
According to General Scheme 1, Method D

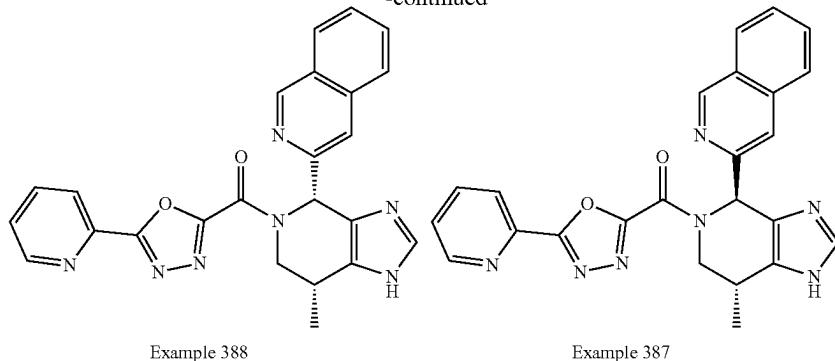


Example 385

Example 386



-continued



Step A1: Preparation of (2S)-2-(1H-imidazol-4-yl)propan-1-amine (B14A)

[0411] To a solution of 2-[(2S)-2-(1H-imidazol-4-yl)propyl]isoindoline-1,3-dione (B13A) (5 g, 19.6 mmol) in EtOH (250 mL) was added $\text{N}_2\text{H}_4 \cdot \text{H}_2\text{O}$ (5.00 g, 97.9 mmol, 4.9 mL, 98% purity, 5 eq). The mixture was stirred at 75° C. for 16 hrs. Reaction progress was checked using TLC (DCM: MeOH=10:1). The reaction mixture was filtered, and the filtrate was concentrated to dryness to afford B14A (2.5 g), which was used without further purification. ^1H NMR (400 MHz, DMSO- d_6) δ 7.50 (s, 1H), 6.73 (s, 1H), 2.56-2.79 (m, 3H), 1.15 (d, 3H).

Step A2: Preparation of (2R)-2-(1H-imidazol-5-yl)propan-1-amine (B14B)

[0412] (2R)-2-(1H-imidazol-5-yl)propan-1-amine (B14B) (2.6 g) was prepared following the procedure of Step A1, starting with 2-[(2R)-2-(1H-imidazol-5-yl)propyl]isoindoline-1,3-dione. ^1H NMR (400 MHz, DMSO- d_6) δ 7.50 (s, 1H), 6.72 (s, 1H), 2.63-2.77 (m, 2H), 2.54-2.61 (m, 1H), 1.15 (d, 3H).

Step B1: Preparation of 3-[(7S)-7-methyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridin-4-yl]isoquinoline (B15A)

[0413] To a solution of (2S)-2-(1H-imidazol-5-yl)propan-1-amine (600 mg, 4.79 mmol) and isoquinoline-3-carbaldehyde (753 mg, 4.79 mmol) in EtOH (15 mL) was added K_2CO_3 (1.99 g, 14.4 mmol, 3 eq). The reaction mixture was stirred at 80° C. for 16 hrs. Reaction progress was checked using LCMS. The reaction mixture was filtered, and the filtrate was concentrated to dryness. The residue was purified by flash silica gel chromatography (ISCO®; 12 g SepaFlash® Silica Flash Column, Eluent of 0-10% DCM: MeOH @30 mL/min) to give B15A (1.2 g, 90% yield). LCMS: m/z 265.2 [M+H] $^+$.

Step B2: Preparation of 3-[(7R)-7-methyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridin-4-yl]isoquinoline (B15B)

[0414] To a solution of (2R)-2-(1H-imidazol-5-yl)propan-1-amine (600 mg, 4.79 mmol) and isoquinoline-3-carbaldehyde (753 mg, 4.79 mmol) in EtOH (20 mL) was added K_2CO_3 (1.99 g, 14.4 mmol, 3 eq). The mixture was stirred at 80° C. for 12 hrs. Reaction progress was checked using

LCMS. The reaction mixture was filtered, and the precipitate was rinsed with EtOAc (100 mL). The filtrate was washed with water (30 mL) and brine (20 mL). The organic layer was dried over Na_2SO_4 , filtered, and concentrated to dryness. The residue was purified by column chromatography on silica gel (DCM:MeOH=20:1 to 10:1) to give B15B (1.05 g, 81% yield). ^1H NMR (400 MHz, DMSO- d_6) δ 11.94 (br s, 1H), 9.19-9.39 (m, 1H), 8.11 (d, 1H), 7.92 (br d, 1H), 7.61-7.82 (m, 3H), 7.33-7.50 (m, 1H), 5.10 (br s, 1H), 3.18-3.24 (m, 1H), 2.87 (br s, 1H), 2.53-2.59 (m, 1H), 1.18 (d, 3H); LCMS: m/z 265.2 [M+H] $^+$.

Step C1: Preparation of (4R,7S)-4-(isoquinolin-3-yl)-7-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(5-(pyridin-2-yl)-1,3,4-oxadiazol-2-yl)methanone and ((4S,7S)-4-(isoquinolin-3-yl)-7-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(5-(pyridin-2-yl)-1,3,4-oxadiazol-2-yl)methanone

[0415] To a solution of 3-[(7S)-7-methyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridin-4-yl]isoquinoline (B15A) (120 mg, 454 μ mol) in DCM (3 mL) was added TEA (230 mg, 2.27 mmol, 316 μ L, 5 eq), and then 5-(2-pyridyl)-1,3,4-oxadiazole-2-carbonyl chloride (190 mg, 908 μ mol, 2 eq) was added at 0° C. The reaction mixture was stirred at rt for 2 hrs. Reaction progress was checked using LCMS. Water (10 mL) was added, and the aqueous portion extracted with DCM (40 mL×3). The combined organic layer was washed with brine (40 mL), dried over Na_2SO_4 , filtered, and concentrated to dryness. The residue was purified by prep-HPLC(column: Boston Prime C18 150*30 mm*5 um; mobile phase: [water(0.05% $\text{NH}_3\text{H}_2\text{O} + 10\text{ mM NH}_4\text{HCO}_3$)-ACN]; B %: 30%-60%, 7 min) to give compound [(7S)-4-(3-isoquinolyl)-7-methyl-1,4,6,7-tetrahydroimidazo[4,5-c]pyridin-5-yl]-[5-(2-pyridyl)-1,3,4-oxadiazol-2-yl]methanone (100 mg, 49% yield).

[0416] SFC Separation: Compound [(7S)-4-(3-isoquinolyl)-7-methyl-1,4,6,7-tetrahydroimidazo[4,5-c]pyridin-5-yl]-[5-(2-pyridyl)-1,3,4-oxadiazol-2-yl]methanone (100 mg) was separated by SFC (column: DAICEL CHIRALCEL OD-H(250 mm*30 mm, 5 um);mobile phase: [0.1% $\text{NH}_3\text{H}_2\text{O}$ ETOH]; B %: 40%-40%, min) to afford Diastereomer 1 (Rt=3.954 min, 63.9 mg, 65% yield) and Diastereomer 2 (Rt=4.405 min, 15.9 mg, 16% yield).

[0417] Diastereomer 1 (Example 385): (4R,7S)-4-(isoquinolin-3-yl)-7-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(5-(pyridin-2-yl)-1,3,4-oxadiazol-2-yl)metha-

none. ¹H NMR (400 MHz, CD₃OD) δ 9.10-9.26 (m, 1H), 8.79 (dd, 1H), 8.32 (dd, 1H), 8.01-8.16 (m, 2H), 7.94-8.00 (m, 1H), 7.59-7.86 (m, 5H), 7.47 (s, 0.5H), 6.95 (s, 0.5H), 4.96 (br d, 0.5H), 4.69 (br d, 0.5H), 4.23 (dd, 0.5H), 3.38 (br d, 0.5H), 3.22 (br s, 1H), 1.38 (dd, 3H); LCMS: m/z 438.2 [M+H]⁺; SFC: 99.4% ee.

[0418] Diastereomer 2 (Example 386): ((4S,7S)-4-(isoquinolin-3-yl)-7-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(5-(pyridin-2-yl)-1,3,4-oxadiazol-2-yl)methanone. ¹H NMR (400 MHz, CD₃OD) δ 9.14-9.29 (m, 1H), 8.76-8.83 (m, 1H), 8.29-8.36 (m, 1H), 8.03-8.14 (m, 2H), 7.95-8.01 (m, 1H), 7.65-7.89 (m, 5H), 7.48 (br s, 0.5H), 6.94 (br s, 0.5H), 4.98 (br dd, 1H), 3.55-3.63 (m, 0.6H), 3.43 (br d, 0.4H), 3.17 (br d, 1H), 1.38 (br d, 3H); LCMS: m/z 438.0 [M+H]⁺; SFC: 92.2% ee.

Step C2: Preparation of (4S,7R)-4-(isoquinolin-3-yl)-7-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(5-(pyridin-2-yl)-1,3,4-oxadiazol-2-yl)methanone and (4R,7R)-4-(isoquinolin-3-yl)-7-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(5-(pyridin-2-yl)-1,3,4-oxadiazol-2-yl)methanone

[0419] To a solution of 3-[(7R)-7-methyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridin-4-yl]isoquinoline (120 mg, 454 μmol) and 5-(2-pyridyl)-1,3,4-oxadiazole-2-carbonyl chloride (143 mg, 681 μmol, 1.5 eq) in DCM (10 mL) was added TEA (138 mg, 1.36 mmol, 190 μL, 3 eq). The reaction mixture was stirred at rt for 12 hrs. Reaction progress was checked using LCMS. The reaction mixture was concentrated to dryness, and EtOAc (100 mL) was added to the residue. The organic portion was washed with sat. Na₂CO₃ solution (30 mL) and brine (30 mL), dried over Na₂SO₄, filtered, and concentrated to dryness. The residue

was purified by prep-HPLC(column: Xtimate C18 150*40 mm*10 um; mobile phase: [water(0.05% NH₃H₂O+10 mM NH₄HCO₃)-ACN];B %: 20%-50%, 9 min) to give compound [(7R)-4-(3-isoquinolyl)-7-methyl-1,4,6,7-tetrahydroimidazo[4,5-c]pyridin-5-yl]-[5-(2-pyridyl)-1,3,4-oxadiazol-2-yl]methanone (135 mg, 67% yield).

[0420] SFC Separation: Compound [(7R)-4-(3-isoquinolyl)-7-methyl-1,4,6,7-tetrahydroimidazo[4,5-c]pyridin-5-yl]-[5-(2-pyridyl)-1,3,4-oxadiazol-2-yl]methanone (100 mg) was separated by SFC (column: DAICEL CHIRALPAK AD(250 mm*50 mm, 10 um);mobile phase: [0.1% NH₃H₂O IPA];B %: 50%-50%, min) to afford Diastereomer 1 (Rt=2.117 min, 41.3 mg, 40% yield) and Diastereomer 2 (Rt=2.448 min, 27.9 mg, 27% yield).

[0421] Diastereomer 1 (Example 387): ((4S,7R)-4-(isoquinolin-3-yl)-7-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(5-(pyridin-2-yl)-1,3,4-oxadiazol-2-yl)methanone. ¹H NMR (400 MHz, CD₃OD) δ 9.07-9.29 (m, 1H), 8.78 (dd, 1H), 8.31 (dd, 1H), 7.94-8.13 (m, 3H), 7.73-7.85 (m, 2H), 7.59-7.73 (m, 3H), 7.47 (s, 0.5H), 6.95 (s, 0.5H), 4.68 (br d, 1H), 4.22 (dd, 0.5H), 3.38 (br d, 0.5H), 3.21 (br s, 1H), 1.38 (dd, 3H); LCMS: m/z 438.2 [M+H]⁺; SFC: 99.4% ee.

[0422] Diastereomer 2 (Example 388): ((4R,7R)-4-(isoquinolin-3-yl)-7-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(5-(pyridin-2-yl)-1,3,4-oxadiazol-2-yl)methanone. ¹H NMR (400 MHz, CD₃OD) δ 9.08-9.32 (m, 1H), 8.79 (t, 1H), 8.29-8.34 (m, 1H), 8.02-8.17 (m, 2H), 7.94-8.00 (m, 1H), 7.63-7.89 (m, 5H), 7.48 (s, 0.5H), 6.93 (s, 0.5H), 4.97 (br dd, 1H), 3.38-3.67 (m, 1H), 2.78-3.30 (m, 1H), 1.38 (dd, 3H); LCMS: m/z 438.2 [M+H]⁺; SFC: 97.3% ee.

[0423] The compounds of Tables 1 through 5 were characterized using proton NMR and LCMS and the enantioselective excess determined. See Tables 6 and 7.

TABLE 6

Ex. #	¹ H NMR (400 MHz)	LCMS: m/z	% ee
1	(CD ₃ OD) δ 8.49 (br s, 1 H), 8.23 (br d, 2 H), 8.10 (br d, 1 H), 7.98 (br s, 1 H), 7.83 (br d, 2 H), 7.57-7.72 (m, 3 H), 7.50 (br d, 1 H), 7.38 (br s, 1 H), 6.72 (br s, 1 H), 4.38-4.51 (m, 1 H), 3.50 (br s, 1 H), 2.97 (br s, 1 H), 2.72 (br d, 1 H)	439.0 [M + H] ⁺	99.1%
2	(CD ₃ OD) δ 8.57 (br s, 1 H), 8.31 (br d, 2 H), 8.18 (br d, 1 H), 8.05 (br s, 1 H), 7.86-7.95 (m, 2 H), 7.64-7.78 (m, 3 H), 7.57 (br t, 1 H), 7.40-7.48 (m, 1 H), 6.78 (br s, 1 H), 4.28-4.58 (m, 1 H), 4.04 (br s, 1 H), 3.05 (br s, 1 H), 2.80 (br d, 1 H)	439.0 [M + H] ⁺	93.5%
3	(CD ₃ OD) δ 8.32 (d, 1 H), 8.05 (br s, 2 H), 7.91 (d, 1 H), 7.63-7.85 (m, 3 H), 7.49-7.62 (m, 1 H), 6.72 (br s, 1 H), 4.63 (br s, 1 H), 4.01 (br s, 1 H), 2.94-3.11 (m, 1 H), 2.80 (br d, 1 H), 1.44 (s, 9 H)	418.2 [M + H] ⁺	98.3%
4	(CD ₃ OD) δ 8.32 (d, 1 H), 7.98-8.27 (m, 2 H), 7.92 (d, 1 H), 7.68-7.80 (m, 3 H), 7.53-7.63 (m, 1 H), 6.75 (br s, 1 H), 4.40-4.69 (m, 1 H), 4.00 (br d, 1 H), 2.94-3.11 (m, 1 H), 2.80 (br d, 1 H), 1.45 (s, 9 H)	418.2 [M + H] ⁺	99.3%
5	(CD ₃ OD) δ 9.13 (br s, 1 H), 8.26-8.50 (m, 3 H), 8.03 (br s, 1 H), 7.90 (br d, 1 H), 7.65-7.79 (m, 3 H), 7.52-7.61 (m, 1 H), 6.21-7.03 (m, 1 H), 4.63 (br s, 1 H), 3.44-4.17 (m, 1 H), 2.94-3.14 (m, 1 H), 2.66-2.84 (m, 1 H)	362.0 [M + H] ⁺	99.9%
6	(CD ₃ OD) δ 9.13 (br s, 1 H), 8.26-8.50 (m, 3 H), 8.03 (br s, 1 H), 7.90 (br d, 1 H), 7.64-7.78 (m, 3 H), 7.56 (br t, 1 H), 6.01-6.97 (m, 1 H), 4.63 (br s, 1 H), 3.46-4.19 (m, 1 H), 2.98-3.16 (m, 1 H), 2.78 (br d, 1 H)	362.1 [M + H] ⁺	99.7%
7	(CD ₃ OD) δ 8.30 (d, 1 H), 8.00 (br d, 1 H), 7.88 (d, 1 H), 7.78 (br s, 1 H), 7.70 (br t, 1 H), 7.65 (s, 1 H), 7.50-7.59 (m, 1 H), 6.33-6.82 (m, 1 H), 4.36 (br s, 1 H), 3.96 (s, 1 H), 3.03 (br s, 1 H), 2.80 (br s, 1 H), 2.32 (s, 3 H), 0.98-1.53 (m, 9 H)	416.1 [M + H] ⁺	100%
8	(CD ₃ OD) δ 8.30 (d, 1 H), 8.00 (br d, 1 H), 7.88 (d, 1 H), 7.77 (br d, 1 H), 7.70 (br t, 1 H), 7.65 (s, 1 H), 7.48-7.58 (m, 1 H),	416.1 [M + H] ⁺	99.7%

TABLE 6-continued

Ex. #	¹ H NMR (400 MHz)	LCMS: m/z	% ee
	6.37-6.81 (m, 1 H), 4.35 (br s, 1 H), 3.95 (s, 1 H), 3.04 (br s, 1 H), 2.80 (br s, 1 H), 2.32 (s, 3 H), 0.96-1.53 (m, 9 H)		
9	(CD ₃ OD) δ 8.21-8.42 (m, 1 H), 7.93-8.03 (m, 1 H), 7.84-7.92 (m, 1 H), 7.75-7.83 (m, 1 H), 7.65-7.72 (m, 2 H), 7.50-7.59 (m, 1 H), 7.28 (s, 0.4 H), 6.81 (s, 0.6 H), 4.92-5.10 (m, 1 H), 3.98 (br t, 0.6 H), 3.33-3.41 (m, 0.4 H), 3.06-3.19 (m, 0.5 H), 2.87-3.01 (m, 0.5 H), 2.75-2.85 (m, 1 H), 2.21-2.34 (m, 1 H), 1.12-1.30 (m, 4 H)	387.2 [M + H] ⁺	100%
10	(CD ₃ OD) δ 8.22-8.34 (m, 1 H), 7.84-8.02 (m, 2 H), 7.63-7.83 (m, 3 H), 7.47-7.59 (m, 1 H), 7.28 (s, 0.4 H), 6.81 (s, 0.6 H), 5.05 (dd, 0.6 H), 4.95 (br dd, 0.4 H), 3.91-4.03 (m, 0.6 H), 3.31-3.39 (m, 0.4 H), 3.07-3.19 (m, 0.6 H), 2.90-3.01 (m, 0.4 H), 2.75-2.85 (m, 1 H), 2.21-2.35 (m, 1 H), 1.15-1.32 (m, 4 H)	387.2 [M + H] ⁺	93.7%
11	(CD ₃ OD) δ 8.22-8.40 (m, 1 H), 8.08-8.21 (m, 2 H), 8.00 (br d, 1 H), 7.87 (br dd, 2 H), 7.60-7.75 (m, 2 H), 7.46-7.59 (m, 1 H), 7.23-7.42 (m, 2 H), 6.87 (br s, 1 H), 4.96-5.23 (m, 1 H), 4.04 (br s, 0.5 H), 3.40 (td, 0.5 H), 3.13-3.24 (m, 0.6 H), 2.94-3.05 (m, 0.4 H), 2.86 (br d, 1 H)	441.1 [M + H]	100%
12	(CD ₃ OD) δ 8.24-8.42 (m, 1 H), 8.10-8.23 (m, 2 H), 8.02 (br d, 1 H), 7.89 (br dd, 2 H), 7.63-7.77 (m, 2 H), 7.48-7.62 (m, 1 H), 7.25-7.44 (m, 2 H), 6.89 (br s, 1 H), 5.17 (br dd, 0.6 H), 5.03 (br dd, 0.4 H), 4.06 (br s, 0.6 H), 3.42 (td, 0.4 H), 3.15-3.27 (m, 0.5 H), 2.96-3.08 (m, 0.5 H), 2.88 (br d, 1 H)	441.1 [M + H]	99.9%
13	Data provided above		
14	Data provided above		
15	(CD ₃ OD) δ 8.31 (br d, 1 H), 7.98-8.27 (m, 2 H), 7.91 (d, 1 H), 7.64-7.83 (m, 3 H), 7.52-7.61 (m, 1 H), 6.76 (br s, 1 H), 4.29-4.73 (m, 1 H), 4.07 (br s, 1 H), 2.96-3.12 (m, 1 H), 2.80 (br d, 1 H), 1.71-1.86 (m, 6 H)	422.0 [M + H] ⁺	99.8%
16	(CD ₃ OD) δ 8.29 (br d, 1 H), 7.96-8.22 (m, 2 H), 7.88 (br d, 1 H), 7.62-7.85 (m, 3 H), 7.50-7.61 (m, 1 H), 6.75 (br s, 1 H), 4.30-4.62 (m, 1 H), 4.05 (br s, 1 H), 2.95-3.08 (m, 1 H), 2.77 (br d, 1 H), 1.57-1.89 (m, 6 H)	422.1 [M + H] ⁺	98.8%
17	(CD ₃ OD) δ 8.33 (d, 1 H), 7.94-8.08 (m, 2 H), 7.90 (br d, 1 H), 7.65-7.85 (m, 3 H), 7.56 (t, 1 H), 6.51-6.96 (m, 1 H), 4.56 (br s, 1 H), 3.91 (br s, 1 H), 3.11 (br s, 1 H), 2.85 (br s, 1 H), 1.51-1.97 (m, 6 H)	406.0 [M + H] ⁺	95.7%
18	(CD ₃ OD) δ 8.30 (d, 1 H), 7.99 (br d, 1 H), 7.88 (br d, 1 H), 7.61-7.83 (m, 4 H), 7.55 (br t, 1 H), 6.42-6.86 (m, 1 H), 4.53 (br s, 1 H), 4.02 (br s, 1 H), 3.09 (br d, 1 H), 2.81 (br d, 1 H), 1.51-1.96 (m, 6 H)	406.0 [M + H] ⁺	97.5%
19	(CD ₃ OD) δ 8.32 (d, 1 H), 7.84-8.07 (m, 4 H), 7.62-7.80 (m, 3 H), 7.55 (t, 1 H), 7.24 (t, 2 H), 6.36 (br s, 1 H), 4.44 (dd, 1 H), 4.07 (br s, 1 H), 3.03-3.17 (m, 1 H), 2.90 (br d, 1 H)	413.1 [M + H] ⁺	100%
20	(CD ₃ OD) δ 8.32 (d, 1 H), 7.86-8.04 (m, 4 H), 7.63-7.79 (m, 3 H), 7.51-7.59 (m, 1 H), 7.24 (t, 2 H), 6.36 (br s, 1 H), 4.44 (dd, 1 H), 4.07 (br s, 1 H), 3.02-3.18 (m, 1 H), 2.90 (br d, 1 H)	413.1 [M + H] ⁺	100%
21	(CD ₃ OD) δ 8.34 (br d, 1 H), 8.02 (br d, 1 H), 7.92 (d, 1 H), 7.81 (br s, 1 H), 7.68-7.78 (m, 2 H), 7.56-7.62 (m, 1 H), 6.37-6.86 (m, 1 H), 4.88 (br s, 0.5 H), 4.39 (br s, 0.5 H), 4.05 (br s, 0.5 H), 3.43-3.74 (m, 0.5 H), 2.96-3.19 (m, 1 H), 2.86 (br s, 1 H), 2.38 (br s, 3 H), 1.31-1.97 (m, 6 H)	420.0 [M + H] ⁺	99.4%
22	(CD ₃ OD) δ 8.34 (br d, 1 H), 8.02 (br d, 1 H), 7.92 (d, 1 H), 7.78-7.90 (m, 1 H), 7.67-7.77 (m, 2 H), 7.55-7.63 (m, 1 H), 6.36-6.86 (m, 1 H), 4.58-4.90 (m, 0.4 H), 4.40 (br s, 0.6 H), 3.84-4.21 (m, 0.5 H), 3.42-3.77 (m, 0.5 H), 2.95-3.19 (m, 1 H), 2.72-2.93 (m, 1 H), 2.29-2.45 (m, 3 H), 1.39-1.97 (m, 6 H)	420.0 [M + H] ⁺	99.0%
23	(CD ₃ OD) δ 8.26-8.42 (m, 1 H), 8.05 (br d, 1 H), 7.92 (br dd, 2 H), 7.67-7.81 (m, 3 H), 7.53-7.62 (m, 1 H), 7.25-7.37 (m, 2 H), 6.91 (br s, 1 H), 5.05 (td, 1 H), 4.11 (br s, 0.6 H), 3.39 (br s, 0.4 H), 2.99-3.30 (m, 1 H), 2.92 (br s, 1 H)	459.0 [M + H] ⁺	99.6%
24	(CD ₃ OD) δ 8.27-8.42 (m, 1 H), 8.05 (br d, 1 H), 7.84-7.96 (m, 2 H), 7.67-7.81 (m, 3 H), 7.53-7.63 (m, 1 H), 7.25-7.37 (m, 2 H), 6.91 (br s, 1 H), 5.00-5.12 (m, 1 H), 3.91-4.22 (m, 0.6H), 3.37-3.42 (m, 0.4 H), 2.98-3.28 (m, 1 H), 2.92 (br s, 1 H)	459.0 [M + H] ⁺	99.6%
25	(CD ₃ OD) δ 8.36 (br d, 1 H), 8.28 (br s, 1 H), 7.88-8.08 (m, 2 H), 7.76 (br d, 2 H), 7.69 (s, 1 H), 7.59 (br t, 2 H), 6.76 (br s, 1 H), 4.61 (br s, 1 H), 3.65-4.18 (m, 4 H), 2.99-3.23 (m, 1 H), 2.87 (br s, 1 H), 2.41 (s, 3 H)	440.1 [M + H] ⁺	99.6%
26	(CD ₃ OD) δ 8.37 (br d, 1 H), 8.28 (br s, 1 H), 7.92-8.08 (m, 2 H), 7.69-7.87 (m, 3 H), 7.30-7.67 (m, 2 H), 6.40-6.92 (m, 1 H), 4.64 (br s, 1 H), 3.57-4.18 (m, 4 H), 3.15 (br s, 1 H), 2.88 (br s, 1 H), 2.42 (s, 3 H)	440.1 [M + H] ⁺	99.6%

TABLE 6-continued

Ex. #	¹ H NMR (400 MHz)	LCMS: m/z	% ee
27	(CD ₃ OD) δ 8.20-8.37 (m, 1 H), 7.84-8.01 (m, 2 H), 7.62-7.83 (m, 3 H), 7.54 (q, 1 H), 7.28 (s, 0.4 H), 6.85 (s, 0.6 H), 4.91-5.07 (m, 1 H), 3.85-4.09 (m, 1 H), 3.08-3.21 (m, 0.7 H), 2.93-3.06 (m, 0.3 H), 2.74-2.88 (m, 1 H), 1.61-1.68 (m, 6 H)	405.2 [M + H] ⁺	99.6%
28	(CD ₃ OD) δ 8.20-8.36 (m, 1 H), 7.77-8.03 (m, 2.5 H), 7.61-7.74 (m, 2.5 H), 7.54 (q, 1 H), 7.27 (br s, 0.4 H), 6.83 (br s, 0.6 H), 4.92-5.05 (m, 1 H), 4.03 (br s, 1 H), 3.06-3.21 (m, 0.6 H), 2.91-3.05 (m, 0.4 H), 2.82 (br d, 1 H), 1.56-1.72 (m, 6 H)	405.2 [M + H] ⁺	99.3%
29	(CD ₃ OD) δ 8.63 (s, 2 H), 8.27 (d, 1 H), 8.00 (br d, 1 H), 7.87 (d, 1 H), 7.59-7.79 (m, 3 H), 7.48-7.58 (m, 1 H), 7.12 (s, 1 H), 5.26 (br dd, 1 H), 3.59-3.91 (m, 1 H), 2.85-3.10 (m, 1 H), 2.71-2.84 (m, 1 H)	397.0 [M + H] ⁺	99.6%
30	(CD ₃ OD) δ 8.49-8.80 (m, 2 H), 8.27 (d, 1 H), 8.00 (d, 1 H), 7.87 (d, 1 H), 7.61-7.78 (m, 3 H), 7.46-7.60 (m, 1 H), 7.13 (s, 1 H), 5.26 (dd, 1 H), 3.62-3.77 (m, 1 H), 2.85-3.02 (m, 1 H), 2.68-2.85 (m, 1 H)	397.0 [M + H] ⁺	96.5%
31	(CD ₃ OD) δ 8.71 (br s, 1 H), 8.35 (br d, 1 H), 8.21 (br s, 1 H), 7.88-8.12 (m, 3 H), 7.66-7.87 (m, 3 H), 7.59 (br t, 2 H), 6.46-7.01 (m, 1 H), 4.58 (br s, 1 H), 3.48-4.24 (m, 1 H), 3.01-3.30 (m, 1 H), 2.87 (br d, 1 H), 2.33-2.56 (m, 3 H)	437.2 [M + H] ⁺	99.7%
32	(CD ₃ OD) δ 8.72 (br s, 1 H), 8.35 (br d, 1 H), 8.22 (br s, 1 H), 7.90-8.10 (m, 2 H), 7.66-7.89 (m, 3 H), 7.59 (br t, 2 H), 6.53-6.97 (m, 1 H), 4.49-4.63 (m, 1 H), 3.53-4.27 (m, 1 H), 2.97-3.29 (m, 1 H), 2.87 (br d, 1 H), 2.47 (br s, 3 H)	437.0 [M + H] ⁺	90.1%
33	(CD ₃ OD) δ 8.67 (s, 1 H), 8.20-8.42 (m, 2 H), 8.00 (d, 0.6 H), 7.79-7.93 (m, 3 H), 7.61-7.75 (m, 2.4 H), 7.48-7.59 (m, 1 H), 7.34 (s, 0.4 H), 6.88 (s, 0.6 H), 5.08 (br dd, 1 H), 3.99-4.12 (m, 0.8 H), 3.34-3.42 (m, 0.7 H), 3.15-3.22 (m, 0.4 H), 2.96-3.06 (m, 0.2 H), 2.80-2.91 (m, 1 H)	442.2 [M + H] ⁺	100%
34	(CD ₃ OD) δ 8.67 (br s, 1 H), 8.20-8.47 (m, 2 H), 8.00 (d, 0.5 H), 7.78-7.94 (m, 3 H), 7.61-7.76 (m, 2.5 H), 7.47-7.60 (m, 1 H), 7.34 (s, 0.4 H), 6.88 (s, 0.6 H), 5.08 (br dd, 1 H), 3.97-4.13 (m, 0.6 H), 3.34-3.43 (m, 0.7 H), 3.14-3.22 (m, 0.3 H), 2.95-3.07 (m, 0.5 H), 2.77-2.91 (m, 1 H)	442.2 [M + H] ⁺	96.3%
35	(CD ₃ OD) δ 8.34 (d, 1 H), 8.04 (br d, 1 H), 7.93 (d, 1 H), 7.70-7.84 (m, 2 H), 7.68 (s, 1 H), 7.54-7.64 (m, 1 H), 6.40-6.86 (m, 1 H), 4.43 (br s, 1 H), 4.00 (br s, 1 H), 3.03 (br s, 1 H), 2.83 (br s, 1 H), 2.32 (s, 3 H), 2.16 (br s, 1 H), 1.14 (br s, 4 H)	400.3 [M + H] ⁺	96.4%
36	(CD ₃ OD) δ 8.34 (d, 1 H), 8.03 (br d, 1 H), 7.92 (d, 1 H), 7.71-7.85 (m, 2 H), 7.68 (s, 1 H), 7.55-7.64 (m, 1 H), 6.29-6.89 (m, 1 H), 4.40 (br s, 1 H), 4.00 (br s, 1 H), 3.03 (br s, 1 H), 2.83 (br s, 1 H), 2.32 (s, 3 H), 2.16 (br s, 1 H), 1.14 (br s, 4 H)	400.2 [M + H] ⁺	99.6%
37	(CD ₃ OD) δ 8.40-8.54 (m, 1 H), 8.20-8.39 (m, 1 H), 7.86-8.06 (m, 2 H), 7.65-7.85 (m, 2.8 H), 7.53-7.62 (m, 1 H), 7.47 (br d, 0.2 H), 6.81 (br s, 0.6 H), 6.03 (br s, 0.4 H), 4.93-5.16 (m, 0.5 H), 3.96-4.31 (m, 0.5 H), 3.80-3.95 (m, 0.7 H), 3.49 (br s, 0.3 H), 2.66-3.10 (m, 2 H)	414.1 [M + H] ⁺	99.8%
38	(CD ₃ OD) δ 8.40-8.56 (m, 1 H), 8.19-8.39 (m, 1 H), 7.86-8.08 (m, 2 H), 7.63-7.85 (m, 2.8 H), 7.58 (t, 1 H), 7.46 (br d, 0.2 H), 6.82 (br s, 0.6 H), 6.04 (br s, 0.4 H), 4.94-5.01 (m, 0.5 H), 4.07 (br s, 0.5 H), 3.89 (br dd, 0.7H), 3.51 (br s, 0.3 H), 2.71-3.05 (m, 2 H)	414.2 [M + H] ⁺	99.7%
39	(CD ₃ OD) δ 7.98-8.52 (m, 2 H), 7.90 (br d, 1 H), 7.47-7.83 (m, 4 H), 6.78 (br s, 1 H), 6.33 (br s, 1 H), 4.37 (br s, 1 H), 4.09 (br d, 1 H), 3.03 (br s, 1 H), 2.78 (br d, 1 H), 2.09 (br t, 3 H)	426.1 [M + H] ⁺	99.4%
40	(CD ₃ OD) δ 8.22-8.51 (m, 2 H), 8.03 (br s, 1 H), 7.89 (br d, 1 H), 7.63-7.80 (m, 2 H), 7.57 (br d, 1 H), 6.79 (br s, 1 H), 6.30 (br s, 1 H), 4.37 (br s, 1 H), 4.08 (br s, 1 H), 3.02 (br s, 1 H), 2.78 (br d, 1 H), 2.09 (br t, 3 H)	426.1 [M + H] ⁺	98.5%
41	(CD ₃ OD) δ 8.30 (d, 1 H), 7.96-8.09 (m, 1 H), 7.90 (br d, 1 H), 7.46-7.81 (m, 4 H), 6.85 (s, 0.7 H), 6.28 (s, 0.3 H), 4.98 (br d, 0.3 H), 4.26 (br dd, 0.7 H), 3.77-3.90 (m, 0.7 H), 3.11-3.26 (m, 0.3 H), 2.71-2.98 (m, 2 H), 2.57-2.71 (m, 1 H), 2.45-2.57 (m, 1 H), 1.04-1.16 (m, 1 H), 0.41-0.64 (m, 2 H), 0.04-0.31 (m, 2 H)	333.2 [M + H] ⁺	99.7%
42	(CD ₃ OD) δ 8.30 (d, 1 H), 7.97-8.07 (m, 1 H), 7.87-7.94 (m, 1 H), 7.53-7.78 (m, 4 H), 6.85 (s, 0.7 H), 6.28 (s, 0.3 H), 4.98 (br d, 0.4 H), 4.26 (br dd, 0.6 H), 3.78-3.88 (m, 0.6 H), 3.12-3.26 (m, 0.3 H), 2.71-2.98 (m, 2 H), 2.57-2.71 (m, 1 H), 2.46-2.57 (m, 1 H), 1.04-1.15 (m, 1 H), 0.45-0.61 (m, 2 H), 0.11-0.29 (m, 2 H)	333.2 [M + H] ⁺	99.7%
43	(CD ₃ OD) δ 8.48-8.80 (m, 1 H), 8.34 (br d, 1 H), 7.91-8.29 (m, 3.5 H), 7.65-7.90 (m, 3.5 H), 7.39-7.64 (m, 2 H), 6.51-7.02 (m, 1 H), 4.87 (s, 1 H), 4.63 (s, 2 H), 3.43-4.30 (m, 1 H), 3.15 (br s, 1 H), 2.87 (br d, 1 H), 2.42 (br s, 1 H), 0.80-1.20 (m, 4 H))	463.2 [M + H] ⁺	99.4%

TABLE 6-continued

Ex. #	¹ H NMR (400 MHz)	LCMS: m/z	% ee
44	(CD ₃ OD) δ 8.67 (br s, 1 H), 8.34 (d, 1 H), 7.89-8.28 (m, 3.5 H), 7.66-7.88 (m, 3.5 H), 7.39-7.63 (m, 2 H), 6.84 (br s, 1 H), 4.78-4.88 (m, 1 H), 3.43-4.34 (m, 1 H), 3.17 (br d, 1 H), 2.87 (br d, 1 H), 2.43 (br s, 1 H), 0.84-1.18 (m, 4 H)	463.2 [M + H] ⁺	99.3%
45	(CD ₃ OD) δ 8.79 (d, 1 H), 8.27-8.40 (m, 2 H), 8.01-8.14 (m, 2 H), 7.83-7.98 (m, 2 H), 7.65-7.78 (m, 3 H), 7.51-7.62 (m, 1 H), 7.38 (s, 0.4 H), 6.92 (br s, 0.6 H), 5.03-5.17 (m, 1 H), 4.11 (br s, 0.6 H), 3.40-3.53 (m, 0.4 H), 2.83-3.29 (m, 2 H)	424.2 [M + H] ⁺	100%
46	(CD ₃ OD) δ 8.79 (d, 1 H), 8.26-8.41 (m, 2 H), 8.00-8.17 (m, 2 H), 7.82-7.98 (m, 2 H), 7.65-7.81 (m, 3 H), 7.51-7.63 (m, 1 H), 7.39 (br s, 0.4 H), 6.92 (br s, 0.6 H), 5.00-5.18 (m, 1 H), 3.98-4.24 (m, 0.5 H), 3.37-3.53 (m, 0.5 H), 2.83-3.30 (m, 2 H)	424.2 [M + H] ⁺	97.6%
47	(CD ₃ OD) δ 8.26-8.44 (m, 2 H), 8.00-8.15 (m, 1.6 H), 7.82-7.97 (m, 2 H), 7.66-7.79 (m, 2.4 H), 7.52-7.63 (m, 1 H), 7.43 (s, 0.4 H), 6.90 (s, 0.6 H), 5.18 (dd, 0.7 H), 5.03 (dd, 0.4 H), 3.93-4.13 (m, 3.7 H), 3.42 (td, 0.4 H), 3.16-3.27 (m, 0.6 H), 2.82-3.08 (m, 1.4 H)	427.1 [M + H] ⁺	100%
48	(CD ₃ OD) δ 8.24-8.43 (m, 2 H), 7.98-8.15 (m, 1.6 H), 7.81-7.95 (m, 2 H), 7.65-7.79 (m, 2.4 H), 7.52-7.62 (m, 1 H), 7.42 (s, 0.4 H), 6.89 (s, 0.6 H), 5.18 (dd, 0.6 H), 5.02 (dd, 0.3 H), 3.95-4.11 (m, 3.7 H), 3.36-3.48 (m, 0.4 H), 3.13-3.27 (m, 0.6 H), 2.96-3.09 (m, 0.4 H), 2.80-2.94 (m, 1 H)	427.1 [M + H] ⁺	99.2%
49	(CD ₃ OD) δ 8.22-8.36 (m, 1 H), 7.95-8.08 (m, 1 H), 7.87 (br d, 1 H), 7.61-7.72 (m, 2 H), 7.54 (br t, 1.3 H), 6.84 (s, 0.7 H), 6.51 (s, 0.3 H), 4.40 (br dd, 1 H), 3.89 (br s, 1 H), 3.36 (br s, 0.5 H), 3.06-3.22 (m, 0.5 H), 2.70-2.98 (m, 2 H), 1.94-2.16 (m, 1 H), 1.69-1.88 (m, 1 H)	355.2 [M + H] ⁺	100%
50	(CD ₃ OD) δ 8.19-8.36 (m, 1 H), 7.92-8.09 (m, 1 H), 7.83-7.91 (m, 1 H), 7.64-7.77 (m, 2 H), 7.47-7.63 (m, 2 H), 6.71 (s, 0.6 H), 6.41 (s, 0.4 H), 4.79 (br d, 0.5 H), 4.41 (br dd, 0.5 H), 3.81-3.92 (m, 0.5 H), 3.51-3.69 (m, 0.5 H), 3.10-3.24 (m, 1 H), 2.93-3.07 (m, 0.5 H), 2.66-2.88 (m, 1.5 H), 1.97-2.20 (m, 1 H), 1.73-1.94 (m, 1 H)	355.2 [M + H] ⁺	100%
51	(CD ₃ OD) δ 8.23-8.49 (m, 2 H), 7.87-8.07 (m, 2 H), 7.51-7.86 (m, 4 H), 6.95-7.32 (m, 1 H), 6.36-6.93 (m, 1 H), 4.28-4.71 (m, 1 H), 3.37-4.17 (m, 1 H), 2.74-3.18 (m, 2 H)	396.10 [M + H] ⁺	98.9%
52	(CD ₃ OD) δ 8.13-8.39 (m, 2 H), 7.76-7.92 (m, 2 H), 7.42-7.74 (m, 4 H), 6.84-7.19 (m, 1 H), 6.34-6.76 (m, 1 H), 4.16-4.63 (m, 1 H), 3.71-4.09 (m, 0.6 H), 3.36 (br d, 0.4 H), 2.59-3.07 (m, 2 H)	396.10 [M + H] ⁺	99.1%
53	(CD ₃ OD) δ 8.20-8.37 (m, 1 H), 7.95-8.08 (m, 1 H), 7.81-7.95 (m, 1 H), 7.50-7.80 (m, 4 H), 6.79 (s, 0.6 H), 6.28 (s, 0.4 H), 4.96-5.20 (m, 1 H), 4.24 (br dd, 1 H), 3.74-3.87 (m, 1 H), 2.93-3.19 (m, 1 H), 2.64-2.93 (m, 4 H), 2.25-2.61 (m, 2 H), 1.86-2.24 (m, 2 H)	365.2 [M + H] ⁺	72.7%
54	(CD ₃ OD) δ 8.24-8.33 (m, 1 H), 7.96-8.11 (m, 1 H), 7.85-7.93 (m, 1 H), 7.49-7.81 (m, 4 H), 6.79 (s, 0.6 H), 6.28 (s, 0.4 H), 5.01-5.25 (m, 1 H), 4.24 (br dd, 1 H), 3.81 (br t, 1 H), 2.93-3.19 (m, 1 H), 2.63-2.92 (m, 4 H), 2.27-2.61 (m, 2 H), 1.94-2.26 (m, 2 H)	365.2 [M + H] ⁺	86.6%
55	(CD ₃ OD) δ 8.29 (br d, 1 H), 8.01 (br d, 1 H), 7.88 (br d, 1 H), 7.70 (br d, 2 H), 7.63 (br s, 1 H), 7.55 (br t, 1 H), 6.75 (br s, 1 H), 4.69 (br d, 1 H), 3.74 (br s, 1 H), 2.94 (br s, 1 H), 2.74 (br d, 1 H), 2.60 (br s, 2 H), 1.96-2.16 (m, 3 H), 1.77 (br d, 1 H)	399.0 [M + H] ⁺	92.8%
56	(CD ₃ OD) δ 8.32 (d, 1 H), 8.05 (d, 1 H), 7.92 (d, 1 H), 7.70-7.77 (m, 2 H), 7.63-7.69 (m, 1 H), 7.55-7.62 (m, 1 H), 6.78 (s, 1 H), 4.73 (br dd, 1 H), 3.78 (br s, 1 H), 2.88-3.04 (m, 1 H), 2.78 (br d, 1 H), 2.63 (br s, 2 H), 1.96-2.24 (m, 3 H), 1.72-1.90 (m, 1 H)	399.2 [M + H] ⁺	97.4%
57	(CD ₃ OD) δ 8.27-8.59 (m, 2 H), 8.01 (br s, 1 H), 7.77-7.96 (m, 2 H), 7.67-7.77 (m, 2 H), 7.58 (td, 1 H), 6.43-6.84 (m, 1 H), 4.41-4.68 (m, 1 H), 4.10 (br s, 1 H), 2.77-3.23 (m, 2 H)	371.0 [M + H] ⁺	98.5%
58	(CD ₃ OD) δ 8.23-8.50 (m, 2 H), 8.01 (br s, 1 H), 7.76-7.96 (m, 1 H), 7.67-7.76 (m, 2 H), 7.56-7.67 (m, 1 H), 6.45-6.87 (m, 1 H), 4.38-4.67 (m, 1 H), 3.97-4.26 (m, 1 H), 2.77-3.23 (m, 2 H)	371.0 [M + H] ⁺	98.9%
59	(CD ₃ OD) δ 8.15-8.22 (m, 1 H), 7.88-7.96 (m, 1 H), 7.75-7.83 (m, 1 H), 7.51-7.68 (m, 3 H), 7.42-7.50 (m, 1 H), 6.31-6.78 (m, 1 H), 4.31 (br dd, 1 H), 3.58-3.71 (m, 1 H), 2.84-3.15 (m, 2 H), 2.57-2.83 (m, 2 H), 1.90-2.20 (m, 4 H), 1.36-1.76 (m, 2 H)	363.1 [M + H] ⁺	100%
60	(CD ₃ OD) δ 8.16-8.21 (m, 1 H), 7.90-7.95 (m, 1 H), 7.76-7.82 (m, 1 H), 7.51-7.68 (m, 3 H), 7.42-7.50 (m, 1 H), 6.32-6.78 (m, 1 H), 4.31 (dd, 1 H), 3.54-3.75 (m, 1 H), 2.85-3.15 (m, 2 H), 2.55-2.84 (m, 2 H), 1.90-2.19 (m, 4 H), 1.42-1.78 (m, 2 H)	363.1 [M + H] ⁺	99.5%

TABLE 6-continued

Ex. #	¹ H NMR (400 MHz)	LCMS: m/z	% ee
61	(CD ₃ OD) δ 8.60 (br s, 1 H), 7.79-8.29 (m, 5 H), 7.23-7.78 (m, 6 H), 6.72 (br s, 1 H), 4.65 (br s, 1 H), 3.30-4.22 (m, 1 H), 2.86-3.16 (m, 1 H), 2.79 (br s, 1 H)	423.1 [M + H] ⁺	99.5%
62	(CD ₃ OD) δ 8.60 (br s, 1 H), 7.78-8.34 (m, 5 H), 7.25-7.76 (m, 6 H), 6.71 (br s, 1 H), 4.64 (br s, 1 H), 3.38-4.14 (m, 1 H), 2.85-3.16 (m, 1 H), 2.79 (br s, 1 H)	423.2 [M + H] ⁺	99.4%
63	(CD ₃ OD) δ 8.87-8.96 (m, 1 H), 8.27-8.38 (m, 2 H), 7.80-8.11 (m, 3 H), 7.37-7.78 (m, 4.5 H), 6.90 (br s, 0.5 H), 5.00-5.24 (m, 1 H), 4.08 (br t, 0.6 H), 3.44 (td, 0.4 H), 2.98-3.26 (m, 1 H), 2.89 (br d, 1 H)	463.2 [M + H] ⁺	100%
64	(CD ₃ OD) δ 8.89-8.94 (m, 1 H), 8.28-8.39 (m, 2 H), 7.78-8.05 (m, 3 H), 7.41-7.76 (m, 4.5 H), 6.90 (s, 0.5 H), 4.99-5.22 (m, 1 H), 4.02-4.14 (m, 0.6 H), 3.39-3.48 (m, 0.4 H), 2.97-3.28 (m, 1 H), 2.81-2.94 (m, 1 H)	463.2 [M + H] ⁺	99.1%
65	(CD ₃ OD) δ 8.35-8.74 (m, 1 H), 8.21 (br dd, 2 H), 7.57-8.03 (m, 6 H), 7.31-7.54 (m, 2 H), 6.92-7.27 (m, 1 H), 6.48-6.81 (m, 1 H), 4.49 (br d, 1 H), 3.85-4.11 (m, 0.6 H), 3.37-3.65 (m, 0.4 H), 2.84-3.17 (m, 1 H), 2.62-2.84 (m, 1 H)	473.1 [M + H] ⁺	100%
66	(CD ₃ OD) δ 8.35-8.70 (m, 1 H), 8.21 (br dd, 2 H), 7.57-8.03 (m, 6 H), 7.32-7.55 (m, 2 H), 6.93-7.25 (m, 1 H), 6.51-6.80 (m, 1 H), 4.49 (br d, 1 H), 3.97 (br t, 0.6 H), 3.33-3.64 (m, 0.4 H), 2.84-3.15 (m, 1 H), 2.77 (br d, 1 H)	473.1 [M + H] ⁺	98.7%
67	Data provided above		
68	Data provided above		
69	(CD ₃ OD) δ 8.23-8.50 (m, 1 H), 7.82-8.16 (m, 4.7 H), 7.64-7.80 (m, 2.3 H), 7.46-7.62 (m, 2 H), 7.41 (s, 0.3 H), 6.90 (s, 0.7 H), 5.19 (dd, 0.7 H), 5.04 (br dd, 0.3 H), 3.97-4.17 (m, 0.7 H), 3.44 (td, 0.3 H), 3.16-3.28 (m, 0.7 H), 2.96-3.09 (m, 0.3 H), 2.81-2.95 (m, 1 H)	459.4 [M + H] ⁺	100%
70	(CD ₃ OD) δ 8.22-8.48 (m, 1 H), 7.81-8.15 (m, 4.7 H), 7.65-7.79 (m, 2.3 H), 7.47-7.63 (m, 2 H), 7.41 (s, 0.3 H), 6.90 (s, 0.7 H), 5.19 (dd, 0.6 H), 5.04 (br dd, 0.4 H), 3.99-4.14 (m, 0.6 H), 3.39-3.51 (m, 0.4 H), 3.17-3.28 (m, 0.6 H), 2.97-3.11 (m, 0.4 H), 2.80-2.94 (m, 1 H)	459.5 [M + H] ⁺	100%
71	(CD ₃ OD) δ 8.34 (br d, 1 H), 7.52-8.12 (m, 6 H), 6.96-7.32 (m, 1 H), 6.47-6.88 (m, 1 H), 4.46 (br s, 0.5 H), 4.03 (br s, 0.5 H), 3.41-3.79 (m, 1.5 H), 2.66-3.23 (m, 6.5 H)	486.1 [M + H] ⁺	99.1%
72	(CD ₃ OD) δ 8.34 (br d, 1 H), 7.47-8.13 (m, 6 H), 6.92-7.43 (m, 1 H), 6.45-6.89 (m, 1 H), 4.46 (br s, 0.7 H), 4.03 (br s, 0.5 H), 3.42-3.81 (m, 1.5 H), 2.61-3.22 (m, 6.3 H)	486.1 [M + H] ⁺	98.6%
73	(CD ₃ OD) δ 8.32 (br s, 1 H), 7.65-8.07 (m, 5 H), 7.47-7.62 (m, 1 H), 6.63-6.93 (m, 3 H), 3.84-4.26 (m, 5 H), 2.93-3.08 (m, 1 H), 2.73-2.88 (m, 1 H)	409.1 [M + H] ⁺	100%
74	(CD ₃ OD) δ 8.33 (br s, 1 H), 7.68-8.06 (m, 5 H), 7.48-7.62 (m, 1 H), 6.60-6.93 (m, 3 H), 3.85-4.23 (m, 5 H), 2.99 (br d, 1 H), 2.78 (br d, 1 H)	409.1 [M + H] ⁺	92.1%
75	(CD ₃ OD) δ 8.00-8.42 (m, 2.6 H), 7.84-7.97 (m, 2 H), 7.65-7.79 (m, 2.4 H), 7.53-7.63 (m, 1 H), 7.20-7.39 (m, 2.4 H), 6.91 (s, 0.6 H), 5.13 (br dd, 0.6 H), 5.04 (br dd, 0.4 H), 4.08 (br t, 0.6 H), 3.42 (td, 0.4 H), 2.99-3.27 (m, 1 H), 2.82-2.94 (m, 1 H)	459.0 [M + H] ⁺	100%
76	(CD ₃ OD) δ 8.00-8.41 (m, 2.6 H), 7.84-7.98 (m, 2 H), 7.66-7.79 (m, 2.4 H), 7.53-7.63 (m, 1 H), 7.19-7.40 (m, 2.4 H), 6.91 (s, 0.6 H), 4.99-5.17 (m, 1 H), 4.08 (br t, 0.6 H), 3.38-3.52 (m, 0.4 H), 2.98-3.26 (m, 1 H), 2.90 (br dd, 1 H)	459.0 [M + H] ⁺	100%
77	(CD ₃ OD) δ 8.32 (br s, 1 H), 7.86-8.06 (m, 2 H), 7.63-7.85 (m, 3 H), 7.57 (t, 1 H), 6.49-7.31 (m, 2 H), 4.66 (br s, 2 H), 4.35-4.47 (m, 1 H), 4.01 (br s, 1 H), 3.37-3.61 (m, 3 H), 2.74-3.26 (m, 2 H)	440.1 [M + H] ⁺	99.4%
78	(CD ₃ OD) δ 8.32 (br s, 1 H), 7.86-8.04 (m, 2 H), 7.63-7.85 (m, 3 H), 7.51-7.61 (m, 1 H), 6.50-7.29 (m, 2 H), 4.53-4.77 (m, 2 H), 4.41 (br s, 1 H), 3.93-4.09 (m, 1 H), 3.35-3.60 (m, 3 H), 2.78-3.26 (m, 2 H)	440.1 [M + H] ⁺	98.3%
79	(CD ₃ OD) δ 8.21-8.37 (m, 1 H), 7.99-8.04 (m, 1 H), 7.84-7.98 (m, 2.4 H), 7.65-7.78 (m, 2 H), 7.45-7.63 (m, 1.6 H), 6.85 (br s, 1 H), 4.98 (br d, 0.4 H), 4.40 (br dd, 0.6 H), 3.98-4.06 (m, 3 H), 3.94 (br s, 0.6 H), 3.21-3.28 (m, 0.4 H), 3.09-3.18 (m, 0.6 H), 2.95-3.05 (m, 0.4 H), 2.70-2.89 (m, 1 H)	360.2 [M + H] ⁺	100%
80	(CD ₃ OD) δ 8.34 (d, 0.6 H), 8.23 (d, 0.4 H), 7.99-8.04 (m, 1 H), 7.81-7.97 (m, 2.5 H), 7.65-7.77 (m, 2 H), 7.46-7.60 (m, 1.5 H), 6.85 (br s, 1 H), 5.00 (dd, 0.4 H), 4.40 (br dd, 0.6 H), 3.98-4.09 (m, 3 H), 3.85-3.97 (m, 0.6 H), 3.23-3.28 (m, 0.4 H), 2.93-3.19 (m, 1 H), 2.70-2.89 (m, 1 H)	360.2 [M + H] ⁺	99.5%
81	(CD ₃ OD) δ 8.19-8.43 (m, 1 H), 7.45-8.14 (m, 8 H), 6.70-6.91 (m, 1.5 H), 6.25 (br s, 0.5 H), 4.15 (br d, 1 H), 3.97 (br s, 1 H), 3.00 (br s, 1 H), 2.77 (br d, 1 H)	395.1 [M + H] ⁺	99.5%

TABLE 6-continued

Ex. #	¹ H NMR (400 MHz)	LCMS: m/z	% ee
82	(CD ₃ OD) δ 8.20-8.45 (m, 1 H), 7.40-8.13 (m, 8 H), 6.72-6.89 (m, 1.5 H), 6.25 (br s, 0.5 H), 4.14 (br d, 1 H), 3.97 (br s, 1 H), 3.00 (br s, 1 H), 2.77 (br d, 1 H)	395.1 [M + H] ⁺	99.8%
83	(CD ₃ OD) δ 8.30 (br d, 1 H), 8.03 (br s, 2 H), 7.90 (d, 1 H), 7.42-7.84 (m, 4 H), 6.66-7.09 (m, 2 H), 4.18 (br s, 1 H), 3.45-4.06 (m, 4 H), 2.86-3.07 (m, 1 H), 2.72 (br dd, 1 H)	409.1 [M + H] ⁺	100%
84	(CD ₃ OD) δ 8.30 (br d, 1 H), 8.04 (br s, 2 H), 7.90 (d, 1 H), 7.62-7.84 (m, 3 H), 7.57 (br t, 1 H), 6.62-7.24 (m, 2 H), 4.19 (br s, 1 H), 3.45-4.00 (m, 4 H), 2.85-3.05 (m, 1 H), 2.64-2.80 (m, 1 H)	409.1 [M + H] ⁺	99.6%
85	(CD ₃ OD) δ 8.21-8.45 (m, 1 H), 7.64-8.09 (m, 6 H), 7.45-7.63 (m, 1 H), 7.39 (s, 0.4 H), 6.95-7.04 (m, 1 H), 6.90 (s, 0.6 H), 4.99-5.21 (m, 1 H), 3.97-4.15 (m, 3.5 H), 3.36-3.44 (m, 0.5 H), 2.97-3.28 (m, 1 H), 2.79-2.94 (m, 1 H)	427.2 [M + H] ⁺	100%
86	(CD ₃ OD) δ 8.22-8.41 (m, 1 H), 7.63-8.10 (m, 6 H), 7.49-7.62 (m, 1 H), 7.39 (s, 0.4 H), 6.85-7.03 (m, 1.6 H), 4.97-5.18 (m, 1 H), 3.98-4.16 (m, 3.5 H), 3.35-3.44 (m, 0.5 H), 3.13-3.27 (m, 0.6 H), 2.79-3.09 (m, 1.4 H)	427.3 [M + H] ⁺	91.7%
87	(CD ₃ OD) δ 8.30 (br d, 1 H), 7.88-8.10 (m, 3 H), 7.64-7.82 (m, 3 H), 7.53-7.60 (m, 1 H), 5.99-6.99 (m, 1 H), 3.87 (br s, 5 H), 2.93-3.03 (m, 1 H), 2.73-2.80 (m, 1 H)	393.1 [M + H] ⁺	99.8%
88	(CD ₃ OD) δ 8.29 (br d, 1 H), 7.87-8.09 (m, 3 H), 7.63-7.81 (m, 3 H), 7.53-7.60 (m, 1 H), 6.07-6.98 (m, 1 H), 3.65-4.31 (m, 5 H), 2.90-3.03 (m, 1 H), 2.76 (dd, 1 H)	393.1 [M + H] ⁺	97.5%
89	(CD ₃ OD) δ 8.64 (dt, 1 H), 8.24-8.38 (m, 1 H), 8.03 (d, 0.5 H), 7.84-7.96 (m, 3 H), 7.64-7.76 (m, 3.5 H), 7.50-7.61 (m, 1 H), 7.33 (s, 0.4 H), 6.90 (s, 0.6 H), 4.97-5.10 (m, 1 H), 3.99-4.16 (m, 0.7 H), 3.35-3.43 (m, 0.4 H), 3.18-3.26 (m, 0.6 H), 2.97-3.09 (m, 0.4 H), 2.81-2.94 (m, 1 H)	442.2 [M + H] ⁺	95.1%
90	(CD ₃ OD) δ 8.63 (d, 1 H), 8.23-8.38 (m, 1 H), 7.83-8.04 (m, 3.5 H), 7.62-7.77 (m, 3.5 H), 7.48-7.59 (m, 1 H), 7.32 (s, 0.4 H), 6.90 (s, 0.6 H), 4.96-5.12 (m, 1 H), 4.07 (br t, 0.6 H), 3.35-3.41 (m, 0.4 H), 3.16-3.26 (m, 0.6 H), 2.97-3.09 (m, 0.4 H), 2.80-2.93 (m, 1 H)	442.2 [M + H] ⁺	97.3%
91	(CD ₃ OD) δ 8.22 (br d, 1 H), 7.42-7.97 (m, 6 H), 6.37-7.19 (m, 2 H), 4.32 (br d, 1 H), 3.91 (br s, 0.6 H), 3.38 (br d, 0.4 H), 2.61-3.10 (m, 2 H), 1.58 (br s, 3 H), 1.14-1.41 (m, 3 H)	454.1 [M + H] ⁺	100%
92	(CD ₃ OD) δ 8.15-8.31 (m, 1 H), 7.39-7.99 (m, 6 H), 6.25-7.27 (m, 2 H), 4.32 (br d, 1 H), 3.90 (br d, 0.6 H), 3.38 (br s, 0.4 H), 2.63-3.12 (m, 2 H), 1.58 (br s, 3 H), 1.10-1.43 (m, 3 H)	454.1 [M + H] ⁺	99.3%
93	(CD ₃ OD) δ 8.21 (br s, 1 H), 7.33-7.98 (m, 7 H), 6.13-6.80 (m, 2 H), 3.62-4.18 (m, 4.5 H), 3.23-3.43 (m, 0.5 H), 2.78-2.96 (m, 1 H), 2.66 (br d, 1 H)	359.1 [M + H] ⁺	99.9%
94	(CD ₃ OD) δ 8.21 (br s, 1 H), 7.32-7.98 (m, 7 H), 6.13-6.81 (m, 2 H), 3.67-4.19 (m, 4.5 H), 3.24-3.40 (m, 0.5 H), 2.87 (br d, 1 H), 2.66 (br d, 1 H)	359.1 [M + H] ⁺	98.8%
95	(CD ₃ OD) δ 8.26-8.41 (m, 2 H), 7.83-8.08 (m, 3 H), 7.64-7.80 (m, 3 H), 7.52-7.62 (m, 1 H), 7.37 (s, 0.4 H), 7.15-7.28 (m, 1 H), 6.91 (s, 0.6 H), 4.99-5.20 (m, 1 H), 4.07 (br t, 0.7 H), 3.37-3.43 (m, 0.3 H), 2.99-3.28 (m, 1 H), 2.82-2.95 (m, 1 H)	463.1 [M + H] ⁺	100%
96	(CD ₃ OD) δ 8.26-8.40 (m, 2 H), 7.82-8.05 (m, 3 H), 7.66-7.80 (m, 3 H), 7.52-7.64 (m, 1 H), 7.37 (s, 0.4 H), 7.15-7.27 (m, 1 H), 6.91 (s, 0.6 H), 4.99-5.18 (m, 1 H), 4.08 (br s, 0.6 H), 3.37-3.46 (m, 0.4 H), 2.99-3.29 (m, 1 H), 2.81-2.95 (m, 1 H)	463.1 [M + H] ⁺	98.5%
97	(CD ₃ OD) δ 8.29 (br s, 1 H), 7.99 (br d, 1 H), 7.88 (br d, 1 H), 7.61-7.81 (m, 3 H), 7.47-7.58 (m, 1 H), 6.14-6.84 (m, 1 H), 3.84-4.37 (m, 1.4 H), 3.45 (br s, 0.6 H), 2.90-3.19 (m, 1 H), 2.81 (br d, 1 H), 1.61 (br s, 3 H), 1.24-1.48 (m, 3 H)	482.0 [M + H] ⁺	99.5%
98	(CD ₃ OD) δ 8.29 (br s, 1 H), 7.99 (br d, 1 H), 7.87 (br d, 1 H), 7.61-7.81 (m, 3 H), 7.47-7.59 (m, 1 H), 6.20-6.80 (m, 1 H), 3.95-4.35 (m, 1.4 H), 3.46 (br s, 0.6 H), 2.89-3.21 (m, 1 H), 2.81 (br d, 1 H), 1.61 (br s, 3 H), 1.22-1.48 (m, 3 H)	482.0 [M + H] ⁺	98.9%
99	(CD ₃ OD) δ 8.21 (br d, 1 H), 7.74-7.98 (m, 2 H), 7.54-7.73 (m, 3 H), 7.38-7.51 (m, 1 H), 6.30-6.79 (m, 1 H), 4.51-4.70 (m, 1 H), 4.32 (br s, 1 H), 3.68-4.01 (m, 1 H), 2.64-3.11 (m, 2 H), 2.13-2.43 (m, 3 H), 1.16-1.62 (m, 3 H)	404.2 [M + H] ⁺	100%
100	(CD ₃ OD) δ 8.21 (br d, 1 H), 7.76-7.95 (m, 2 H), 7.54-7.73 (m, 3 H), 7.39-7.49 (m, 1 H), 6.29-6.80 (m, 1 H), 4.54-4.75 (m, 1 H), 4.32 (br s, 1 H), 3.80-4.03 (m, 1 H), 2.61-3.09 (m, 2 H), 2.24 (br s, 3 H), 1.47 (br s, 3 H)	404.2 [M + H] ⁺	100%
101	(CD ₃ OD) δ 8.21 (br d, 1 H), 7.90 (d, 1 H), 7.80 (d, 1 H), 7.54-7.75 (m, 3 H), 7.38-7.50 (m, 1 H), 6.37-6.81 (m, 1 H), 4.33 (br s, 0.6 H), 3.90 (br s, 0.5 H), 3.35-3.62 (m, 0.4 H), 2.36-3.11 (m, 4.5 H), 2.25-2.33 (m, 3 H), 1.30-2.23 (m, 4 H)	430.2 [M + H] ⁺	100%

TABLE 6-continued

Ex. #	¹ H NMR (400 MHz)	LCMS: m/z	% ee
102	(CD ₃ OD) δ 8.33 (br d, 1 H), 8.03 (d, 1 H), 7.92 (d, 1 H), 7.64-7.86 (m, 3 H), 7.51-7.62 (m, 1 H), 6.42-6.86 (m, 1 H), 4.46 (br s, 0.6 H), 3.44-4.20 (m, 1 H), 2.54-3.25 (m, 4 H), 2.39 (br s, 3 H), 1.36-2.27 (m, 4.4 H)	430.3 [M + H] ⁺	99.6%
103	(CD ₃ OD) δ 8.63 (s, 1 H), 8.26-8.43 (m, 1 H), 8.15-8.23 (m, 1 H), 8.04 (d, 0.7 H), 7.84-7.96 (m, 3 H), 7.50-7.79 (m, 3.5 H), 7.39 (s, 0.3 H), 6.91 (s, 0.5 H), 5.00-5.16 (m, 1 H), 4.09 (br s, 0.6 H), 3.36-3.43 (m, 0.4 H), 3.19-3.28 (m, 0.7 H), 2.99-3.07 (m, 0.3 H), 2.89 (br d, 1 H), 2.49 (s, 3 H)	438.1 [M + H] ⁺	100%
104	(CD ₃ OD) δ 8.62 (s, 1 H), 8.25-8.44 (m, 1 H), 8.13-8.24 (m, 1 H), 8.04 (d, 0.6 H), 7.83-7.98 (m, 3 H), 7.49-7.79 (m, 3.5 H), 7.39 (s, 0.4 H), 6.91 (s, 0.5 H), 4.99-5.16 (m, 1 H), 4.08 (br s, 0.6 H), 3.37-3.46 (m, 0.4 H), 3.16-3.29 (m, 0.6 H), 2.99-3.10 (m, 0.4 H), 2.89 (br d, 1 H), 2.49 (s, 3 H)	438.1 [M + H] ⁺	100%
105	(CD ₃ OD) δ 8.26-8.39 (m, 1 H), 8.01 (d, 1 H), 7.86-7.95 (m, 2 H), 7.82 (d, 1 H), 7.65-7.76 (m, 1 H), 7.53-7.61 (m, 1 H), 7.31 (s, 0.5 H), 6.92 (s, 0.5 H), 4.94-5.10 (m, 1 H), 3.96 (ddd, 1 H), 3.14-3.27 (m, 0.7 H), 2.97-3.06 (m, 0.4 H), 2.81-2.92 (m, 1 H), 1.80-1.94 (m, 6 H)	407.0 [M + H] ⁺	100%
106	(CD ₃ OD) δ 8.56-8.61 (m, 1 H), 8.32-8.48 (m, 1 H), 7.90-8.02 (m, 2 H), 7.70-7.83 (m, 2 H), 7.56-7.65 (m, 1 H), 7.47 (s, 0.3 H), 7.07 (s, 0.7 H), 4.93-5.18 (m, 1 H), 3.78 (ddd, 1 H), 3.23-3.29 (m, 0.7 H), 3.02-3.15 (m, 0.3 H), 2.84-2.99 (m, 1 H), 1.82-1.95 (m, 6 H)	407.1 [M + H] ⁺	94.5%
107	(CD ₃ OD) δ 9.03 (d, 1 H), 8.46-8.57 (m, 1 H), 8.24-8.40 (m, 1 H), 7.85-8.05 (m, 3.5 H), 7.49-7.78 (m, 3.5 H), 7.36 (s, 0.4 H), 6.91 (s, 0.6 H), 4.98-5.18 (m, 1 H), 4.08 (br s, 0.6 H), 3.38-3.46 (m, 0.4 H), 3.18-3.27 (m, 0.6 H), 2.97-3.10 (m, 0.4 H), 2.80-2.94 (m, 1 H)	492.0 [M + H] ⁺	100%
108	(CD ₃ OD) δ 9.04 (br d, 1 H), 8.48-8.59 (m, 1 H), 8.24-8.39 (m, 1 H), 7.86-8.06 (m, 3.5 H), 7.50-7.77 (m, 3.5 H), 7.36 (s, 0.4 H), 6.91 (br s, 0.6 H), 5.00-5.16 (m, 1 H), 4.09 (br s, 0.5 H), 3.40 (br dd, 0.5 H), 2.98-3.23 (m, 1 H), 2.90 (br s, 1 H)	492.1 [M + H] ⁺	96.9%
109	(CD ₃ OD) δ 9.40 (br s, 0.5 H), 8.90 (br s, 0.5 H), 8.45 (br s, 1 H), 7.30-8.37 (m, 10 H), 6.90 (br s, 0.5 H), 6.28 (br s, 0.5 H), 4.21 (br s, 1 H), 4.04 (br s, 1 H), 2.96-3.10 (m, 1 H), 2.80 (br d, 1 H)	456.0 [M + H] ⁺	100%
110	(CD ₃ OD) δ 9.40 (br s, 0.3 H), 8.89 (br s, 0.7 H), 8.44 (br s, 1 H), 7.27-8.34 (m, 10 H), 6.91 (br s, 0.6 H), 6.28 (br s, 0.4 H), 4.19 (br s, 1 H), 4.03 (br s, 1 H), 2.95-3.09 (m, 1 H), 2.79 (br d, 1 H)	456.0 [M + H] ⁺	99.6%
111	(CD ₃ OD) δ 8.29 (br d, 1 H), 7.84-8.04 (m, 2 H), 7.60-7.82 (m, 3 H), 7.49-7.58 (m, 1 H), 6.29-6.85 (m, 1 H), 4.71-4.84 (m, 1 H), 4.40 (br s, 1 H), 3.97 (br s, 1 H), 2.65-3.16 (m, 2 H), 2.32 (br s, 3 H), 1.19-1.78 (m, 3 H)	404.1 [M + H] ⁺	100%
112	(CD ₃ OD) δ 8.29 (br d, 1 H), 7.82-8.07 (m, 2 H), 7.60-7.80 (m, 3 H), 7.49-7.58 (m, 1 H), 6.13-6.97 (m, 1 H), 4.77-4.85 (m, 1 H), 4.41 (br s, 1 H), 3.96 (br s, 1 H), 2.71-3.17 (m, 2 H), 2.18-2.49 (m, 3 H), 1.31-1.72 (m, 3 H)	404.1 [M + H] ⁺	98.7%
113	(CD ₃ OD) δ 8.33 (br s, 1 H), 8.03 (br d, 1 H), 7.92 (br d, 1 H), 7.63-7.87 (m, 3 H), 7.53-7.62 (m, 1 H), 6.27-6.89 (m, 1 H), 4.31 (br s, 1 H), 4.11 (br s, 0.6 H), 3.38-3.57 (m, 0.4 H), 2.94-3.23 (m, 1 H), 2.86 (br d, 1 H), 1.32-1.79 (m, 6 H)	438.1 [M + H] ⁺	99.6%
114	(CD ₃ OD) δ 8.33 (br s, 1 H), 8.03 (br d, 1 H), 7.92 (br d, 1 H), 7.62-7.87 (m, 3 H), 7.54-7.61 (m, 1 H), 6.31-6.89 (m, 1 H), 4.31 (br s, 1 H), 4.11 (br s, 0.6 H), 3.37-3.55 (m, 0.4 H), 2.94-3.24 (m, 1 H), 2.86 (br d, 1 H), 1.34-1.78 (m, 6 H)	438.1 [M + H] ⁺	99.4%
115	(CD ₃ OD) δ 8.23-8.44 (m, 1 H), 7.82-8.09 (m, 4.5 H), 7.54-7.77 (m, 3 H), 6.87-7.15 (m, 1.5 H), 4.99-5.20 (m, 1 H), 3.96-4.18 (m, 0.5 H), 3.36-3.55 (m, 0.5 H), 2.80-3.29 (m, 2 H)	413.2 [M + H] ⁺	96.5%
116	(CD ₃ OD) δ 8.17-8.54 (m, 2 H), 7.44-8.10 (m, 6.5 H), 6.98-7.18 (m, 1.5 H), 4.99-5.29 (m, 1 H), 3.76-3.98 (m, 1 H), 2.79-3.30 (m, 2 H)	413.2 [M + H] ⁺	93.3%
117	(CD ₃ OD) δ 8.32 (d, 1 H), 8.01 (br d, 1 H), 7.90 (d, 1 H), 7.64-7.85 (m, 3 H), 7.49-7.62 (m, 1 H), 6.32-6.85 (m, 1 H), 3.39-4.51 (m, 2 H), 2.71-3.23 (m, 2 H), 2.36 (br s, 3 H), 1.32-1.99 (m, 6 H)	427.3 [M + H] ⁺	99.8%
118	(CD ₃ OD) δ 8.32 (d, 1 H), 8.01 (br d, 1 H), 7.90 (d, 1 H), 7.64-7.87 (m, 3 H), 7.50-7.61 (m, 1 H), 6.27-6.87 (m, 1 H), 3.38-4.47 (m, 2 H), 2.72-3.19 (m, 2 H), 2.18-2.55 (m, 3 H), 1.34-2.07 (m, 6 H)	427.3 [M + H] ⁺	100%
119	(CD ₃ OD) δ 8.33 (br d, 1 H), 7.86-8.05 (m, 2 H), 7.81 (br d, 1 H), 7.64-7.75 (m, 2 H), 7.56 (t, 1 H), 6.90-7.27 (m, 1 H), 6.51-6.84 (m, 1 H), 4.96-4.99 (m, 1 H), 4.44 (br d, 1 H), 4.01 (br s,	440.2 [M + H] ⁺	98.6%

TABLE 6-continued

Ex. #	¹ H NMR (400 MHz)	LCMS: m/z	% ee
	0.6 H), 3.48 (br s, 0.2 H), 2.91-3.18 (m, 1 H), 2.83 (br d, 1 H), 1.31-1.72 (m, 3 H)		
120	(CD ₃ OD) δ 8.32 (br d, 1 H), 7.86-8.03 (m, 2 H), 7.81 (br d, 1 H), 7.63-7.75 (m, 2 H), 7.51-7.59 (m, 1 H), 6.93-7.28 (m, 1 H), 6.52-6.83 (m, 1 H), 4.95-4.98 (m, 1 H), 4.43 (br d, 1 H), 4.01 (br s, 0.6 H), 3.48 (br s, 0.2 H), 2.92-3.21 (m, 1 H), 2.83 (br d, 1 H), 1.31-1.71 (m, 3 H)	440.2 [M + H] ⁺	97.0%
121	(CD ₃ OD) δ 8.33 (br d, 1 H), 7.85-8.04 (m, 2 H), 7.80 (br s, 1 H), 7.64-7.76 (m, 2 H), 7.57 (t, 1 H), 6.93-7.26 (m, 1 H), 6.52-6.83 (m, 1 H), 4.98 (br s, 1 H), 4.42 (br s, 1 H), 4.01 (br s, 0.6 H), 3.49 (br s, 0.3 H), 2.90-3.22 (m, 1 H), 2.83 (br d, 1 H), 1.34-1.67 (m, 3 H)	440.2 [M + H] ⁺	83.1%
122	(CD ₃ OD) δ 8.32 (br s, 1 H), 7.86-8.04 (m, 2 H), 7.81 (br s, 1 H), 7.64-7.75 (m, 2 H), 7.52-7.61 (m, 1 H), 6.94-7.28 (m, 1 H), 6.51-6.83 (m, 1 H), 4.98 (br s, 1 H), 4.44 (br d, 1 H), 4.02 (br s, 0.6 H), 3.48 (br s, 0.4 H), 2.92-3.18 (m, 1 H), 2.83 (br d, 1 H), 1.33-1.69 (m, 3 H)	440.2 [M + H] ⁺	98.2%
123	(CD ₃ OD) δ 8.29 (br s, 1 H), 8.03 (br s, 2 H), 7.90 (d, 1 H), 7.62-7.82 (m, 3 H), 7.57 (br t, 1 H), 6.87 (br s, 0.7 H), 6.18 (br s, 0.3 H), 3.81-4.28 (m, 1 H), 3.35 (br s, 1 H), 2.91-3.06 (m, 1 H), 2.76 (br d, 1 H)	379.2 [M + H] ⁺	99.1%
124	(CD ₃ OD) δ 8.29 (br s, 1 H), 8.03 (br s, 2 H), 7.90 (d, 1 H), 7.63-7.82 (m, 3 H), 7.57 (br t, 1 H), 6.87 (br s, 0.6 H), 6.19 (br s, 0.3 H), 3.84-4.28 (m, 1 H), 3.48 (br s, 1 H), 2.90-3.06 (m, 1 H), 2.76 (br d, 1 H)	379.2 [M + H] ⁺	100%
125	(CD ₃ OD) δ 8.30 (br s, 1 H), 7.88-8.17 (m, 3 H), 7.63-7.87 (m, 2.7 H), 7.43-7.62 (m, 1.3 H), 6.83-7.42 (m, 1.6 H), 6.19 (br s, 0.4 H), 5.12 (br s, 3 H), 3.86-4.27 (m, 1 H), 2.91-3.08 (m, 1 H), 2.75 (dd, 1 H)	477.3 [M + H] ⁺	98.2%
126	(CD ₃ OD) δ 8.30 (br s, 1 H), 7.88-8.17 (m, 3 H), 7.63-7.87 (m, 2.7 H), 7.43-7.62 (m, 1.3 H), 6.83-7.42 (m, 1.7 H), 6.19 (br s, 0.3 H), 5.12 (br s, 3 H), 3.86-4.27 (m, 1 H), 2.91-3.08 (m, 1 H), 2.75 (dd, 1 H)	477.3 [M + H] ⁺	95.8%
127	(CD ₃ OD) δ 8.23 (br d, 1 H), 7.40-8.00 (m, 5 H), 6.81-7.24 (m, 1 H), 6.35-6.73 (m, 1 H), 3.85-4.36 (m, 1.5 H), 3.26-3.51 (m, 0.5 H), 2.63-3.14 (m, 2 H), 1.37-2.03 (m, 6 H)	463.2 [M + H] ⁺	100%
128	(CD ₃ OD) δ 8.22 (br d, 1 H), 7.39-7.97 (m, 5 H), 6.82-7.21 (m, 1 H), 6.36-6.74 (m, 1 H), 3.85-4.38 (m, 1.5 H), 3.38 (br s, 0.5 H), 2.58-3.14 (m, 2 H), 1.37-2.00 (m, 6 H)	463.2 [M + H] ⁺	100%
129	(CD ₃ OD) δ 8.30 (br d, 1 H), 7.85-8.04 (m, 2 H), 7.64-7.84 (m, 3 H), 7.50-7.59 (m, 1 H), 6.45-7.27 (m, 2 H), 4.43 (br s, 1 H), 3.98 (br s, 0.6 H), 3.46 (br s, 0.4 H), 2.72-3.19 (m, 2 H), 0.97-1.51 (m, 4 H)	452.30 [M + H] ⁺	97.0%
130	(CD ₃ OD) δ 8.30 (br d, 1 H), 7.85-8.02 (m, 2 H), 7.63-7.82 (m, 3 H), 7.50-7.58 (m, 1 H), 6.37-7.26 (m, 2 H), 4.43 (br s, 1 H), 3.98 (br s, 0.6 H), 3.45 (br d, 0.4 H), 2.63-3.19 (m, 2 H), 1.02-1.50 (m, 4 H)	452.20 [M + H] ⁺	99.3%
131	(CD ₃ OD) δ 8.21 (br s, 1 H), 7.91 (br d, 1 H), 7.80 (br d, 1 H), 7.40-7.73 (m, 4 H), 6.16-6.74 (m, 1 H), 5.10 (br s, 1 H), 4.13 (br s, 1 H), 3.98 (br d, 0.5 H), 3.36 (br d, 0.5 H), 2.87-3.09 (m, 1 H), 2.68-2.81 (m, 1 H), 1.27-1.53 (m, 3 H)	470.1 [M + H] ⁺	100%
132	(CD ₃ OD) δ 8.33 (br s, 1 H), 8.03 (br d, 1 H), 7.92 (br d, 1 H), 7.54-7.86 (m, 4 H), 6.79 (br s, 0.6 H), 6.37 (br s, 0.4 H), 5.01-5.11 (m, 1 H), 4.26 (br s, 1 H), 4.08 (br s, 0.6 H), 3.45 (br s, 0.4 H), 2.96-3.20 (m, 1 H), 2.86 (br d, 1 H), 1.40-1.67 (m, 3 H)	468.1 [M + H] ⁺	97.6%
133	(CD ₃ OD) δ 8.21 (br s, 1 H), 7.91 (d, 1 H), 7.80 (br d, 1 H), 7.39-7.71 (m, 4 H), 6.21-6.73 (m, 1 H), 5.09 (br s, 1 H), 4.11-4.24 (m, 1 H), 3.96 (br s, 0.6 H), 3.33 (br s, 0.4 H), 2.80-3.11 (m, 1 H), 2.70-2.77 (m, 1 H), 1.29-1.55 (m, 3 H)	470.1 [M + H] ⁺	97.6%
134	(CD ₃ OD) δ 8.33 (br s, 1 H), 8.03 (br d, 1 H), 7.92 (br d, 1 H), 7.53-7.85 (m, 4 H), 6.79 (br s, 0.6 H), 6.36 (br s, 0.4 H), 5.22 (br s, 1 H), 4.25 (br s, 1 H), 4.09 (br s, 0.6 H), 3.45 (br s, 0.4 H), 2.96-3.24 (m, 1 H), 2.86 (br d, 1 H), 1.39-1.67 (m, 3 H)	470.2 [M + H] ⁺	98.0%
135	(CD ₃ OD) δ 8.30 (br s, 1 H), 8.00 (d, 1 H), 7.90 (d, 1 H), 7.65-7.83 (m, 3 H), 7.56 (ddd, 1 H), 6.29-6.84 (m, 1 H), 4.92-5.13 (m, 1 H), 3.95-4.40 (m, 1.5 H), 3.34-3.62 (m, 0.5 H), 2.77-3.20 (m, 2 H), 1.33-1.67 (m, 3 H)	424.2 [M + H] ⁺	100%
136	(CD ₃ OD) δ 8.30 (br s, 1 H), 8.00 (d, 1 H), 7.90 (d, 1 H), 7.62-7.83 (m, 3 H), 7.50-7.60 (m, 1 H), 6.29-6.84 (m, 1 H), 4.93-5.03 (m, 1 H), 3.90-4.42 (m, 1.5 H), 3.33-3.57 (m, 0.5 H), 2.75-3.21 (m, 2 H), 1.33-1.65 (m, 3 H)	424.2 [M + H] ⁺	98.9%
137	(CD ₃ OD) δ 8.30 (br s, 1 H), 8.00 (d, 1 H), 7.90 (d, 1 H), 7.63-7.84 (m, 3 H), 7.51-7.60 (m, 1 H), 6.24-6.84 (m, 1 H), 4.92-5.05 (m, 1 H), 3.94-4.42 (m, 1.5 H), 3.33-3.62 (m, 0.5 H), 2.78-3.18 (m, 2 H), 1.37-1.65 (m, 3 H)	424.2 [M + H] ⁺	98.6%

TABLE 6-continued

Ex. #	¹ H NMR (400 MHz)	LCMS: m/z	% ee
138	(CD ₃ OD) δ 8.31 (br s, 1 H), 8.00 (d, 1 H), 7.90 (d, 1 H), 7.63-7.84 (m, 3 H), 7.52-7.61 (m, 1 H), 6.22-6.83 (m, 1 H), 4.92-5.03 (m, 1 H), 3.93-4.42 (m, 1.5 H), 3.34-3.54 (m, 0.5 H), 2.76-3.20 (m, 2 H), 1.31-1.66 (m, 3 H)	424.2 [M + H] ⁺	98%
139	(CD ₃ OD) δ 9.32-9.50 (m, 1 H), 7.81-8.08 (m, 3 H), 7.44-7.71 (m, 2 H), 7.11-7.33 (m, 0.4 H), 6.59-7.00 (m, 0.6 H), 4.89-5.18 (m, 1 H), 3.90-4.25 (m, 0.6 H), 3.36-3.65 (m, 0.5 H), 2.59-3.07 (m, 2 H), 1.97-2.35 (m, 1 H), 0.91-1.31 (m, 4 H)	388.1 [M + H] ⁺	100%
140	(CD ₃ OD) δ 9.22-9.54 (m, 1 H), 7.74-8.09 (m, 3 H), 7.45-7.67 (m, 2 H), 7.12-7.34 (m, 0.5 H), 6.56-6.86 (m, 0.5 H), 4.91-5.25 (m, 1 H), 3.96-4.24 (m, 0.6 H), 3.34-3.60 (m, 0.4H), 2.93-3.12 (m, 1 H), 2.55-2.90 (m, 1 H), 2.01-2.32 (m, 1 H), 0.98-1.30 (m, 4 H)	388.0 [M + H] ⁺	97.9%
141	(CD ₃ OD) δ 9.52 (s, 1 H), 8.75-9.00 (m, 1 H), 7.87-8.20 (m, 3 H), 7.69 (dt, 1 H), 7.35-7.59 (m, 1 H), 6.88 (br s, 0.6 H), 6.09 (br d, 0.3 H), 4.29-4.67 (m, 0.5 H), 3.39-3.93 (m, 1.5 H), 2.67-3.17 (m, 2 H), 2.07-2.45 (m, 3H), 1.11-1.69 (m, 6 H)	419.2 [M + H] ⁺	6.7%
142	(CD ₃ OD) δ 9.42 (s, 1 H), 7.87-8.05 (m, 3 H), 7.56-7.75 (m, 1 H), 7.50 (s, 1 H), 6.19-6.75 (m, 1 H), 4.82-4.93 (m, 0.5 H), 3.95-4.55 (m, 1.5 H), 2.61-3.12 (m, 2 H), 2.10-2.36 (m, 3 H), 1.10-1.69 (m, 6 H)	419.1 [M + H] ⁺	98.8%
143	(CD ₃ OD) δ 9.43-9.67 (m, 1 H), 8.24-8.48 (m, 1 H), 7.94-8.17 (m, 4 H), 7.59-7.84 (m, 2 H), 7.44 (br s, 0.4 H), 6.88 (br s, 0.6 H), 5.07-5.37 (m, 1 H), 4.13-4.42 (m, 0.6 H), 3.90-4.07 (m, 3 H), 3.66 (br s, 0.4 H), 2.77-3.18 (m, 2 H)	428.2 [M + H] ⁺	100%
144	(CD ₃ OD) δ 9.46-9.64 (m, 1 H), 8.27-8.47 (m, 1 H), 7.95-8.19 (m, 4 H), 7.58-7.84 (m, 2 H), 7.44 (br s, 0.4 H), 6.88 (s, 0.6 H), 5.31 (br dd, 0.7 H), 5.17 (br s, 0.3 H), 4.27 (br s, 0.5 H), 3.96-4.07 (m, 3 H), 3.66 (br s, 0.5 H), 2.78-3.17 (m, 2 H)	428.2 [M + H] ⁺	99.0%
145	(CD ₃ OD) δ 9.46-9.69 (m, 1 H), 8.69-8.85 (m, 1 H), 8.19-8.37 (m, 1 H), 7.92-8.17 (m, 4 H), 7.60-7.81 (m, 3 H), 7.37 (br s, 0.4 H), 6.91 (s, 0.6 H), 5.09-5.31 (m, 1 H), 4.14-4.52 (m, 0.6 H), 3.69 (br s, 0.4 H), 3.15-3.23 (m, 0.5 H), 3.02 (br d, 0.5 H), 2.87 (br d, 1 H)	425.1 [M + H] ⁺	100%
146	(CD ₃ OD) δ 9.24-9.52 (m, 1 H), 8.55-8.77 (m, 1 H), 8.08-8.27 (m, 1 H), 7.79-8.06 (m, 4 H), 7.48-7.73 (m, 3 H), 7.27 (br s, 0.4 H), 6.79 (br s, 0.6 H), 5.07 (br d, 1 H), 3.87-4.43 (m, 0.7 H), 3.56 (br d, 0.3 H), 3.05-3.14 (m, 0.7 H), 2.89 (br d, 0.3 H), 2.77 (br s, 1 H)	425.1 [M + H] ⁺	98.0%
147	(CD ₃ OD) δ 9.55 (br s, 1 H), 8.30-8.62 (m, 1 H), 7.93-8.20 (m, 3 H), 7.54-7.86 (m, 2 H), 6.47-6.88 (m, 1 H), 4.97-5.08 (m, 0.3 H), 4.50-4.63 (m, 0.7 H), 4.28 (br s, 0.7 H), 3.74 (br s, 0.3 H), 2.74-3.15 (m, 2 H)	372.2 [M + H] ⁺	100%
148	(CD ₃ OD) δ 9.55 (br s, 1 H), 8.25-8.67 (m, 1 H), 7.96-8.19 (m, 3 H), 7.55-7.85 (m, 2 H), 6.50-6.85 (m, 1 H), 4.99-5.08 (m, 0.2 H), 4.46-4.63 (m, 0.8 H), 4.27 (br s, 0.5 H), 3.73 (br s, 0.5 H), 2.75-3.15 (m, 2 H)	372.1 [M + H] ⁺	100%
149	(CD ₃ OD) δ 9.55 (br s, 1 H), 8.25-8.51 (m, 1 H), 7.99-8.17 (m, 3 H), 7.71-7.95 (m, 2 H), 7.63 (s, 1 H), 6.76 (br s, 1 H), 4.72 (br s, 1 H), 4.27 (br s, 0.6 H), 3.83 (br s, 0.4 H), 3.11 (br s, 1 H), 2.84 (br d, 1 H)	347.0 [M + H] ⁺	100%
150	(CD ₃ OD) δ 9.55 (br s, 1 H), 8.22-8.54 (m, 1 H), 7.60-8.17 (m, 6 H), 6.77 (br s, 1 H), 4.72 (br s, 1 H), 4.27 (br s, 0.6 H), 3.84 (br s, 0.4 H), 3.13 (br d, 1 H), 2.84 (br d, 1 H)	347.1 [M + H] ⁺	100%
151	(CD ₃ OD) δ 9.42-9.59 (m, 1 H), 7.88-8.16 (m, 3 H), 7.54-7.78 (m, 2 H), 7.28 (br s, 0.5 H), 6.82 (s, 0.5 H), 5.05-5.22 (m, 1 H), 4.21 (br s, 1 H), 3.41-3.84 (m, 2 H), 2.96-3.15 (m, 4 H), 2.82 (br s, 1 H)	438.3 [M + H] ⁺	100%
152	(CD ₃ OD) δ 9.35-9.60 (m, 1 H), 7.82-8.15 (m, 3 H), 7.51-7.76 (m, 2 H), 7.32 (br s, 0.5 H), 6.82 (br s, 0.5 H), 5.04-5.23 (m, 1 H), 4.22 (br s, 1 H), 3.49-3.84 (m, 2 H), 2.68-3.12 (m, 4 H), 2.82 (br s, 1 H)	438.3 [M + H] ⁺	97.5%
153	(CD ₃ OD) δ 9.57 (s, 1 H), 8.62 (br s, 1 H), 8.45 (br s, 1 H), 7.91-8.17 (m, 4 H), 7.75 (br t, 1 H), 7.62 (s, 1 H), 7.42 (br d, 1 H), 6.80 (br s, 1 H), 4.76 (br s, 1 H), 4.54 (s, 2 H), 4.16 (br s, 1 H), 3.44 (s, 3 H), 3.03-3.16 (m, 1 H), 2.81 (br d, 1 H)	440.2 [M + H] ⁺	100%
154	(CD ₃ OD) δ 9.57 (s, 1 H), 8.62 (s, 1 H), 8.45 (br s, 1 H), 7.90-8.15 (m, 4 H), 7.75 (br t, 1 H), 7.62 (s, 1 H), 7.42 (br d, 1 H), 6.79 (br s, 1 H), 4.77 (br s, 1 H), 4.54 (s, 2 H), 4.14 (br s, 1 H), 3.44 (s, 3 H), 3.02-3.16 (m, 1 H), 2.81 (br d, 1 H)	440.2 [M + H] ⁺	99.1%
155	(CD ₃ OD) δ 9.57 (s, 1 H), 8.61 (s, 1 H), 8.45 (br s, 1 H), 7.90-8.18 (m, 4 H), 7.71-7.82 (m, 1 H), 7.62 (s, 1 H), 7.46 (br d, 1 H), 6.80 (br s, 1 H), 4.75 (br s, 1 H), 4.15 (br s, 1 H), 3.58 (s, 2 H), 3.03-3.14 (m, 1 H), 2.81 (br d, 1 H), 2.32 (s, 6 H)	453.3 [M + H] ⁺	99.0%

TABLE 6-continued

Ex. #	¹ H NMR (400 MHz)	LCMS: m/z	% ee
156	(CD ₃ OD) δ 9.57 (br s, 1 H), 8.61 (s, 1 H), 8.46 (br s, 1 H), 7.88-8.16 (m, 4 H), 7.72-7.81 (m, 1 H), 7.62 (br s, 1 H), 7.46 (br d, 1 H), 6.80 (br s, 1 H), 4.76 (br s, 1 H), 4.15 (br s, 1 H), 3.58 (s, 2 H), 3.11 (br d, 1 H), 2.81 (br d, 1 H), 2.32 (s, 6 H)	453.3 [M + H] ⁺	97.4%
157	(CD ₃ OD) δ 9.52 (br s, 1 H), 8.36-8.90 (m, 1 H), 7.44-8.25 (m, 9 H), 6.77 (br s, 0.5 H), 4.93-5.06 (m, 0.5 H), 4.29 (br s, 0.5 H), 3.68-4.06 (m, 0.5 H), 3.31-3.46 (m, 0.5 H), 2.69-3.22 (m, 2 H)	424.20 [M + H] ⁺	99.8%
158	(CD ₃ OD) δ 9.53 (br s, 1 H), 8.24-8.81 (m, 1 H), 7.35-8.19 (m, 9 H), 6.77 (br s, 1 H), 4.95-5.02 (m, 0.2 H), 4.30 (br s, 0.8 H), 3.90 (br s, 0.5 H), 3.33 (br s, 0.5 H), 2.77-3.22 (m, 2 H)	424.20 [M + H] ⁺	99.4%
159	(CD ₃ OD) δ 9.51-9.56 (m, 1 H), 7.98-8.13 (m, 3 H), 7.59-7.78 (m, 2 H), 7.50 (s, 0.3 H), 6.82 (s, 0.7 H), 5.45 (br dd, 0.6 H), 5.11 (br dd, 0.4 H), 4.20 (br t, 0.5 H), 3.56-3.77 (m, 4.5 H), 2.90-3.20 (m, 1 H), 2.74-2.88 (m, 1 H), 1.84-2.14 (m, 4 H)	449.30 [M + H] ⁺	100%
160	(CD ₃ OD) δ 9.51-9.56 (m, 1 H), 7.96-8.18 (m, 3 H), 7.60-7.83 (m, 2 H), 7.50 (s, 0.3 H), 6.82 (s, 0.7 H), 5.45 (br dd, 0.7 H), 5.11 (br dd, 0.3 H), 4.12-4.32 (m, 0.5 H), 3.54-3.78 (m, 4.5 H), 2.91-3.21 (m, 1 H), 2.74-2.87 (m, 1 H), 1.77-2.20 (m, 4 H)	449.20 [M + H] ⁺	99.8%
161	(CD ₃ OD) δ 9.37-9.67 (m, 1 H), 7.85-8.18 (m, 3 H), 7.51-7.81 (m, 2 H), 7.26 (br s, 0.3 H), 6.83 (br s, 0.7 H), 5.03-5.19 (m, 1 H), 4.18 (br s, 0.8 H), 3.61 (br s, 0.2 H), 2.90-3.17 (m, 1 H), 2.81 (br d, 1 H), 1.72-1.97 (m, 6 H)	408.2 [M + H] ⁺	100%
162	(CD ₃ OD) δ 9.39-9.58 (m, 1 H), 7.90-8.14 (m, 3 H), 7.54-7.78 (m, 2 H), 7.26 (s, 0.4 H), 6.83 (s, 0.6 H), 5.04-5.22 (m, 1 H), 4.20 (br s, 0.7 H), 3.55-3.67 (m, 0.3 H), 3.06-3.18 (m, 0.6 H), 2.90-3.01 (m, 0.4 H), 2.81 (br d, 1 H), 1.73-1.92 (m, 6 H)	408.2 [M + H] ⁺	99.4%
163	(CD ₃ OD) δ 9.44-9.65 (m, 1 H), 8.48-8.74 (m, 1 H), 7.57-8.21 (m, 7.3 H), 7.32 (br s, 0.2 H), 6.91 (s, 0.5 H), 5.09-5.30 (m, 1 H), 4.09-4.44 (m, 0.6 H), 3.58-3.91 (m, 0.4 H), 2.81-3.23 (m, 2 H)	443.20 [M + H] ⁺	98.4%
164	(CD ₃ OD) δ 9.41-9.64 (m, 1 H), 8.46-8.77 (m, 1 H), 7.55-8.23 (m, 7.2 H), 7.32 (br s, 0.3 H), 6.91 (s, 0.5 H), 5.13-5.28 (m, 1 H), 4.31 (br s, 0.6 H), 3.69 (br s, 0.4 H), 2.71-3.21 (m, 2 H)	443.20 [M + H] ⁺	98.7%
165	(CD ₃ OD) δ 9.44-9.62 (m, 1 H), 7.93-8.18 (m, 3 H), 7.59-7.86 (m, 3 H), 7.23-7.55 (m, 1 H), 7.01 (d, 0.7 H), 6.83-6.95 (m, 1 H), 5.07-5.31 (m, 1 H), 4.11-4.49 (m, 0.6 H), 3.94-4.10 (m, 3 H), 3.66 (br s, 0.4 H), 2.95-3.26 (m, 1 H), 2.88 (br s, 1 H)	428.1 [M + H] ⁺	100%
166	(CD ₃ OD) δ 9.41-9.65 (m, 1 H), 7.96-8.15 (m, 3 H), 7.65-7.84 (m, 3 H), 7.39 (br s, 0.4 H), 7.01 (d, 0.6 H), 6.91 (d, 1 H), 5.10-5.32 (m, 1 H), 4.23-4.37 (m, 0.6 H), 3.94-4.10 (m, 3 H), 3.57-3.74 (m, 0.4 H), 2.94-3.26 (m, 1 H), 2.86 (br d, 1 H)	428.1 [M + H] ⁺	97.3%
167	(CD ₃ OD) δ 9.48-9.60 (m, 1 H), 8.58-8.80 (m, 1 H), 8.25-8.43 (m, 1 H), 7.95-8.18 (m, 3 H), 7.81-7.94 (m, 1 H), 7.63-7.79 (m, 2 H), 7.37 (br s, 0.3 H), 6.90 (s, 0.7 H), 5.11-5.29 (m, 1 H), 4.30 (br s, 0.6 H), 3.59-3.76 (m, 0.4 H), 2.97-3.26 (m, 1 H), 2.87 (br d, 1 H)	443.1 [M + H] ⁺	96.8%
168	(CD ₃ OD) δ 9.29-9.54 (m, 1 H), 8.46-8.67 (m, 1 H), 8.13-8.32 (m, 1 H), 7.83-8.04 (m, 3 H), 7.69-7.81 (m, 1 H), 7.51-7.67 (m, 2 H), 7.25 (s, 0.4 H), 6.78 (s, 0.6 H), 4.99-5.19 (m, 1 H), 4.18 (br t, 0.4 H), 3.50-3.62 (m, 0.6 H), 2.83-3.18 (m, 1 H), 2.67-2.80 (m, 1 H)	443.1 [M + H] ⁺	98.0%
169	(CD ₃ OD) δ 9.50-9.59 (m, 1 H), 8.93-9.19 (m, 1 H), 8.32-8.64 (m, 2 H), 7.89-8.18 (m, 3 H), 7.59-7.84 (m, 2 H), 7.36 (s, 0.3 H), 6.91 (s, 0.7 H), 5.11-5.33 (m, 1 H), 4.19-4.43 (m, 0.6 H), 3.70 (td, 0.4 H), 2.97-3.27 (m, 1 H), 2.79-2.94 (m, 1 H)	493.1 [M + H] ⁺	97.8%
170	(CD ₃ OD) δ 9.35-9.48 (m, 1 H), 8.86-9.04 (m, 1 H), 8.23-8.43 (m, 2 H), 7.82-8.07 (m, 3 H), 7.43-7.72 (m, 2 H), 7.24 (s, 0.4 H), 6.79 (s, 0.6 H), 5.00-5.16 (m, 1 H), 4.10-4.25 (m, 0.6 H), 3.48-3.66 (m, 0.4 H), 2.85-3.14 (m, 1 H), 2.68-2.81 (m, 1 H)	493.1 [M + H] ⁺	98.8%
171	(CD ₃ OD) δ 9.42-9.66 (m, 1 H), 8.52-8.66 (m, 1 H), 7.82-8.27 (m, 5 H), 7.62-7.80 (m, 2 H), 7.37 (br s, 0.3 H), 6.90 (s, 0.7 H), 5.09-5.35 (m, 1 H), 4.30 (br s, 0.6 H), 3.68 (br s, 0.4 H), 3.14-3.27 (m, 0.7 H), 2.97-3.10 (m, 0.3 H), 2.87 (br d, 1 H), 2.39-2.58 (m, 3 H)	439.1 [M + H] ⁺	100%
172	(CD ₃ OD) δ 9.35-9.74 (m, 1 H), 8.49-8.69 (m, 1 H), 7.83-8.27 (m, 5 H), 7.59-7.81 (m, 2 H), 7.39 (br s, 0.3 H), 6.90 (s, 0.7 H), 5.10-5.34 (m, 1 H), 4.31 (br s, 0.5 H), 3.56-3.78 (m, 0.5 H), 3.12-3.27 (m, 0.6 H), 2.96-3.12 (m, 0.4 H), 2.87 (br d, 1 H), 2.41-2.55 (m, 3 H)	439.1 [M + H] ⁺	94.8%
173	(CD ₃ OD) δ 9.46-9.72 (m, 1 H), 8.94-9.11 (m, 1 H), 8.40-8.67 (m, 1 H), 7.89-8.23 (m, 4 H), 7.58-7.86 (m, 2 H), 7.39 (br s, 0.3 H), 6.92 (br s, 0.7 H), 5.12-5.34 (m, 1 H), 4.31 (s, 0.5 H), 3.70 (br s, 0.5 H), 3.14-3.26 (m, 0.6 H), 3.03 (br s, 0.4 H), 2.89 (br s, 1 H)	493.1 [M + H] ⁺	100%

TABLE 6-continued

Ex. #	¹ H NMR (400 MHz)	LCMS: m/z	% ee
174	(CD ₃ OD) δ 9.37-9.81 (m, 1 H), 8.92-9.18 (m, 1 H), 8.37-8.66 (m, 1 H), 7.90-8.29 (m, 4 H), 7.59-7.84 (m, 2 H), 7.39 (br s, 0.4 H), 6.92 (s, 0.6 H), 5.12-5.32 (m, 1 H), 4.35 (br s, 0.5 H), 3.70 (br s, 0.5 H), 3.13-3.27 (m, 0.6 H), 3.02 (br d, 0.4 H), 2.89 (br s, 1 H)	493.0 [M + H] ⁺	97.5%
175	(CD ₃ OD) δ 9.43-9.65 (m, 1 H), 7.95-8.20 (m, 3 H), 7.59-7.93 (m, 3 H), 6.82-7.52 (m, 2 H), 5.09-5.32 (m, 1 H), 4.29 (br s, 0.5 H), 3.64 (br s, 0.5 H), 2.97-3.26 (m, 1 H), 2.88 (br s, 1 H)	414.2 [M + H] ⁺	97.0%
176	(CD ₃ OD) δ 9.44-9.65 (m, 1 H), 7.95-8.17 (m, 3 H), 7.61-7.93 (m, 3 H), 6.80-7.47 (m, 2 H), 5.08-5.31 (m, 1 H), 4.29 (br s, 0.6 H), 3.65 (br s, 0.4 H), 2.96-3.25 (m, 1 H), 2.88 (br s, 1 H)	414.3 [M + H] ⁺	98.3%
177	(CD ₃ OD) δ 9.51-9.62 (m, 1 H), 9.17-9.38 (m, 1 H), 8.72-8.88 (m, 1 H), 8.41-8.61 (m, 1 H), 7.95-8.19 (m, 3 H), 7.58-7.87 (m, 3 H), 6.80-7.51 (m, 1 H), 5.10-5.39 (m, 1 H), 3.62-4.43 (m, 1 H), 2.97-3.27 (m, 1 H), 2.87 (br s, 1 H)	425.3 [M + H] ⁺	100%
178	(CD ₃ OD) δ 9.51-9.62 (m, 1 H), 9.17-9.40 (m, 1 H), 8.74-8.93 (m, 1 H), 8.43-8.62 (m, 1 H), 7.95-8.16 (m, 3 H), 7.62-7.80 (m, 3 H), 6.80-7.54 (m, 1 H), 5.12-5.38 (m, 1 H), 3.58-4.50 (m, 1 H), 2.95-3.25 (m, 1 H), 2.87 (br s, 1 H)	425.3 [M + H] ⁺	100%
179	(CD ₃ OD) δ 9.49-9.61 (m, 1 H), 8.77-8.93 (m, 2 H), 7.97-8.18 (m, 5 H), 7.63-7.80 (m, 2 H), 6.87-7.43 (m, 1 H), 5.11-5.35 (m, 1 H), 3.63-4.43 (m, 1 H), 2.97-3.27 (m, 1 H), 2.89 (br d, 1 H)	425.3 [M + H] ⁺	100%
180	(CD ₃ OD) δ 9.50-9.60 (m, 1 H), 8.78-8.88 (m, 2 H), 7.96-8.17 (m, 5 H), 7.64-7.79 (m, 2 H), 6.75-7.53 (m, 1 H), 5.09-5.36 (m, 1 H), 3.57-4.53 (m, 1 H), 2.96-3.22 (m, 1 H), 2.87 (br s, 1 H)	425.2 [M + H] ⁺	100%
181	(DMSO-d ₆) δ 12.19 (br s, 1 H), 9.44-9.79 (m, 1 H), 8.40-8.64 (m, 1 H), 7.43-8.21 (m, 7.3 H), 6.50-7.25 (m, 0.7 H), 4.72-5.13 (m, 1 H), 4.35 (br s, 0.3 H), 3.81-4.08 (m, 3.7 H), 2.70-3.05 (m, 2 H)	455.4 [M + H] ⁺	100%
182	(CD ₃ OD) δ 9.35-9.58 (m, 0.8 H), 7.91-8.45 (m, 6 H), 7.36-7.81 (m, 3 H), 6.90 (br s, 0.2 H), 5.03-5.30 (m, 1 H), 3.73-3.97 (m, 4 H), 3.41-3.51 (m, 1 H), 2.80 (br d, 1 H)	455.4 [M + H] ⁺	97.7%
183	(CD ₃ OD) δ 9.40-9.63 (m, 1 H), 7.89-8.15 (m, 4 H), 7.62-7.79 (m, 2 H), 6.83-6.94 (m, 1 H), 5.08 (dd, 0.4 H), 4.50 (dd, 0.6 H), 4.07-4.15 (m, 0.6 H), 3.97-4.07 (m, 3 H), 3.47 (td, 0.4 H), 2.93-3.19 (m, 1 H), 2.62-2.87 (m, 1 H)	361.2 [M + H] ⁺	100%
184	(CD ₃ OD) δ 9.28-9.54 (m, 1 H), 7.76-8.03 (m, 4 H), 7.48-7.67 (m, 2 H), 6.66-6.82 (m, 1 H), 4.96 (dd, 0.4 H), 4.38 (dd, 0.6 H), 3.95-4.03 (m, 0.6 H), 3.85-3.95 (m, 3 H), 3.35 (td, 0.4 H), 2.81-3.06 (m, 1 H), 2.57-2.76 (m, 1 H)	361.2 [M + H] ⁺	100%
185	(CD ₃ OD) δ 9.45-9.60 (m, 1 H), 8.78-8.96 (m, 1 H), 8.21-8.40 (m, 1 H), 7.96-8.12 (m, 3 H), 7.57-7.84 (m, 3 H), 7.30-7.54 (m, 0.5 H), 6.87 (s, 0.5 H), 5.10-5.33 (m, 1 H), 4.27 (br s, 0.5 H), 3.67 (br s, 0.5 H), 3.09-3.24 (m, 1 H), 2.77-3.02 (m, 1 H)	464.2 [M + H] ⁺	98.6%
186	(CD ₃ OD) δ 9.41-9.61 (m, 1 H), 8.75-8.98 (m, 1 H), 8.19-8.43 (m, 1 H), 7.93-8.15 (m, 3 H), 7.56-7.86 (m, 3 H), 7.37-7.52 (m, 0.5 H), 6.87 (s, 0.5 H), 5.07-5.34 (m, 1 H), 4.26 (br s, 0.5 H), 3.68 (br d, 0.5 H), 3.11-3.25 (m, 1 H), 2.81-3.02 (m, 1 H)	464.2 [M + H] ⁺	100%
187	(CD ₃ OD) δ 9.44-9.59 (m, 1 H), 8.34-8.54 (m, 1 H), 7.90-8.21 (m, 4 H), 7.60-7.81 (m, 2 H), 7.42 (s, 0.4 H), 6.87 (s, 0.6 H), 5.10-5.35 (m, 1 H), 4.91-4.99 (m, 1 H), 4.25 (br t, 0.6 H), 3.58-3.72 (m, 0.4 H), 2.93-3.40 (m, 1 H), 2.76-2.92 (m, 1 H), 2.43-2.70 (m, 4 H), 1.86-2.00 (m, 2 H)	468.0 [M + H] ⁺	100%
188	(CD ₃ OD) δ 9.44-9.60 (m, 1 H), 8.32-8.55 (m, 1 H), 7.92-8.19 (m, 4 H), 7.59-7.81 (m, 2 H), 7.41 (s, 0.4 H), 6.86 (s, 0.6 H), 5.08-5.35 (m, 1 H), 4.91-5.01 (m, 1 H), 4.25 (br t, 0.6 H), 3.56-3.74 (m, 0.4 H), 2.90-3.25 (m, 1 H), 2.73-2.89 (m, 1 H), 2.44-2.68 (m, 4 H), 1.86-1.97 (m, 2 H)	468.2 [M + H] ⁺	99.4%
189	(CD ₃ OD) δ 9.45-9.60 (m, 1 H), 8.25-8.38 (m, 1 H), 7.90-8.17 (m, 3 H), 7.45-7.86 (m, 3 H), 7.07-7.48 (m, 1.4 H), 6.88 (s, 0.6 H), 5.09-5.28 (m, 1 H), 4.27 (br s, 0.6 H), 3.58-3.72 (m, 0.4 H), 2.95-3.25 (m, 1 H), 2.85 (br d, 1 H)	464.2 [M + H] ⁺	100%
190	(CD ₃ OD) δ 9.45-9.58 (m, 1 H), 8.26-8.38 (m, 1 H), 7.90-8.16 (m, 3 H), 7.49-7.86 (m, 3 H), 7.07-7.48 (m, 1.4 H), 6.88 (s, 0.6 H), 5.08-5.29 (m, 1 H), 4.27 (br s, 0.6 H), 3.58-3.73 (m, 0.4 H), 2.95-3.24 (m, 1 H), 2.85 (br d, 1 H)	464.1 [M + H] ⁺	99.6%
191	(CD ₃ OD) δ 9.44-9.67 (m, 1.5 H), 9.39 (s, 0.5 H), 8.73-8.93 (m, 2 H), 7.92-8.20 (m, 3 H), 7.55-7.83 (m, 2 H), 7.38 (br s, 0.4 H), 6.91 (br s, 0.6 H), 5.08-5.33 (m, 1 H), 4.30 (br s, 0.6 H), 3.71 (br s, 0.4 H), 3.11-3.27 (m, 1 H), 2.76-3.09 (m, 1 H)	426.2 [M + H] ⁺	98.6%
192	(CD ₃ OD) δ 9.44-9.61 (m, 1.6 H), 9.39 (s, 0.4 H), 8.72-8.92 (m, 2 H), 7.92-8.21 (m, 3 H), 7.60-7.82 (m, 2 H), 7.37 (br s, 0.4 H), 6.91 (s, 0.6 H), 5.07-5.34 (m, 1 H), 4.31 (br s, 0.6 H), 3.71 (br s, 0.4 H), 3.12-3.28 (m, 1 H), 2.81-3.09 (m, 1 H)	426.2 [M + H] ⁺	100%

TABLE 6-continued

Ex. #	¹ H NMR (400 MHz)	LCMS: m/z	% ee
193	(CD ₃ OD) δ 9.56 (s, 1 H), 8.74 (br s, 0.6 H), 8.19-8.40 (m, 1 H), 8.13 (br s, 1 H), 8.03 (br d, 2.4 H), 7.54-7.82 (m, 3.6 H), 7.42 (br s, 0.4 H), 6.53-6.91 (m, 1 H), 5.00-5.10 (m, 0.2 H), 4.67 (br s, 0.8 H), 3.89-4.57 (m, 1 H), 2.97-3.26 (m, 1 H), 2.85 (br d, 1 H), 2.39-2.51 (m, 3 H)	438.2 [M + H] ⁺	97.1%
194	(CD ₃ OD) δ 9.56 (s, 1 H), 8.75 (br s, 0.6 H), 8.20-8.39 (m, 1 H), 8.14 (br s, 1 H), 8.03 (br d, 2.4 H), 7.59-7.80 (m, 3.6 H), 7.42 (br s, 0.4 H), 6.54-6.87 (m, 1 H), 5.02 (br s, 0.3 H), 4.60-4.73 (m, 0.7 H), 3.84-4.41 (m, 1 H), 2.95-3.25 (m, 1 H), 2.85 (br d, 1 H), 2.39-2.50 (m, 3 H)	438.2 [M + H] ⁺	96.3%
195	(CD ₃ OD) δ 9.39-9.67 (m, 1 H), 8.62-8.88 (m, 1 H), 8.31-8.52 (m, 1 H), 7.91-8.21 (m, 4.3 H), 7.62-7.82 (m, 2 H), 7.37 (s, 0.3 H), 6.91 (s, 0.4 H), 5.11-5.31 (m, 1 H), 4.30 (br s, 0.5 H), 3.69 (br s, 0.5 H), 3.12-3.28 (m, 0.6 H), 2.95-3.10 (m, 0.4 H), 2.87 (br d, 1 H)	509.2 [M + H] ⁺	100%
196	(CD ₃ OD) δ 9.46-9.65 (m, 1 H), 8.68-8.85 (m, 1 H), 8.32-8.52 (m, 1 H), 7.84-8.15 (m, 5.3 H), 7.69-7.82 (m, 1 H), 7.46 (s, 0.3 H), 6.94 (s, 0.4 H), 5.13-5.35 (m, 1 H), 4.19-4.31 (m, 0.5 H), 3.60-3.75 (m, 0.5 H), 3.18-3.29 (m, 0.5 H), 2.98-3.11 (m, 0.5 H), 2.89 (br d, 1 H)	509.1 [M + H] ⁺	96.9%
197	(CD ₃ OD) δ 8.49 (br s, 1 H), 8.23 (br d, 2 H), 8.10 (br d, 1 H), 7.98 (br s, 1 H), 7.83 (br d, 2 H), 7.57-7.72 (m, 3 H), 7.50 (br d, 1 H), 7.38 (br s, 1 H), 6.72 (br s, 1 H), 4.38-4.51 (m, 1 H), 3.50 (br s, 1 H), 2.97 (br s, 1 H), 2.72 (br d, 1 H)	439.0 [M + H] ⁺	99.1%
198	(CD ₃ OD) δ 8.57 (br s, 1 H), 8.31 (br d, 2 H), 8.18 (br d, 1 H), 8.05 (br s, 1 H), 7.86-7.95 (m, 2 H), 7.64-7.78 (m, 3 H), 7.57 (br t, 1 H), 7.40-7.48 (m, 1 H), 6.78 (br s, 1 H), 4.28-4.58 (m, 1 H), 4.04 (br s, 1 H), 3.05 (br s, 1 H), 2.80 (br d, 1 H)	439.0 [M + H] ⁺	93.5%
199	(CD ₃ OD) δ 8.32 (d, 1 H), 8.05 (br s, 2 H), 7.91 (d, 1 H), 7.63-7.85 (m, 3 H), 7.49-7.62 (m, 1 H), 6.72 (br s, 1 H), 4.63 (br s, 1 H), 4.01 (br s, 1 H), 2.94-3.11 (m, 1 H), 2.80 (br d, 1 H), 1.44 (s, 9 H)	418.2 [M + H] ⁺	98.3%
200	(CD ₃ OD) δ 8.32 (d, 1 H), 7.98-8.27 (m, 2 H), 7.92 (d, 1 H), 7.68-7.80 (m, 3 H), 7.53-7.63 (m, 1 H), 6.75 (br s, 1 H), 4.40-4.69 (m, 1 H), 4.00 (br d, 1 H), 2.94-3.11 (m, 1 H), 2.80 (br d, 1 H), 1.45 (s, 9 H)	418.2 [M + H] ⁺	99.3%
201	(CD ₃ OD) δ 9.13 (br s, 1 H), 8.26-8.50 (m, 3 H), 8.03 (br s, 1 H), 7.90 (br d, 1 H), 7.65-7.79 (m, 3 H), 7.52-7.61 (m, 1 H), 6.21-7.03 (m, 1 H), 4.63 (br s, 1 H), 3.44-4.17 (m, 1 H), 2.94-3.14 (m, 1 H), 2.66-2.84 (m, 1 H)	362.0 [M + H] ⁺	99.9%
202	(CD ₃ OD) δ 9.13 (br s, 1 H), 8.26-8.50 (m, 3 H), 8.03 (br s, 1 H), 7.90 (br d, 1 H), 7.64-7.78 (m, 3 H), 7.56 (br t, 1 H), 6.01-6.97 (m, 1 H), 4.63 (br s, 1 H), 3.46-4.19 (m, 1 H), 2.98-3.16 (m, 1 H), 2.78 (br d, 1 H)	362.1 [M + H] ⁺	99.7%
203	(CD ₃ OD) δ 8.30 (d, 1 H), 8.00 (br d, 1 H), 7.88 (d, 1 H), 7.78 (br s, 1 H), 7.70 (br t, 1 H), 7.65 (s, 1 H), 7.50-7.59 (m, 1 H), 6.33-6.82 (m, 1 H), 4.36 (br s, 1 H), 3.96 (s, 1 H), 3.03 (br s, 1 H), 2.80 (br s, 1 H), 2.32 (s, 3 H), 0.98-1.53 (m, 9 H)	416.1 [M + H] ⁺	100%
204	(CD ₃ OD) δ 8.30 (d, 1 H), 8.00 (br d, 1 H), 7.88 (d, 1 H), 7.77 (br d, 1 H), 7.70 (br t, 1 H), 7.65 (s, 1 H), 7.48-7.58 (m, 1 H), 6.37-6.81 (m, 1 H), 4.35 (br s, 1 H), 3.95 (s, 1 H), 3.04 (br s, 1 H), 2.80 (br s, 1 H), 2.32 (s, 3 H), 0.96-1.53 (m, 9 H)	416.1 [M + H] ⁺	99.7%
205	(CD ₃ OD) δ 8.57 (br d, 1 H), 8.14-8.51 (m, 3.5 H), 7.81-8.10 (m, 4.5 H), 7.69 (br s, 1 H), 7.46 (dd, 1 H), 6.94 (br s, 1 H), 4.60 (s, 1 H), 4.13 (br s, 1 H), 3.12 (br s, 1 H), 2.88 (br s, 1 H)	440.1 [M + H] ⁺	100%
206	(CD ₃ OD) δ 8.57 (br s, 1 H), 8.13-8.52 (m, 3.5 H), 7.82-8.13 (m, 4.5 H), 7.69 (br s, 1 H), 7.40-7.53 (m, 1 H), 6.95 (br s, 1 H), 4.40-4.61 (m, 1 H), 4.14 (br s, 1 H), 3.11 (br s, 1 H), 2.87 (br s, 1 H)	440.1 [M + H] ⁺	99.9%
207	(CD ₃ OD) δ 8.35-8.83 (m, 3 H), 7.80-8.28 (m, 5 H), 7.42-7.77 (m, 2 H), 7.01 (br s, 1 H), 4.54-4.64 (m, 1 H), 3.59-4.29 (m, 1 H), 2.77-3.30 (m, 2 H), 2.46 (s, 3 H)	438.2 [M + H] ⁺	100%
208	(CD ₃ OD) δ 8.19-8.71 (m, 3 H), 7.68-8.17 (m, 5 H), 7.29-7.66 (m, 2 H), 6.89 (br s, 1 H), 4.34-4.51 (m, 1 H), 3.47-4.14 (m, 1 H), 2.68-3.18 (m, 2 H), 2.34 (s, 3 H)	438.2 [M + H] ⁺	99.6%
209	(CD ₃ OD) δ 8.34 (d, 1 H), 8.25 (br s, 1 H), 7.96 (br d, 1 H), 7.86 (ddd, 1 H), 7.74-7.82 (m, 1 H), 7.59 (s, 1 H), 6.72-7.22 (m, 2 H), 4.36 (br d, 1 H), 3.32-4.03 (m, 1 H), 2.64-3.16 (m, 2 H), 1.57 (br s, 4 H), 1.25-1.48 (m, 2 H)	455.2 [M + H] ⁺	94.4%
210	(CD ₃ OD) δ 8.46 (d, 1 H), 8.37 (br s, 1 H), 8.08 (br d, 1 H), 7.98 (ddd, 1 H), 7.86-7.93 (m, 1 H), 7.71 (s, 1 H), 6.84-7.36 (m, 2 H), 4.48 (br d, 1 H), 3.45-4.15 (m, 1 H), 2.81-3.27 (m, 2 H), 1.69 (br s, 4 H), 1.44-1.59 (m, 2 H)	455.2 [M + H] ⁺	90.2%

TABLE 6-continued

Ex. #	¹ H NMR (400 MHz)	LCMS: m/z	% ee
211	(CD ₃ OD) δ 8.30-8.37 (m, 1 H), 8.01-8.29 (m, 2 H), 7.95 (br d, 1 H), 7.85 (ddd, 1 H), 7.73-7.81 (m, 1 H), 7.60 (s, 1 H), 6.83 (br s, 1 H), 4.53 (br s, 1 H), 3.93 (br s, 1 H), 2.64-3.10 (m, 2 H), 2.16-2.31 (m, 3 H)	361.1 [M + H] ⁺	100%
212	(CD ₃ OD) δ 8.33 (d, 1 H), 8.02-8.28 (m, 2 H), 7.95 (br d, 1 H), 7.81-7.89 (m, 1 H), 7.72-7.81 (m, 1 H), 7.60 (br s, 1 H), 6.83 (br s, 1 H), 4.59 (br s, 1 H), 3.93 (br s, 1 H), 2.64-3.12 (m, 2 H), 2.24 (s, 3 H)	361.1 [M + H] ⁺	100%
213	(CD ₃ OD) δ 8.32-8.52 (m, 1.6 H), 7.86-8.13 (m, 3.4 H), 7.46-7.84 (m, 3 H), 6.56-7.17 (m, 2 H), 4.20 (br d, 1 H), 4.04 (br s, 0.6 H), 3.01-3.24 (m, 1.4 H), 2.85 (br d, 1 H)	396.2 [M + H] ⁺	98.7%
214	(CD ₃ OD) δ 8.28-8.57 (m, 1.6 H), 7.87-8.20 (m, 3.4 H), 7.42-7.85 (m, 3 H), 6.57-7.12 (m, 2 H), 4.19 (br s, 1 H), 4.05 (br s, 0.6 H), 2.97-3.21 (m, 1.4 H), 2.85 (br d, 1 H)	396.1 [M + H] ⁺	99.6%
215	(CD ₃ OD) δ 8.39-8.58 (m, 1 H), 7.82-8.27 (m, 4 H), 7.60-7.79 (m, 1 H), 6.75-7.13 (m, 1 H), 4.67-4.86 (m, 1 H), 3.90-4.06 (m, 0.6 H), 3.13-3.29 (m, 0.3 H), 2.59-3.10 (m, 2 H), 2.12-2.21 (m, 1 H), 0.80-1.09 (m, 4 H)	320.2 [M + H] ⁺	100%
216	(CD ₃ OD) δ 8.27-8.37 (m, 1 H), 7.71-8.12 (m, 4 H), 7.46-7.66 (m, 1 H), 6.80-6.96 (m, 1 H), 4.54-4.74 (m, 1 H), 3.77-3.93 (m, 0.6 H), 3.03-3.15 (m, 0.3 H), 2.51-2.98 (m, 2 H), 1.97-2.11 (m, 1 H), 0.70-1.00 (m, 4 H)	320.2 [M + H] ⁺	100%
217	(CD ₃ OD) δ 8.42-8.58 (m, 1 H), 8.14-8.41 (m, 1 H), 7.83-8.12 (m, 3 H), 7.69-7.82 (m, 1 H), 7.08 (br s, 1 H), 4.98-5.19 (m, 1 H), 3.36-4.17 (m, 1 H), 2.84-3.28 (m, 2 H), 1.79-2.00 (m, 6 H)	408.2 [M + H] ⁺	100%
218	(CD ₃ OD) δ 8.31-8.38 (m, 1 H), 8.02-8.29 (m, 1 H), 7.73-8.00 (m, 3 H), 7.58-7.70 (m, 1 H), 6.97 (s, 1 H), 4.99 (br dd, 1 H), 3.27-3.99 (m, 1 H), 2.71-3.16 (m, 2 H), 1.70-1.91 (m, 6 H)	408.2 [M + H] ⁺	98.3%
219	(CD ₃ OD) δ 7.75-7.87 (m, 2 H), 7.69-7.74 (m, 1 H), 7.60-7.68 (m, 2 H), 7.55 (s, 1 H), 7.33-7.48 (m, 4 H), 6.92 (br s, 0.8 H), 6.24 (br s, 0.2 H), 4.71 (m, 0.2 H), 4.06 (dd, 0.8 H), 3.36-3.46 (m, 3 H), 2.81-3.15 (m, 3 H), 2.57-2.77 (m, 1 H)	389.0 [M + H] ⁺	100%
220	(CD ₃ OD) δ 7.67-7.80 (m, 2 H), 7.61-7.67 (m, 1 H), 7.52-7.61 (m, 2 H), 7.43-7.51 (m, 1 H), 7.25-7.40 (m, 4 H), 6.84 (br s, 0.8 H), 6.16 (br s, 0.2 H), 4.59-4.71 (m, 0.2 H), 3.98 (dd, 0.8 H), 3.25-3.41 (m, 3 H), 2.74-3.12 (m, 3 H), 2.51-2.71 (m, 1 H)	389.0 [M + H] ⁺	99.4%
221	(CD ₃ OD) δ 9.05 (s, 1 H), 8.10 (s, 1 H), 7.72-7.80 (m, 2 H), 7.67-7.71 (m, 1 H), 7.64 (s, 1 H), 7.60 (s, 1 H), 7.53 (d, 1 H), 7.34-7.41 (m, 2 H), 6.86 (br s, 1 H), 3.92-4.27 (m, 1 H), 3.29-3.51 (m, 1 H), 2.87-3.00 (m, 1 H), 2.70 (dd, 1 H)	361.1 [M + H] ⁺	99.7%
222	(CD ₃ OD) δ 9.06 (s, 1 H), 8.10 (s, 1 H), 7.73-7.82 (m, 2 H), 7.69 (d, 1 H), 7.57-7.65 (m, 2 H), 7.53 (br d, 1 H), 7.34-7.41 (m, 2 H), 6.86 (br s, 1 H), 3.93-4.23 (m, 1 H), 3.31-3.53 (m, 1 H), 2.87-3.01 (m, 1 H), 2.65-2.77 (m, 1 H)	361.1 [M + H] ⁺	99.3%
223	(CD ₃ OD) δ 8.62 (d, 1 H), 8.14-8.29 (m, 2 H), 7.85-8.00 (m, 3 H), 7.65-7.85 (m, 4 H), 7.44-7.56 (m, 3 H), 7.02 (br s, 1 H), 4.27 (br s, 1 H), 3.56 (br s, 1 H), 3.02-3.19 (m, 1 H), 2.75-2.95 (m, 1 H)	438.1 [M + H] ⁺	100%
224	(CD ₃ OD) δ 8.62 (d, 1 H), 8.14-8.28 (m, 2 H), 7.86-8.00 (m, 3 H), 7.65-7.85 (m, 4 H), 7.46-7.57 (m, 3 H), 7.02 (br s, 1 H), 4.27 (s, 1 H), 3.43-3.72 (m, 1 H), 3.05-3.17 (m, 1 H), 2.79-2.91 (m, 1 H)	438.1 [M + H] ⁺	98.8%
225	(CD ₃ OD) δ 8.62 (d, 1.5 H), 8.38 (d, 1.5 H), 7.95 (d, 1 H), 7.65 (s, 2 H), 7.54 (br d, 1 H), 7.37-7.46 (m, 1 H), 7.24-7.35 (m, 1 H), 6.98-7.16 (m, 1 H), 6.56-6.97 (m, 2 H), 4.61 (br s, 1 H), 3.31-3.91 (m, 1 H), 2.99-3.14 (m, 1 H), 2.75 (br d, 1 H)	384.1 [M + H] ⁺	100%
226	(CD ₃ OD) δ 8.63 (d, 1.5 H), 8.38 (d, 1.5 H), 7.96 (d, 1 H), 7.66 (s, 2 H), 7.54 (br d, 1 H), 7.43 (ddd, 1 H), 7.26-7.35 (m, 1 H), 7.05 (td, 1 H), 6.58-6.99 (m, 2 H), 4.62 (br s, 1 H), 3.36-3.91 (m, 1 H), 2.98-3.17 (m, 1 H), 2.76 (br d, 1 H)	384.1 [M + H] ⁺	100%
227	(CD ₃ OD) δ 8.12-8.48 (m, 2 H), 7.57-7.90 (m, 2 H), 7.48 (d, 1 H), 7.22-7.35 (m, 1 H), 6.37-7.01 (m, 2 H), 4.28 (br s, 1 H), 3.75 (br s, 1 H), 2.91-3.19 (m, 1 H), 2.79 (br d, 1 H), 2.37 (s, 3 H)	349.0 [M + H] ⁺	99.5%
228	(CD ₃ OD) δ 8.13-8.46 (m, 2 H), 7.58-7.90 (m, 2 H), 7.48 (d, 1 H), 7.22-7.36 (m, 1 H), 6.39-6.96 (m, 2 H), 4.28 (br s, 1 H), 3.55-3.90 (m, 1 H), 2.92-3.16 (m, 1 H), 2.79 (br d, 1 H), 2.37 (s, 3 H)	349.0 [M + H] ⁺	99.3%
229	(CD ₃ OD) δ 8.37 (d, 1 H), 7.62-7.83 (m, 2 H), 7.48 (br d, 1 H), 7.24-7.37 (m, 1 H), 6.79-7.16 (m, 2 H), 6.29 (br s, 1 H), 4.27 (dd, 1 H), 3.63-3.84 (m, 1 H), 2.96-3.16 (m, 1 H), 2.81 (br dd, 1 H)	358.2 [M + H] ⁺	100%
230	(CD ₃ OD) δ 8.38 (br d, 1 H), 7.60-7.90 (m, 2 H), 7.48 (br d, 1 H), 7.30 (br t, 1 H), 6.75-7.17 (m, 2 H), 6.29 (br s, 1 H), 4.27	358.1 [M + H] ⁺	99.6%

TABLE 6-continued

Ex. #	¹ H NMR (400 MHz)	LCMS: m/z	% ee
	(dd, 1 H), 3.59-3.90 (m, 1 H), 2.97-3.20 (m, 1 H), 2.82 (br d, 1 H)		
231	(CD ₃ OD) δ 8.65 (br s, 2 H), 8.34 (d, 1 H), 7.58-7.82 (m, 2 H), 7.45 (br d, 1 H), 7.09-7.31 (m, 2 H), 6.87 (td, 1 H), 5.12 (br dd, 1 H), 3.42-3.59 (m, 1 H), 2.82-2.98 (m, 1 H), 2.62-2.81 (m, 1 H)	386.1 [M + H] ⁺	100%
232	(CD ₃ OD) δ 8.56-8.71 (m, 2 H), 8.36 (br s, 1 H), 7.52-7.95 (m, 2 H), 7.45 (br s, 1 H), 7.11-7.33 (m, 2 H), 6.87 (br s, 1 H), 5.13 (br d, 1 H), 3.50 (br s, 1 H), 2.60-3.07 (m, 2 H)	386.2 [M + H] ⁺	99.7%
233	(CD ₃ OD) δ 8.31-8.57 (m, 2 H), 7.87 (s, 1 H), 7.61-7.74 (m, 1 H), 7.51 (d, 1 H), 7.32 (t, 1 H), 6.93 (t, 1 H), 6.85 (s, 0.7 H), 5.97 (s, 0.3 H), 4.81 (br d, 0.3 H), 3.83-3.93 (m, 0.7 H), 3.73-3.82 (m, 0.7 H), 3.44-3.60 (m, 0.3 H), 2.88-3.04 (m, 1 H), 2.77-2.88 (m, 1 H)	403.1 [M + H] ⁺	100%
234	(CD ₃ OD) δ 8.31-8.54 (m, 2 H), 7.87 (s, 1 H), 7.60-7.71 (m, 1 H), 7.51 (d, 1 H), 7.30-7.35 (m, 1 H), 6.89-6.95 (m, 1 H), 6.84 (br s, 0.7 H), 5.96 (br s, 0.3 H), 4.80-4.85 (m, 0.3 H), 3.83-3.94 (m, 0.7 H), 3.74-3.82 (m, 0.7 H), 3.47-3.62 (m, 0.3 H), 2.88-3.04 (m, 1 H), 2.76-2.87 (m, 1 H)	403.1 [M + H] ⁺	100%
235	Data provided above		
236	Data provided above		
237	(CD ₃ OD) δ 8.19-8.48 (m, 1 H), 7.38-7.81 (m, 3 H), 7.20-7.35 (m, 1 H), 6.73-6.97 (m, 1.7 H), 6.18 (s, 0.3 H), 4.77 (br dd, 0.3 H), 4.12 (br dd, 0.7 H), 3.53-3.78 (m, 0.6 H), 3.01-3.16 (m, 0.4 H), 2.56-2.98 (m, 2.8 H), 2.29-2.56 (m, 1.2 H), 0.87-1.16 (m, 1 H), 0.40-0.64 (m, 2 H), 0.21 (td, 2 H)	322.2 [M + H] ⁺	100%
238	(CD ₃ OD) δ 8.18-8.46 (m, 1 H), 7.38-7.81 (m, 3 H), 7.18-7.36 (m, 1 H), 6.69-6.99 (m, 1.7 H), 6.17 (s, 0.3 H), 4.76 (br dd, 0.4 H), 4.11 (br dd, 0.6 H), 3.58-3.76 (m, 0.7 H), 3.07 (td, 0.3 H), 2.57-2.96 (m, 3 H), 2.46 (dd, 1 H), 0.98-1.09 (m, 1 H), 0.47-0.58 (m, 2 H), 0.21 (td, 2 H)	322.2 [M + H] ⁺	99.9%
239	(CD ₃ OD) δ 8.34-8.45 (m, 1 H), 7.86 (s, 0.7 H), 7.68 (s, 1 H), 7.47-7.63 (m, 1.3 H), 7.26-7.39 (m, 1 H), 6.93 (t, 1 H), 6.81 (br s, 0.7 H), 6.02 (br s, 0.3 H), 4.78 (br dd, 0.3 H), 3.81-3.91 (m, 1.4 H), 3.37-3.51 (m, 0.3 H), 2.74-3.02 (m, 2 H), 2.17-2.27 (m, 1 H), 1.09-1.28 (m, 4 H)	443.0 [M + H] ⁺	100%
240	(CD ₃ OD) δ 8.36-8.47 (m, 1 H), 7.86 (s, 0.7 H), 7.68 (s, 1 H), 7.47-7.63 (m, 1.3 H), 7.28-7.38 (m, 1 H), 6.93 (t, 1 H), 6.81 (s, 0.7 H), 6.02 (s, 0.3 H), 4.79 (br dd, 0.4 H), 3.83-3.90 (m, 1.4 H), 3.39-3.48 (m, 0.2 H), 2.77-3.01 (m, 2 H), 2.16-2.26 (m, 1 H), 1.08-1.28 (m, 4 H)	443.0 [M + H] ⁺	98.8%
241	(CD ₃ OD) δ 8.29-8.38 (m, 1 H), 7.71 (s, 0.6 H), 7.57-7.65 (m, 1.4 H), 7.51 (d, 0.4 H), 7.44 (d, 0.6 H), 7.21-7.32 (m, 1 H), 6.76-6.92 (m, 1.6 H), 6.27 (s, 0.4 H), 4.73 (br dd, 0.3 H), 4.17 (dd, 5.0 Hz, 0.7 H), 3.55-3.75 (m, 0.7 H), 2.53-3.11 (m, 4.3 H), 1.41-1.64 (m, 2 H), 0.63-0.87 (m, 1 H), 0.24-0.51 (m, 2 H), 0.06-0.13 (m, 2 H)	336.1 [M + H] ⁺	100%
242	(CD ₃ OD) δ 8.29-8.37 (m, 1 H), 7.71 (s, 0.6 H), 7.55-7.65 (m, 1.4 H), 7.50 (br d, 0.4 H), 7.44 (d, 0.6 H), 7.21-7.33 (m, 1 H), 6.77-6.91 (m, 1.6 H), 6.27 (s, 0.4 H), 4.74 (br dd, 0.4 H), 4.17 (dd, 0.6 H), 3.61-3.75 (m, 0.6 H), 2.52-3.12 (m, 4.4 H), 1.39-1.62 (m, 2 H), 0.64-0.81 (m, 1 H), 0.26-0.45 (m, 2 H), 0.06-0.11 (m, 2 H)	336.1 [M + H] ⁺	100%
243	(CD ₃ OD) δ 8.38 (br d, 1 H), 8.13 (br s, 1 H), 7.58-7.90 (m, 2 H), 7.48 (br d, 1 H), 7.29 (br t, 1 H), 6.41-7.03 (m, 2 H), 4.62 (br s, 1 H), 4.34 (br s, 0.4 H), 3.77 (br s, 0.6 H), 2.92-3.18 (m, 1 H), 2.80 (br d, 1 H), 2.22-2.48 (m, 1 H), 0.95 (br d, 4 H)	375.0 [M + H] ⁺	100%
244	(CD ₃ OD) δ 8.38 (br d, 1 H), 8.14 (br s, 1 H), 7.59-7.90 (m, 2 H), 7.48 (br d, 1 H), 7.29 (br t, 1 H), 6.42-7.03 (m, 2 H), 4.51-4.86 (m, 1 H), 4.34 (br s, 0.6 H), 3.78 (br s, 0.4 H), 3.03 (br s, 1 H), 2.80 (br d, 1 H), 2.35 (br s, 1 H), 0.95 (br d, 4 H)	375.2 [M + H] ⁺	100%
245	(CD ₃ OD) δ 8.41 (br d, 2 H), 7.80 (br s, 2 H), 7.55 (br d, 1 H), 7.29-7.40 (m, 1 H), 6.88-6.99 (m, 1 H), 6.81 (br s, 1 H), 4.38 (br s, 1 H), 3.47-3.99 (m, 1 H), 2.97-3.12 (m, 1 H), 2.80 (br d, 1 H), 1.48 (s, 9 H)	407.0 [M + H] ⁺	99.6%
246	(CD ₃ OD) δ 8.40 (br d, 2 H), 7.69 (s, 2 H), 7.53 (br s, 1 H), 7.26-7.37 (m, 1 H), 6.93 (t, 1 H), 6.40-6.84 (m, 1 H), 4.33 (br s, 1 H), 3.68-3.99 (m, 1 H), 3.02 (br d, 1 H), 2.67-2.88 (m, 1 H), 1.48 (s, 9 H)	407.0 [M + H] ⁺	98.9%
247	(CD ₃ OD) δ 8.38 (br d, 1.5 H), 7.42-8.19 (m, 3.5 H), 7.31 (br t, 1 H), 6.65-7.01 (m, 1.6 H), 6.42 (br s, 0.4 H), 4.28 (br s, 1 H), 3.57-4.01 (m, 1 H), 2.95-3.10 (m, 1 H), 2.68-2.87 (m, 1 H), 1.70-1.87 (m, 6 H)	411.1 [M + H] ⁺	100%
248	(CD ₃ OD) δ 8.38 (br d, 1.5 H), 7.45-8.25 (m, 3.5 H), 7.31 (br t, 1 H), 6.62-7.03 (m, 1.6 H), 6.43 (br s, 0.4 H), 4.12-4.55 (m, 1 H)	411.1 [M + H] ⁺	99.4%

TABLE 6-continued

Ex. #	¹ H NMR (400 MHz)	LCMS: m/z	% ee
	H), 3.81 (br s, 1 H), 2.95-3.09 (m, 1 H), 2.66-2.90 (m, 1 H), 1.72-1.87 (m, 6 H)		
249	(CD ₃ OD) δ 8.38 (br d, 1 H), 7.40-7.97 (m, 4 H), 7.30 (br t, 1 H), 6.54-6.95 (m, 2 H), 4.44 (br s, 1 H), 3.44-3.95 (m, 1 H), 2.62-3.26 (m, 2 H), 1.41 (br s, 9 H)	391.1 [M + H] ⁺	100%
250	(CD ₃ OD) δ 8.38 (br d, 1 H), 7.40-7.98 (m, 4 H), 7.30 (br t, 1 H), 6.51-6.96 (m, 2 H), 4.45 (br s, 1 H), 3.40-3.91 (m, 1 H), 2.57-3.25 (m, 2 H), 1.26-1.59 (m, 9 H)	391.2 [M + H] ⁺	100%
251	(CD ₃ OD) δ 8.70 (br s, 0.4 H), 8.40 (br d, 1 H), 8.13 (br s, 0.6 H), 7.47-7.90 (m, 3 H), 7.33 (br t, 1 H), 6.78-7.00 (m, 1.5 H), 6.44 (br s, 0.5 H), 4.30 (br s, 1 H), 3.81 (br s, 1 H), 2.97-3.10 (m, 1 H), 2.64-2.88 (m, 5 H), 1.87-2.17 (m, 2 H)	423.1 [M + H] ⁺	97.1%
252	(CD ₃ OD) δ 8.70 (br s, 0.4 H), 8.40 (br d, 1 H), 8.05-8.28 (m, 0.6 H), 7.48-7.88 (m, 3 H), 7.33 (br t, 1 H), 6.77-7.04 (m, 1.5 H), 6.43 (br s, 0.5 H), 4.30 (br s, 1 H), 3.82 (br s, 1 H), 2.96-3.12 (m, 1 H), 2.60-2.90 (m, 5 H), 1.79-2.25 (m, 2 H)	423.1 [M + H] ⁺	92.8%
253	(CD ₃ OD) δ 8.31-8.39 (m, 1 H), 7.42-7.76 (m, 3 H), 7.23-7.35 (m, 1 H), 6.89 (q, 1 H), 6.16-6.81 (m, 1 H), 4.99-5.29 (m, 1 H), 4.69-4.77 (m, 0.4 H), 4.12 (dd, 0.6 H), 3.64 (ddd, 1 H), 2.60-3.10 (m, 5 H), 2.07-2.56 (m, 4 H)	354.1 [M + H] ⁺	100%
254	(CD ₃ OD) δ 8.32-8.38 (m, 1 H), 7.43-7.72 (m, 3 H), 7.29 (dt, 1 H), 6.89 (q, 1 H), 6.16-6.82 (m, 1 H), 4.99-5.28 (m, 1 H), 4.73 (br dd, 0.4 H), 4.12 (dd, 0.6 H), 3.60-3.68 (m, 0.4 H), 2.62-3.08 (m, 5 H), 2.07-2.46 (m, 4 H)	354.0 [M + H] ⁺	100%
255	(CD ₃ OD) δ 8.65-8.82 (m, 1 H), 8.34-8.51 (m, 1 H), 8.22-8.34 (m, 1 H), 7.87-8.12 (m, 2 H), 7.58-7.78 (m, 2 H), 7.46-7.58 (m, 1 H), 7.30-7.38 (m, 1 H), 6.83-7.04 (m, 1.7 H), 6.22 (s, 0.3 H), 3.90-4.08 (m, 1.5 H), 3.58-3.80 (m, 0.5 H), 2.98-3.13 (m, 1 H), 2.75-2.96 (m, 1 H)	480.0 [M + H] ⁺	93.2%
256	(CD ₃ OD) δ 8.68-8.84 (m, 1 H), 8.37-8.55 (m, 1 H), 8.23-8.32 (m, 1 H), 7.90-8.09 (m, 2 H), 7.59-7.76 (m, 2 H), 7.46-7.56 (m, 1 H), 7.30-7.39 (m, 1 H), 6.86-6.98 (m, 1.7 H), 6.22 (s, 0.3 H), 3.89-4.07 (m, 1.5 H), 3.60-3.78 (m, 0.5 H), 2.97-3.11 (m, 1 H), 2.78-2.94 (m, 1 H)	480.0 [M + H] ⁺	98.4%
257	(CD ₃ OD) δ 8.35 (d, 1 H), 8.04 (br d, 1 H), 7.93 (d, 1 H), 7.64-7.87 (m, 4 H), 7.55-7.63 (m, 1 H), 6.78 (br s, 1 H), 4.62 (br s, 1 H), 4.03 (br s, 1 H), 2.66-3.24 (m, 2 H), 0.96-1.68 (m, 9 H)	402.2 [M + H] ⁺	99.7%
258	(CD ₃ OD) δ 8.35 (d, 1 H), 8.04 (br d, 1 H), 7.93 (d, 1 H), 7.65-7.88 (m, 4 H), 7.54-7.64 (m, 1 H), 6.78 (br s, 1 H), 4.61 (s, 1 H), 3.45-4.22 (m, 1 H), 2.73-3.18 (m, 2 H), 1.18-1.60 (m, 9 H)	402.2 [M + H] ⁺	98.7%
259	(CD ₃ OD) δ 8.29 (br d, 1 H), 8.05 (br s, 2 H), 7.90 (d, 1 H), 7.63-7.83 (m, 3 H), 7.56 (br t, 1 H), 6.18-7.10 (m, 2 H), 4.16 (br s, 1 H), 3.87 (br s, 1 H), 2.94-2.95 (m, 1 H), 2.68-2.76 (m, 1 H)	395.1 [M + H] ⁺	99.5%
260	(CD ₃ OD) δ 8.30 (br d, 1 H), 8.05 (br s, 2 H), 7.90 (d, 1 H), 7.63-7.81 (m, 3 H), 7.57 (br t, 1 H), 6.14-7.16 (m, 2 H), 4.16 (br s, 1 H), 3.86 (br s, 1 H), 2.95 (br s, 1 H), 2.69-2.76 (m, 1 H)	395.1 [M + H] ⁺	99.0%
261	(CD ₃ OD) δ 8.17-8.46 (m, 1 H), 7.53-8.08 (m, 10 H), 7.43 (br d, 0.4 H), 7.07 (br s, 1 H), 6.91 (s, 0.6 H), 6.71 (s, 0.6 H), 6.61 (d, 0.4 H), 5.87 (s, 0.2 H), 5.00 (br d, 0.6 H), 3.85 (br s, 1 H), 3.63 (br s, 0.4 H), 3.13 (br s, 0.4 H), 2.58-2.88 (m, 1.6 H)	422.2 [M + H] ⁺	100%
262	(CD ₃ OD) δ 8.17-8.45 (m, 1 H), 7.53-8.07 (m, 10 H), 7.43 (br d, 0.3 H), 7.07 (br s, 1 H), 6.91 (s, 0.7 H), 6.71 (d, 0.6 H), 6.61 (d, 0.3 H), 5.87 (s, 0.3 H), 4.96-5.02 (m, 0.6 H), 3.84 (br s, 1.3 H), 3.54-3.71 (m, 0.3 H), 3.06-3.19 (m, 0.4 H), 2.74-2.89 (m, 1 H), 2.60-2.70 (m, 0.6 H)	422.2 [M + H] ⁺	99.6%
263	(CD ₃ OD) δ 8.32 (br d, 1 H), 7.99 (br d, 1 H), 7.38-7.93 (m, 4.8 H), 6.81 (br s, 1 H), 6.57 (br s, 1 H), 6.28 (br s, 0.2 H), 4.15 (br s, 1 H), 3.71-4.06 (m, 4 H), 2.91-3.07 (m, 1 H), 2.77 (br d, 1 H)	393.2 [M + H] ⁺	100%
264	(CD ₃ OD) δ 8.32 (br d, 1 H), 7.99 (br d, 1 H), 7.41-7.94 (m, 4.7 H), 6.81 (br s, 1 H), 6.57 (br s, 1 H), 6.28 (br s, 0.3 H), 4.90-4.98 (m, 0.5 H), 4.16 (br d, 0.5 H), 3.71-4.08 (m, 3.4 H), 3.32-3.39 (m, 0.6 H), 2.89-3.04 (m, 1 H), 2.77 (br d, 1 H)	393.2 [M + H] ⁺	99.0%
265	(CD ₃ OD) δ 8.19-8.34 (m, 1 H), 7.98 (d, 0.5 H), 7.79-7.94 (m, 2 H), 7.64-7.76 (m, 2 H), 7.48-7.59 (m, 1.5 H), 6.75-6.89 (m, 1 H), 4.91-4.98 (m, 0.5 H), 4.47 (br dd, 0.5 H), 3.95-4.02 (m, 3 H), 3.84-3.94 (m, 0.5 H), 2.93-3.25 (m, 1.5 H), 2.71-2.86 (m, 1 H)	394.2 [M + H] ⁺	99.2%
266	(CD ₃ OD) δ 8.21-8.36 (m, 1 H), 8.00 (d, 0.5 H), 7.80-7.95 (m, 2 H), 7.65-7.77 (m, 2 H), 7.49-7.60 (m, 1.5 H), 6.75-6.93 (m, 1 H), 4.92-4.99 (m, 0.5 H), 4.49 (br dd, 0.5 H), 3.98-4.03 (m, 3 H), 3.85-3.97 (m, 0.5 H), 2.93-3.29 (m, 1.5 H), 2.72-2.89 (m, 1 H)	394.2 [M + H] ⁺	99.4%

TABLE 6-continued

Ex. #	¹ H NMR (400 MHz)	LCMS: m/z	% ee
267	(CD ₃ OD) δ 8.35 (br d, 1 H), 7.83-8.15 (m, 2.5 H), 7.23-7.82 (m, 4.5 H), 5.97-7.02 (m, 2 H), 4.23 (br d, 1 H), 3.81-4.08 (m, 1 H), 2.98 (br s, 1 H), 2.71-2.86 (m, 1 H)	410.2 [M + H] ⁺	97.9%
268	(CD ₃ OD) δ 8.33 (br d, 1 H), 7.82-8.09 (m, 2.4 H), 7.20-7.81 (m, 4.6 H), 6.03-6.89 (m, 2 H), 4.21 (br d, 1 H), 3.81-4.06 (m, 1 H), 2.96 (br s, 1 H), 2.76 (dd, 1 H)	410.2 [M + H] ⁺	98.7%
269	(CD ₃ OD) δ 8.58-8.71 (m, 1 H), 8.20-8.38 (m, 1 H), 7.82-8.01 (m, 3 H), 7.65-7.77 (m, 2 H), 7.51-7.60 (m, 1 H), 6.80-6.99 (m, 1 H), 5.03 (br dd, 0.4 H), 4.47 (br dd, 0.6 H), 4.21-4.33 (m, 2 H), 3.91-4.05 (m, 0.6 H), 3.39 (td, 0.5 H), 3.11-3.23 (m, 0.6 H), 2.94-3.08 (m, 0.4 H), 2.72-2.90 (m, 1 H), 1.28-1.45 (m, 3 H)	374.1 [M + H] ⁺	100%
270	(CD ₃ OD) δ 8.59-8.72 (m, 1 H), 8.20-8.38 (m, 1 H), 7.83-8.01 (m, 3 H), 7.67-7.76 (m, 2 H), 7.52-7.61 (m, 1 H), 6.82-7.00 (m, 1 H), 5.03 (br dd, 0.3 H), 4.47 (dd, 0.7 H), 4.22-4.33 (m, 2 H), 3.93-4.05 (m, 0.6 H), 3.34-3.43 (m, 0.4 H), 3.11-3.24 (m, 0.7 H), 2.95-3.06 (m, 0.3 H), 2.73-2.89 (m, 1 H), 1.28-1.46 (m, 3 H)	374.1 [M + H] ⁺	97.9%
271	(CD ₃ OD) δ 8.15 (d, 1 H), 7.88 (br d, 1 H), 7.77 (br d, 1 H), 7.34-7.69 (m, 5 H), 7.20-7.32 (m, 1 H), 6.70 (s, 0.6 H), 6.20 (br s, 0.4 H), 4.82 (br s, 1 H), 4.15 (br dd, 0.5 H), 3.69 (br s, 0.5 H), 3.26-3.34 (m, 2 H), 2.96-3.19 (m, 2 H), 2.54-2.84 (m, 2 H)	390.1 [M + H] ⁺	98.2%
272	(CD ₃ OD) δ 8.14 (d, 1 H), 7.87 (br d, 1 H), 7.75 (br d, 1 H), 7.33-7.67 (m, 5 H), 7.19-7.30 (m, 1 H), 6.69 (s, 0.5 H), 6.20 (s, 0.5 H), 4.80-4.91 (m, 1 H), 4.14 (br dd, 0.5 H), 3.68 (br t, 0.5 H), 3.25-3.33 (m, 2 H), 2.91-3.19 (m, 2 H), 2.53-2.85 (m, 2 H)	390.1 [M + H] ⁺	98.5%
273	(CD ₃ OD) δ 9.49 (d, 1 H), 7.92-8.15 (m, 3 H), 7.53-7.83 (m, 2.6 H), 7.25-7.53 (m, 1.4 H), 6.78 (s, 0.6 H), 6.40 (s, 0.4 H), 4.93-4.98 (m, 0.5 H), 4.40 (br dd, 0.5 H), 4.06 (br t, 0.6 H), 3.46-3.63 (m, 0.4 H), 3.35-3.45 (m, 2 H), 3.14-3.31 (m, 2 H), 2.66-3.01 (m, 2 H)	391.1 [M + H] ⁺	100%
274	(CD ₃ OD) δ 9.49 (d, 1 H), 7.88-8.18 (m, 3 H), 7.54-7.85 (m, 2.6 H), 7.19-7.53 (m, 1.4 H), 6.78 (s, 0.6 H), 6.40 (s, 0.4 H), 4.93-4.98 (m, 0.5 H), 4.40 (br dd, 0.5 H), 3.98-4.17 (m, 0.6 H), 3.48-3.63 (m, 0.4 H), 3.35-3.45 (m, 2 H), 3.13-3.31 (m, 2 H), 2.68-2.99 (m, 2 H)	391.1 [M + H] ⁺	99.3%
275	(CD ₃ OD) δ 9.44-9.62 (m, 1 H), 7.93-8.16 (m, 3 H), 7.58-7.80 (m, 2 H), 6.54-7.07 (m, 2 H), 5.07 (br dd, 0.3 H), 4.58 (dd, 0.7 H), 4.11-4.18 (m, 0.6 H), 4.01-4.11 (m, 3 H), 3.45 (td, 0.4 H), 2.92-3.21 (m, 1 H), 2.71-2.90 (m, 1 H)	411.2 [M + H] ⁺	100%
276	(CD ₃ OD) δ 9.31-9.51 (m, 1 H), 7.81-8.07 (m, 3 H), 7.48-7.70 (m, 2 H), 6.39-6.97 (m, 2 H), 4.95 (dd, 0.3 H), 4.46 (dd, 0.7 H), 3.99-4.06 (m, 0.5 H), 3.90-3.99 (m, 3 H), 3.33 (td, 0.5 H), 2.82-3.09 (m, 1 H), 2.61-2.78 (m, 1 H)	411.2 [M + H] ⁺	100%
277	(CD ₃ OD) δ 9.56 (s, 1 H), 8.32-9.19 (m, 2 H), 7.92-8.25 (m, 4 H), 7.57-7.82 (m, 2 H), 7.00-7.41 (m, 1 H), 6.58-6.87 (m, 1 H), 5.08 (br d, 0.4 H), 4.72 (br d, 0.6 H), 3.85-4.42 (m, 1 H), 2.97-3.29 (m, 1 H), 2.87 (br d, 1 H)	542.1 [M + H] ⁺	97.1%
278	(CD ₃ OD) δ 9.56 (s, 1 H), 8.32-9.19 (m, 2 H), 7.92-8.25 (m, 4 H), 7.57-7.82 (m, 2 H), 7.00-7.41 (m, 1 H), 6.58-6.87 (m, 1 H), 5.08 (br d, 0.4 H), 4.72 (br d, 0.6 H), 3.85-4.42 (m, 1 H), 2.97-3.29 (m, 1 H), 2.87 (br d, 1 H)	542.1 [M + H] ⁺	97.5%
279	(CD ₃ OD) δ 9.55 (s, 1 H), 7.98-8.15 (m, 3 H), 7.76 (t, 1 H), 7.62 (s, 1 H), 6.90-7.31 (m, 1 H), 6.69 (s, 1 H), 4.56 (br s, 2 H), 4.02 (br s, 0.6 H), 3.50 (br s, 4.2 H), 3.01 (br s, 1 H), 2.80 (br d, 1 H), 1.54-2.01 (m, 4 H)	498.0 [M + H] ⁺	98.4%
280	(CD ₃ OD) δ 9.45 (s, 1 H), 7.81-8.12 (m, 3 H), 7.41-7.78 (m, 2 H), 6.77-7.23 (m, 1 H), 6.58 (s, 1 H), 4.26-4.76 (m, 2 H), 3.78 (br s, 0.9 H), 3.22-3.72 (m, 4.1 H), 2.89 (br s, 1 H), 2.69 (br d, 1 H), 1.35-1.93 (m, 4 H)	498.0 [M + H] ⁺	97.0%
281	(CD ₃ OD) δ 9.57 (br s, 1 H), 8.13 (br d, 1 H), 7.99-8.09 (m, 2 H), 7.96 (br s, 0.5 H), 7.71-7.90 (m, 2 H), 7.64 (br s, 1 H), 6.95-7.42 (m, 1.5 H), 6.78 (br s, 1 H), 5.05 (br s, 0.4 H), 4.64 (br d, 0.6 H), 3.80-4.41 (m, 4 H), 2.95-3.23 (m, 1 H), 2.88 (br d, 1 H)	477.2 [M + H] ⁺	100%
282	(CD ₃ OD) δ 9.45 (br s, 1 H), 8.00 (br d, 1 H), 7.87-7.97 (m, 2 H), 7.84 (br s, 0.5 H), 7.59-7.78 (m, 2 H), 7.52 (br s, 1 H), 6.83-7.28 (m, 1.5 H), 6.65 (br d, 1 H), 4.93 (br s, 0.3 H), 4.55 (br d, 0.7 H), 3.69-4.29 (m, 4 H), 2.83-3.11 (m, 1 H), 2.76 (br d, 1 H)	477.2 [M + H] ⁺	99.6%
283	(CD ₃ OD) δ 8.38 (s, 1 H), 7.86 (br t, 2 H), 7.72-7.80 (m, 3 H), 7.57-7.71 (m, 2 H), 7.37-7.51 (m, 2 H), 6.95 (br s, 1 H), 4.38	345.1 [M + H] ⁺	99.8%

TABLE 6-continued

Ex. #	¹ H NMR (400 MHz)	LCMS: m/z	% ee
	(br s, 1 H), 3.48 (br s, 1 H), 3.02-3.19 (m, 1 H), 2.83 (br d, 1 H)		
284	(CD ₃ OD) δ 8.38 (s, 1 H), 7.85 (br t, 2 H), 7.71-7.80 (m, 3 H), 7.57-7.70 (m, 2 H), 7.41-7.52 (m, 2 H), 6.95 (br s, 1 H), 4.37 (br s, 1 H), 3.48 (br s, 1 H), 3.09 (br s, 1 H), 2.83 (br d, 1 H)	345.1 [M + H] ⁺	99.3%

TABLE 7

Ex. #	¹ H NMR (400 MHz)	LCMS: m/z	% ee
300	(CD ₃ OD) δ 9.26 (br s, 1 H), 8.74 (br s, 0.2 H), 8.57 (d, 1 H), 8.18 (d, 1 H), 8.08 (br d, 1 H), 7.91 (td, 2.6 H), 7.75 (t, 1 H), 7.50-7.71 (m, 2.8 H), 7.40-7.49 (m, 1 H), 6.19-7.03 (m, 1.4 H), 4.40 (br s, 1 H), 3.99 (br s, 1 H), 3.00-3.14 (m, 1 H), 2.81 (br s, 1 H)	439.0 [M + H] ⁺	99.2%
301	(CD ₃ OD) δ 9.12-9.40 (m, 1 H), 8.73 (br s, 0.2 H), 8.57 (d, 1 H), 8.18 (d, 1 H), 8.07 (br d, 1 H), 7.78-8.00 (m, 2.8 H), 7.75 (t, 1 H), 7.51-7.71 (m, 3 H), 7.38-7.50 (m, 1 H), 6.44-6.94 (m, 1 H), 4.41 (br s, 1 H), 3.99 (br s, 1 H), 2.95-3.14 (m, 1 H), 2.79 (br d, 1 H)	439.0 [M + H] ⁺	99.5%
302	(CD ₃ OD) δ 9.50 (br s, 1 H), 8.21 (s, 1 H), 8.10 (br d, 1 H), 7.95-8.00 (m, 1 H), 7.96 (s, 1 H), 7.89 (br s, 1 H), 7.77 (t, 1 H), 7.60-7.73 (m, 3 H), 6.73 (br s, 1 H), 4.34-4.60 (m, 1 H), 3.94 (s, 4 H), 2.98-3.12 (m, 1 H), 2.79 (br d, 1 H)	442.1 [M + H] ⁺	100%
303	(CD ₃ OD) δ 9.28 (br s, 1 H), 8.20 (s, 1 H), 8.08 (br d, 1 H), 7.95 (s, 1 H), 7.89 (br d, 1 H), 7.76 (br t, 2 H), 7.62-7.73 (m, 3 H), 6.70 (br s, 1 H), 4.34-4.60 (m, 1 H), 3.94 (s, 4 H), 2.98-3.12 (m, 1 H), 2.79 (br d, 1 H)	442.2 [M + H] ⁺	98.4%
304	(CD ₃ OD) δ 9.27 (br s, 1 H), 8.44 (br s, 1 H), 8.10 (br d, 2 H), 7.91 (br s, 1 H), 7.74-7.83 (m, 3 H), 7.61-7.73 (m, 2 H), 6.82 (br s, 1 H), 5.06 (br d, 2 H), 4.66-4.80 (m, 1 H), 3.73-4.19 (m, 1 H), 3.13 (br s, 1 H), 2.87 (br s, 1 H)	494.2 [M + H] ⁺	98.9%
305	(CD ₃ OD) δ 9.26 (br s, 1 H), 8.43 (br s, 1 H), 7.99-8.15 (m, 1 H), 7.91 (br s, 2 H), 7.73-7.85 (m, 3 H), 7.64-7.73 (m, 2 H), 6.82 (br s, 1 H), 5.06 (br d, 2 H), 4.63-4.79 (m, 1 H), 3.74-4.23 (m, 1 H), 3.13 (br s, 1 H), 2.88 (br s, 1 H)	494.2 [M + H] ⁺	95.4%
306	(CD ₃ OD) δ 9.27 (br s, 1 H), 8.39 (s, 1 H), 8.04-8.12 (m, 2 H), 7.88 (br s, 1 H), 7.76 (br t, 2 H), 7.53-7.70 (m, 3 H), 6.69 (br s, 1 H), 5.02 (q, 2 H), 4.60 (br s, 1 H), 3.39-4.20 (m, 1 H), 2.94-3.16 (m, 1 H), 2.80 (br s, 1 H)	510.1 [M + H] ⁺	98.3%
307	(CD ₃ OD) δ 9.27 (br s, 1 H), 8.38 (s, 1 H), 8.02-8.13 (m, 2 H), 7.88 (br s, 1 H), 7.76 (br t, 2 H), 7.56-7.71 (m, 3 H), 6.68 (br s, 1 H), 5.01 (q, 2 H), 4.57 (br s, 1 H), 4.00 (br s, 1 H), 2.96-3.14 (m, 1 H), 2.75-2.88 (m, 1 H)	510.2 [M + H] ⁺	100%
308	(CD ₃ OD) δ 9.24 (br s, 1 H), 8.63-8.75 (m, 1 H), 8.22 (br s, 1 H), 8.08 (br d, 1 H), 7.82-8.05 (m, 4 H), 7.75-7.75 (m, 1 H), 7.77 (br t, 1 H), 7.65-7.70 (m, 2 H), 7.51-7.59 (m, 1 H), 6.86 (br s, 1 H), 4.64-4.76 (m, 1 H), 3.84-4.16 (m, 1 H), 3.01-3.25 (m, 1 H), 2.75-2.96 (m, 1 H)	423.1 [M + H] ⁺	100%
309	(CD ₃ OD) δ 9.25 (br s, 1 H), 8.72 (br d, 1 H), 8.23 (br s, 1 H), 8.10 (br d, 1 H), 7.84-8.06 (m, 4 H), 7.79 (br t, 1 H), 7.66-7.74 (m, 2 H), 7.55-7.61 (m, 1 H), 6.87 (br s, 1 H), 4.66-4.82 (m, 1 H), 3.90-4.24 (m, 1 H), 3.03-3.32 (m, 1 H), 2.74-3.02 (m, 1 H)	423.1 [M + H] ⁺	99.8%
310	(CD ₃ OD) δ 9.25 (br s, 1 H), 8.06-8.34 (m, 2H), 7.97-8.04 (m, 1 H), 7.88 (br s, 2 H), 7.76 (br t, 2 H), 7.63-7.72 (m, 2 H), 6.77 (br s, 1 H), 4.70 (br s, 1 H), 3.93 (m, 4 H), 3.11 (br s, 1 H), 2.83 (br s, 1 H)	426.2 [M + H] ⁺	100%
311	(CD ₃ OD) δ 9.28 (br s, 1 H), 8.07-8.36 (m, 2 H), 8.02-8.10 (m, 1 H), 7.92 (br s, 2 H), 7.80 (br t, 2 H), 7.65-7.76 (m, 2 H), 6.82 (br s, 1 H), 4.69 (br s, 1 H), 3.97 (m, 4 H), 3.10 (br s, 1 H), 2.87 (br s, 1 H)	426.0 [M + H] ⁺	99.1%
312	(CD ₃ OD) δ 9.28 (br s, 1 H), 8.91 (br s, 0.5 H), 8.67 (d, 1 H), 8.53 (d, 1 H), 8.31-8.48 (m, 0.5 H), 8.26 (t, 1 H), 8.09 (br d, 1 H), 7.88 (br s, 2 H), 7.62-7.81 (m, 3 H), 6.31-7.09 (m, 1 H), 4.40 (br s, 1 H), 4.03 (br s, 1 H), 3.01-3.15 (m, 1 H), 2.81 (br d, 1 H)	457.1 [M + H] ⁺	100%
313	(CD ₃ OD) δ 9.28 (br s, 1 H), 8.93 (br s, 0.5 H), 8.67 (d, 1 H), 8.53 (d, 1 H), 8.32-8.45 (m, 0.5 H), 8.22-8.29 (m, 1 H), 8.21-8.32 (m, 1 H), 8.08 (br d, 1.5 H), 7.88 (br s, 1.5 H),	457.1 [M + H] ⁺	100%

TABLE 7-continued

Ex. #	¹ H NMR (400 MHz)	LCMS: m/z	% ee
314	7.63-7.72 (m, 2 H), 6.28-7.18 (m, 1 H), 4.23-4.68 (m, 1 H), 4.08 (br d, 1 H), 2.96-3.21 (m, 1 H), 2.69-2.92 (m, 1 H) (CD ₃ OD) δ 9.32 (br s, 1 H), 8.32-9.08 (m, 2 H), 8.11 (d, 1 H), 7.92 (br d, 2 H), 7.62-7.87 (m, 4 H), 7.42 (d, 1 H), 6.81 (br s, 1 H), 4.57-4.73 (m, 1 H), 4.53 (s, 2 H), 3.48-4.23 (m, 1 H), 3.44 (s, 3 H), 3.03-3.17 (m, 1 H), 2.74-2.87 (m, 1 H)	439.1 [M + H] ⁺	99.2%
315	7.63-7.72 (m, 2 H), 6.28-7.18 (m, 1 H), 4.23-4.68 (m, 1 H), 4.08 (br d, 1 H), 2.96-3.21 (m, 1 H), 2.69-2.92 (m, 1 H) (CD ₃ OD) δ 9.32 (br s, 1 H), 8.62 (s, 2 H), 8.12 (d, 1 H), 7.92 (br d, 2 H), 7.52-7.88 (m, 4 H), 7.42 (d, 1 H), 6.80 (br s, 1 H), 4.58-4.73 (m, 1 H), 4.54 (s, 2 H), 3.52-4.22 (m, 1 H), 3.44 (s, 3 H), 3.03-3.18 (m, 1 H), 2.80 (br d, 1 H)	439.1 [M + H] ⁺	99.3%
316	7.63-7.72 (m, 2 H), 6.28-7.18 (m, 1 H), 4.23-4.68 (m, 1 H), 4.08 (br d, 1 H), 2.96-3.21 (m, 1 H), 2.69-2.92 (m, 1 H) (CD ₃ OD) δ 9.28 (br s, 1 H), 8.60 (br s, 0.5 H), 8.09 (br d, 1 H), 7.89 (br s, 1.5 H), 7.56-7.80 (m, 3 H), 6.08-7.54 (m, 2 H), 4.23-4.88 (m, 1 H), 3.94 (br s, 1 H), 2.94-3.14 (m, 1 H), 2.79 (br d, 1 H), 1.45 (s, 9 H)	418.2 [M + H] ⁺	100%
317	7.63-7.72 (m, 2 H), 6.28-7.18 (m, 1 H), 4.23-4.68 (m, 1 H), 4.08 (br d, 1 H), 2.96-3.21 (m, 1 H), 2.69-2.92 (m, 1 H) (CD ₃ OD) δ 9.29 (br s, 1 H), 8.55 (s, 0.5 H), 8.10 (br d, 1 H), 7.89 (br s, 1.5 H), 7.62-7.81 (m, 3 H), 6.14-7.60 (m, 2 H), 4.35-4.87 (m, 1 H), 3.34-4.13 (m, 1 H), 2.95-3.15 (m, 1 H), 2.81 (br s, 1 H), 1.45 (s, 9 H)	418.2 [M + H] ⁺	100%
318	7.63-7.72 (m, 2 H), 6.28-7.18 (m, 1 H), 4.23-4.68 (m, 1 H), 4.08 (br d, 1 H), 2.96-3.21 (m, 1 H), 2.69-2.92 (m, 1 H) (CD ₃ OD) δ 9.12-9.24 (m, 1 H), 8.03-8.12 (m, 1 H), 7.91-7.96 (m, 1 H), 7.53-7.88 (m, 4 H), 7.44 (s, 0.4 H), 6.88 (s, 0.6 H), 4.96-5.01 (m, 0.79 H), 4.84 (br d, 0.24 H), 3.88-3.97 (m, 0.7 H), 3.19-3.28 (m, 0.54 H), 3.10-3.18 (m, 0.67 H), 2.94-3.03 (m, 0.52 H), 2.79-2.89 (m, 1 H), 2.48-2.69 (m, 3 H)	361.2 [M + H] ⁺	100%
319	7.63-7.72 (m, 2 H), 6.28-7.18 (m, 1 H), 4.23-4.68 (m, 1 H), 4.08 (br d, 1 H), 2.96-3.21 (m, 1 H), 2.69-2.92 (m, 1 H) (CD ₃ OD) δ 9.15-9.23 (m, 1 H), 8.02-8.15 (m, 1 H), 7.92-7.96 (m, 1 H), 7.62-7.87 (m, 4 H), 7.44 (s, 0.44 H), 6.88 (s, 0.67 H), 4.97-5.01 (m, 0.71 H), 4.83-4.86 (m, 0.24 H), 3.88-3.96 (m, 0.74 H), 3.20-3.27 (m, 0.51 H), 3.10-3.18 (m, 0.74 H), 2.93-3.03 (m, 0.59 H), 2.80-2.89 (m, 1 H), 2.58-2.69 (m, 3 H)	361.2 [M + H] ⁺	100%
320	7.63-7.72 (m, 2 H), 6.28-7.18 (m, 1 H), 4.23-4.68 (m, 1 H), 4.08 (br d, 1 H), 2.96-3.21 (m, 1 H), 2.69-2.92 (m, 1 H) (CD ₃ OD) δ 9.23 (br s, 1 H), 8.39 (s, 1 H), 8.08 (br d, 1 H), 7.90 (br s, 2 H), 7.63-7.82 (m, 4 H), 6.82 (br s, 1 H), 4.48-4.80 (m, 1 H), 3.99 (br s, 1 H), 3.07 (br s, 1 H), 2.86 (br s, 1 H)	346.0 [M + H] ⁺	100%
321	7.63-7.72 (m, 2 H), 6.28-7.18 (m, 1 H), 4.23-4.68 (m, 1 H), 4.08 (br d, 1 H), 2.96-3.21 (m, 1 H), 2.69-2.92 (m, 1 H) (CD ₃ OD) δ 9.21 (br s, 1 H), 8.36 (s, 1 H), 8.06 (br d, 1 H), 7.88 (br s, 2 H), 7.60-7.80 (m, 4 H), 6.78 (br s, 1 H), 4.42-4.71 (m, 1 H), 3.97 (br s, 1 H), 3.05 (br s, 1 H), 2.81 (br s, 1 H)	346.1 [M + H] ⁺	100%
322	7.63-7.72 (m, 2 H), 6.28-7.18 (m, 1 H), 4.23-4.68 (m, 1 H), 4.08 (br d, 1 H), 2.96-3.21 (m, 1 H), 2.69-2.92 (m, 1 H) (CD ₃ OD) δ 9.10-9.26 (m, 1 H), 8.38 (s, 1 H), 8.01-8.14 (m, 2 H), 7.91-7.97 (m, 1 H), 7.61-7.87 (m, 4 H), 7.53 (s, 1 H), 6.92 (s, 1 H), 5.10 (br dd, 1 H), 3.86-4.07 (m, 3 H), 3.09-3.28 (m, 0.7 H), 2.94-3.08 (m, 0.3 H), 2.75-2.93 (m, 1 H)	427.1 [M + H] ⁺	100%
323	7.63-7.72 (m, 2 H), 6.28-7.18 (m, 1 H), 4.23-4.68 (m, 1 H), 4.08 (br d, 1 H), 2.96-3.21 (m, 1 H), 2.69-2.92 (m, 1 H) (CD ₃ OD) δ 9.04-9.30 (m, 1 H), 8.38 (s, 1 H), 8.00-8.13 (m, 2 H), 7.89-7.97 (m, 1 H), 7.60-7.86 (m, 4 H), 6.90 (s, 1 H), 5.09 (br dd, 1 H), 3.85-4.09 (m, 4 H), 3.11-3.27 (m, 0.7 H), 2.94-3.08 (m, 0.3 H), 2.87 (br d, 1 H)	427.1 [M + H] ⁺	98.9%
324	7.63-7.72 (m, 2 H), 6.28-7.18 (m, 1 H), 4.23-4.68 (m, 1 H), 4.08 (br d, 1 H), 2.96-3.21 (m, 1 H), 2.69-2.92 (m, 1 H) (CD ₃ OD) δ 9.08-9.22 (m, 1 H), 8.71-8.78 (m, 1 H), 8.24-8.31 (m, 1 H), 7.98-8.10 (m, 2 H), 7.91-7.96 (m, 1 H), 7.59-7.85 (m, 5 H), 7.46 (s, 0.4 H), 6.91 (s, 0.6 H), 5.01 (br dd, 1 H), 3.91-4.03 (m, 0.6 H), 3.10-3.27 (m, 1 H), 2.94-3.08 (m, 0.4 H), 2.80-2.93 (m, 1 H)	424.2 [M + H] ⁺	100%
325	7.63-7.72 (m, 2 H), 6.28-7.18 (m, 1 H), 4.23-4.68 (m, 1 H), 4.08 (br d, 1 H), 2.96-3.21 (m, 1 H), 2.69-2.92 (m, 1 H) (CD ₃ OD) δ 9.08-9.23 (m, 1 H), 8.70-8.78 (m, 1 H), 8.22-8.33 (m, 1 H), 7.98-8.10 (m, 2 H), 7.89-7.96 (m, 1 H), 7.59-7.83 (m, 5 H), 7.46 (s, 0.4 H), 6.91 (s, 0.6 H), 5.02 (br dd, 1 H), 3.91-4.03 (m, 0.6 H), 3.13-3.27 (m, 1 H), 2.94-3.06 (m, 0.4 H), 2.81-2.91 (m, 1 H)	424.2 [M + H] ⁺	99.2%
326	7.63-7.72 (m, 2 H), 6.28-7.18 (m, 1 H), 4.23-4.68 (m, 1 H), 4.08 (br d, 1 H), 2.96-3.21 (m, 1 H), 2.69-2.92 (m, 1 H) (CD ₃ OD) δ 9.07-9.26 (m, 1 H), 8.00-8.09 (m, 1 H), 7.86-7.93 (m, 1 H), 7.69-7.85 (m, 2 H), 7.57-7.69 (m, 2 H), 7.40 (s, 0.4 H), 6.85 (s, 0.6 H), 4.98 (dd, 0.5 H), 4.83 (br dd, 0.5 H), 3.82-3.95 (m, 0.6 H), 3.20 (td, 0.4 H), 3.05-3.14 (m, 0.6 H), 2.90-3.02 (m, 0.4 H), 2.68-2.85 (m, 1 H), 2.22-2.37 (m, 1 H), 1.08-1.33 (m, 4 H)	387.2 [M + H] ⁺	99.8%
327	7.63-7.72 (m, 2 H), 6.28-7.18 (m, 1 H), 4.23-4.68 (m, 1 H), 4.08 (br d, 1 H), 2.96-3.21 (m, 1 H), 2.69-2.92 (m, 1 H) (CD ₃ OD) δ 9.16 (d, 1 H), 8.00-8.09 (m, 1 H), 7.87-7.94 (m, 1 H), 7.70-7.85 (m, 2 H), 7.57-7.70 (m, 2 H), 7.40 (s, 0.6 H), 6.85 (s, 0.4 H), 4.99 (dd, 0.6 H), 4.77-4.85 (m, 0.4 H), 3.77-3.95 (m, 0.6 H), 3.14-3.24 (m, 0.4 H), 3.06-3.13 (m, 0.6 H), 2.89-2.99 (m, 0.4 H), 2.74-2.87 (m, 1 H), 2.22-2.35 (m, 1 H), 1.15-1.29 (m, 4 H)	387.2 [M + H] ⁺	99.3%
328	7.63-7.72 (m, 2 H), 6.28-7.18 (m, 1 H), 4.23-4.68 (m, 1 H), 4.08 (br d, 1 H), 2.96-3.21 (m, 1 H), 2.69-2.92 (m, 1 H) (CD ₃ OD) δ 9.27 (br s, 1 H), 8.55 (br s, 0.5 H), 8.09 (br d, 1 H), 7.89 (br s, 1.5 H), 7.77 (br t, 1 H), 7.40-7.72 (m, 3 H), 6.78 (br s, 1 H), 4.42 (br s, 1 H), 3.98 (br s, 1 H), 2.96-3.10 (m, 1 H), 2.80 (br s, 1 H), 1.61 (br d, 6 H)	420.1 [M + H] ⁺	100%
329	7.63-7.72 (m, 2 H), 6.28-7.18 (m, 1 H), 4.23-4.68 (m, 1 H), 4.08 (br d, 1 H), 2.96-3.21 (m, 1 H), 2.69-2.92 (m, 1 H) (CD ₃ OD) δ 9.27 (br s, 1 H), 8.51 (br s, 0.5 H), 8.05-8.35 (m, 1.5 H), 7.54-8.04 (m, 5 H), 6.34-7.05 (m, 1 H), 4.44 (br s, 1 H)	420.1 [M + H] ⁺	99.6%

TABLE 7-continued

Ex. #	¹ H NMR (400 MHz)	LCMS: m/z	% ee
	H), 3.70-4.15 (m, 1 H), 2.90-3.15 (m, 1 H), 2.79 (br d, 1 H), 1.60 (br d, 6 H)		
330	(CD ₃ OD) δ 9.28 (br s, 1 H), 8.56 (s, 2 H), 8.07 (d, 1 H), 7.87 (br d, 2 H), 7.53-7.80 (m, 4 H), 7.41 (d, 1 H), 6.76 (br s, 1 H), 4.57-4.69 (m, 1 H), 3.38-4.08 (m, 3 H), 2.98-3.13 (m, 1 H), 2.76 (br d, 1 H), 2.27 (s, 6 H)	452.2 [M + H] ⁺	100%
331	(CD ₃ OD) δ 9.32 (br s, 1 H), 8.28-9.09 (m, 2 H), 8.11 (d, 1 H), 7.91 (br d, 2 H), 7.64-7.86 (m, 4 H), 7.45 (dd, 1 H), 6.81 (br s, 1 H), 4.62 (br s, 1 H), 3.42-4.13 (m, 3 H), 3.00-3.17 (m, 1 H), 2.80 (br d, 1 H), 2.30 (s, 6 H)	452.1 [M + H] ⁺	99.7%
332	(CD ₃ OD) δ 9.27 (br s, 1 H), 8.65 (br s, 0.5 H), 8.09 (br d, 1.5 H), 7.35-7.99 (m, 5 H), 6.29-7.08 (m, 1 H), 4.25-4.64 (m, 1 H), 3.99 (br s, 1 H), 2.98-3.08 (m, 1 H), 2.81 (br s, 1 H), 1.73-1.85 (m, 6 H)	422.1 [M + H] ⁺	100%
333	(CD ₃ OD) δ 9.28 (br s, 1 H), 8.67 (br s, 0.5 H), 8.10 (br d, 1 H), 7.90 (br s, 1.5 H), 7.78 (br t, 1 H), 7.34-7.73 (m, 3 H), 6.27-7.01 (m, 1 H), 4.38 (br s, 1 H), 3.97 (br s, 1 H), 2.98-3.12 (m, 1 H), 2.81 (br s, 1 H), 1.71-1.91 (m, 6 H)	422.1 [M + H] ⁺	97.3%
334	(CD ₃ OD) δ 9.10-9.30 (m, 1 H), 8.02-8.13 (m, 1 H), 7.93-8.01 (m, 1 H), 7.61-7.88 (m, 5 H), 7.43 (br s, 0.4 H), 7.30 (td, 2 H), 6.94 (s, 0.6 H), 5.01 (br dd, 1 H), 3.91-4.05 (m, 1 H), 3.17-3.30 (m, 1 H), 2.90 (br d, 1 H)	459.1 [M + H] ⁺	100%
335	(CD ₃ OD) δ 9.09-9.29 (m, 1 H), 8.03-8.15 (m, 1 H), 7.93-8.00 (m, 1 H), 7.60-7.88 (m, 5 H), 7.43 (s, 0.4 H), 7.30 (td, 2 H), 6.94 (s, 0.6 H), 5.01 (br dd, 1 H), 3.88-4.10 (m, 1 H), 3.17-3.30 (m, 1 H), 2.82-2.96 (m, 1 H)	459.1 [M + H] ⁺	99.7%
336	(CD ₃ OD) δ 9.21 (s, 1 H), 8.06 (d, 1 H), 7.98 (dd, 2 H), 7.91 (d, 1 H), 7.84 (s, 1 H), 7.73-7.79 (m, 1 H), 7.61-7.70 (m, 2 H), 7.25 (t, 2 H), 6.36 (s, 1 H), 4.35 (br dd, 1 H), 3.89 (ddd, 1 H), 3.04-3.17 (m, 1 H), 2.86 (br dd, 1 H)	413.2 [M + H] ⁺	99.1%
337	(CD ₃ OD) δ 9.21 (s, 1 H), 8.06 (d, 1 H), 7.95-8.02 (m, 2 H), 7.92 (d, 1 H), 7.84 (s, 1 H), 7.77 (td, 1 H), 7.62-7.71 (m, 2 H), 7.22-7.31 (m, 2 H), 6.37 (s, 1 H), 4.35 (br dd, 1 H), 3.89 (ddd, 1 H), 3.03-3.20 (m, 1 H), 2.86 (br dd, 1 H)	413.2 [M + H] ⁺	99.0%
338	(CD ₃ OD) δ 9.20 (s, 1 H), 8.06 (d, 1 H), 7.89 (br s, 1.6 H), 7.46-7.78 (m, 4 H), 6.49-6.89 (m, 1 H), 4.48 (br s, 1 H), 3.97 (br s, 1 H), 2.71-3.13 (m, 2 H), 1.64-1.91 (m, 6 H)	406.2 [M + H] ⁺	100%
339	(CD ₃ OD) δ 9.20 (br s, 1 H), 8.06 (br d, 1.3 H), 7.89 (br s, 1.7 H), 7.46-7.78 (m, 4 H), 6.52-6.89 (m, 1 H), 4.48 (br s, 1 H), 3.95 (br s, 1 H), 2.66-3.15 (m, 2 H), 1.79 (br d, 6 H)	406.1 [M + H] ⁺	99.7%
340	(CD ₃ OD) δ 9.09-9.29 (m, 1 H), 8.71 (dd, 1 H), 8.38 (td, 1 H), 8.02-8.14 (m, 1 H), 7.93-8.00 (m, 1.2 H), 7.85-7.93 (m, 1.2 H), 7.73-7.84 (m, 1.6 H), 7.62-7.73 (m, 2 H), 7.50 (br s, 0.4 H), 6.94 (s, 0.6 H), 5.05 (br dd, 0.5 H), 4.94-4.99 (m, 0.5 H), 3.95-4.05 (m, 0.6 H), 3.16-3.29 (m, 1 H), 2.99-3.09 (m, 0.4 H), 2.81-2.96 (m, 1 H)	442.1 [M + H] ⁺	100%
341	(CD ₃ OD) δ 9.12-9.29 (m, 1 H), 8.71 (dd, 1 H), 8.33-8.43 (m, 1 H), 8.03-8.13 (m, 1 H), 7.95-7.99 (m, 1 H), 7.85-7.93 (m, 1.2 H), 7.78-7.85 (m, 1.2 H), 7.70-7.78 (m, 1.6 H), 7.63-7.69 (m, 1 H), 7.47-7.53 (m, 0.4 H), 6.94 (s, 0.6 H), 5.05 (br dd, 0.5 H), 4.93-4.97 (m, 0.5 H), 3.96-4.05 (m, 0.6 H), 3.17-3.29 (m, 1 H), 3.00-3.09 (m, 0.4 H), 2.80-2.95 (m, 1 H)	442.1 [M + H] ⁺	100%
342	(CD ₃ OD) δ 9.02-9.40 (m, 1 H), 8.20 (dd, 2 H), 8.01-8.12 (m, 1 H), 7.92-7.96 (m, 1 H), 7.58-7.85 (m, 4 H), 7.36 (td, 2 H), 6.93 (s, 1 H), 4.98-5.27 (m, 1 H), 3.88-4.10 (m, 1 H), 2.69-3.26 (m, 2 H)	441.2 [M + H] ⁺	100%
343	(CD ₃ OD) δ 9.08-9.40 (m, 1 H), 8.13-8.27 (m, 2 H), 8.00-8.12 (m, 1 H), 7.91-7.98 (m, 1 H), 7.54-7.83 (m, 4 H), 7.28-7.43 (m, 2 H), 6.93 (s, 1 H), 5.11 (br dd, 1 H), 3.72-4.06 (m, 1 H), 2.85-3.23 (m, 2 H)	441.1 [M + H] ⁺	99.0%
344	(CD ₃ OD) δ 9.33 (br s, 1 H), 8.23-9.01 (m, 1 H), 8.12 (d, 1 H), 7.66-7.98 (m, 6 H), 7.45 (dd, 1 H), 7.18 (d, 1 H), 6.82 (br s, 1 H), 4.64 (br s, 1 H), 3.51-4.20 (m, 1 H), 3.00-3.18 (m, 1 H), 2.81 (br d, 1 H), 2.05 (d, 3 H), 1.99 (d, 3 H)	455.2 [M + H] ⁺	98.1%
345	(CD ₃ OD) δ 9.10-9.33 (m, 1 H), 8.00-8.12 (m, 1 H), 7.83-7.95 (m, 1 H), 7.76 (br t, 1.5H), 7.52-7.72 (m, 2.5 H), 6.80 (s, 0.6 H), 6.34 (br s, 0.4 H), 4.78 (br s, 0.3 H), 4.22 (br s, 0.7 H), 3.79 (br s, 1 H), 3.44-3.66 (m, 1H), 2.93-3.26 (m, 4 H), 2.60-2.89 (m, 1 H), 2.45 (d, 3 H)	389.2 [M + H] ⁺	96.3%
346	(CD ₃ OD) δ 9.02-9.35 (m, 1 H), 8.02-8.13 (m, 1 H), 7.83-7.95 (m, 1 H), 7.50-7.82 (m, 4 H), 6.90-7.34 (m, 1 H), 6.80 (s, 0.6 H), 6.36 (br s, 0.4 H), 4.76 (br d, 0.4 H), 4.25 (br d, 0.6 H), 3.64-3.88 (m, 1 H), 3.32-3.41 (m, 1.5 H), 3.12-3.29 (m, 2 H), 2.93-3.11 (m, 1 H), 2.61-2.89 (m, 1.5 H)	425.2 [M + H] ⁺	99.2%

TABLE 7-continued

Ex. #	¹ H NMR (400 MHz)	LCMS: m/z	% ee
347	(CD ₃ OD) δ 9.09-9.22 (m, 1 H), 8.04 (dd, 1 H), 7.87-7.95 (m, 1 H), 7.51-7.84 (m, 4 H), 7.32 (br s, 0.4 H), 6.87 (s, 0.6 H), 4.92 (br s, 0.4 H), 3.79-3.99 (m, 0.6 H), 3.30-3.36 (m, 0.5 H), 3.06-3.24 (m, 1 H), 2.90-3.05 (m, 0.5 H), 2.83 (br d, 1 H), 1.67 (dd, 6 H)	405.0 [M + H] ⁺	100%
348	(CD ₃ OD) δ 8.94-9.37 (m, 1 H), 8.35 (s, 1 H), 8.14 (br d, 1 H), 7.81-8.01 (m, 2 H), 7.51-7.77 (m, 5 H), 6.98-7.27 (m, 4 H), 3.62-4.10 (m, 2 H), 2.59-3.13 (m, 2 H)	422.2 [M + H] ⁺	99.4%
349	(DMSO-d ₆) δ 11.82-12.26 (m, 1 H), 9.53 (s, 1 H), 9.11-9.43 (m, 1 H), 8.12 (br dd, 1 H), 7.93-8.00 (m, 1 H), 7.75-7.83 (m, 1.5 H), 7.62-7.73 (m, 2 H), 7.54 (s, 0.5 H), 6.35-6.74 (m, 1 H), 4.80-4.95 (m, 1H), 4.63-4.77 (m, 0.6 H), 4.60 (br s, 1H), 4.26 (br d, 0.4 H), 3.88 (br s, 0.4H), 3.39-3.43 (m, 0.6 H), 2.87-3.04 (m, 1 H), 2.68-2.77 (m, 1 H),	377.0 [M + H] ⁺	98.5%
350	(CD ₃ OD) δ 9.56-9.61 (m, 1 H), 9.10-9.24 (m, 1 H), 7.99-8.10 (m, 1 H), 7.89-7.93 (m, 1 H), 7.62-7.82 (m, 4 H), 7.48 (s, 0.4 H), 6.90 (s, 0.6 H), 5.05 (dd, 0.5 H), 4.88-4.91 (m, 0.5 H), 3.76-3.95 (m, 0.6 H), 3.31-3.36 (m, 0.4 H), 3.10-3.20 (m, 0.8 H), 3.00 (s, 0.2 H), 2.74-2.86 (m, 1 H)	363.0 [M + H] ⁺	99.3%
351	(CD ₃ OD) δ 9.14-9.33 (m, 1 H), 8.10 (dd, 1 H), 7.88-7.95 (m, 1 H), 7.86 (br d, 0.6 H), 7.64-7.82 (m, 3 H), 7.56 (s, 0.4 H), 6.84 (s, 0.5 H), 6.48 (br s, 0.5 H), 4.88-4.90 (m, 2 H), 4.80 (br dd, 1 H), 4.32 (br dd, 0.5 H), 3.82-3.92 (m, 0.5 H), 2.94-3.11 (m, 1 H), 2.80-2.93 (m, 1 H), 2.76 (s, 3 H)	391.0 [M + H] ⁺	98.6%
352	(CD ₃ OD) δ 9.29 (br s, 1 H), 8.89 (s, 1 H), 8.32-8.80 (m, 1 H), 8.09 (br d, 1 H), 7.81-7.96 (m, 2 H), 7.56-7.81 (m, 4 H), 7.50 (br d, 1 H), 6.76 (br s, 1 H), 4.59-4.67 (m, 1 H), 3.60 (br s, 1 H), 3.00-3.17 (m, 1 H), 2.78 (br d, 1 H)	473.0 [M + H] ⁺	100%
353	(CD ₃ OD) δ 9.19 (br s, 1 H), 8.34 (br d, 2 H), 8.06 (br t, 1 H), 7.70-7.99 (m, 3 H), 7.52-7.70 (m, 2 H), 6.90-7.21 (m, 2 H), 6.84 (br t, 1 H), 5.55 (br s, 1 H), 3.78 (br s, 1 H), 3.13 (br s, 1 H), 2.77 (br d, 1 H)	395.0 [M + H]	100%
354	(CD ₃ OD) δ 9.08-9.33 (m, 1 H), 8.36-8.42 (m, 1 H), 8.15 (d, 1 H), 7.88-8.09 (m, 4 H), 7.71-7.87 (m, 3 H), 7.57-7.70 (m, 1 H), 7.28-7.39 (m, 1 H), 7.16-7.37 (m, 1 H), 4.96-5.06 (m, 1 H), 3.87 (br d, 0.6 H), 3.49 (td, 0.4 H), 2.87-3.23 (m, 1 H), 2.63-2.87 (m, 1 H)	423.0 [M + H] ⁺	100%
355	(CD ₃ OD) δ 9.29 (br s, 1 H), 8.79 (s, 1 H), 8.08 (d, 1 H), 7.84-7.99 (m, 2 H), 7.58-7.82 (m, 4 H), 7.23-7.43 (m, 2 H), 6.76 (br s, 1 H), 4.91-5.02 (m, 1 H), 3.33-3.43 (m, 1 H), 2.91-3.15 (m, 1 H), 2.77 (br d, 1 H)	473.1 [M + H] ⁺	100%
356	(CD ₃ OD) δ 9.30 (br s, 1 H), 8.52 (d, 2 H), 8.06-8.18 (m, 2 H), 7.89 (br d, 1 H), 7.55-7.82 (m, 4 H), 7.11 (dd, 1 H), 6.77 (br s, 1 H), 4.63 (br s, 1 H), 3.37-4.16 (m, 1 H), 3.04-3.17 (m, 1 H), 2.74-2.86 (m, 1 H)	475.0 [M + H] ⁺	100%
357	(CD ₃ OD) δ 9.23 (br s, 1 H), 8.48-8.58 (d, 1.7 H), 8.07 (d, 1 H), 7.90 (br s, 1 H), 7.75 (br s, 1 H), 7.54-7.68 (m, 2.5 H), 7.36 (br s, 0.5 H), 6.68-7.14 (m, 3 H), 6.27 (br s, 0.3 H), 3.62-4.33 (m, 2 H), 2.65-3.09 (m, 2 H)	413.1 [M + H] ⁺	98.9%
358	(CD ₃ OD) δ 9.25 (s, 0.6 H), 8.97 (s, 0.4 H), 8.03-8.15 (m, 2.3 H), 7.88-8.03 (m, 2 H), 7.77 (t, 0.7 H), 7.57-7.71 (m, 3 H), 7.17-7.57 (m, 2 H), 7.03 (s, 0.7 H), 6.53 (br s, 0.3 H), 5.02 (br dd, 0.5 H), 4.03 (br s, 0.5 H), 3.75-3.88 (m, 0.6 H), 3.40-3.54 (m, 0.4 H), 2.97-3.13 (m, 1 H), 2.64-2.94 (m, 1 H)	412.0 [M + H] ⁺	100%
359	(CD ₃ OD) δ 9.01-9.29 (m, 1 H), 7.99-8.17 (m, 1 H), 7.95 (br dd, 2 H), 7.71-7.79 (m, 1 H), 7.62-7.71 (m, 2 H), 7.54-7.61 (m, 2 H), 7.38-7.46 (m, 1 H), 7.30 (t, 0.3 H), 7.20 (br t, 1 H), 7.03 (s, 0.7 H), 4.98 (br s, 1 H), 3.77-3.92 (m, 0.6 H), 3.46 (br s, 0.4 H), 2.99-3.19 (m, 1 H), 2.68-2.87 (m, 1 H)	395.0 [M + H] ⁺	98.3%
360	(CD ₃ OD) δ 9.00-9.36 (m, 1 H), 7.88-8.17 (m, 3.5 H), 7.60-7.79 (m, 4 H), 7.39-7.56 (m, 1.5 H), 7.25 (br t, 1 H), 7.04 (s, 1 H), 5.05 (br d, 1 H), 3.99-4.27 (m, 3 H), 3.77-3.96 (m, 0.6 H), 3.48 (br s, 0.4 H), 2.94-3.23 (m, 1 H), 2.66-2.91 (m, 1 H)	409.0 [M + H] ⁺	98.8%
361	(CD ₃ OD) δ 9.05-9.27 (m, 1 H), 7.98-8.15 (m, 1 H), 7.45-7.93 (m, 5.4 H), 6.87 (s, 0.6 H), 5.09 (br d, 1 H), 3.76-3.88 (m, 1 H), 2.88-3.21 (m, 1 H), 2.72-2.87 (m, 4 H)	377.0 [M + H] ⁺	100%
362	(CD ₃ OD) δ 9.25 (s, 1 H), 8.01-8.20 (m, 3 H), 7.87 (br d, 1 H), 7.68-7.82 (m, 3 H), 7.57-7.67 (m, 2 H), 7.32 (br s, 1 H), 6.79 (dd, 2 H), 4.61-4.69 (m, 1 H), 3.69 (br s, 1 H), 2.98-3.09 (m, 1 H), 2.74 (br dd, 1 H)	395.0 [M + H] ⁺	100%
363	(CD ₃ OD) δ 9.22 (s, 1 H), 8.09 (d, 1 H), 7.87-7.99 (m, 2 H), 7.74-7.83 (m, 1 H), 7.63-7.74 (m, 2 H), 6.39 (s, 1 H), 4.40	390.2 [M + H] ⁺	98.4%

TABLE 7-continued

Ex. #	¹ H NMR (400 MHz)	LCMS: m/z	% ee
	(dd, 1 H), 3.86-4.02 (m, 1 H), 3.47 (s, 3 H), 3.02-3.17 (m, 4 H), 2.87 (dd, 1 H)		
364	(CD ₃ OD) δ 9.19-9.27 (m, 1 H), 8.05-8.13 (m, 3 H), 7.94-7.98 (m, 1 H), 7.76-7.89 (m, 2 H), 7.65-7.75 (m, 2 H), 7.54-7.62 (m, 3.5 H), 6.95 (s, 0.5 H), 5.26 (dd, 0.7 H), 4.65 (br s, 0.3 H), 3.86-3.98 (m, 0.6 H), 3.36-3.42 (m, 0.4 H), 2.98-3.29 (m, 1 H), 2.81-2.92 (m, 1 H)	439.1 [M + H] ⁺	98.7%
365	Data provided above		
366	(CD ₃ OD) δ 9.05-9.31 (m, 1 H), 8.06 (br t, 1 H), 7.83-7.96 (m, 1.5 H), 7.64-7.81 (m, 3.5 H), 7.60 (s, 0.5 H), 6.86 (s, 0.5 H), 5.23 (br d, 1 H), 3.82-3.92 (m, 1 H), 2.94-3.23 (m, 7 H), 2.83 (br d, 1 H)	390.2 [M + H] ⁺	100%
367	(CD ₃ OD) δ 9.12-9.25 (m, 1 H), 8.01-8.14 (m, 1 H), 7.83-7.97 (m, 1.5 H), 7.73-7.82 (m, 1.5 H), 7.63-7.72 (m, 2 H), 7.61 (s, 0.5 H), 6.86 (s, 0.5 H), 5.23 (dd, 1 H), 3.81-3.93 (m, 1 H), 2.95-3.21 (m, 7 H), 2.74-2.90 (m, 1 H)	390.2 [M + H] ⁺	100%
368	(CD ₃ OD) δ 9.31 (s, 0.5 H), 9.21 (s, 0.5 H), 8.07-8.15 (m, 2 H), 7.84-7.95 (m, 1.6 H), 7.74-7.82 (m, 1.4 H), 7.64-7.72 (m, 1.6 H), 7.56 (s, 0.4 H), 6.86 (s, 0.5 H), 6.49 (br s, 0.5 H), 5.01 (br s, 0.5 H), 4.78-4.87 (m, 0.7 H), 4.64 (s, 0.3 H), 4.42-4.49 (m, 0.5 H), 4.34 (br dd, 0.5 H), 3.81-3.92 (m, 0.5 H), 2.65-3.19 (m, 3 H)	444.2 [M + H] ⁺	100%
369	(CD ₃ OD) δ 9.08-9.43 (m, 1 H), 8.43-8.59 (m, 1 H), 7.95-8.21 (m, 2 H), 7.61-7.94 (m, 5 H), 7.54 (s, 0.5 H), 6.76 (s, 0.5 H), 6.31-6.49 (m, 0.3 H), 6.14-6.21 (m, 0.3 H), 5.78 (d, 0.4 H), 5.47 (s, 1 H), 4.71 (br dd, 1 H), 4.19 (br dd, 0.5 H), 3.91 (br t, 0.5 H), 2.97-3.22 (m, 1 H), 2.77-2.94 (m, 1 H)	360.0 [M + H] ⁺	100%
370	(CD ₃ OD) δ 9.09-9.27 (m, 1 H), 8.02-8.13 (m, 1 H), 7.82-7.97 (m, 1.5 H), 7.72-7.81 (m, 1.5 H), 7.56-7.71 (m, 2.5 H), 6.85 (s, 0.5 H), 5.19 (br dd, 1 H), 3.76-3.99 (m, 1 H), 3.07-3.21 (m, 0.7 H), 2.93-3.00 (m, 0.3 H), 2.83 (br d, 1 H), 2.65-2.75 (m, 1 H), 0.73-0.96 (m, 2 H), 0.57-0.70 (m, 2 H)	402.1 [M + H] ⁺	100%
371	(CD ₃ OD) δ 9.13-9.26 (m, 1 H), 8.02-8.12 (m, 1 H), 7.83-7.96 (m, 1.6 H), 7.72-7.81 (m, 1.4 H), 7.63-7.72 (m, 2 H), 7.60 (s, 0.4 H), 6.85 (s, 0.6 H), 5.20 (br dd, 1 H), 4.80-4.86 (m, 0.5 H), 3.77-3.96 (m, 0.5 H), 3.06-3.20 (m, 0.7 H), 2.91-3.01 (m, 0.3 H), 2.77-2.89 (m, 1 H), 2.64-2.75 (m, 1 H), 0.75-0.89 (m, 2 H), 0.58-0.69 (m, 2 H)	402.0 [M + H] ⁺	100%
372	(CD ₃ OD) δ 9.12-9.33 (m, 1 H), 8.08 (dd, 1 H), 7.72-7.96 (m, 3 H), 7.61-7.71 (m, 1.6 H), 7.52 (s, 0.4 H), 6.83 (br d, 1.6 H), 6.40 (s, 0.4 H), 4.77 (br dd, 0.3 H), 4.44 (s, 0.7 H), 4.25 (br dd, 0.8 H), 4.04 (s, 1.2 H), 3.78-3.92 (m, 0.6 H), 3.04 (td, 0.4 H), 2.66-2.99 (m, 2 H), 2.37 (d, 3 H)	374.2 [M + H] ⁺	97.9%
373	(CD ₃ OD) δ 9.30 (s, 0.5 H), 9.17 (s, 0.5 H), 8.90 (d, 1 H), 8.07 (dd, 1 H), 7.71-7.95 (m, 4 H), 7.60-7.71 (m, 1.6 H), 7.53 (s, 0.4 H), 6.82 (s, 0.6 H), 6.44 (s, 0.4 H), 4.71-4.81 (m, 0.6 H), 4.52-4.70 (m, 0.8 H), 4.29-4.36 (m, 0.4 H), 4.20-4.38 (m, 1.2 H), 3.75-3.88 (m, 0.5 H), 3.02 (td, 0.5 H), 2.67-2.94 (m, 2 H)	376.1 [M + H] ⁺	100%
374	(CD ₃ OD) δ 9.30 (br s, 1 H), 8.31-8.60 (m, 1 H), 8.08 (br s, 1 H), 7.45-7.94 (m, 6 H), 7.14-7.44 (m, 2 H), 6.17-7.00 (m, 1 H), 4.57-4.86 (m, 0.5 H), 4.29-4.33 (m, 1 H), 4.12 (br s, 1.3 H), 3.66-3.91 (m, 0.7 H), 3.11 (br s, 0.3 H), 2.76 (br s, 1.7 H)	370.2 [M + H] ⁺	100%
375	(CD ₃ OD) δ 9.12-9.37 (m, 1 H), 8.35-8.53 (m, 1 H), 8.04-8.16 (m, 1 H), 7.44-7.94 (m, 7 H), 7.15-7.24 (m, 0.4 H), 7.00-7.10 (m, 0.6 H), 6.80-6.89 (m, 1.6 H), 6.49 (s, 0.4 H), 4.83 (br dd, 0.5 H), 4.27-4.55 (m, 1.5 H), 4.01-4.18 (m, 1 H), 3.71-3.84 (m, 0.6 H), 3.03-3.17 (m, 0.4 H), 2.78-2.92 (m, 0.4 H), 2.66-2.76 (m, 1.6 H)	409.2 [M + H] ⁺	100%
376	(CD ₃ OD) δ 9.73 (br s, 1 H), 9.03 (s, 1 H), 7.94-8.56 (m, 6 H), 7.12 (br s, 1 H), 4.47 (br s, 1 H), 3.79 (br s, 1 H), 3.22-3.30 (m, 1 H), 3.07 (br d, 1 H), 2.02-2.20 (m, 3 H)	426.1 [M + H] ⁺	100%
377	(CD ₃ OD) δ 9.22 (s, 1 H), 8.65 (br s, 1 H), 7.73-8.20 (m, 6 H), 7.63-7.70 (m, 2 H), 7.52 (br s, 1 H), 6.87 (br s, 1 H), 4.60 (br s, 1 H), 3.49-4.10 (m, 1 H), 3.15 (br s, 1 H), 2.86 (br d, 1 H), 2.34 (br s, 1 H), 0.92-1.14 (m, 4 H)	463.2 [M + H] ⁺	97.3%
378	(CD ₃ OD) δ 9.19 (s, 1 H), 8.05 (d, 1 H), 7.90 (br d, 2 H), 7.75 (br t, 1 H), 7.61-7.68 (m, 2 H), 4.41 (s, 1 H), 3.90 (br s, 1 H), 3.05 (br s, 1 H), 2.80 (br d, 1 H), 2.26 (br s, 1 H), 1.54 (br s, 6 H), 0.91 (br s, 4 H)	444.3 [M + H] ⁺	100%
379	Data provided above		
380	Data provided above		

TABLE 7-continued

Ex. #	¹ H NMR (400 MHz)	LCMS: m/z	% ee
381	(CD ₃ OD) δ 9.25 (br s, 1 H), 8.72 (br d, 1 H), 7.55-8.27 (m, 10 H), 6.93 (br s, 1 H), 4.19 (br s, 0.5 H), 3.50 (br s, 0.5 H), 3.19 (br s, 2 H), 1.37 (d, 3 H)	437.1 [M + H] ⁺	99.4%
382	(CD ₃ OD) δ 9.25 (br s, 1 H), 8.73 (br s, 1 H), 7.54-8.30 (m, 10 H), 6.89 (br s, 1 H), 3.34-3.73 (m, 1 H), 2.84-3.30 (m, 2 H), 1.38 (br s, 3 H)	437.2 [M + H] ⁺	80.3%
383	(DMSO-d ₆) δ 11.72-12.38 (m, 1 H), 9.27 (br d, 1 H), 8.75 (br d, 1 H), 8.05-8.22 (m, 2.5 H), 7.92-8.05 (m, 2.5 H), 7.89 (br s, 1 H), 7.72-7.82 (m, 1 H), 7.64-7.72 (m, 1 H), 7.59 (br dd, 2 H), 6.59-6.88 (m, 1 H), 4.02-4.65 (m, 1.5 H), 3.45 (br s, 0.5 H), 2.91-3.18 (m, 1 H), 1.15-1.31 (m, 3 H)	437.0 [M + H] ⁺	99.5%
384	(CD ₃ OD) δ 9.23 (br s, 1 H), 8.70 (br s, 1 H), 8.23 (br s, 1 H), 7.98-8.11 (m, 1.8 H), 7.90 (br s, 2.2 H), 7.78 (br t, 1.6 H), 7.69 (br d, 2 H), 7.56 (br s, 1.4 H), 6.63-6.95 (m, 1 H), 4.64 (br s, 2 H), 3.49-4.09 (m, 0.8 H), 3.00 (br s, 0.2 H), 1.36 (br s, 3 H)	437.0 [M + H] ⁺	96.7%
385	Data provided above		
386	Data provided above		
387	Data provided above		
388	Data provided above		
389	(CD ₃ OD) δ 9.20 (s, 1 H), 8.06 (br d, 1 H), 7.62-7.94 (m, 5 H), 6.42-7.02 (m, 1 H), 4.60 (br s, 1 H), 3.99-4.35 (m, 1 H), 3.12 (br d, 1 H), 2.31 (s, 3 H), 1.60 (br s, 6 H), 1.29 (br d, 3 H)	432.2 [M + H] ⁺	99.8%
390	(CD ₃ OD) δ 9.21 (br s, 1 H), 8.07 (d, 1 H), 7.63-7.97 (m, 5 H), 6.40-6.82 (m, 1 H), 4.55-4.76 (m, 1 H), 4.25 (br s, 0.5 H), 3.50 (br d, 0.5 H), 2.89-3.20 (m, 1 H), 2.34 (s, 3 H), 1.25-1.68 (m, 9 H)	432.2 [M + H] ⁺	94.3%
391	(CD ₃ OD) δ 9.21 (s, 1 H), 8.07 (d, 1 H), 7.90 (br s, 1 H), 7.59-7.84 (m, 4 H), 6.40-7.07 (m, 1 H), 3.39-4.43 (m, 2 H), 3.12 (br s, 1 H), 2.32 (s, 3 H), 1.61 (br s, 6 H), 1.30 (br d, 3 H)	432.2 [M + H] ⁺	99.6%
392	(CD ₃ OD) δ 9.23 (s, 1 H), 8.09 (d, 1 H), 7.60-7.98 (m, 5 H), 6.39-6.88 (m, 1 H), 3.41-4.42 (m, 2 H), 2.93-3.27 (m, 1 H), 2.35 (s, 3 H), 1.41-1.75 (m, 6 H), 1.35 (br d, 3 H)	432.2 [M + H] ⁺	99.5%
393	(CD ₃ OD) δ 9.27 (br s, 1 H), 8.35-8.98 (m, 0.5 H), 8.08 (br d, 1.5 H), 7.39-8.02 (m, 5 H), 6.17-7.06 (m, 1 H), 4.74 (s, 2 H), 4.18-4.70 (m, 1 H), 3.53-4.16 (m, 1 H), 3.49 (s, 3 H), 2.93-3.17 (m, 1 H), 2.78 (br d, 1 H)	406.1 [M + H] ⁺	100%
394	(CD ₃ OD) δ 9.25 (br s, 1 H), 8.10 (br d, 1 H), 7.59-8.01 (m, 5 H), 6.50-7.06 (m, 1 H), 4.62 (s, 3.5 H), 3.84-4.09 (m, 0.5 H), 3.36-3.54 (m, 3 H), 2.76-3.18 (m, 2 H)	390.1 [M + H] ⁺	100%
395	(CD ₃ OD) δ 9.21 (br s, 1 H), 8.06 (d, 1 H), 7.89 (br s, 2 H), 7.76 (br t, 2 H), 7.64-7.70 (m, 2 H), 6.87 (br s, 1 H), 4.42-4.73 (m, 1 H), 3.88-4.25 (m, 0.6 H), 3.36-3.59 (m, 0.4 H), 3.14 (br s, 1 H), 1.61 (br s, 6 H), 1.32 (d, 3 H)	418.0 [M + H] ⁺	100%
396	(CD ₃ OD) δ 9.19 (br s, 1 H), 8.06 (br d, 1 H), 7.89 (br s, 2 H), 7.75 (br t, 2 H), 7.62-7.67 (m, 2 H), 6.58-6.84 (m, 1 H), 4.29-4.73 (m, 1 H), 3.52 (br s, 1 H), 3.11 (s, 0.7 H), 2.74-3.02 (m, 0.3 H), 1.53-1.68 (m, 6 H), 1.32 (br s, 3 H)	418.0 [M + H] ⁺	99.0%
397	(CD ₃ OD) δ 9.19 (br s, 1 H), 8.05 (br d, 1 H), 7.59-7.94 (m, 6 H), 6.84 (br s, 1 H), 4.59 (s, 1 H), 4.09 (br s, 0.3 H), 3.46 (br s, 1 H), 3.12 (br s, 0.7 H), 1.59 (br s, 6 H), 1.30 (br d, 3 H)	418.0 [M + H] ⁺	100%
398	(CD ₃ OD) δ 9.19 (br s, 1 H), 8.06 (br d, 1 H), 7.89 (br s, 1.5 H), 7.51-7.82 (m, 4.5 H), 6.53-6.86 (m, 1 H), 4.58 (s, 1 H), 4.43 (br s, 0.5 H), 3.46 (br s, 1 H), 2.86 (s, 0.5 H), 1.62 (br s, 6 H), 1.32 (br s, 3 H)	418.1 [M + H] ⁺	98.9%
399	(CD ₃ OD) δ 9.20 (s, 1 H), 8.06 (d, 1 H), 7.88 (br s, 1 H), 7.76 (br t, 2 H), 7.62-7.71 (m, 2 H), 6.51-7.10 (m, 1 H), 4.19-4.72 (m, 1 H), 3.91-4.15 (m, 0.5 H), 3.36-3.72 (m, 0.5 H), 3.11 (br s, 1 H), 2.22 (br s, 1 H), 1.54 (br s, 6 H), 1.24-1.42 (m, 3 H), 0.83-0.99 (m, 4 H)	458.1 [M + H] ⁺	99.6%
400	(CD ₃ OD) δ 9.19 (s, 1 H), 8.05 (d, 1 H), 7.89 (br s, 1 H), 7.75 (br t, 2 H), 7.61-7.67 (m, 2 H), 6.46-6.82 (m, 1 H), 4.18-4.80 (m, 1 H), 3.50 (br s, 0.5 H), 2.90-3.28 (m, 1.5 H), 2.28 (br s, 1 H), 1.27-1.60 (m, 9 H), 0.91 (br s, 4 H)	458.1 [M + H] ⁺	100%
401	(CD ₃ OD) δ 9.17 (s, 1 H), 8.04 (br d, 1 H), 7.57-7.95 (m, 5 H), 6.41-7.08 (m, 1 H), 4.16-4.75 (m, 1 H), 3.84-4.11 (m, 0.5 H), 3.46 (br s, 0.5 H), 3.09 (br s, 1 H), 2.20 (br s, 1 H), 1.24-1.62 (m, 9 H), 0.76-1.04 (m, 4 H)	458.1 [M + H] ⁺	100%
402	(CD ₃ OD) δ 9.19 (s, 1 H), 8.05 (br d, 1 H), 7.89 (br s, 1.8 H), 7.75 (br t, 1.2 H), 7.61-7.70 (m, 2 H), 6.48-6.87 (m, 1	458.1 [M + H] ⁺	100%

TABLE 7-continued

Ex. #	¹ H NMR (400 MHz)	LCMS: m/z	% ee
	H), 4.70 (br s, 0.5 H), 4.30 (br s, 0.5 H), 3.47 (br s, 1 H), 3.01 (br s, 1 H), 2.28 (br s, 1 H), 1.28-1.61 (m, 9 H), 0.91 (br s, 4 H)		
403	(CD ₃ OD) δ 9.21 (s, 1 H), 8.65 (br s, 1 H), 7.44-8.25 (m, 9 H), 6.51-7.09 (m, 1 H), 4.24-4.75 (m, 1 H), 4.12 (br s, 0.5 H), 3.41-3.73 (m, 0.5 H), 3.13 (br s, 1 H), 2.41 (s, 3 H), 1.20-1.46 (m, 3 H)	451.0 [M + H] ⁺	100%
404	(CD ₃ OD) δ 9.24 (br s, 1 H), 8.71 (br s, 1 H), 7.85-8.20 (m, 4.2 H), 7.44-7.83 (m, 4.8 H), 6.50-6.96 (m, 1 H), 4.66-4.83 (m, 0.5 H), 4.44 (br s, 0.5 H), 3.37-3.64 (m, 1 H), 3.08-3.26 (m, 1 H), 2.45 (s, 3 H), 1.36 (br d, 3 H), 1.20-1.46 (m, 3 H)	451.0 [M + H] ⁺	98.0%
405	(CD ₃ OD) δ 9.21 (s, 1 H), 8.66 (br s, 1 H), 7.59-8.22 (m, 8 H), 7.53 (br s, 1 H), 6.97 (br s, 0.7 H), 6.64 (br s, 0.3 H), 4.62 (br s, 0.3 H), 4.36 (br s, 0.6 H), 4.12 (br s, 0.6 H), 3.47-3.74 (m, 0.4 H), 3.13 (br d, 1 H), 2.41 (s, 3 H), 1.32 (br s, 3 H)	451.1 [M + H] ⁺	100%
406	(CD ₃ OD) δ 9.23 (br s, 1 H), 8.69 (br s, 1 H), 7.65-8.22 (m, 8 H), 7.55 (br s, 1 H), 6.86 (br s, 0.6 H), 6.60 (br s, 0.4 H), 4.41 (br s, 1 H), 3.46-3.63 (m, 1 H), 3.06-3.29 (m, 1 H), 2.44 (s, 3 H), 1.35 (d, 3 H)	451.1 [M + H] ⁺	100%
407	(CD ₃ OD) δ 9.20 (s, 1 H), 8.63 (br d, 1 H), 8.06 (br d, 1 H), 7.61-8.00 (m, 7 H), 7.47-7.54 (m, 1 H), 6.61-7.08 (m, 1 H), 4.36-4.63 (m, 1 H), 3.54-4.18 (m, 1 H), 3.14 (br s, 1 H), 2.19-2.37 (m, 1 H), 1.33 (br d, 3 H), 0.91-1.08 (m, 4 H)	477.0 [M + H] ⁺	99.7%
408	(CD ₃ OD) δ 9.23 (s, 1 H), 8.65 (br s, 1 H), 8.06-8.15 (m, 1 H), 7.64-8.01 (m, 7 H), 7.53 (br s, 1 H), 6.56-6.93 (m, 1 H), 4.29-4.56 (m, 1 H), 3.41-3.77 (m, 1 H), 3.14 (br s, 1 H), 2.35 (br s, 1 H), 1.36 (br d, 3 H), 0.95-1.12 (m, 4 H)	477.0 [M + H] ⁺	91.0%
409	(CD ₃ OD) δ 9.23 (s, 1 H), 8.66 (br d, 1 H), 8.04-8.31 (m, 1.7 H), 7.74-8.03 (m, 4 H), 7.61-7.74 (m, 1.3 H), 7.46-7.60 (m, 1 H), 6.45-7.20 (m, 1 H), 4.31-4.78 (m, 1 H), 4.13 (br s, 0.6 H), 3.59 (br s, 0.4 H), 3.17 (br s, 1 H), 2.09-2.50 (m, 1 H), 1.35 (br d, 3 H), 0.84-1.15 (m, 4 H)	477.0 [M + H] ⁺	100%
410	(CD ₃ OD) δ 9.26 (s, 1 H), 8.69 (br s, 1 H), 8.08-8.27 (m, 1.6 H), 7.93 (br s, 1 H), 7.80 (br t, 1.4 H), 7.66-7.75 (m, 2 H), 7.55 (br s, 1 H), 6.56-6.99 (m, 1 H), 4.68-4.87 (m, 0.6 H), 4.49 (br s, 0.4 H), 3.52-3.94 (m, 0.5 H), 3.42 (br s, 0.5 H), 3.17-3.31 (m, 1 H), 2.38 (br s, 1 H), 1.38 (d, 3 H), 0.98-1.16 (m, 4 H)	477.0 [M + H] ⁺	100%
411	Number not used		
412	Number not used		
413	Number not used		
414	Number not used		
415	Number not used		
416	Number not used		
417	Number not used		
418	Number not used		
419	(CD ₃ OD) δ 9.11-9.29 (m, 1 H), 8.09 (dd, 1 H), 7.91-8.01 (m, 1 H), 7.73-7.87 (m, 2 H), 7.58-7.73 (m, 2 H), 7.38 (s, 0.4 H), 6.92 (s, 0.6 H), 4.97-5.06 (m, 0.5 H), 4.87 (br d, 0.5 H), 3.66-3.74 (m, 0.5 H), 3.64-4.04 (m, 1.5 H), 2.76-2.92 (m, 1 H), 1.82-1.98 (m, 6 H)	407.1 [M + H] ⁺	100%
420	(CD ₃ OD) δ 9.04-9.35 (m, 1 H), 8.00-8.19 (m, 1 H), 7.45-7.96 (m, 5 H), 6.77 (s, 0.6 H), 6.04 (br s, 0.4 H), 3.98-4.65 (m, 1 H), 3.69-3.93 (m, 4 H), 3.35-3.62 (m, 2 H), 3.06-3.21 (m, 2 H), 2.58-2.93 (m, 2 H)	416.1 [M + H] ⁺	96.6%
421	(CD ₃ OD) δ 9.16-9.25 (m, 1 H), 8.04-8.14 (m, 1 H), 7.55-7.99 (m, 5 H), 6.67-6.96 (m, 1 H), 4.96 (br s, 0.3 H), 4.17 (dd, 0.7 H), 3.91-4.05 (m, 0.7 H), 3.44 (td, 0.3 H), 2.94-3.13 (m, 1 H), 2.77-2.91 (m, 1 H), 1.65-1.74 (m, 6 H)	405.1 [M + H] ⁺	100%
422	(CD ₃ OD) δ 9.05-9.39 (m, 1 H), 7.55-8.15 (m, 6 H), 6.77-7.15 (m, 1 H), 4.44 (br dd, 1 H), 3.87-4.06 (m, 1 H), 2.75-3.18 (m, 2 H), 1.48-1.72 (m, 6 H)	405.1 [M + H] ⁺	100%
423	(CD ₃ OD) δ 9.18-9.27 (m, 1 H), 8.07 (dd, 1 H), 7.86-7.99 (m, 1 H), 7.42-7.82 (m, 4 H), 6.63-7.04 (m, 2 H), 4.44 (br d, 0.5 H), 4.04-4.20 (m, 3 H), 3.78-3.90 (m, 0.5 H), 2.71-3.28 (m, 3 H)	410.2 [M + H] ⁺	100%
424	(CD ₃ OD) δ 9.08-9.28 (m, 1 H), 8.02-8.12 (m, 1 H), 7.63-7.95 (m, 5 H), 7.56 (s, 0.4 H), 6.85 (s, 0.6 H), 5.37-5.62 (m, 1 H), 5.17 (br dd, 1 H), 4.50-4.61 (m, 2 H), 4.25-4.44 (m, 2 H), 3.78-3.99 (m, 1 H), 2.74-3.19 (m, 2 H)	420.2 [M + H] ⁺	100%
425	(CD ₃ OD) δ 9.14-9.23 (m, 1 H), 8.03-8.10 (m, 1 H), 7.83-7.95 (m, 2 H), 7.58-7.81 (m, 4 H), 6.86 (s, 1 H), 5.23 (dd, 1 H), 4.92-4.97 (m, 1 H), 3.80-3.95 (m, 1 H), 3.55-3.75 (m, 5 H), 2.73-3.17 (m, 2 H), 1.84-2.09 (m, 5 H)	448.2 [M + H] ⁺	100%

TABLE 7-continued

Ex. #	¹ H NMR (400 MHz)	LCMS: m/z	% ee
426	(CD ₃ OD) δ 9.10-9.26 (m, 1 H), 8.33 (dd, 1 H), 8.01-8.10 (m, 1 H), 7.90-7.99 (m, 1 H), 7.60-7.88 (m, 5 H), 7.34-7.55 (m, 1 H), 7.10-7.23 (m, 1 H), 6.92 (s, 1 H), 5.05 (br dd, 1 H), 3.89-4.04 (m, 1 H), 2.84-3.27 (m, 2 H)	463.2	99.4%
427	(CD ₃ OD) δ 9.09-9.43 (m, 1 H), 8.06-8.31 (m, 2 H), 7.87-8.03 (m, 1.7 H), 7.64-7.86 (m, 2.3 H), 7.44 (br s, 0.4 H), 6.96 (s, 0.6 H), 5.03 (br dd, 1 H), 3.38-3.56 (m, 1 H), 3.26 (br s, 0.5 H), 2.87-2.98 (m, 0.5 H), 1.45-1.51 (m, 9 H), 1.36-1.41 (m, 3 H)	417.2	100%
428	(CD ₃ OD) δ 9.08-9.27 (m, 1 H), 8.02-8.15 (m, 1 H), 7.91-8.02 (m, 1 H), 7.74-7.89 (m, 2 H), 7.64-7.74 (m, 1.5 H), 7.57 (s, 0.5 H), 7.37 (s, 0.5 H), 6.91 (s, 0.5 H), 4.85-4.89 (m, 0.5 H), 4.67 (s, 0.5 H), 4.15 (dd, 0.6 H), 3.30 (br s, 0.4 H), 3.20 (br d, 1 H), 1.49 (d, 9 H), 1.34 (dd, 3 H)	417.2	100%
429	(CD ₃ OD) δ 9.09-9.22 (m, 1 H), 8.05 (t, 1 H), 7.86-7.99 (m, 1 H), 7.49-7.85 (m, 4 H), 7.35 (s, 0.5 H), 6.89 (s, 0.5 H), 4.93-4.96 (m, 0.5 H), 4.61 (br s, 0.5 H), 4.13 (dd, 0.5 H), 3.09-3.30 (m, 1.5 H), 1.47 (d, 9 H), 1.24-1.38 (m, 3 H)	417.2	100%
430	(CD ₃ OD) δ 9.11-9.24 (m, 1 H), 8.03-8.11 (m, 1 H), 7.91-7.96 (m, 1 H), 7.59-7.87 (m, 4 H), 6.80-7.40 (m, 1 H), 4.91-4.93 (m, 0.7 H), 4.80 (dd, 0.3 H), 3.49 (dd, 0.6 H), 3.36 (br dd, 0.6 H), 3.15-3.24 (m, 0.4 H), 2.78-2.85 (m, 0.4 H), 1.46-1.48 (m, 9 H), 1.33 (d, 3 H)	417.2	99.2%
431	(CD ₃ OD) δ 9.28 (br s, 1 H), 8.61 (d, 1.5 H), 8.08 (d, 1 H), 7.89 (br t, 2 H), 7.55-7.79 (m, 4.5 H), 7.35-7.43 (m, 1 H), 7.03 (t, 1 H), 6.76 (br s, 1 H), 4.39-4.59 (m, 1 H), 3.39-3.95 (m, 1 H), 2.98-3.14 (m, 1 H), 2.71-2.83 (m, 1 H)	395.1	100%
432	(CD ₃ OD) δ 9.28 (br s, 1 H), 8.61 (d, 1.5 H), 8.07 (br d, 1 H), 7.89 (br t, 2 H), 7.53-7.79 (m, 4.5 H), 7.29-7.44 (m, 1 H), 7.03 (t, 1 H), 6.76 (br s, 1 H), 4.44-4.60 (m, 1 H), 3.41-3.89 (m, 1 H), 2.99-3.15 (m, 1 H), 2.77 (br d, 1 H)	395.2	99.7%
433	(CD ₃ OD) δ 9.19 (br d, 1 H), 8.07 (br t, 1 H), 7.82-7.96 (m, 1.5 H), 7.65-7.81 (m, 3.5 H), 7.59 (br s, 0.5 H), 6.86 (s, 0.5 H), 5.22 (br d, 1 H), 3.88 (br t, 1 H), 3.73-3.83 (m, 4 H), 3.54-3.68 (m, 4 H), 3.10 (br d, 1 H), 2.84 (br d, 1 H)	432.2	100%
434	(CD ₃ OD) δ 9.19 (br d, 1 H), 8.07 (br t, 1 H), 7.83-7.97 (m, 1.5 H), 7.63-7.81 (m, 3.5 H), 7.59 (br s, 0.5 H), 6.86 (br s, 0.5 H), 5.22 (br d, 1 H), 3.84-3.96 (m, 1 H), 3.72-3.83 (m, 4 H), 3.51-3.65 (m, 4 H), 2.99-3.21 (m, 1 H), 2.84 (br d, 1 H)	432.2	99.5%
435	(CD ₃ OD) δ 9.24 (br s, 1 H), 8.09 (d, 1 H), 7.92 (br s, 2 H), 7.64-7.82 (m, 4 H), 6.57-6.90 (m, 1 H), 4.54 (br s, 1 H), 3.98 (br s, 1 H), 3.07 (br s, 1 H), 2.64-2.98 (m, 1 H), 1.26-1.51 (m, 9 H)	402.1	99.9%
436	(CD ₃ OD) δ 9.24 (br s, 1 H), 8.10 (d, 1 H), 7.92 (br s, 2 H), 7.64-7.83 (m, 4 H), 6.61-6.91 (m, 1 H), 4.54 (br s, 1 H), 3.95 (br s,, 1 H), 3.08 (br s, 1 H), 2.87 (br s, 1 H), 1.52-1.57 (m, 1 H), 1.26-1.53 (m, 9 H)	402.1	99.4%
437	(CD ₃ OD) δ 9.11-9.24 (m, 1 H), 8.60-8.68 (m, 1 H), 8.00-8.11 (m, 1 H), 7.90-7.99 (m, 2.5 H), 7.60-7.86 (m, 5.5 H), 7.43 (s, 0.4 H), 6.93 (s, 0.6 H), 4.98 (br dd, 1 H), 3.93-4.04 (m, 0.7 H), 2.81-3.28 (m, 2.3 H)	442.2	100%
438	(CD ₃ OD) δ 9.08-9.30 (m, 1 H), 8.38-8.52 (m, 1 H), 8.20-8.30 (m, 1 H), 8.01-8.11 (m, 1 H), 7.95 (br d, 1 H), 7.57-7.86 (m, 5 H), 7.29-7.49 (m, 0.5 H), 6.93 (br s, 0.5 H), 5.04 (br dd, 0.6 H), 3.86-4.07 (m, 4 H), 3.12-3.28 (m, 1 H), 2.98-3.07 (m, 0.4 H), 2.82-2.94 (m, 1 H)	454.2	100%
439	(CD ₃ OD) δ 9.12-9.26 (m, 1 H), 8.57-8.66 (m, 1 H), 8.15-8.20 (m, 1 H), 8.01-8.12 (m, 1 H), 7.59-7.99 (m, 6 H), 7.47 (s, 0.4 H), 6.93 (s, 0.6 H), 5.02 (br dd, 1 H), 3.87-4.03 (m, 0.6 H), 2.75-3.26 (m, 2.4 H), 2.40-2.52 (m, 3 H)	438.2	100%
440	(CD ₃ OD) δ 9.11-9.28 (m, 1 H), 8.84-9.00 (m, 1 H), 8.29-8.46 (m, 1 H), 8.00-8.14 (m, 1 H), 7.92-7.97 (m, 1 H), 7.49-7.86 (m, 5.4 H), 6.92 (s, 0.6 H), 5.09 (br dd, 1 H), 3.89-4.08 (m, 0.6 H), 3.12-3.28 (m, 1 H), 2.97-3.07 (m, 0.4 H), 2.82-2.92 (m, 1 H)	463.2	100%
441	(CD ₃ OD) δ 9.11-9.27 (m, 1 H), 8.01-8.12 (m, 1 H), 7.91-7.98 (m, 1 H), 7.61-7.86 (m, 5 H), 7.48 (s, 0.4 H), 6.97-7.01 (m, 1 H), 6.92 (s, 0.6 H), 5.04 (br dd, 1 H), 3.89-4.08 (m, 4 H), 2.83-3.26 (m, 2 H)	427.2	100%
442	(CD ₃ OD) δ 9.23 (s, 0.5 H), 9.10-9.15 (m, 1 H), 8.40-8.55 (m, 2.5 H), 8.00-8.12 (m, 1 H), 7.91-7.99 (m, 1 H), 7.60-7.88 (m, 4 H), 7.47 (s, 0.4 H), 6.94 (s, 0.6 H), 5.03 (dd, 1 H), 3.89-4.10 (m, 1 H), 2.80-3.26 (m, 2 H)	492.2	100%
443	(CD ₃ OD) δ 9.11-9.27 (m, 1 H), 8.02-8.13 (m, 1 H), 7.92-8.01 (m, 2 H), 7.60-7.92 (m, 5 H), 7.50 (s, 0.4 H), 6.92 (s,	427.2	100%

TABLE 7-continued

Ex. #	¹ H NMR (400 MHz)	LCMS: m/z	% ee
	0.6 H), 5.08 (dd, 1 H), 4.10 (s, 3 H), 3.91-4.05 (m, 1 H), 2.80-3.26 (m, 2 H)		
444	(CD ₃ OD) δ 9.07-9.29 (m, 1 H), 7.91-8.13 (m, 3 H), 7.59-7.87 (m, 5 H), 7.47 (br s, 0.4 H), 6.91 (s, 0.6 H), 5.03 (br dd, 1 H), 3.96 (br t, 1 H), 3.79-3.89 (m, 3 H), 2.81-3.26 (m, 2 H)	427.2 [M + H] ⁺	100%
445	(CD ₃ OD) δ 9.26-9.35 (m, 1 H), 9.22 (s, 0.6 H), 9.15 (s, 0.4 H), 8.79 (td, 1 H), 8.46-8.59 (m, 1 H), 8.01-8.13 (m, 1 H), 7.92-7.99 (m, 1 H), 7.60-7.89 (m, 5 H), 7.53 (s, 0.4 H), 6.93 (s, 0.6 H), 5.04-5.23 (m, 0.7 H), 3.89-4.13 (m, 0.7 H), 3.16-3.29 (m, 1 H), 2.83-3.07 (m, 1.6 H)	424.2 [M + H] ⁺	100%
446	(CD ₃ OD) δ 9.11-9.26 (m, 1 H), 7.88-8.12 (m, 3 H), 7.59-7.87 (m, 4 H), 7.44-7.56 (m, 0.4 H), 6.91 (s, 0.6 H), 5.11 (br dd, 0.6 H), 3.81-4.02 (m, 4 H), 3.11-3.29 (m, 1 H), 2.79-3.07 (m, 1.5 H), 2.58-2.74 (m, 3 H)	441.2 [M + H] ⁺	95.8%
447	(CD ₃ OD) δ 9.07-9.29 (m, 1 H), 8.00-8.13 (m, 1 H), 7.94 (br d, 1 H), 7.56-7.88 (m, 5 H), 7.49 (s, 0.4 H), 7.06 (br d, 1 H), 6.91 (s, 0.6 H), 4.99-5.17 (m, 0.6 H), 4.27-4.33 (m, 3 H), 3.86-4.04 (m, 0.4 H), 3.10-3.31 (m, 2 H), 2.75-3.09 (m, 1 H)	427.2 [M + H] ⁺	100%
448	(CD ₃ OD) δ 9.05-9.42 (m, 1 H), 8.77-8.95 (m, 2 H), 7.88-8.18 (m, 4.5 H), 7.61-7.88 (m, 3.5 H), 7.50 (br s, 0.5 H), 6.93 (br s, 0.5 H), 5.08 (br dd, 1 H), 3.89-4.09 (m, 1 H), 2.85-3.26 (m, 2 H)	424.1 [M + H] ⁺	100%
449	(CD ₃ OD) δ 9.02-9.34 (m, 1 H), 8.47 (s, 1 H), 8.02-8.16 (m, 2 H), 7.91-7.97 (m, 1 H), 7.61-7.87 (m, 4 H), 7.52 (s, 0.4 H), 6.91 (s, 0.6 H), 5.10 (br dd, 1 H), 4.94-4.98 (m, 1 H), 3.45-4.03 (m, 1 H), 2.82-3.28 (m, 2 H), 2.46-2.71 (m, 4 H), 1.81-2.12 (m, 2 H)	467.2 [M + H] ⁺	95.8%
450	(CD ₃ OD) δ 9.12-9.23 (m, 1 H), 8.24 (s, 1 H), 8.01-8.09 (m, 1 H), 7.91-7.95 (m, 1 H), 7.62-7.85 (m, 4 H), 7.50 (br s, 0.5 H), 6.90 (br s, 0.5 H), 5.09 (br dd, 0.6 H), 3.93-3.99 (m, 0.4 H), 3.88-3.92 (m, 3 H), 2.81-3.29 (m, 3 H), 2.50-2.53 (m, 3 H)	441.2 [M + H] ⁺	100%
451	(CD ₃ OD) δ 9.13-9.23 (m, 1 H), 8.13-8.50 (m, 2 H), 8.02-8.11 (m, 1 H), 7.91-7.97 (m, 1 H), 7.62-7.86 (m, 4 H), 7.54 (s, 0.4 H), 6.91 (s, 0.6 H), 5.10 (br dd, 1 H), 3.90-4.00 (m, 0.6 H), 3.12-3.28 (m, 1 H), 2.95-3.06 (m, 0.4 H), 2.81-2.92 (m, 1 H)	413.2 [M + H] ⁺	100%
452	(CD ₃ OD) δ 9.31 (br s, 1 H), 8.43 (s, 2 H), 8.11 (d, 1 H), 7.91 (br d, 1 H), 7.60-7.86 (m, 5 H), 7.19 (d, 1 H), 6.79 (br s, 1 H), 4.93 (br s, 1 H), 3.41-4.22 (m, 1 H), 3.08 (br s, 1 H), 2.80 (br d, 1 H), 1.95-2.10 (m, 1 H), 0.97-1.10 (m, 2 H), 0.79 (q, 2 H)	435.2 [M + H] ⁺	100%
453	(CD ₃ OD) δ 9.31 (br s, 1 H), 8.51 (s, 2 H), 8.11 (d, 1 H), 7.91 (br d, 1 H), 7.86 (br d, 1 H), 7.60-7.82 (m, 4 H), 7.39 (d, 1 H), 6.80 (br s, 1 H), 4.68-4.87 (m, 1 H), 3.68 (t, 3 H), 3.36 (s, 3 H), 3.02-3.16 (m, 1 H), 2.93 (t, 2 H), 2.80 (br d, 1 H)	453.2 [M + H] ⁺	100%
454	(CD ₃ OD) δ 9.13-9.25 (m, 1 H), 8.12-8.51 (m, 2 H), 8.02-8.11 (m, 1 H), 7.92-7.97 (m, 1 H), 7.62-7.86 (m, 4 H), 7.54 (s, 0.4 H), 6.92 (s, 0.6 H), 5.11 (br dd, 1 H), 3.91-4.00 (m, 0.6 H), 3.13-3.28 (m, 1 H), 2.95-3.06 (m, 0.4 H), 2.81-2.92 (m, 1 H)	413.2 [M + H] ⁺	100%
455	(CD ₃ OD) δ 9.05-9.29 (m, 1 H), 8.03-8.15 (m, 1 H), 7.96 (br d, 1 H), 7.64-7.88 (m, 4 H), 7.31-7.58 (m, 1.4 H), 6.93 (s, 0.6 H), 5.11 (br dd, 1 H), 4.24 (s, 3 H), 3.86-4.11 (m, 1 H), 2.98-3.29 (m, 1 H), 2.82-2.95 (m, 1 H), 2.38 (s, 3 H)	441.2 [M + H] ⁺	100%
456	(CD ₃ OD) δ 9.32 (br s, 1 H), 8.25-9.06 (m, 2 H), 8.04-8.19 (m, 2 H), 7.86-8.01 (m, 3 H), 7.58-7.86 (m, 5 H), 6.83 (br d, 1 H), 4.97-5.09 (m, 1 H), 4.65 (br s, 1 H), 3.96 (s, 3 H), 3.01-3.20 (m, 1 H), 2.73-2.89 (m, 1 H)	475.2 [M + H] ⁺	100%
457	(CD ₃ OD) δ 9.31 (br s, 1 H), 8.19-8.95 (m, 1 H), 8.05-8.16 (m, 2 H), 7.91 (br d, 1 H), 7.62-7.87 (m, 5 H), 7.42 (dd, 1 H), 6.55-7.08 (m, 1 H), 4.66-4.80 (m, 1 H), 3.53-4.13 (m, 1 H), 3.17-3.26 (m, 4 H), 3.01-3.16 (m, 1 H), 2.80 (br d, 1 H), 2.60-2.72 (m, 4 H), 2.38 (s, 3 H)	493.3 [M + H] ⁺	100%
458	(CD ₃ OD) δ 9.32 (br s, 1 H), 8.21-8.95 (m, 1 H), 8.05-8.15 (m, 2 H), 7.91 (br d, 1 H), 7.58-7.88 (m, 5 H), 7.43 (dd, 1 H), 6.81 (br s, 1 H), 4.67-4.86 (m, 1 H), 3.83-3.92 (m, 4 H), 3.53-3.83 (m, 1 H), 3.13-3.20 (m, 4 H), 3.02-3.13 (m, 1 H), 2.80 (br d, 1 H)	480.2 [M + H] ⁺	100%

TABLE 7-continued

Ex. #	¹ H NMR (400 MHz)	LCMS: m/z	% ee
459	(CD ₃ OD) δ 9.31 (br s, 1 H), 8.20-9.18 (m, 2 H), 8.05-8.18 (m, 2 H), 7.47-8.03 (m, 5 H), 6.76 (br s, 1 H), 4.49-4.63 (m, 1 H), 3.39-4.30 (m, 1 H), 2.72-3.19 (m, 2 H)	509.0 [M + H] ⁺	100%
460	(CD ₃ OD) δ 9.30 (br s, 1 H), 8.27 (d, 2 H), 8.09 (d, 1 H), 7.53-7.99 (m, 6 H), 7.20 (dd, 1 H), 6.78 (br s, 1 H), 4.62 (br dd, 1 H), 3.88 (s, 3 H), 3.18-3.30 (m, 1 H), 2.94-3.17 (m, 1 H), 2.68-2.88 (m, 1 H)	425.2 [M + H] ⁺	100%
461	(CD ₃ OD) δ 9.13-9.49 (m, 2 H), 8.27-8.98 (m, 2 H), 7.90-8.22 (m, 6 H), 7.56-7.89 (m, 4 H), 7.41 (ddd, 1 H), 6.62-7.03 (m, 1 H), 5.03-5.15 (m, 1 H), 4.71 (br s, 1 H), 3.02-3.23 (m, 1 H), 2.70-2.94 (m, 1 H)	472.2 [M + H] ⁺	100%
462	(CD ₃ OD) δ 9.30 (br s, 1 H), 8.36 -9.01 (m, 2 H), 8.09 (d, 1 H), 7.96 (d, 1 H), 7.89 (br d, 1 H), 7.62-7.82 (m, 4 H), 7.04 (dd, 1 H), 6.68-6.80 (m, 1 H), 4.61-4.72 (m, 1 H), 3.43-3.91 (m, 1 H), 3.03-3.15 (m, 1 H), 2.79 (br d, 1 H)	429.2 [M + H] ⁺	100%
463	(CD ₃ OD) δ 9.32 (br s, 1 H), 8.22-9.05 (m, 2 H), 8.12 (d, 1 H), 8.03 (s, 1 H), 7.91 (br d, 1 H), 7.56-7.83 (m, 4 H), 6.78 (br s, 1 H), 4.95-5.14 (m, 1 H), 4.63-4.73 (m, 1 H), 3.82-3.94 (m, 4 H), 2.97-3.20 (m, 5 H), 2.81 (br d, 1 H)	514.2 [M + H] ⁺	100%
464	(CD ₃ OD) δ 9.32 (br s, 1 H), 8.32-9.12 (m, 2 H), 8.11 (d, 1 H), 8.02 (s, 1 H), 7.91 (br d, 1 H), 7.52-7.84 (m, 4 H), 6.60-7.16 (m, 1 H), 4.94-5.07 (m, 1 H), 3.38-4.36 (m, 1 H), 3.14 (br s, 5 H), 2.51-2.87 (m, 5 H), 2.40 (s, 3 H)	527.2 [M + H] ⁺	100%
465	(CD ₃ OD) δ 9.04-9.36 (m, 1 H), 8.03-8.15 (m, 1 H), 7.90-8.00 (m, 1 H), 7.60-7.89 (m, 4 H), 6.85-7.42 (m, 1 H), 5.05-5.19 (m, 1 H), 4.96 (br d, 1 H), 4.82-4.88 (m, 0.5 H), 3.82-4.03 (m, 0.5 H), 2.98-3.30 (m, 1 H), 2.78-2.94 (m, 1 H), 1.63-1.69 (m, 3 H)	391.2 [M + H] ⁺	100%
466	(CD ₃ OD) δ 9.29 (br s, 1 H), 8.42 (s, 1.7 H), 8.08 (d, 1 H), 7.52-7.97 (m, 6.3 H), 7.29 (d, 1 H), 6.78 (br s, 1 H), 4.56-4.61 (m, 1 H), 3.42-4.07 (m, 1 H), 2.97-3.16 (m, 1 H), 2.78 (br dd, 1 H), 2.37 (s, 3 H)	409.2 [M + H] ⁺	100%
467	(CD ₃ OD) δ 9.28 (br s, 1 H), 8.78 (d, 2 H), 8.08 (br d, 1 H), 7.61-8.01 (m, 6 H), 7.40 (dd, 1 H), 6.76 (br s, 1 H), 4.96-5.01 (m, 1 H), 4.51-4.62 (m, 1 H), 3.00-3.13 (m, 1 H), 2.78 (br d, 1 H)	429.1 [M + H] ⁺	100%
468	(CD ₃ OD) δ 9.31 (br s, 1 H), 8.54 (s, 2 H), 8.11 (d, 1 H), 7.83-7.98 (m, 2 H), 7.61-7.82 (m, 4 H), 7.38 (dd, 1 H), 6.80 (br s, 1 H), 4.69-4.74 (m, 1 H), 3.42-3.91 (m, 1 H), 3.01-3.17 (m, 1 H), 2.85-2.94 (m, 2 H), 2.76-2.84 (m, 1 H), 2.62-2.71 (m, 2 H), 2.34 (s, 6 H)	466.3 [M + H] ⁺	99.0%
469	(CD ₃ OD) δ 9.42-9.47 (m, 1 H), 9.10-9.28 (m, 1 H), 8.79-8.87 (m, 2 H), 8.01-8.10 (m, 1 H), 7.93-7.97 (m, 1 H), 7.61-7.88 (m, 4 H), 7.48 (s, 0.5 H), 6.94 (s, 0.5 H), 5.05 (br dd, 1 H), 3.89-4.06 (m, 1 H), 2.88-3.26 (m, 2 H)	425.1 [M + H] ⁺	100%
470	(CD ₃ OD) δ 9.25-9.28 (m, 1 H), 9.27 (br s, 1 H), 8.25-8.50 (m, 1 H), 7.61-7.88 (m, 7 H), 7.31 (dd, 1 H), 6.79 (br s, 1 H), 4.62 (br s, 1 H), 3.48-3.82 (m, 1 H), 3.00-3.11 (m, 1 H), 2.73-2.93 (m, 7 H)	438.2 [M + H] ⁺	99.7%
471	(CD ₃ OD) δ 9.42 (d, 1 H), 9.02-9.33 (m, 2 H), 8.25-8.38 (m, 1 H), 8.01-8.15 (m, 1 H), 7.93-8.01 (m, 1 H), 7.57-7.93 (m, 4 H), 6.88-7.56 (m, 1 H), 5.02 (br dd, 1 H), 3.93-4.14 (m, 1 H), 3.04-3.29 (m, 1 H), 2.74-2.97 (m, 1 H)	425.2 [M + H] ⁺	100%
472	(CD ₃ OD) δ 9.03-9.31 (m, 1 H), 8.01-8.13 (m, 1 H), 7.90-7.98 (m, 1 H), 7.36-7.86 (m, 4.5 H), 6.53-7.06 (m, 1.5 H), 5.02 (br d, 1 H), 3.83-4.02 (m, 4 H), 3.00-3.26 (m, 1 H), 2.88 (br s, 1 H), 2.36-2.45 (m, 3 H)	441.1 [M + H] ⁺	100%
473	(CD ₃ OD) δ 9.13-9.30 (m, 1 H), 9.00-9.09 (m, 2 H), 8.01-8.14 (m, 1 H), 7.97 (br d, 1 H), 7.63-7.88 (m, 5 H), 6.95 (s, 1 H), 5.01 (br dd, 1 H), 3.92-4.07 (m, 0.5 H), 2.83-3.30 (m, 2.5 H)	425.1 [M + H] ⁺	100%
474	(400 MHz, METHANOL-d ₄) δ 9.32 (br s, 1 H), 8.48 (br s, 1 H), 8.07-8.20 (m, 2 H), 7.92 (br d, 1 H), 7.65-7.85 (m, 5 H), 7.33-7.51 (m, 1 H), 6.81 (br s, 1 H), 4.76 (br d, 2 H), 3.71 (s, 1 H), 3.26-3.31 (m, 1 H), 3.02-3.22 (m, 4 H), 2.81 (br d, 1 H), 1.93-2.21 (m, 4 H)	496.3 [M + H] ⁺	100%
475	(CD ₃ OD) δ 9.24-9.39 (m, 1 H), 8.35-9.12 (m, 4 H), 8.21 (dt, 1 H), 8.01-8.14 (m, 2 H), 7.91 (br d, 1 H), 7.54-7.81 (m, 6 H), 6.82 (br s, 1 H), 4.63 (br s, 1 H), 3.37-4.12 (m, 1 H), 2.71-3.21 (m, 2 H)	472.2 [M + H] ⁺	100%
476	(CD ₃ OD) δ 9.46 (s, 1 H), 9.11-9.28 (m, 2 H), 8.74 (d, 1 H), 8.40 (br d, 0.5 H), 7.89-8.11 (m, 4 H), 7.52-7.88 (m, 5.5 H), 6.68 (br s, 1 H), 4.52-4.62 (m, 1 H), 3.54 (s, 1 H), 3.01 (br d, 1 H), 2.71 (br d, 1 H)	473.2 [M + H] ⁺	100%

TABLE 7-continued

Ex. #	¹ H NMR (400 MHz)	LCMS: m/z	% ee
477	(CD ₃ OD) δ 9.46 (s, 1 H), 9.34 (br s, 1 H), 9.25 (s, 1 H), 8.50-8.92 (m, 3 H), 8.02-8.26 (m, 3 H), 7.92 (br d, 1 H), 7.66-7.85 (m, 4 H), 6.81 (br s, 1 H), 4.64-4.75 (m, 1 H), 3.75 (s, 1 H), 3.02-3.20 (m, 1 H), 2.83 (br d, 1 H)	473.2 [M + H] ⁺	100%
478	(CD ₃ OD) δ 9.30 (br s, 1 H), 8.24-8.76 (m, 1 H), 8.05-8.13 (m, 2 H), 7.90 (br d, 1 H), 7.74-7.84 (m, 3 H), 7.66-7.73 (m, 2 H), 7.40 (dd, 1 H), 6.80 (br s, 1 H), 4.79-4.87 (m, 1 H), 4.63 (br s, 1 H), 3.75-3.83 (m, 1 H), 3.46-3.53 (m, 2 H), 3.01-3.14 (m, 1 H), 2.84-2.93 (m, 2 H), 2.79 (br d, 1 H), 2.01 (br d, 2 H), 1.66-1.75 (m, 2 H)	494.2 [M + H] ⁺	100%
479	(CD ₃ OD) δ 9.25-9.55 (m, 2 H), 8.24-9.18 (m, 1 H), 7.65-8.16 (m, 10 H), 7.28 (d, 1 H), 6.81 (br s, 1 H), 4.67 (br s, 1 H), 3.81 (s, 1 H), 3.04-3.19 (m, 1 H), 2.73-2.90 (m, 1 H), 2.63 (s, 3 H)	486.2 [M + H] ⁺	100%
480	(CD ₃ OD) δ 9.31 (br s, 1 H), 8.38-9.03 (m, 3 H), 8.10 (br d, 1 H), 8.00 (d, 1 H), 7.90 (br d, 1 H), 7.64-7.85 (m, 5 H), 7.34-7.48 (m, 2 H), 6.56-7.01 (m, 1 H), 4.64 (br s, 1 H), 3.45-4.01 (m, 1 H), 2.73-3.20 (m, 2 H), 2.54 (s, 3 H)	486.2 [M + H] ⁺	100%
481	(CD ₃ OD) δ 11.90-12.13 (m, 1 H), 9.07-9.49 (m, 2 H), 7.51-8.30 (m, 10 H), 6.90 (d, 2 H), 4.46-4.61 (m, 1 H), 3.85-4.07 (m, 4 H), 2.95-3.06 (m, 1 H), 2.68-2.75 (m, 1 H)	475.2 [M + H] ⁺	100%
482	(CD ₃ OD) δ 9.02-9.81 (m, 2 H), 8.56 (br d, 2 H), 7.99-8.18 (m, 3 H), 7.92 (br d, 1 H), 7.57-7.86 (m, 5 H), 7.49 (dt, 1 H), 6.82 (br d, 1 H), 4.53-4.76 (m, 1 H), 3.37 (br s, 1 H), 3.04-3.22 (m, 1 H), 2.82 (br d, 1 H)	490.1 [M + H] ⁺	100%
483	(CD ₃ OD) δ 9.64 (s, 1 H), 9.18-9.50 (m, 1 H), 8.20-9.17 (m, 4 H), 8.13 (d, 1 H), 8.02 (d, 1 H), 7.92 (br d, 1 H), 7.57-7.86 (m, 4 H), 7.42 (t, 1 H), 6.53-7.10 (m, 1 H), 4.62 (s, 1 H), 3.35-3.66 (m, 1 H), 3.12 (br s, 1 H), 2.82 (br d, 1 H)	473.2 [M + H] ⁺	100%
484	(CD ₃ OD) δ 9.24-9.36 (m, 1 H), 8.58 (s, 2 H), 8.09 (br d, 1 H), 7.88 (br d, 2 H), 7.63-7.80 (m, 4 H), 7.46 (d, 1 H), 6.69-6.88 (m, 1 H), 4.61 (br s, 1 H), 3.51-3.77 (m, 7 H), 2.99-3.12 (m, 1 H), 2.78 (br d, 1 H), 2.50 (br s, 4 H)	494.3 [M + H] ⁺	100%
485	(CD ₃ OD) δ 9.32 (br s, 1 H), 8.26-9.07 (m, 2 H), 8.11 (d, 1 H), 8.00 (d, 1 H), 7.91 (br d, 1 H), 7.61-7.86 (m, 7 H), 7.51 (t, 2 H), 7.38-7.46 (m, 1 H), 6.83 (br s, 1 H), 4.65 (br s, 1 H), 3.65 (br s, 1 H), 3.02-3.18 (m, 1 H), 2.81 (br d, 1 H)	471.2 [M + H] ⁺	100%
486	(CD ₃ OD) δ 9.32 (br s, 1 H), 9.16 (s, 1 H), 8.64 (d, 2 H), 8.02-8.13 (m, 2 H), 7.55-7.98 (m, 9 H), 6.81 (br s, 1 H), 4.61 (br s, 1 H), 3.42-4.01 (m, 1 H), 3.03-3.14 (m, 1 H), 2.80 (br d, 1 H)	472.2 [M + H] ⁺	100%
487	(CD ₃ OD) δ 9.30 (br s, 1 H), 9.15-9.19 (m, 3 H), 9.12 (s, 1 H), 8.34-8.98 (m, 1 H), 8.08 (dd, 2 H), 7.90 (br d, 1 H), 7.73-7.82 (m, 4 H), 7.62-7.71 (m, 1 H), 6.81 (br s, 1 H), 4.65 (br s, 1 H), 3.45-3.79 (m, 1 H), 3.04-3.16 (m, 1 H), 2.81 (br d, 1 H)	473.2 [M + H] ⁺	100%
488	(CD ₃ OD) δ 9.30 (br s, 1 H), 8.58 (s, 2 H), 7.63-8.14 (m, 7.4 H), 7.44 (d, 1 H), 6.60-6.93 (m, 0.6 H), 4.61 (br s, 1 H), 3.60 (s, 3 H), 3.01-3.14 (m, 1 H), 2.78 (br d, 1 H), 2.41-2.71 (m, 8 H), 2.31 (s, 3 H)	507.3 [M + H] ⁺	100%
489	(CD ₃ OD) δ 9.29 (br s, 1 H), 8.01-8.59 (m, 2 H), 7.64-7.91 (m, 7 H), 7.17 (dd, 1 H), 6.80 (br s, 1 H), 4.64 (br d, 1 H), 3.48-3.74 (m, 1 H), 3.25-3.30 (m, 4 H), 3.01-3.12 (m, 1 H), 2.77 (br d, 1 H), 2.02-2.08 (m, 4 H)	464.2 [M + H] ⁺	100%
490	(CD ₃ OD) δ 9.13-9.27 (m, 1 H), 8.03-8.11 (m, 1 H), 7.83-7.98 (m, 2 H), 7.73-7.82 (m, 1 H), 7.61-7.71 (m, 2 H), 7.51 (br d, 0.5 H), 6.99 (br s, 0.5 H), 4.45 (br d, 0.5 H), 4.25 (br d, 0.5 H), 4.15 (br d, 0.5 H), 3.46-3.61 (m, 0.5 H), 2.58-2.68 (m, 3 H), 1.25-1.39 (m, 2 H), 0.85-1.12 (m, 2 H)	387.2 [M + H] ⁺	99.6%
491	(CD ₃ OD) δ 9.19 (d, 1 H), 8.03-8.09 (m, 1 H), 7.83-7.96 (m, 2 H), 7.71-7.81 (m, 1 H), 7.65-7.70 (m, 1 H), 7.61-7.64 (m, 1 H), 7.54 (br s, 0.5 H), 6.99 (s, 0.5 H), 4.44 (d, 0.5 H), 4.25 (d, 0.5 H), 4.15 (br d, 0.5 H), 3.50-3.62 (m, 0.5 H), 2.58-2.67 (m, 3 H), 1.28-1.37 (m, 2 H), 0.85-1.11 (m, 2 H)	387.2 [M + H] ⁺	99.7%
492	(CD ₃ OD) δ 9.23 (s, 1 H), 8.22 (br s, 1 H), 8.08 (br d, 1 H), 7.91 (br s, 1 H), 7.77 (br t, 1.5 H), 7.54-7.72 (m, 2.5 H), 6.45-7.16 (m, 1 H), 4.21 (br s, 1 H), 3.65 (br s, 1 H), 2.33 (s, 3 H), 1.30 (br d, 1 H), 0.93 (br s, 3 H)	386.0 [M + H] ⁺	100%
493	(CD ₃ OD) δ 9.22 (s, 1 H), 8.21 (s, 1 H), 8.07 (br d, 1 H), 7.90 (br s, 1 H), 7.76 (br t, 1.5 H), 7.54-7.71 (m, 2.5 H), 6.40-7.13 (m, 1 H), 4.18 (br s, 1 H), 3.64 (br s, 1 H), 2.32 (s, 3 H), 1.29 (br d, 1 H), 0.92 (br s, 3 H)	386.1 [M + H] ⁺	100%
494	(CD ₃ OD) δ 9.13-9.26 (m, 1 H), 8.67-8.75 (m, 1 H), 8.33-8.43 (m, 1 H), 8.03-8.15 (m, 1 H), 7.95-8.01 (m, 1 H), 7.62-	456.2 [M + H] ⁺	100%

TABLE 7-continued

Ex. #	¹ H NMR (400 MHz)	LCMS: m/z	% ee
	7.95 (m, 5 H), 7.48 (s, 0.4 H), 6.93 (s, 0.6 H), 4.99 (br dd, 0.7 H), 4.84 (br d, 0.3 H), 3.58 (dd, 0.6 H), 3.39-3.48 (m, 0.6 H), 3.20-3.29 (m, 0.4 H), 2.83-2.94 (m, 0.4 H), 1.38 (dd, 3 H)		
495	(CD ₃ OD) δ 8.99-9.14 (m, 1 H), 8.59 (dd, 1 H), 8.27 (ddd, 1 H), 7.90-8.01 (m, 1 H), 7.83-7.88 (m, 1 H), 7.47-7.82 (m, 5 H), 7.36 (s, 0.5 H), 6.82 (s, 0.5 H), 4.86 (br d, 0.6 H), 4.50-4.61 (m, 0.7 H), 4.10 (dd, 0.4 H), 3.25 (br d, 0.3 H), 3.10 (br d, 1 H), 1.26 (t, 3 H)	456.2 [M + H] ⁺	100%
496	(CD ₃ OD) δ 9.09-9.23 (m, 1 H), 8.69 (dd, 1 H), 8.32-8.41 (m, 1 H), 7.59-8.09 (m, 7 H), 7.46 (s, 0.5 H), 6.93 (s, 0.5 H), 4.96 (br d, 1 H), 4.59-4.69 (m, 0.8 H), 4.20 (dd, 0.2 H), 3.21 (br d, 1 H), 1.36 (t, 3 H)	456.0 [M + H] ⁺	100%
497	(CD ₃ OD) δ 9.12-9.24 (m, 1 H), 8.67-8.71 (m, 1 H), 8.33-8.39 (m, 1 H), 8.01-8.11 (m, 1 H), 7.62-7.97 (m, 6 H), 7.46 (s, 0.5 H), 6.91 (s, 0.5 H), 4.97 (br dd, 1 H), 3.51-3.63 (m, 0.7 H), 3.41 (br dd, 0.6 H), 3.23 (br dd, 0.4 H), 2.81-2.90 (m, 0.3 H), 1.35 (dd, 3 H)	456.0 [M + H] ⁺	98.6%
498	(CD ₃ OD) δ 9.01-9.37 (m, 1 H), 8.00-8.16 (m, 1 H), 7.89-7.99 (m, 1 H), 7.60-7.85 (m, 3.3 H), 7.23-7.52 (m, 1.2 H), 6.90 (s, 0.5 H), 4.45-4.60 (m, 1 H), 3.39-3.54 (m, 1 H), 3.26 (br s, 0.5 H), 2.83 (br t, 0.5 H), 1.81-1.97 (m, 6 H), 1.35 (br d, 3 H)	421.2 [M + H] ⁺	100%
499	(CD ₃ OD) δ 9.01-9.27 (m, 1 H), 8.03-8.14 (m, 1 H), 7.91-8.01 (m, 1 H), 7.63-7.90 (m, 3.5 H), 7.56 (s, 0.5 H), 7.36 (s, 0.5 H), 6.91 (s, 0.5 H), 4.66 (s, 1 H), 4.17 (dd, 0.5 H), 3.29 (br d, 0.5 H), 3.21 (br d, 1 H), 1.85-1.97 (m, 6 H), 1.35 (d, 3 H)	421.2 [M + H] ⁺	100%
500	(CD ₃ OD) δ 9.11-9.22 (m, 1 H), 8.01-8.11 (m, 1 H), 7.88-8.01 (m, 1 H), 7.62-7.84 (m, 3.5 H), 7.55 (s, 0.5 H), 7.35 (s, 0.5 H), 6.89 (s, 0.5 H), 4.85 (br s, 0.7 H), 4.64 (s, 0.3 H), 4.15 (dd, 0.5 H), 3.11-3.28 (m, 1.5 H), 1.81-1.96 (m, 6 H), 1.33 (d, 3 H)	421.2 [M + H] ⁺	100%
501	(CD ₃ OD) δ 9.10-9.25 (m, 1 H), 8.03-8.11 (m, 1 H), 7.91-7.95 (m, 1 H), 7.58-7.87 (m, 4 H), 6.84-7.38 (m, 1 H), 4.90-4.93 (m, 0.7 H), 4.80 (dd, 0.3 H), 3.46-3.57 (m, 0.6 H), 3.37 (br d, 0.6 H), 3.20 (br d, 0.4 H), 2.80 (br t, 0.4 H), 1.84-1.93 (m, 6 H), 1.34 (d, 3 H)	421.2 [M + H] ⁺	99.8%
502	(CD ₃ OD) δ 9.22 (br s, 1 H), 8.38 (s, 1 H), 8.08 (br d, 1.3 H), 7.91 (br s, 1.7 H), 7.53-7.81 (m, 4 H), 6.55-6.88 (m, 1 H), 4.43 (br s, 1 H), 3.38-3.70 (m, 1 H), 2.68-3.16 (m, 1 H), 1.33 (br d, 3 H)	360.2 [M + H] ⁺	98.8%
503	(CD ₃ OD) δ 9.22 (br s, 1 H), 8.37 (s, 1 H), 8.07 (d, 1 H), 7.88 (br s, 2 H), 7.59-7.82 (m, 4 H), 6.60-6.94 (m, 1 H), 3.97-4.51 (m, 1 H), 3.33-3.73 (m, 1 H), 2.99-3.23 (m, 1 H), 1.30 (br d, 3 H)	360.2 [M + H] ⁺	99.7%
504	(CD ₃ OD) δ 9.20 (br s, 1 H), 8.35 (s, 1 H), 8.05 (br d, 1 H), 7.60-7.94 (m, 6 H), 6.79 (br s, 1 H), 4.59 (s, 1 H), 4.42 (br s, 0.6 H), 3.90-4.22 (m, 0.4 H), 3.11 (br s, 1 H), 1.28 (br d, 3 H)	360.0 [M + H] ⁺	100%
505	(CD ₃ OD) δ 9.20 (br s, 1 H), 8.36 (s, 1 H), 8.06 (br d, 1 H), 7.89 (br s, 2 H), 7.61-7.78 (m, 4 H), 6.49-6.90 (m, 1 H), 4.93-4.99 (m, 0.6 H), 4.62-4.82 (m, 0.5 H), 4.41 (br s, 0.6 H), 3.37-3.67 (m, 0.5 H), 3.14-3.25 (m, 0.6 H), 2.64-3.03 (m, 0.2 H), 1.26-1.38 (m, 3 H)	360.1 [M + H] ⁺	100%
506	(CD ₃ OD) δ 9.24 (s, 1 H), 8.33-8.51 (m, 1 H), 8.03-8.22 (m, 2 H), 7.90-8.03 (m, 1 H), 7.59-7.88 (m, 3 H), 6.71-7.53 (m, 1 H), 4.48 (br s, 1 H), 3.62-4.17 (m, 1 H), 3.20 (br dd, 1 H), 2.31 (dt, 1 H), 1.34 (br d, 3 H), 0.87-1.02 (m, 4 H)	400.0 [M + H] ⁺	95.1%
507	(CD ₃ OD) δ 9.21 (s, 1 H), 8.02-8.16 (m, 2 H), 7.91 (br s, 2 H), 7.77 (br t, 1 H), 7.60-7.73 (m, 2 H), 6.44-6.89 (m, 1 H), 4.32 (br s, 1 H), 3.41-3.65 (m, 1 H), 3.10-3.27 (m, 1 H), 2.02-2.35 (m, 1 H), 1.32 (d, 3 H), 0.93 (br d, 4 H)	400.0 [M + H] ⁺	91.5%
508	(CD ₃ OD) δ 9.19 (s, 1 H), 8.02-8.12 (m, 2 H), 7.89 (br s, 2 H), 7.75 (br t, 1 H), 7.62-7.69 (m, 1 H), 7.60-7.69 (m, 1 H), 6.28-6.94 (m, 1 H), 4.29 (br s, 1 H), 3.46 (br s, 1 H), 3.04-3.25 (m, 1 H), 2.05-2.40 (m, 1 H), 1.30 (d, 3 H), 0.91 (br d, 4 H)	400.1 [M + H] ⁺	98.9%
509	(CD ₃ OD) δ 9.17 (s, 1 H), 7.97-8.20 (m, 2 H), 7.85 (br s, 1 H), 7.67-7.79 (m, 2.5 H), 7.64 (br t, 1.5 H), 6.47-7.08 (m, 1 H), 3.86-4.46 (m, 1 H), 3.46 (br s, 1 H), 3.09 (br s, 1 H), 2.15 (br s, 1 H), 1.25 (br d, 3 H), 0.85-0.97 (m, 4 H)	400.0 [M + H] ⁺	100%
510	(CD ₃ OD) δ 9.12-9.28 (m, 1 H), 8.04-8.15 (m, 1 H), 7.82-8.00 (m, 2 H), 7.66-7.81 (m, 3 H), 7.63 (s, 0.3 H), 7.42 (s, 1 H)	401.2 [M + H] ⁺	100%

TABLE 7-continued

Ex. #	¹ H NMR (400 MHz)	LCMS: m/z	% ee
	0.3 H), 6.87 (s, 0.4 H), 4.75-4.88 (m, 1 H), 3.45-3.55 (m, 0.7 H), 3.35-3.40 (m, 0.6 H), 3.11-3.26 (m, 0.4 H), 2.75-2.92 (m, 0.3 H), 2.22-2.41 (m, 1 H), 1.21-1.37 (m, 7 H)		
511	(CD ₃ OD) δ 9.18 (d, 1 H), 8.08 (t, 1 H), 7.90-7.99 (m, 1 H), 7.73-7.88 (m, 2 H), 7.64-7.73 (m, 1.5 H), 7.58 (s, 0.5 H), 7.42 (s, 0.5 H), 6.89 (s, 0.5 H), 4.97 (s, 0.6 H), 4.65 (br s, 0.4 H), 4.13 (dd, 0.5 H), 3.30 (br s, 0.5 H), 3.18 (br s, 1 H), 2.22-2.43 (m, 1 H), 1.16-1.37 (m, 7 H)	401.2 [M + H] ⁺	97.9%
512	(CD ₃ OD) δ 9.17 (d, 1 H), 8.06 (t, 1 H), 7.89-7.97 (m, 1 H), 7.56-7.85 (m, 4 H), 7.41 (s, 0.5 H), 6.87 (s, 0.5 H), 4.98 (br s, 0.6 H), 4.60 (br s, 0.4 H), 4.11 (dd, 0.5 H), 3.12-3.29 (m, 1.5 H), 2.26-2.37 (m, 1 H), 1.16-1.34 (m, 7 H)	401.2 [M + H] ⁺	100%
513	(CD ₃ OD) δ 9.11-9.25 (m, 1 H), 8.03-8.10 (m, 1 H), 7.73-7.96 (m, 3 H), 7.58-7.72 (m, 2 H), 6.80-7.47 (m, 1 H), 4.92-4.97 (m, 0.6 H), 4.77 (dd, 0.4 H), 3.45-3.52 (m, 0.6 H), 3.32-3.38 (m, 0.6 H), 3.12-3.23 (m, 0.4 H), 2.81 (t, 0.4 H), 2.24-2.36 (m, 1 H), 1.33 (dd, 3 H), 1.18-1.29 (m, 4 H)	401.2 [M + H] ⁺	100%
514	(CD ₃ OD) δ 9.10-9.24 (m, 1 H), 8.43 (dd, 1 H), 8.24 (dd, 1 H), 7.93-8.09 (m, 2 H), 7.58-7.82 (m, 5 H), 7.47 (s, 0.5 H), 6.93 (s, 0.5 H), 4.96 (br d, 0.5 H), 4.66 (d, 0.5 H), 4.19 (dd, 0.5 H), 3.98 (d, 3 H), 3.36 (br d, 0.5 H), 3.15-3.23 (m, 1 H), 1.36 (dd, 3 H)	468.2 [M + H] ⁺	100%
515	(CD ₃ OD) δ 9.00-9.43 (m, 1 H), 8.39-8.53 (m, 1 H), 8.21-8.32 (m, 1 H), 8.02-8.17 (m, 1 H), 7.92-8.00 (m, 1 H), 7.57-7.90 (m, 5 H), 7.49 (br s, 0.4 H), 6.93 (s, 0.6 H), 4.98 (br d, 1 H), 3.91-4.09 (m, 3 H), 3.58 (br s, 0.5 H), 3.42 (br s, 0.5 H), 3.25 (br s, 0.5 H), 2.87 (br t, 0.5 H), 1.37 (dd, 3 H)	468.2 [M + H] ⁺	97.6%
516	(CD ₃ OD) δ 8.88-9.54 (m, 1 H), 8.45 (dd, 1 H), 8.26 (dd, 1 H), 7.92-8.16 (m, 2 H), 7.56-7.90 (m, 5 H), 7.49 (s, 0.5 H), 6.95 (s, 0.5 H), 4.98 (br d, 0.5 H), 4.68 (d, 0.5 H), 4.21 (dd, 0.5 H), 4.00 (d, 3 H), 3.38 (d, 0.5 H), 3.21 (br dd, 1 H), 1.38 (dd, 3 H)	468.2 [M + H] ⁺	98.3%
517	(CD ₃ OD) δ 9.20 (s, 1 H), 8.48 (br s, 1 H), 8.07 (br d, 1 H), 7.50-8.00 (m, 5 H), 6.81 (br s, 0.6 H), 6.56 (br s, 0.4 H), 4.70-4.83 (m, 0.5 H), 4.40 (br s, 0.5 H), 3.99 (br s, 0.6 H), 3.47 (br s, 0.4 H), 2.66-3.25 (m, 2 H)	371.1 [M + H] ⁺	100%
518	(CD ₃ OD) δ 9.16-9.29 (m, 1 H), 8.07 (dd, 1 H), 7.99 (d, 1 H), 7.88-7.96 (m, 1 H), 7.59-7.83 (m, 3.5 H), 7.42 (s, 0.5 H), 6.92 (s, 0.5 H), 6.68 (br s, 0.5 H), 4.27-4.51 (m, 0.5 H), 3.95-4.18 (m, 3 H), 3.79-3.93 (m, 0.5 H), 3.35-3.50 (m, 0.4 H), 3.07-3.23 (m, 0.6 H), 2.93-3.05 (m, 1 H), 2.69-2.91 (m, 1 H)	360.1 [M + H] ⁺	100%

Cell Based Phenylalanine Flux Assay

[0424] Cells expressing R408W PAH were made by transducing A375 cells with lentivirus encoding human PAH with the R408W mutation in pLVX-Puro, then selecting with puromycin until stable cell lines were generated. A375 R408W cells were seeded into 96 well plates in DMEM+10% FBS at a density of 40,000 cells/well one hour prior to compound addition. Compounds were resuspended in DMSO, and 2-fold serial dilutions were performed to generate a 10-point dose curve. Compounds were added to plated cells in a total volume of 100 μ l, and a final DMSO concentration of 0.5%. Each compound was tested in duplicate. Following compound addition, cells were placed in a 5% CO₂, 37° C. tissue culture incubator for 24 hrs. After the incubation period, 20 μ M sepiapterin and 800 μ M 13C9, 15N-Phenylalanine were added. After 4 hours, cell media was removed. An aliquot of 10 μ l of cell media was combined with 200 μ l of extraction buffer (80% acetonitrile/20% H₂O) for each well. Determination of ¹³C-Tyrosine concentration was assessed by liquid chromatography mass spectrometry.

[0425] Specific compounds disclosed herein were tested in the foregoing assay and they were determined to have an

AC₅₀ according to the following scores: (A) less than or equal to 0.500 μ M, (B) greater than 0.500 and less than 1.000 μ M, (C) greater than or equal to 1.000 and less than 5.000 μ M, (D) greater than or equal to 5.000 μ M, (E) no fit, and (NT) not tested, as shown below. Where a compound was tested multiple times, the average value of the tests is reported.

Ex. #	AC ₅₀
1	A
2	C
3	A
4	D
5	B
6	D
7	B
8	E
9	B
10	C
11	A
12	D
13	C
14	D
15	B
16	D

-continued

-continued

Ex. #	AC ₅₀	Ex. #	AC ₅₀
17	A	91	A
18	E	92	C
19	D	93	A
20	B	94	C
21	D	95	C
22	A	96	B
23	A	97	A
24	D	98	C
25	D	99	C
26	A	100	E
27	D	101	B
28	C	102	D
29	A	103	C
30	D	104	A
31	B	105	B
32	D	106	C
33	C	107	B
34	D	108	C
35	A	109	C
36	D	110	C
37	A	111	B
38	C	112	E
39	B	113	A
40	C	114	D
41	A	115	A
42	C	116	C
43	A	117	C
44	C	118	A
45	A	119	C
46	D	120	A
47	B	121	C
48	D	122	A
49	A	123	C
50	D	124	B
51	A	125	C
52	C	126	D
53	A	127	C
54	C	128	A
55	B	129	C
56	C	130	A
57	A	131	C
58	C	132	C
59	A	133	A
60	C	134	A
61	B	135	D
62	D	136	C
63	A	137	A
64	D	138	A
65	A	139	B
66	C	140	D
67	B	141	A
68	D	142	D
69	B	143	B
70	D	144	D
71	A	145	A
72	C	146	C
73	B	147	A
74	C	148	C
75	B	149	A
76	D	150	D
77	A	151	B
78	A	152	D
79	D	153	B
80	B	154	D
81	A	155	B
82	D	156	D
83	A	157	D
84	C	158	B
85	A	159	C
86	C	160	D
87	C	161	B
88	A	162	D
89	A	163	A
90	C	164	D

-continued

-continued

Ex. #	AC ₅₀	Ex. #	AC ₅₀
165	B	239	E
166	C	240	A
167	C	241	D
168	A	242	A
169	C	243	C
170	B	244	B
171	A	245	B
172	C	246	D
173	A	247	D
174	C	248	B
175	B	249	E
176	D	250	B
177	A	251	C
178	C	252	D
179	A	253	C
180	D	254	A
181	A	255	E
182	C	256	A
183	C	257	E
184	A	258	A
185	A	259	A
186	D	260	E
187	A	261	A
188	C	262	E
189	A	263	A
190	C	264	E
191	D	265	B
192	B	266	E
193	A	267	B
194	C	268	E
195	A	269	E
196	D	270	B
197	B	271	B
198	D	272	D
199	D	273	A
200	A	274	D
201	A	275	E
202	D	276	A
203	A	277	E
204	C	278	A
205	B	279	E
206	C	280	A
207	D	281	B
208	B	282	E
209	A	283	B
210	C	284	E
211	A	300	A
212	E	301	D
213	A	302	A
214	C	303	D
215	C	304	D
216	C	305	A
217	E	306	B
218	B	307	D
219	B	308	A
220	E	309	D
221	C	310	D
222	D	311	A
223	C	312	A
224	D	313	C
225	A	314	A
226	D	315	D
227	D	316	A
228	C	317	D
229	E	318	A
230	B	319	D
231	A	320	A
232	D	321	C
233	D	322	A
234	A	323	D
235	D	324	A
236	C	325	D
237	D	326	A
238	A	327	D

-continued

-continued

Ex. #	AC ₅₀	Ex. #	AC ₅₀
328	B	402	A
329	D	403	A
330	A	404	D
331	D	405	C
332	A	406	A
333	C	407	A
334	A	408	B
335	C	409	E
336	D	410	A
337	A	411	C
338	D	412	A
339	A	413	A
340	A	414	C
341	D	415	C
342	A	416	A
343	D	417	A
344	B	418	D
345	B	419	A
346	C	420	C
347	B	421	B
348	A	422	C
349	A	423	A
350	A	424	A
351	B	425	A
352	A	426	A
353	A	427	C
354	A	428	B
355	A	429	C
356	A	430	A
357	A	431	A
358	A	432	E
359	A	433	B
360	A	434	E
361	B	435	A
362	A	436	E
363	B	437	A
364	A	438	A
365	B	439	A
366	A	440	A
367	D	441	A
368	A	442	A
369	B	443	A
370	B	444	B
371	D	445	A
372	A	446	A
373	A	447	A
374	A	448	A
375	A	449	A
376	A	450	A
377	A	451	A
378	A	452	A
379	C	453	A
380	D	454	B
381	C	455	A
382	D	456	A
383	E	457	A
384	C	458	A
385	B	459	A
386	D	460	A
387	E	461	A
388	B	462	A
389	A	463	A
390	D	464	A
391	E	465	B
392	B	466	A
393	B	467	A
394	B	468	A
395	B	469	A
396	C	470	A
397	E	471	A
398	C	472	A
399	A	473	A
400	C	474	C
401	C	475	A

-continued

Ex. #	AC ₅₀
476	A
477	A
478	B
479	A
480	A
481	A
482	A
483	A
484	A
485	A
486	A
487	A
488	A
489	A
490	A
491	E
492	D
493	A
494	C
495	E
496	C
497	C
498	C

-continued

Ex. #	AC ₅₀
499	B
500	E
501	A
502	E
503	B
504	E
505	A
506	A
507	C
508	E
509	E
510	E
511	B
512	E
513	B
514	E
515	C
516	B
517	A
518	A

[0426] Additionally, the following compounds were tested with an AC₅₀ of B, C, D, or E:

Compound(s)	AC ₅₀
(4R, 7S), (4R,7R), (4S, 7S), and (4S, 7R) diastereomers of 3-[5-[6-(methoxymethyl)pyrazolo[1,5-a]pyridine-3-carbonyl]-7-methyl-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]isoquinoline	C, C, C, E
(4R, 7S), (4R,7R), (4S, 7S), and (4S, 7R) diastereomers of 3-[7-methyl-5-[5-(pyridin-2-yl)-1,3,4-oxadiazol-2-yl]-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]isoquinoline	C, C, D, E
(4R, 7S), (4R,7R), (4S, 7S), and (4S, 7R) diastereomers of 3-[7-methyl-5-[5-(4-methylpiperazin-1-yl)-1,3,4-oxadiazole-2-carbonyl]-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]isoquinoline	C, C, E, E
(4R, 7S), (4R,7R), (4S, 7S), and (4S, 7R) diastereomers of 3-[5-[5-(4-fluoropiperidin-1-yl)-1,3,4-oxadiazole-2-carbonyl]-7-methyl-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]isoquinoline	C, C, D, E
(4R, 7S), (4R,7R), (4S, 7S), and (4S, 7R) diastereomers of 3-[7-methyl-5-[5-methyl-1,3,4-oxadiazole-2-carbonyl]-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]isoquinoline	C, C, E, E
(4R, 7S), (4R,7R), (4S, 7S), and (4S, 7R) diastereomers of ({3-[4-(isoquinolin-3-yl)-7-methyl-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridine-5-carbonyl]pyrazolo[1,5-al]pyridin-6-yl}methyl)dimethylamine	C, C, C, D
(4R, 7S), (4R,7R), (4S, 7S), and (4S, 7R) diastereomers of 2-[5-[4-(isoquinolin-3-yl)-7-methyl-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridine-5-carbonyl]-1,3,4-oxadiazol-2-yl]propan-2-ol	C, C, E, E
(4R, 7S), (4R,7R), (4S, 7S), and (4S, 7R) diastereomers of 3-[7-methyl-5-[5-(morpholin-4-yl)-1,3,4-oxadiazole-2-carbonyl]-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]isoquinoline	C, C, D, E
(4R, 7S), (4R,7R), (4S, 7S), and (4S, 7R) diastereomers of 5-[4-(isoquinolin-3-yl)-7-methyl-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridine-5-carbonyl]-N,N-dimethyl-1,3,4-oxadiazol-2-amine	C, C, D, E
(4R, 7S), (4R,7R), (4S, 7S), and (4S, 7R) diastereomers of 3-[7-methyl-5-[5-(1-methyl-1H-pyrazol-4-yl)-1,3,4-oxadiazole-2-carbonyl]-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]isoquinoline	C, C, D, E
(4R, 7S), (4R,7R), (4S, 7S), and (4S, 7R) diastereomers of 3-[7-methyl-5-(4-methyl-1,3-oxazole-5-carbonyl)-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]isoquinoline	D, D, E, E
(4R, 7S), (4R,7R), (4S, 7S), and (4S, 7R) diastereomers of N-cyclopropyl-5-[4-(isoquinolin-3-yl)-7-methyl-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridine-5-carbonyl]-1,3,4-oxadiazol-2-amine	C, C, D, E
(4R, 7S), (4R,7R), (4S, 7S), and (4S, 7R) diastereomers of (2-(2-hydroxypropan-2-yl)-4-(trifluoromethyl)oxazol-5-yl)(4-(isoquinolin-3-yl)-7-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5-(4H-yl)methanone	E, E, E, E
(4R, 7S), (4R,7R), (4S, 7S), and (4S, 7R) diastereomers of 5-[4-(isoquinolin-3-yl)-7-methyl-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridine-5-carbonyl]-N-(2-methoxyethyl)-1,3,4-oxadiazol-2-amine	C, D, E, E
(4R, 7S), (4R,7R), (4S, 7S), and (4S, 7R) diastereomers of 3-[7-methyl-5-[4-(trifluoromethyl)-1,3-oxazole-5-carbonyl]-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]isoquinoline	C, E, E, E

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Compound(s)	AC ₅₀
(4R, 7S), (4R,7R), (4S, 7S), and (4S, 7R) diastereomers of 3-[5-[3-fluoroazetidin-1-yl]-1,3,4-oxadiazole-2-carbonyl]-7-methyl-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]isoquinoline	C, D, D, E
(4R, 7S), (4R,7R), (4S, 7S), and (4S, 7R) diastereomers of (4-(isoquinolin-3-yl)-7-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(2-(pyridin-2-yl)-4-(trifluoromethyl)oxazol-5-yl)methanone	B, E, E, E
3-[(4R)-5-[4-methyl-2-(methyl-1H-pyrazol-4-yl)-1,3-oxazole-5-carbonyl]-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]isoquinoline	E
3-[(4R)-5-[2-(pyridin-2-yl)-4-(trifluoromethyl)-1,3-oxazole-5-carbonyl]-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]isoquinoline	E
3-[(4R)-5-[4-methyl-2-(pyridin-2-yl)-1,3-oxazole-5-carbonyl]-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]isoquinoline	E
3-[(4R)-5-(2-cyclopropyl-4-methyl-1,3-oxazole-5-carbonyl)-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]isoquinoline	E
3-[(4R)-5-[4-(trifluoromethyl)-1,3-oxazole-5-carbonyl]-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]isoquinoline	E
1-[(4R)-4-(isoquinolin-3-yl)-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-5-yl]-2-(1,3-thiazol-4-yl)ethan-1-one	E
2-{5-[(4R)-4-(isoquinolin-3-yl)-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridine-5-carbonyl]-4-(trifluoromethyl)-1,3-oxazol-2-yl} propan-2-ol	E
3-[(4R)-5-cyclopropanecarbonyl-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]isoquinoline	E
2-cyclopropyl-1-[(4R)-4-(isoquinolin-3-yl)-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-5-yl]ethan-1-one	E
3-[(4R)-5-[4-(difluoromethyl)-1,3-oxazole-5-carbonyl]-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]isoquinoline	E
3-[(4R)-5-[2-cyclopropyl-4-(difluoromethyl)-1,3-oxazole-5-carbonyl]-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]isoquinoline	E
3-[(4R)-5-[(1R)-2,2-difluorocyclopropanecarbonyl]-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]isoquinoline	E
2-(3-fluorocyclobutyl)-1-[(4R)-4-(isoquinolin-3-yl)-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-5-yl]ethan-1-one	E
2-(1-hydroxycyclobutyl)-1-[(4R)-4-(isoquinolin-3-yl)-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-5-yl]ethan-1-one	E
2,2-difluoro-2-(1-hydroxycyclobutyl)-1-[(4R)-4-(isoquinolin-3-yl)-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-5-yl]ethan-1-one	E
3-[(4R)-5-[(1-pyridin-2-yl)azetidine-3-carbonyl]-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]isoquinoline	C
2-{5-[(4R)-4-(isoquinolin-3-yl)-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridine-5-carbonyl]-1,2-oxazol-3-yl} propan-2-ol	C
2-{3-[(4R)-4-(isoquinolin-3-yl)-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridine-5-carbonyl]-1,2-oxazol-5-yl} propan-2-ol	C
2-[(4R)-5-[(4R)-4-(isoquinolin-3-yl)-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridine-5-carbonyl]-1,3-oxazol-2-yl]propan-2-ol	E
3-[(4R)-5-[(1-difluoromethyl)-1H-pyrazole-5-carbonyl]-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]isoquinoline	E
3-[(4R)-5-[(1S)-2,2-difluorocyclopropanecarbonyl]-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]isoquinoline	E
3-[(4R)-5-[(1S)-2,2-difluorocyclopropanecarbonyl]-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]isoquinoline	E
3-[(4R)-5-[(1-pyridin-2-yl)azetidine-3-carbonyl]-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]isoquinoline	C
2-{5-[(4R)-4-(isoquinolin-3-yl)-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridine-5-carbonyl]-1,2-oxazol-3-yl} propan-2-ol	C
2-{3-[(4R)-4-(isoquinolin-3-yl)-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridine-5-carbonyl]-1,2-oxazol-5-yl} propan-2-ol	C
2-[(4R)-5-[(4R)-4-(isoquinolin-3-yl)-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridine-5-carbonyl]-1,3-oxazol-2-yl]propan-2-ol	E
3-[(4R)-5-[(1-difluoromethyl)-1H-pyrazole-5-carbonyl]-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]isoquinoline	E
3-[(4R)-5-[(5-(4-methylpiperazin-1-yl)-1,3,4-oxadiazole-2-carbonyl)-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]isoquinoline	C
3-[(4R)-5-[(4-(2,2-difluoroethyl)-1,3-oxazole-5-carbonyl)-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]isoquinoline	E
3-[(4R)-5-[(1-cyclopropanesulfonyl)-1H-pyrazol-4-yl]-1,3,4-oxadiazole-2-carbonyl]-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]isoquinoline	D
3-[(4R)-5-[(6-fluoropyrazolo[1,5-a]pyridine-3-carbonyl)-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]isoquinoline	E
(1S)-1-[(5-[(4R)-4-(isoquinolin-3-yl)-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridine-5-carbonyl]-1,3,4-oxadiazol-2-yl)ethan-1-ol	C
1-[(4R)-4-(isoquinolin-3-yl)-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-5-yl]-3-(1,3-thiazol-2-yl)propan-1-one	E
methyl 3-[(4R)-4-(isoquinolin-3-yl)-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridine-5-carbonyl]azetidine-1-carboxylate	C
3-[(4R)-5-[2-(trifluoromethyl)pyrazolo[1,5-a]pyridine-3-carbonyl]-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]isoquinoline	E
3-[(4R)-5-(4-ethyl-4H-1,2,4-triazole-3-carbonyl)-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]isoquinoline	E
3-[(4S,7R)-5-[3-(3-fluoropyridin-2-yl)-1,3,4-oxadiazole-2-carbonyl]-7-methyl-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]isoquinoline	E
3-[(4S,7R)-7-methyl-5-[5-(pyrazin-2-yl)-1,3,4-oxadiazole-2-carbonyl]-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]isoquinoline	E
3-[(4S,7R)-5-[5-(1,5-dimethyl-1H-pyrazol-4-yl)-1,3,4-oxadiazole-2-carbonyl]-7-methyl-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]isoquinoline	C

-continued

Compound(s)	AC ₅₀
3-[(4S,7R)-7-methyl-5-[5-(1-methylcyclopropyl)-1,3,4-oxadiazole-2-carbonyl]-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]isoquinoline	C
4R and 4S enantiomers of 3-[5-(1,3-thiazole-5-carbonyl)-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]isoquinoline	D, E
4R and 4S enantiomers of 3-[5-(4-methyl-1,3-oxazole-5-carbonyl)-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]isoquinoline	C, E
4R and 4S enantiomers of 3-[5-(2-tert-butyl-4-methyl-1,3-oxazole-5-carbonyl)-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]isoquinoline	C, E
4R and 4S enantiomers of 2-{5-[4-(isoquinolin-3-yl)-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridine-5-carbonyl]-1,3-oxazol-2-yl}propan-2-ol	C, C
4R and 4S enantiomers of 2-{5-[4-(isoquinolin-3-yl)-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridine-5-carbonyl]-4-methyl-1,3-oxazol-2-yl} propan-2-ol	C, E
4R and 4S enantiomers of 2-{3-[4-(isoquinolin-3-yl)-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridine-5-carbonyl]pyrazolo[1,5-a]pyridin-6-yl}propan-2-ol	C, D
4R and 4S enantiomers of 3-[5-[2-(2-fluoropropan-2-yl)-4-methyl-1,3-oxazole-5-carbonyl]-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]isoquinoline	C, E
4R and 4S enantiomers of 3-[5-[5-(difluoromethyl)-1,3,4-oxadiazol-2-yl]-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]isoquinoline	D, E
4R and 4S enantiomers of 3-[5-[5-(trifluoromethyl)pyrimidin-2-yl]-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]isoquinoline	C, E
4R and 4S enantiomers of 3-[5-[5-(pyridin-2-yl)-1,3,4-oxadiazole-2-carbonyl]-1H,4H,5H,6H,7H,8H-imidazo[4,5-c]azepin-4-yl]isoquinoline	C, E
4R and 4S enantiomers of 3-[5-(4-cyclopropyl-1,3-oxazole-5-carbonyl)-1H,4H,5H,6H,7H,8H-imidazo[4,5-c]azepin-4-yl]isoquinoline	D, E
4R and 4S enantiomers of 2-{4-cyclopropyl-5-[4-(isoquinolin-3-yl)-1H,4H,5H,6H,7H,8H-imidazo[4,5-c]azepine-5-carbonyl]-1,3-oxazol-2-yl} propan-2-ol	C, C
4R and 4S enantiomers of 3-[5-(4-cyclopropyl-2-(1-methyl-1H-pyrazol-4-yl)-1,3-oxazole-5-carbonyl]-1H,4H,5H,6H,7H,8H-imidazo[4,5-c]azepin-4-yl]isoquinoline	C, E
4R and 4S enantiomers of [(3-{{1'-(isoquinolin-3-yl)}-1',4',5',6'-tetrahydrospiro[cyclopropane-1,7'-imidazo[4,5-c]pyridin]-5'-yl}carbonyl}pyrazolo[1,5-a]pyridin-6-yl)methyl]dimethylamine	C, E
4R and 4S enantiomers of ((3-[4-(isoquinolin-3-yl)-7,7-dimethyl-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridine-5-carbonyl]pyrazolo[1,5-a]pyridin-6-yl)methyl)dimethylamine	D, E
4R and 4S enantiomers of 3-[7,7-dimethyl-5-(5-methyl-1,3,4-oxadiazole-2-carbonyl)-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]isoquinoline	C, E
4R and 4S enantiomers of 2-[5-(1,3-oxazole-5-carbonyl)-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]quinoline	C, D
4R and 4S enantiomers of 2-[5-(4-methyl-1,3-oxazole-5-carbonyl)-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]quinoline	C, E
4R and 4S enantiomers of 2-[5-(4-quinolin-2-yl)-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridine-5-carbonyl]-1,3-thiazo[2-yl] propan-2-ol	C, D
4R and 4S enantiomers of 2-[5-(5-methyl-1,3,4-oxadiazole-2-carbonyl)-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]quinoline	C, D
4R and 4S enantiomers of 2-[5-{4-(quinolin-2-yl)-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridine-5-carbonyl]-1,3-oxazol-2-yl} propan-2-ol	C, E
4R and 4S enantiomers of 2-[5-(4-quinolin-2-yl)-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridine-5-carbonyl]-1,3-thiazo[2-yl] propan-2-ol	C, D
4R and 4S enantiomers of 2-[5-(5-methyl-1,3,4-oxadiazole-2-carbonyl)-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]quinoline	C, D
4R and 4S enantiomers of 2-[5-{4-(quinolin-2-yl)-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridine-5-carbonyl]-1,3-oxazol-2-yl} propan-2-ol	C, E
4R and 4S enantiomers of 2-[3-{4-(quinolin-2-yl)-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridine-5-carbonyl]pyrazolo[1,5-a]pyridin-6-yl} propan-2-ol	C, D
4R and 4S enantiomers of 2-[5-[5-(difluoromethyl)-1,3,4-oxadiazol-2-yl]-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]quinoline	C, D
4R and 4S enantiomers of dimethyl({3-[4-(quinolin-2-yl)-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridine-5-carbonyl]pyrazolo[1,5-a]pyridin-6-yl}methyl)amine	C, D
4R and 4S enantiomers of 2-[5-[6-(2-fluoropropan-2-yl)pyrazolo[1,5-a]pyridine-3-carbonyl]-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]isoquinoline	C, D
4R and 4S enantiomers of 2-[5-{4-(pyridin-2-yl)-1,3-oxazole-5-carbonyl}-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]quinoline	C, E
4R and 4S enantiomers of 1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]quinoline	C, E
4R and 4S enantiomers of 2-[5-{imidazo[1,5-a]pyridine-1-carbonyl}-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]quinoline	C, D
4R and 4S enantiomers of 2-[5-(1H-indazole-3-carbonyl)-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]quinoline	C, D
4R and 4S enantiomers of 2-[5-(1-methyl-1H-indazole-3-carbonyl)-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]quinoline	C, C
4R and 4S enantiomers of pyrrole[1,2-b]pyridazin-5-yl(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone	C, E
4R and 4S enantiomers of 2-[5-(1,2-benzothiazole-3-carbonyl)-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]quinoline	D, E
4R and 4S enantiomers of (2-(2-hydroxypropan-2-yl)-4-(trifluoromethyl)oxazol-5-yl)(4-(quinolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone	E, E
4R and 4S enantiomers of 2-{4-cyclopropyl-5-[4-(quinolin-2-yl)-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridine-5-carbonyl]-1,3-oxazol-2-yl} propan-2-ol	C, C

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Compound(s)	AC ₅₀
4R and 4S enantiomers of 2-{pyrazolo[1,5-a]pyridin-3-y}-1-[4-(quinolin-2-yl)-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-5-yl]ethan-1-one	C, C
4R and 4S enantiomers of 2-[5-cyclopropanecarbonyl-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]quinoline	C, C
4R and 4S enantiomers of 2-[5-[5-(4-methylpiperazin-1-yl)-1,3,4-oxadiazole-2-carbonyl]-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]quinoline	C, D
4R and 4S enantiomers of 2-[5-[5-(morpholin-4-yl)-1,3,4-oxadiazole-2-carbonyl]-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]quinoline	C, D
4R and 4S enantiomers of 2-[5-[4-cyclopropyl-2-(pyridin-2-yl)-1,3-oxazole-5-carbonyl]-1H,4H,5H,6H,7H,8H-imidazo[4,5-c]azepin-4-yl]quinoline	C, D
4R and 4S enantiomers of 2-[5-[5-(pyridin-2-yl)-1,3,4-oxadiazole-2-carbonyl]-1H,4H,5H,6H,7H,8H-imidazo[4,5-c]azepin-4-yl]quinoline	D, D
4R and 4S enantiomers of 2-[5-[2-cyclopropyl-4-(difluoromethyl)-1,3-oxazole-5-carbonyl]-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]quinoline	C, E
4R and 4S enantiomers of 2-[5-[(1R)-2,2-difluorocyclopropanecarbonyl]-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]quinoline	C, C
4R and 4S enantiomers of 2-[5-[5-(4-fluoropiperidin-1-yl)-1,3,4-oxadiazole-2-carbonyl]-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]quinoline	C, D
4R and 4S enantiomers of dimethyl(2-[4-methyl-5-[4-(quinolin-2-yl)-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridine-5-carbonyl]-1,3-oxazol-2-yl}ethyl)amine	C, E
4R and 4S enantiomers of N,N,4-trimethyl-5-[4-(quinolin-2-yl)-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridine-5-carbonyl]-1,3-oxazol-2-amine	C, D
4R and 4S enantiomers of N,N-dimethyl-5-[4-(quinolin-2-yl)-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridine-5-carbonyl]-1,3,4-oxadiazol-2-amine	C, D
4R and 4S enantiomers of 2-[5-{2-[2-(3-fluorooazetidin-1-yl)ethyl]-4-methyl-1,3-oxazole-5-carbonyl}-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]quinoline	C, D
4R and 4S enantiomers of N-cyclopropyl-4-methyl-5-[4-(quinolin-2-yl)-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridine-5-carbonyl]-1,3-oxazol-2-amine	C, D
4R and 4S enantiomers of 2-[5-[4-methyl-2-(4-methylpiperazin-1-yl)-1,3-oxazole-5-carbonyl]-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]quinoline	C, E
4R and 4S enantiomers of 2-[5-[4-methyl-2-(morpholin-4-yl)-1,3-oxazole-5-carbonyl]-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]quinoline	C, D
4R and 4S enantiomers of 2-[5-[2-(4-fluoropiperidin-1-yl)-4-methyl-1,3-oxazole-5-carbonyl]-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]quinoline	C, D
4R and 4'S enantiomers of 5'-[4-methyl-1,3-oxazole-5-carbonyl)-4'-(quinolin-2-yl)-1',4',5',6'-tetrahydrospiro[cyclopropane-1,7'-imidazo[4,5-c]pyridine]	C, D
4R and 4S enantiomers of 2-[5-[5-(3-fluorooazetidin-1-yl)-1,3,4-oxadiazole-2-carbonyl]-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]quinoline	C, D
4R and 4S enantiomers of N-cyclopropyl-5-[4-(quinolin-2-yl)-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridine-5-carbonyl]-1,3,4-oxadiazol-2-amine	C, D
4R and 4S enantiomers of 4-methyl-5-[4-(quinolin-2-yl)-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridine-5-carbonyl]-1,3-oxazol-2-amine	C, D
4R and 4S enantiomers of 2-[5-[2-(methoxymethyl)-1,3-thiazole-5-carbonyl]-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]quinoline	C, D
4R and 4S enantiomers of 2-[5-[2-(methoxymethyl)-1,3-oxazole-5-carbonyl]-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]quinoline	C, E
4R and 4S enantiomers of N-(2-methoxyethyl)-5-[4-(quinolin-2-yl)-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridine-5-carbonyl]-1,3,4-oxadiazol-2-amine	C, D
4R and 4S enantiomers of dimethyl({5-[4-(quinolin-2-yl)-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridine-5-carbonyl]-1,3,4-oxadiazol-2-yl} methyl)amine	C, D
4R and 4S enantiomers of 2-[5-{5-[2-(morpholin-4-yl)ethyl]-1,3,4-oxadiazole-2-carbonyl}-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]quinoline	C, D
4R and 4S enantiomers of 2-[5-{2-(1-methyl-1H-pyrazol-4-yl)-1,3-oxazole-5-carbonyl}-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]quinoline	C, C
4R and 4S enantiomers of 2-[5-[6-(methoxymethyl)pyrazolo[1,5-a]pyridine-3-carbonyl]-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]quinoline	D, D
4R and 4S enantiomers of N-(2-{5-[4-(quinolin-2-yl)-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridine-5-carbonyl]-1,3,4-oxadiazol-2-yl}ethyl)cyclopropanamine	C, D
4R and 4S enantiomers of 2-[5-[1-(pyridin-2-yl)-1H-pyrazole-4-carbonyl]-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]quinoline	C, C
4R and 4S enantiomers of 2-[5-[5-(methoxymethyl)-1,3,4-oxadiazole-2-carbonyl]-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]quinoline	C, C
4R and 4S enantiomers of 2-[5-[5-(3,3-difluorocyclobutyl)-1,3,4-oxadiazole-2-carbonyl]-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]quinoline	C, D
4R and 4S enantiomers of 2-[5-[5-(4-(trifluoromethyl)phenyl)-1,3,4-oxadiazole-2-carbonyl]-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]quinoline	C, D
4R and 4S enantiomers of 2-[5-[5-(4-fluoro-2-methylphenyl)-1,3,4-oxadiazole-2-carbonyl]-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]quinoline	C, E
4R and 4S enantiomers of 2-[5-[5-(difluoromethyl)-1-methyl-1H-pyrazole-4-carbonyl]-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]quinoline	C, E
4R and 4S enantiomers of 2-[5-[6-(2-methoxyethyl)pyrazolo[1,5-a]pyridine-3-carbonyl]-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]quinoline	C, D
4R and 4S enantiomers of 2-[5-[1-(pyridin-2-yl)azetidine-3-carbonyl]-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]quinoline	C, D

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Compound(s)	AC ₅₀
4R and 4S enantiomers of 2-[5-{5-[(trifluoromethoxy)methyl]-1,3,4-oxadiazole-2-carbonyl}-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]quinoline	C, D
4R and 4S enantiomers of 2-[5-{5-[(trifluoromethyl)pyridin-2-yl]-1,3,4-oxadiazole-2-carbonyl}-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]quinoline	C, D
4R and 4S enantiomers of 2-[5-{5-(1H-pyrazol-4-yl)-1,3,4-oxadiazole-2-carbonyl}-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]quinoline	C, D
4R and 4S enantiomers of methyl 3-[4-(quinolin-2-yl)-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridine-5-carbonyl]azetidine-1-carboxylate	D, D
4R and 4S enantiomers of 2-[5-[1-(2,2,2-trifluoroethyl)azetidine-3-carbonyl]-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]quinoline	C, D
4R and 4S enantiomers of 2-[5-{5-[1-(2,2-difluoroethyl)-1H-pyrazol-3-yl]-1,3,4-oxadiazole-2-carbonyl}-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]quinoline	C, D
4R and 4S enantiomers of 2-[5-[5-chloro-1-(pyridin-2-yl)-1H-pyrazole-4-carbonyl]-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]quinoline	C, D
4R and 4S enantiomers of 2-[5-[2-(2-methoxypropan-2-yl)-4-methyl-1,3-oxazole-5-carbonyl]-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]quinoline	C, E
4R and 4S enantiomers of 2-[5-{1-methyl-3-[(trifluoromethoxy)methyl]-1H-pyrazole-5-carbonyl}-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]quinoline	C, D
4R and 4S enantiomers of 2-[5-{4-(quinolin-2-yl)-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridine-5-carbonyl]-1H-pyrazol-3-yl} propan-2-ol	D, E
4R and 4S enantiomers of 2-[1-methyl-5-{4-(quinolin-2-yl)-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridine-5-carbonyl}-1H-pyrazol-3-yl] propan-2-ol	D, E
4R and 4S enantiomers of 1-[4-methyl-5-{4-(quinolin-2-yl)-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridine-5-carbonyl}-1,3-oxazol-2-yl]cyclopropan-1-ol	C, D
4R and 4S enantiomers of 2-[5-[2-(2-methanesulfonylpropan-2-yl)-4-methyl-1,3-oxazole-5-carbonyl]-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]quinoline	C, E
4R and 4S enantiomers of 2-[5-(1H-pyrazole-4-carbonyl)-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]quinoline	C, E
4R and 4S enantiomers of 2-[5-{2-[(2S)-azetidin-2-yl]-4-methyl-1,3-oxazole-5-carbonyl}-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]quinoline	C, D
4R and 4S enantiomers of 2-[5-(1H-pyrazole-5-carbonyl)-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]quinoline	C, D
4R and 4S enantiomers of 2-[5-(1-methyl-1H-pyrazole-3-carbonyl)-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]quinoline	C, E
4R and 4S enantiomers of 2-[5-[5-chloro-1-(2,2,2-trifluoroethyl)-1H-pyrazole-4-carbonyl]-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]quinoline	C, D
4R and 4S enantiomers of 2-[5-[1-methyl-3-(trifluoromethyl)-1H-1,2,4-triazole-5-carbonyl]-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]quinoline	C, E
4R and 4S enantiomers of 2-[5-{4-(quinolin-2-yl)-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridine-5-carbonyl]-1,2-oxazol-3-yl} propan-2-ol	C, D
4R and 4S enantiomers of 2-[3-{4-(quinolin-2-yl)-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridine-5-carbonyl}-1,2-oxazol-5-yl} propan-2-ol	C, D
2-[5-{4-(quinolin-2-yl)-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridine-5-carbonyl]-1,3,4-oxadiazol-2-yl}ethan-1-ol	D
4S and 4R enantiomers of (2-(1-methyl-1H-pyrazol-4-yl)oxazol-5-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone	C, D
4S and 4R enantiomers of (2-(2-hydroxypropan-2-yl)oxazol-5-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone	D, E
4S and 4R enantiomers of (4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(4-(trifluoromethyl)oxazol-5-yl)methanone	E, E
4S and 4R enantiomers of (4-(difluoromethyl)oxazol-5-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone	E, E
4S and 4R enantiomers of (5-(2-hydroxypropan-2-yl)-1,3,4-oxadiazol-2-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone	C, D
4S and 4R enantiomers of (4-methyloxazol-5-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone	C, E
4S and 4R enantiomers of (5-(4-methylpiperazin-1-yl)-1,3,4-oxadiazol-2-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone	C, E
4S and 4R enantiomers of (5-(3-fluoroazetidin-1-yl)-1,3,4-oxadiazol-2-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone	C, E
4S and 4R enantiomers of (5-(dimethylamino)-1,3,4-oxadiazol-2-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone	C, D
4S and 4R enantiomers of (5-(morpholin-1,3,4-oxadiazol-2-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone	C, E
4S and 4R enantiomers of (5-methyl-1,3,4-oxadiazol-2-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone	C, D
4S and 4R enantiomers of (5-(1H-pyrazol-4-yl)-1,3,4-oxadiazol-2-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone	C, C
4S and 4R enantiomers of (4-(difluoromethyl)-2-(pyridin-4-yl)oxazol-5-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone	E, E
4S and 4R enantiomers of (4-(difluoromethyl)-2-(pyridin-3-yl)oxazol-5-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone	E, E
4S and 4R enantiomers of (4-(difluoromethyl)-2-(pyridin-2-yl)oxazol-5-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone	E, E

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Compound(s)	AC ₅₀
4S and 4R enantiomers of (5-(pyrimidin-2-yl)-1,3,4-oxadiazol-2-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone	C, D
4S and 4R enantiomers of (4-(difluoromethyl)-2-(5-methoxypyridin-2-yl)oxazol-5-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone	E, E
4S and 4R enantiomers of (4-(difluoromethyl)-2-(1-methyl-1H-pyrazol-3-yl)oxazol-5-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone	E, E
4S and 4R enantiomers of (4-(difluoromethyl)-2-(4-methylpiperazin-1-yl)oxazol-5-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone	E, E
4S and 4R enantiomers of (2-(pyridin-2-yl)-4-(trifluoromethyl)oxazol-5-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone	E, E
4S and 4R enantiomers of (4-(difluoromethyl)-2-(5-fluoropyridin-2-yl)oxazol-5-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone	E, E
4S and 4R enantiomers of (4-(difluoromethyl)-2-(1-methyl-1H-pyrazol-4-yl)oxazol-5-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone	E, E
4S and 4R enantiomers of (4-(difluoromethyl)-2-morpholinooxazol-5-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone	E, E
4S and 4R enantiomers of (1-(difluoromethyl)-1H-pyrazol-5-yl)(4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone	E, E
4S and 4R enantiomers of 2-[5-[2-(1-methyl-1H-pyrazol-4-yl)-4-(trifluoromethyl)-1,3-oxazole-5-carbonyl]-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]quinazoline	E, E
4S and 4R enantiomers of 2-[5-[4-methyl-2-(1-methyl-1H-pyrazol-4-yl)-1,3-oxazole-5-carbonyl]-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]quinazoline	D, E
4S and 4R enantiomers of 2-[5-[4-(difluoromethyl)-2-(1-methyl-1H-imidazol-4-yl)-1,3-oxazole-5-carbonyl]-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]quinazoline	E, E
4S and 4R enantiomers of 2-[5-[4-(difluoromethyl)-2-(pyrimidin-2-yl)-1,3-oxazole-5-carbonyl]-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]quinazoline	E, E
4S and 4R enantiomers of 2-[5-[4-(difluoromethyl)-2-(pyrazin-2-yl)oxazol-5-yl](4-(quinazolin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone	E, E
4S and 4R enantiomers of 1-[3-[4-(quinazolin-2-yl)-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridine-5-carbonyl]pyrazolo[1,5-a]pyridin-6-yl] piperidin-4-ol	C, E
4S and 4R enantiomers of 2-[5-[5-(1-methyl-1H-imidazol-5-yl)-1,3,4-oxadiazole-2-carbonyl]-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]quinazoline	C, E
4S and 4R enantiomers of 2-[5-[4-(difluoromethyl)-2-(pyrimidin-4-yl)-1,3-oxazole-5-carbonyl]-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-5(4H)-yl]methanone	E, E
4S and 4R enantiomers of 1-[3-[4-(quinazolin-2-yl)-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridine-5-carbonyl]pyrazolo[1,5-a]pyridin-6-yl] piperidin-4-ol	E, E
4S and 4R enantiomers of 2-[5-[4-(difluoromethyl)-2-(pyrimidin-2-yl)-1,3-oxazol-2-yl]propan-2-ol	E, E
4S and 4R enantiomers of 2-[5-[4-(difluoromethyl)-2-(pyrimidin-4-yl)-1,3-oxazole-5-carbonyl]-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]quinazoline	E, E
4S and 4R enantiomers of 2-[5-[1-(3-dimethyl-1H-1,2,4-triazole-5-carbonyl)-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]quinazoline	E, E
4S and 4R enantiomers of 2-[5-[4-(quinazolin-2-yl)-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridine-5-carbonyl]-4-(trifluoromethyl)-1,3-oxazol-2-yl] propan-2-ol	E, E
4S and 4R enantiomers of 2-[4-(difluoromethyl)-5-[4-(quinazolin-2-yl)-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridine-5-carbonyl]-1,3-oxazol-2-yl]propan-2-ol	E, E
4S and 4R enantiomers of 2-[5-[4-(difluoromethyl)-2-(pyrimidin-4-yl)-1,3-oxazole-5-carbonyl]-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]quinazoline	E, E
4S and 4R enantiomers of 2-[5-[1-(3-dimethyl-1H-1,2,4-triazole-5-carbonyl)-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]quinazoline	E, E
4S and 4R enantiomers of 3-[5-[4-(quinazolin-2-yl)-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]cinnoline	C, E
4S and 4R enantiomers of 3-[5-[5-methyl-1,3,4-oxadiazole-2-carbonyl]-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]cinnoline	D, E
4S and 4R enantiomers of ({3-[4-(cinnolin-3-yl)-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridine-5-carbonyl]pyrazolo[1,5-a]pyridin-6-yl}methyl)dimethylamine	D, E
4S and 4R enantiomers of 3-[5-[2-(pyridin-2-yl)-1,3-oxazole-5-carbonyl]-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]cinnoline	C, D
4S and 4R enantiomers of 3-[5-[4-(difluoromethyl)-2-(pyridin-2-yl)-1,3-oxazole-5-carbonyl]-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]cinnoline	D, E
4S and 4R enantiomers of 3-[5-[4-(difluoromethyl)-1,3-oxazole-5-carbonyl]-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]cinnoline	E, E
4S and 4R enantiomers of 3-[5-[5-methyl-1,3,4-oxadiazole-2-carbonyl]-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]cinnoline	C, E
4S and 4R enantiomers of 3-[5-[5-(pyridin-2-yl)-1,3-oxazole-5-carbonyl]-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]cinnoline	C, D
4S and 4R enantiomers of 3-[5-[4-(difluoromethyl)-2-(pyridin-2-yl)-1,3-oxazole-5-carbonyl]-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]cinnoline	C, E
4S and 4R enantiomers of 3-[5-[5-(5-methyl-1,3,4-oxadiazole-2-carbonyl)-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]cinnoline	C, C
4S and 4R enantiomers of 3-[5-[5-(1-methyl-1H-pyrazol-3-yl)-1,3,4-oxadiazole-2-carbonyl]-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]cinnoline	C, E
4S and 4R enantiomers of 3-[5-[5-(1-methyl-1H-pyrazol-4-yl)-1,3,4-oxadiazole-2-carbonyl]-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]cinnoline	C, C
4S and 4R enantiomers of 3-[5-[5-(1-methyl-1H-pyrazol-4-yl)-1,3,4-oxadiazole-2-carbonyl]-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]cinnoline	C, E
4S and 4R enantiomers of 3-[5-[5-(5-cyclopropyl)-1,3,4-oxadiazole-2-carbonyl]-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]cinnoline	C, C
4S and 4R enantiomers of 2-[5-[4-(cinnolin-3-yl)-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridine-5-carbonyl]-1,3,4-oxadiazol-2-yl] propan-2-ol	C, E

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Compound(s)	AC ₅₀
4S and 4R enantiomers of 3-[5-(5-tert-butyl-1,3,4-oxadiazole-2-carbonyl)-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-4-yl]cinnoline	C, C
4S and 4R enantiomers of (1R)-1-{5-[4-(cinnolin-3-yl)-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridine-5-carbonyl]-1,3,4-oxadiazol-2-yl}ethan-1-ol	D, E
4S and 4R enantiomers of (1S)-1-{5-[4-(cinnolin-3-yl)-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridine-5-carbonyl]-1,3,4-oxadiazol-2-yl}ethan-1-ol	C, E
4S and 4R enantiomers of 1-[4-(cinnolin-3-yl)-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-5-yl]-3-(1,3-thiazol-2-yl)propan-1-one	C, E
4,4-dimethyl-1-[4-(naphthalen-2-yl)-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-5-yl]pentan-1-one	E
3-(4-fluorophenyl)-1-[4-(naphthalen-2-yl)-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-5-yl]propan-1-one	D
2-[4-(naphthalen-2-yl)-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridine-5-carbonyl]-1,3-benzothiazole	D
4R and 4S enantiomers of 1-[4-{imidazo[1,2-a]pyridin-2-yl}-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-5-yl]-3-(1,3-thiazol-2-yl)propan-1-one	C, E
4R and 4S enantiomers of 5-[4-{imidazo[1,2-a]pyridin-2-yl}-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridine-5-carbonyl]-1,3-thiazole	C, D
4R and 4S enantiomers of 5-[4-{imidazo[1,2-a]pyridin-2-yl}-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridine-5-carbonyl]-1,3-oxazole	C, E
4R and 4S enantiomers of 2-[4-{imidazo[1,2-a]pyridin-2-yl}-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridine-5-carbonyl]-5-methyl-1,3,4-oxadiazole	C, E
4R and 4S enantiomers of 2-[5-{4-[imidazo[1,2-a]pyridin-2-yl]-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridine-5-carbonyl]-4-methyl-1,3-oxazol-2-yl} propan-2-ol	C, E
4R and 4S enantiomers of ((3-[4-{imidazo[1,2-a]pyridin-2-yl}-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridine-5-carbonyl]pyrazolo[1,5-a]pyridin-6-yl)methyl)dimethylamine	D, E
4R and 4S enantiomers of 1-[4-{imidazo[1,2-a]pyridin-2-yl}-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-5-yl]-2-(5-methyl-1,3,4-thiadiazol-2-yl)ethan-1-one	D, E
4R and 4S enantiomers of 1-[4-{imidazo[1,2-a]pyridin-2-yl}-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-5-yl]-2-[4-(trifluoromethyl)-1,3-thiazol-2-yl]ethan-1-one	C, D
4R and 4S enantiomers of 1-[4-{imidazo[1,2-a]pyridin-2-yl}-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-5-yl]-2-(2-methyl-1,3-oxazol-5-yl)ethan-1-one	D, E
4R and 4S enantiomers of 1-[4-{imidazo[1,2-a]pyridin-2-yl}-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-5-yl]-2-(1,3-thiazol-4-yl)ethan-1-one	C, E
4R and 4S enantiomers of 1-[4-{imidazo[1,2-a]pyridin-2-yl}-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-5-yl]-2-(1,3,4-thiadiazol-2-yl)ethan-1-one	D, E
4R and 4S enantiomers of 1-[4-{imidazo[1,2-a]pyridin-2-yl}-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-5-yl]-2-(1,3,4-thiadiazol-2-yl)ethan-1-one	D, E
4R and 4S enantiomers of 1-[4-{imidazo[1,2-a]pyridin-2-yl}-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-5-yl]-2-(1,3-thiazol-5-yl)ethan-1-one	D, E
4R and 4S enantiomers of 1-[4-{imidazo[1,2-a]pyridin-2-yl}-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-5-yl]-2-(1,3-oxazol-5-yl)ethan-1-one	D, E
4R and 4S enantiomers of 1-[4-{imidazo[1,2-a]pyridin-2-yl}-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-5-yl]-2-(5-methyl-1,3-oxazol-4-yl)ethan-1-one	E, E
4R and 4S enantiomers of 1-[4-{imidazo[1,2-a]pyridin-2-yl}-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-5-yl]-2-(4-methyl-1,3-oxazol-5-yl)ethan-1-one	D, E
4R and 4S enantiomers of 1-[4-{imidazo[1,2-a]pyridin-2-yl}-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-5-yl]-2-{pyrazolo[1,5-a]pyridin-3-yl} ethan-1-one	D, E
4R and 4S enantiomers of 2-[5-{4-[imidazo[1,2-a]pyridin-2-yl]-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridine-5-carbonyl]-4-(trifluoromethyl)-1,3-oxazol-2-yl} propan-2-ol	C, E
4R and 4S enantiomers of 2-[2-(difluoromethyl)-1,3-oxazol-4-yl]-1-[4-{imidazo[1,2-a]pyridin-2-yl}-3H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-5-yl]ethan-1-one	C, D
4R and 4S enantiomers of 5-cyclopropanecarbonyl-4-{imidazo[1,2-a]pyridin-2-yl}-3H,4H,5H,6H,7H-imidazo[4,5-c]pyridine	C, E
4R and 4S enantiomers of 5-[4-{imidazo[1,2-a]pyridin-2-yl}-3H,4H,5H,6H,7H-imidazo[4,5-c]pyridine-5-carbonyl]-2-methyl-4-(trifluoromethyl)-1,3-oxazole	E, E
4R and 4S enantiomers of 5-[4-{imidazo[1,2-a]pyridin-2-yl}-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridine-5-carbonyl]-4-(trifluoromethyl)-1,3-oxazol-2-amine	E, E
4R and 4S enantiomers of 1-[4-{imidazo[1,2-a]pyridin-2-yl}-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-5-yl]-2-(pyridin-2-yl)ethan-1-one	D, E
4R and 4S enantiomers of 2-[5-{4-[imidazo[1,2-a]pyridin-2-yl]-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridine-5-carbonyl]-1,3,4-oxadiazol-2-yl}pyridine	C, E
4R and 4S enantiomers of 2-[5-{4-[imidazo[1,2-a]pyridin-2-yl]-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridine-5-carbonyl]-4-methyl-1,3-oxazol-2-yl}pyridine	C, D
4R and 4S enantiomers of 1-[4-{imidazo[1,2-a]pyridin-2-yl}-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-5-yl]-3-(5-methyl-1,3,4-oxadiazol-2-yl)propan-1-one	D, E
4R and 4S enantiomers of 1-[4-{imidazo[1,2-a]pyridin-2-yl}-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-5-yl]-3-(5-methyl-1,3,4-thiadiazol-2-yl)propan-1-one	D, E
4R and 4S enantiomers of 1-[4-{imidazo[1,2-a]pyridin-2-yl}-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-5-yl]-3-(1,3-oxazol-2-yl)propan-1-one	C, E

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Compound(s)	AC ₅₀
4R and 4S enantiomers of 1-[4-{imidazo[1,2-a]pyridin-2-yl}-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-5-yl]-3-phenylpropan-1-one	C, D
4R and 4S enantiomers of 4-(difluoromethyl)-5-[4-{imidazo[1,2-a]pyridin-2-yl}-3H,4H,5H,6H,7H-imidazo[4,5-c]pyridine-5-carbonyl]-1,3-oxazole	C, E
4R and 4S enantiomers of 2-[4-cyclopropyl-5-[4-{imidazo[1,2-a]pyridin-2-yl}-3H,4H,5H,6H,7H-imidazo[4,5-c]pyridine-5-carbonyl]-1,3-oxazol-2-yl] pyridine	C, D
4R and 4S enantiomers of 1-[4-{imidazo[1,2-a]pyridin-2-yl}-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-5-yl]-3-(1,3-oxazol-5-yl)propan-1-one	C, E
4R and 4S enantiomers of 1-[4-{imidazo[1,2-a]pyridin-2-yl}-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-5-yl]-3-(1-thiazol-5-yl)propan-1-one	D, E
4R and 4S enantiomers of 1-[4-{imidazo[1,2-a]pyridin-2-yl}-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-5-yl]-2-(H-1,2,4-triazol-1-yl)ethan-1-one	D, E
4R and 4S enantiomers of 3-[5-(difluoromethyl)-1,3,4-oxadiazol-2-yl]-1-[4-{imidazo[1,2-a]pyridin-2-yl}-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-5-yl]propan-1-one	D, E
4R and 4S enantiomers of 3-(1,3-benzoxazol-2-yl)-1-[4-{imidazo[1,2-a]pyridin-2-yl}-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-5-yl]propan-1-one	C, E
4R and 4S enantiomers of 4-[5-[4-{imidazo[1,2-a]pyridin-2-yl}-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridine-5-carbonyl]-1,3,4-oxadiazol-2-yl] morpholine	D, E
4R and 4S enantiomers of 1-[4-{imidazo[1,2-a]pyridin-2-yl}-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-5-yl]-2-(5-methyl-1,3,4-oxadiazol-2-yl)ethan-1-one	E, E
4R and 4S enantiomers of 2-[4-cyclopropyl-5-[4-{imidazo[1,2-a]pyridin-2-yl}-1H,4H,5H,6H,7H,8H-imidazo[4,5-c]azepine-5-carbonyl]-1,3-oxazol-2-yl] pyridine	D, D
4R and 4S enantiomers of 2-[5-[4-{imidazo[1,2-a]pyridin-2-yl}-1H,4H,5H,6H,7H-imidazo[4,5-c]azepine-5-carbonyl]-1,3,4-oxadiazol-2-yl] pyridine	D, E
4R and 4S enantiomers of 2-[4-cyclopropyl-5-[4-{imidazo[1,2-a]pyridin-2-yl}-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridine-5-carbonyl]-1,3-oxazol-2-yl] propan-2-ol	C, E
4R and 4S enantiomers of 2-[4-{imidazo[1,2-a]pyridin-2-yl}-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridine-5-carbonyl]-5-(1-methyl-1H-pyrazol-4-yl)-1,3,4-oxadiazole	C, E
4R and 4S enantiomers of 1-[5-[4-{imidazo[1,2-a]pyridin-2-yl}-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridine-5-carbonyl]-1,3,4-oxadiazol-2-yl]-4-methylpiperazine	D, E
4R and 4S enantiomers of 2-[5-[4-{imidazo[1,2-a]pyridin-2-yl}-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridine-5-carbonyl]-1,3-oxazol-4-yl] pyridine	C, E
4R and 4S enantiomers of 2-cyclopropyl-5-[4-{imidazo[1,2-a]pyridin-2-yl}-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridine-5-carbonyl]-1,3,4-oxadiazole	C, E
4R and 4S enantiomers of 2-(difluoromethyl)-5-[4-{imidazo[1,2-a]pyridin-2-yl}-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridine-5-carbonyl]-1,3-thiazole	C, C
4R and 4S enantiomers of 5-[4-{imidazo[1,2-a]pyridin-2-yl}-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridine-5-carbonyl]-2-(trifluoromethyl)-1,3-thiazole	C, D
4R and 4S enantiomers of 2-[5-[4-{imidazo[1,2-a]pyridin-2-yl}-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridine-5-carbonyl]-1,3-thiazol-2-yl] propan-2-ol	C, E
4R and 4S enantiomers of 2-cyclopropyl-5-[4-{imidazo[1,2-a]pyridin-2-yl}-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridine-5-carbonyl]-1,3-thiazole	C, D
4R and 4S enantiomers of 5-[4-{imidazo[1,2-a]pyridin-2-yl}-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridine-5-carbonyl]-2-(trifluoromethyl)-1,3-oxazole	C, E
4R and 4S enantiomers of 2-(2-fluoropropan-2-yl)-5-[4-{imidazo[1,2-a]pyridin-2-yl}-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridine-5-carbonyl]-1,3-oxazole	C, E
4R and 4S enantiomers of 2-[5-[4-{imidazo[1,2-a]pyridin-2-yl}-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridine-5-carbonyl]-1,3-oxazol-2-yl] propan-2-ol	D, E
4R and 4S enantiomers of 2-cyclopropyl-5-[4-{imidazo[1,2-a]pyridin-2-yl}-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridine-5-carbonyl]-1,3-oxazole	C, E
4R and 4S enantiomers of 5-[1(R)-2,2-difluorocyclopropanecarbonyl]-4-[imidazo[1,2-a]pyridin-2-yl]-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridine	C, E
4R and 4S enantiomers of 5-[1(S)-2,2-difluorocyclopropanecarbonyl]-4-[imidazo[1,2-a]pyridin-2-yl]-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridine	C, D
4R and 4S enantiomers of 1-[5-[4-{imidazo[1,2-a]pyridin-2-yl}-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridine-5-carbonyl]-1,3-thiazol-2-yl]cyclobutan-1-ol	C, E
4R and 4S enantiomers of 2,2-difluoro-2-(1-hydroxycyclobutyl)-1-[4-{imidazo[1,2-a]pyridin-2-yl}-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-5-yl]ethan-1-one	C, E
4R and 4S enantiomers of 2-(1-hydroxycyclobutyl)-1-[4-{imidazo[1,2-a]pyridin-2-yl}-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridin-5-yl]ethan-1-one	E, E
4R and 4S enantiomers of 5-[4-{imidazo[1,2-a]pyridin-2-yl}-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridine-5-carbonyl]-1,3-oxazole-4-carbonitrile	C, D
4R and 4S enantiomers of 4'-{imidazo[1,2-a]pyridin-2-yl}-5-(4-methyl-1,3-oxazole-5-carbonyl)-1',4',5',6'-tetrahydrospiro[cyclopropane-1,7'-imidazo[4,5-c]pyridine]	C, E

-continued

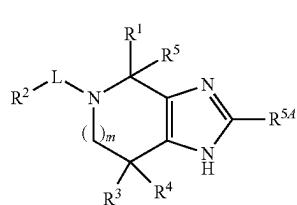
Compound(s)	AC ₅₀
4R and 4S enantiomers of 5-[4-{imidazo[1,2-a]pyridin-2-yl}-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridine-5-carbonyl]-2-(methoxymethyl)-1,3-thiazole	D, E
4R and 4S enantiomers of 5-[4-{imidazo[1,2-a]pyridin-2-yl}-1H,4H,5H,6H,7H-imidazo[4,5-c]pyridine-5-carbonyl]-2-(methoxymethyl)-1,3-oxazole	D, E

[0427] Having now fully described the methods, compounds, and compositions of matter provided herein, it will be understood by those of skill in the art that the same can be performed within a wide and equivalent range of conditions, formulations, and other parameters without affecting the scope of the methods, compounds, and compositions provided herein or any embodiment thereof.

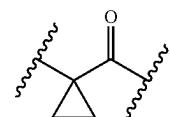
[0428] All patents, patent applications and publications cited herein are fully incorporated by reference herein in their entirety.

1. A compound of Formula I:

R³ is H or C₁₋₆alkyl;
 R⁴ is H or C₁₋₆alkyl;
 or R³ and R⁴, together with the atom to which they are attached, form a C₃₋₆cycloalkyl;
 R⁵ is H or D;
 R^{5A} is H or D; and
 L is a bond, —C(O)—, —C(O)CH₂—, —C(O)
 CH₂CH₂—, —C(O)CH₂CH₂CH₂—, —C(O)CF₂—,
 —C(O)CHF—, —C(O)C(CH₃)₂—, —C(O)
 CH=CH—,



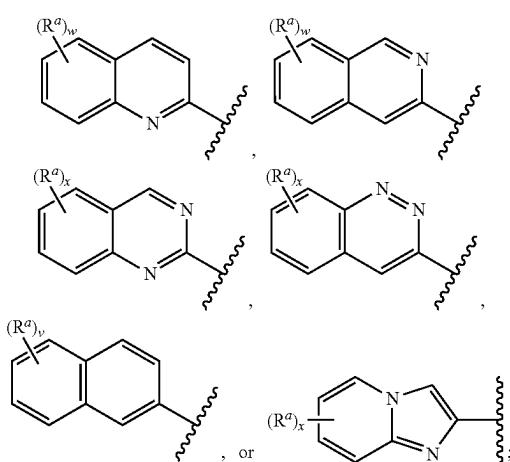
I



or a pharmaceutically acceptable salt thereof, wherein:

m is 1 or 2;

R¹ is



v is 0 to 7;

w is 0 to 6;

x is 0 to 5;

each R^a independently is halo, C₁₋₆alkyl, C₃₋₆cycloalkyl, C₁₋₆haloalkyl, C₁₋₆alkoxy or C₁₋₆haloalkoxy;

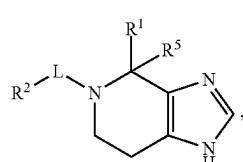
R² is C₁₋₄alkyl, optionally substituted C₃₋₈cycloalkyl, optionally substituted heterocycl, optionally substituted aryl, or optionally substituted heteroaryl;

—C(O)NHCH₂—, —CH₂—, or —CH₂CH₂—.

2. (canceled)

3. (canceled)

4. The compound of claim 1, wherein the compound is of Formula I-A-1:

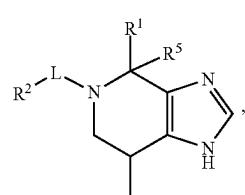


I-A-1

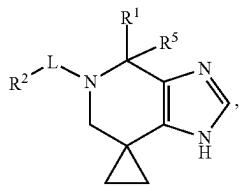
pharmaceutically acceptable salt thereof.

5.-9. (canceled)

10. The compound of claim 1, wherein the compound is of Formula I-L-1



or a pharmaceutically acceptable salt thereof, or Formula I-M-1



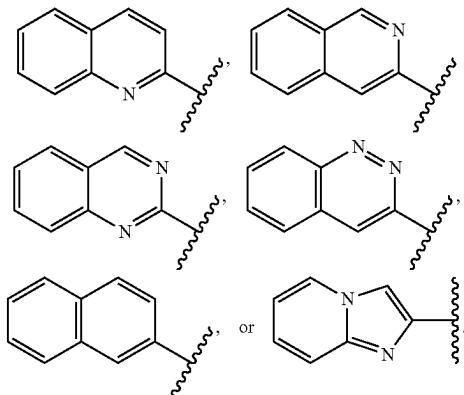
or a pharmaceutically acceptable salt thereof.

11.-14. (canceled)

15. The compound of claim **4**, or a pharmaceutically acceptable salt thereof, wherein L is a bond, —C(O)—, —C(O)CH₂—, —C(O)CH₂CH₂—, or —C(O)CF₃—.

16.-22. (canceled)

23. The compound according to claim **15**, or a pharmaceutically acceptable salt thereof wherein R¹ is



24.-27. (canceled)

28. The compound of claim **1**, or a pharmaceutically acceptable salt thereof, wherein R² is cyclopentyl, cyclobutyl, cyclopropyl, cyclohexyl, azetidinyl, phenyl, pyrazolyl, oxazolyl, thiazolyl, triazolyl, oxadiazolyl, pyridinyl, pyrimidinyl, pyrazolo[1,5-a]pyridinyl, indazolyl, thia-diazolyl, imidazol[1,5-a]pyridinyl, pyrrolo[1,2]pyridazinyl, thiophenyl, isoxazolyl, isothiazolyl, benzo[d]thiazolyl, benzo[d]imidazolyl, benzo[d]oxazolyl, benzo[d]isoxazolyl, benzo[c]isoxazolyl, benzo[d]isothiazolyl, furanyl, pyrazinyl or quinolinyl, each of which is unsubstituted.

29. (canceled)

30. (canceled)

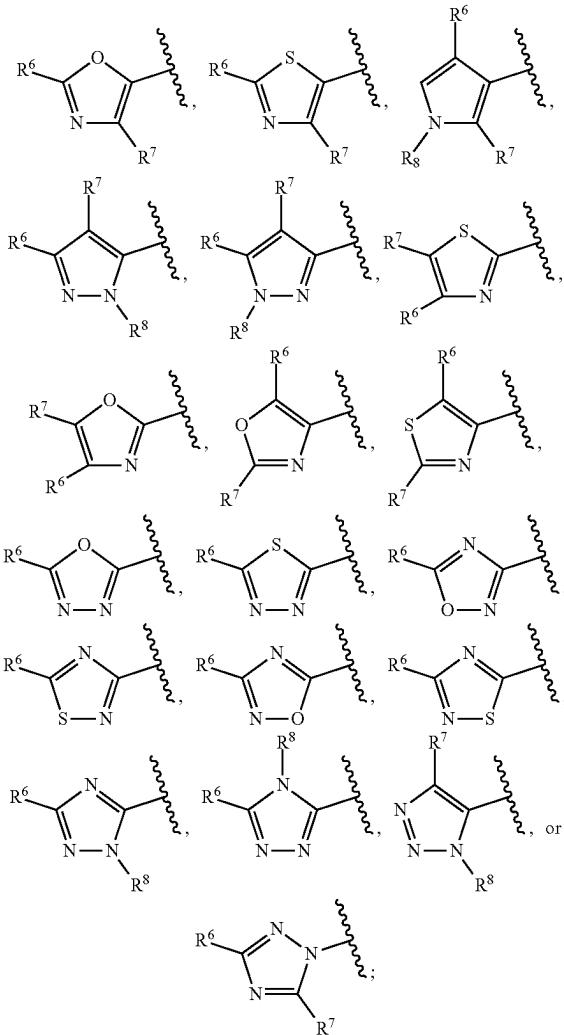
31. The compound of claim **23**, or a pharmaceutically acceptable salt thereof, wherein R² is heterocyclyl, optionally substituted with one or more of halo, C₁₋₆haloalkyl, or optionally substituted heteroaryl; R² is C₃₋₈cycloalkyl, optionally substituted with one or more of halo, C₁₋₆alkyl, C₁₋₆haloalkyl, or OH; or R² is aryl, optionally substituted with one or more of halo or C₁₋₆alkoxy.

32.-35. (canceled)

36. The compound of claim **23**, or a pharmaceutically acceptable salt thereof, wherein R² is optionally substituted pyridinyl, optionally substituted pyrimidinyl, or optionally substituted pyrazinyl, wherein R² is optionally substituted with one or more of halo, C₁₋₆haloalkyl, cyano, or NR^yR^z, wherein R^y and R^z are independently H or C₁₋₆alkyl.

37.-49. (canceled)

50. The compound of claim **23**, or a pharmaceutically acceptable salt thereof, wherein R² is:



wherein:

R⁶ and R⁷ are, independently, H, CN, C₁₋₆alkyl, C₁₋₆haloalkyl, C₁₋₆cyanoalkyl, C₁₋₆hydroxyalkyl, C₁₋₆alkoxy, C₁₋₆alkoxy(alkylene), C₁₋₆haloalkoxy, C₁₋₆haloalkoxy(alkylene), C₁₋₆deuteratedalkoxy(alkylene), halo, (CR^yR^x)_pNR^yR^z, C(O)NR^yR^z, C₁₋₆alkylcarbonyl, optionally substituted C₃₋₈cycloalkyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted C₂₋₆alkenyl, optionally substituted C₃₋₈cycloalkenyl, optionally substituted C₃₋₈cycloalkyl(alkylene), optionally substituted aryl(alkylene), optionally substituted heterocyclyl(alkylene), or C₁₋₆alkylsulfonyl;

R⁸ is H, C₁₋₆alkyl, C₁₋₆haloalkyl, C₁₋₆alkoxy, C₁₋₆alkylcarbonyl, C₁₋₆hydroxyalkyl, (CR^yR^x)_pNR^yR^z, optionally substituted C₃₋₈cycloalkyl, optionally substituted aryl, optionally substituted heteroaryl, or optionally substituted C₃₋₈cycloalkyl(alkylene);

R^y and R^x are, independently, H or C₁₋₆alkyl;

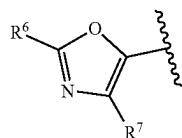
R^y and R^z are, independently, H, C_{1-6} alkyl, C_{1-6} alkoxy(alkylene), or C_{3-6} cycloalkyl;

R^{y2} and R^{z2} are, independently, H, C_{1-6} alkyl, or C_{3-6} cycloalkyl; and

p is 0, 1, 2, or 3.

51.-63. (canceled)

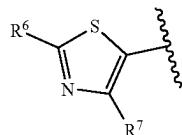
64. The compound of claim **50**, or a pharmaceutically acceptable salt thereof, wherein R^2 is:



wherein:

R^6 is H, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{1-6} cyanoalkyl, C_{1-6} hydroxyalkyl, C_{1-6} alkoxy, C_{1-6} alkoxy(alkylene), optionally substituted C_{3-6} cycloalkyl, optionally substituted heteroaryl, or optionally substituted heterocyclyl; and
 R^7 is H, CN, C_{1-6} alkyl, C_{1-6} haloalkyl, halo, C_{3-6} cycloalkyl, aryl, or heteroaryl.

65. The compound of claim **50**, or a pharmaceutically acceptable salt thereof, wherein R^2 is:

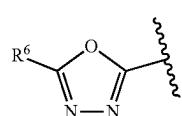


wherein:

R^6 is H, CN, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{1-6} hydroxyalkyl, C_{1-6} alkoxy, C_{1-6} alkoxy(alkylene), optionally substituted C_{3-6} cycloalkyl, or optionally substituted heteroaryl; and

R^7 is H, C_{1-6} alkyl, C_{1-6} haloalkyl, halo, or C_{3-6} cycloalkyl.

66. The compound of claim **50**, or a pharmaceutically acceptable salt thereof, wherein R^2 is:



wherein:

R^6 is H, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{1-6} hydroxyalkyl, $C(O)NR^{y2}R^{z2}$, $(CR^yR^x)_pNR^yR^z$, optionally substituted C_{3-6} cycloalkyl, optionally substituted aryl, optionally substituted heterocyclyl, or optionally substituted heteroaryl;

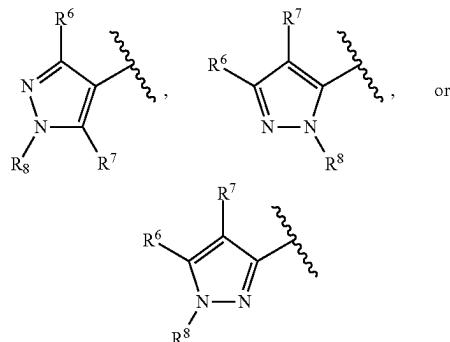
R^y and R^x are, independently, H or C_{1-6} alkyl;

R^y and R^z are, independently, H, C_{1-6} alkyl, C_{1-6} alkoxy(alkylene), or C_{3-6} cycloalkyl;

R^{y2} and R^{z2} are, independently, H, C_{1-6} alkyl, or C_{3-6} cycloalkyl; and

p is 0, 1, 2, or 3.

67. The compound of claim **50**, or a pharmaceutically acceptable salt thereof, wherein R^2 is:

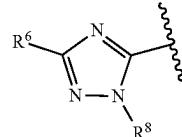


wherein:

R^6 and R^7 are independently H, halo, C_{1-6} alkyl, C_{1-6} haloalkyl, or NR^yR^z ; and

R^8 is H, C_{1-6} alkyl, C_{1-6} haloalkyl, or heteroaryl; and
 R^y and R^z are independently H or C_{1-6} alkyl.

68. The compound of claim **50**, or a pharmaceutically acceptable salt thereof, wherein R^2 is:

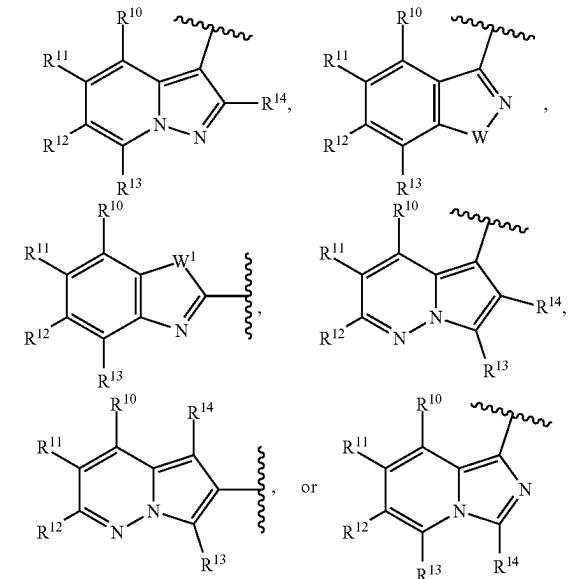


wherein:

R^6 is H, C_{1-6} alkyl, halo, or C_{1-6} haloalkyl; and

R^8 is H, C_{1-6} alkyl, or C_{1-6} haloalkyl.

69. The compound of claim **23**, or a pharmaceutically acceptable salt thereof, wherein R^2 is:



wherein:

W is S or NR¹⁵;

W¹ is S, O, or NR¹⁵;

R¹⁰, R¹¹, R¹², R¹³, and R¹⁴ are independently H, C₁₋₆alkyl, C₁₋₆haloalkyl, C₁₋₆alkoxy, C₁₋₆alkoxy(alkylene), C₁₋₆hydroxyalkyl, C₁₋₆haloalkoxy, C₁₋₆haloalkoxy(alkylene), C₂₋₆alkenyl, CN, halo, (CR'R²)_pNR'R², C(O)NR¹²R², optionally substituted C₃₋₈cycloalkyl, optionally substituted heterocyclyl, optionally substituted heterocyclyl(alkylene), optionally substituted aryl, or optionally substituted heteroaryl;

R^v and R^x are independently H or C₁₋₆alkyl;

R^y and R^z are independently H, C₁₋₆alkyl, C₃₋₆cycloalkyl, C₁₋₆hydroxyalkyl, C₁₋₆haloalkyl, C₁₋₆alkoxy(alkylene), or C(O)OC₁₋₆alkyl;

R^{v2} and R^{z2} are independently H, C₁₋₆alkyl, or C₃₋₆cycloalkyl;

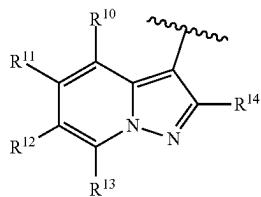
p is 0, 1, 2, or 3; and

R¹⁵ is H or C₁₋₆alkyl.

70. (canceled)

71. (canceled)

72. The compound of claim **69**, or a pharmaceutically acceptable salt thereof, wherein R² is:



wherein:

R¹⁰, R¹¹, R¹², R¹³ and R¹⁴ are independently H, C₁₋₆alkyl, C₁₋₆haloalkyl, C₃₋₆cycloalkyl, C₁₋₆alkoxy, C₁₋₆alkoxy(alkylene), halo, optionally substituted aryl, optionally substituted heterocyclyl, optionally substituted heterocyclyl(alkylene), optionally substituted heteroaryl, or (CR'R²)_pNR'R²;

R^v and R^x are, independently, H or C₁₋₆alkyl;

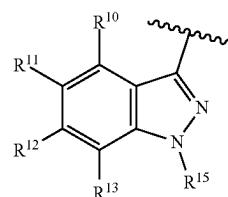
R^y and R^z are, independently, H, C₁₋₆alkyl, C₃₋₆cycloalkyl, or C(O)OC₁₋₆; and

p is 0, 1, 2, or 3.

73. The compound of claim **72**, or a pharmaceutically acceptable salt thereof, wherein the optionally substituted heterocyclyl and optionally substituted heterocyclyl(alkylene) are each substituted with one or more of halo, C₁₋₆haloalkyl, C₁₋₆alkyl, C₁₋₆hydroxyalkyl, C₁₋₆alkoxy, or C₃₋₆cycloalkyl; and the optionally substituted heteroaryl is substituted with one or more of halo, C₁₋₆haloalkyl, C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆haloalkoxy, C₃₋₆cycloalkyl, or C₃₋₆cycloalkylsulfonyl.

74.-77. (canceled)

78. The compound of claim **69**, or a pharmaceutically acceptable salt thereof, wherein R² is:



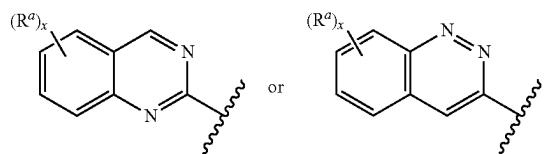
wherein:

R¹⁰, R¹¹, R¹², and R¹³ are, independently, H, C₁₋₆alkyl, or halo; and

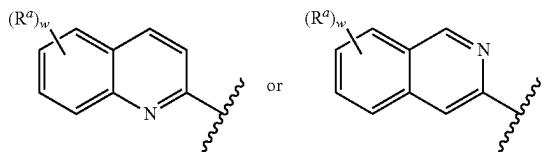
R¹⁵ is H or C₁₋₆alkyl.

79. (canceled)

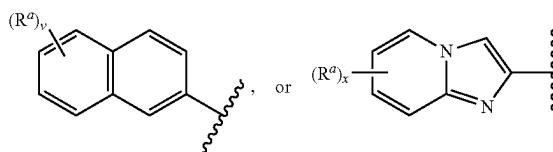
80. The compound of claim **1**, that is an S-enantiomer, or a pharmaceutically acceptable salt thereof, and wherein R¹ is



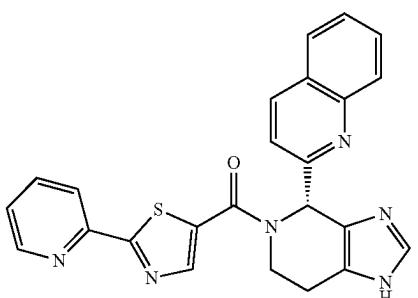
81. The compound of claim **1** that is an R-enantiomer, or a pharmaceutically acceptable salt thereof, and wherein R¹ is



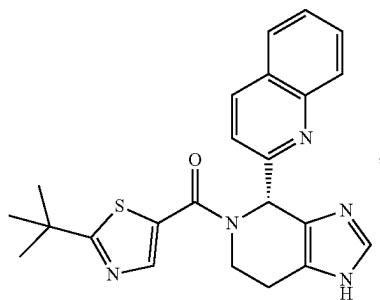
82. The compound of claim **1** that is an R-enantiomer, or a pharmaceutically acceptable salt thereof, and wherein R¹ is



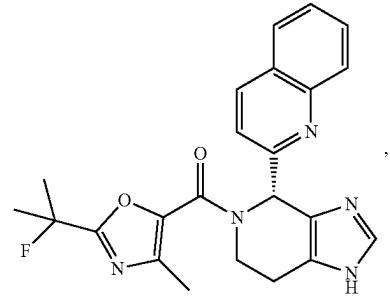
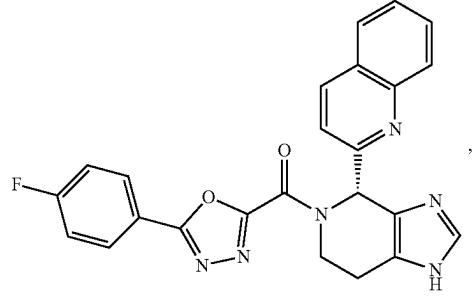
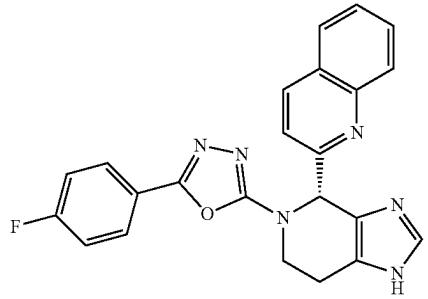
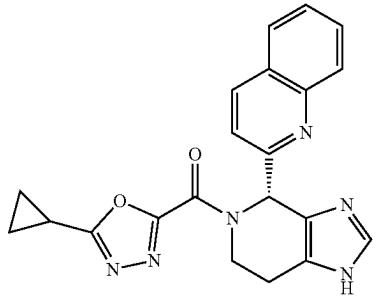
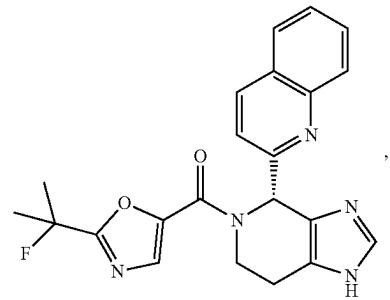
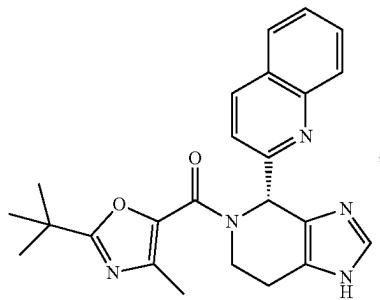
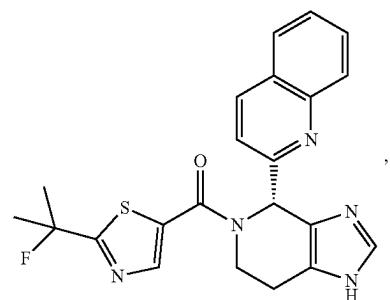
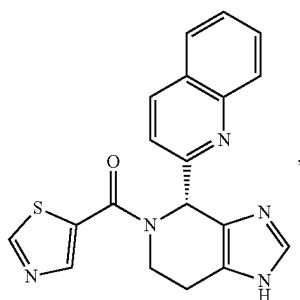
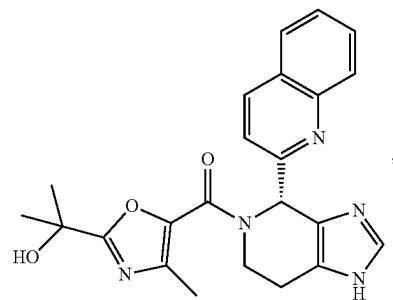
83. The compound of claim **1**, or a pharmaceutically acceptable salt thereof, wherein the compound is selected from the following:



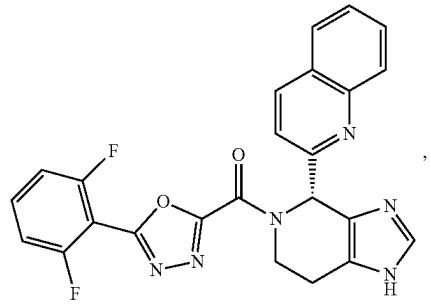
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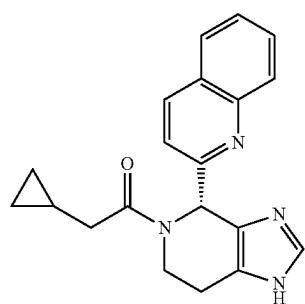
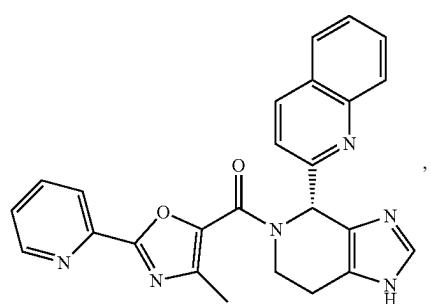
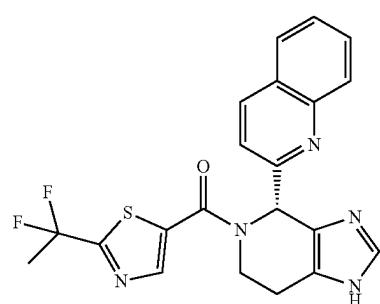
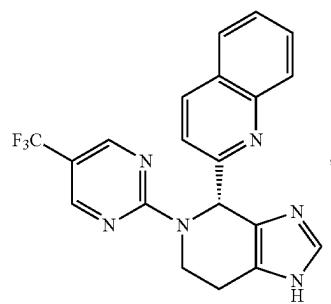
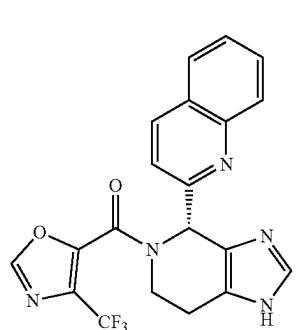
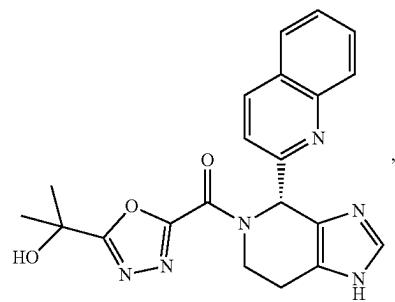
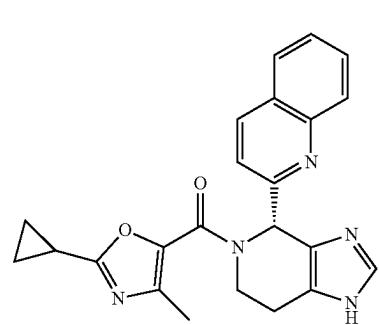
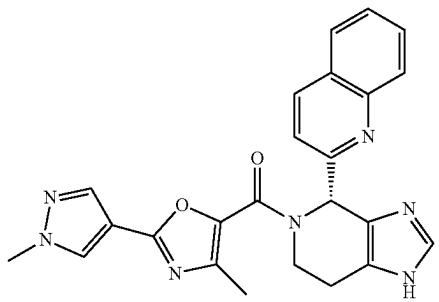
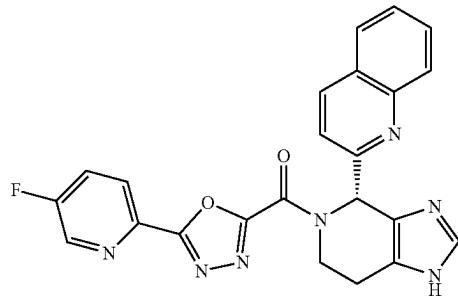
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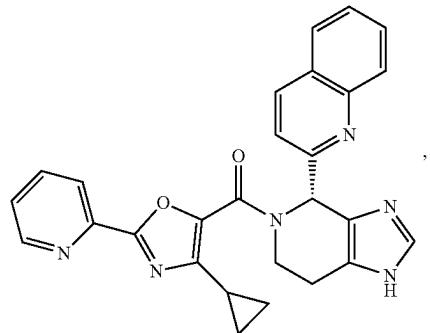
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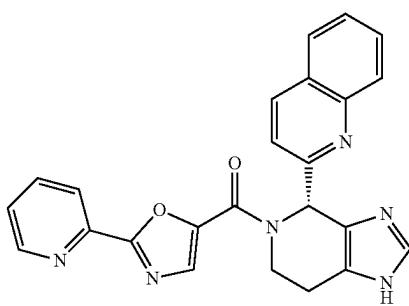
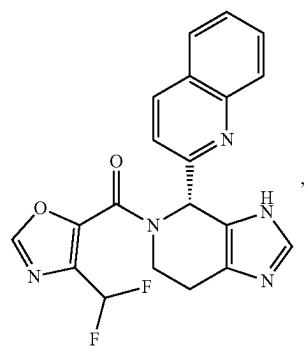
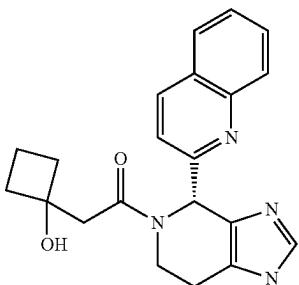
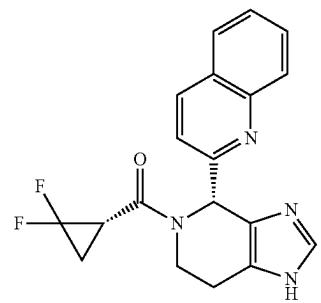
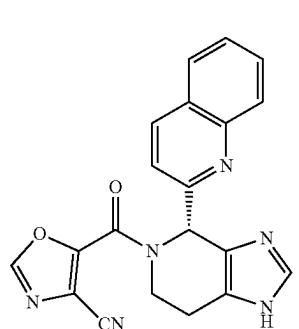
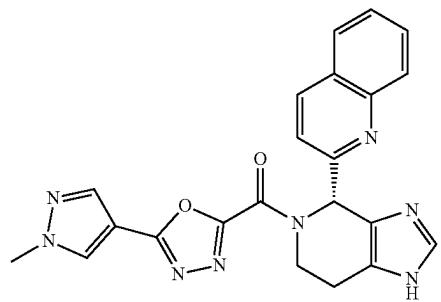
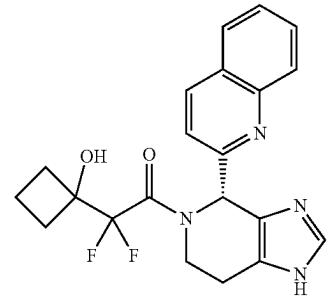
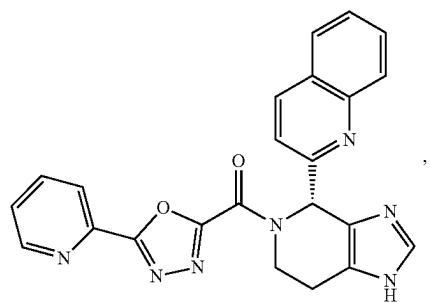
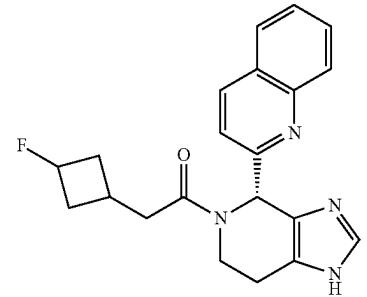
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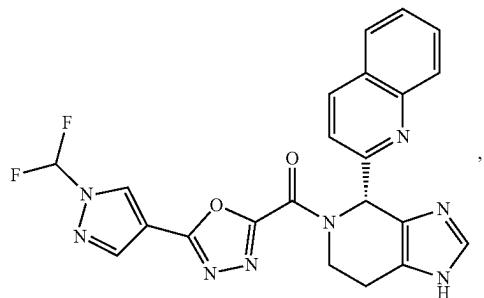
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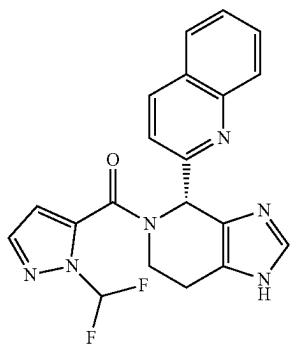
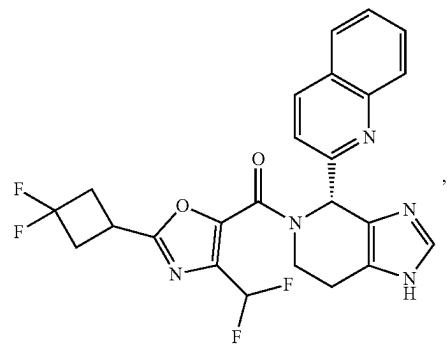
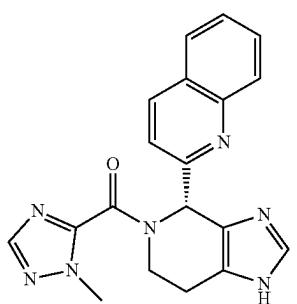
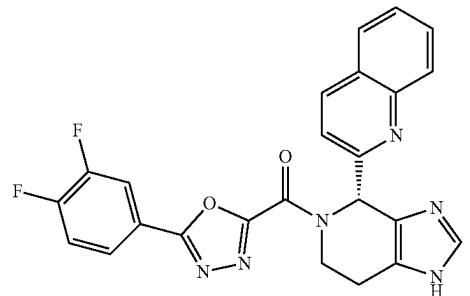
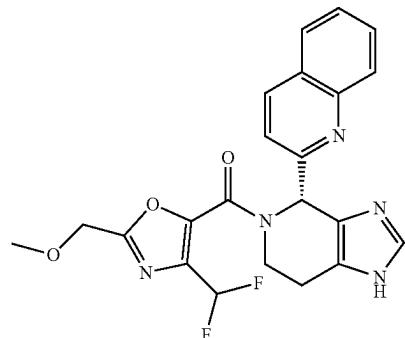
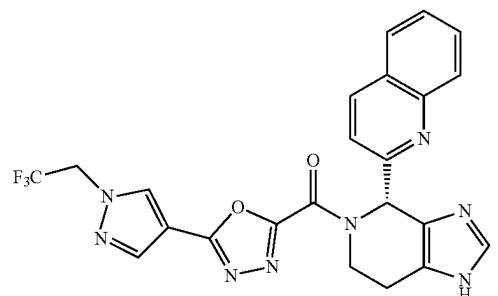
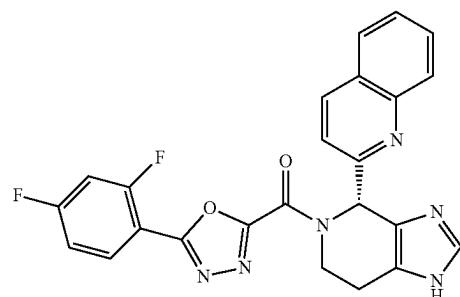
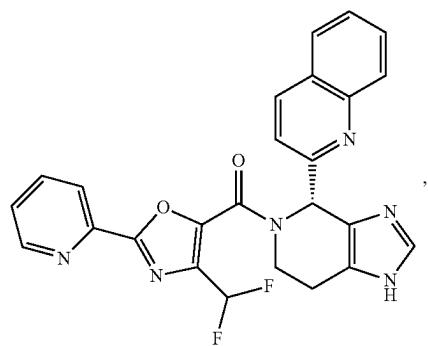
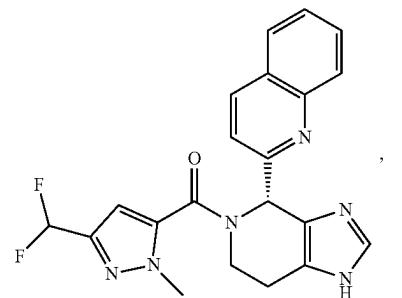
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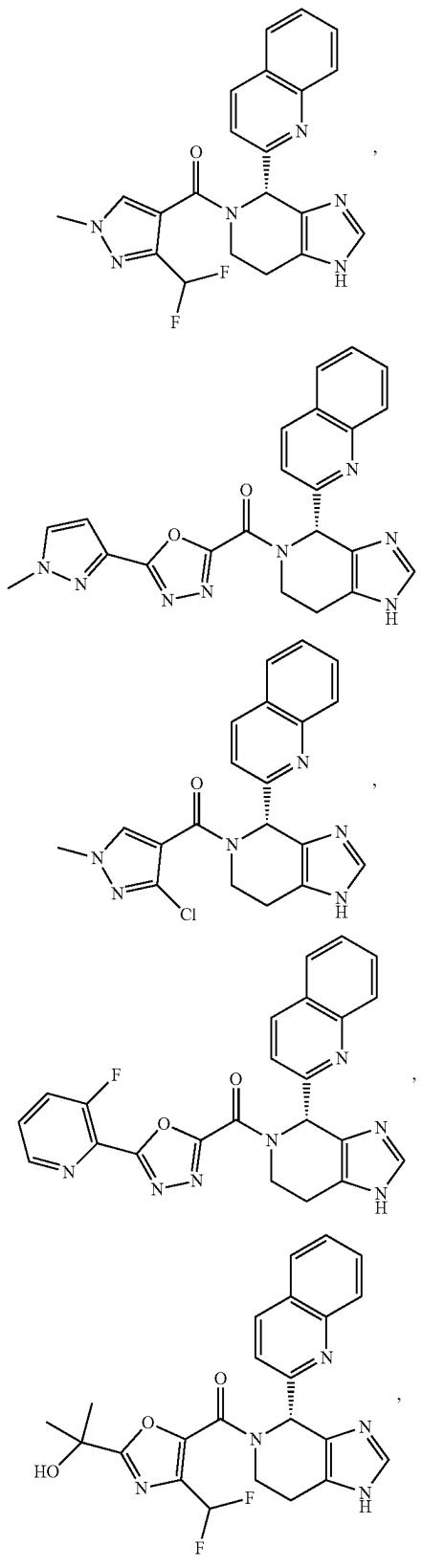
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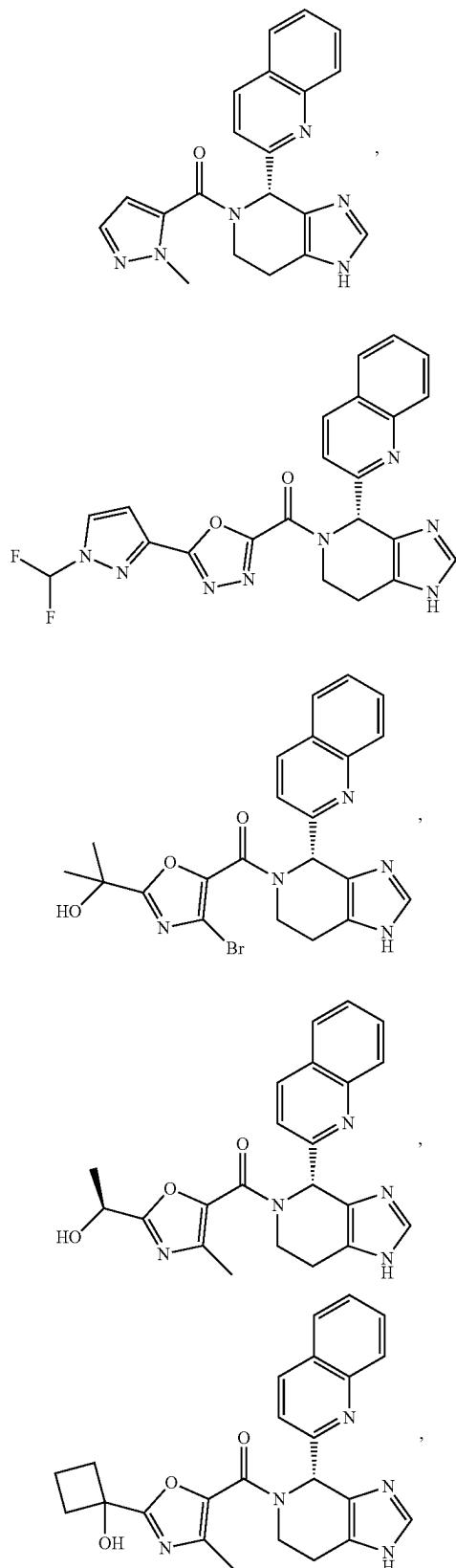
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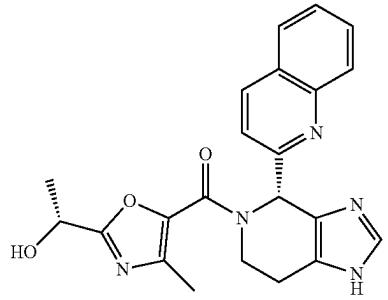
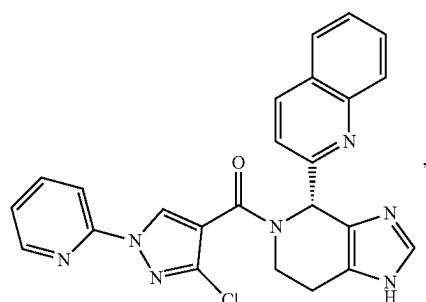
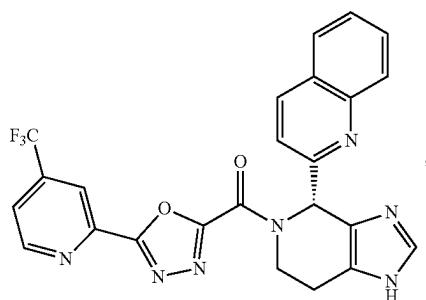
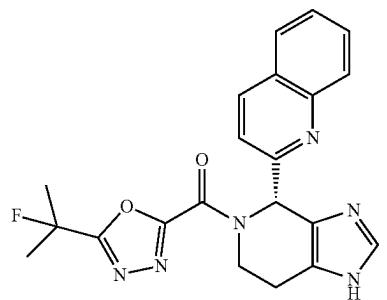
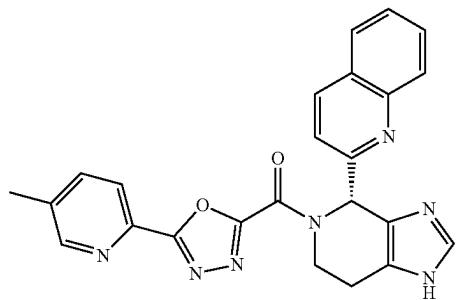
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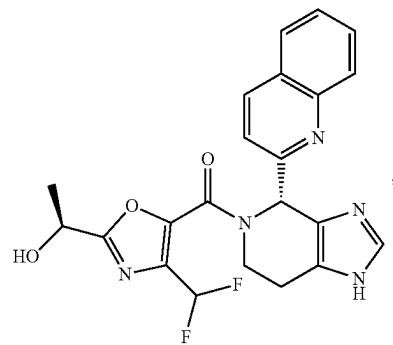
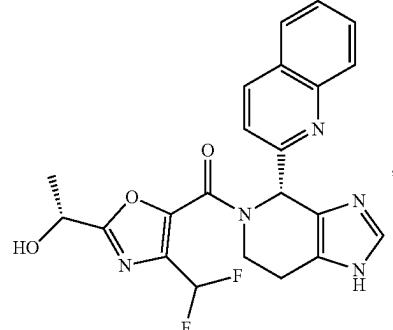
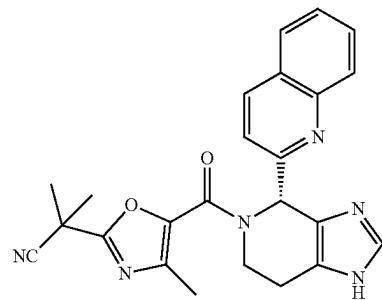
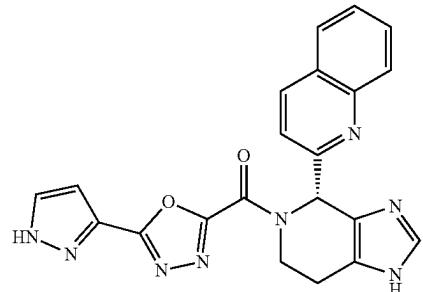
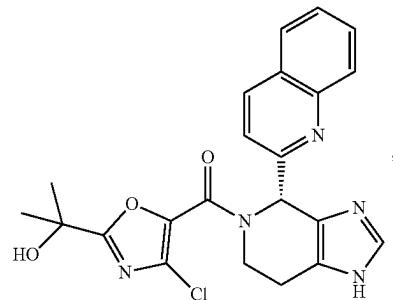
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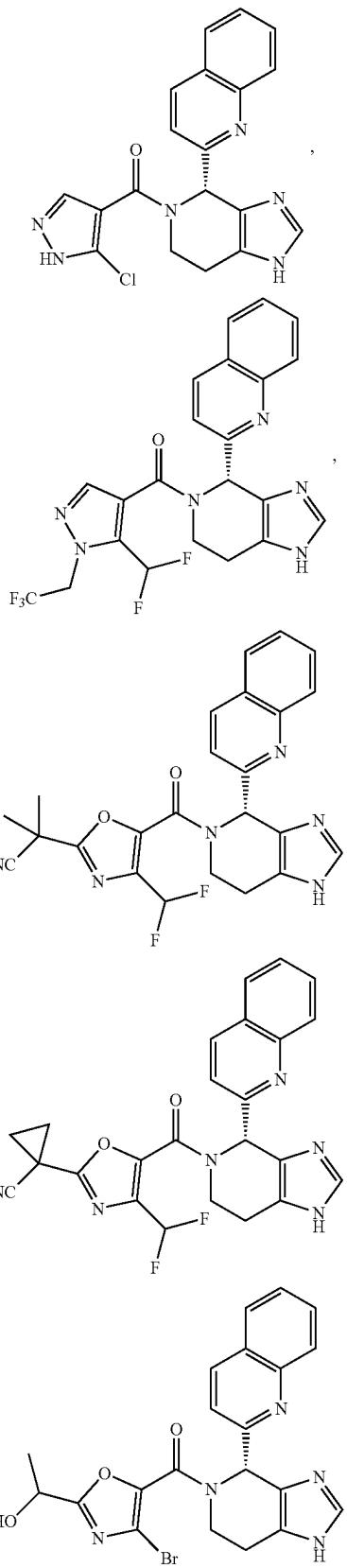
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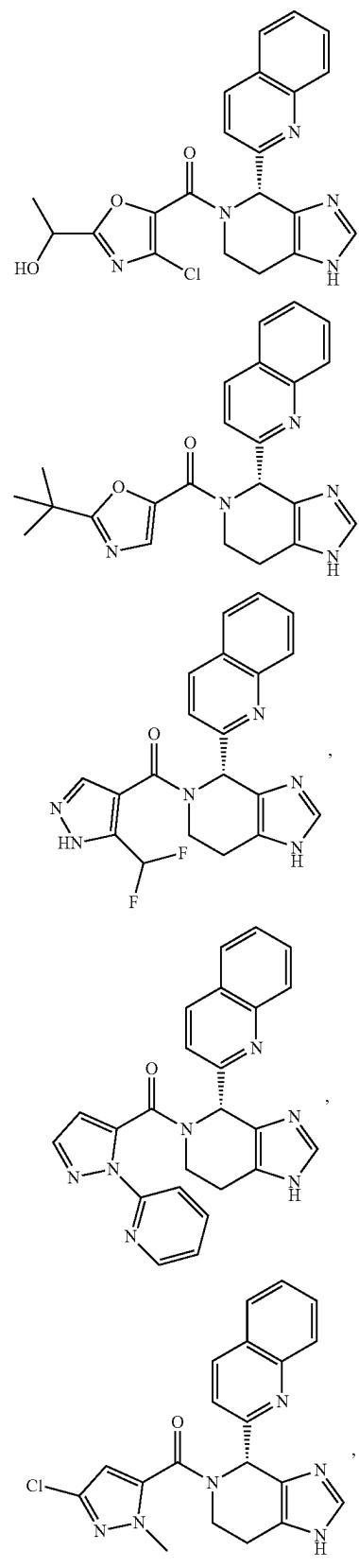
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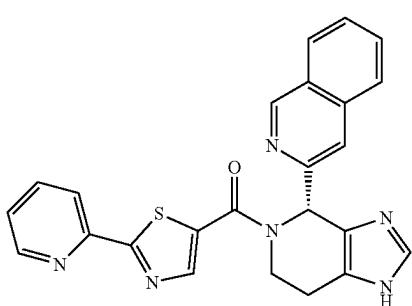
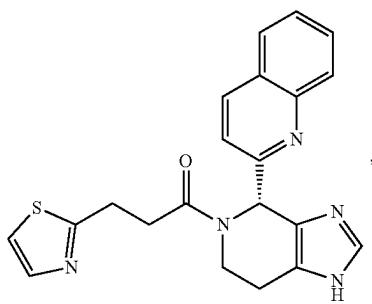
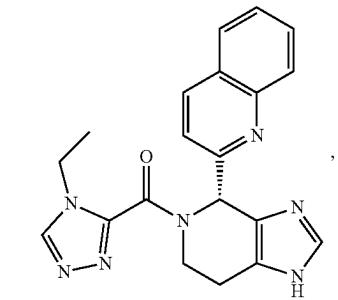
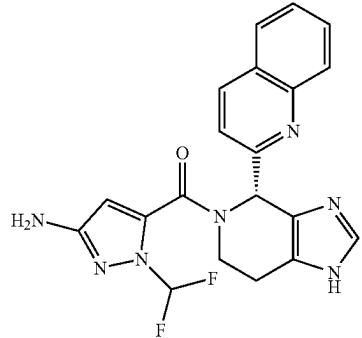
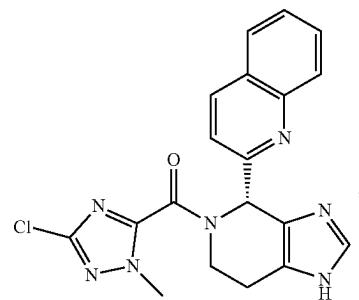
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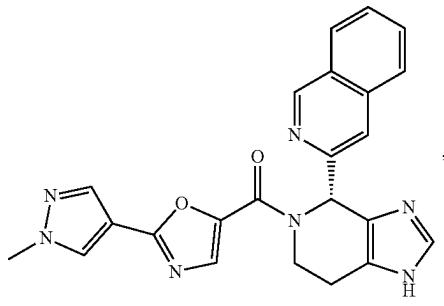
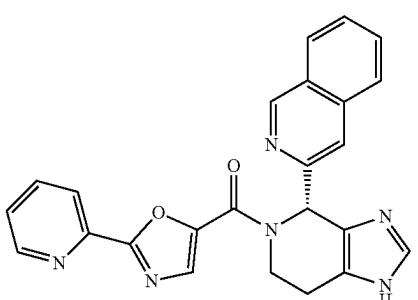
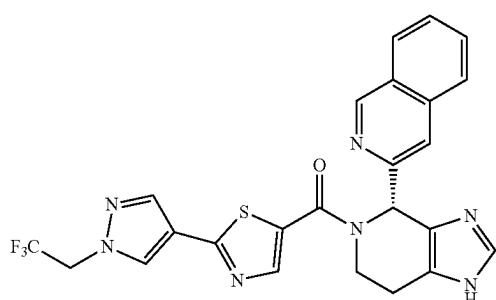
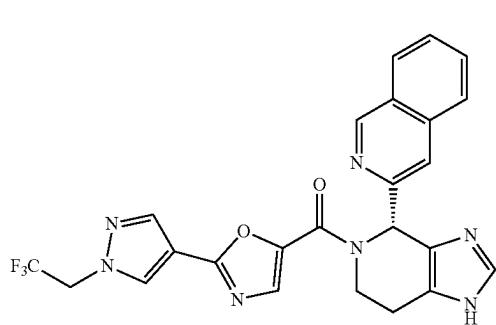
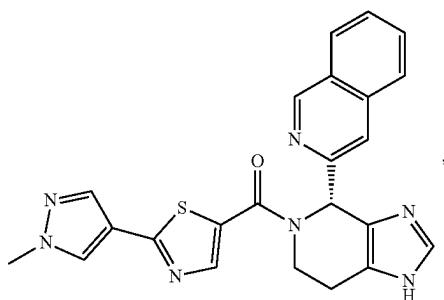
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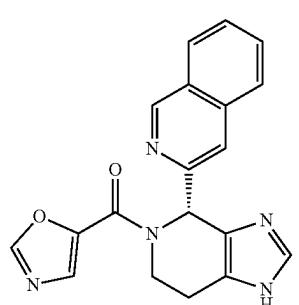
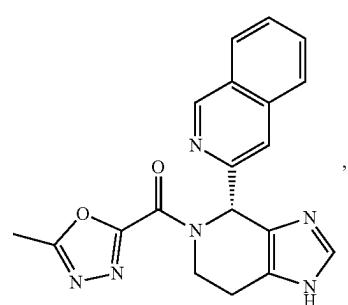
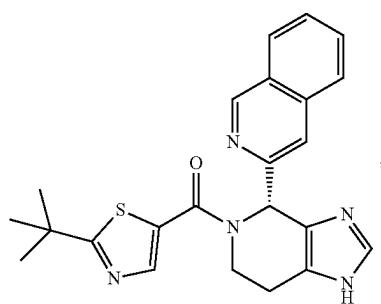
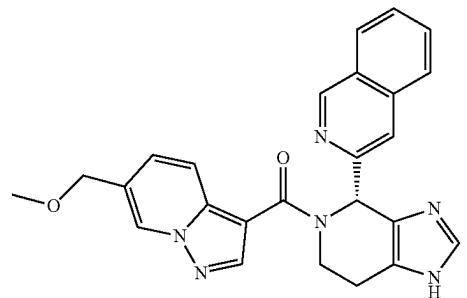
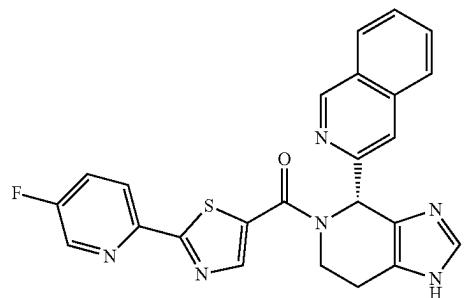
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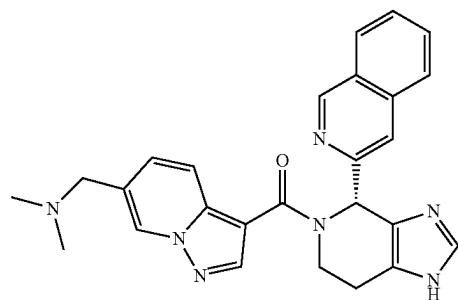
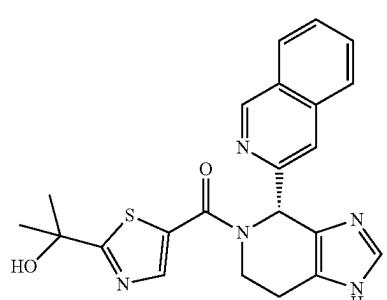
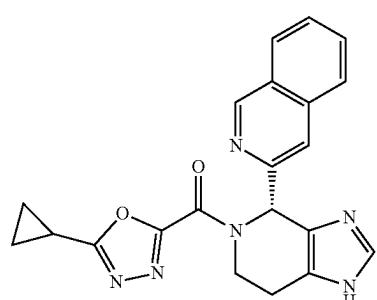
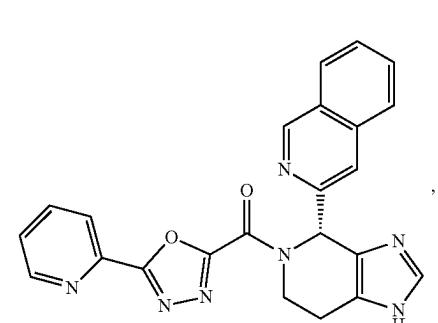
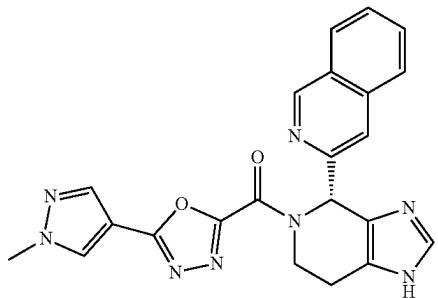
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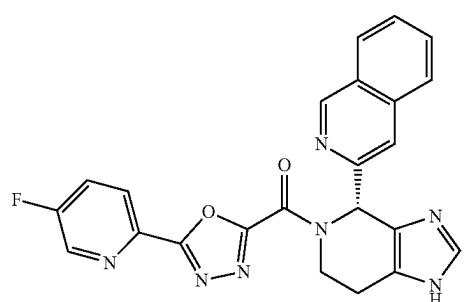
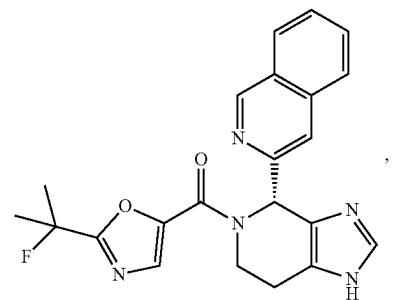
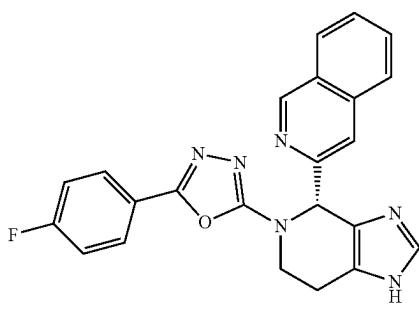
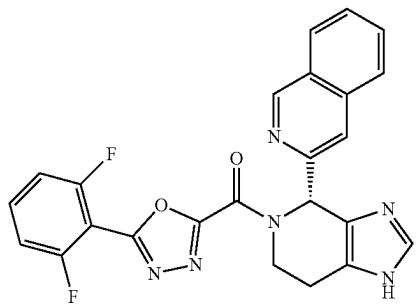
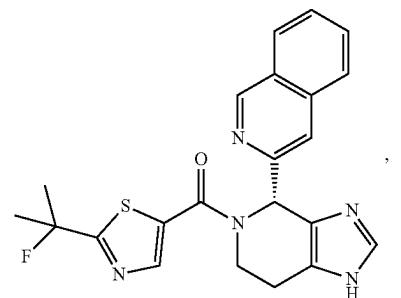
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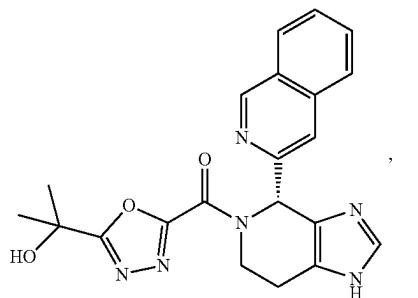
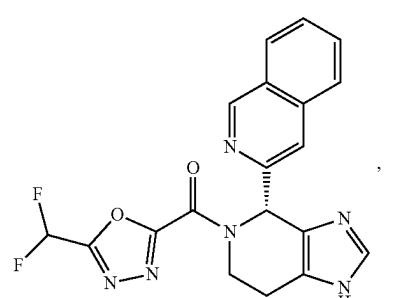
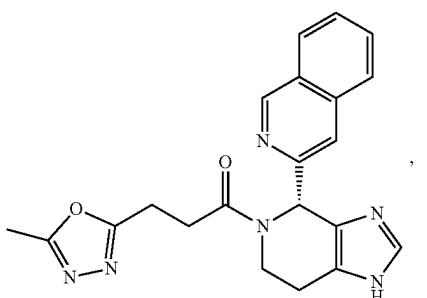
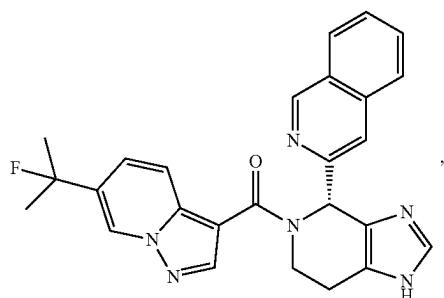
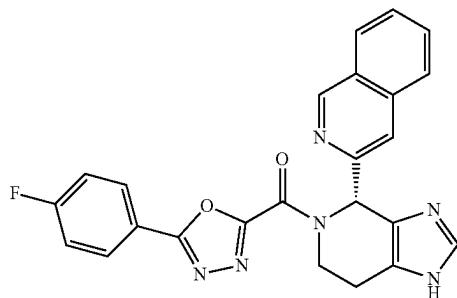
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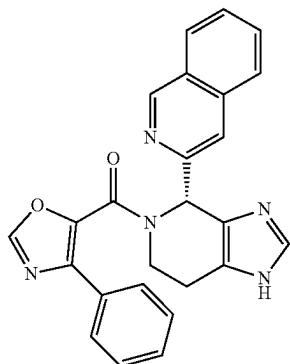
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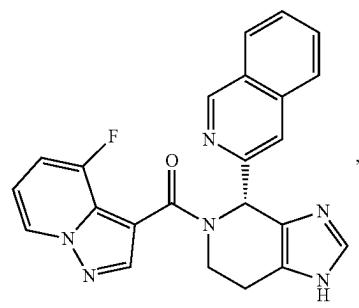
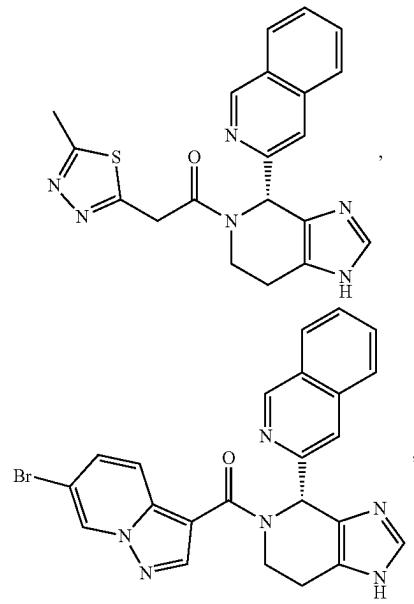
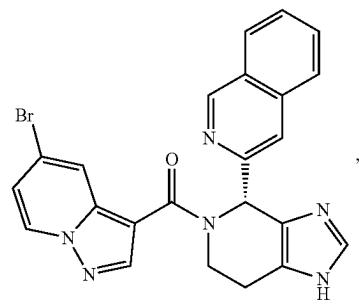
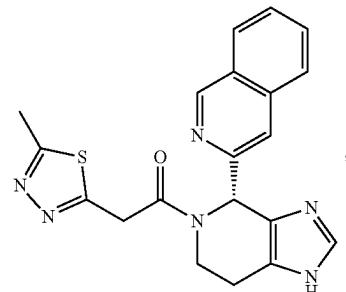
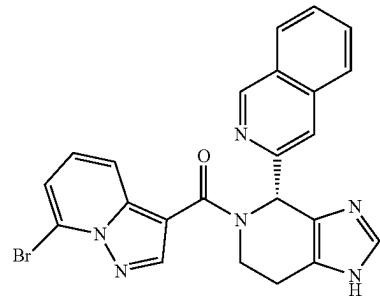
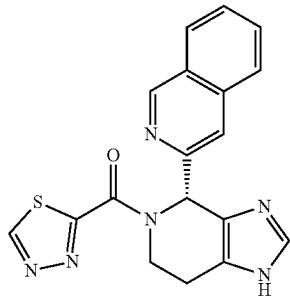
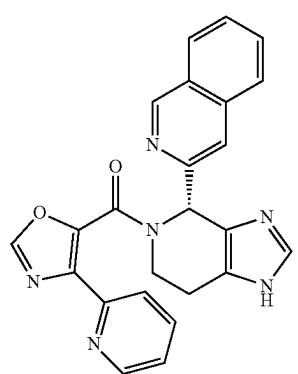
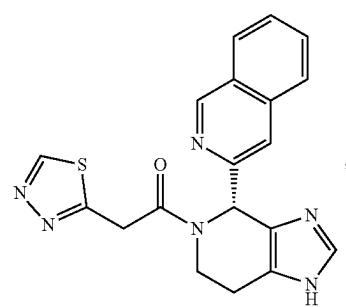
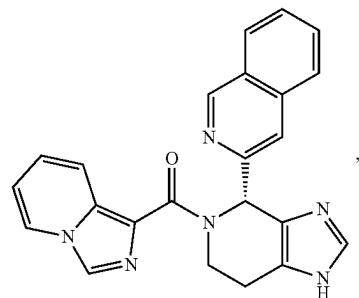
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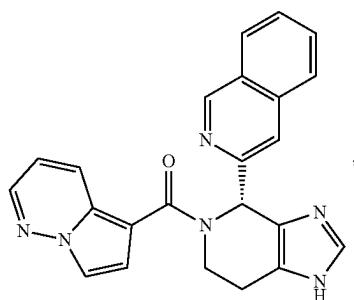
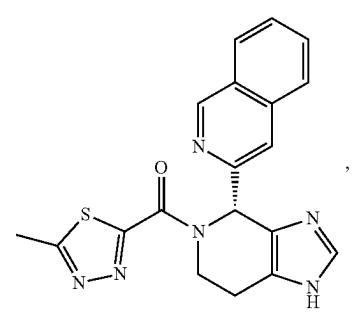
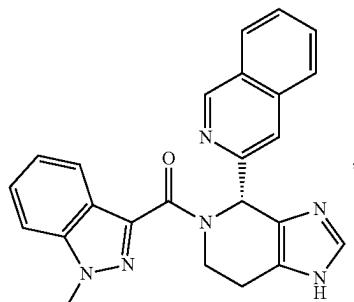
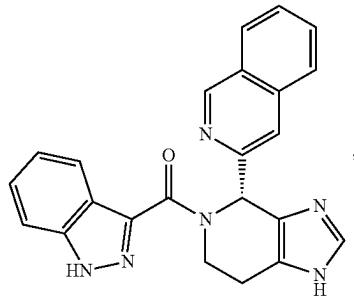
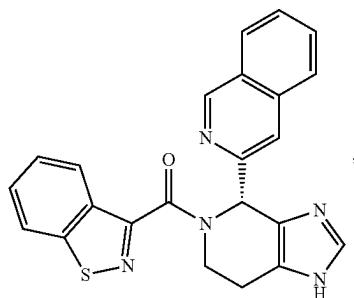
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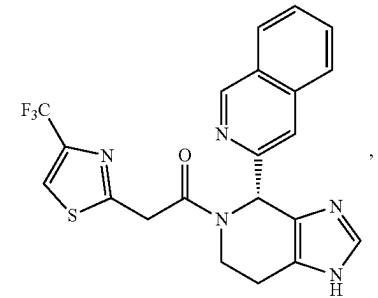
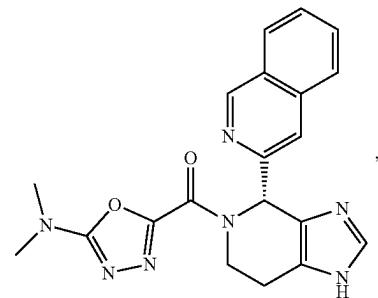
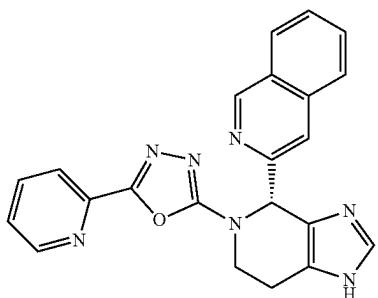
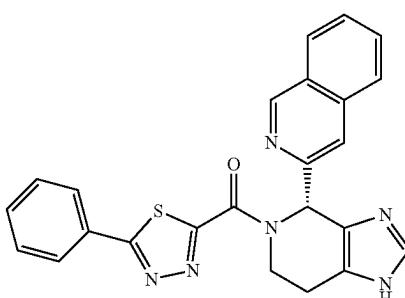
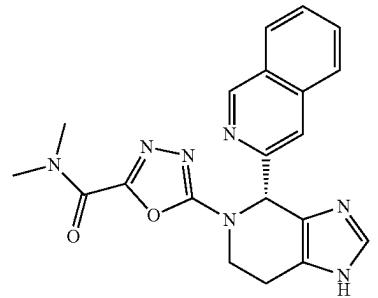
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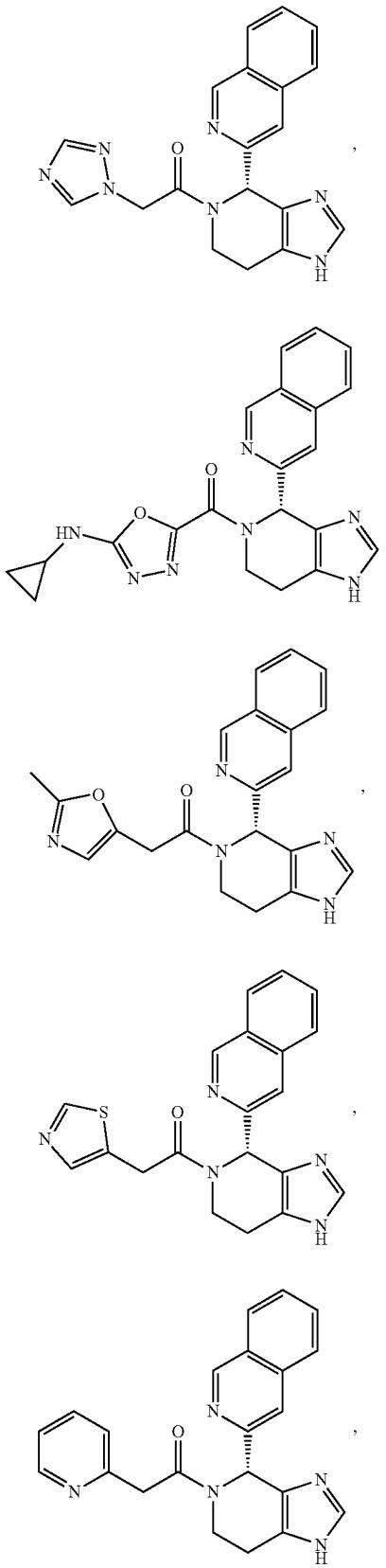
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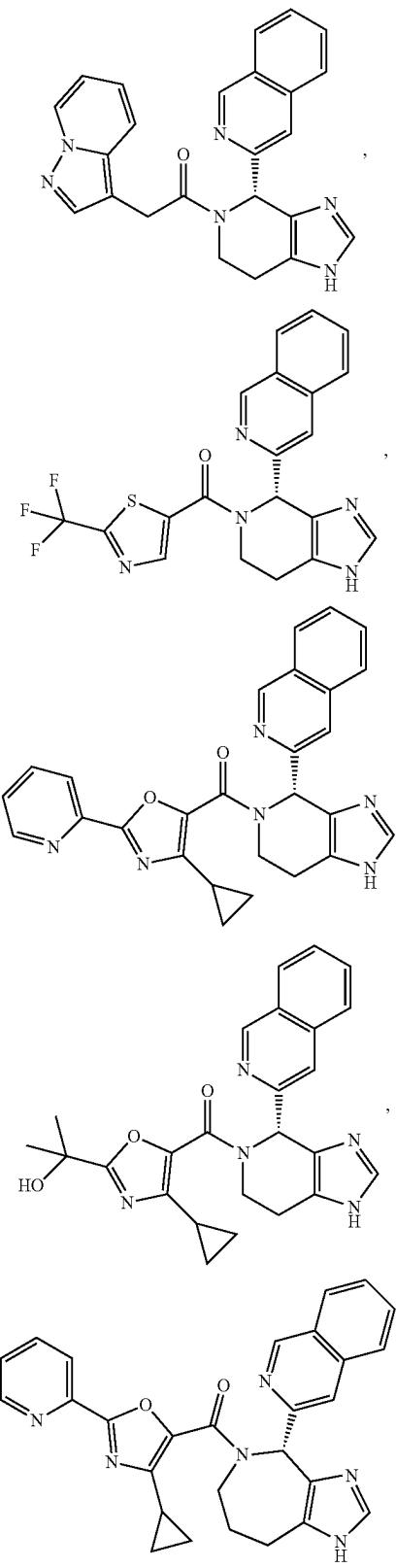
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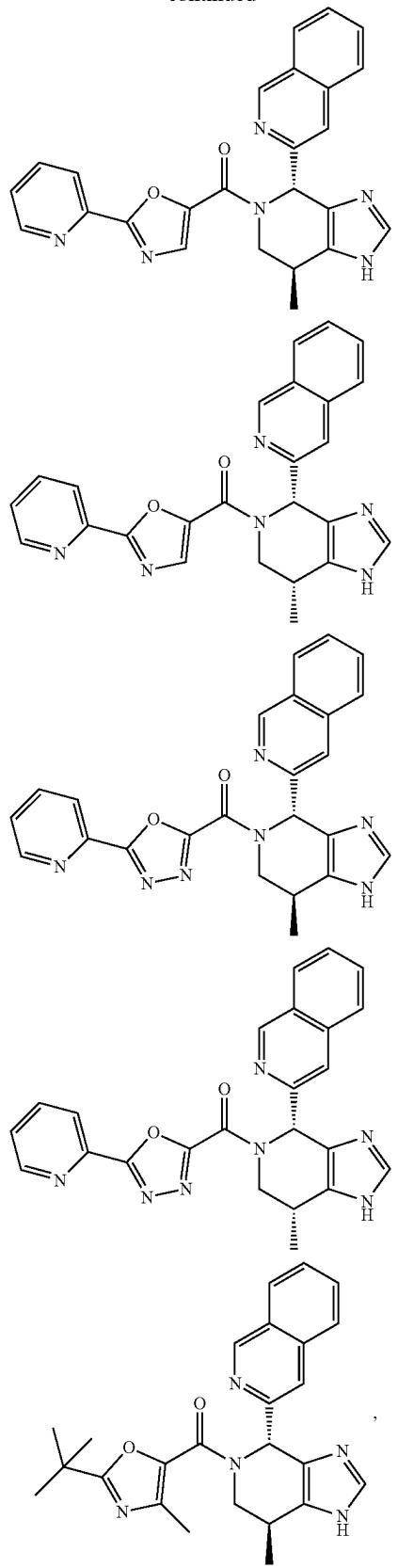
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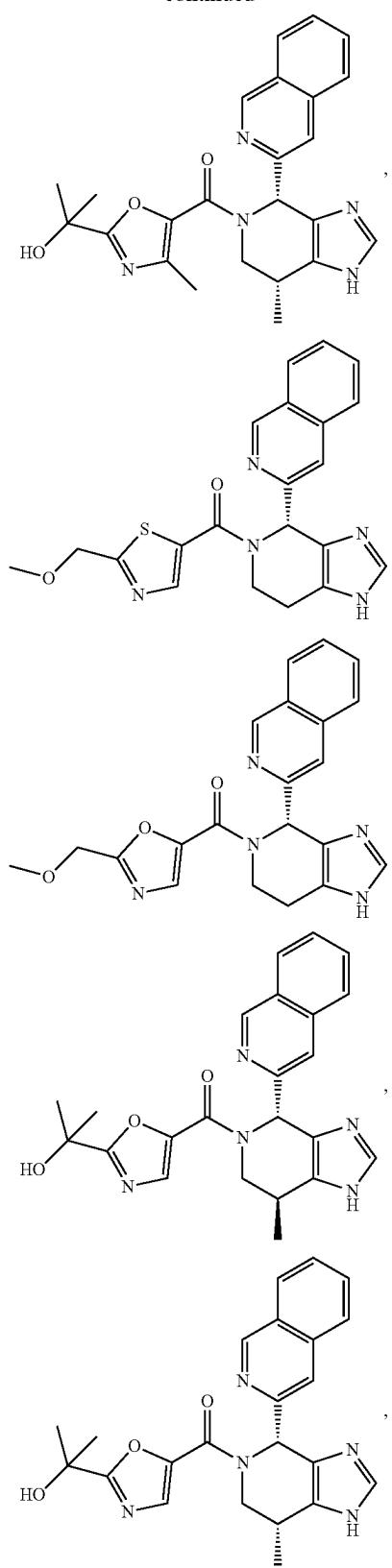
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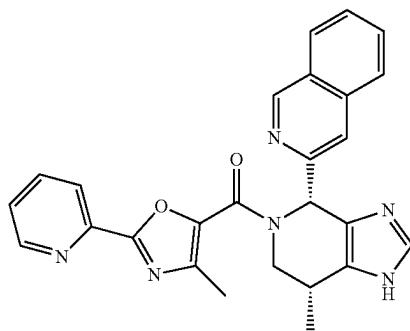
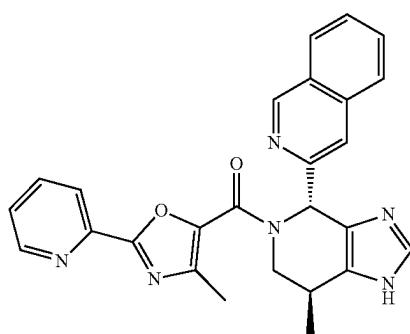
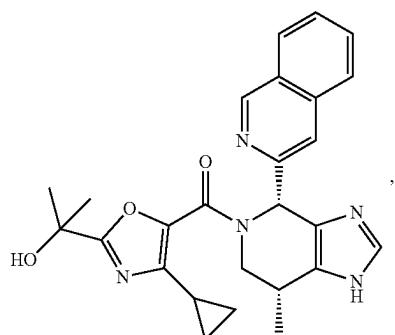
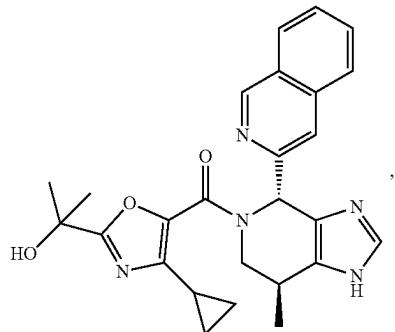
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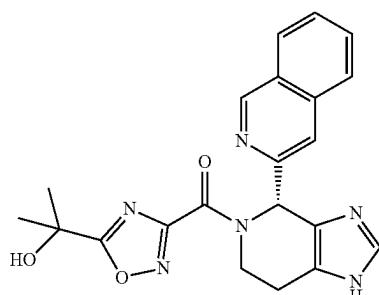
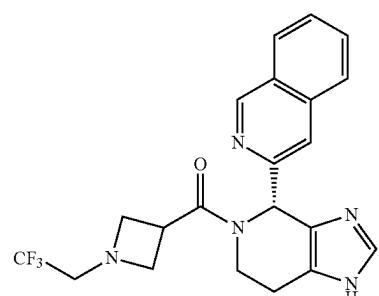
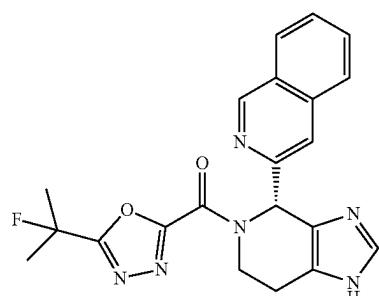
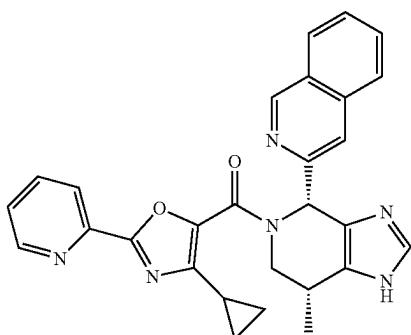
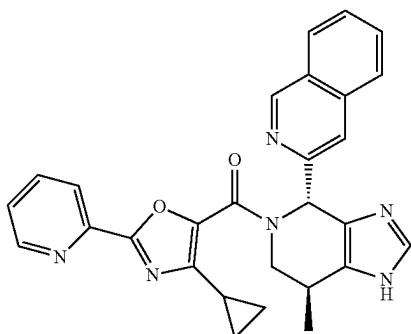
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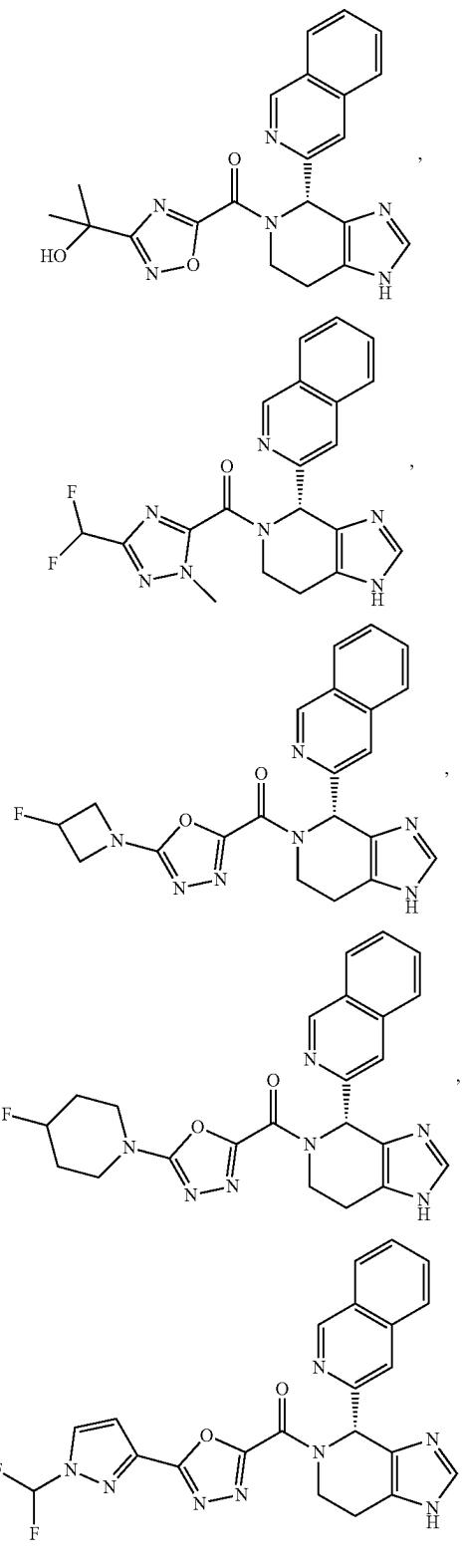
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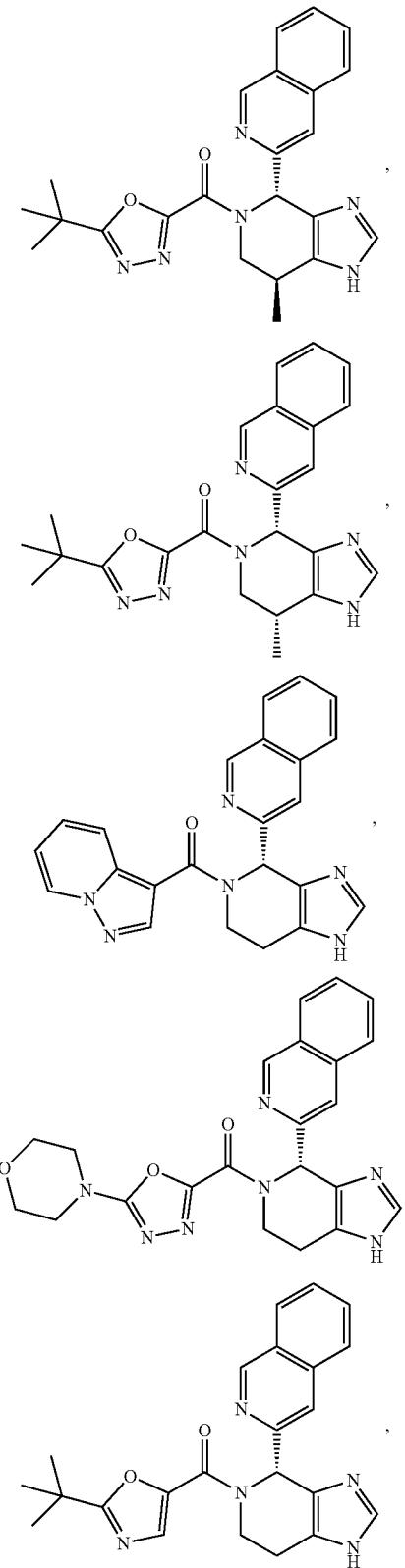
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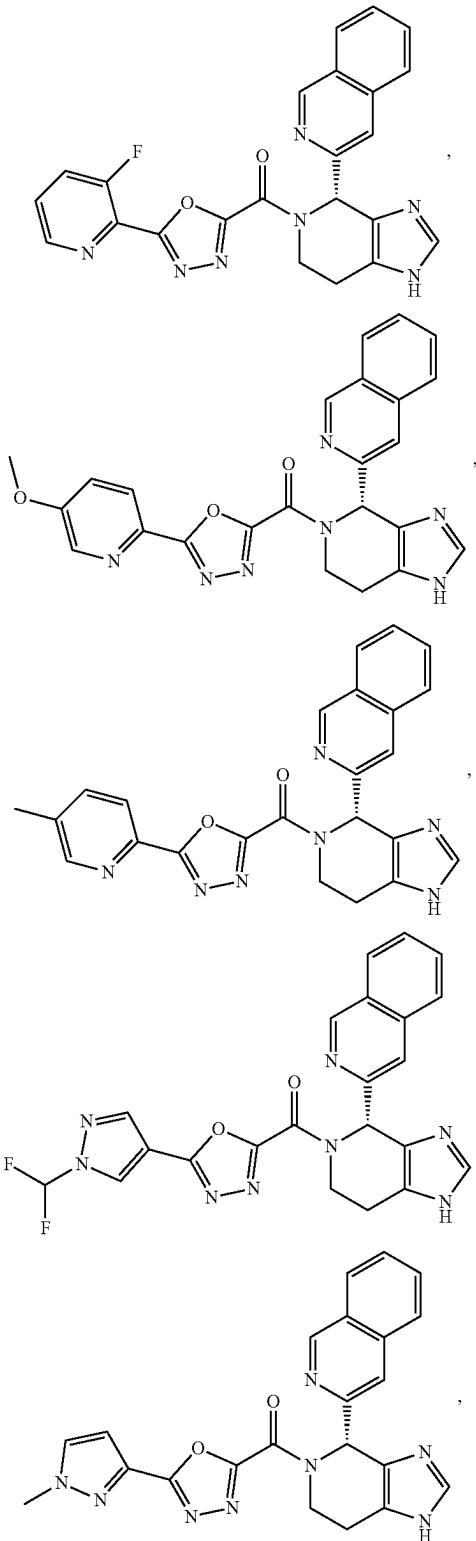
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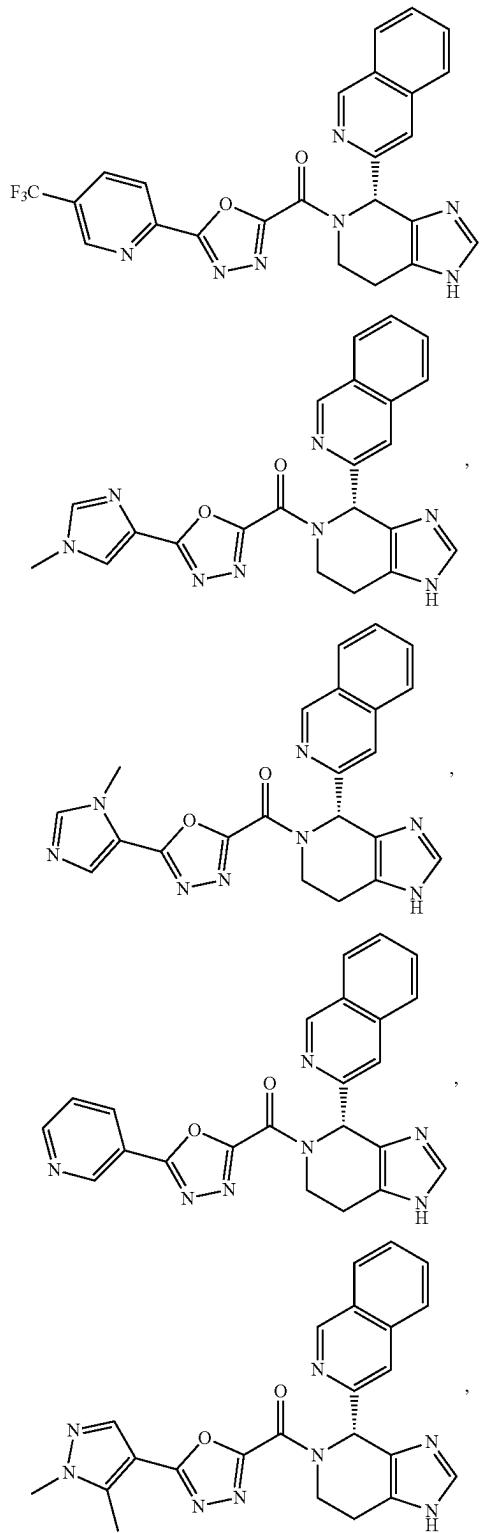
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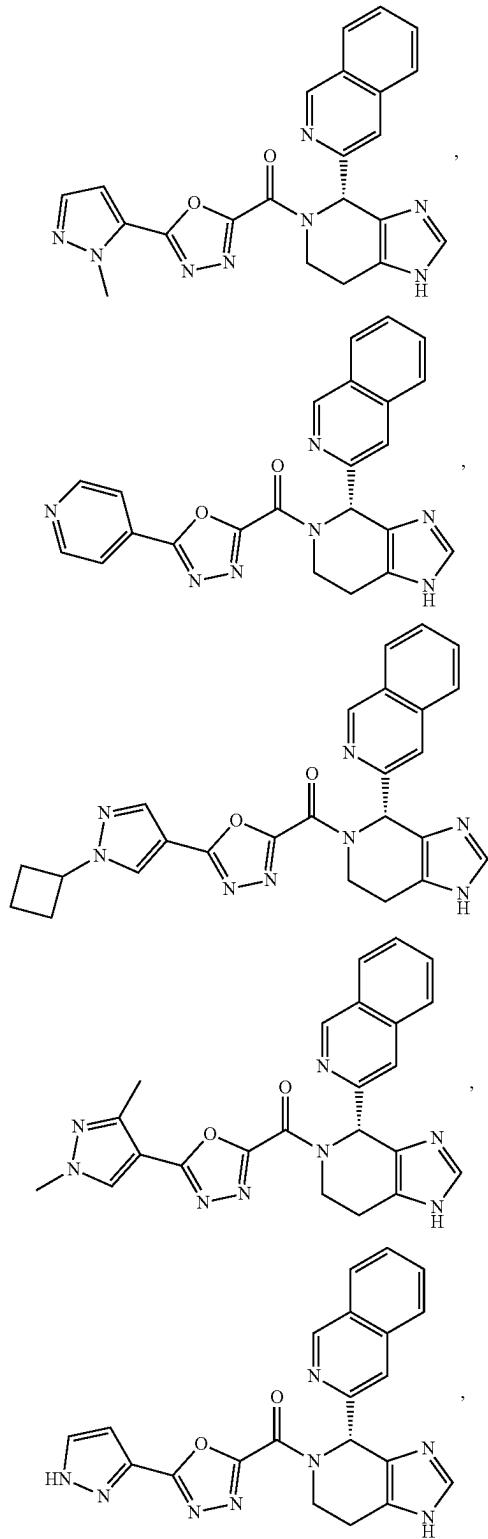
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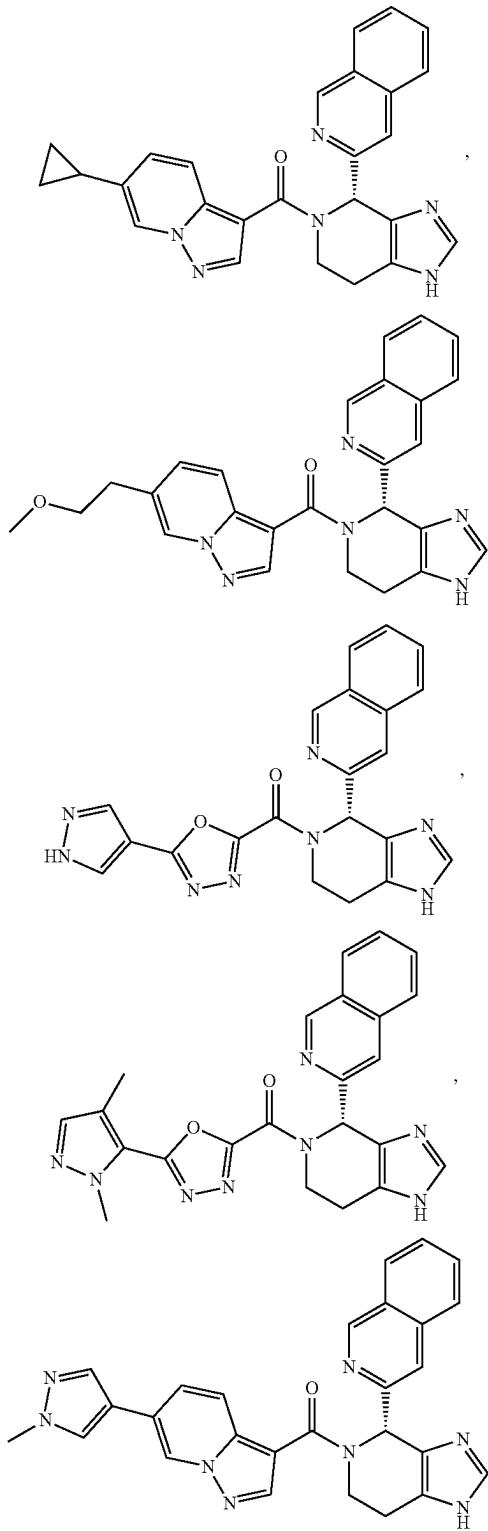
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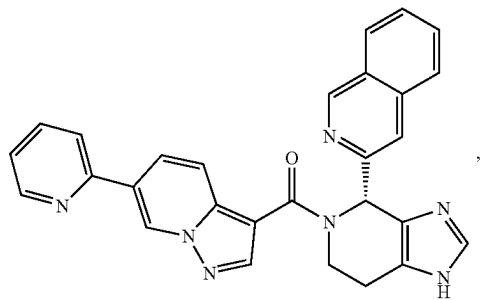
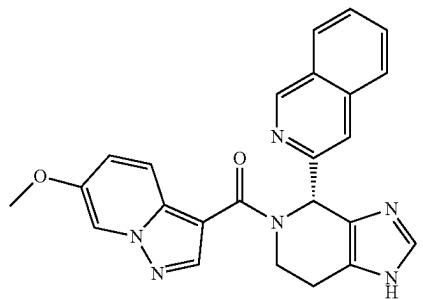
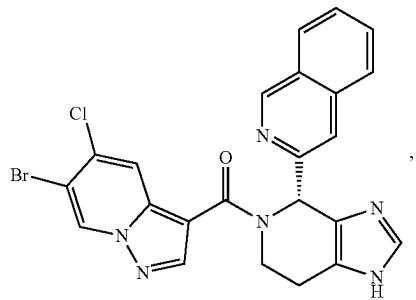
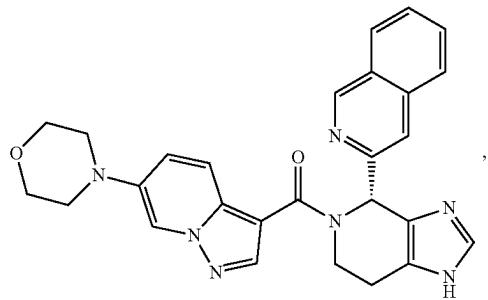
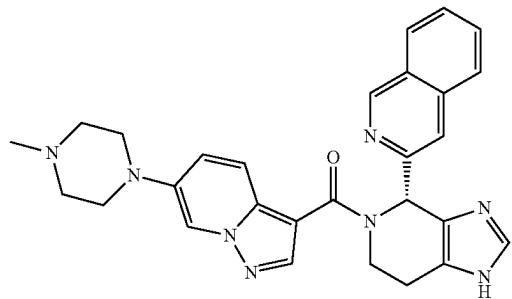
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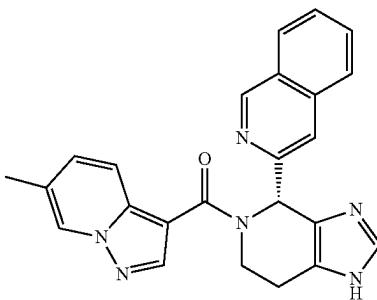
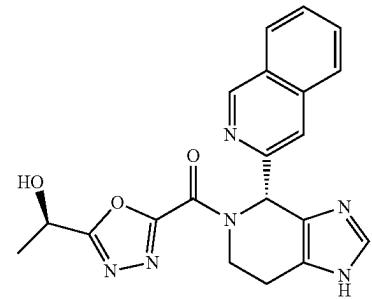
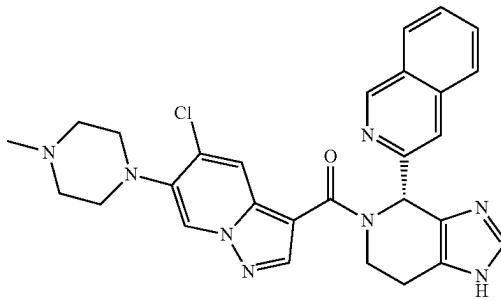
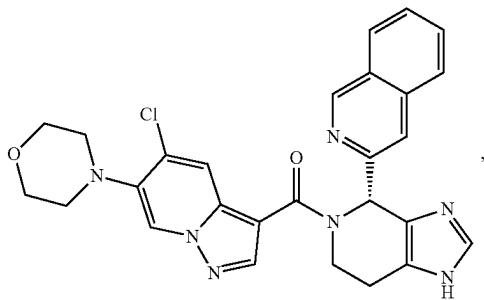
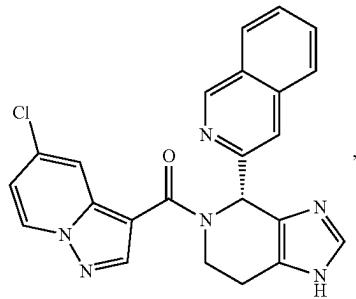
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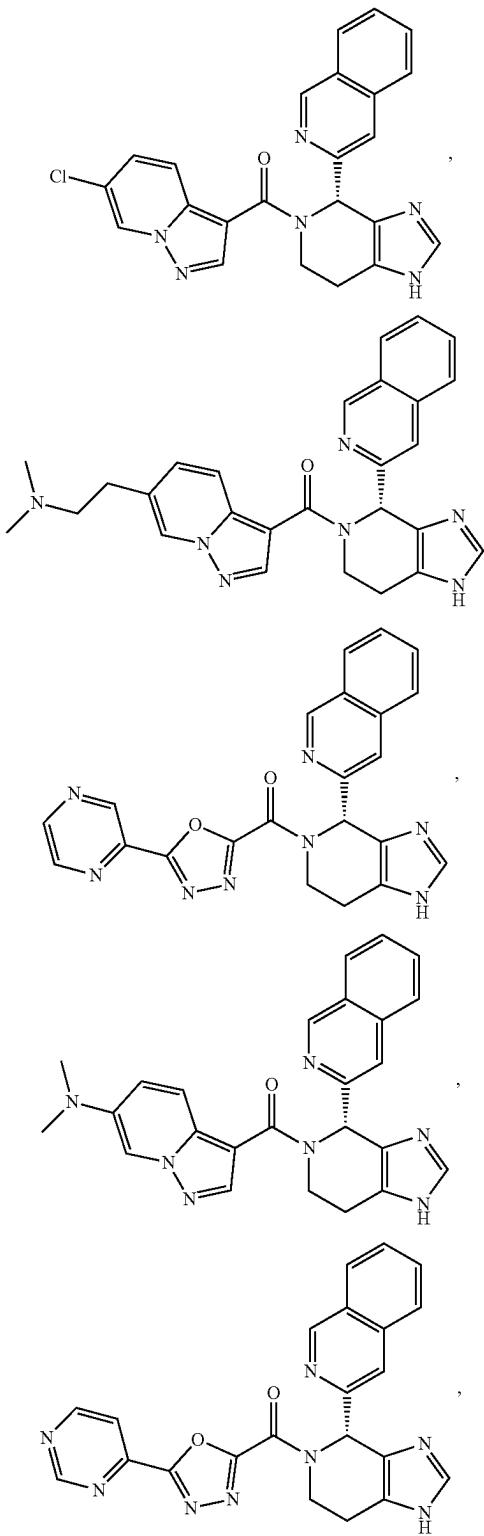
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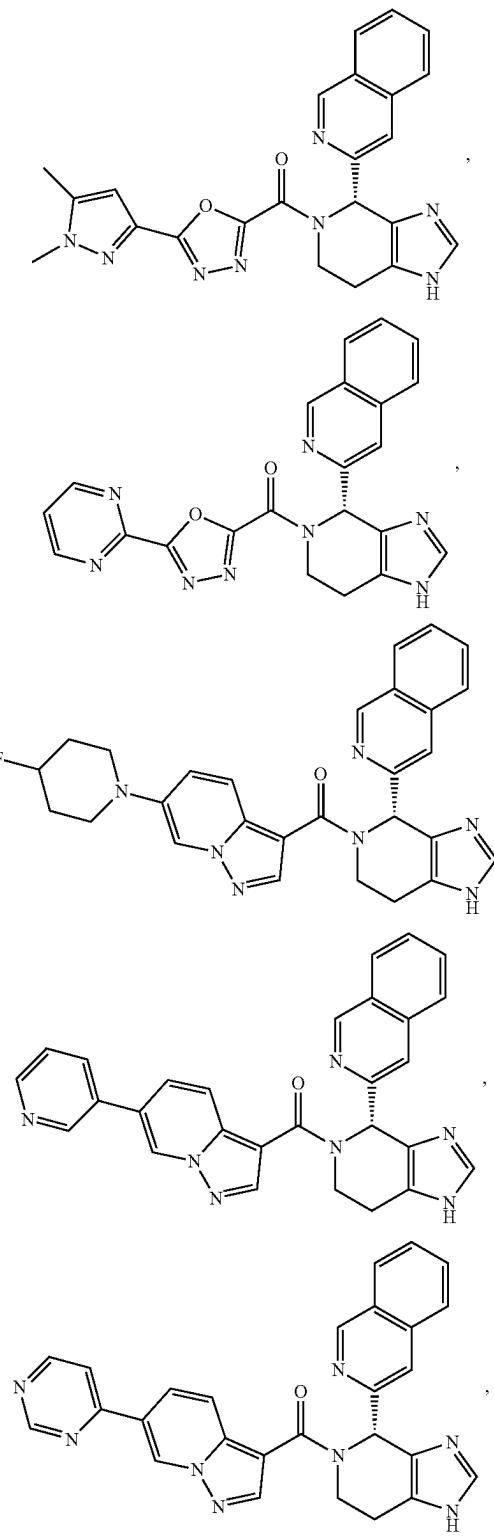
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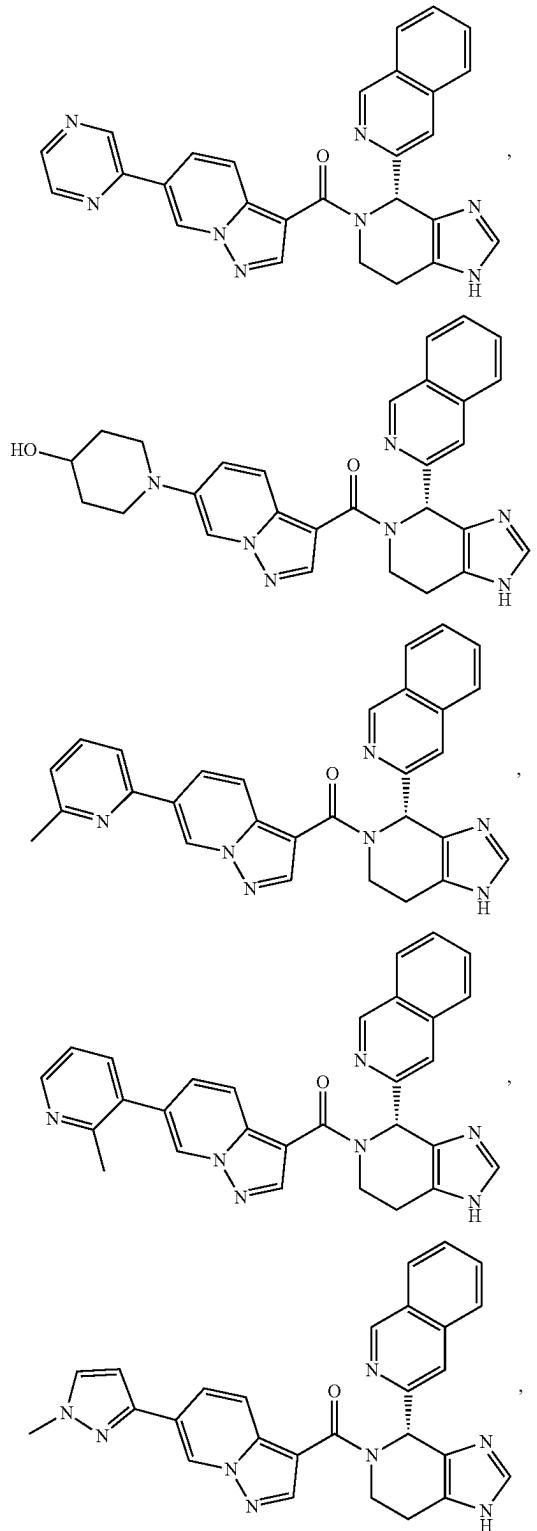
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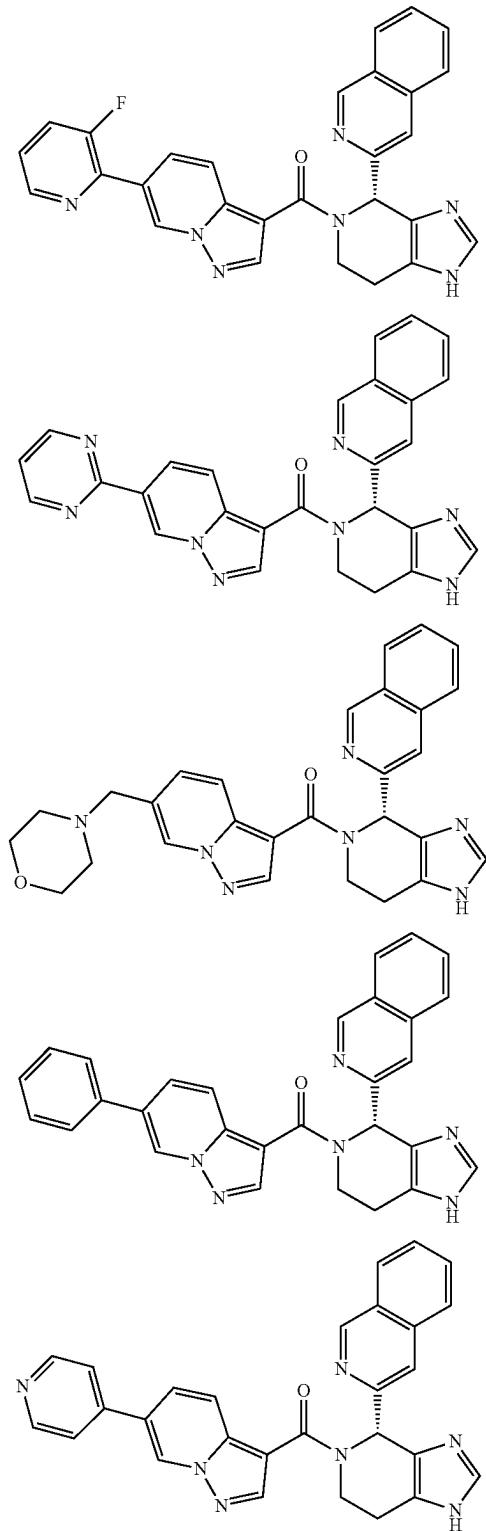
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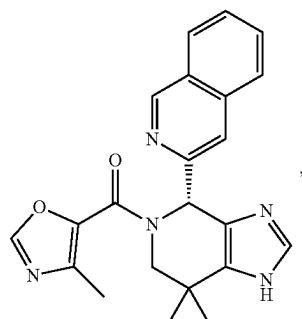
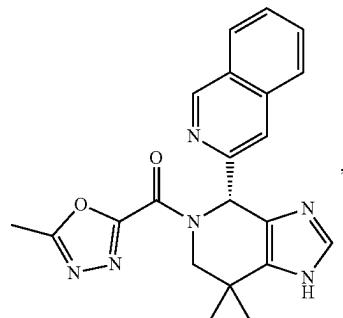
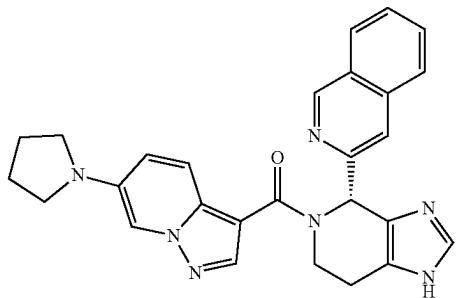
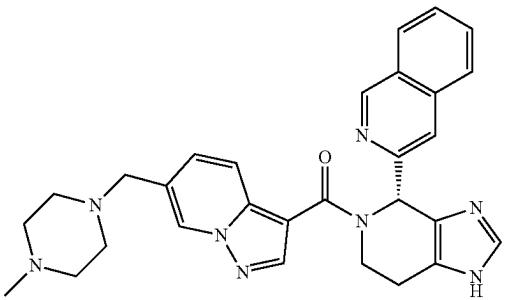
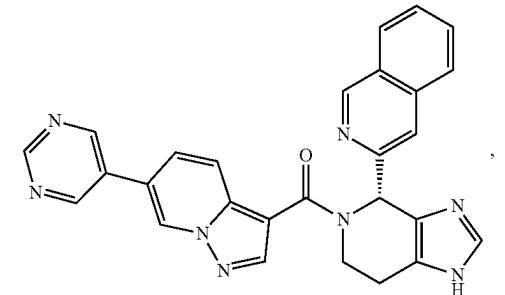
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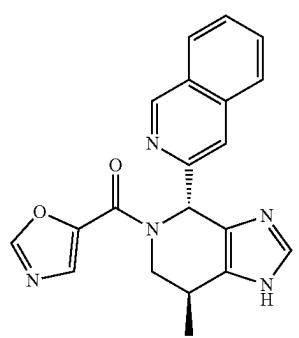
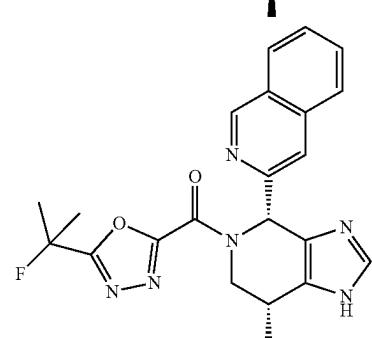
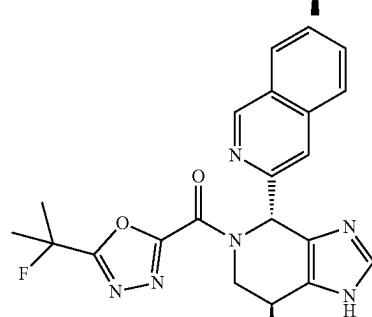
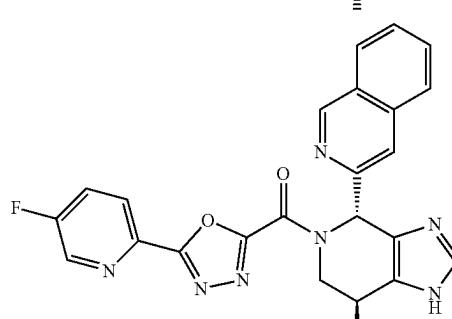
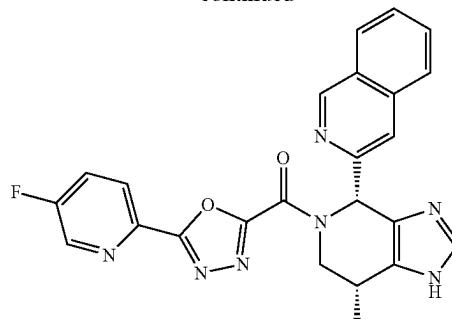
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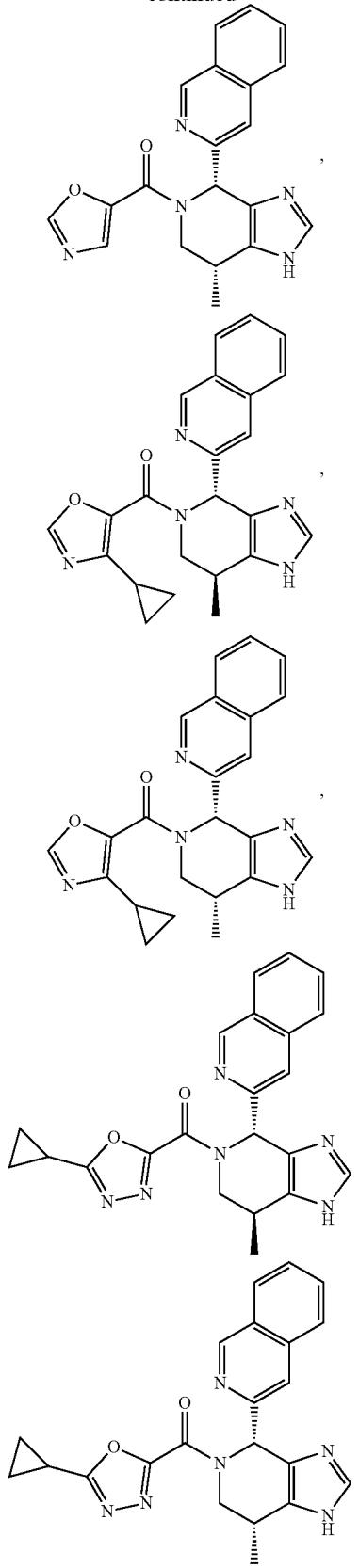
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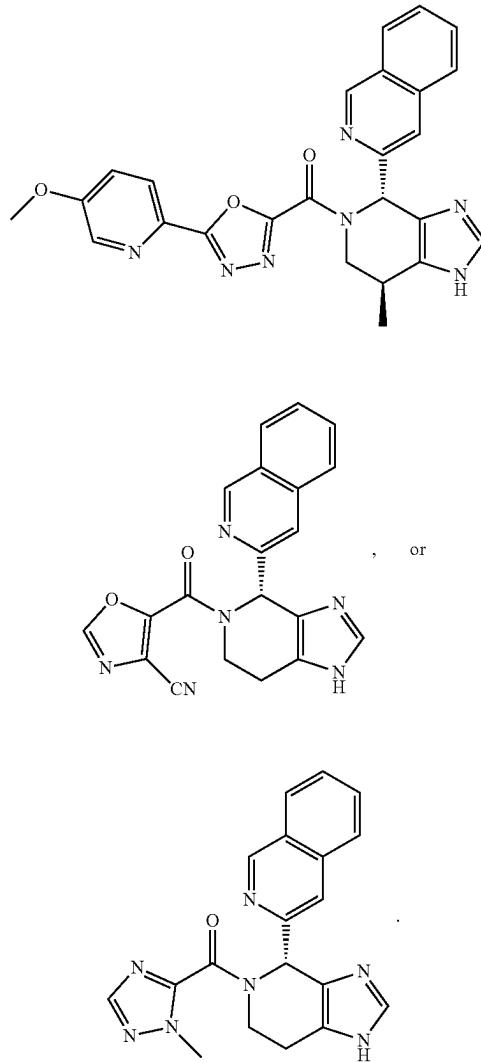
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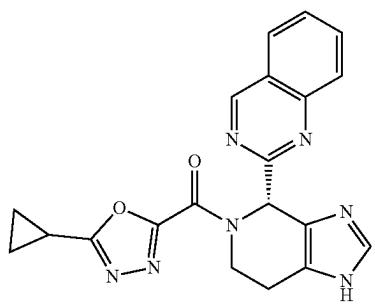
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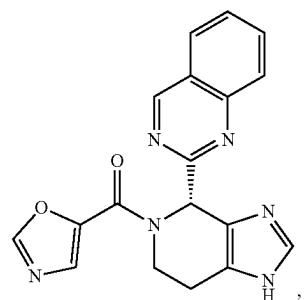
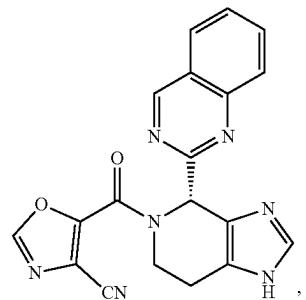
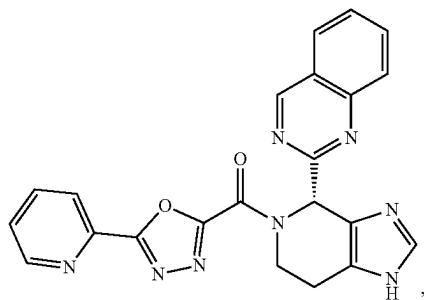
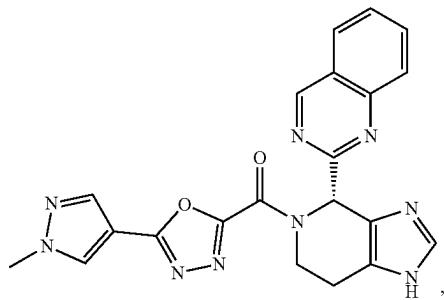
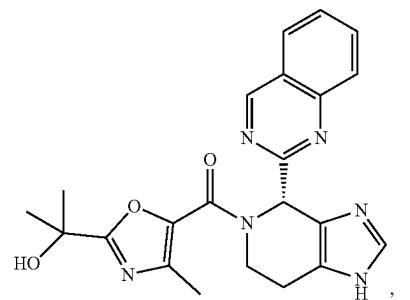
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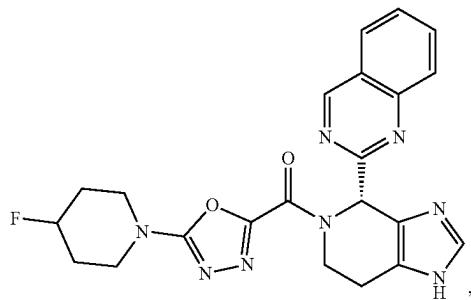
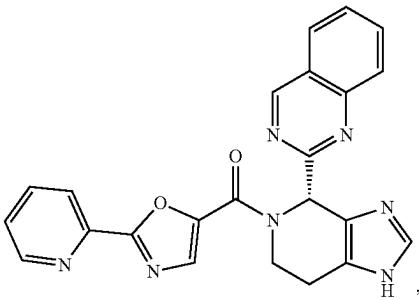
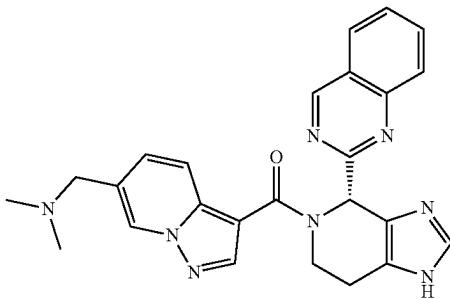
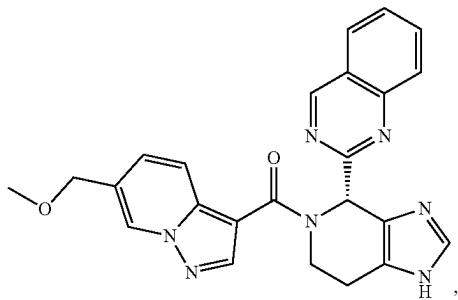
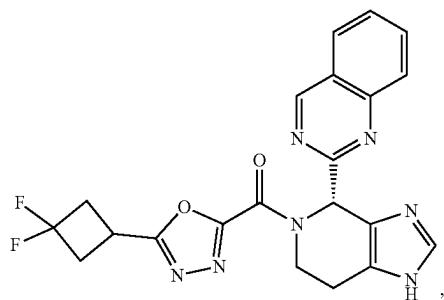
85. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein the compound is selected from the following:



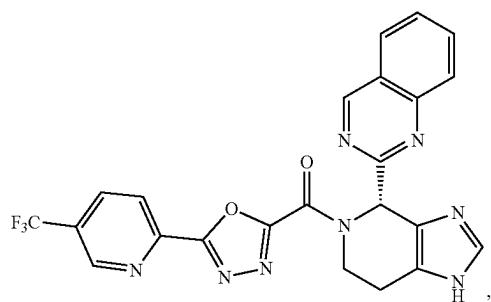
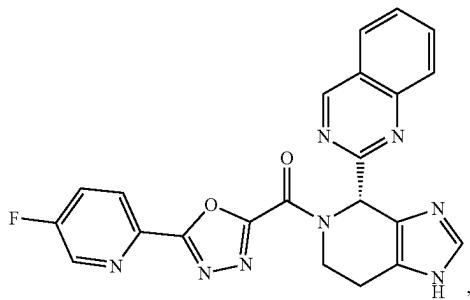
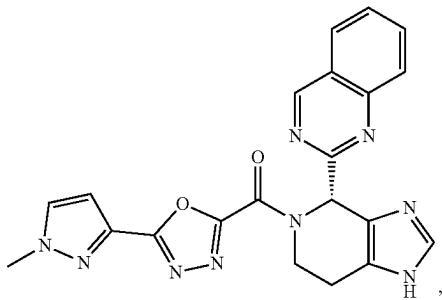
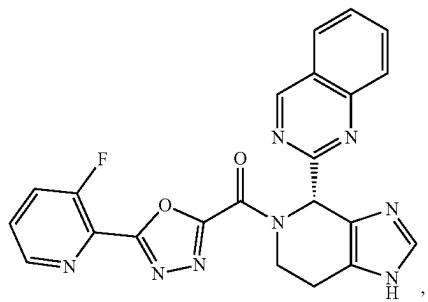
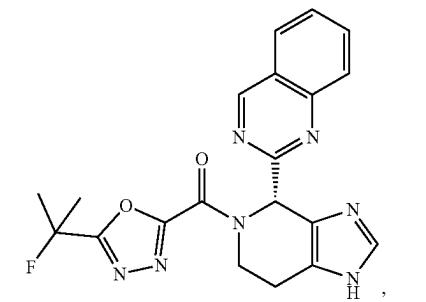
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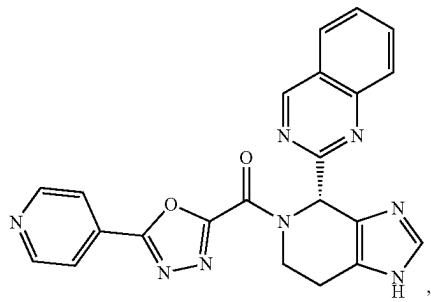
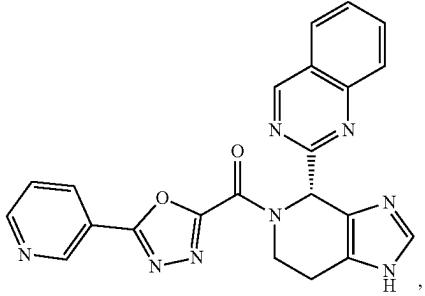
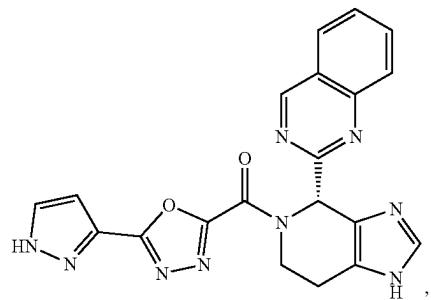
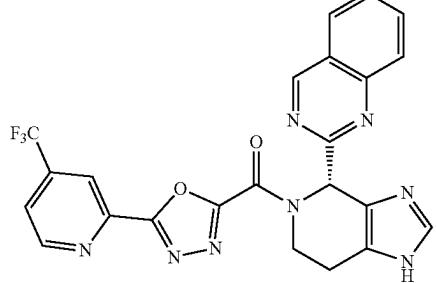
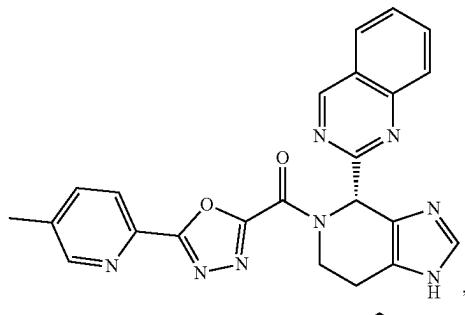
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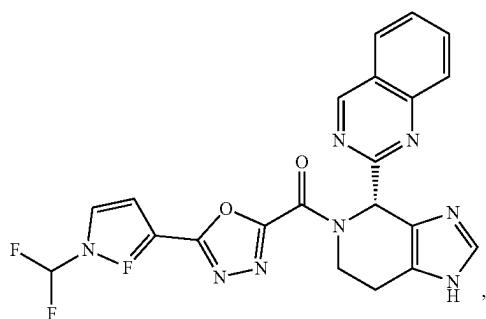
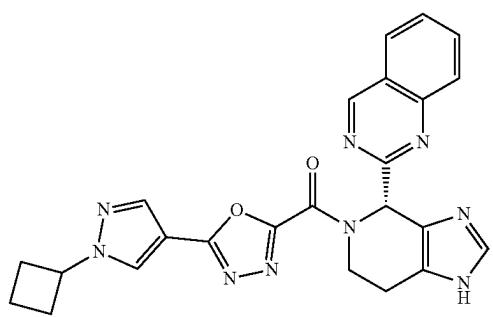
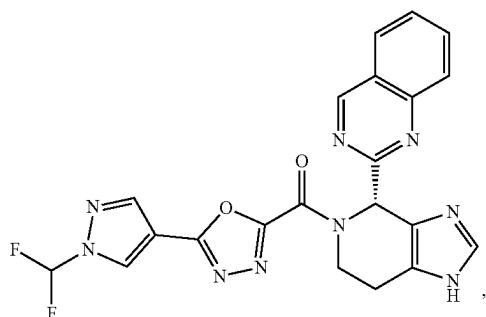
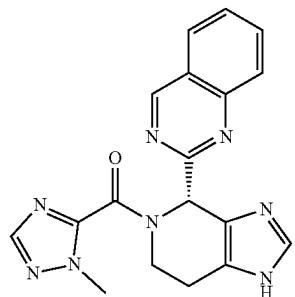
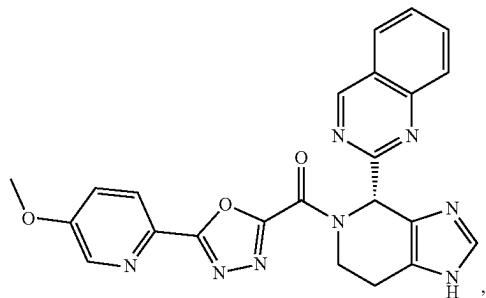
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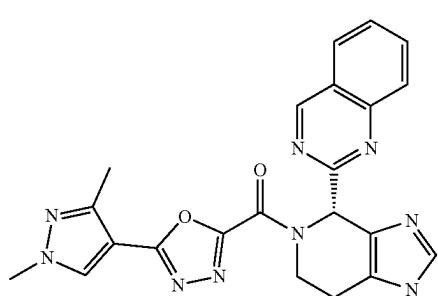
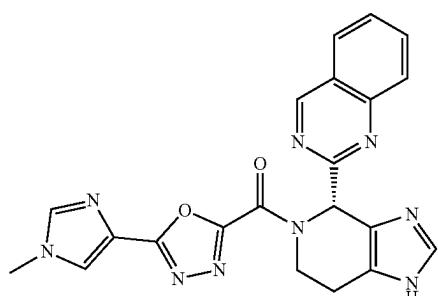
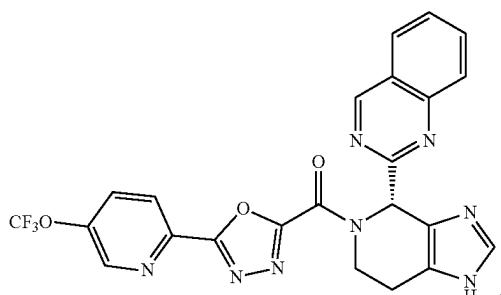
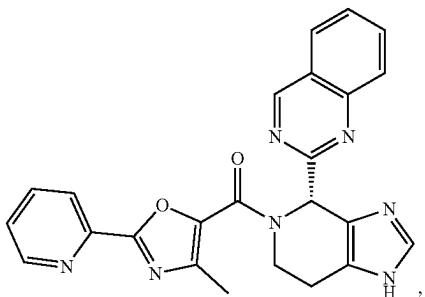
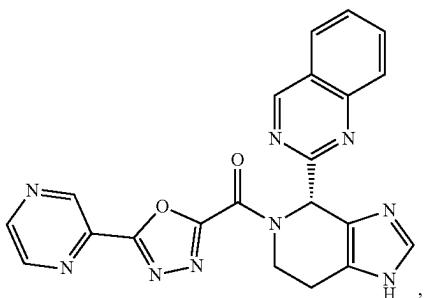
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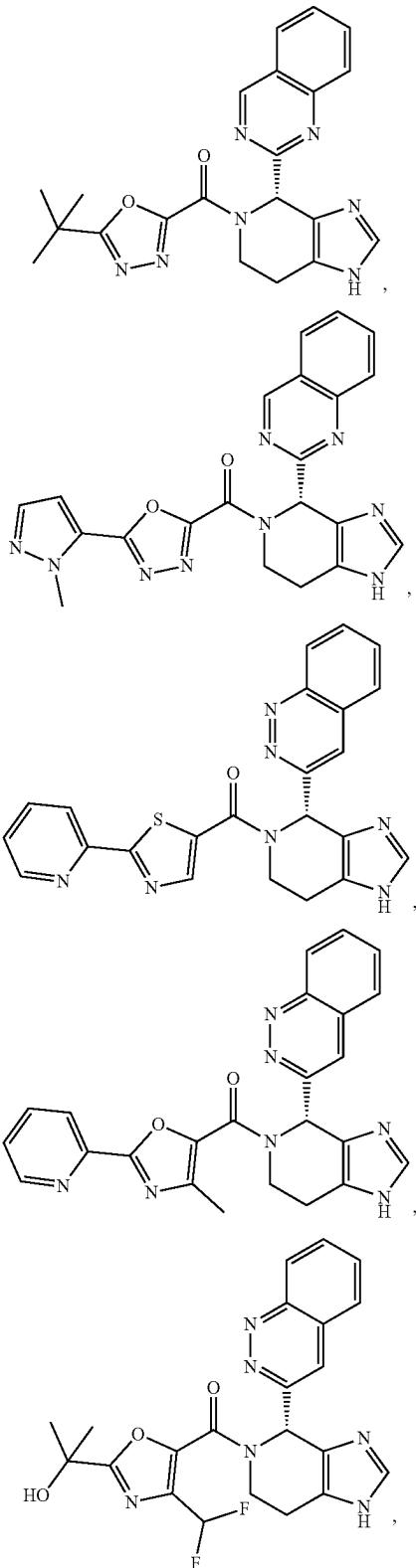
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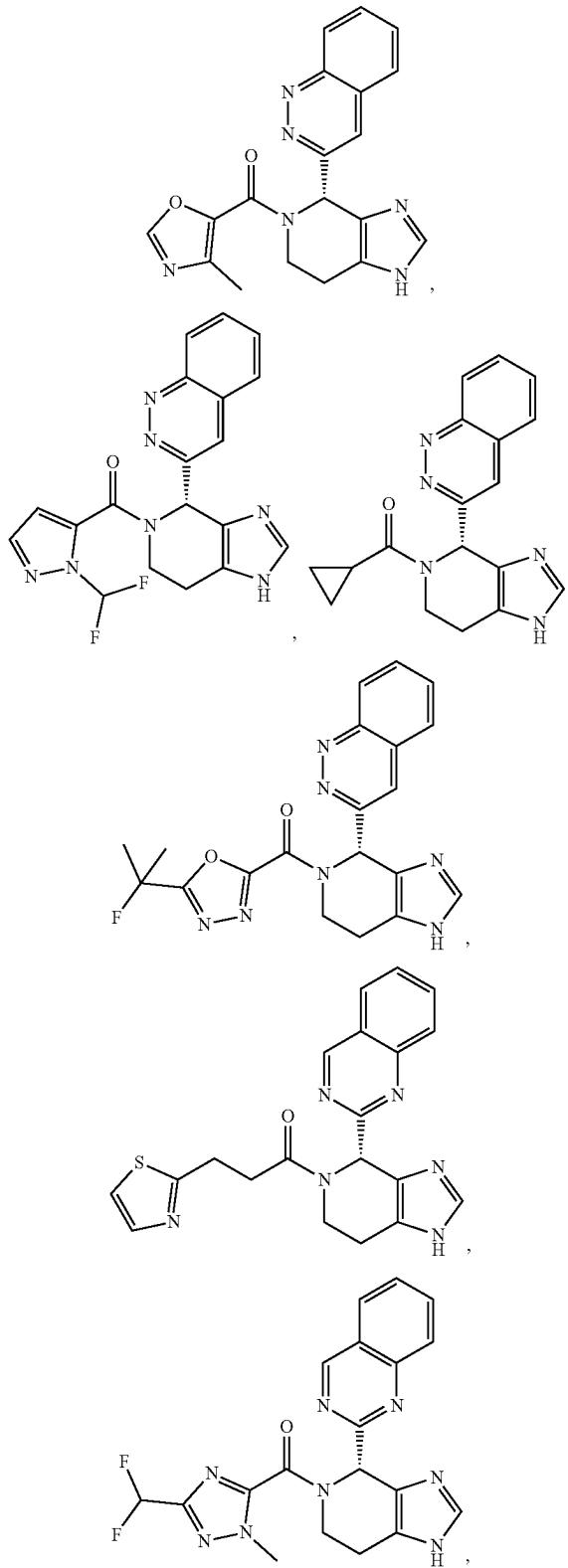
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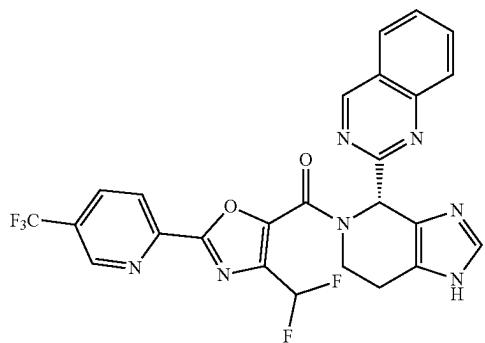
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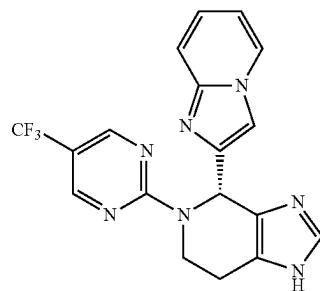
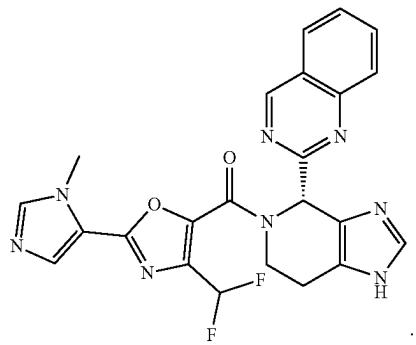
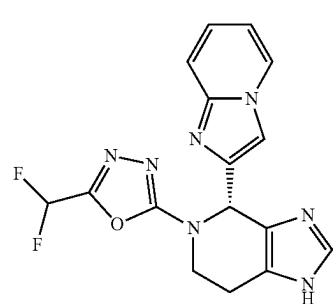
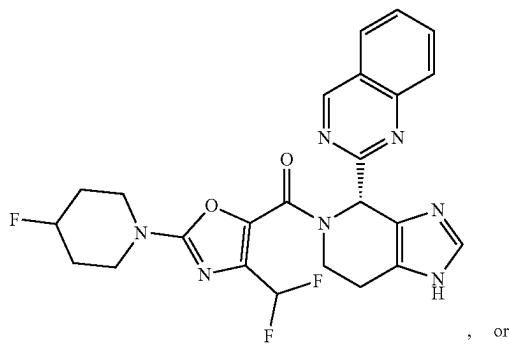
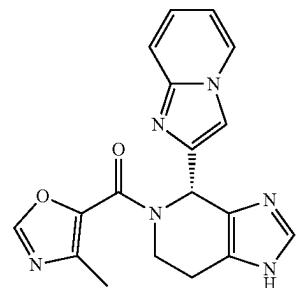
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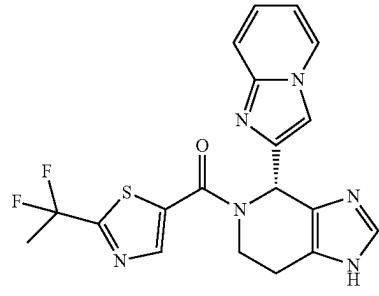
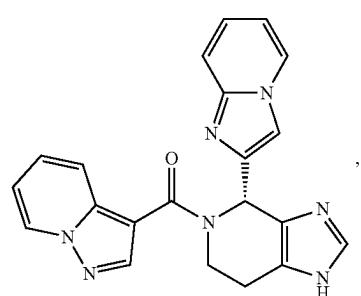
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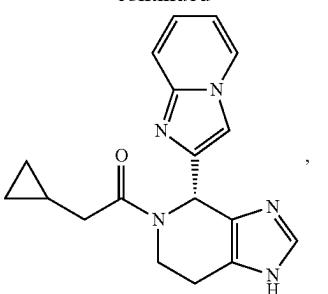
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**86.** (canceled)

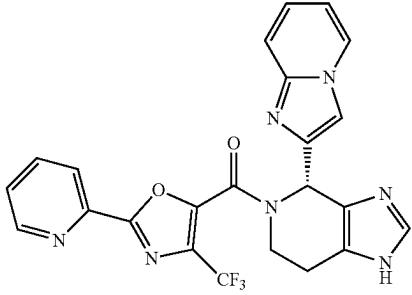
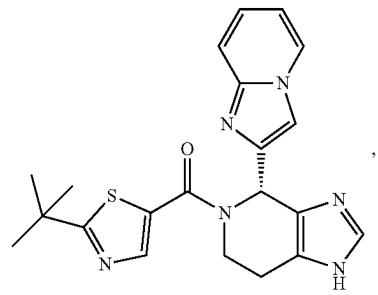
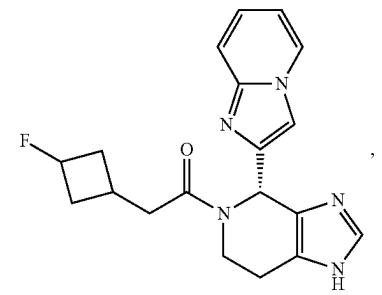
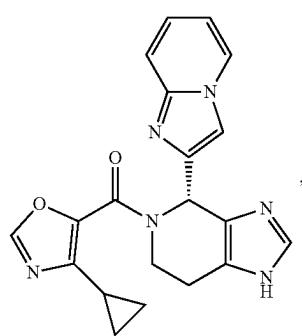
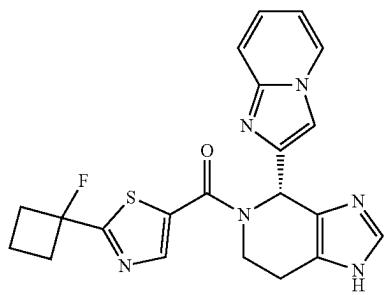
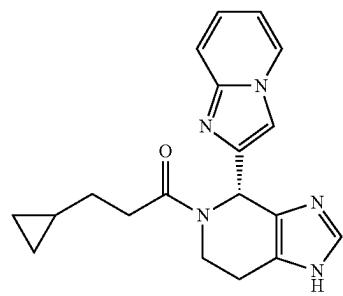
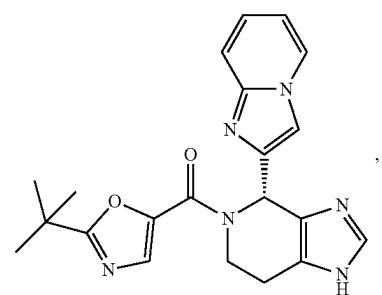
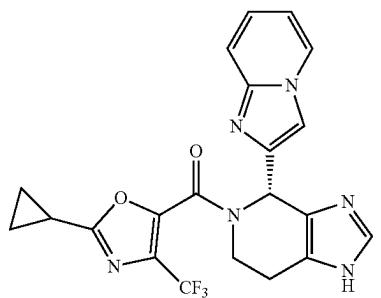
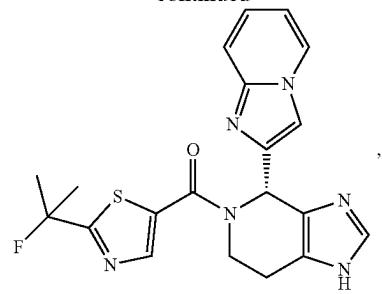
87. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein the compound is selected from the following:



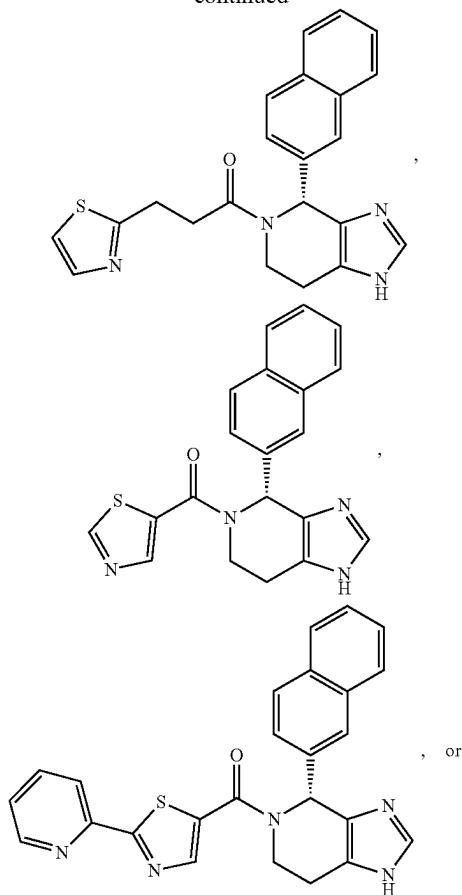
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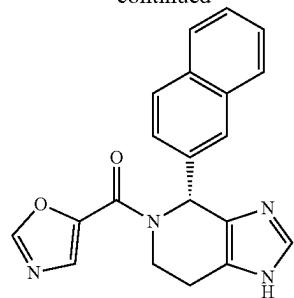
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**88-92.** (canceled)**93.** A pharmaceutical composition comprising a compound of claim 1, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient.**94.** (canceled)**95.** A method for stabilizing a mutant PAH protein, comprising contacting the protein with a compound of claim 1, or a pharmaceutically acceptable salt thereof.**96.** (canceled)**97.** (canceled)**98.** The method of claim 95, wherein the mutant PAH protein contains at least one R408W mutation.**99.** (canceled)**100.** A method for reducing blood phenylalanine concentration in a subject suffering from phenylketonuria comprising administering a compound of claim 1, or a pharmaceutically acceptable salt thereof.**101-104.** (canceled)

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