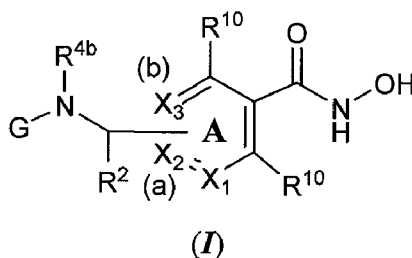




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- (71) **Applicant (for all designated States except US):** **MILLENNIUM PHARMACEUTICALS, INC.** [US/US]; 40 Landsdowne Street, Cambridge, MA 02139 (US).
- (72) **Inventors; and**
- (75) **Inventors/Applicants (for US only):** **BLACKBURN, Christopher** [US/US]; 25 Western Avenue, Natick, MA 01760 (US). **GIGSTAD, Kenneth, M.** [US/US]; 18 Briarwood Drive, Westford, MA 01886 (US). **HARRISON, Sean, J.** [US/US]; 87 Agassiz Avenue, Belmont, MA 02478 (US). **XU, He** [CN/US]; 43 Clover Road, Needham, MA 02494 (US).
- (74) **Agents:** **GRIFFITHS, Sian, L.** et al.; Millennium Pharmaceuticals, Inc., 40 Landsdowne Street, Cambridge, MA 02139 (US).
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(54) **Title:** SUBSTITUTED HYDROXAMIC ACIDS AND USES THEREOF



(57) **Abstract:** This invention provides compounds of formula (I) wherein ring A, X₁, X₂, X₃, R², R^{4b}, R¹⁰, and G have values as described in the specification, useful as inhibitors of HDAC6. The invention also provides pharmaceutical compositions comprising the compounds of the invention, and methods of using the compositions in the treatment of proliferative, inflammatory, infectious, neurological or cardiovascular diseases or disorders.

SUBSTITUTED HYDROXAMIC ACIDS AND USES THEREOF

PRIORITY CLAIM

[0001] This application claims the benefit of U.S. Provisional Patent Application Serial No. 61/339,138, filed February 26, 2010, incorporated by reference in its entirety, and U.S. Provisional Patent Application Serial No. 61/426,314, filed December 22, 2010, incorporated by reference in its entirety.

FIELD OF THE INVENTION

[0002] The invention relates to compounds and methods for the selective inhibition of HDAC6. The present invention relates to compounds useful as HDAC6 inhibitors. The invention also provides pharmaceutical compositions comprising the compounds of the invention and methods of using the compositions in the treatment of various diseases.

BACKGROUND OF THE INVENTION

[0003] Histone deacetylase 6 (HDAC6) is a member of a family of amidohydrolases commonly referred as histone or lysine deacetylases (HDACs or KDACs) as they catalyze the removal of acetyl groups from the ϵ -amino group of lysine residues from proteins. The family includes 18 enzymes which can be divided in 3 main classes based on their sequence homology to yeast enzymes Rpd3 (Class I), Hda1 (Class II) and Sir2 (Class III). A fourth class was defined with the finding of a distinct mammalian enzyme - HDAC11 (reviewed in Yang, *et al.*, *Nature Rev. Mol. Cell Biol.* **2008**, 9:206–218 and in Saunders and Verdin, *Oncogene* **2007**, 26(37):5489–5504). Biochemically, Class I (HDAC1, 2, 3, 8) and Class II (HDAC4, 5, 6, 7, 9, 10) and Class IV (HDAC11) are Zn^{2+} -dependent enzymes, while Class III (SIRT1–7) are dependent on nicotinamide adenine dinucleotide (NAD^+) for activity. Unlike all other HDACs, HDAC6 resides primarily in the cytosol. It has 2 functional catalytic domains and a carboxy-terminal Zn^{2+} -finger ubiquitin binding domain that binds ubiquitinated misfolded proteins (Kawaguchi *et al.*, *Cell* **2003**, 115(6):727–738), ubiquitin (Boyault *et al.*, *EMBO J.* **2006**, 25(14): 3357–3366), as well as ubiquitin-like FAT10 modifier (Kalveram *et al.*, *J. Cell Sci.* **2008**, 121(24):4079–4088). Known substrates of HDAC6 include cytoskeletal proteins α -tubulin and cortactin; β -catenin which forms part of adherens junctions and anchors the actin cytoskeleton; the chaperone Hsp90; and the redox regulatory proteins peroxiredoxin (Prx) I and Prx II (reviewed in Boyault *et al.*, *Oncogene* **2007**, 26(37):5468–5476; Matthias *et al.*, *Cell Cycle* **2008**, 7(1):7–10; Li *et al.*, *J Biol. Chem.* **2008**, 283(19):12686–12690; Parmigiani *et al.*, *Proc. Natl. Acad. Sci. USA* **2009**, 105(28):9633–9638). Thus, HDAC6 mediates a wide range of cellular functions including microtubule-dependent trafficking and signaling, membrane

remodeling and chemotactic motility, involvement in control of cellular adhesion, ubiquitin level sensing, regulation of chaperone levels and activity, and responses to oxidative stress. All of these functions may be important in tumorigenesis, tumor growth and survival as well as metastasis (Simms-Waldrup *et al.*, *Mol. Genet. Metabolism* **2008**, 94(3):283-286; Rodriguez-Gonzalez *et al.*, *Cancer Res.* **2008**, 68(8):2557-2560; Kapoor, *Int. J. Cancer* **2009**, 124:509; Lee *et al.*, *Cancer Res.* **2008**, 68(18):7561-7569). Recent studies have shown HDAC6 to be important in autophagy, an alternative pathway for protein degradation that compensates for deficiencies in the activity of the ubiquitin proteasome system or expression of proteins prone to form aggregates and can be activated following treatment with a proteasome inhibitor (Kawaguchi *et al.*, *Cell* **2003**, 115(6):727-738; Iwata *et al.*, *J. Biol. Chem.* **2005**, 280(48): 40282-40292; Ding *et al.*, *Am. J. Pathol.* **2007**, 171:513-524, Pandey *et al.*, *Nature* **2007**, 447(7146):860-864).

Although the molecular mechanistic details are not completely understood, HDAC6 binds ubiquitinated or ubiquitin-like conjugated misfolded proteins which would otherwise induce proteotoxic stress and then serves as an adaptor protein to traffic the ubiquitinated cargo to the microtubule organizing center using the microtubule network via its known association with dynein motor protein. The resulting perinuclear aggregates, known as aggresomes, are then degraded by fusion with lysosomes in an HDAC6- and cortactin-dependent process which induces remodeling of the actin cytoskeleton proximal to aggresomes (Lee *et al.*, *EMBO J.* **2010**, 29:969-980). In addition, HDAC6 regulates a variety of biological processes dependent on its association with the microtubular network including cellular adhesion (Tran *et al.*, *J. Cell Sci.* **2007**, 120(8):1469-1479) and migration (Zhang *et al.*, *Mol. Cell* **2007**, 27(2):197-213; reviewed in Valenzuela-Fernandez *et al.*, *Trends Cell. Biol.* **2008**, 18(6):291-297), epithelial to mesenchymal transition (Shan *et al.*, *J. Biol. Chem.* **2008**, 283(30):21065-21073), resistance to anoikis (Lee *et al.*, *Cancer Res.* **2008**, 68(18):7561-7569), epithelial growth factor-mediated Wnt signaling via β -catenin deacetylation (Li *et al.*, *J. Biol. Chem.* **2008**, 283(19):12686-12690) and epithelial growth factor receptor stabilization by endocytic trafficking (Lissanu Deribe *et al.*, *Sci. Signal.* **2009**, 2(102):ra84; Gao *et al.*, *J. Biol. Chem.* **2010**, 285:11219-11226); all events that promote oncogenesis and metastasis (Lee *et al.*, *Cancer Res.* **2008**, 68(18):7561-7569). HDAC6 activity is known to be upregulated by Aurora A kinase in cilia formation (Pugacheva *et al.*, *Cell* **2007**, 129(7):1351-1363) and indirectly by farnesyl transferase with which HDAC6 forms a complex with microtubules (Zhou *et al.*, *J. Biol. Chem.* **2009**, 284(15): 9648-9655). Also, HDAC6 is negatively regulated by tau protein (Perez *et al.*, *J. Neurochem.* **2009**, 109(6):1756-1766).

[0004] Diseases in which selective HDAC6 inhibition could have a potential benefit include cancer (reviewed in Simms-Waldrup *et al.*, *Mol. Genet. Metabolism* **2008**, 94(3):283-286 and Rodriguez-Gonzalez *et al.*, *Cancer Res.* **2008**, 68(8):2557-2560), specifically: multiple myeloma (Hideshima *et al.*, *Proc. Natl. Acad. Sci. USA* **2005**, 102(24):8567-8572); lung cancer (Kamemura *et al.*, *Biochem. Biophys.*

Res. Commun. **2008**, 374(1):84-89); ovarian cancer (Bazzaro *et al.*, *Clin. Cancer Res.* **2008**, 14(22):7340-7347); breast cancer (Lee *et al.*, *Cancer Res.* **2008**, 68(18):7561-7569); prostate cancer (Mellado *et al.*, *Clin. Trans. Onco.* **2009**, 11(1):5-10); pancreatic cancer (Nawrocki *et al.*, *Cancer Res.* **2006**, 66(7):3773-3781); renal cancer (Cha *et al.*, *Clin. Cancer Res.* **2009**, 15(3):840-850); and leukemias such as acute myeloid leukemia (AML) (Fiskus *et al.*, *Blood* **2008**, 112(7):2896-2905) and acute lymphoblastic leukemia (ALL) (Rodriguez-Gonzalez *et al.*, *Blood* **2008**, 112(11): Abstract 1923).

[0005] Inhibition of HDAC6 may also have a role in cardiovascular disease, i.e. cardiovascular stress, including pressure overload, chronic ischemia, and infarction-reperfusion injury (Tannous *et al.*, *Circulation* **2008**, 117(24):3070-3078); bacterial infection, including those caused by uropathogenic *Escherichia coli* (Dhakal and Mulve, *J. Biol. Chem.* **2008**, 284(1):446-454); neurological diseases caused by accumulation of intracellular protein aggregates such as Huntington's disease (reviewed in Kazantsev *et al.*, *Nat. Rev. Drug Disc.* **2008**, 7(10):854-868; see also Dompierre *et al.*, *J. Neurosci.* **2007**, 27(13):3571-3583; Kozikowski *et al.*, *J. Med. Chem.* **2007**, 50:3054-3061) or central nervous system trauma caused by tissue injury, oxidative-stress induced neuronal or axonal degeneration (Rivieccio *et al.*, *Proc. Natl. Acad. Sci. USA* **2009**, 106(46):19599-195604); and inflammation, including reduction of pro-inflammatory cytokine IL-1 β (Carta *et al.*, *Blood* **2006**, 108(5):1618-1626), increased expression of the FOXP3 transcription factor, which induces immunosuppressive function of regulatory T-cells resulting in benefits in chronic diseases such as rheumatoid arthritis, psoriasis, multiple sclerosis, lupus and organ transplant rejection (reviewed in Wang *et al.*, *Nat. Rev. Drug Disc.* **2009**, 8(12):969-981).

[0006] Given the complex function of HDAC6, selective inhibitors could have potential utility when used alone or in combination with other chemotherapeutics such as microtubule destabilizing agents (Zhou *et al.*, *J. Biol. Chem.* **2009**, 284(15): 9648-9655); Hsp90 inhibitors (Rao *et al.*, *Blood* **2008**, 112(5):1886-1893); inhibitors of Hsp90 client proteins, including receptor tyrosine kinases such as Her-2 or VEGFR (Bhalla *et al.*, *J. Clin. Oncol.* **2006**, 24(18S): Abstract 1923; Park *et al.*, *Biochem. Biophys. Res. Commun.* **2008**, 368(2):318-322), and signaling kinases such as Bcr-Abl, Akt, mutant FLT-3, c-Raf, and MEK (Bhalla *et al.*, *J. Clin. Oncol.* **2006**, 24(18S): Abstract 1923; Kamemura *et al.*, *Biochem. Biophys. Res. Commun.* **2008**, 374(1):84-89); inhibitors of cell cycle kinases Aurora A and Aurora B (Pugacheva *et al.*, *Cell* **2007**, 129(7):1351-1363; Park *et al.*, *J. Mol. Med.* **2008**, 86(1):117-128; Cha *et al.*, *Clin. Cancer Res.* **2009**, 15(3):840-850); EGFR inhibitors (Lissanu Deribe *et al.*, *Sci. Signal.* **2009**, 2(102): ra84; Gao *et al.*, *J. Biol. Chem.* **2010**, 285:11219-11226) and proteasome inhibitors (Hideshima *et al.*, *Proc. Natl. Acad. Sci. USA* **2005**, 102(24):8567-8572) or other inhibitors of the ubiquitin proteasome system such as ubiquitin and ubiquitin-like activating (E1), conjugation (E2), ligase enzymes (E3, E4) and deubiquitinase enzymes (DUBs) as well as modulators of autophagy and protein homeostasis pathways.

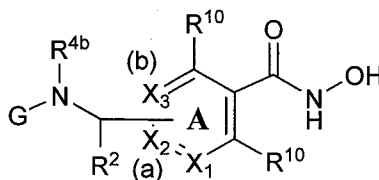
In addition, HDAC6 inhibitors could be combined with radiation therapy (Kim *et al.*, *Radiother. Oncol.* **2009**, 92(1):125-132.

[0007] Clearly, it would be beneficial to provide novel HDAC6 inhibitors that possess good therapeutic properties, especially for the treatment of proliferative diseases or disorders.

DETAILED DESCRIPTION OF THE INVENTION

1. General Description of Compounds of the Invention

[0008] The present invention provides compounds that are effective inhibitors of HDAC6. These compounds are useful for inhibiting HDAC6 activity *in vitro* and *in vivo*, and are especially useful for the treatment of various cell proliferative diseases or disorders. The compounds of the invention are represented by formula (I):



(I);

or a pharmaceutically acceptable salt thereof; wherein:

ring A is an aromatic 6-membered ring connected through one of positions (a) or (b);

X_1 is CR^1 or N;

(i) when ring A is connected through position (a), X_2 is C; and X_3 is CR^1 or N; or

(ii) when ring A is connected through position (b), X_3 is C; and X_2 is CR^1 or N;

each occurrence of R^1 is independently hydrogen, halogen, C_{1-4} alkyl, C_{1-3} fluoroalkyl, $-O-C_{1-3}$ alkyl, $-O-C_{1-3}$ fluoroalkyl, cyano, hydroxy, $-NHC(O)C_{1-3}$ alkyl, $-NHC_{1-3}$ alkyl, $-N(C_{1-3} \text{ alkyl})_2$, $-C(O)NHC_{1-3}$ alkyl, $-NHC(O)NHC_{1-3}$ alkyl, or $-NHS(O)_2C_{1-3}$ alkyl;

each occurrence of R^{10} is independently hydrogen, halogen, hydroxy, $-O-C_{1-3}$ alkyl, or $-O-C_{1-3}$ fluoroalkyl;

R^2 is C_{1-6} aliphatic, C_{1-6} fluoroaliphatic, or unsubstituted or substituted 6-10-membered aryl;

R^{4b} is hydrogen, or C_{1-4} aliphatic;

G is $-R^3$, $-V_1-R^3$, $-V_1-L_1-R^3$, $-L_2-V_1-R^3$, $-L_2-V_2-R^3$, or $-L_1-R^3$;

L_1 is an unsubstituted or substituted C_{1-3} alkylene chain;

L_2 is an unsubstituted or substituted C_{2-3} alkylene chain;

V_1 is $-C(O)-$, $-C(S)-$, $-C(O)-CR^A=CR^A-$, $-C(O)-N(R^{4a})-$, $-C(O)-O-$, or $-S(O)_2-$;

V_2 is $-N(R^{4a})-$, $-N(R^{4a})-C(O)-$, $-SO_2-N(R^{4a})-$, $-N(R^{4a})-SO_2-$, $-O-$, $-S-$, $-S(O)-$,
 $-N(R^{4a})-C(O)-N(R^{4a})-$, $-N(R^{4a})-C(O)-O-$, $-O-C(O)-N(R^{4a})-$, or $-N(R^{4a})-SO_2-N(R^{4a})-$;

R^3 is unsubstituted or substituted C_{1-6} aliphatic, unsubstituted or substituted 3-10-membered cycloaliphatic, unsubstituted or substituted 4-10-membered heterocyclyl having 1-5 heteroatoms independently selected from nitrogen, oxygen, and sulfur, unsubstituted or substituted 6-10-membered aryl, or unsubstituted or substituted 5-10-membered heteroaryl having 1-5 heteroatoms independently selected from nitrogen, oxygen, and sulfur;

each occurrence of R^A is independently hydrogen, fluoro, or unsubstituted or substituted C_{1-4} aliphatic; and

each occurrence of R^{4a} is independently hydrogen, or unsubstituted or substituted C_{1-4} aliphatic.

2. Compounds and Definitions:

[0009] Compounds of this invention include those described generally for formula (I) above, and are further illustrated by the classes, subclasses, and species disclosed herein. As used herein, the following definitions shall apply unless otherwise indicated.

[0010] As described herein, compounds of the invention may be optionally substituted with one or more substituents, such as are illustrated generally above, or as exemplified by particular classes, subclasses, and species of the invention. It will be appreciated that the phrase "optionally substituted" is used interchangeably with the phrase "substituted or unsubstituted." In general, the term "substituted", whether preceded by the term "optionally" or not, means that a hydrogen radical of the designated moiety is replaced with the radical of a specified substituent, provided that the substitution results in a stable or chemically feasible compound. The term "substitutable", when used in reference to a designated atom, means that attached to the atom is a hydrogen radical, which hydrogen atom can be replaced with the radical of a suitable substituent. Unless otherwise indicated, an "optionally substituted" group may have a substituent at each substitutable position of the group, and when more than one position in any given structure may be substituted with more than one substituent selected from a specified group, the substituent may be either the same or different at every position. Combinations of substituents envisioned by this invention are preferably those that result in the formation of stable or chemically feasible compounds.

[0011] A stable compound or chemically feasible compound is one in which the chemical structure is not substantially altered when kept at a temperature from about -80°C to about $+40^{\circ}\text{C}$, in the absence of moisture or other chemically reactive conditions, for at least a week, or a compound which maintains its integrity long enough to be useful for therapeutic or prophylactic administration to a patient.

[0012] The phrase "one or more substituents", as used herein, refers to a number of substituents that equals from one to the maximum number of substituents possible based on the number of available bonding sites, provided that the above conditions of stability and chemical feasibility are met.

[0013] As used herein, the term "independently selected" means that the same or different values may be selected for multiple instances of a given variable in a single compound.

[0014] As used herein, the term "aromatic" includes aryl and heteroaryl groups as described generally below and herein.

[0015] The term "aliphatic" or "aliphatic group", as used herein, means an optionally substituted straight-chain or branched C_{1-12} hydrocarbon, or a cyclic C_{1-12} hydrocarbon which is completely saturated or which contains one or more units of unsaturation, but which is not aromatic (also referred to herein as "carbocycle", "cycloaliphatic", "cycloalkyl", or "cycloalkenyl"). For example, suitable aliphatic groups include optionally substituted linear, branched or cyclic alkyl, alkenyl, alkynyl groups and hybrids thereof, such as (cycloalkyl)alkyl, (cycloalkenyl)alkyl, or (cycloalkyl)alkenyl. Unless otherwise specified, in various embodiments, aliphatic groups have 1-12, 1-10, 1-8, 1-6, 1-4, 1-3, or 1-2 carbon atoms.

[0016] The term "alkyl", used alone or as part of a larger moiety, refers to an optionally substituted straight or branched chain hydrocarbon group having 1-12, 1-10, 1-8, 1-6, 1-4, 1-3, or 1-2 carbon atoms.

[0017] The term "alkenyl", used alone or as part of a larger moiety, refers to an optionally substituted straight or branched chain hydrocarbon group having at least one double bond and having 2-12, 2-10, 2-8, 2-6, 2-4, or 2-3 carbon atoms.

[0018] The term "alkynyl", used alone or as part of a larger moiety, refers to an optionally substituted straight or branched chain hydrocarbon group having at least one triple bond and having 2-12, 2-10, 2-8, 2-6, 2-4, or 2-3 carbon atoms.

[0019] The terms "cycloaliphatic", "carbocycle", "carbocyclyl", "carbocyclo", or "carbocyclic", used alone or as part of a larger moiety, refer to an optionally substituted saturated or partially unsaturated cyclic aliphatic ring system having from 3 to about 14 ring carbon atoms. In some embodiments, the cycloaliphatic group is an optionally substituted monocyclic hydrocarbon having 3-8 or 3-6 ring carbon atoms. Cycloaliphatic groups include, without limitation, optionally substituted cyclopropyl, cyclobutyl, cyclopentyl, cyclopentenyl, cyclohexyl, cyclohexenyl, cycloheptyl, cycloheptenyl, cyclooctyl, cyclooctenyl, or cyclooctadienyl. The terms "cycloaliphatic", "carbocycle", "carbocyclyl", "carbocyclo",

or “carbocyclic” also include optionally substituted bridged or fused bicyclic rings having 6-12, 6-10, or 6-8 ring carbon atoms, wherein any individual ring in the bicyclic system has 3-8 ring carbon atoms.

[0020] The term “cycloalkyl” refers to an optionally substituted saturated ring system of about 3 to about 10 ring carbon atoms. Exemplary monocyclic cycloalkyl rings include cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl.

[0021] The term “cycloalkenyl” refers to an optionally substituted non-aromatic monocyclic or multicyclic ring system containing at least one carbon-carbon double bond and having about 3 to about 10 carbon atoms. Exemplary monocyclic cycloalkenyl rings include cyclopentyl, cyclohexenyl, and cycloheptenyl.

[0022] The terms “haloaliphatic”, “haloalkyl”, “haloalkenyl” and “haloalkoxy” refer to an aliphatic, alkyl, alkenyl or alkoxy group, as the case may be, which is substituted with one or more halogen atoms. As used herein, the term “halogen” or “halo” means F, Cl, Br, or I. The term “fluoroaliphatic” refers to a haloaliphatic wherein the halogen is fluoro, including perfluorinated aliphatic groups. Examples of fluoroaliphatic groups include, without limitation, fluoromethyl, difluoromethyl, trifluoromethyl, 2-fluoroethyl, 2,2,2-trifluoroethyl, 1,1,2-trifluoroethyl, 1,2,2-trifluoroethyl, and pentafluoroethyl.

[0023] The term “heteroatom” refers to one or more of oxygen, sulfur, nitrogen, phosphorus, or silicon (including, any oxidized form of nitrogen, sulfur, phosphorus, or silicon; the quaternized form of any basic nitrogen or; a substitutable nitrogen of a heterocyclic ring, for example N (as in 3,4-dihydro-2*H*-pyrrolyl), NH (as in pyrrolidiny) or NR⁺ (as in N-substituted pyrrolidiny)).

[0024] The terms “aryl” and “ar-”, used alone or as part of a larger moiety, e.g., “aralkyl”, “aralkoxy”, or “aryloxyalkyl”, refer to an optionally substituted C₆₋₁₄aromatic hydrocarbon moiety comprising one to three aromatic rings. Preferably, the aryl group is a C₆₋₁₀aryl group. Aryl groups include, without limitation, optionally substituted phenyl, naphthyl, or anthracenyl. The terms “aryl” and “ar-”, as used herein, also include groups in which an aryl ring is fused to one or more cycloaliphatic rings to form an optionally substituted cyclic structure such as a tetrahydronaphthyl, indenyl, or indanyl ring. The term “aryl” may be used interchangeably with the terms “aryl group”, “aryl ring”, and “aromatic ring”.

[0025] An “aralkyl” or “arylalkyl” group comprises an aryl group covalently attached to an alkyl group, either of which independently is optionally substituted. Preferably, the aralkyl group is C₆₋₁₀arylC₁₋₆alkyl, including, without limitation, benzyl, phenethyl, and naphthylmethyl.

[0026] The terms “heteroaryl” and “heteroar-”, used alone or as part of a larger moiety, e.g., “heteroaralkyl”, or “heteroaralkoxy”, refer to groups having 5 to 14 ring atoms, preferably 5, 6, 9, or 10 ring atoms; having 6, 10, or 14 π electrons shared in a cyclic array; and having, in addition to carbon atoms, from one to five heteroatoms. A heteroaryl group may be mono-, bi-, tri-, or polycyclic, preferably

mono-, bi-, or tricyclic, more preferably mono- or bicyclic. The term "heteroatom" refers to nitrogen, oxygen, or sulfur, and includes any oxidized form of nitrogen or sulfur, and any quaternized form of a basic nitrogen. For example, a nitrogen atom of a heteroaryl may be a basic nitrogen atom and may also be optionally oxidized to the corresponding N-oxide. When a heteroaryl is substituted by a hydroxy group, it also includes its corresponding tautomer. The terms "heteroaryl" and "heteroar-", as used herein, also include groups in which a heteroaromatic ring is fused to one or more aryl, cycloaliphatic, or heterocycloaliphatic rings. Nonlimiting examples of heteroaryl groups include thienyl, furanyl, pyrrolyl, imidazolyl, pyrazolyl, triazolyl, tetrazolyl, oxazolyl, isoxazolyl, oxadiazolyl, thiazolyl, isothiazolyl, thiadiazolyl, pyridyl, pyridazinyl, pyrimidinyl, pyrazinyl, indoliziny, purinyl, naphthyridinyl, pteridinyl, indolyl, isoindolyl, benzothienyl, benzofuranyl, dibenzofuranyl, indazolyl, benzimidazolyl, benzthiazolyl, quinolyl, isoquinolyl, cinnolinyl, phthalazinyl, quinazolinyl, quinoxalinyl, 4*H*-quinoliziny, carbazolyl, acridinyl, phenazinyl, phenothiazinyl, phenoxazinyl, tetrahydroquinolinyl, tetrahydroisoquinolinyl, and pyrido[2,3-*b*]-1,4-oxazin-3(4*H*)-one. The term "heteroaryl" may be used interchangeably with the terms "heteroaryl ring", "heteroaryl group", or "heteroaromatic", any of which terms include rings that are optionally substituted. The term "heteroaralkyl" refers to an alkyl group substituted by a heteroaryl, wherein the alkyl and heteroaryl portions independently are optionally substituted.

[0027] As used herein, the terms "heterocycle", "heterocyclyl", "heterocyclic radical", and "heterocyclic ring" are used interchangeably and refer to a stable 3- to 8-membered monocyclic or 7-10-membered bicyclic heterocyclic moiety that is either saturated or partially unsaturated, and having, in addition to carbon atoms, one or more, preferably one to four, heteroatoms, as defined above. When used in reference to a ring atom of a heterocycle, the term "nitrogen" includes a substituted nitrogen. As an example, in a saturated or partially unsaturated ring having 0-3 heteroatoms selected from oxygen, sulfur or nitrogen, the nitrogen may be N (as in 3,4-dihydro-2*H*-pyrrolyl), NH (as in pyrrolidinyl), or NR⁺ (as in *N*-substituted pyrrolidinyl).

[0028] A heterocyclic ring can be attached to its pendant group at any heteroatom or carbon atom that results in a stable structure and any of the ring atoms can be optionally substituted. Examples of such saturated or partially unsaturated heterocyclic radicals include, without limitation, tetrahydrofuranyl, tetrahydrothienyl, piperidinyl, decahydroquinolinyl, oxazolidinyl, piperazinyl, dioxanyl, dioxolanyl, diazepinyl, oxazepinyl, thiazepinyl, morpholinyl, and thiamorpholinyl. A heterocyclyl group may be mono-, bi-, tri-, or polycyclic, preferably mono-, bi-, or tricyclic, more preferably mono- or bicyclic. The term "heterocyclylalkyl" refers to an alkyl group substituted by a heterocyclyl, wherein the alkyl and heterocyclyl portions independently are optionally substituted. Additionally, a heterocyclic ring also includes groups in which the heterocyclic ring is fused to one or more aryl rings.

[0029] As used herein, the term “partially unsaturated” refers to a ring moiety that includes at least one double or triple bond between ring atoms. The term “partially unsaturated” is intended to encompass rings having multiple sites of unsaturation, but is not intended to include aromatic (e.g., aryl or heteroaryl) moieties, as herein defined.

[0030] The term “alkylene” refers to a bivalent alkyl group. An “alkylene chain” is a polymethylene group, i.e., $-(CH_2)_n-$, wherein n is a positive integer, preferably from 1 to 6, from 1 to 4, from 1 to 3, from 1 to 2, or from 2 to 3. An optionally substituted alkylene chain is a polymethylene group in which one or more methylene hydrogen atoms is optionally replaced with a substituent. Suitable substituents include those described below for a substituted aliphatic group and also include those described in the specification herein. It will be appreciated that two substituents of the alkylene group may be taken together to form a ring system. In certain embodiments, two substituents can be taken together to form a 3-7-membered ring. The substituents can be on the same or different atoms.

[0031] An alkylene chain also can be optionally interrupted by a functional group. An alkylene chain is “interrupted” by a functional group when an internal methylene unit is interrupted by the functional group. Examples of suitable “interrupting functional groups” are described in the specification and claims herein.

[0032] For purposes of clarity, all bivalent groups described herein, including, e.g., the alkylene chain linkers described above, are intended to be read from left to right, with a corresponding left-to-right reading of the formula or structure in which the variable appears.

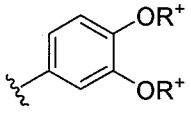
[0033] An aryl (including aralkyl, aralkoxy, aryloxyalkyl and the like) or heteroaryl (including heteroaralkyl and heteroarylalkoxy and the like) group may contain one or more substituents and thus may be “optionally substituted”. In addition to the substituents defined above and herein, suitable substituents on the unsaturated carbon atom of an aryl or heteroaryl group also include and are generally selected from -halo, $-NO_2$, $-CN$, $-R^+$, $-C(R^+)=C(R^+)_2$, $-C\equiv C-R^+$, $-OR^+$, $-SR^0$, $-S(O)R^0$, $-SO_2R^0$, $-SO_3R^+$, $-SO_2N(R^+)_2$, $-N(R^+)_2$, $-NR^+C(O)R^+$, $-NR^+C(S)R^+$, $-NR^+C(O)N(R^+)_2$, $-NR^+C(S)N(R^+)_2$, $-N(R^+)C(=NR^+)-N(R^+)_2$, $-N(R^+)C(=NR^+)-R^0$, $-NR^+CO_2R^+$, $-NR^+SO_2R^0$, $-NR^+SO_2N(R^+)_2$, $-O-C(O)R^+$, $-O-CO_2R^+$, $-OC(O)N(R^+)_2$, $-C(O)R^+$, $-C(S)R^0$, $-CO_2R^+$, $-C(O)-C(O)R^+$, $-C(O)N(R^+)_2$, $-C(S)N(R^+)_2$, $-C(O)N(R^+)-OR^+$, $-C(O)N(R^+)C(=NR^+)-N(R^+)_2$, $-N(R^+)C(=NR^+)-N(R^+)-C(O)R^+$, $-C(=NR^+)-N(R^+)_2$, $-C(=NR^+)-OR^+$, $-N(R^+)-N(R^+)_2$, $-C(=NR^+)-N(R^+)-OR^+$, $-C(R^0)=N-OR^+$, $-P(O)(R^+)_2$, $-P(O)(OR^+)_2$, $-O-P(O)-OR^+$, and $-P(O)(NR^+)-N(R^+)_2$, wherein R^+ , independently, is hydrogen or an optionally substituted aliphatic, aryl, heteroaryl, cycloaliphatic, or heterocyclyl group, or two independent occurrences of R^+ are taken together with their intervening atom(s) to form an optionally substituted 5-7-membered aryl, heteroaryl, cycloaliphatic, or heterocyclyl ring. Each R^0 is an optionally substituted aliphatic, aryl, heteroaryl, cycloaliphatic, or heterocyclyl group.

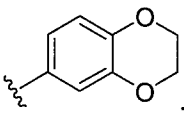
[0034] An aliphatic or heteroaliphatic group, or a non-aromatic carbocyclic or heterocyclic ring may contain one or more substituents and thus may be “optionally substituted”. Unless otherwise defined above and herein, suitable substituents on the saturated carbon of an aliphatic or heteroaliphatic group, or of a non-aromatic carbocyclic or heterocyclic ring are selected from those listed above for the unsaturated carbon of an aryl or heteroaryl group and additionally include the following: $=O$, $=S$, $=C(R^*)_2$, $=N-N(R^*)_2$, $=N-OR^*$, $=N-NHC(O)R^*$, $=N-NHCO_2R^o$, $=N-NHSO_2R^o$ or $=N-R^*$ where R^o is defined above, and each R^* is independently selected from hydrogen or an optionally substituted C_{1-6} aliphatic group.

[0035] In addition to the substituents defined above and herein, optional substituents on the nitrogen of a non-aromatic heterocyclic ring also include and are generally selected from $-R^+$, $-N(R^+)_2$, $-C(O)R^+$, $-C(O)OR^+$, $-C(O)C(O)R^+$, $-C(O)CH_2C(O)R^+$, $-S(O)_2R^+$, $-S(O)_2N(R^+)_2$, $-C(S)N(R^+)_2$, $-C(=NH)-N(R^+)_2$, or $-N(R^+)S(O)_2R^+$; wherein each R^+ is defined above. A ring nitrogen atom of a heteroaryl or non-aromatic heterocyclic ring also may be oxidized to form the corresponding N-hydroxy or N-oxide compound. A nonlimiting example of such a heteroaryl having an oxidized ring nitrogen atom is N-oxidopyridyl.

[0036] As detailed above, in some embodiments, two independent occurrences of R^+ (or any other variable similarly defined in the specification and claims herein), are taken together with their intervening atom(s) to form a monocyclic or bicyclic ring selected from 3–13-membered cycloaliphatic, 3–12-membered heterocyclyl having 1–5 heteroatoms independently selected from nitrogen, oxygen, or sulfur, 6–10-membered aryl, or 5–10-membered heteroaryl having 1–5 heteroatoms independently selected from nitrogen, oxygen, or sulfur.

[0037] Exemplary rings that are formed when two independent occurrences of R^+ (or any other variable similarly defined in the specification and claims herein), are taken together with their intervening atom(s) include, but are not limited to the following: a) two independent occurrences of R^+ (or any other variable similarly defined in the specification or claims herein) that are bound to the same atom and are taken together with that atom to form a ring, for example, $N(R^+)_2$, where both occurrences of R^+ are taken together with the nitrogen atom to form a piperidin-1-yl, piperazin-1-yl, or morpholin-4-yl group; and b) two independent occurrences of R^+ (or any other variable similarly defined in the specification or claims herein) that are bound to different atoms and are taken together with both of those atoms to form a ring,

for example where a phenyl group is substituted with two occurrences of OR^+ , these two occurrences of R^+ are taken together with the oxygen atoms to which they are bound to form a fused 6-

membered oxygen containing ring: . It will be appreciated that a variety of other rings (e.g., spiro and bridged rings) can be formed when two independent occurrences of R^+ (or any other

variable similarly defined in the specification and claims herein) are taken together with their intervening atom(s) and that the examples detailed above are not intended to be limiting.

[0038] Unless otherwise stated, structures depicted herein are also meant to include all isomeric (e.g., enantiomeric, diastereomeric, and geometric (or conformational)) forms of the structure; for example, the R and S configurations for each asymmetric center, (Z) and (E) double bond isomers, and (Z) and (E) conformational isomers. Therefore, single stereochemical isomers as well as enantiomeric, diastereomeric, and geometric (or conformational) mixtures of the present compounds are within the scope of the invention. Unless otherwise stated, all tautomeric forms of the compounds of the invention are within the scope of the invention. Additionally, unless otherwise stated, structures depicted herein are also meant to include compounds that differ only in the presence of one or more isotopically enriched atoms. For example, compounds having the present structures except for the replacement of hydrogen by deuterium or tritium, or the replacement of a carbon by a ^{13}C - or ^{14}C -enriched carbon are within the scope of this invention. Such compounds are useful, for example, as analytical tools or probes in biological assays.

[0039] The terms "stereoisomer", "enantiomer", "diastereomer", "epimer", and "chiral center", are used herein in accordance with the meaning each is given in ordinary usage by those of ordinary skill in the art. Thus, stereoisomers are compounds that have the same atomic connectivity, but differ in the spatial arrangement of the atoms. Enantiomers are stereoisomers that have a mirror image relationship, that is, the stereochemical configuration at all corresponding chiral centers is opposite. Diastereomers are stereoisomers having more than one chiral center, which differ from one another in that the stereochemical configuration of at least one, but not all, of the corresponding chiral centers is opposite. Epimers are diastereomers that differ in stereochemical configuration at only one chiral center.

[0040] It is to be understood that, when a disclosed compound has at least one chiral center, the present invention encompasses one enantiomer of the compound, substantially free from the corresponding optical isomer, a racemic mixture of both optical isomers of the compound, and mixtures enriched in one enantiomer relative to its corresponding optical isomer. When a mixture is enriched in one enantiomer relative to its optical isomer, the mixture contains, for example, an enantiomeric excess of at least 50%, 75%, 90%, 95%, 99%, or 99.5%.

[0041] The enantiomers of the present invention may be resolved by methods known to those skilled in the art, for example by formation of diastereoisomeric salts which may be separated, for example, by crystallization; formation of diastereoisomeric derivatives or complexes which may be separated, for example, by crystallization, gas-liquid or liquid chromatography; selective reaction of one enantiomer with an enantiomer-specific reagent, for example enzymatic esterification; or gas-liquid or liquid chromatography in a chiral environment, for example on a chiral support for example silica with a bound

chiral ligand or in the presence of a chiral solvent. Where the desired enantiomer is converted into another chemical entity by one of the separation procedures described above, a further step is required to liberate the desired enantiomeric form. Alternatively, specific enantiomers may be synthesized by asymmetric synthesis using optically active reagents, substrates, catalysts or solvents, or by converting one enantiomer into the other by asymmetric transformation.

[0042] When a disclosed compound has at least two chiral centers, the present invention encompasses a diastereomer substantially free of other diastereomers, an enantiomeric pair of diastereomers substantially free of other stereoisomers, mixtures of diastereomers, mixtures of enantiomeric pairs of diastereomers, mixtures of diastereomers in which one diastereomer is enriched relative to the other diastereomer(s), and mixtures of enantiomeric pairs of diastereomers in which one enantiomeric pair of diastereomers is enriched relative to the other stereoisomers. When a mixture is enriched in one diastereomer or enantiomeric pair of diastereomers relative to the other stereoisomers, the mixture is enriched with the depicted or referenced diastereomer or enantiomeric pair of diastereomers relative to other stereoisomers for the compound, for example, by a molar excess of at least 50%, 75%, 90%, 95%, 99%, or 99.5%.

[0043] As used herein, the term "diastereomeric ratio" refers to the ratio between diastereomers which differ in the stereochemical configuration at one chiral center, relative to a second chiral center in the same molecule. By way of example, a chemical structure with two chiral centers provides four possible stereoisomers: R^*R , R^*S , S^*R , and S^*S , wherein the asterisk denotes the corresponding chiral center in each stereoisomer. The diastereomeric ratio for such a mixture of stereoisomers is the ratio of one diastereomer and its enantiomer to the other diastereomer and its enantiomer = $(R^*R + S^*S) : (R^*S + S^*R)$.

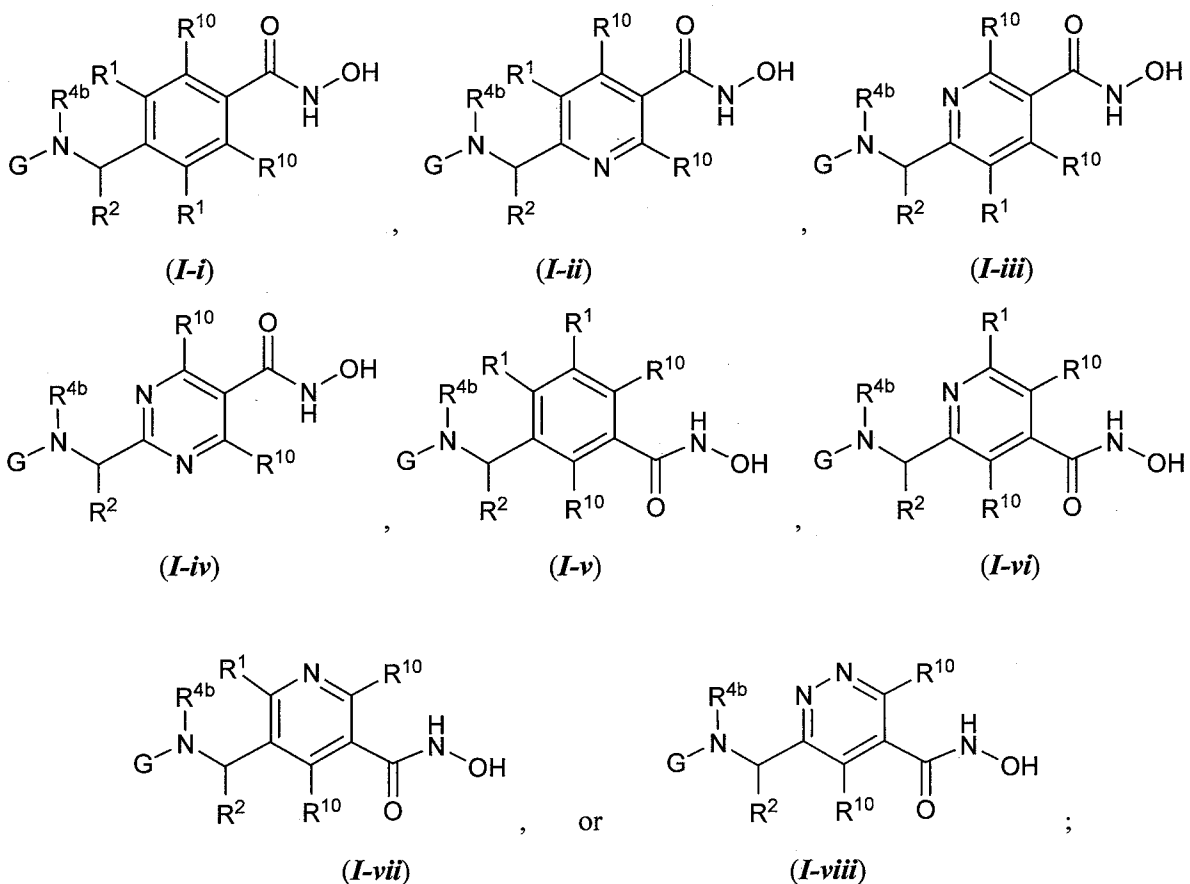
[0044] One of ordinary skill in the art will recognize that additional stereoisomers are possible when the molecule has more than two chiral centers. For purposes of the present invention, the term "diastereomeric ratio" has identical meaning in reference to compounds with multiple chiral centers as it does in reference to compounds having two chiral centers. Thus, the term "diastereomeric ratio" refers to the ratio of all compounds having R^*R or S^*S configuration at the specified chiral centers to all compounds having R^*S or S^*R configuration at the specified chiral centers. For convenience, this ratio is referred to herein as the diastereomeric ratio at the asterisked carbon, relative to the second specified chiral center.

[0045] The diastereomeric ratio can be measured by any analytical method suitable for distinguishing between diastereomeric compounds having different relative stereochemical configurations at the specified chiral centers. Such methods include, without limitation, nuclear magnetic resonance (NMR), gas chromatography (GC), and high performance liquid chromatography (HPLC) methods.

[0046] The diastereoisomeric pairs may be separated by methods known to those skilled in the art, for example chromatography or crystallization and the individual enantiomers within each pair may be separated as described above. Specific procedures for chromatographically separating diastereomeric pairs of precursors used in the preparation of compounds disclosed herein are provided the examples herein.

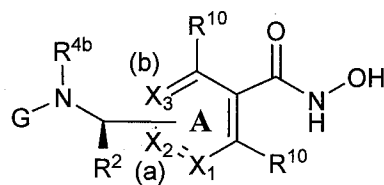
3. Description of Exemplary Compounds:

[0047] In some embodiments, the compound of formula (I) is represented by:



wherein R^1 , R^{10} , R^2 , R^{4b} , and G have the values described herein. In certain embodiments, the compound of formula (I) is represented by formulas (I-i) or (I-v), wherein R^1 , R^{10} , R^2 , R^{4b} , and G have the values described herein.

[0048] In some embodiments, the compound of formula (I) is represented by formula (II-a):



(II-a);

wherein:

ring A is an aromatic 6-membered ring connected through one of positions (a) or (b);

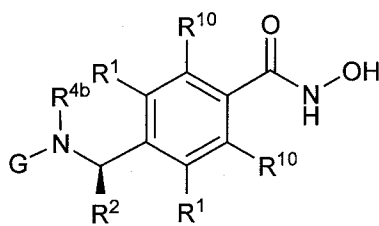
X₁ is CR¹ or N;

(i) when ring A is connected through position (a), X₂ is C; and X₃ is CR¹ or N; or

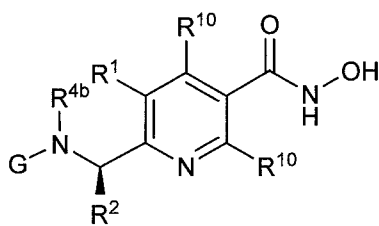
(ii) when ring A is connected through position (b), X₃ is C; and X₂ is CR¹ or N;

and R¹, R¹⁰, R², R^{4b}, and G have the values described herein.

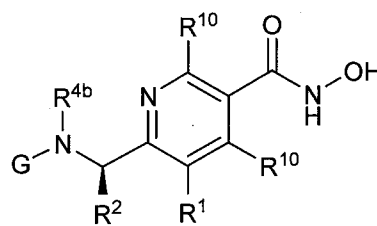
[0049] In some embodiments, the compound of formula (II-a) is represented by:



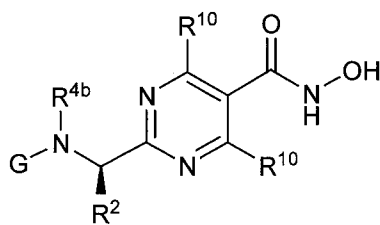
(II-a-i)



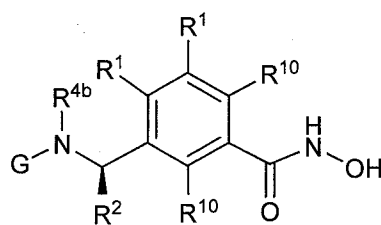
(II-a-ii)



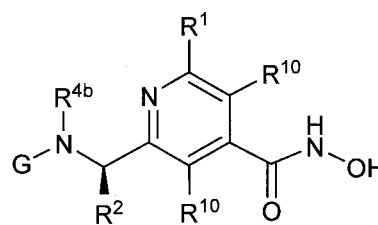
(II-a-iii)



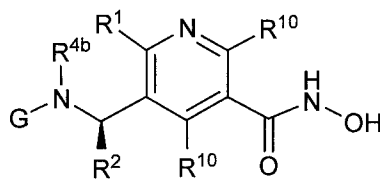
(II-a-iv)



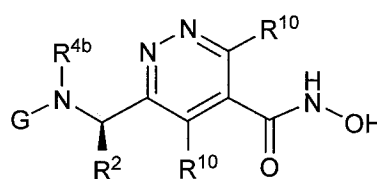
(II-a-v)



(II-a-vi)



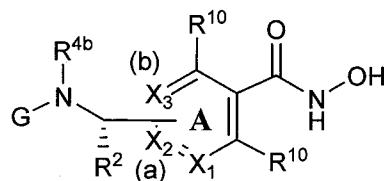
(II-a-vii)



(II-a-viii)

wherein R^1 , R^{10} , R^2 , R^{4b} , and G have the values described herein. In certain embodiments, the compound of formula (II-a) is represented by formulas (II-a-i) or (II-a-v), wherein R^1 , R^{10} , R^2 , R^{4b} , and G have the values described herein.

[0050] In some embodiments, the compound of formula (I) is represented by formula (II-b):



(II-b);

wherein:

ring A is an aromatic 6-membered ring connected through one of positions (a) or (b);

wherein:

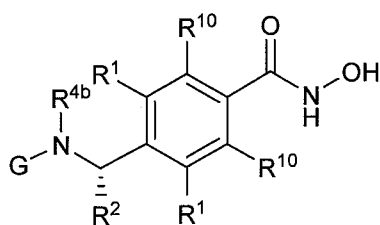
X_1 is CR^1 or N;

(i) when ring A is connected through position (a), X_2 is C; and X_3 is CR^1 or N; or

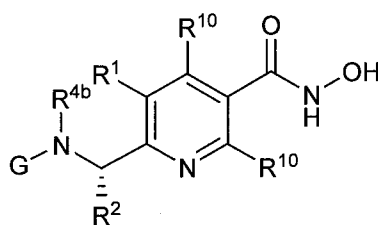
(ii) when ring A is connected through position (b), X_3 is C; and X_2 is CR^1 or N;

and R^1 , R^{10} , R^2 , R^{4b} , and G have the values described herein.

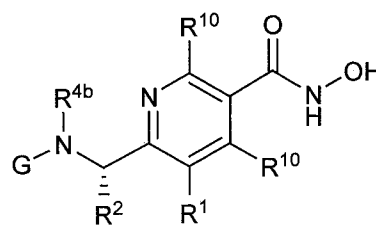
[0051] In some embodiments, the compound of formula (II-b) is represented by:



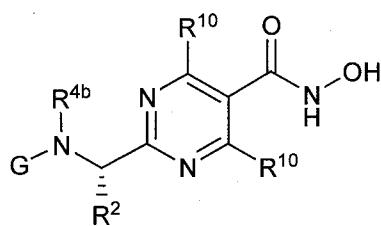
(II-b-i)



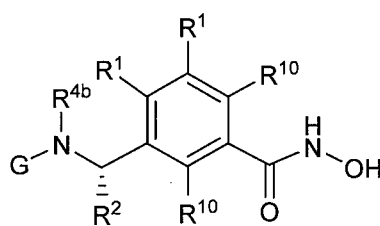
(II-b-ii)



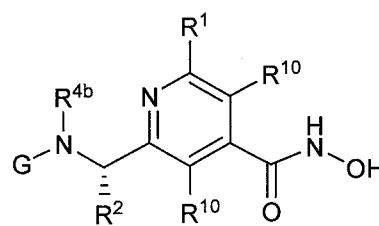
(II-b-iii)



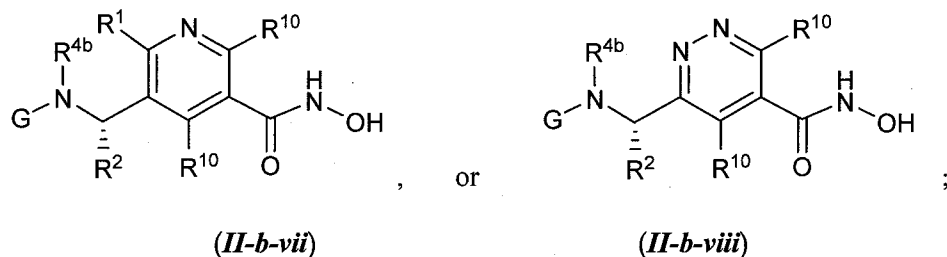
(II-b-iv)



(II-b-v)

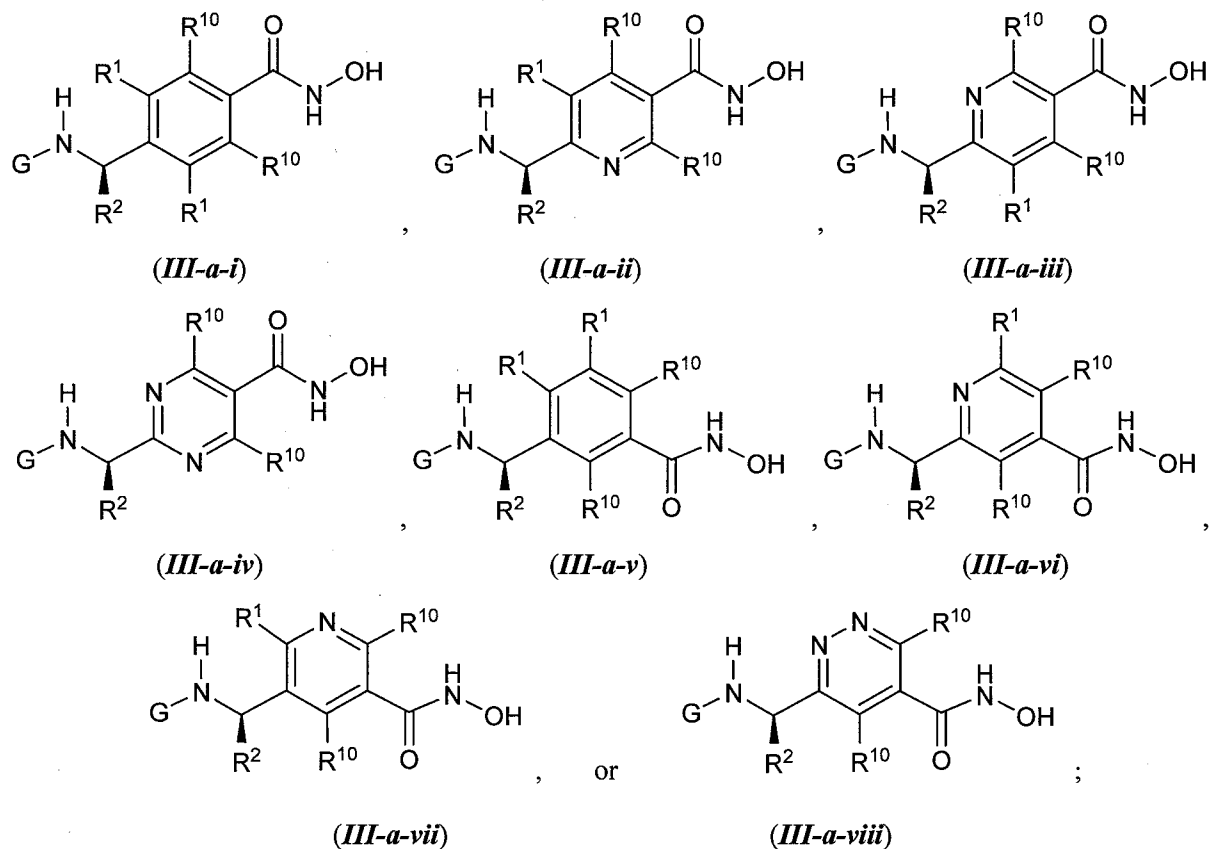


(II-b-vi)



wherein R^1 , R^{10} , R^2 , R^{4b} , and G have the values described herein. In certain embodiments, the compound of formula (II) is represented by formulas (II-b-i) or (II-b-v), wherein R^1 , R^{10} , R^2 , R^{4b} , and G have the values described herein.

[0052] In some embodiments, the compound of formula (I) is represented by:



wherein R^1 , R^{10} , R^2 , and G have the values described herein. In certain embodiments, the compound of formula (I) is represented by formulas (III-a-i) or (III-a-v), wherein R^1 , R^{10} , R^2 , and G have the values described herein.

[0053] The values described below for each variable are with respect to any of formulas (I), (II), (III), (IV), (V), (VI), or their sub-formulas as described herein.

[0054] Each occurrence of the variable R^1 is independently hydrogen, halogen, C_{1-4} alkyl, C_{1-3} fluoroalkyl, $-O-C_{1-3}$ alkyl, $-O-C_{1-3}$ fluoroalkyl, cyano, hydroxy, $-NHC(O)C_{1-3}$ alkyl, $-NHC_{1-3}$ alkyl, $-N(C_{1-3} \text{ alkyl})_2$, $-C(O)NHC_{1-3}$ alkyl, $-NHC(O)NHC_{1-3}$ alkyl, or $-NHS(O)_2C_{1-3}$ alkyl. In some embodiments, each occurrence of R^1 is independently hydrogen, chloro, fluoro, C_{1-4} alkyl, $-O-C_{1-3}$ alkyl, trifluoromethyl, hydroxy, or cyano. In certain embodiments, each occurrence of R^1 is independently hydrogen, chloro, fluoro, hydroxy, methoxy, ethoxy, n-propoxy, isopropoxy, cyano, trifluoromethyl, methyl, ethyl, isopropyl, n-propyl, or tert-butyl. In certain embodiments, each occurrence of R^1 is independently hydrogen, chloro, fluoro, hydroxy, trifluoromethyl, or methyl. In certain embodiments, R^1 is hydrogen.

[0055] Each occurrence of the variable R^{10} is independently hydrogen, halogen, hydroxy, $-O-C_{1-3}$ alkyl, or $-O-C_{1-3}$ fluoroalkyl. In some embodiments, R^{10} is hydrogen, chloro, fluoro, hydroxy, methoxy, or ethoxy. In some embodiments, R^{10} is hydrogen.

[0056] The variable R^2 is C_{1-6} aliphatic, C_{1-6} fluoroaliphatic, or unsubstituted or substituted 6-10-membered aryl. In some embodiments, R^2 is methyl, ethyl, isopropyl, n-propyl, n-butyl, isobutyl, sec-butyl, tert-butyl, pentyl, hexyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, trifluoromethyl, or phenyl. In certain embodiments, R^2 is methyl, ethyl, isopropyl, n-propyl, trifluoromethyl, tert-butyl, cyclopropyl, or phenyl. In certain embodiments, R^2 is methyl, ethyl, isopropyl, or n-propyl.

[0057] The variable R^{4b} is hydrogen, or C_{1-4} aliphatic. In some embodiments, R^{4b} is hydrogen.

[0058] The variable G is $-R^3$, $-V_1-R^3$, $-V_1-L_1-R^3$, $-L_2-V_1-R^3$, $-L_2-V_2-R^3$, or $-L_1-R^3$, wherein L_1 , L_2 , V_1 , V_2 , and R^3 have the values described herein. In some embodiments, G is $-V_1-R^3$, or $-V_1-L_1-R^3$, wherein L_1 , V_1 , and R^3 have the values described herein. In certain embodiments, G is $-V_1-R^3$, wherein V_1 and R^3 have the values described herein.

[0059] The variable L_1 is an unsubstituted or substituted C_{1-3} alkylene chain. In some embodiments, L_1 is $-CH_2-$, $-CH_2CH_2-$, or $-CH_2CH_2CH_2-$. In certain embodiments, L_1 is $-CH_2-$.

[0060] The variable L_2 is an unsubstituted or substituted C_{2-3} alkylene chain. In some embodiments, L_2 is $-CH_2CH_2-$ or $-CH_2CH_2CH_2-$.

[0061] The variable V_1 is $-C(O)-$, $-C(S)-$, $-C(O)-CR^A=CR^A-$, $-C(O)-N(R^{4a})-$, $-C(O)-O-$, or $-S(O)_2-$, wherein R^A and R^{4a} have the values described herein. In some embodiments, V_1 is $-C(O)-$, $-C(O)-N(R^{4a})-$, or $-S(O)_2-$, wherein R^{4a} has the values described herein. In certain embodiments, V_1 is $-C(O)-$, $-C(O)-NH-$, or $-S(O)_2-$. In other certain embodiments, V_1 is $-C(O)-$.

[0062] Each occurrence of the variable R^A is independently hydrogen, halo, or an optionally substituted C_{1-4} aliphatic group. In some embodiments, each occurrence of R^A is independently hydrogen, fluoro or methyl. In certain embodiments, each occurrence of R^A is hydrogen.

[0063] Each occurrence of the variable R^{4a} is independently hydrogen, or unsubstituted or substituted C_{1-4} aliphatic. In certain embodiments, R^{4a} is hydrogen.

[0064] The variable V_2 is $-N(R^{4a})-$, $-N(R^{4a})-C(O)-$, $-SO_2-N(R^{4a})-$, $-N(R^{4a})-SO_2-$, $-O-$, $-S-$, $-S(O)-$, $-N(R^{4a})-C(O)-N(R^{4a})-$, $-N(R^{4a})-C(O)-O-$, $-O-C(O)-N(R^{4a})-$, or $-N(R^{4a})-SO_2-N(R^{4a})-$, wherein R^{4a} has the values described herein. In some embodiments, V_2 is $-N(R^{4a})-$, $-NR^{4a}-C(O)-$, $-SO_2-N(R^{4a})-$, $-N(R^{4a})-SO_2-$, $-O-$, or $-S-$, wherein R^{4a} has the values described herein. In certain embodiments, V_2 is $-N(R^{4a})-$, $-O-$, or $-S-$, wherein R^{4a} has the values described herein. In certain embodiments, V_2 is $-NH-$, or $-O-$.

[0065] The variable R^3 is unsubstituted or substituted C_{1-6} aliphatic, unsubstituted or substituted 3-10-membered cycloaliphatic, unsubstituted or substituted 4-10-membered heterocyclyl having 1-5 heteroatoms independently selected from nitrogen, oxygen, and sulfur, unsubstituted or substituted 6-10-membered aryl, or unsubstituted or substituted 5-10-membered heteroaryl having 1-5 heteroatoms independently selected from nitrogen, oxygen, and sulfur.

[0066] In some embodiments, R^3 is unsubstituted or substituted C_{1-6} aliphatic, unsubstituted or substituted 3-10-membered cycloaliphatic, unsubstituted or substituted 4-10-membered heterocyclyl having 1-5 heteroatoms independently selected from nitrogen, oxygen, and sulfur, unsubstituted or substituted 6-10-membered aryl, or unsubstituted or substituted 5-10-membered heteroaryl having 1-5 heteroatoms independently selected from nitrogen, oxygen, and sulfur; wherein:

each substitutable carbon chain atom in R^3 is unsubstituted or substituted with 1-2 occurrences of $-R^{5dd}$,

each substitutable saturated ring carbon atom in R^3 is unsubstituted or substituted with $=O$, $=S$, $=C(R^5)_2$, $=N-N(R^4)_2$, $=N-OR^5$, $=N-NHC(O)R^5$, $=N-NHCO_2R^6$, $=N-NHSO_2R^6$, $=N-R^5$ or $-R^{5a}$;

each substitutable unsaturated ring carbon atom in R^3 is unsubstituted or is substituted with $-R^{5a}$; and

each substitutable ring nitrogen atom in R^3 is unsubstituted or substituted with $-R^{9b}$;

wherein R^{5dd} , R^4 , R^5 , R^6 , R^{5a} , and R^{9b} have the values described herein.

[0067] In some embodiments, R^3 is unsubstituted or substituted C_{1-6} aliphatic, unsubstituted or substituted 3-10-membered cycloaliphatic, unsubstituted or substituted 4-10-membered heterocyclyl having 1-5 heteroatoms independently selected from nitrogen, oxygen, and sulfur, unsubstituted or substituted 6-10-membered aryl, or unsubstituted or substituted 5-10-membered heteroaryl having 1-5 heteroatoms independently selected from nitrogen, oxygen, and sulfur; wherein:

each substitutable carbon chain atom in R^3 is unsubstituted or substituted with 1-2 occurrences of

$-R^{5dd}$;

each substitutable saturated ring carbon atom in R^3 is unsubstituted or substituted with $=O$, $=S$, $=C(R^5)_2$, $=N-R^5$ or $-R^{5a}$;

each substitutable unsaturated ring carbon atom in R^3 is unsubstituted or is substituted with $-R^{5a}$;
and

each substitutable ring nitrogen atom in R^3 is unsubstituted or substituted with $-R^{9b}$;

wherein R^{5dd} , R^5 , R^{5a} , and R^{9b} have the values described herein.

[0068] In certain embodiments, R^3 is unsubstituted or substituted C_{1-6} aliphatic, unsubstituted or substituted 3-10-membered cycloaliphatic, unsubstituted or substituted 4-10-membered heterocyclyl having 1-5 heteroatoms independently selected from nitrogen, oxygen, and sulfur, unsubstituted or substituted 6-10-membered aryl, or unsubstituted or substituted 5-10-membered heteroaryl having 1-5 heteroatoms independently selected from nitrogen, oxygen, and sulfur; wherein:

each substitutable carbon chain atom in R^3 is unsubstituted or substituted with 1-2 occurrences of $-R^{5dd}$;

each substitutable saturated ring carbon atom in R^3 is unsubstituted or substituted with $-R^{5a}$;

each substitutable unsaturated ring carbon atom in R^3 is unsubstituted or is substituted with $-R^{5a}$;
the total number of R^{5a} substituents is p ; and

each substitutable ring nitrogen atom in R^3 is unsubstituted or substituted with $-R^{9b}$;

wherein R^{5dd} , R^{5a} , R^{9b} , and p have the values described herein.

[0069] In some embodiments, R^3 is unsubstituted or substituted C_{1-6} aliphatic. In certain embodiments, each substitutable carbon chain atom in R^3 is unsubstituted or substituted with 1-2 occurrences of $-R^{5dd}$, wherein R^{5dd} has the values described herein. In certain embodiments, R^3 is methyl, ethyl, n-propyl, isopropyl, tert-butyl, n-butyl, iso-butyl, pentyl, hexyl, butenyl, propenyl, pentenyl, or hexenyl, wherein each of the forementioned groups is unsubstituted or substituted. In certain embodiments, R^3 is methyl, ethyl, n-propyl, isopropyl, tert-butyl, n-butyl, iso-butyl, pentyl, hexyl, butenyl, propenyl, pentenyl, or hexenyl, wherein each substitutable carbon chain atom in R^3 is unsubstituted or substituted with 1-2 occurrences of $-R^{5dd}$, wherein R^{5dd} has the values described herein.

[0070] In some embodiments, R^3 is unsubstituted or substituted unsubstituted or substituted 3-10-membered cycloaliphatic, unsubstituted or substituted 4-10-membered heterocyclyl having 1-5

heteroatoms independently selected from nitrogen, oxygen, and sulfur, unsubstituted or substituted 6-10-membered aryl, or unsubstituted or substituted 5-10-membered heteroaryl having 1-5 heteroatoms independently selected from nitrogen, oxygen, and sulfur.

[0071] In certain embodiments, R^3 is unsubstituted or substituted unsubstituted or substituted 3-10-membered cycloaliphatic, unsubstituted or substituted 4-10-membered heterocyclyl having 1-5 heteroatoms independently selected from nitrogen, oxygen, and sulfur, unsubstituted or substituted 6-10-membered aryl, or unsubstituted or substituted 5-10-membered heteroaryl having 1-5 heteroatoms independently selected from nitrogen, oxygen, and sulfur, wherein:

each substitutable saturated ring carbon atom in R^3 is unsubstituted or substituted with $=O$, $=S$, $=C(R^5)_2$, $=N-N(R^4)_2$, $=N-OR^5$, $=N-NHC(O)R^5$, $=N-NHCO_2R^6$, $=N-NHSO_2R^6$, $=N-R^5$ or $-R^{5a}$;

each substitutable unsaturated ring carbon atom in R^3 is unsubstituted or is substituted with $-R^{5a}$; and

each substitutable ring nitrogen atom in R^3 is unsubstituted or substituted with $-R^{9b}$;

wherein R^4 , R^5 , R^6 , R^{5a} , and R^{9b} have the values described herein.

[0072] In certain embodiments, R^3 is unsubstituted or substituted unsubstituted or substituted 3-10-membered cycloaliphatic, unsubstituted or substituted 4-10-membered heterocyclyl having 1-5 heteroatoms independently selected from nitrogen, oxygen, and sulfur, unsubstituted or substituted 6-10-membered aryl, or unsubstituted or substituted 5-10-membered heteroaryl having 1-5 heteroatoms independently selected from nitrogen, oxygen, and sulfur, wherein:

each substitutable saturated ring carbon atom in R^3 is unsubstituted or substituted with $=O$, $=S$, $=C(R^5)_2$, $=N-R^5$ or $-R^{5a}$;

each substitutable unsaturated ring carbon atom in R^3 is unsubstituted or is substituted with $-R^{5a}$; and

each substitutable ring nitrogen atom in R^3 is unsubstituted or substituted with $-R^{9b}$;

wherein R^5 , R^{5a} , and R^{9b} have the values described herein.

[0073] In certain embodiments, R^3 is unsubstituted or substituted unsubstituted or substituted 3-10-membered cycloaliphatic, unsubstituted or substituted 4-10-membered heterocyclyl having 1-5 heteroatoms independently selected from nitrogen, oxygen, and sulfur, unsubstituted or substituted 6-10-membered aryl, or unsubstituted or substituted 5-10-membered heteroaryl having 1-5 heteroatoms independently selected from nitrogen, oxygen, and sulfur, wherein:

each substitutable saturated ring carbon atom in R^3 is unsubstituted or substituted with

$-R^{5a}$;

each substitutable unsaturated ring carbon atom in R^3 is unsubstituted or is substituted with $-R^{5a}$;

the total number of R^{5a} substituents is p; and

each substitutable ring nitrogen atom in R^3 is unsubstituted or substituted with $-R^{9b}$;

wherein R^{5a} , R^{9b} , and p have the values described herein.

[0074] In certain embodiments, R^3 is furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, thiadiazolyl, phenyl, naphthyl, pyranlyl, pyridyl, pyridazinyl, pyrimidinyl, pyrazinyl, triazinyl, indoliziny, imidazopyridyl, indolyl, isoindolyl, indazolyl, benzimidazolyl, benzthiazolyl, benzothienyl, benzofuranyl, benzoxazolyl, benzodioxolyl, benzthiadiazolyl, 2,3-dihydrobenzofuranyl, 4H-furo[3,2-b]pyrrolyl, pyrazolopyrimidinyl, purinyl, quinolyl, isoquinolyl, tetrahydroquinolyl, tetrahydroisoquinolyl, cinnolyl, phthalazinyl, quinazolinyl, quinoxalinyl, naphthyridinyl, pteridinyl, tetrahydrofuranyl, tetrahydropyranlyl, tetrahydrothienyl, indanyl, tetrahydroindazolyl, pyrrolidinyl, pyrrolidonyl, piperidinyl, pyrrolinyl, decahydroquinolyl, oxazolidinyl, piperazinyl, dioxanyl, diazepinyl, oxazepinyl, thiazepinyl, morpholinyl, thiamorpholinyl, quinuclidinyl, phenanthridinyl, tetrahydronaphthyl, indolinyl, benzodioxanyl, chromanyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, cyclooctyl, cyclopentenyl, cyclohexenyl, cycloheptenyl, cyclooctenyl, bicycloheptanyl, bicyclooctanyl, or adamantyl; wherein:

each substitutable saturated ring carbon atom in R^3 is unsubstituted or substituted with $=O$, $=S$, $=C(R^5)_2$, $=N-N(R^4)_2$, $=N-OR^5$, $=N-NHC(O)R^5$, $=N-NHCO_2R^6$, $=N-NHSO_2R^6$, $=N-R^5$ or $-R^{5a}$;

each substitutable unsaturated ring carbon atom in R^3 is unsubstituted or is substituted with $-R^{5a}$; and

each substitutable ring nitrogen atom in R^3 is unsubstituted or substituted with $-R^{9b}$;

wherein R^4 , R^5 , R^6 , R^{5a} , and R^{9b} have the values described herein.

[0075] In certain embodiments, R^3 is furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, thiadiazolyl, phenyl, naphthyl, pyranlyl, pyridyl, pyridazinyl, pyrimidinyl, pyrazinyl, triazinyl, indoliziny, imidazopyridyl, indolyl, isoindolyl, indazolyl, benzimidazolyl, benzthiazolyl, benzothienyl, benzofuranyl, benzoxazolyl, benzodioxolyl,

benzthiadiazolyl, 2,3-dihydrobenzofuranyl, 4H-furo[3,2-b]pyrrolyl, pyrazolopyrimidinyl, purinyl, quinolyl, isoquinolyl, tetrahydroquinolyl, tetrahydroisoquinolyl, cinnolyl, phthalazinyl, quinazolinyl, quinoxalinyl, naphthyridinyl, pteridinyl, tetrahydrofuranlyl, tetrahydropyranlyl, tetrahydrothienyl, indanyl, tetrahydroindazolyl, pyrrolidinyl, pyrrolidonyl, piperidinyl, pyrrolinyl, decahydroquinolyl, oxazolidinyl, piperazinyl, dioxanyl, diazepinyl, oxazepinyl, thiazepinyl, morpholinyl, thiamorpholinyl, quinuclidinyl, phenanthridinyl, tetrahydronaphthyl, indolinyl, benzodioxanyl, chromanyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, cyclooctyl, cyclopentenyl, cyclohexenyl, cycloheptenyl, cyclooctenyl, bicycloheptanyl, bicyclooctanyl, or adamantyl; wherein:

each substitutable saturated ring carbon atom in R^3 is unsubstituted or substituted with $=O$, $=S$, $=C(R^{5a})_2$, $=N-R^{5a}$, or $-R^{5a}$;

each substitutable unsaturated ring carbon atom in R^3 is unsubstituted or is substituted with $-R^{5a}$; and

each substitutable ring nitrogen atom in R^3 is unsubstituted or substituted with $-R^{9b}$;

wherein R^5 , R^{5a} , and R^{9b} have the values described herein.

[0076] In certain embodiments, R^3 is furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, thiadiazolyl, phenyl, naphthyl, pyranlyl, pyridyl, pyridazinyl, pyrimidinyl, pyrazinyl, triazinyl, indoliziny, imidazopyridyl, indolyl, isoindolyl, indazolyl, benzimidazolyl, benzthiazolyl, benzothienyl, benzofuranyl, benzoxazolyl, benzodioxolyl, benzthiadiazolyl, 2,3-dihydrobenzofuranyl, 4H-furo[3,2-b]pyrrolyl, pyrazolopyrimidinyl, purinyl, quinolyl, isoquinolyl, tetrahydroquinolyl, tetrahydroisoquinolyl, cinnolyl, phthalazinyl, quinazolinyl, quinoxalinyl, naphthyridinyl, pteridinyl, tetrahydrofuranlyl, tetrahydropyranlyl, tetrahydrothienyl, indanyl, tetrahydroindazolyl, pyrrolidinyl, pyrrolidonyl, piperidinyl, pyrrolinyl, decahydroquinolyl, oxazolidinyl, piperazinyl, dioxanyl, diazepinyl, oxazepinyl, thiazepinyl, morpholinyl, thiamorpholinyl, quinuclidinyl, phenanthridinyl, tetrahydronaphthyl, indolinyl, benzodioxanyl, chromanyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, cyclooctyl, cyclopentenyl, cyclohexenyl, cycloheptenyl, cyclooctenyl, bicycloheptanyl, bicyclooctanyl, or adamantyl; wherein:

each substitutable saturated ring carbon atom in R^3 is unsubstituted or substituted with $-R^{5a}$;

each substitutable unsaturated ring carbon atom in R^3 is unsubstituted or is substituted with $-R^{5a}$;

the total number of R^{5a} substituents is p ; and

each substitutable ring nitrogen atom in R^3 is unsubstituted or substituted with $-R^{9b}$;

wherein R^{5a} , R^{9b} , and p have the values described herein.

[0077] In some embodiments, each occurrence of R^{5dd} is independently halogen, hydroxy, $-O(C_{1-3} \text{ alkyl})$, cyano, $-N(R^4)_2$, $-C(O)(C_{1-3} \text{ alkyl})$, $-CO_2H$, $-CO_2(C_{1-3} \text{ alkyl})$, $-C(O)NH_2$, or $-C(O)NH(C_{1-3} \text{ alkyl})$. In certain embodiments, each occurrence of R^{5dd} is independently fluoro, hydroxy, methoxy, ethoxy, or $-C(O)NHCH_3$.

[0078] Each R^4 is independently hydrogen, unsubstituted or substituted 3-10-membered cycloaliphatic, unsubstituted or substituted 4-10-membered heterocyclyl having 1-5 heteroatoms independently selected from nitrogen, oxygen, and sulfur, unsubstituted or substituted 6-10-membered aryl, or unsubstituted or substituted 5-10-membered heteroaryl having 1-5 heteroatoms independently selected from nitrogen, oxygen, and sulfur; or two R^4 on the same nitrogen atom, taken together with the nitrogen atom, form an unsubstituted or substituted 5- to 6-membered heteroaryl or an unsubstituted or substituted 4- to 8-membered heterocyclyl having, in addition to the nitrogen atom, 0-2 ring heteroatoms selected from nitrogen, oxygen, and sulfur.

[0079] Each R^5 is independently hydrogen, unsubstituted or substituted C_{1-6} aliphatic, unsubstituted or substituted 3-10-membered cycloaliphatic, unsubstituted or substituted 4-10-membered heterocyclyl having 1-5 heteroatoms independently selected from nitrogen, oxygen, and sulfur, unsubstituted or substituted 6-10-membered aryl, or unsubstituted or substituted 5-10-membered heteroaryl having 1-5 heteroatoms independently selected from nitrogen, oxygen, and sulfur.

[0080] Each R^6 is independently unsubstituted or substituted C_{1-6} aliphatic, or unsubstituted or substituted 6-10-membered aryl.

[0081] Each R^7 is independently unsubstituted or substituted 4-10-membered heterocyclyl having 1-5 heteroatoms independently selected from nitrogen, oxygen, and sulfur, unsubstituted or substituted 6-10-membered aryl, or unsubstituted or substituted 5-10-membered heteroaryl having 1-5 heteroatoms independently selected from nitrogen, oxygen, and sulfur.

[0082] Each R^{9b} is independently $-C(O)R^5$, $-C(O)N(R^4)_2$, $-CO_2R^6$, $-SO_2R^6$, $-SO_2N(R^4)_2$, unsubstituted C_{1-4} aliphatic, or C_{1-4} aliphatic substituted with 1-2 independent occurrences of R^7 or R^8 , wherein R^7 and R^8 have the values described herein.

[0083] Each R^8 is independently halogen, $-OH$, $-O(C_{1-3} \text{ alkyl})$, $-CN$, $-N(R^4)_2$, $-C(O)(C_{1-3} \text{ alkyl})$, $-CO_2H$, $-CO_2(C_{1-3} \text{ alkyl})$, $-C(O)NH_2$, or $-C(O)NH(C_{1-3} \text{ alkyl})$, wherein R^4 has the values described herein.

[0084] Each R^{5a} is independently halogen, $-NO_2$, $-CN$, $-C(R^5)=C(R^5)_2$, $-C\equiv C-R^5$, $-OR^5$, $-SR^6$,

-S(O)R⁶, -SO₂R⁶, -SO₂N(R⁴)₂, -N(R⁴)₂, -NR⁴C(O)R⁵, -NR⁴C(O)N(R⁴)₂, -NR⁴CO₂R⁶, -OC(O)N(R⁴)₂, -C(O)-C(O)R⁵, -C(O)R⁵, -C(O)N(R⁴)₂, -C(=NR⁴)-N(R⁴)₂, -C(=NR⁴)-OR⁵, -N(R⁴)-N(R⁴)₂, -N(R⁴)C(=NR⁴)-N(R⁴)₂, -N(R⁴)SO₂R⁶, -N(R⁴)SO₂N(R⁴)₂, -P(O)(R⁵)₂, -P(O)(OR⁵)₂, unsubstituted or substituted C₁₋₆ aliphatic, unsubstituted or substituted 3-10-membered cycloaliphatic, unsubstituted or substituted 4-10-membered heterocyclyl having 1-5 heteroatoms independently selected from nitrogen, oxygen, and sulfur, unsubstituted or substituted 6-10-membered aryl, or unsubstituted or substituted 5-10-membered heteroaryl having 1-5 heteroatoms independently selected from nitrogen, oxygen, and sulfur; or two adjacent R^{5a}, taken together with the intervening ring atoms, form an unsubstituted or substituted fused aromatic ring or an unsubstituted or substituted non-aromatic ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, and sulfur, wherein R⁵, R⁶, and R⁴ have the values described herein.

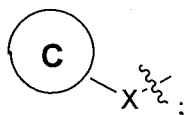
[0085] In some embodiments, each R^{5a} is independently halogen, -CN, -OH, C₁₋₄ alkyl, C₁₋₃ fluoroalkyl, -O-C₁₋₃ alkyl, -O-C₁₋₃ fluoroalkyl, -NHC(O)C₁₋₃ alkyl, -C(O)NHC₁₋₃ alkyl, -NHC(O)NHC₁₋₃ alkyl, -NHS(O)₂C₁₋₃ alkyl, 3-10-membered cycloaliphatic substituted with 0-2 occurrences of -R^{7a}, 4-10-membered heterocyclyl having 1-5 heteroatoms independently selected from nitrogen, oxygen, and sulfur substituted with 0-2 occurrences of -R^{7a}, 6-10-membered aryl substituted with 0-2 occurrences of -R^{7a}, or 5-10-membered heteroaryl having 1-5 heteroatoms independently selected from nitrogen, oxygen, and sulfur substituted with 0-2 occurrences of -R^{7a} wherein R^{7a} has the values described herein.

[0086] In certain embodiments, each R^{5a} is independently chloro, fluoro, hydroxy, methoxy, ethoxy, n-propoxy, isopropoxy, cyano, trifluoromethyl, methyl, ethyl, isopropyl, n-propyl, tert-butyl or phenyl.

[0087] Each occurrence of the variable R^{7a} is independently halogen, C₁₋₃ alkyl, C₁₋₃ fluoroalkyl, -O-C₁₋₃ alkyl, -O-C₁₋₃ fluoroalkyl, -NHC(O)C₁₋₃ alkyl, -C(O)NHC₁₋₃ alkyl, -NHC(O)NHC₁₋₃ alkyl, or -NHS(O)₂C₁₋₃ alkyl.

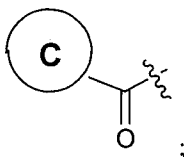
[0088] The variable p is 1-2. In some embodiments, p is 1.

[0089] In some embodiments, G is:



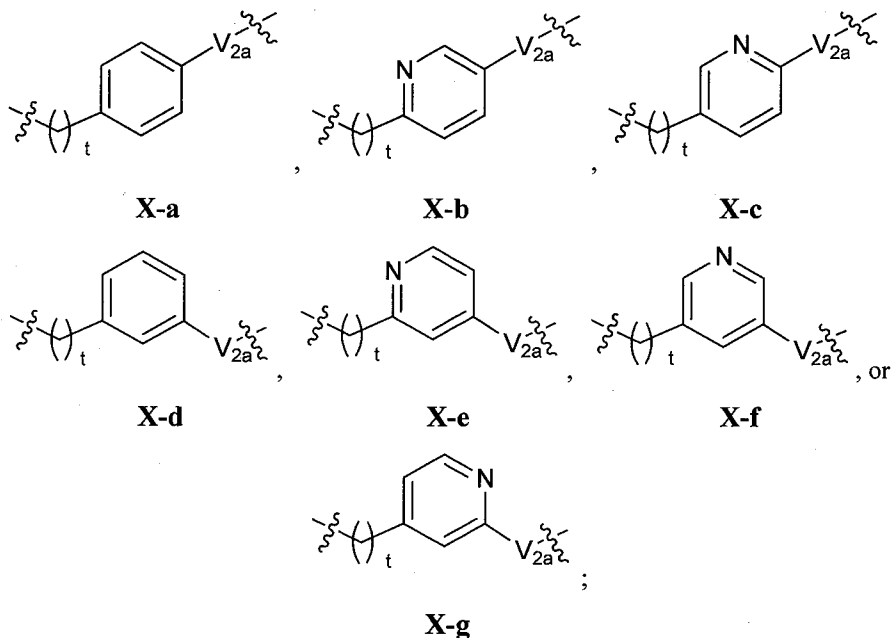
wherein X and Ring C have the values described herein.

[0090] In certain embodiments, G is:



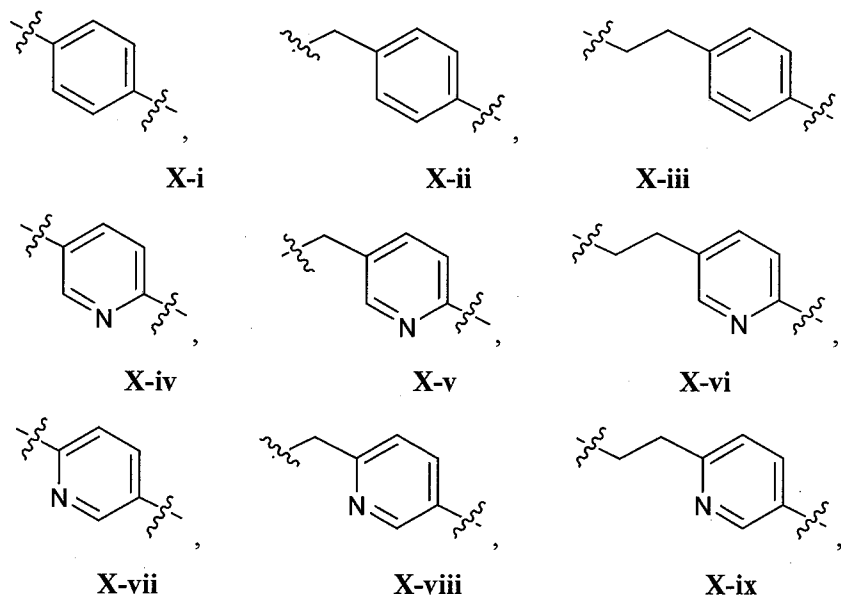
wherein Ring C has the values described herein.

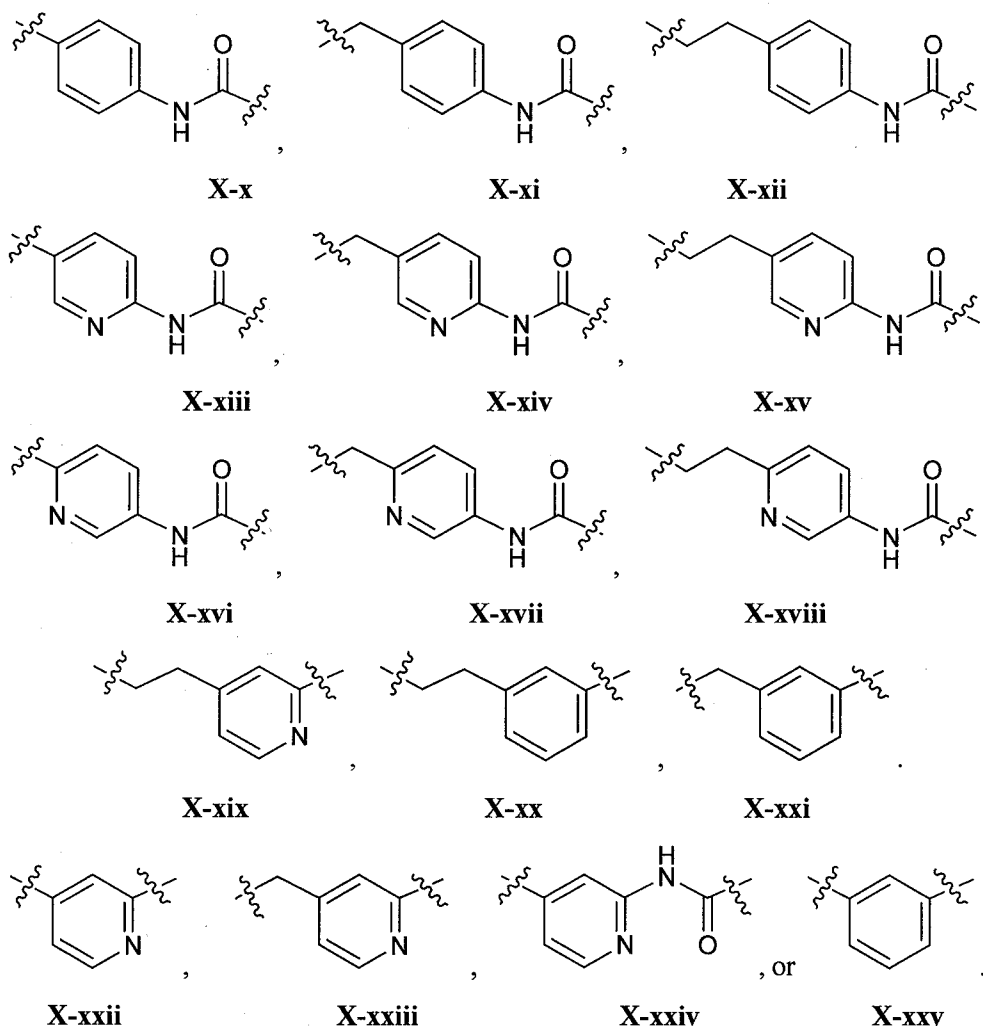
[0091] The variable X is $-\text{C}(\text{O})-$ or $-\text{L}_{2a}-\text{R}^{3aa}-\text{V}_{2a}-$, wherein L_{2a} , R^{3aa} , and V_{2a} have the values described herein. In some embodiments, X is $-\text{C}(\text{O})-$. In some embodiments, X is $-\text{L}_{2a}-\text{R}^{3aa}-\text{V}_{2a}-$, wherein L_{2a} , R^{3aa} , and V_{2a} have the values described herein. In some embodiments, X is $-\text{C}(\text{O})-$,



wherein V_{2a} and t have the values described herein.

[0092] In certain embodiments, X is $-\text{C}(\text{O})-$,

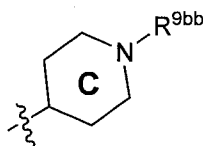




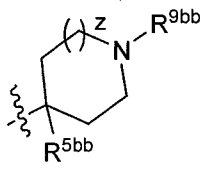
[0093] In certain embodiments, X is -C(O)-, X-ii, X-iii, X-xi, X-xii, X-xxii, X-xxiv, or X-xxv.

[0094] Ring C is a 4-7 membered heterocyclic ring containing one nitrogen atom, wherein the nitrogen atom is not the atom bound to X, and wherein the nitrogen atom in Ring C is substituted with R^{9bb} and Ring C is unsubstituted or substituted by 1-4 occurrences of R^{5b} ; wherein R^{9bb} , X, and R^{5b} have the values described herein. In some embodiments, Ring C is a 4-7 membered heterocyclic ring containing one nitrogen atom, wherein the nitrogen atom is not the atom bound to X, and wherein the nitrogen atom in Ring C is substituted with R^{9bb} and Ring C is unsubstituted or substituted by 1-2 occurrences of R^{5b} ; wherein R^{9bb} , X, and R^{5b} have the values described herein.

[0095] In certain embodiments, Ring C is:



wherein Ring C is unsubstituted or substituted with 1 occurrence of R^{5b} , wherein R^{9bb} and R^{5b} have the values described herein. In certain embodiments, Ring C is:



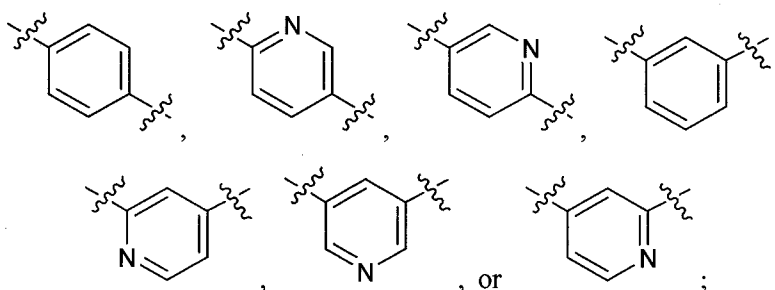
wherein R^{9bb} , z and R^{5bb} have the values described herein.

[0096] The variable V_{2a} is a bond, $-NH-C(O)-$, $-NH-S(O)_2-$, or $-NH-C(O)-NH-$. In some embodiments, V_{2a} is a bond or $-NH-C(O)-$. In certain embodiments, V_{2a} is a bond. In certain embodiments, V_{2a} is $-NH-C(O)-$.

[0097] The variable t is 0-2. In some embodiments, t is 0-1. In certain embodiments, t is 0. In certain embodiments, t is 1. In certain embodiments, t is 2.

[0098] The variable L_{2a} is a bond or unsubstituted or substituted C_{1-3} alkylene chain. In some embodiments, L_{2a} is a bond, $-CH_2-$, $-CH_2CH_2-$, or $-CH_2CH_2CH_2-$. In certain embodiments, L_{2a} is a bond. In certain embodiments, L_{2a} is $-CH_2-$. In certain embodiments, L_{2a} is $-CH_2CH_2-$.

[0099] The variable R^{3aa} is a 6-membered aromatic ring containing 0-2 nitrogen atoms which is unsubstituted or substituted with 1-2 independent occurrences of R^{4c} , wherein R^{4c} has the values described herein. In some embodiments, R^{3aa} is phenyl or pyridyl, each of which is unsubstituted or substituted with 1-2 independent occurrences of R^{4c} , wherein R^{4c} has the values described herein. In some embodiments, R^{3aa} is:



wherein each ring is unsubstituted or substituted with 1-2 independent occurrences of R^{4c} .

[00100] The variable R^{4c} is chloro, fluoro, cyano, hydroxy, methoxy, ethoxy, trifluoromethoxy, trifluoromethyl, methyl, or ethyl. In some embodiments, R^{4c} is chloro, fluoro, methyl or ethyl.

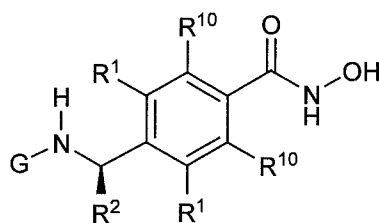
[00101] The variable z is 0-1. In some embodiments, z is 0. In some embodiments, z is 1.

[00102] Each occurrence of the variable R^{5b} is independently chloro, fluoro, hydroxy, methyl, ethyl, methoxy, ethoxy, trifluoromethyl, trifluoromethoxy, $-C(O)NH_2$, or $-CO_2H$. In some embodiments, each occurrence of the variable R^{5b} is independently chloro, fluoro, hydroxy, methyl, or ethyl. In certain embodiments, each occurrence of the variable R^{5b} is methyl.

[00103] The variable R^{5bb} is hydrogen or methyl. In some embodiments, R^{5bb} is hydrogen. In some embodiments, R^{5bb} is methyl.

[00104] The variable R^{9bb} is hydrogen, unsubstituted $C(O)-O-C_{1-6}$ aliphatic, unsubstituted $C(O)-C_{1-6}$ aliphatic, unsubstituted $C(O)-C_{3-10}$ cycloaliphatic, or unsubstituted C_{1-6} aliphatic. In some embodiments, R^{9bb} is hydrogen, methyl, ethyl, isopropyl, or tert-butoxycarbonyl. In some embodiments, R^{9bb} is methyl, ethyl, or isopropyl. In certain embodiments, R^{9bb} is hydrogen.

[00105] In certain embodiments, the compound of formula (I) is represented by:



(III-a-i);

wherein:

each occurrence of R^1 is independently hydrogen, chloro, fluoro, hydroxy, trifluoromethyl, or methyl;

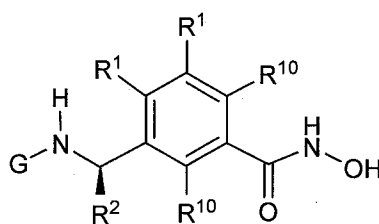
R^{10} is hydrogen;

G is $-V_1-R^3$; and

V_1 is $-C(O)-$, $-C(O)-N(R^{4a})-$ or $-S(O)_2-$;

wherein R^2 , R^3 , and R^{4a} have the values described herein.

[00106] In certain embodiments, the compound of formula (I) is represented by:



(III-a-v);

wherein:

each occurrence of R^1 is independently hydrogen, chloro, fluoro, hydroxy, trifluoromethyl, or methyl;

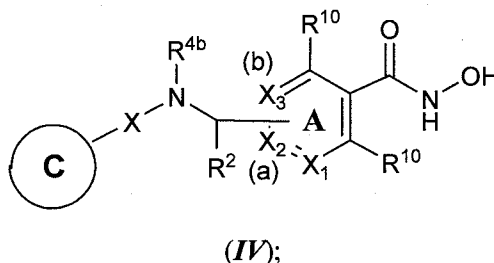
R^{10} is hydrogen;

G is $-V_1-R^3$; and

V_1 is $-C(O)-$, $-C(O)-N(R^{4a})-$ or $-S(O)_2-$;

wherein R^2 , R^3 , and R^{4a} have the values described herein.

[00107] In certain embodiments, the compound of formula (I) is represented by:



wherein:

ring A is an aromatic 6-membered ring connected through one of positions (a) or (b);

X_1 is CR^1 or N;

(i) when ring A is connected through position (a), X_2 is C; and X_3 is CR^1 or N; or

(ii) when ring A is connected through position (b), X_3 is C; and X_2 is CR^1 or N;

R^{4b} is hydrogen, or C_{1-4} aliphatic;

R^2 is methyl, ethyl, isopropyl, n-propyl, trifluoromethyl, tert-butyl, cyclopropyl, or phenyl;

R^1 is hydrogen, chloro, fluoro, hydroxy, methoxy, ethoxy, n-propoxy, isopropoxy, cyano, trifluoromethyl, methyl, ethyl, isopropyl, n-propyl, or tert-butyl;

R^{10} is hydrogen; and

wherein Ring C and X have the values described herein.

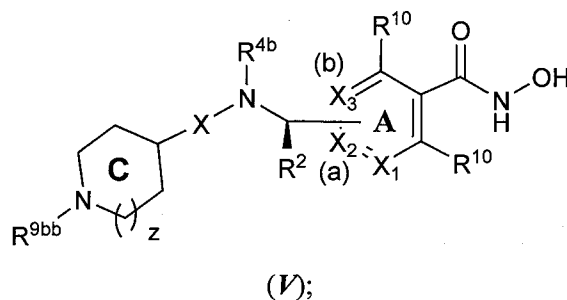
[00108] In such embodiments:

R^2 is methyl, ethyl, isopropyl, or n-propyl;

R^1 is hydrogen; and

R^{4b} is hydrogen.

[00109] In certain embodiments, the compound of formula (I) is represented by:



wherein:

ring A is an aromatic 6-membered ring connected through one of positions (a) or (b);

X_1 is CR^1 or N;

(i) when ring A is connected through position (a), X_2 is C; and X_3 is CR^1 or N; or

(ii) when ring A is connected through position (b), X_3 is C; and X_2 is CR^1 or N;

R^{4b} is hydrogen;

R^2 is methyl, ethyl, isopropyl, n-propyl, trifluoromethyl, tert-butyl, cyclopropyl, or phenyl;

each occurrence of R^1 is independently hydrogen, chloro, fluoro, hydroxy, trifluoromethyl, or methyl;

R^{10} is hydrogen;

R^{9bb} is hydrogen, methyl, ethyl, isopropyl, or tert-butoxycarbonyl;

X is -C(O)-, X-a, X-b, X-c, X-d, X-e, X-f, or X-g;

Ring C is unsubstituted or substituted with one occurrence of R^{5b} ; and

z, R^{5b} , t, and V_{2a} have the values described herein.

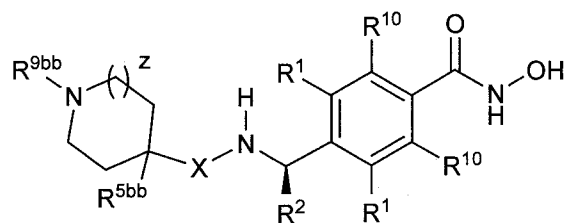
[00110] In such embodiments:

R^2 is methyl, ethyl, isopropyl, or n-propyl;

R^1 is hydrogen; and

R^{5b} is methyl.

[00111] In certain embodiments, the compound of formula (I) is represented by:



(VI-a-i);

wherein:

each occurrence of R¹ is independently hydrogen, chloro, fluoro, hydroxy, trifluoromethyl, or methyl;

R² is methyl, ethyl, isopropyl, n-propyl, trifluoromethyl, tert-butyl, cyclopropyl, or phenyl;

R¹⁰ is hydrogen;

R^{9bb} is hydrogen, methyl, ethyl, isopropyl, or tert-butoxycarbonyl;

X is -C(O)-, X-ii, X-iii, X-xi, X-xii, X-xxii, X-xxiv, or X-xxv;

R^{5bb} is hydrogen or methyl; and

z has the values described herein.

[00112] In certain such embodiments,

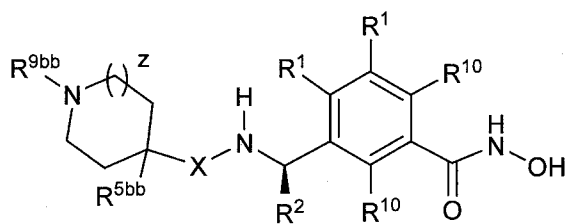
R¹ is hydrogen;

R² is methyl, ethyl, isopropyl, or n-propyl;

R^{5bb} is methyl; and

z is 1.

[00113] In certain embodiments, the compound of formula (I) is represented by:



(VI-a-v);

wherein:

each occurrence of R^1 is independently hydrogen, chloro, fluoro, hydroxy, trifluoromethyl, or methyl;

R^2 is methyl, ethyl, isopropyl, n-propyl, trifluoromethyl, tert-butyl, cyclopropyl, or phenyl;

R^{10} is hydrogen;

R^{9bb} is hydrogen, methyl, ethyl, isopropyl, or tert-butoxycarbonyl;

X is -C(O)-, X-ii, X-iii, X-xi, X-xii, X-xxii, X-xxiv, or X-xxv;

R^{5bb} is hydrogen or methyl; and

z has the values described herein.

[00114] In certain such embodiments,

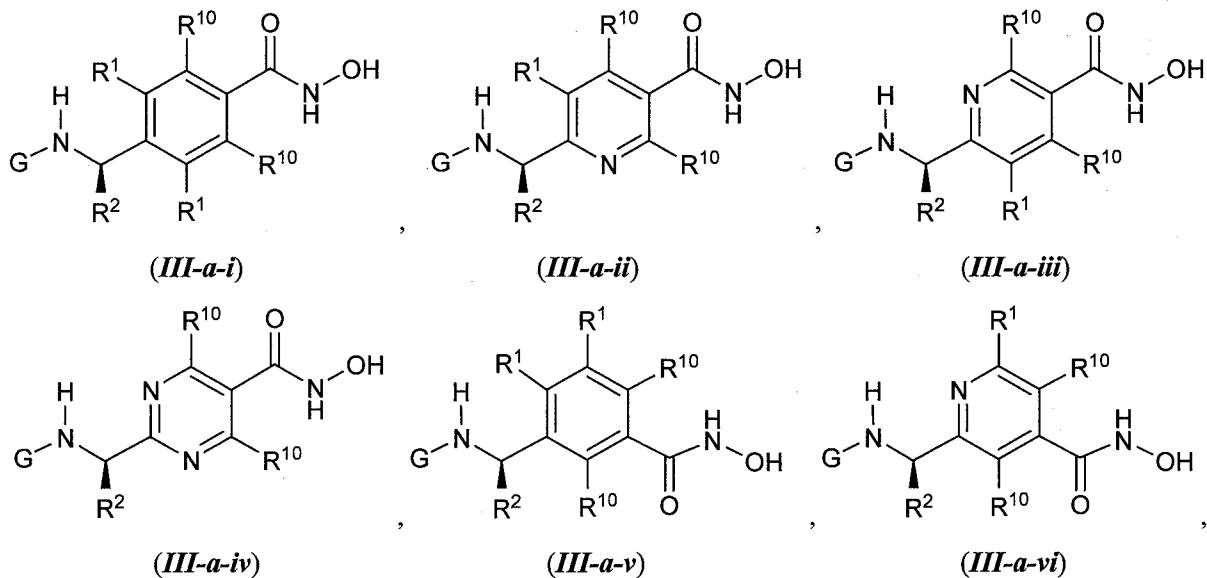
R^1 is hydrogen;

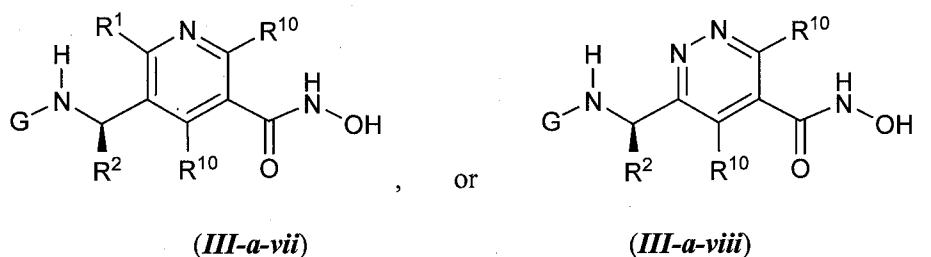
R^2 is methyl, ethyl, isopropyl, or n-propyl;

R^{5bb} is methyl; and

z is 1.

[00115] In certain embodiments, the compound of formula (I) is represented by:





wherein:

each occurrence of R¹ is independently hydrogen, chloro, fluoro, hydroxy, trifluoromethyl, or methyl;

R¹⁰ is hydrogen;

G is -V₁-R³;

V₁ is -C(O)-, -C(O)-NH- or -S(O)₂-;

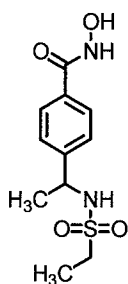
R² is methyl, ethyl, isopropyl, or n-propyl; and

wherein R³ has the values described herein.

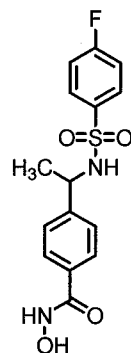
[00116] In certain such embodiments, the compound of formula (I) is represented by formula (III-a-i). In certain such embodiments, the compound of formula (I) is represented by formula (III-a-ii). In certain such embodiments, the compound of formula (I) is represented by formula (III-a-iii). In certain such embodiments, the compound of formula (I) is represented by formula (III-a-iv). In certain such embodiments, the compound of formula (I) is represented by formula (III-a-v). In certain such embodiments, the compound of formula (I) is represented by formula (III-a-vi). In certain such embodiments, the compound of formula (I) is represented by formula (III-a-vii). In certain such embodiments, the compound of formula (I) is represented by formula (III-a-viii).

[00117] In certain such embodiments, the compound of formula (I) is represented by formula (III-a-i), wherein R¹ is hydrogen. In certain such embodiments, the compound of formula (I) is represented by formula (III-a-ii), wherein R¹ is hydrogen. In certain such embodiments, the compound of formula (I) is represented by formula (III-a-iii), wherein R¹ is hydrogen. In certain such embodiments, the compound of formula (I) is represented by formula (III-a-iv), wherein R¹ is hydrogen. In certain such embodiments, the compound of formula (I) is represented by formula (III-a-v), wherein R¹ is hydrogen. In certain such embodiments, the compound of formula (I) is represented by formula (III-a-vi), wherein R¹ is hydrogen. In certain such embodiments, the compound of formula (I) is represented by formula (III-a-vii), wherein R¹ is hydrogen. In certain such embodiments, the compound of formula (I) is represented by formula (III-a-viii), wherein R¹ is hydrogen.

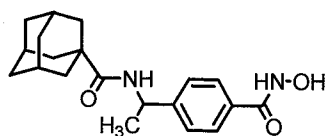
[00118] Representative examples of compounds of formula (I) are shown in Table 1.



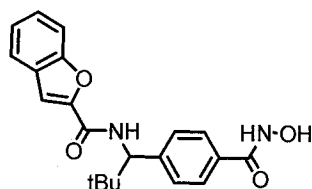
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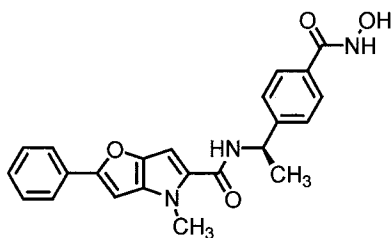
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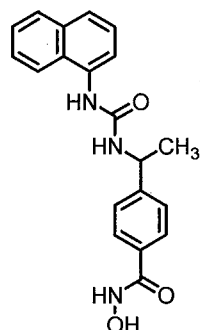
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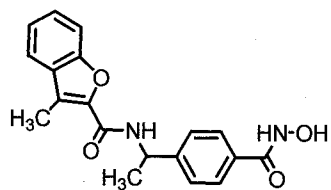
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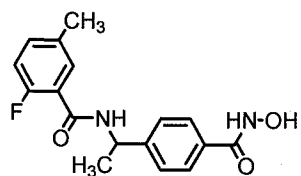
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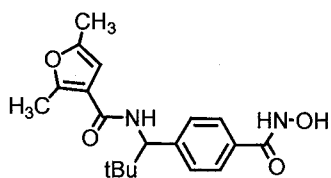
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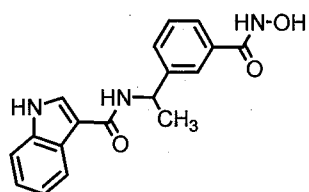
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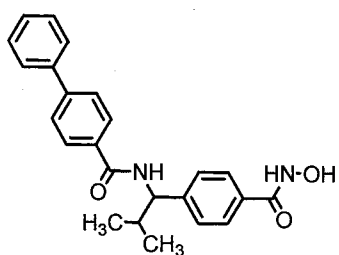
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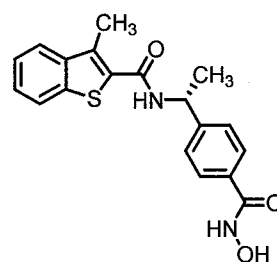
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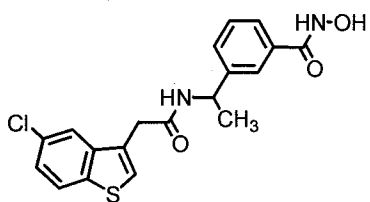
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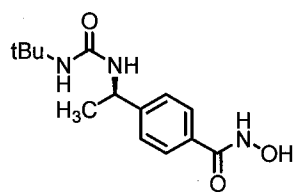
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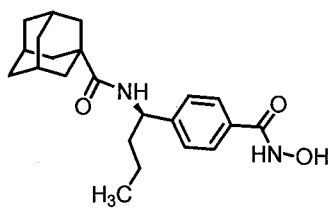
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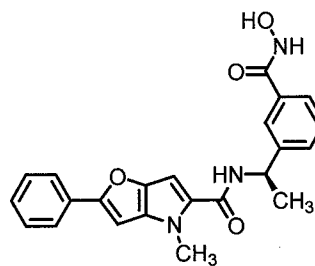
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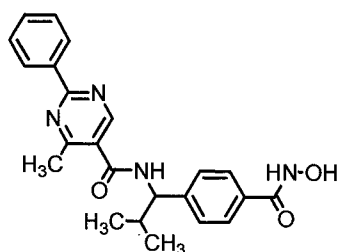
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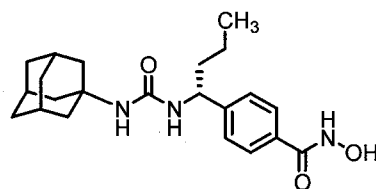
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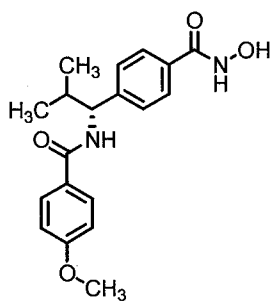
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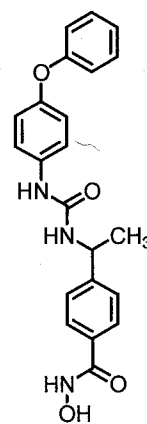
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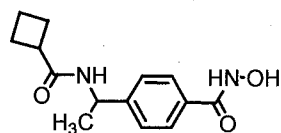
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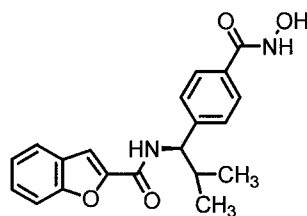
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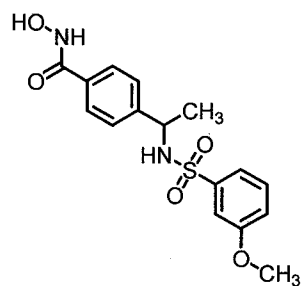
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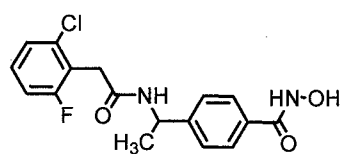
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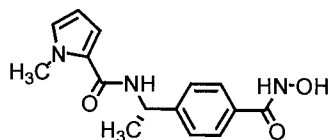
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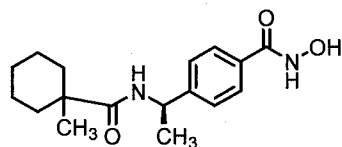
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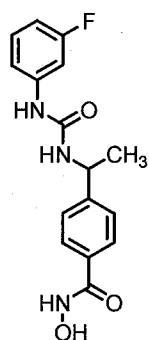
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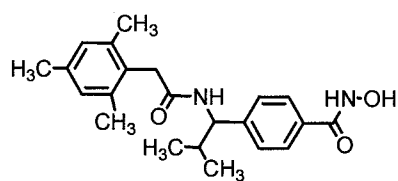
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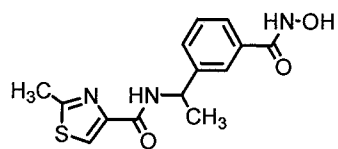
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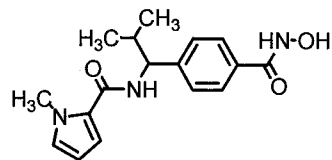
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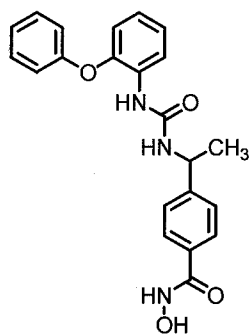
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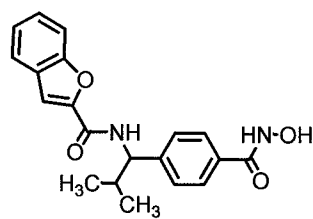
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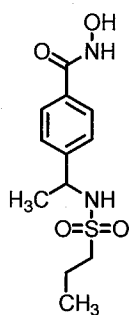
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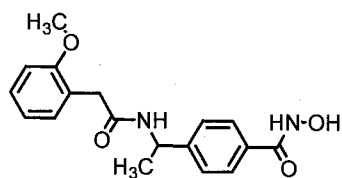
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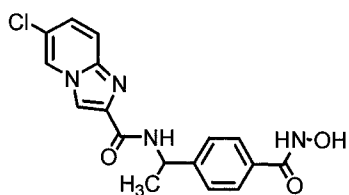
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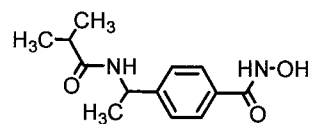
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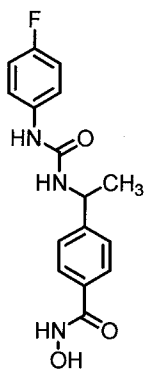
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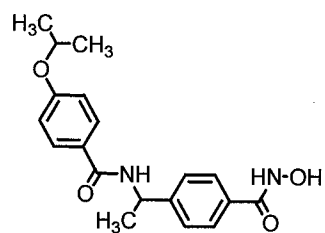
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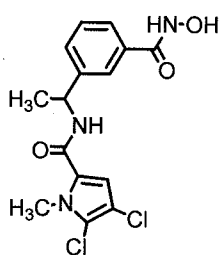
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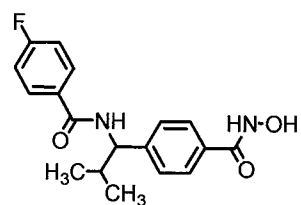
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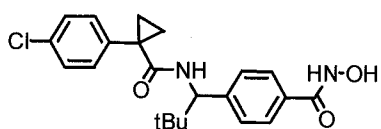
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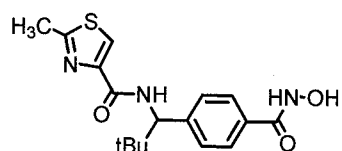
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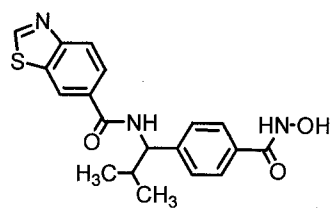
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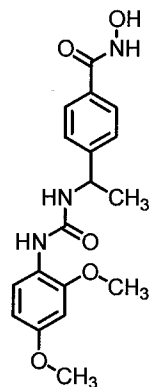
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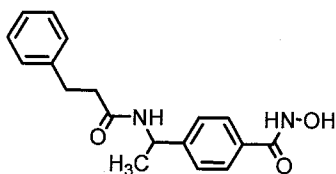
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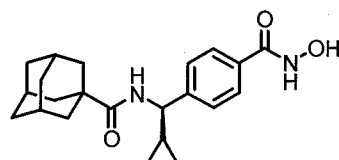
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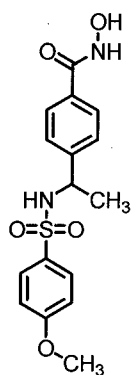
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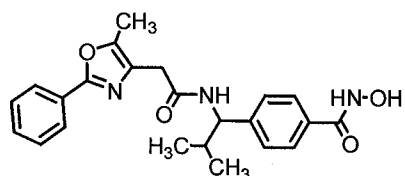
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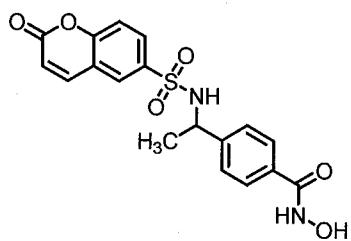
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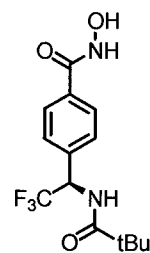
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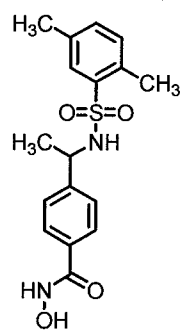
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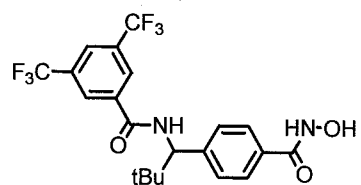
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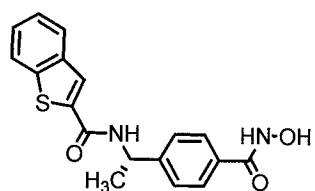
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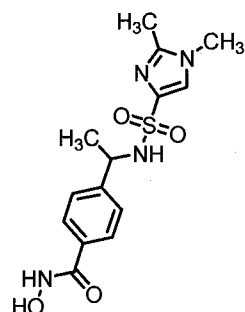
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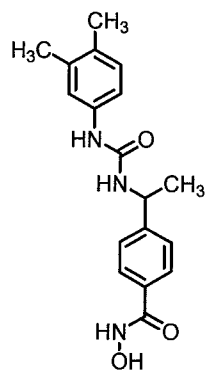
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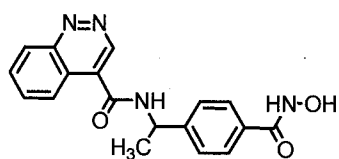
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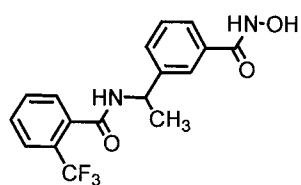
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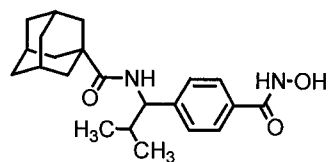
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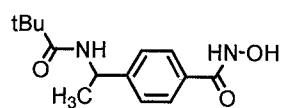
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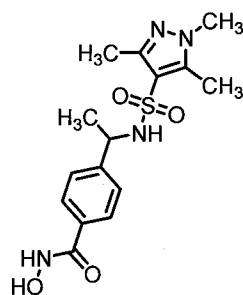
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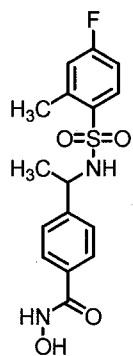
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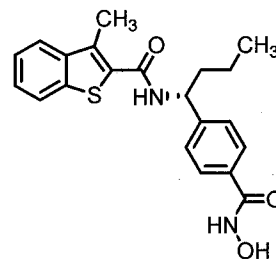
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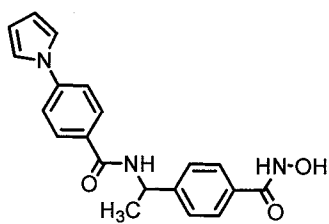
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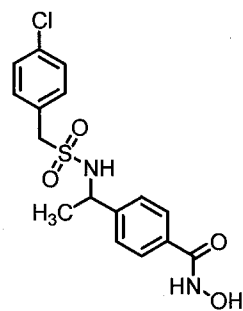
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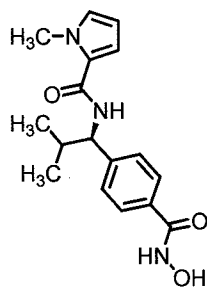
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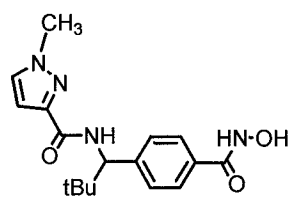
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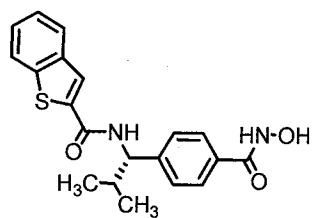
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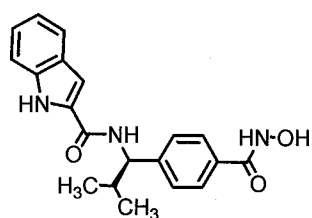
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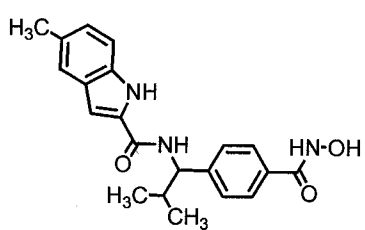
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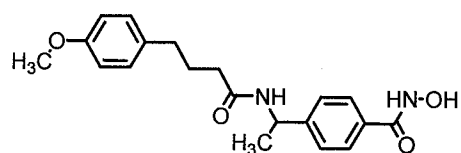
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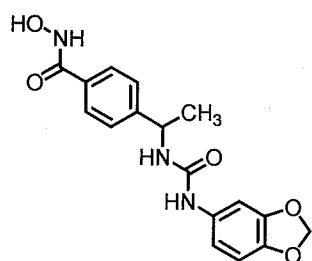
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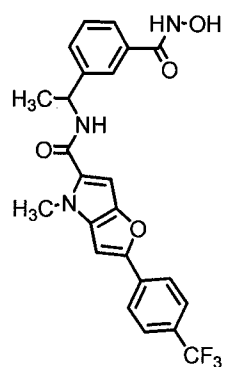
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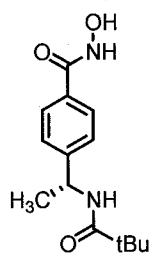
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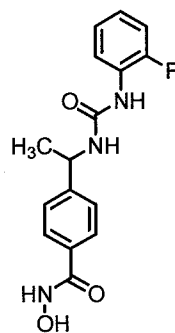
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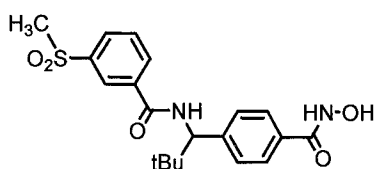
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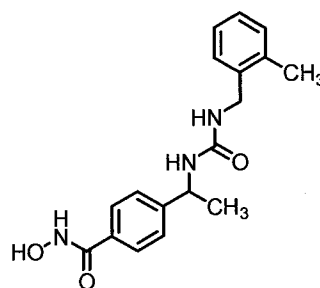
I-73



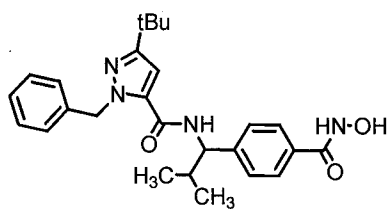
I-74



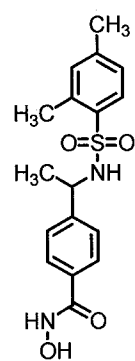
I-75



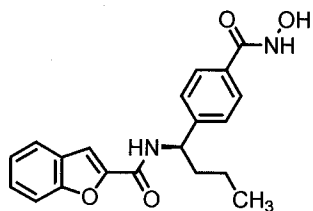
I-76



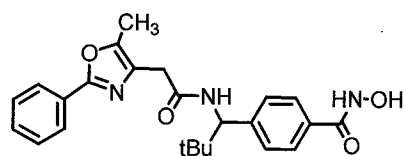
I-77



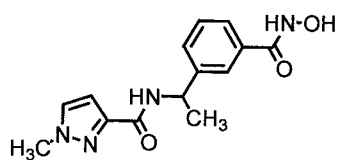
I-78



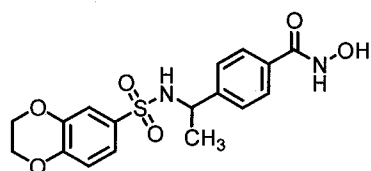
I-79



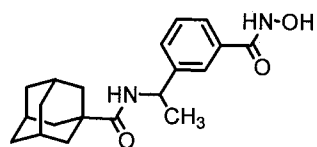
I-80



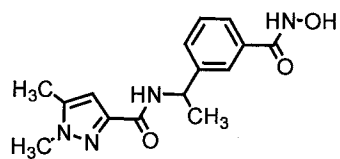
I-81



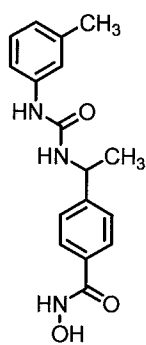
I-82



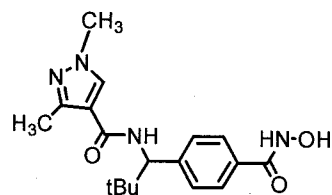
I-83



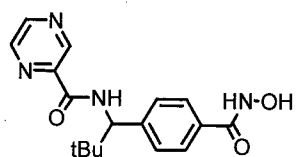
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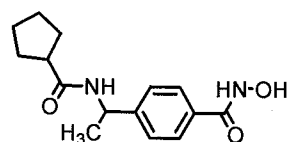
I-85



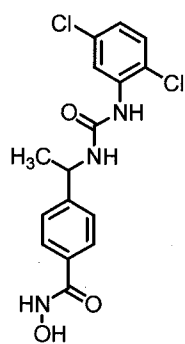
I-86



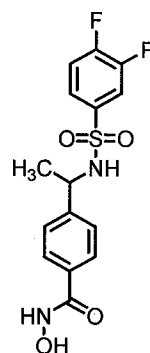
I-87



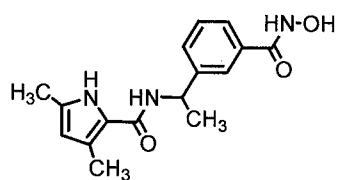
I-88



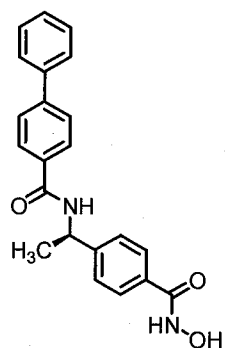
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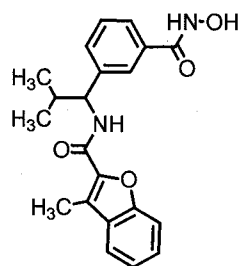
I-90



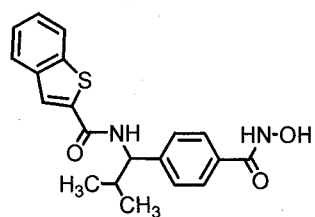
I-91



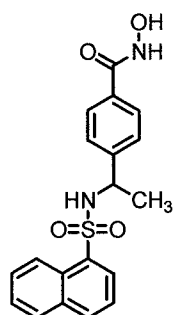
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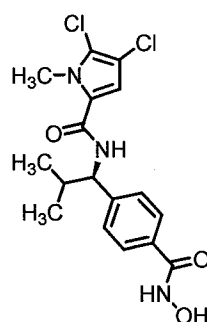
I-93



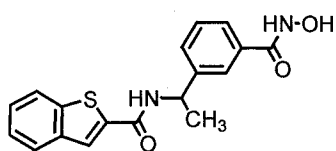
I-94



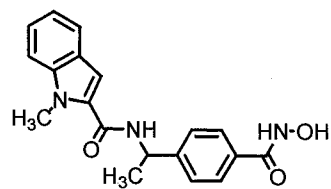
I-95



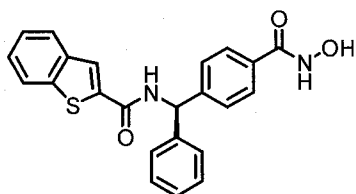
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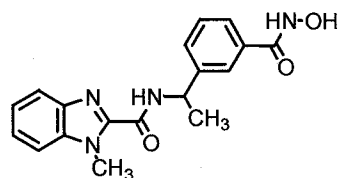
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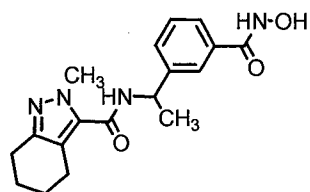
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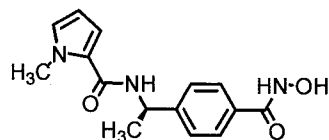
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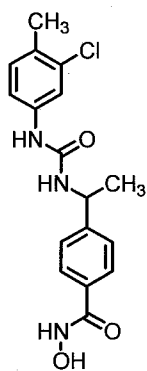
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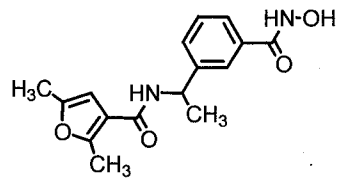
I-101



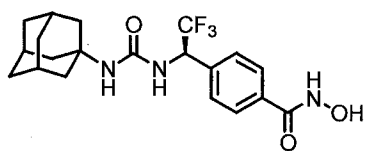
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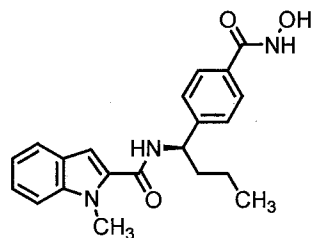
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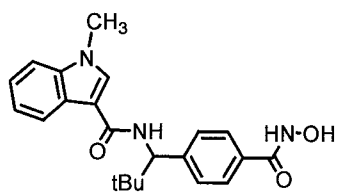
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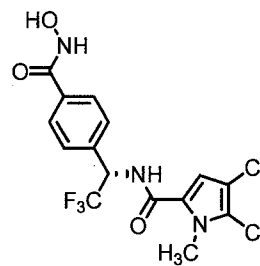
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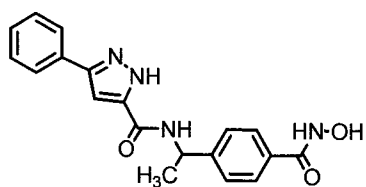
I-106



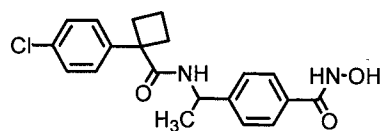
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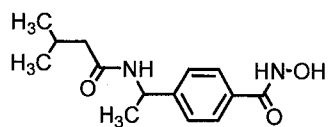
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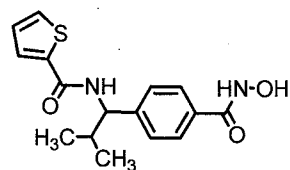
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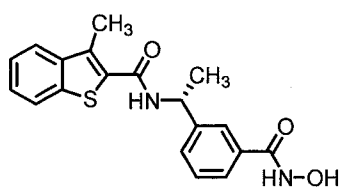
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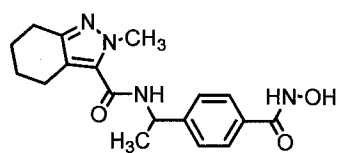
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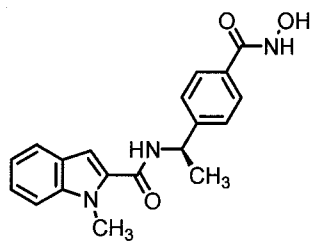
I-112



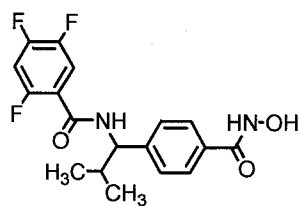
I-113



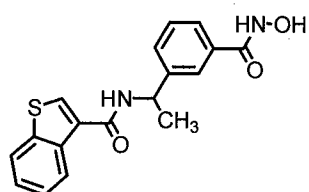
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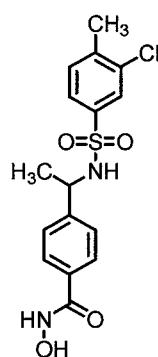
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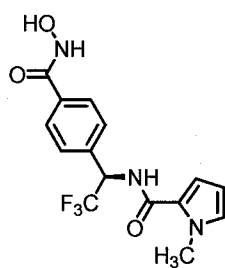
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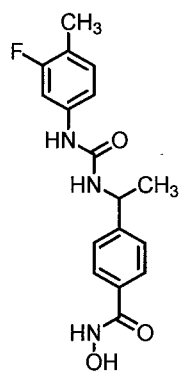
I-117



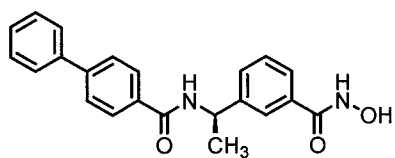
I-118



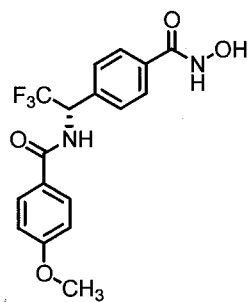
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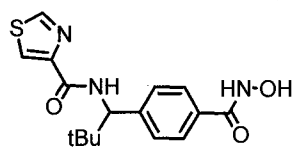
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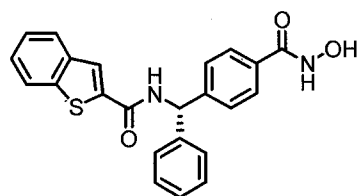
I-121



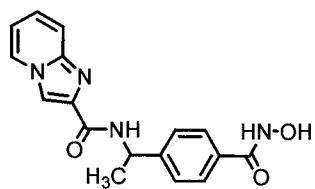
I-122



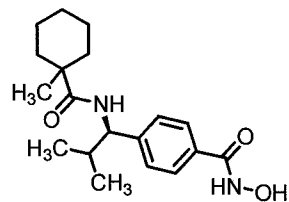
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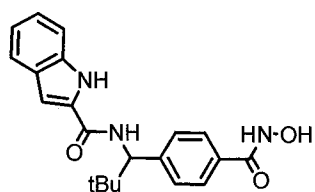
I-124



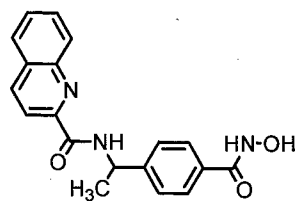
I-125



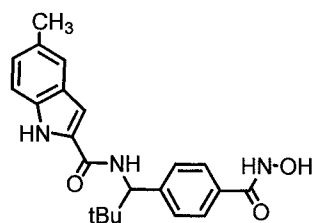
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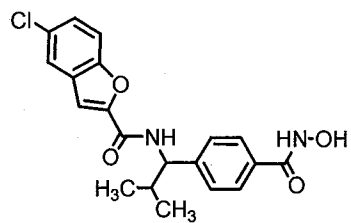
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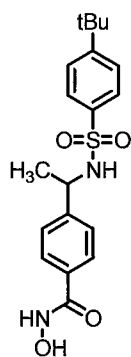
I-128



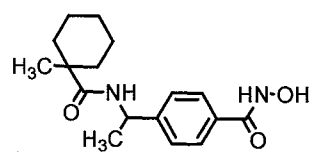
I-129



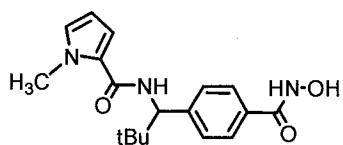
I-130



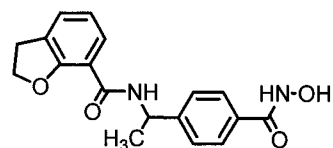
I-131



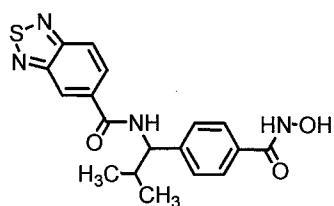
I-132



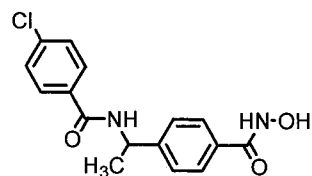
I-133



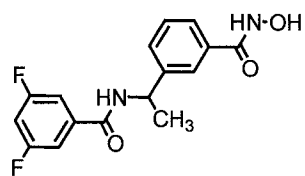
I-134



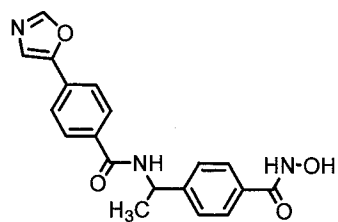
I-135



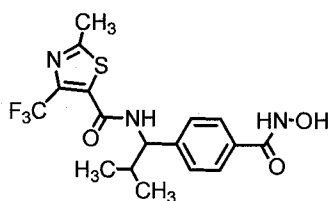
I-136



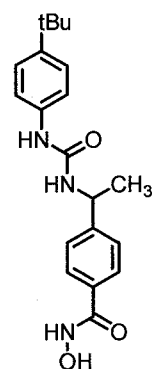
I-137



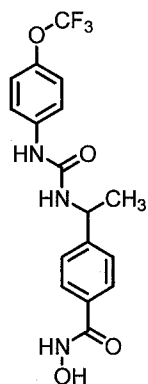
I-138



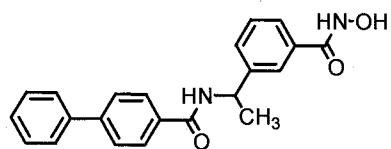
I-139



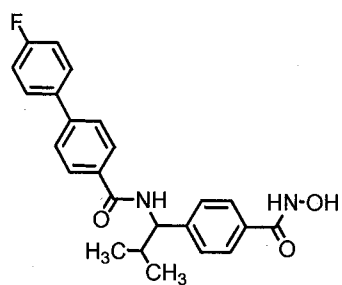
I-140



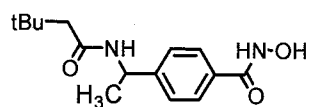
I-141



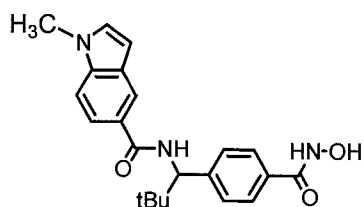
I-142



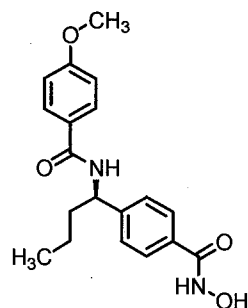
I-143



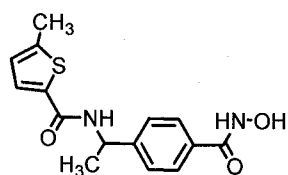
I-144



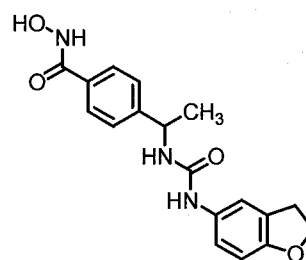
I-145



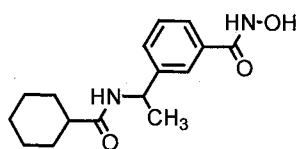
I-146



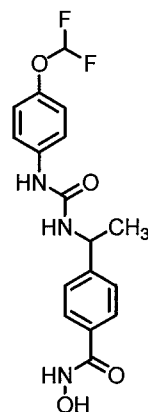
I-147



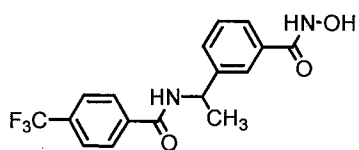
I-148



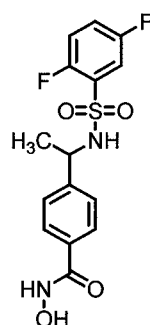
I-149



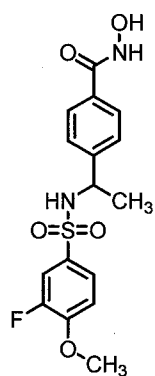
I-150



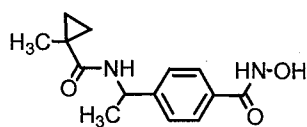
I-151



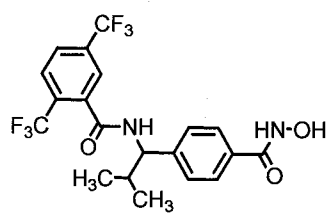
I-152



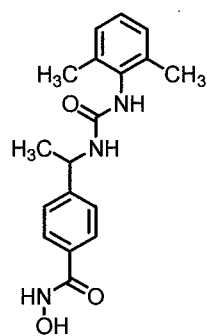
I-153



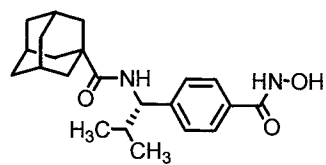
I-154



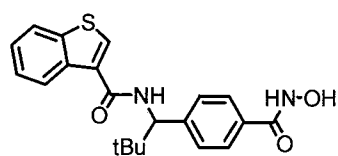
I-155



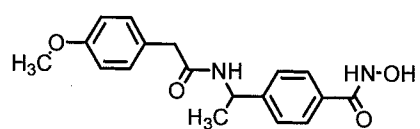
I-156



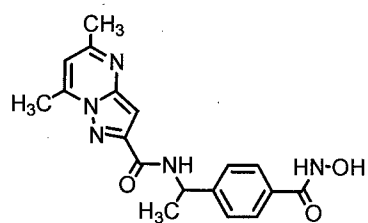
I-157



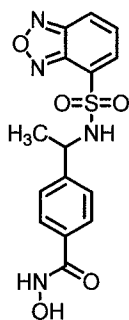
I-158



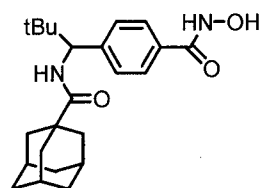
I-159



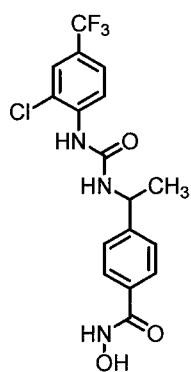
I-160



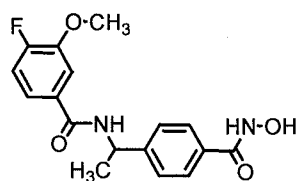
I-161



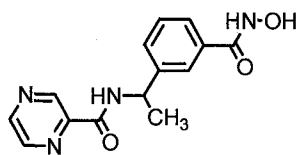
I-162



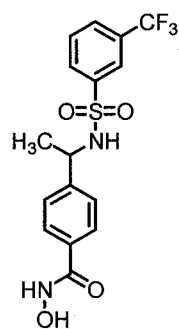
I-163



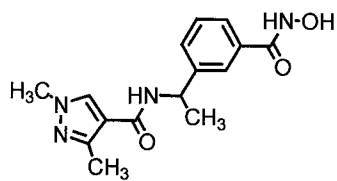
I-164



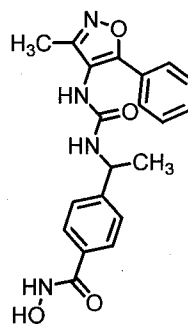
I-165



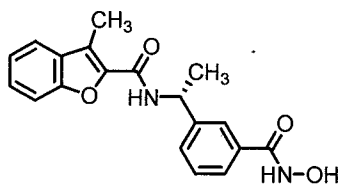
I-166



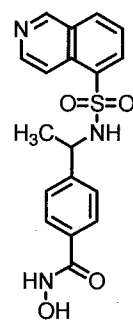
I-167



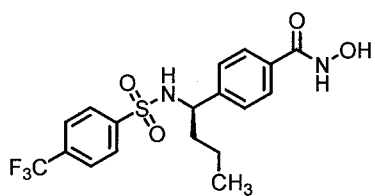
I-168



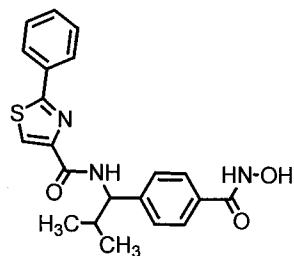
I-169



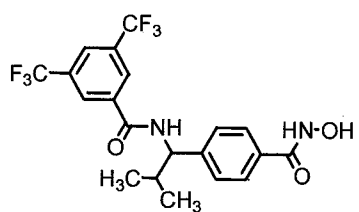
I-170



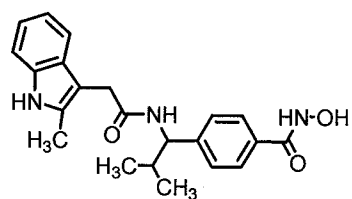
I-171



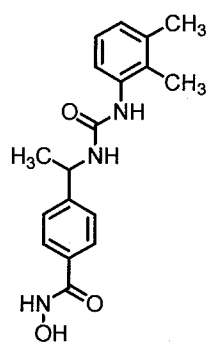
I-172



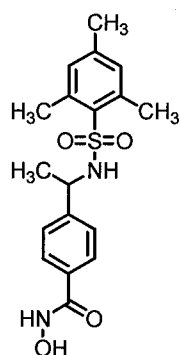
I-173



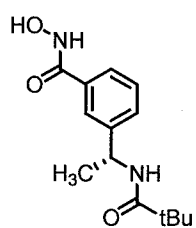
I-174



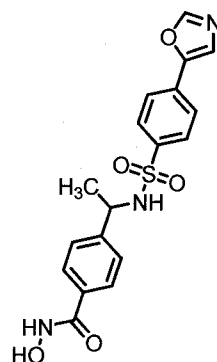
I-175



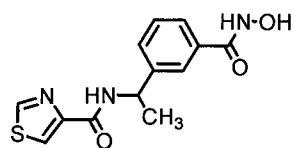
I-176



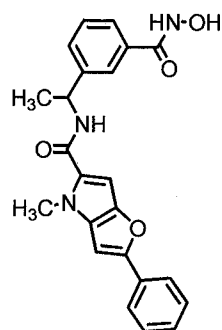
I-177



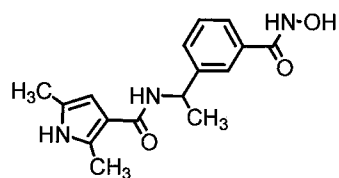
I-178



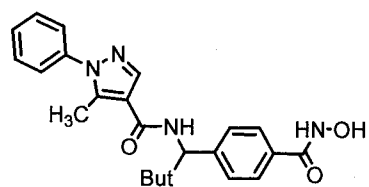
I-179



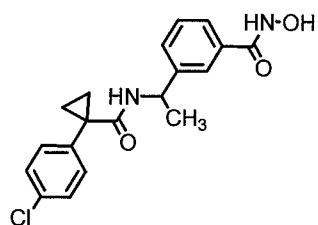
I-180



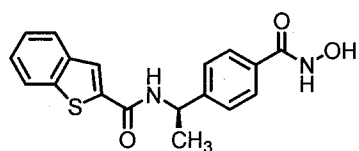
I-181



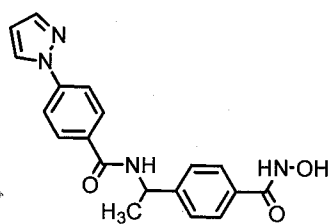
I-182



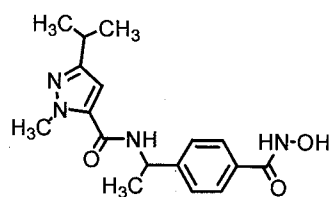
I-183



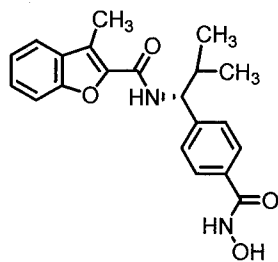
I-184



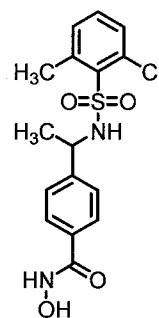
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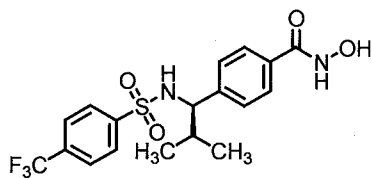
I-186



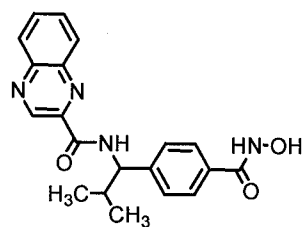
I-187



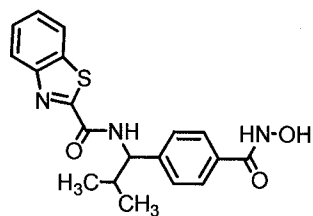
I-188



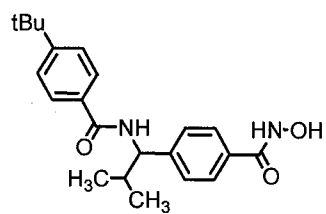
I-189



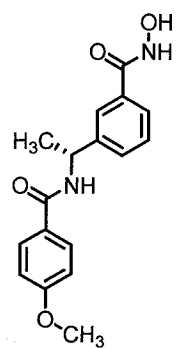
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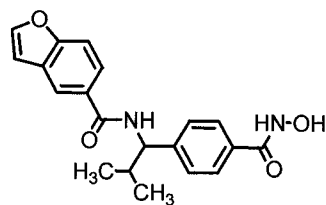
I-191



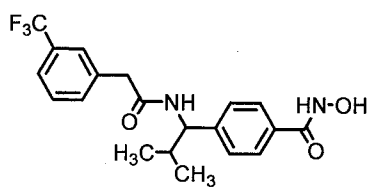
I-192



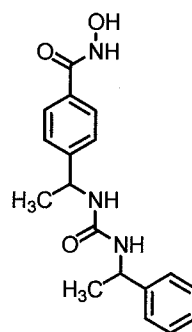
I-193



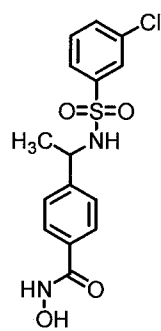
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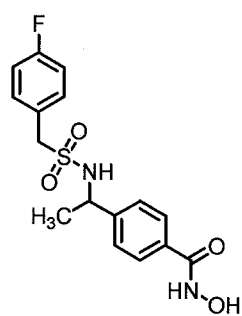
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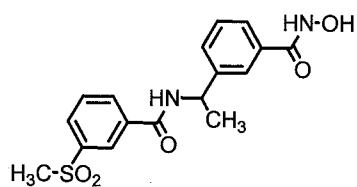
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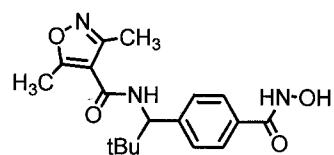
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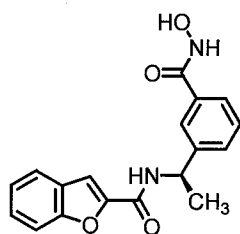
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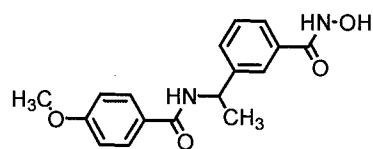
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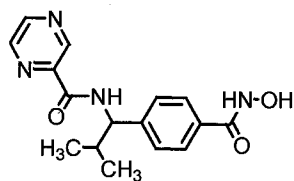
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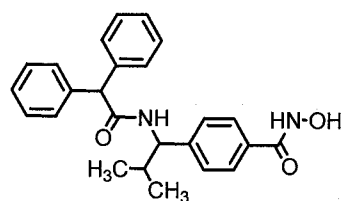
I-201



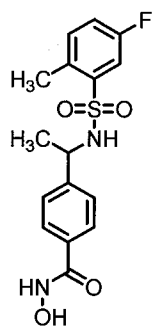
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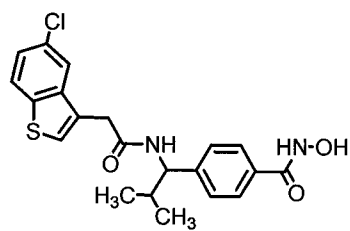
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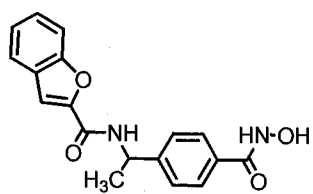
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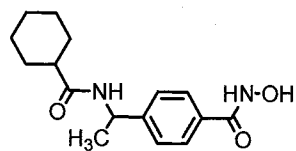
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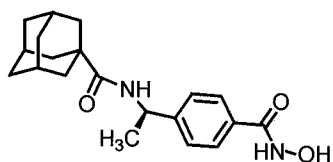
I-206



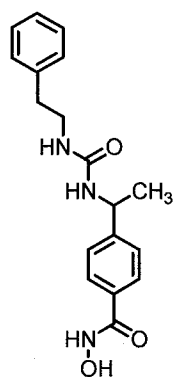
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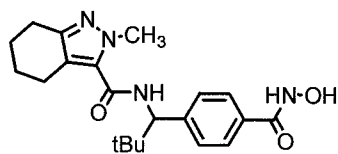
I-208



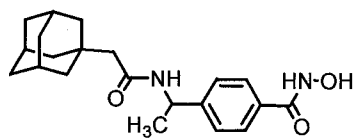
I-209



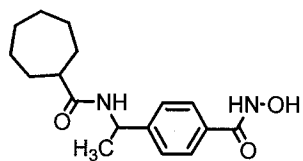
I-210



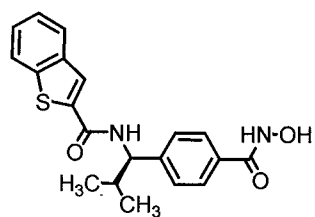
I-211



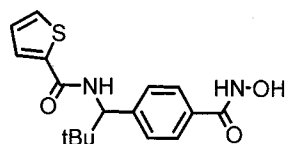
I-212



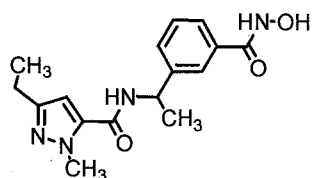
I-213



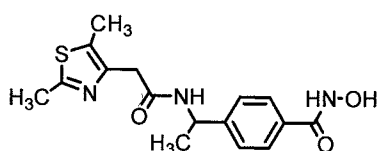
I-214



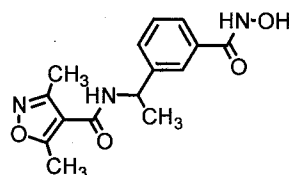
I-215



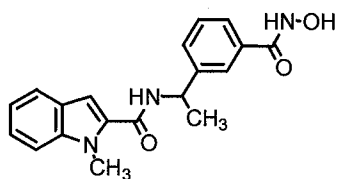
I-216



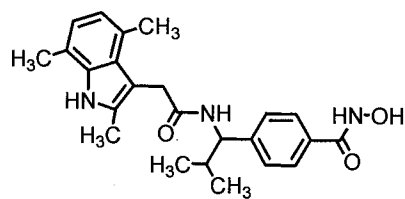
I-217



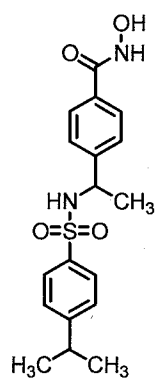
I-218



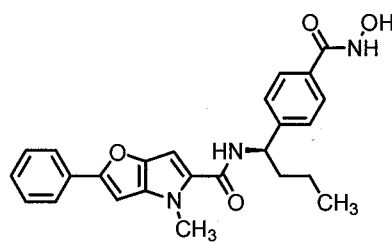
I-219



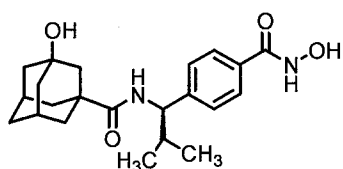
I-220



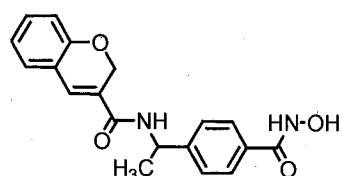
I-221



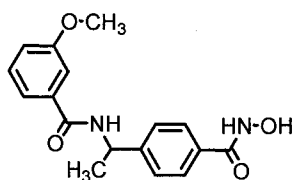
I-222



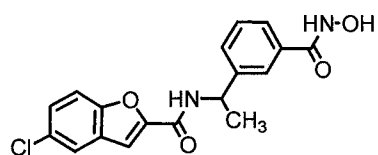
I-223



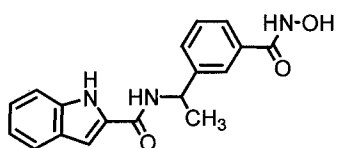
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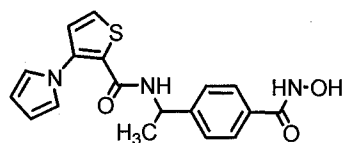
I-225



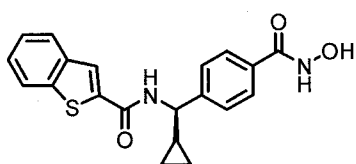
I-226



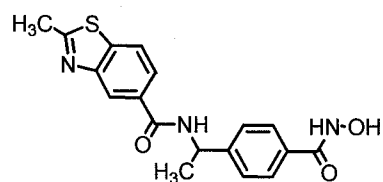
I-227



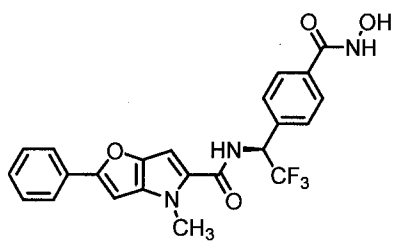
I-228



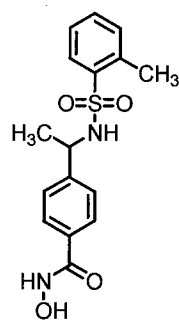
I-229



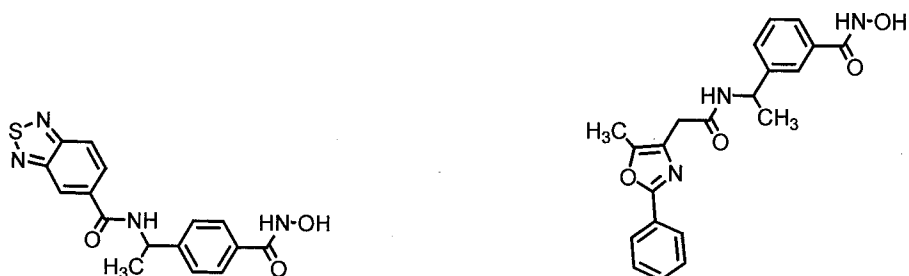
I-230



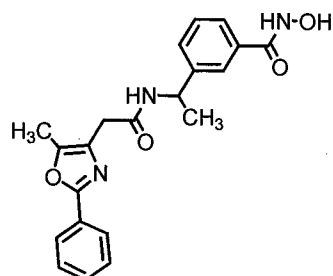
I-231



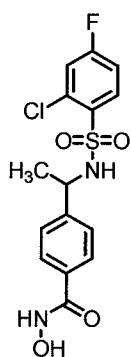
I-232



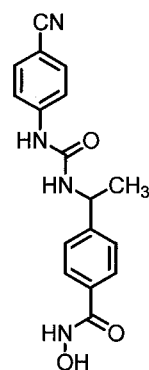
I-233



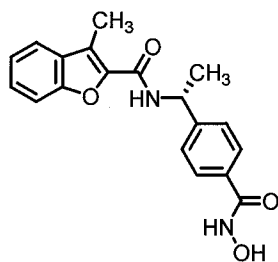
I-234



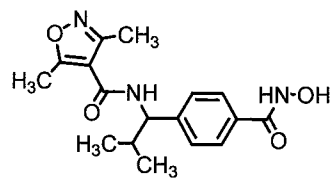
I-235



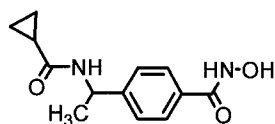
I-236



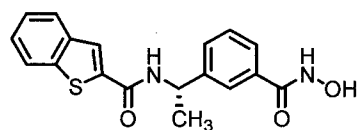
I-237



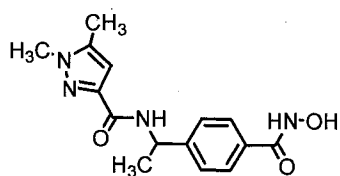
I-238



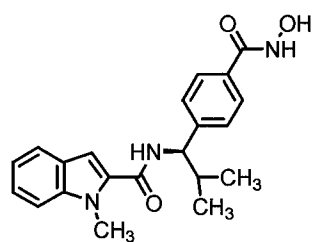
I-239



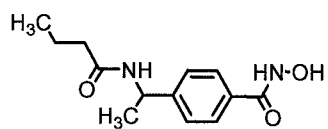
I-240



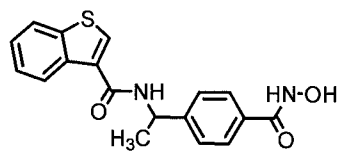
I-241



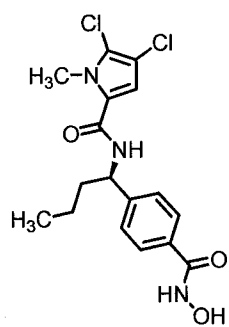
I-242



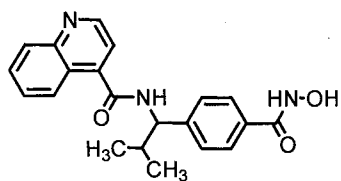
I-243



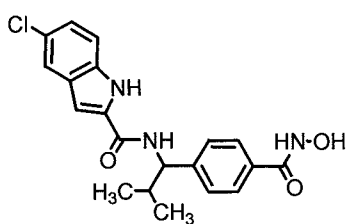
I-244



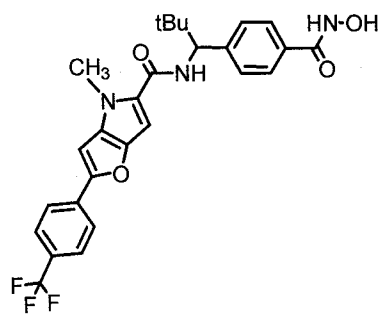
I-245



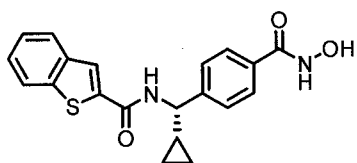
I-246



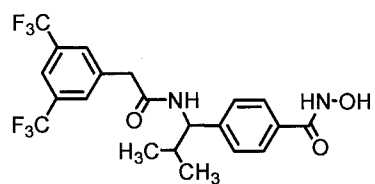
I-247



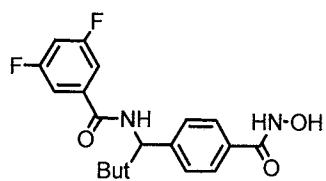
I-248



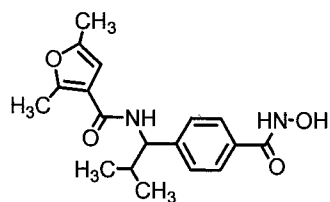
I-249



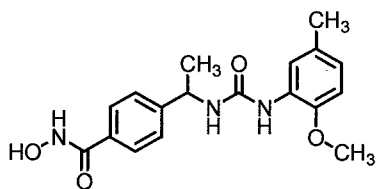
I-250



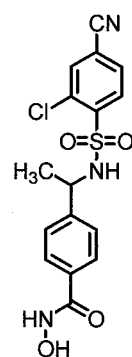
I-251



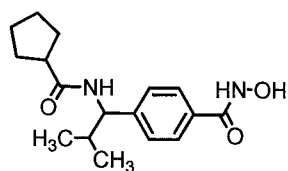
I-252



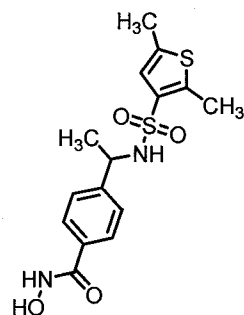
I-253



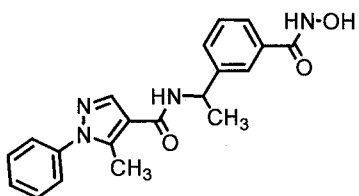
I-254



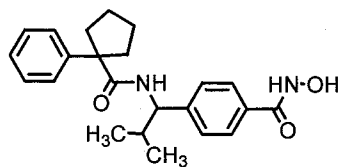
I-255



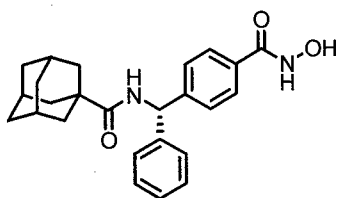
I-256



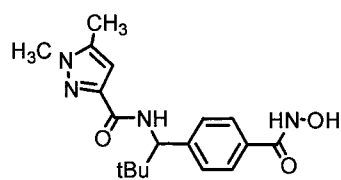
I-257



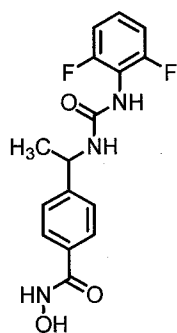
I-258



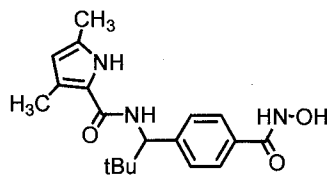
I-259



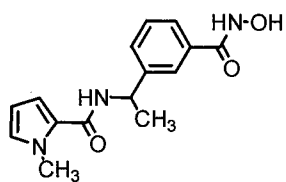
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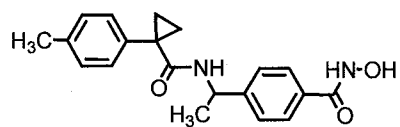
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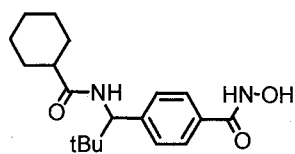
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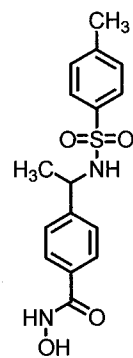
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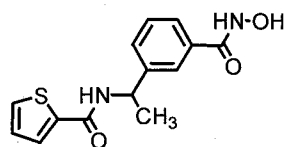
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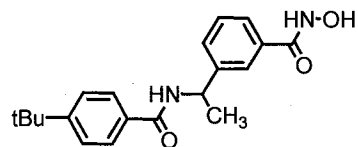
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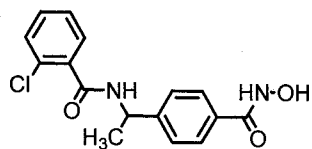
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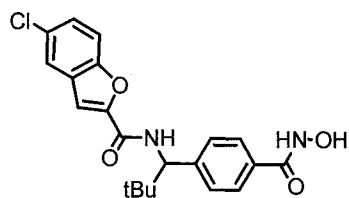
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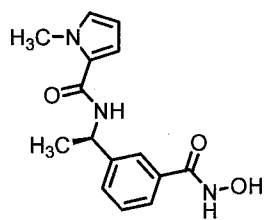
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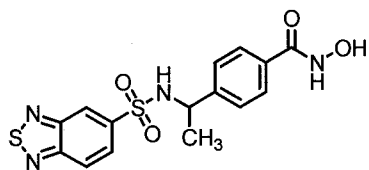
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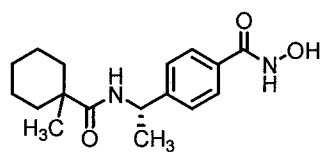
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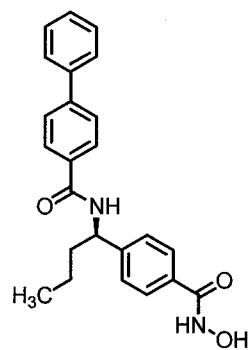
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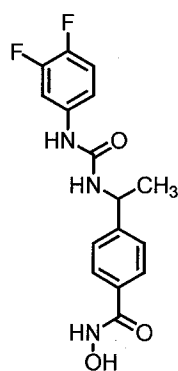
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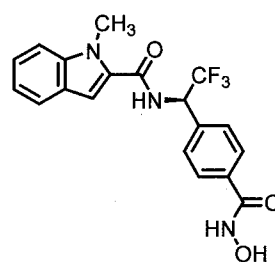
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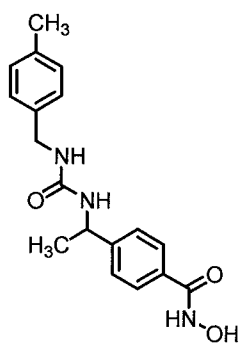
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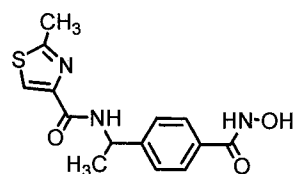
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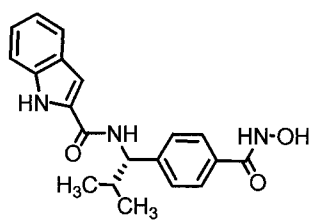
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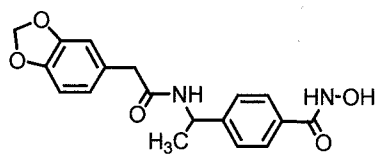
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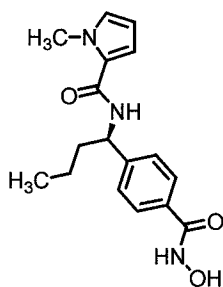
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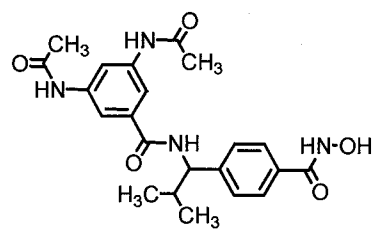
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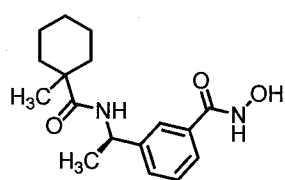
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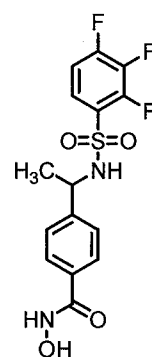
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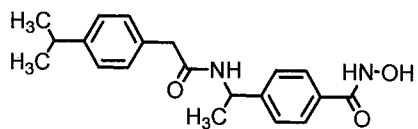
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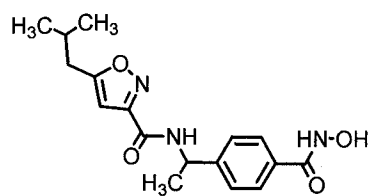
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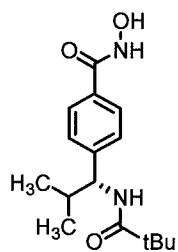
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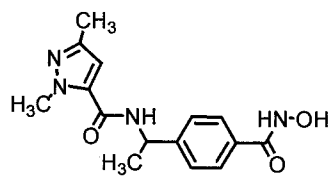
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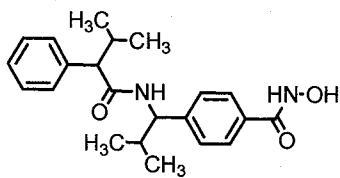
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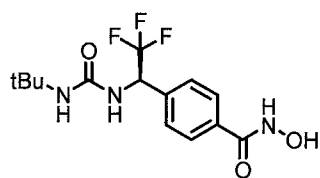
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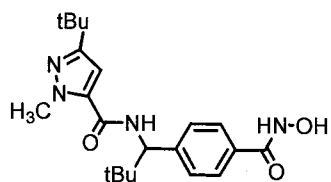
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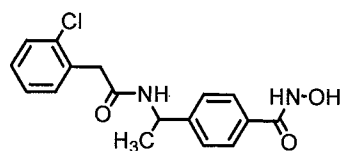
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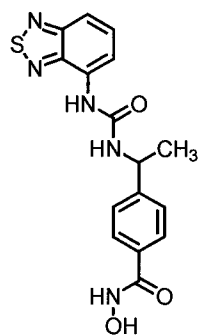
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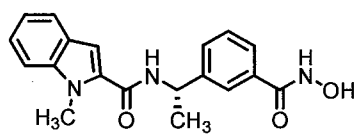
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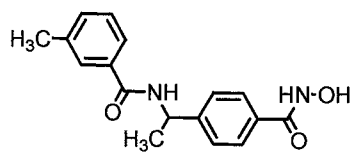
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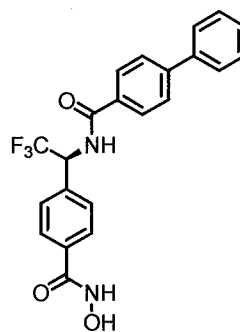
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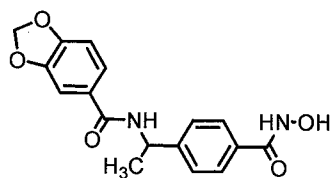
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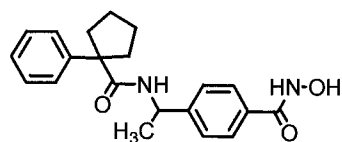
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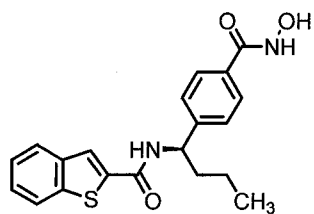
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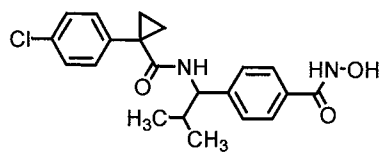
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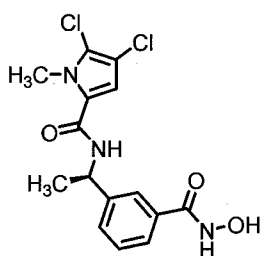
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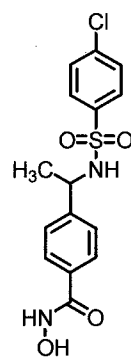
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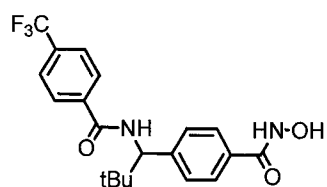
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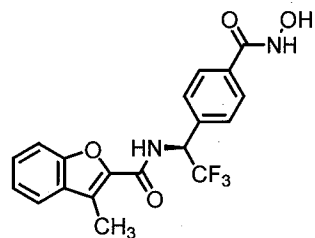
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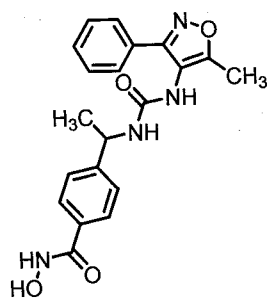
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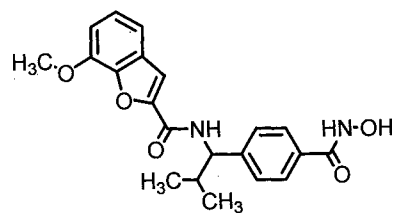
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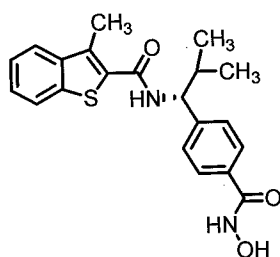
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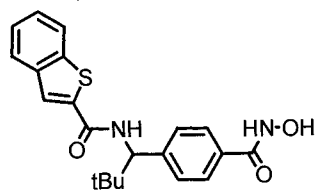
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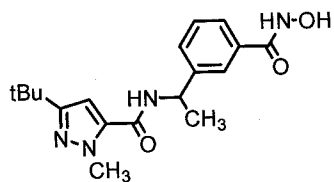
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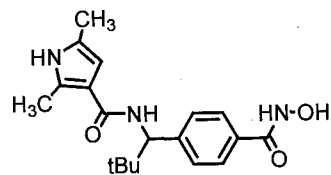
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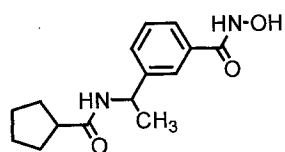
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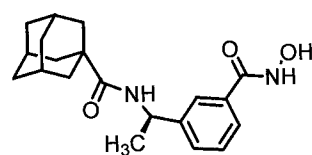
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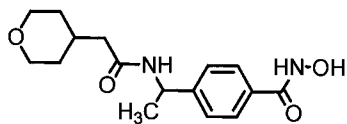
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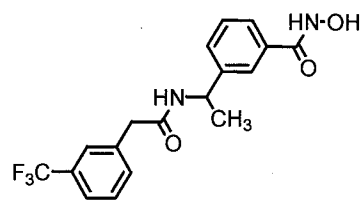
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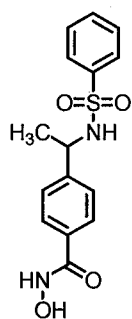
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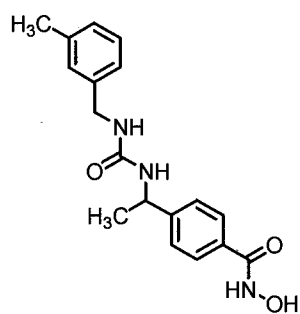
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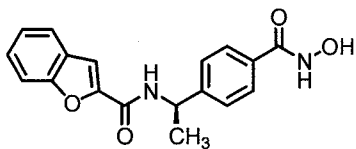
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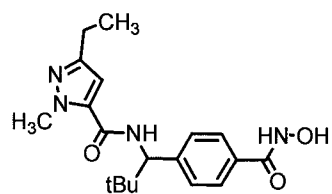
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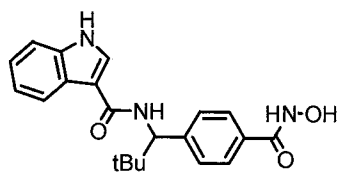
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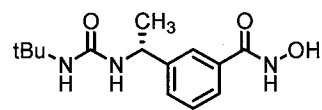
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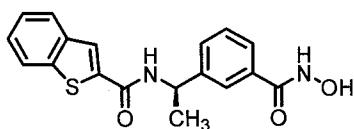
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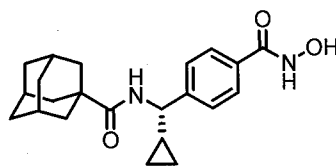
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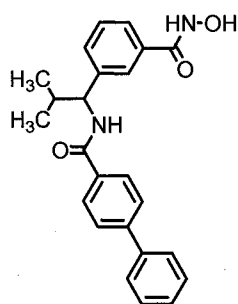
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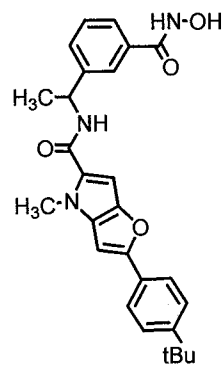
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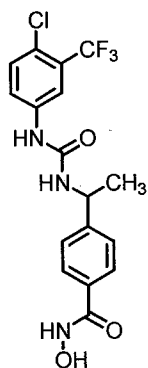
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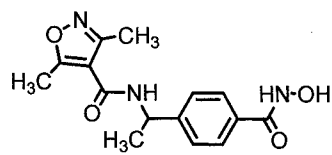
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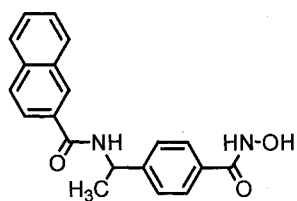
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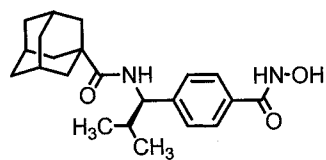
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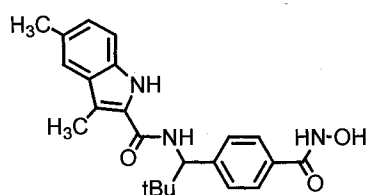
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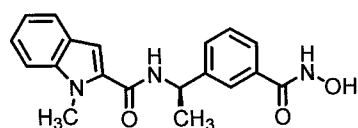
I-327



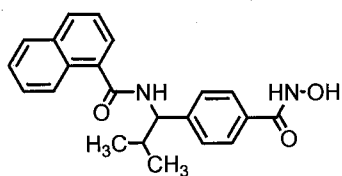
I-328



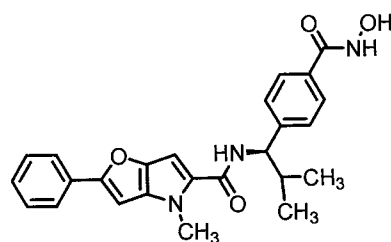
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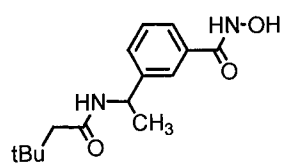
I-330



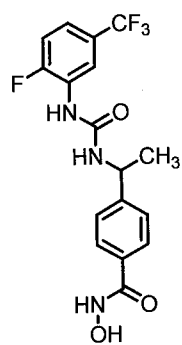
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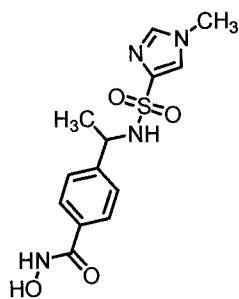
I-332



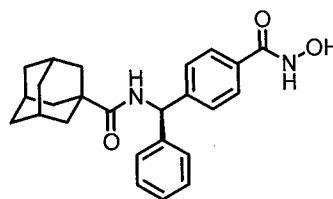
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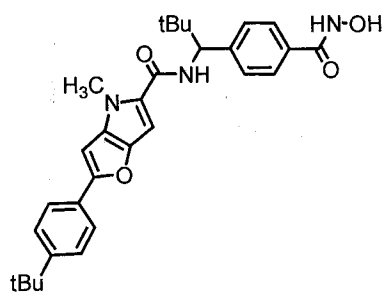
I-334



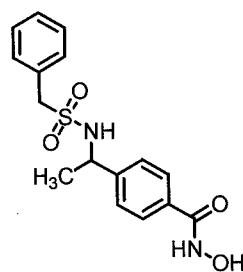
I-335



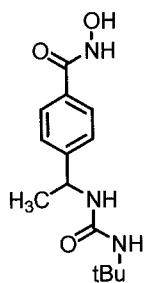
I-336



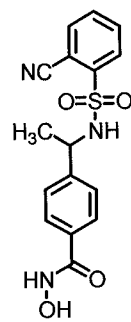
I-337



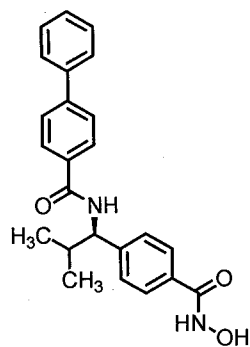
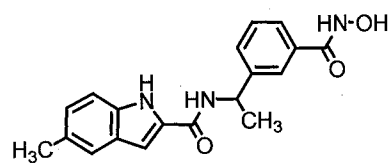
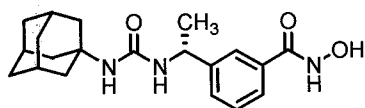
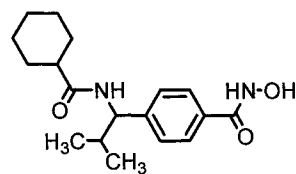
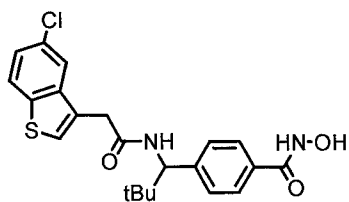
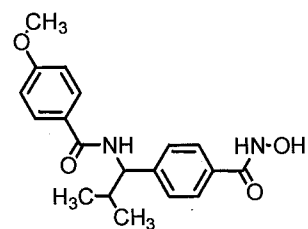
I-338

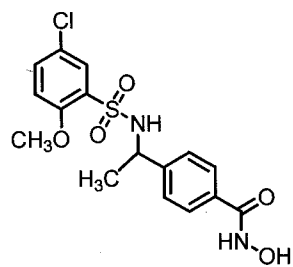


I-339

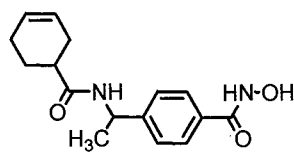


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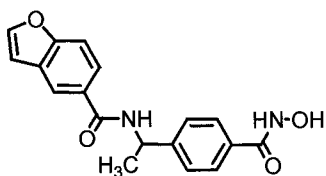
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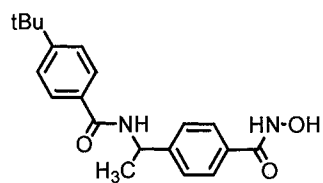
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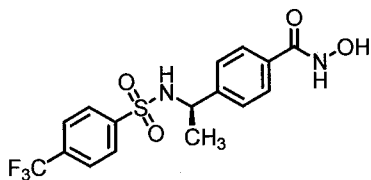
I-348



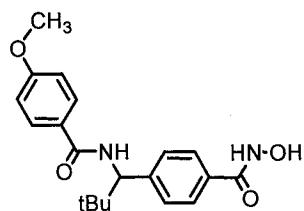
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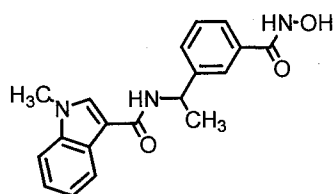
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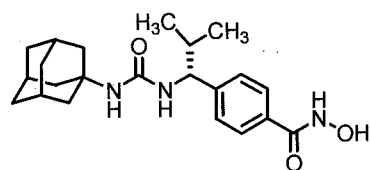
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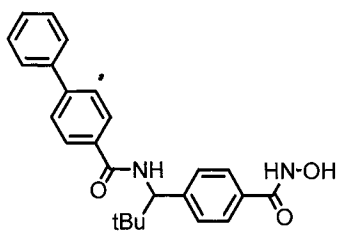
I-352



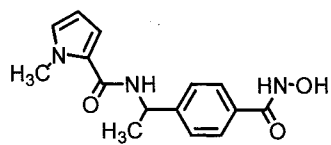
I-353



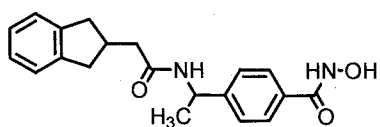
I-354



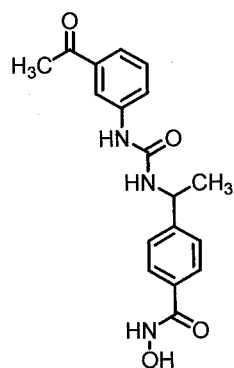
I-355



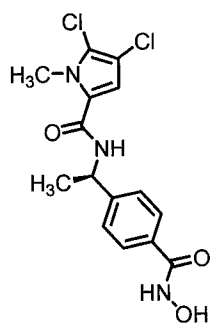
I-356



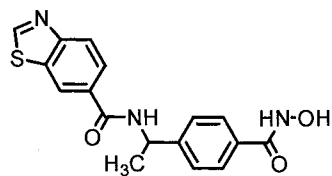
I-357



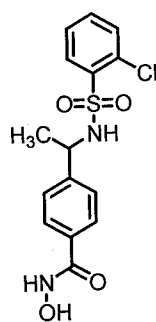
I-358



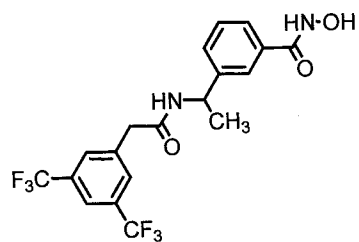
I-359



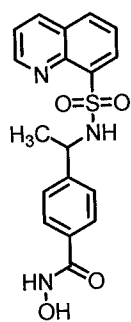
I-360



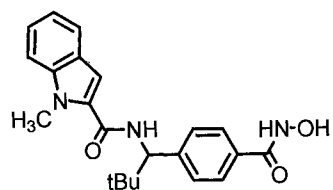
I-361



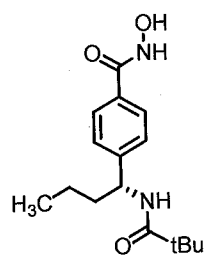
I-362



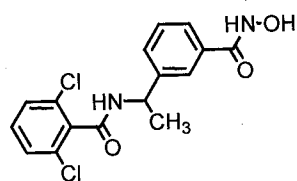
I-363



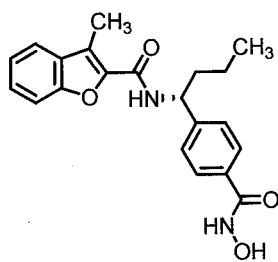
I-364



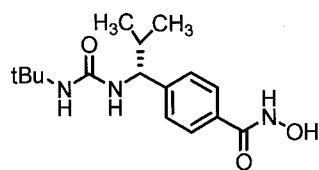
I-365



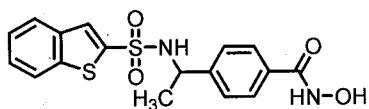
I-366



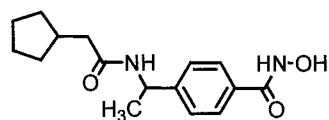
I-367



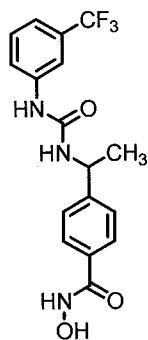
I-368



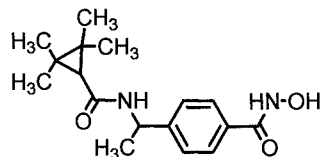
I-369



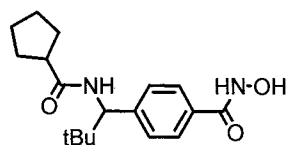
I-370



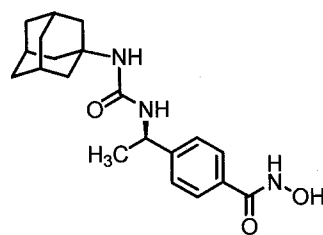
I-371



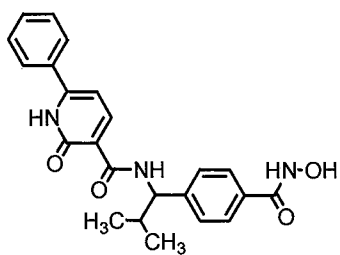
I-372



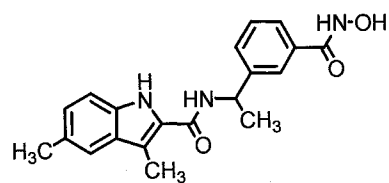
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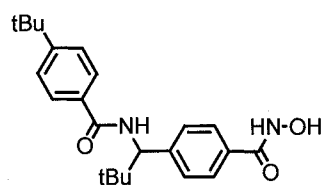
I-374



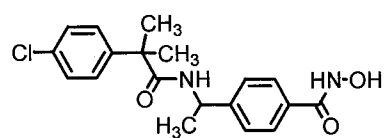
I-375



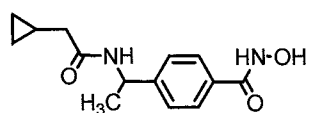
I-376



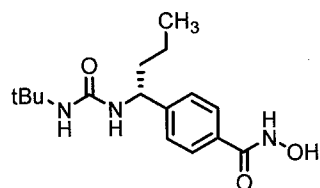
I-377



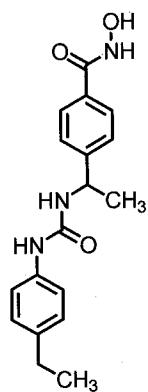
I-378



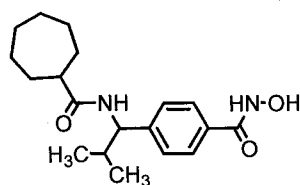
I-379



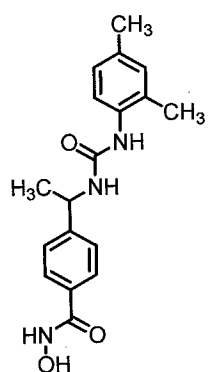
I-380



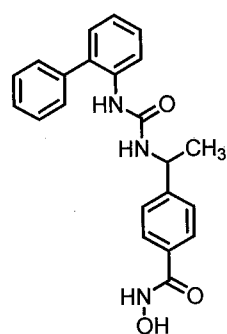
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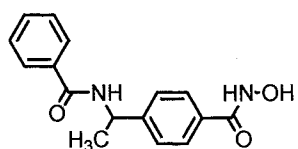
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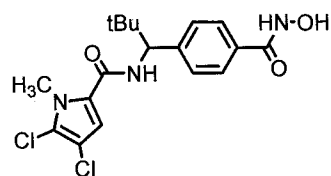
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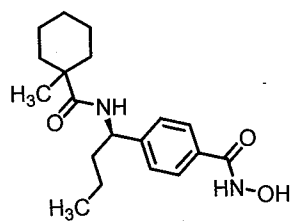
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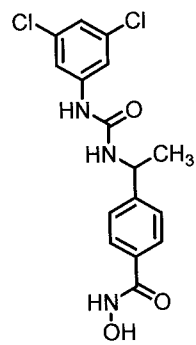
I-385



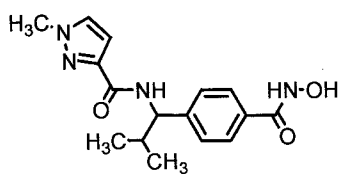
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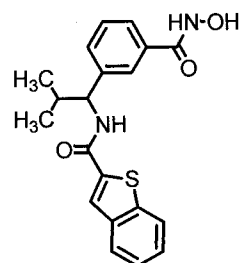
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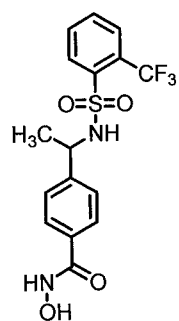
I-388



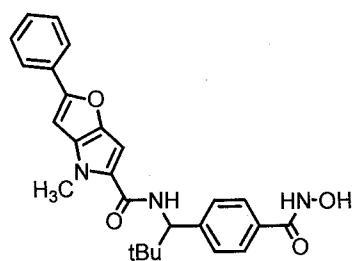
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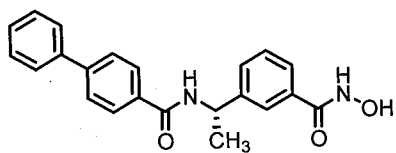
I-390



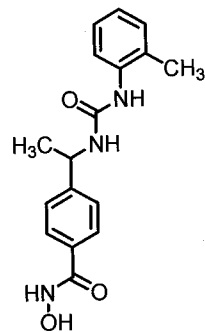
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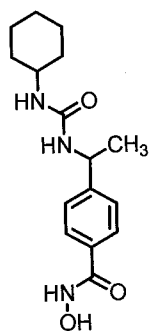
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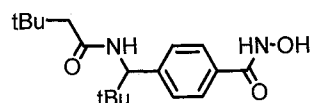
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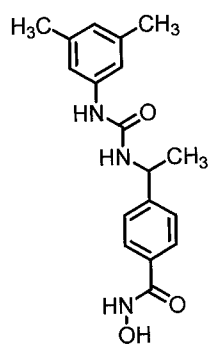
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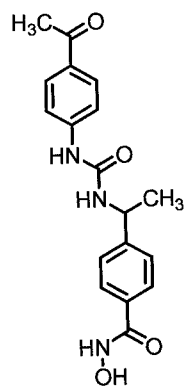
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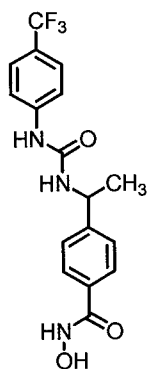
I-396



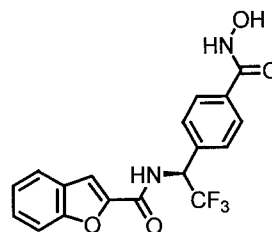
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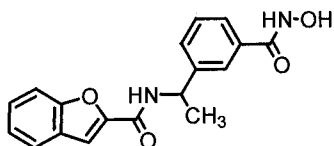
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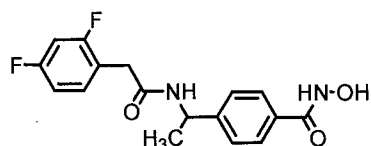
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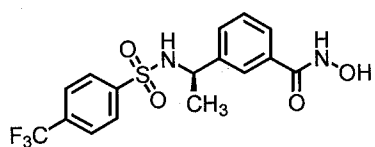
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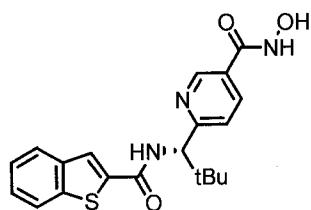
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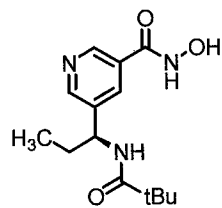
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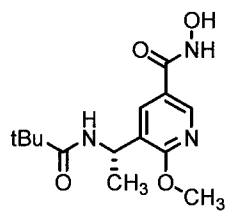
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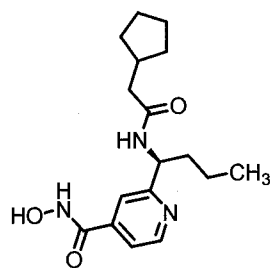
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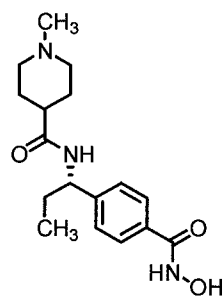
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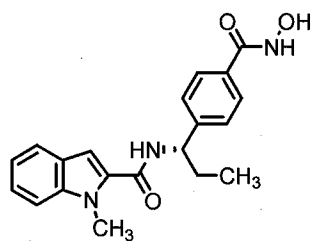
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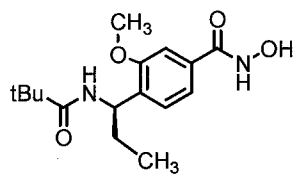
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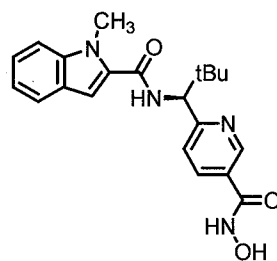
I-408



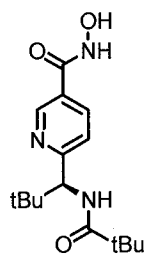
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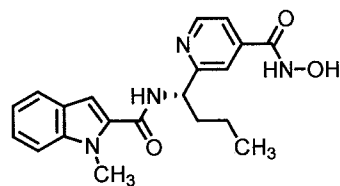
I-410



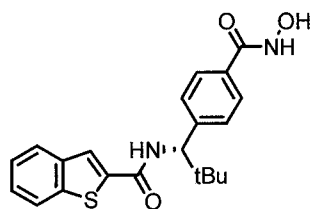
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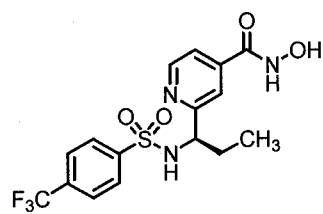
I-412



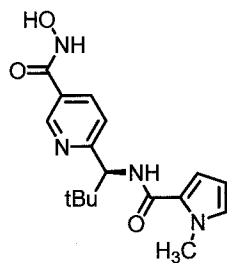
I-413



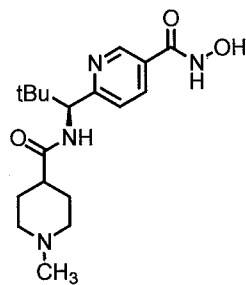
I-414



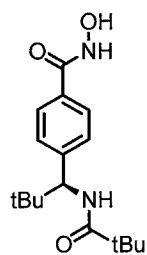
I-415



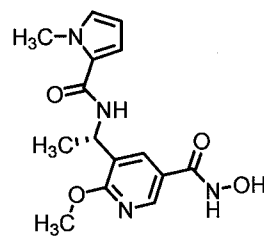
I-416



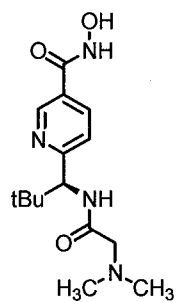
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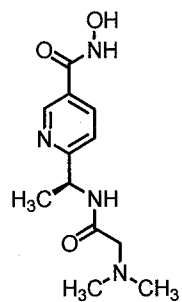
I-418



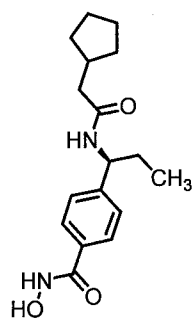
I-419



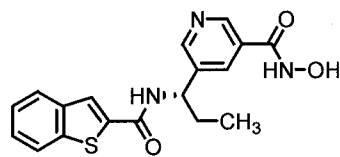
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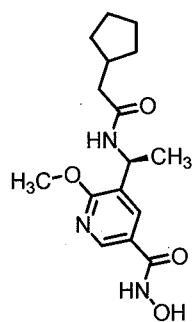
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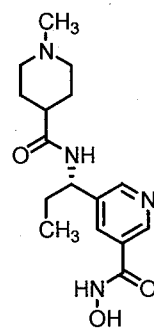
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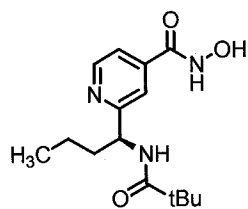
I-423



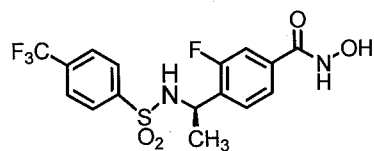
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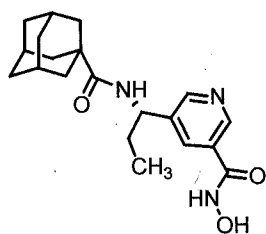
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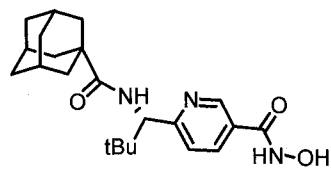
I-426



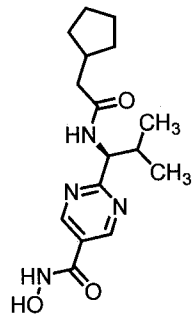
I-427



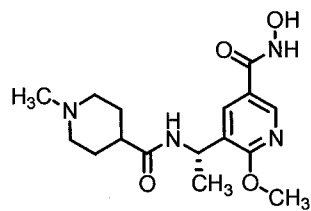
I-428



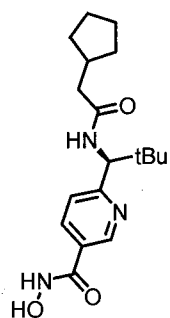
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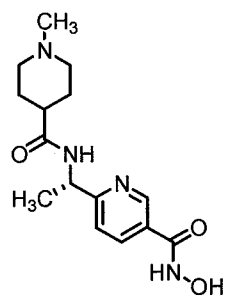
I-430



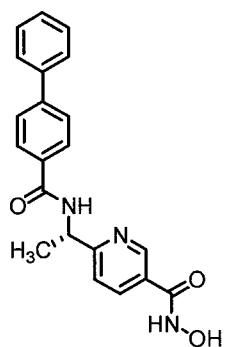
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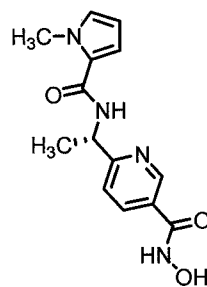
I-432



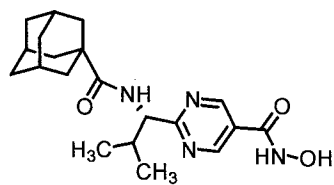
I-433



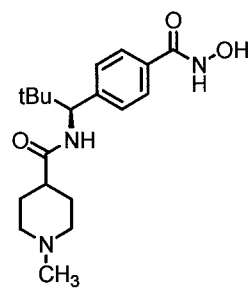
I-434



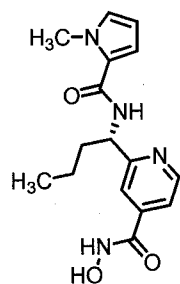
I-435



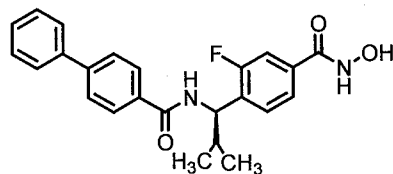
I-436



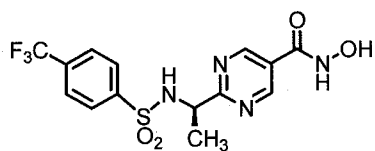
I-437



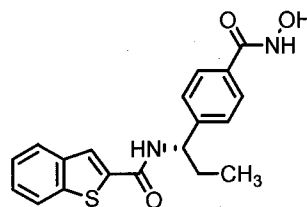
I-438



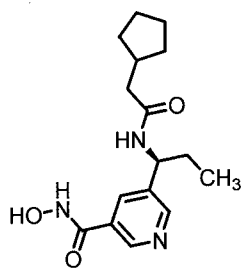
I-439



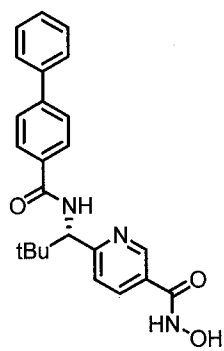
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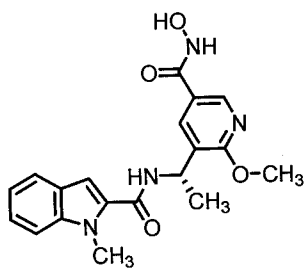
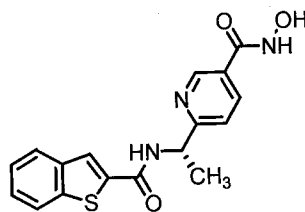
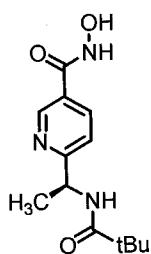
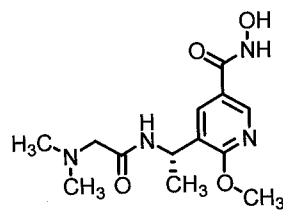
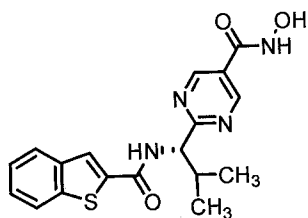
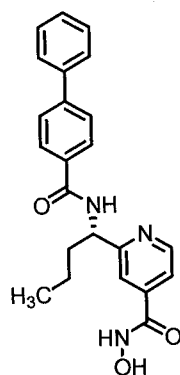
I-441

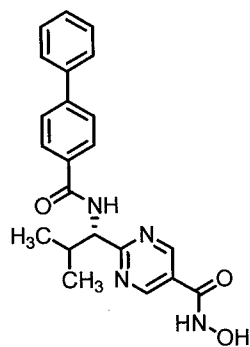


I-442

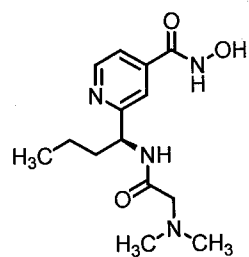


I-443

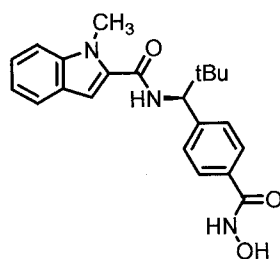
**I-444****I-445****I-446****I-447****I-448****I-449**



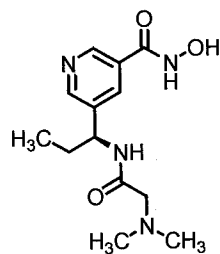
I-450



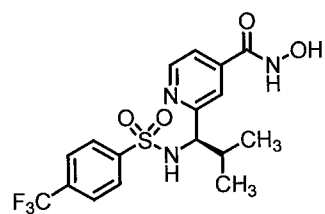
I-451



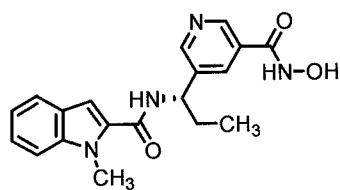
I-452



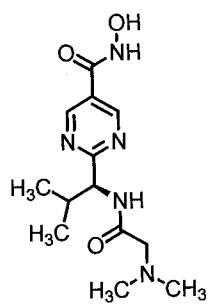
I-453



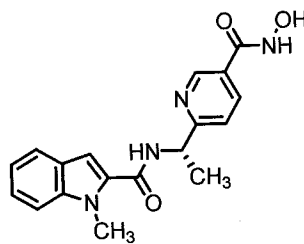
I-454



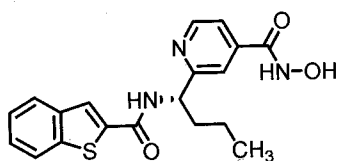
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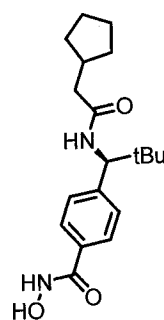
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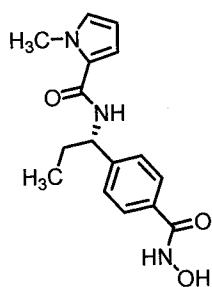
I-457



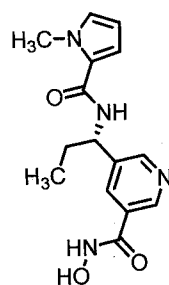
I-458



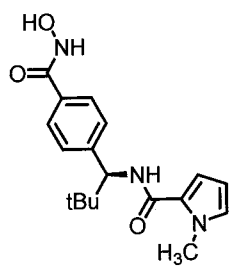
I-459



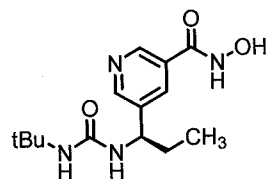
I-460



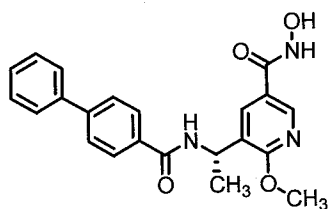
I-461



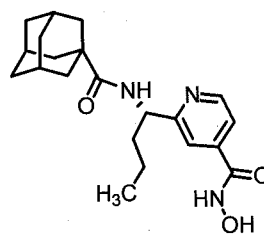
I-462



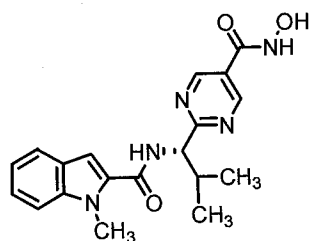
I-463



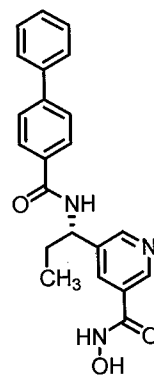
I-464



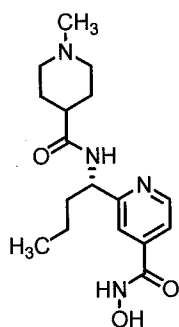
I-465



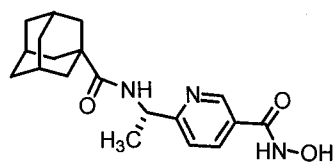
I-466



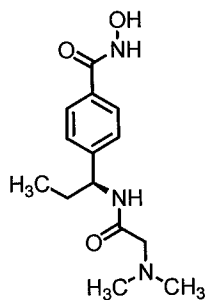
I-467



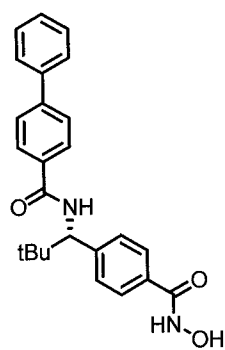
I-468



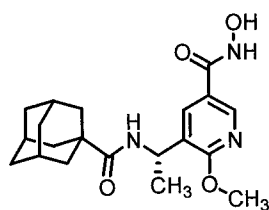
I-469



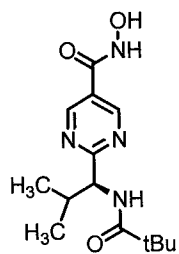
I-470



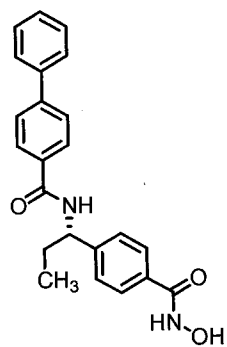
I-471



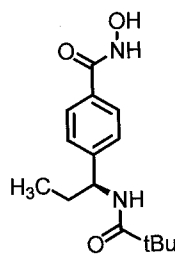
I-472



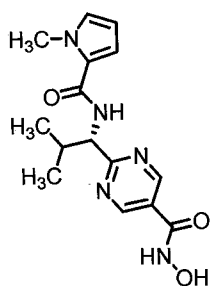
I-473



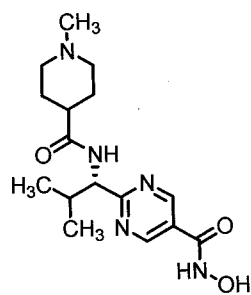
I-474



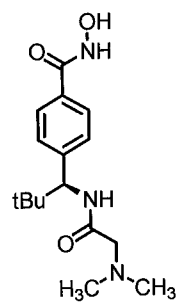
I-475



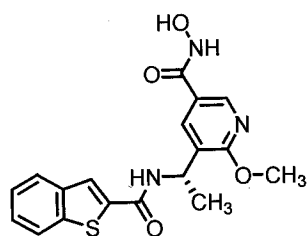
I-476



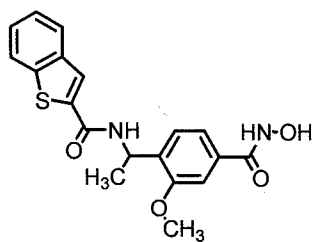
I-477



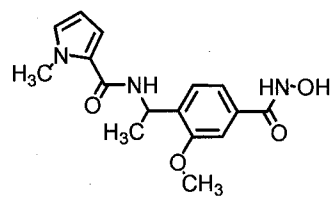
I-478



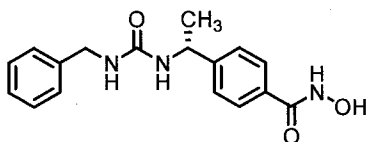
I-479



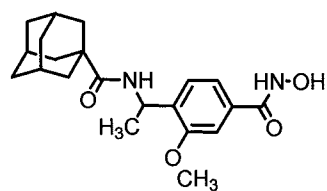
I-480



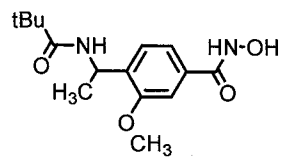
I-481



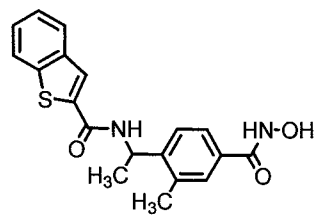
I-482



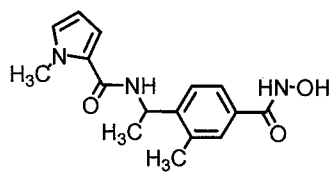
I-483



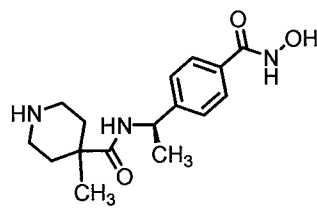
I-484



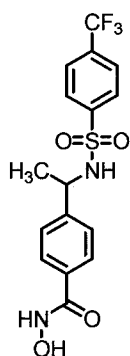
I-485



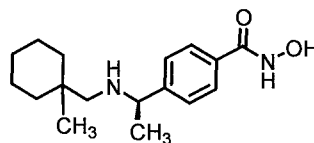
I-486



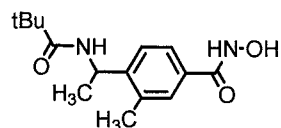
I-487



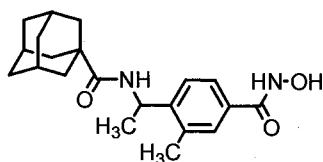
I-488



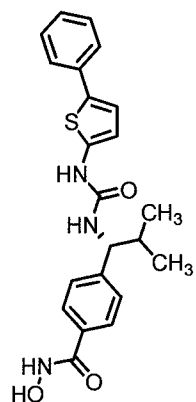
I-489



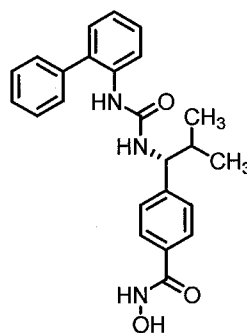
I-490



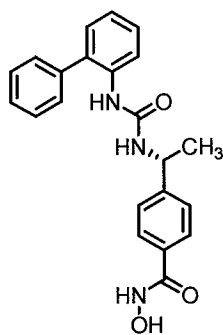
I-491



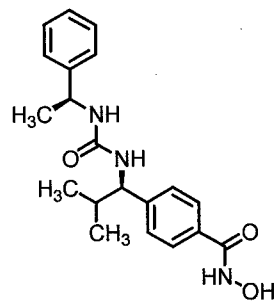
I-492



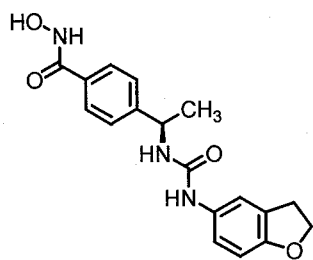
I-493



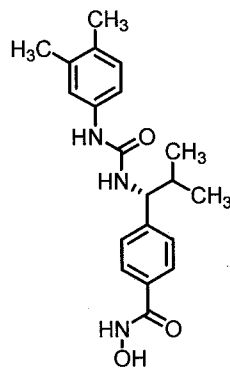
I-494



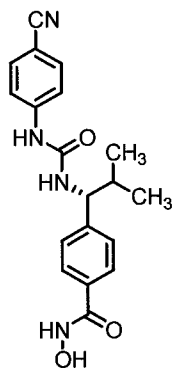
I-495



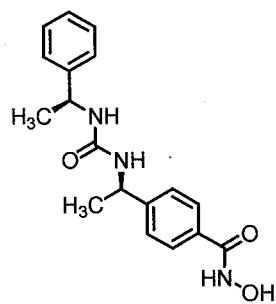
I-496



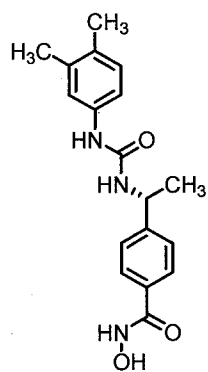
I-497



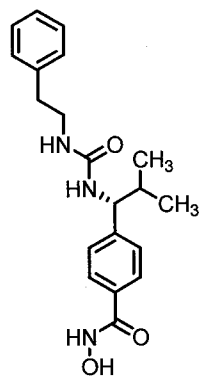
I-498



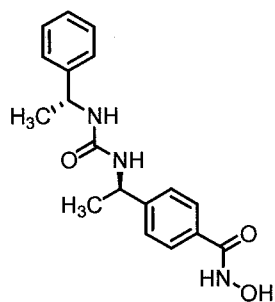
I-499



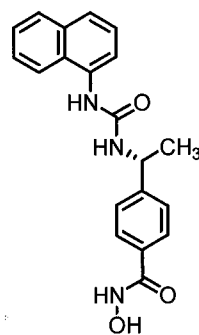
I-500



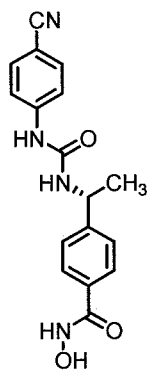
I-501



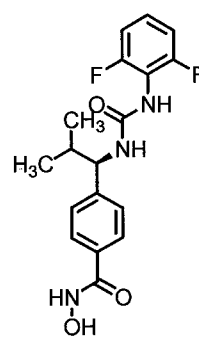
I-502



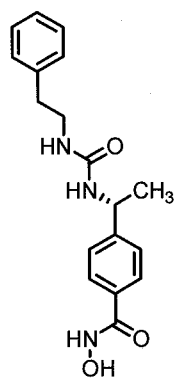
I-503



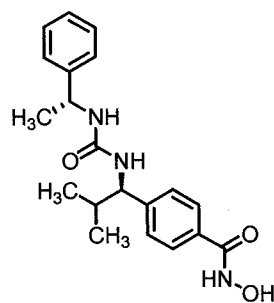
I-504



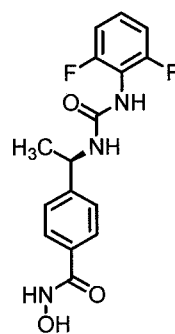
I-505



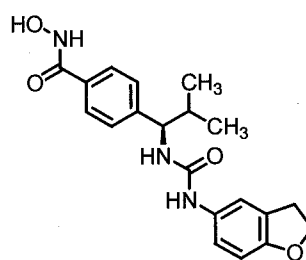
I-506



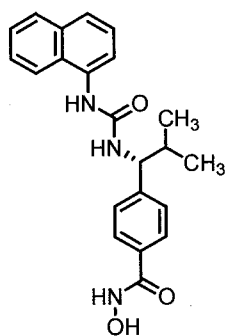
I-507



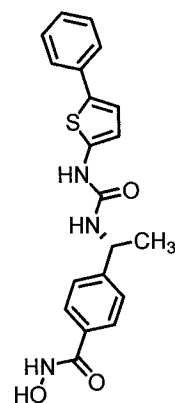
I-508



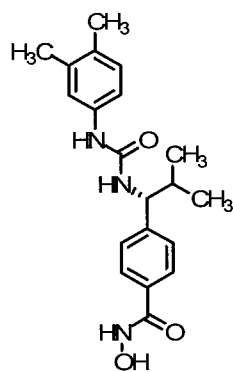
I-509



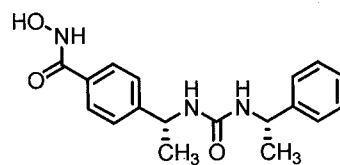
I-510



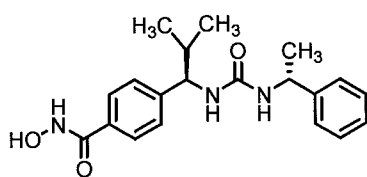
I-511



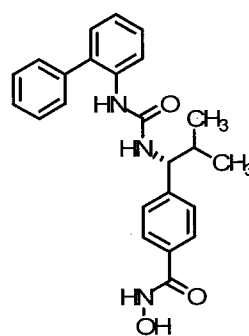
I-512



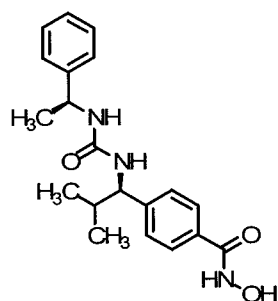
I-513



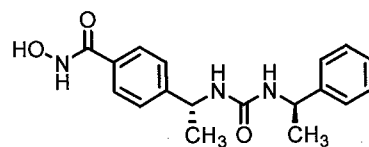
I-514



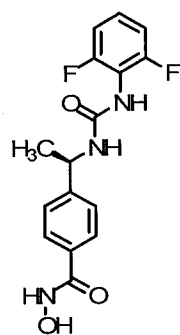
I-515



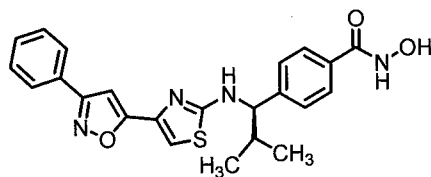
I-516



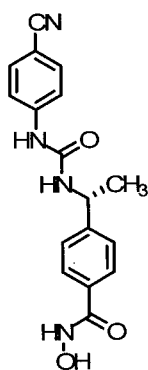
I-517



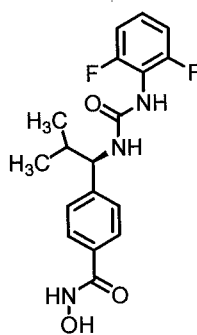
I-518



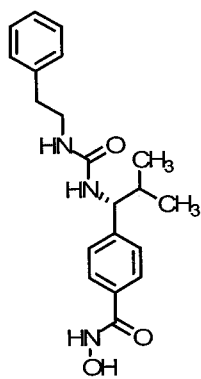
I-519



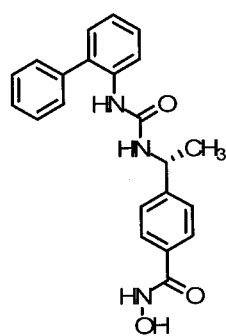
I-520



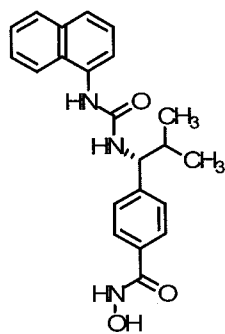
I-521



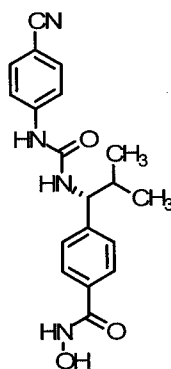
I-522



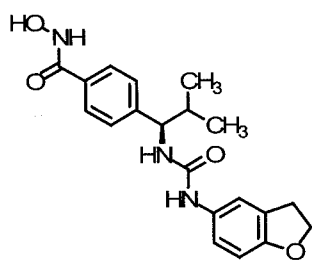
I-523



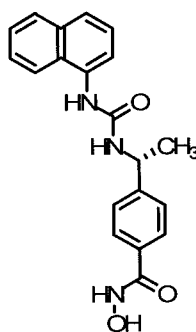
I-524



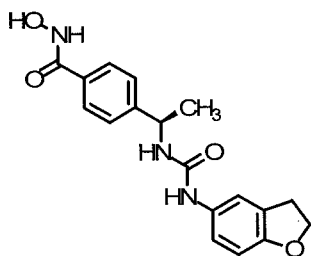
I-525



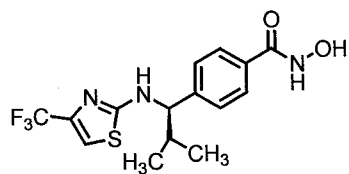
I-526



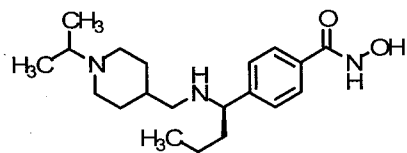
I-527



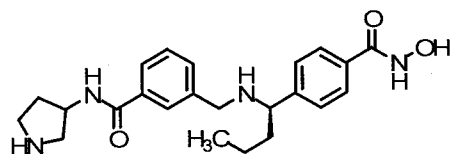
I-528



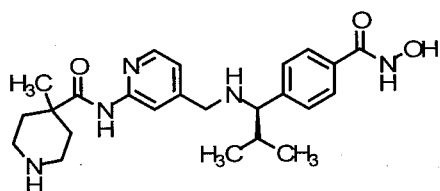
I-529



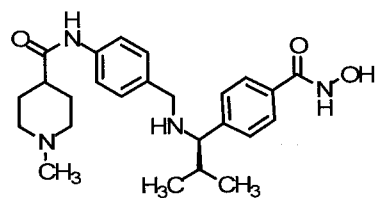
I-530



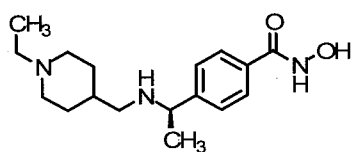
I-531



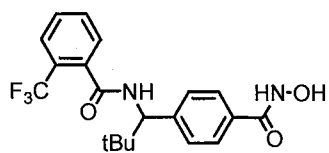
I-532



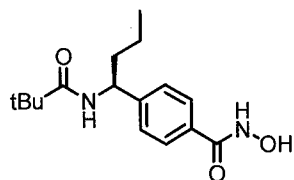
I-533



I-534



I-535



I-536

[00119] The compounds in Table 1 above may also be identified by the following chemical names:

I-1	4-{1-[(ethylsulfonyl)amino]ethyl}- <i>N</i> -hydroxybenzamide
I-2	4-(1-{[(4-fluorophenyl)sulfonyl]amino}ethyl)- <i>N</i> -hydroxybenzamide
I-3	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)adamantane-1-carboxamide
I-4	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}-2,2-dimethylpropyl)-1-benzofuran-2-carboxamide
I-5	<i>N</i> -((1 <i>R</i>)-1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-4-methyl-2-phenyl-4 <i>H</i> -furo[3,2- <i>b</i>]pyrrole-5-carboxamide
I-6	<i>N</i> -hydroxy-4-(1-{[(1-naphthylamino)carbonyl]amino}ethyl)benzamide
I-7	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-3-methyl-1-benzofuran-2-carboxamide
I-8	2-fluoro- <i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-5-methylbenzamide
I-9	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}-2,2-dimethylpropyl)-2,5-dimethyl-3-furamide
I-10	<i>N</i> -(1-{3-[(hydroxyamino)carbonyl]phenyl}ethyl)-1 <i>H</i> -indole-3-carboxamide
I-11	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)biphenyl-4-carboxamide
I-12	<i>N</i> -((1 <i>R</i>)-1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-3-methyl-1-benzothiophene-2-carboxamide
I-13	3-(1-{[(5-chloro-1-benzothien-3-yl)acetyl]amino}ethyl)- <i>N</i> -hydroxybenzamide
I-14	4-((1 <i>R</i>)-1-{[(<i>tert</i> -butylamino)carbonyl]amino}ethyl)- <i>N</i> -hydroxybenzamide
I-15	<i>N</i> -((1 <i>R</i>)-1-{4-[(hydroxyamino)carbonyl]phenyl}butyl)adamantane-1-carboxamide
I-16	<i>N</i> -((1 <i>R</i>)-1-{3-[(hydroxyamino)carbonyl]phenyl}ethyl)-4-methyl-2-phenyl-4 <i>H</i> -furo[3,2- <i>b</i>]pyrrole-5-carboxamide
I-17	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)-4-methyl-2-phenylpyrimidine-5-carboxamide
I-18	4-[(1 <i>R</i>)-1-({[1-adamantylamino]carbonyl}amino)butyl]- <i>N</i> -hydroxybenzamide
I-19	<i>N</i> -((1 <i>R</i>)-1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)-4-methoxybenzamide
I-20	<i>N</i> -hydroxy-4-[1-({[(4-phenoxyphenyl)amino]carbonyl}amino)ethyl]benzamide
I-21	4-{1-[(cyclobutylcarbonyl)amino]ethyl}- <i>N</i> -hydroxybenzamide
I-22	<i>N</i> -((1 <i>R</i>)-1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)-1-benzofuran-2-carboxamide
I-23	<i>N</i> -hydroxy-4-(1-{[(3-methoxyphenyl)sulfonyl]amino}ethyl)benzamide

I-24	4-(1-{[(2-chloro-6-fluorophenyl)acetyl]amino}ethyl)- <i>N</i> -hydroxybenzamide
I-25	<i>N</i> -((1 <i>S</i>)-1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-1-methyl-1 <i>H</i> -pyrrole-2-carboxamide
I-26	<i>N</i> -hydroxy-4-((1 <i>R</i>)-1-{[(1-methylcyclohexyl)carbonyl]amino}ethyl)benzamide
I-27	4-[1-({[(3-fluorophenyl)amino]carbonyl}amino)ethyl]- <i>N</i> -hydroxybenzamide
I-28	<i>N</i> -hydroxy-4-{1-[(mesitylacetyl)amino]-2-methylpropyl}benzamide
I-29	<i>N</i> -(1-{3-[(hydroxyamino)carbonyl]phenyl}ethyl)-2-methyl-1,3-thiazole-4-carboxamide
I-30	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)-1-methyl-1 <i>H</i> -pyrrole-2-carboxamide
I-31	<i>N</i> -hydroxy-4-[1-({[(2-phenoxyphenyl)amino]carbonyl}amino)ethyl]benzamide
I-32	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)-1-benzofuran-2-carboxamide
I-33	<i>N</i> -hydroxy-4-{1-[(propylsulfonyl)amino]ethyl}benzamide
I-34	<i>N</i> -hydroxy-4-(1-{{[(2-methoxyphenyl)acetyl]amino}ethyl})benzamide
I-35	6-chloro- <i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)imidazo[1,2- <i>a</i>]pyridine-2-carboxamide
I-36	<i>N</i> -hydroxy-4-[1-(isobutyrylamino)ethyl]benzamide
I-37	4-[1-({[(4-fluorophenyl)amino]carbonyl}amino)ethyl]- <i>N</i> -hydroxybenzamide
I-38	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-4-isopropoxybenzamide
I-39	4,5-dichloro- <i>N</i> -(1-{3-[(hydroxyamino)carbonyl]phenyl}ethyl)-1-methyl-1 <i>H</i> -pyrrole-2-carboxamide
I-40	4-fluoro- <i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)benzamide
I-41	4-[1-({[1-(4-chlorophenyl)cyclopropyl]carbonyl}amino)-2,2-dimethylpropyl]- <i>N</i> -hydroxybenzamide
I-42	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}-2,2-dimethylpropyl)-2-methyl-1,3-thiazole-4-carboxamide
I-43	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)-1,3-benzothiazole-6-carboxamide
I-44	4-[1-({[(2,4-dimethoxyphenyl)amino]carbonyl}amino)ethyl]- <i>N</i> -hydroxybenzamide
I-45	<i>N</i> -hydroxy-4-{1-[(3-phenylpropanoyl)amino]ethyl}benzamide
I-46	<i>N</i> -((<i>R</i>)-cyclopropyl{4-[(hydroxyamino)carbonyl]phenyl}methyl)adamantane-1-carboxamide
I-47	<i>N</i> -hydroxy-4-(1-{{[(4-methoxyphenyl)sulfonyl]amino}ethyl})benzamide

I-48	<i>N</i> -hydroxy-4-(2-methyl-1-{[(5-methyl-2-phenyl-1,3-oxazol-4-yl)acetyl]amino}propyl)benzamide
I-49	<i>N</i> -hydroxy-4-(1-{[(2-oxo-2 <i>H</i> -chromen-6-yl)sulfonyl]amino}ethyl)benzamide
I-50	4-{(1 <i>R</i>)-1-[(2,2-dimethylpropanoyl)amino]-2,2,2-trifluoroethyl}- <i>N</i> -hydroxybenzamide
I-51	4-(1-{[(2,5-dimethylphenyl)sulfonyl]amino}ethyl)- <i>N</i> -hydroxybenzamide
I-52	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}-2,2-dimethylpropyl)-3,5-bis(trifluoromethyl)benzamide
I-53	<i>N</i> -((1 <i>S</i>)-1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-1-benzothiophene-2-carboxamide
I-54	4-(1-{[(1,2-dimethyl-1 <i>H</i> -imidazol-4-yl)sulfonyl]amino}ethyl)- <i>N</i> -hydroxybenzamide
I-55	4-[1-({[(3,4-dimethylphenyl)amino]carbonyl}amino)ethyl]- <i>N</i> -hydroxybenzamide
I-56	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)cinnoline-4-carboxamide
I-57	<i>N</i> -(1-{3-[(hydroxyamino)carbonyl]phenyl}ethyl)-2-(trifluoromethyl)benzamide
I-58	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)adamantane-1-carboxamide
I-59	4-{1-[(2,2-dimethylpropanoyl)amino]ethyl}- <i>N</i> -hydroxybenzamide
I-60	<i>N</i> -hydroxy-4-(1-{[(1,3,5-trimethyl-1 <i>H</i> -pyrazol-4-yl)sulfonyl]amino}ethyl)benzamide
I-61	4-(1-{[(4-fluoro-2-methylphenyl)sulfonyl]amino}ethyl)- <i>N</i> -hydroxybenzamide
I-62	<i>N</i> -((1 <i>R</i>)-1-{4-[(hydroxyamino)carbonyl]phenyl}butyl)-3-methyl-1-benzothiophene-2-carboxamide
I-63	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-4-(1 <i>H</i> -pyrrol-1-yl)benzamide
I-64	4-(1-{[(4-chlorobenzyl)sulfonyl]amino}ethyl)- <i>N</i> -hydroxybenzamide
I-65	<i>N</i> -((1 <i>R</i>)-1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)-1-methyl-1 <i>H</i> -pyrrole-2-carboxamide
I-66	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}-2,2-dimethylpropyl)-1-methyl-1 <i>H</i> -pyrazole-3-carboxamide
I-67	<i>N</i> -((1 <i>S</i>)-1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)-1-benzothiophene-2-carboxamide
I-68	<i>N</i> -((1 <i>R</i>)-1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)-1 <i>H</i> -indole-2-carboxamide
I-69	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)-5-methyl-1 <i>H</i> -indole-2-carboxamide
I-70	<i>N</i> -hydroxy-4-(1-{[4-(4-methoxyphenyl)butanoyl]amino}ethyl)benzamide
I-71	4-(1-{[(1,3-benzodioxol-5-ylamino)carbonyl]amino}ethyl)- <i>N</i> -hydroxybenzamide

I-72	<i>N</i> -(1-{3-[(hydroxyamino)carbonyl]phenyl}ethyl)-4-methyl-2-[4-(trifluoromethyl)phenyl]-4 <i>H</i> -furo[3,2- <i>b</i>]pyrrole-5-carboxamide
I-73	4-{(1 <i>R</i>)-1-[(2,2-dimethylpropanoyl)amino]ethyl}- <i>N</i> -hydroxybenzamide
I-74	4-[1-({[(2-fluorophenyl)amino]carbonyl}amino)ethyl]- <i>N</i> -hydroxybenzamide
I-75	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}-2,2-dimethylpropyl)-3-(methylsulfonyl)benzamide
I-76	<i>N</i> -hydroxy-4-[1-({[(2-methylbenzyl)amino]carbonyl}amino)ethyl]benzamide
I-77	1-benzyl-3- <i>tert</i> -butyl- <i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)-1 <i>H</i> -pyrazole-5-carboxamide
I-78	4-(1-{[(2,4-dimethylphenyl)sulfonyl]amino}ethyl)- <i>N</i> -hydroxybenzamide
I-79	<i>N</i> -((1 <i>R</i>)-1-{4-[(hydroxyamino)carbonyl]phenyl}butyl)-1-benzofuran-2-carboxamide
I-80	4-(2,2-dimethyl-1-{[(5-methyl-2-phenyl-1,3-oxazol-4-yl)acetyl]amino}propyl)- <i>N</i> -hydroxybenzamide
I-81	<i>N</i> -(1-{3-[(hydroxyamino)carbonyl]phenyl}ethyl)-1-methyl-1 <i>H</i> -pyrazole-3-carboxamide
I-82	4-{1-[(2,3-dihydro-1,4-benzodioxin-6-ylsulfonyl)amino]ethyl}- <i>N</i> -hydroxybenzamide
I-83	<i>N</i> -(1-{3-[(hydroxyamino)carbonyl]phenyl}ethyl)adamantane-1-carboxamide
I-84	<i>N</i> -(1-{3-[(hydroxyamino)carbonyl]phenyl}ethyl)-1,5-dimethyl-1 <i>H</i> -pyrazole-3-carboxamide
I-85	<i>N</i> -hydroxy-4-[1-({[(3-methylphenyl)amino]carbonyl}amino)ethyl]benzamide
I-86	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}-2,2-dimethylpropyl)-1,3-dimethyl-1 <i>H</i> -pyrazole-4-carboxamide
I-87	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}-2,2-dimethylpropyl)pyrazine-2-carboxamide
I-88	4-{1-[(cyclopentylcarbonyl)amino]ethyl}- <i>N</i> -hydroxybenzamide
I-89	4-[1-({[(2,5-dichlorophenyl)amino]carbonyl}amino)ethyl]- <i>N</i> -hydroxybenzamide
I-90	4-(1-{[(3,4-difluorophenyl)sulfonyl]amino}ethyl)- <i>N</i> -hydroxybenzamide
I-91	<i>N</i> -(1-{3-[(hydroxyamino)carbonyl]phenyl}ethyl)-3,5-dimethyl-1 <i>H</i> -pyrrole-2-carboxamide
I-92	<i>N</i> -((1 <i>R</i>)-1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)biphenyl-4-carboxamide
I-93	<i>N</i> -(1-{3-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)-3-methyl-1-benzofuran-2-carboxamide
I-94	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)-1-benzothiophene-2-carboxamide
I-95	<i>N</i> -hydroxy-4-{1-[(1-naphthylsulfonyl)amino]ethyl}benzamide

I-96	4,5-dichloro- <i>N</i> -((1 <i>R</i>)-1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)-1-methyl-1 <i>H</i> -pyrrole-2-carboxamide
I-97	<i>N</i> -(1-{3-[(hydroxyamino)carbonyl]phenyl}ethyl)-1-benzothiophene-2-carboxamide
I-98	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-1-methyl-1 <i>H</i> -indole-2-carboxamide
I-99	<i>N</i> -[(<i>R</i>)-{4-[(hydroxyamino)carbonyl]phenyl}(phenyl)methyl]-1-benzothiophene-2-carboxamide
I-100	<i>N</i> -(1-{3-[(hydroxyamino)carbonyl]phenyl}ethyl)-1-methyl-1 <i>H</i> -benzimidazole-2-carboxamide
I-101	<i>N</i> -(1-{3-[(hydroxyamino)carbonyl]phenyl}ethyl)-2-methyl-4,5,6,7-tetrahydro-2 <i>H</i> -indazole-3-carboxamide
I-102	<i>N</i> -((1 <i>R</i>)-1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-1-methyl-1 <i>H</i> -pyrrole-2-carboxamide
I-103	4-[1-({[(3-chloro-4-methylphenyl)amino]carbonyl}amino)ethyl]- <i>N</i> -hydroxybenzamide
I-104	<i>N</i> -(1-{3-[(hydroxyamino)carbonyl]phenyl}ethyl)-2,5-dimethyl-3-furamide
I-105	4-((1 <i>R</i>)-1-{[(1-adamantylamino)carbonyl]amino}-2,2,2-trifluoroethyl)- <i>N</i> -hydroxybenzamide
I-106	<i>N</i> -((1 <i>R</i>)-1-{4-[(hydroxyamino)carbonyl]phenyl}butyl)-1-methyl-1 <i>H</i> -indole-2-carboxamide
I-107	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}-2,2-dimethylpropyl)-1-methyl-1 <i>H</i> -indole-3-carboxamide
I-108	4,5-dichloro-1-methyl- <i>N</i> -((1 <i>S</i>)-2,2,2-trifluoro-1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-1 <i>H</i> -pyrrole-2-carboxamide
I-109	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-3-phenyl-1 <i>H</i> -pyrazole-5-carboxamide
I-110	4-[1-({[1-(4-chlorophenyl)cyclobutyl]carbonyl}amino)ethyl]- <i>N</i> -hydroxybenzamide
I-111	<i>N</i> -hydroxy-4-{1-[(3-methylbutanoyl)amino]ethyl}benzamide
I-112	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)thiophene-2-carboxamide
I-113	<i>N</i> -((1 <i>R</i>)-1-{3-[(hydroxyamino)carbonyl]phenyl}ethyl)-3-methyl-1-benzothiophene-2-carboxamide
I-114	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-2-methyl-4,5,6,7-tetrahydro-2 <i>H</i> -indazole-3-carboxamide
I-115	<i>N</i> -((1 <i>R</i>)-1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-1-methyl-1 <i>H</i> -indole-2-carboxamide
I-116	2,4,5-trifluoro- <i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)benzamide
I-117	<i>N</i> -(1-{3-[(hydroxyamino)carbonyl]phenyl}ethyl)-1-benzothiophene-3-carboxamide
I-118	4-(1-{[(3-chloro-4-methylphenyl)sulfonyl]amino}ethyl)- <i>N</i> -hydroxybenzamide

I-119	1-methyl- <i>N</i> -((1 <i>R</i>)-2,2,2-trifluoro-1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-1 <i>H</i> -pyrrole-2-carboxamide
I-120	4-[1-({[(3-fluoro-4-methylphenyl)amino]carbonyl}amino)ethyl]- <i>N</i> -hydroxybenzamide
I-121	<i>N</i> -((1 <i>R</i>)-1-{3-[(hydroxyamino)carbonyl]phenyl}ethyl)biphenyl-4-carboxamide
I-122	4-methoxy- <i>N</i> -((1 <i>S</i>)-2,2,2-trifluoro-1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)benzamide
I-123	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}-2,2-dimethylpropyl)-1,3-thiazole-4-carboxamide
I-124	<i>N</i> -[(<i>S</i>)-{4-[(hydroxyamino)carbonyl]phenyl}(phenyl)methyl]-1-benzothiophene-2-carboxamide
I-125	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)imidazo[1,2- <i>a</i>]pyridine-2-carboxamide
I-126	<i>N</i> -hydroxy-4-((1 <i>R</i>)-2-methyl-1-{[(1-methylcyclohexyl)carbonyl]amino}propyl)benzamide
I-127	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}-2,2-dimethylpropyl)-1 <i>H</i> -indole-2-carboxamide
I-128	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)quinoline-2-carboxamide
I-129	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}-2,2-dimethylpropyl)-5-methyl-1 <i>H</i> -indole-2-carboxamide
I-130	5-chloro- <i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)-1-benzofuran-2-carboxamide
I-131	4-(1-({[(4- <i>tert</i> -butylphenyl)sulfonyl]amino}ethyl)- <i>N</i> -hydroxybenzamide
I-132	<i>N</i> -hydroxy-4-(1-({[(1-methylcyclohexyl)carbonyl]amino}ethyl)benzamide
I-133	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}-2,2-dimethylpropyl)-1-methyl-1 <i>H</i> -pyrrole-2-carboxamide
I-134	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-2,3-dihydro-1-benzofuran-7-carboxamide
I-135	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)-2,1,3-benzothiadiazole-5-carboxamide
I-136	4-chloro- <i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)benzamide
I-137	3,5-difluoro- <i>N</i> -(1-{3-[(hydroxyamino)carbonyl]phenyl}ethyl)benzamide
I-138	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-4-(1,3-oxazol-5-yl)benzamide
I-139	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)-2-methyl-4-(trifluoromethyl)-1,3-thiazole-5-carboxamide
I-140	4-[1-({[(4- <i>tert</i> -butylphenyl)amino]carbonyl}amino)ethyl]- <i>N</i> -hydroxybenzamide
I-141	<i>N</i> -hydroxy-4-{1-[(4-(trifluoromethoxy)phenyl)amino]carbonyl}amino]ethyl}benzamide

I-142	<i>N</i> -(1-{3-[(hydroxyamino)carbonyl]phenyl}ethyl)biphenyl-4-carboxamide
I-143	4'-fluoro- <i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)biphenyl-4-carboxamide
I-144	4-{1-[(3,3-dimethylbutanoyl)amino]ethyl}- <i>N</i> -hydroxybenzamide
I-145	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}-2,2-dimethylpropyl)-1-methyl-1 <i>H</i> -indole-5-carboxamide
I-146	<i>N</i> -((1 <i>R</i>)-1-{4-[(hydroxyamino)carbonyl]phenyl}butyl)-4-methoxybenzamide
I-147	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-5-methylthiophene-2-carboxamide
I-148	4-(1-{[(2,3-dihydro-1-benzofuran-5-ylamino)carbonyl]amino}ethyl)- <i>N</i> -hydroxybenzamide
I-149	3-{1-[(cyclohexylcarbonyl)amino]ethyl}- <i>N</i> -hydroxybenzamide
I-150	4-{1-[[{4-(difluoromethoxy)phenyl]amino}carbonyl]amino}ethyl}- <i>N</i> -hydroxybenzamide
I-151	<i>N</i> -hydroxy-3-(1-{[4-(trifluoromethyl)benzoyl]amino}ethyl)benzamide
I-152	4-(1-{[(2,5-difluorophenyl)sulfonyl]amino}ethyl)- <i>N</i> -hydroxybenzamide
I-153	4-(1-{[(3-fluoro-4-methoxyphenyl)sulfonyl]amino}ethyl)- <i>N</i> -hydroxybenzamide
I-154	<i>N</i> -hydroxy-4-(1-{[(1-methylcyclopropyl)carbonyl]amino}ethyl)benzamide
I-155	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)-2,5-bis(trifluoromethyl)benzamide
I-156	4-[1-({[(2,6-dimethylphenyl)amino]carbonyl}amino)ethyl]- <i>N</i> -hydroxybenzamide
I-157	<i>N</i> -((1 <i>S</i>)-1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)adamantane-1-carboxamide
I-158	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}-2,2-dimethylpropyl)-1-benzothiophene-3-carboxamide
I-159	<i>N</i> -hydroxy-4-(1-{[(4-methoxyphenyl)acetyl]amino}ethyl)benzamide
I-160	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-5,7-dimethylpyrazolo[1,5- <i>a</i>]pyrimidine-2-carboxamide
I-161	4-{1-[(2,1,3-benzoxadiazol-4-ylsulfonyl)amino]ethyl}- <i>N</i> -hydroxybenzamide
I-162	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}-2,2-dimethylpropyl)adamantane-1-carboxamide
I-163	4-{1-[[{2-chloro-4-(trifluoromethyl)phenyl]amino}carbonyl]amino}ethyl}- <i>N</i> -hydroxybenzamide
I-164	4-fluoro- <i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-3-methoxybenzamide
I-165	<i>N</i> -(1-{3-[(hydroxyamino)carbonyl]phenyl}ethyl)pyrazine-2-carboxamide

I-166	<i>N</i> -hydroxy-4-[1-({[3-(trifluoromethyl)phenyl]sulfonyl}amino)ethyl]benzamide
I-167	<i>N</i> -(1-{3-[(hydroxyamino)carbonyl]phenyl}ethyl)-1,3-dimethyl-1 <i>H</i> -pyrazole-4-carboxamide
I-168	<i>N</i> -hydroxy-4-[1-({[(3-methyl-5-phenylisoxazol-4-yl)amino]carbonyl}amino)ethyl]benzamide
I-169	<i>N</i> -((1 <i>R</i>)-1-{3-[(hydroxyamino)carbonyl]phenyl}ethyl)-3-methyl-1-benzofuran-2-carboxamide
I-170	<i>N</i> -hydroxy-4-{1-[(isoquinolin-5-ylsulfonyl)amino]ethyl}benzamide
I-171	<i>N</i> -hydroxy-4-[(1 <i>R</i>)-1-({[4-(trifluoromethyl)phenyl]sulfonyl}amino)butyl]benzamide
I-172	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)-2-phenyl-1,3-thiazole-4-carboxamide
I-173	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)-3,5-bis(trifluoromethyl)benzamide
I-174	<i>N</i> -hydroxy-4-(2-methyl-1-{[(2-methyl-1 <i>H</i> -indol-3-yl)acetyl]amino}propyl)benzamide
I-175	4-[1-({[(2,3-dimethylphenyl)amino]carbonyl}amino)ethyl]- <i>N</i> -hydroxybenzamide
I-176	<i>N</i> -hydroxy-4-{1-[(mesitylsulfonyl)amino]ethyl}benzamide
I-177	3-{(1 <i>R</i>)-1-[(2,2-dimethylpropanoyl)amino]ethyl}- <i>N</i> -hydroxybenzamide
I-178	<i>N</i> -hydroxy-4-[1-({[4-(1,3-oxazol-5-yl)phenyl]sulfonyl}amino)ethyl]benzamide
I-179	<i>N</i> -(1-{3-[(hydroxyamino)carbonyl]phenyl}ethyl)-1,3-thiazole-4-carboxamide
I-180	<i>N</i> -(1-{3-[(hydroxyamino)carbonyl]phenyl}ethyl)-4-methyl-2-phenyl-4 <i>H</i> -furo[3,2- <i>b</i>]pyrrole-5-carboxamide
I-181	<i>N</i> -(1-{3-[(hydroxyamino)carbonyl]phenyl}ethyl)-2,5-dimethyl-1 <i>H</i> -pyrrole-3-carboxamide
I-182	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}-2,2-dimethylpropyl)-5-methyl-1-phenyl-1 <i>H</i> -pyrazole-4-carboxamide
I-183	3-[1-({[1-(4-chlorophenyl)cyclopropyl]carbonyl}amino)ethyl]- <i>N</i> -hydroxybenzamide
I-184	<i>N</i> -((1 <i>R</i>)-1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-1-benzothiophene-2-carboxamide
I-185	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-4-(1 <i>H</i> -pyrazol-1-yl)benzamide
I-186	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-3-isopropyl-1-methyl-1 <i>H</i> -pyrazole-5-carboxamide
I-187	<i>N</i> -((1 <i>R</i>)-1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)-3-methyl-1-benzofuran-2-carboxamide
I-188	4-(1-({[(2-chloro-6-methylphenyl)sulfonyl]amino}ethyl)- <i>N</i> -hydroxybenzamide
I-189	<i>N</i> -hydroxy-4-[(1 <i>R</i>)-2-methyl-1-({[4-(trifluoromethyl)phenyl]sulfonyl}amino)propyl]benzamide

I-190	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)quinoxaline-2-carboxamide
I-191	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)-1,3-benzothiazole-2-carboxamide
I-192	4- <i>tert</i> -butyl- <i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)benzamide
I-193	<i>N</i> -hydroxy-3-{(1 <i>R</i>)-1-[(4-methoxybenzoyl)amino]ethyl}benzamide
I-194	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)-1-benzofuran-5-carboxamide
I-195	<i>N</i> -hydroxy-4-[2-methyl-1-({[3-(trifluoromethyl)phenyl]acetyl}amino)propyl]benzamide
I-196	<i>N</i> -hydroxy-4-[1-({[(1-phenylethyl)amino]carbonyl}amino)ethyl]benzamide
I-197	4-(1-{[(3-chlorophenyl)sulfonyl]amino}ethyl)- <i>N</i> -hydroxybenzamide
I-198	4-(1-{[(4-fluorobenzyl)sulfonyl]amino}ethyl)- <i>N</i> -hydroxybenzamide
I-199	<i>N</i> -(1-{3-[(hydroxyamino)carbonyl]phenyl}ethyl)-3-(methylsulfonyl)benzamide
I-200	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}-2,2-dimethylpropyl)-3,5-dimethylisoxazole-4-carboxamide
I-201	<i>N</i> -((1 <i>R</i>)-1-{3-[(hydroxyamino)carbonyl]phenyl}ethyl)-1-benzofuran-2-carboxamide
I-202	<i>N</i> -hydroxy-3-{1-[(4-methoxybenzoyl)amino]ethyl}benzamide
I-203	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)pyrazine-2-carboxamide
I-204	4-{1-[(diphenylacetyl)amino]-2-methylpropyl}- <i>N</i> -hydroxybenzamide
I-205	4-(1-{[(5-fluoro-2-methylphenyl)sulfonyl]amino}ethyl)- <i>N</i> -hydroxybenzamide
I-206	4-(1-{[(5-chloro-1-benzothien-3-yl)acetyl]amino}-2-methylpropyl)- <i>N</i> -hydroxybenzamide
I-207	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-1-benzofuran-2-carboxamide
I-208	4-{1-[(cyclohexylcarbonyl)amino]ethyl}- <i>N</i> -hydroxybenzamide
I-209	<i>N</i> -((1 <i>R</i>)-1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)adamantane-1-carboxamide
I-210	<i>N</i> -hydroxy-4-[1-({[(2-phenylethyl)amino]carbonyl}amino)ethyl]benzamide
I-211	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}-2,2-dimethylpropyl)-2-methyl-4,5,6,7-tetrahydro-2 <i>H</i> -indazole-3-carboxamide
I-212	4-(1-{[(1-adamantylacetyl)amino]ethyl}- <i>N</i> -hydroxybenzamide
I-213	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)cycloheptanecarboxamide
I-214	<i>N</i> -((1 <i>R</i>)-1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)-1-benzothiophene-2-carboxamide

I-215	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}-2,2-dimethylpropyl)thiophene-2-carboxamide
I-216	3-ethyl- <i>N</i> -(1-{3-[(hydroxyamino)carbonyl]phenyl}ethyl)-1-methyl-1 <i>H</i> -pyrazole-5-carboxamide
I-217	4-(1-{[(2,5-dimethyl-1,3-thiazol-4-yl)acetyl]amino}ethyl)- <i>N</i> -hydroxybenzamide
I-218	<i>N</i> -(1-{3-[(hydroxyamino)carbonyl]phenyl}ethyl)-3,5-dimethylisoxazole-4-carboxamide
I-219	<i>N</i> -(1-{3-[(hydroxyamino)carbonyl]phenyl}ethyl)-1-methyl-1 <i>H</i> -indole-2-carboxamide
I-220	<i>N</i> -hydroxy-4-(2-methyl-1-{[(2,4,7-trimethyl-1 <i>H</i> -indol-3-yl)acetyl]amino}propyl)benzamide
I-221	<i>N</i> -hydroxy-4-(1-{[(4-isopropylphenyl)sulfonyl]amino}ethyl)benzamide
I-222	<i>N</i> -((1 <i>R</i>)-1-{4-[(hydroxyamino)carbonyl]phenyl}butyl)-4-methyl-2-phenyl-4 <i>H</i> -furo[3,2- <i>b</i>]pyrrole-5-carboxamide
I-223	3-hydroxy- <i>N</i> -((1 <i>R</i>)-1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)adamantane-1-carboxamide
I-224	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-2 <i>H</i> -chromene-3-carboxamide
I-225	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-3-methoxybenzamide
I-226	5-chloro- <i>N</i> -(1-{3-[(hydroxyamino)carbonyl]phenyl}ethyl)-1-benzofuran-2-carboxamide
I-227	<i>N</i> -(1-{3-[(hydroxyamino)carbonyl]phenyl}ethyl)-1 <i>H</i> -indole-2-carboxamide
I-228	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-3-(1 <i>H</i> -pyrrol-1-yl)thiophene-2-carboxamide
I-229	<i>N</i> -((<i>R</i>)-cyclopropyl{4-[(hydroxyamino)carbonyl]phenyl}methyl)-1-benzothiophene-2-carboxamide
I-230	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-2-methyl-1,3-benzothiazole-5-carboxamide
I-231	4-methyl-2-phenyl- <i>N</i> -((1 <i>S</i>)-2,2,2-trifluoro-1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-4 <i>H</i> -furo[3,2- <i>b</i>]pyrrole-5-carboxamide
I-232	<i>N</i> -hydroxy-4-(1-{[(2-methylphenyl)sulfonyl]amino}ethyl)benzamide
I-233	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-2,1,3-benzothiadiazole-5-carboxamide
I-234	<i>N</i> -hydroxy-3-(1-{[(5-methyl-2-phenyl-1,3-oxazol-4-yl)acetyl]amino}ethyl)benzamide
I-235	4-(1-{[(2-chloro-4-fluorophenyl)sulfonyl]amino}ethyl)- <i>N</i> -hydroxybenzamide
I-236	4-[1-{[(4-cyanophenyl)amino]carbonyl}amino]ethyl]- <i>N</i> -hydroxybenzamide
I-237	<i>N</i> -((1 <i>R</i>)-1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-3-methyl-1-benzofuran-2-carboxamide
I-238	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)-3,5-dimethylisoxazole-4-carboxamide

I-239	4-{1-[(cyclopropylcarbonyl)amino]ethyl}- <i>N</i> -hydroxybenzamide
I-240	<i>N</i> -((1 <i>S</i>)-1-{3-[(hydroxyamino)carbonyl]phenyl}ethyl)-1-benzothiophene-2-carboxamide
I-241	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-1,5-dimethyl-1 <i>H</i> -pyrazole-3-carboxamide
I-242	<i>N</i> -((1 <i>R</i>)-1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)-1-methyl-1 <i>H</i> -indole-2-carboxamide
I-243	4-[1-(butyrylamino)ethyl]- <i>N</i> -hydroxybenzamide
I-244	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-1-benzothiophene-3-carboxamide
I-245	4,5-dichloro- <i>N</i> -((1 <i>R</i>)-1-{4-[(hydroxyamino)carbonyl]phenyl}butyl)-1-methyl-1 <i>H</i> -pyrrole-2-carboxamide
I-246	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)quinoline-4-carboxamide
I-247	5-chloro- <i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)-1 <i>H</i> -indole-2-carboxamide
I-248	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}-2,2-dimethylpropyl)-4-methyl-2-[4-(trifluoromethyl)phenyl]-4 <i>H</i> -furo[3,2- <i>b</i>]pyrrole-5-carboxamide
I-249	<i>N</i> -((<i>S</i>)-cyclopropyl{4-[(hydroxyamino)carbonyl]phenyl}methyl)-1-benzothiophene-2-carboxamide
I-250	4-[1-({[3,5-bis(trifluoromethyl)phenyl]acetyl}amino)-2-methylpropyl]- <i>N</i> -hydroxybenzamide
I-251	3,5-difluoro- <i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}-2,2-dimethylpropyl)benzamide
I-252	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)-2,5-dimethyl-3-furamide
I-253	<i>N</i> -hydroxy-4-[1-({[(2-methoxy-5-methylphenyl)amino]carbonyl}amino)ethyl]benzamide
I-254	4-(1-{[(2-chloro-4-cyanophenyl)sulfonyl]amino}ethyl)- <i>N</i> -hydroxybenzamide
I-255	4-{1-[(cyclopentylcarbonyl)amino]-2-methylpropyl}- <i>N</i> -hydroxybenzamide
I-256	4-(1-{[(2,5-dimethyl-3-thienyl)sulfonyl]amino}ethyl)- <i>N</i> -hydroxybenzamide
I-257	<i>N</i> -(1-{3-[(hydroxyamino)carbonyl]phenyl}ethyl)-5-methyl-1-phenyl-1 <i>H</i> -pyrazole-4-carboxamide
I-258	<i>N</i> -hydroxy-4-(2-methyl-1-{[(1-phenylcyclopentyl)carbonyl]amino}propyl)benzamide
I-259	<i>N</i> -[(<i>S</i>)-{4-[(hydroxyamino)carbonyl]phenyl}(phenyl)methyl]adamantane-1-carboxamide
I-260	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}-2,2-dimethylpropyl)-1,5-dimethyl-1 <i>H</i> -pyrazole-3-carboxamide
I-261	4-[1-({[(2,6-difluorophenyl)amino]carbonyl}amino)ethyl]- <i>N</i> -hydroxybenzamide

I-262	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}-2,2-dimethylpropyl)-3,5-dimethyl-1 <i>H</i> -pyrrole-2-carboxamide
I-263	<i>N</i> -(1-{3-[(hydroxyamino)carbonyl]phenyl}ethyl)-1-methyl-1 <i>H</i> -pyrrole-2-carboxamide
I-264	<i>N</i> -hydroxy-4-[1-({[1-(4-methylphenyl)cyclopropyl]carbonyl}amino)ethyl]benzamide
I-265	4-{1-[(cyclohexylcarbonyl)amino]-2,2-dimethylpropyl}- <i>N</i> -hydroxybenzamide
I-266	<i>N</i> -hydroxy-4-(1-{[(4-methylphenyl)sulfonyl]amino}ethyl)benzamide
I-267	<i>N</i> -(1-{3-[(hydroxyamino)carbonyl]phenyl}ethyl)thiophene-2-carboxamide
I-268	3-{1-[(4- <i>tert</i> -butylbenzoyl)amino]ethyl}- <i>N</i> -hydroxybenzamide
I-269	2-chloro- <i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)benzamide
I-270	5-chloro- <i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}-2,2-dimethylpropyl)-1-benzofuran-2-carboxamide
I-271	<i>N</i> -((1 <i>R</i>)-1-{3-[(hydroxyamino)carbonyl]phenyl}ethyl)-1-methyl-1 <i>H</i> -pyrrole-2-carboxamide
I-272	4-{1-[(2,1,3-benzothiadiazol-5-ylsulfonyl)amino]ethyl}- <i>N</i> -hydroxybenzamide
I-273	<i>N</i> -hydroxy-4-((1 <i>S</i>)-1-{[(1-methylcyclohexyl)carbonyl]amino}ethyl)benzamide
I-274	<i>N</i> -((1 <i>R</i>)-1-{4-[(hydroxyamino)carbonyl]phenyl}butyl)biphenyl-4-carboxamide
I-275	4-[1-({[(3,4-difluorophenyl)amino]carbonyl}amino)ethyl]- <i>N</i> -hydroxybenzamide
I-276	1-methyl- <i>N</i> -((1 <i>R</i>)-2,2,2-trifluoro-1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-1 <i>H</i> -indole-2-carboxamide
I-277	<i>N</i> -hydroxy-4-[1-({[(4-methylbenzyl)amino]carbonyl}amino)ethyl]benzamide
I-278	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-2-methyl-1,3-thiazole-4-carboxamide
I-279	<i>N</i> -((1 <i>S</i>)-1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)-1 <i>H</i> -indole-2-carboxamide
I-280	4-{1-[(1,3-benzodioxol-5-ylacetyl)amino]ethyl}- <i>N</i> -hydroxybenzamide
I-281	<i>N</i> -((1 <i>R</i>)-1-{4-[(hydroxyamino)carbonyl]phenyl}butyl)-1-methyl-1 <i>H</i> -pyrrole-2-carboxamide
I-282	3,5-bis(acetylamino)- <i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)benzamide
I-283	<i>N</i> -hydroxy-3-((1 <i>R</i>)-1-{[(1-methylcyclohexyl)carbonyl]amino}ethyl)benzamide
I-284	<i>N</i> -hydroxy-4-(1-{[(2,3,4-trifluorophenyl)sulfonyl]amino}ethyl)benzamide
I-285	<i>N</i> -hydroxy-4-(1-{[(4-isopropylphenyl)acetyl]amino}ethyl)benzamide
I-286	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-5-isobutylisoxazole-3-carboxamide

I-287	4-((1 <i>R</i>)-1-[(2,2-dimethylpropanoyl)amino]-2-methylpropyl)- <i>N</i> -hydroxybenzamide
I-288	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-1,3-dimethyl-1 <i>H</i> -pyrazole-5-carboxamide
I-289	<i>N</i> -hydroxy-4-{2-methyl-1-[(3-methyl-2-phenylbutanoyl)amino]propyl}benzamide
I-290	4-((1 <i>R</i>)-1-{[(<i>tert</i> -butylamino)carbonyl]amino}-2,2,2-trifluoroethyl)- <i>N</i> -hydroxybenzamide
I-291	3- <i>tert</i> -butyl- <i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}-2,2-dimethylpropyl)-1-methyl-1 <i>H</i> -pyrazole-5-carboxamide
I-292	4-(1-{[(2-chlorophenyl)acetyl]amino}ethyl)- <i>N</i> -hydroxybenzamide
I-293	4-(1-{[(2,1,3-benzothiadiazol-4-ylamino)carbonyl]amino}ethyl)- <i>N</i> -hydroxybenzamide
I-294	<i>N</i> -((1 <i>S</i>)-1-{3-[(hydroxyamino)carbonyl]phenyl}ethyl)-1-methyl-1 <i>H</i> -indole-2-carboxamide
I-295	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-3-methylbenzamide
I-296	<i>N</i> -((1 <i>S</i>)-2,2,2-trifluoro-1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)biphenyl-4-carboxamide
I-297	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-1,3-benzodioxole-5-carboxamide
I-298	<i>N</i> -hydroxy-4-(1-{[(1-phenylcyclopentyl)carbonyl]amino}ethyl)benzamide
I-299	<i>N</i> -((1 <i>R</i>)-1-{4-[(hydroxyamino)carbonyl]phenyl}butyl)-1-benzothiophene-2-carboxamide
I-300	4-[1-({[1-(4-chlorophenyl)cyclopropyl]carbonyl}amino)-2-methylpropyl]- <i>N</i> -hydroxybenzamide
I-301	4,5-dichloro- <i>N</i> -((1 <i>R</i>)-1-{3-[(hydroxyamino)carbonyl]phenyl}ethyl)-1-methyl-1 <i>H</i> -pyrrole-2-carboxamide
I-302	4-(1-{[(4-chlorophenyl)sulfonyl]amino}ethyl)- <i>N</i> -hydroxybenzamide
I-303	4-(2,2-dimethyl-1-{[4-(trifluoromethyl)benzoyl]amino}propyl)- <i>N</i> -hydroxybenzamide
I-304	3-methyl- <i>N</i> -((1 <i>S</i>)-2,2,2-trifluoro-1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-1-benzofuran-2-carboxamide
I-305	<i>N</i> -hydroxy-4-[1-({[(5-methyl-3-phenylisoxazol-4-yl)amino]carbonyl}amino)ethyl]benzamide
I-306	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)-7-methoxy-1-benzofuran-2-carboxamide
I-307	<i>N</i> -((1 <i>R</i>)-1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)-3-methyl-1-benzothiophene-2-carboxamide
I-308	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}-2,2-dimethylpropyl)-1-benzothiophene-2-carboxamide
I-309	3- <i>tert</i> -butyl- <i>N</i> -(1-{3-[(hydroxyamino)carbonyl]phenyl}ethyl)-1-methyl-1 <i>H</i> -pyrazole-5-

	carboxamide
I-310	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}-2,2-dimethylpropyl)-2,5-dimethyl-1 <i>H</i> -pyrrole-3-carboxamide
I-311	3-{1-[(cyclopentylcarbonyl)amino]ethyl}- <i>N</i> -hydroxybenzamide
I-312	<i>N</i> -((1 <i>R</i>)-1-{3-[(hydroxyamino)carbonyl]phenyl}ethyl)adamantane-1-carboxamide
I-313	<i>N</i> -hydroxy-4-{1-[(tetrahydro-2 <i>H</i> -pyran-4-ylacetyl)amino]ethyl}benzamide
I-314	<i>N</i> -hydroxy-3-{1-({[3-(trifluoromethyl)phenyl]acetyl}amino)ethyl}benzamide
I-315	<i>N</i> -hydroxy-4-{1-[(phenylsulfonyl)amino]ethyl}benzamide
I-316	<i>N</i> -hydroxy-4-{1-({[(3-methylbenzyl)amino]carbonyl}amino)ethyl}benzamide
I-317	<i>N</i> -((1 <i>R</i>)-1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-1-benzofuran-2-carboxamide
I-318	3-ethyl- <i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}-2,2-dimethylpropyl)-1-methyl-1 <i>H</i> -pyrazole-5-carboxamide
I-319	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}-2,2-dimethylpropyl)-1 <i>H</i> -indole-3-carboxamide
I-320	3-((1 <i>R</i>)-1-{[(<i>tert</i> -butylamino)carbonyl]amino}ethyl)- <i>N</i> -hydroxybenzamide
I-321	<i>N</i> -((1 <i>R</i>)-1-{3-[(hydroxyamino)carbonyl]phenyl}ethyl)-1-benzothiophene-2-carboxamide
I-322	<i>N</i> -((<i>S</i>)-cyclopropyl{4-[(hydroxyamino)carbonyl]phenyl}methyl)adamantane-1-carboxamide
I-323	<i>N</i> -(1-{3-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)biphenyl-4-carboxamide
I-324	2-(4- <i>tert</i> -butylphenyl)- <i>N</i> -(1-{3-[(hydroxyamino)carbonyl]phenyl}ethyl)-4-methyl-4 <i>H</i> -furo[3,2- <i>b</i>]pyrrole-5-carboxamide
I-325	4-{1-[(4-chloro-3-(trifluoromethyl)phenyl)amino]carbonyl}amino]ethyl}- <i>N</i> -hydroxybenzamide
I-326	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-3,5-dimethylisoxazole-4-carboxamide
I-327	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-2-naphthamide
I-328	<i>N</i> -((1 <i>R</i>)-1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)adamantane-1-carboxamide
I-329	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}-2,2-dimethylpropyl)-3,5-dimethyl-1 <i>H</i> -indole-2-carboxamide
I-330	<i>N</i> -((1 <i>R</i>)-1-{3-[(hydroxyamino)carbonyl]phenyl}ethyl)-1-methyl-1 <i>H</i> -indole-2-carboxamide
I-331	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)-1-naphthamide
I-332	<i>N</i> -((1 <i>R</i>)-1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)-4-methyl-2-phenyl-4 <i>H</i> -

	furo[3,2- <i>b</i>]pyrrole-5-carboxamide
I-333	3-{1-[(3,3-dimethylbutanoyl)amino]ethyl}- <i>N</i> -hydroxybenzamide
I-334	4-{1-[(2-fluoro-5-(trifluoromethyl)phenyl)amino]carbonyl}aminoethyl}- <i>N</i> -hydroxybenzamide
I-335	<i>N</i> -hydroxy-4-(1-{[(1-methyl-1 <i>H</i> -imidazol-4-yl)sulfonyl]amino}ethyl)benzamide
I-336	<i>N</i> -[(<i>R</i>)-{4-[(hydroxyamino)carbonyl]phenyl}(phenyl)methyl]adamantane-1-carboxamide
I-337	2-(4- <i>tert</i> -butylphenyl)- <i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}-2,2-dimethylpropyl)-4-methyl-4 <i>H</i> -furo[3,2- <i>b</i>]pyrrole-5-carboxamide
I-338	4-{1-[(benzylsulfonyl)amino]ethyl}- <i>N</i> -hydroxybenzamide
I-339	4-(1-{[(<i>tert</i> -butylamino)carbonyl]amino}ethyl)- <i>N</i> -hydroxybenzamide
I-340	4-(1-{[(2-cyanophenyl)sulfonyl]amino}ethyl)- <i>N</i> -hydroxybenzamide
I-341	<i>N</i> -[(1 <i>R</i>)-1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl]biphenyl-4-carboxamide
I-342	<i>N</i> -(1-{3-[(hydroxyamino)carbonyl]phenyl}ethyl)-5-methyl-1 <i>H</i> -indole-2-carboxamide
I-343	3-[(1 <i>R</i>)-1-{[1-adamantylamino]carbonyl}amino]ethyl)- <i>N</i> -hydroxybenzamide
I-344	4-{1-[(cyclohexylcarbonyl)amino]-2-methylpropyl}- <i>N</i> -hydroxybenzamide
I-345	4-(1-{[(5-chloro-1-benzothien-3-yl)acetyl]amino}-2,2-dimethylpropyl)- <i>N</i> -hydroxybenzamide
I-346	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)-4-methoxybenzamide
I-347	4-(1-{[(5-chloro-2-methoxyphenyl)sulfonyl]amino}ethyl)- <i>N</i> -hydroxybenzamide
I-348	4-{1-[(cyclohex-3-en-1-ylcarbonyl)amino]ethyl}- <i>N</i> -hydroxybenzamide
I-349	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-1-benzofuran-5-carboxamide
I-350	4- <i>tert</i> -butyl- <i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)benzamide
I-351	<i>N</i> -hydroxy-4-[(1 <i>R</i>)-1-{[4-(trifluoromethyl)phenyl]sulfonyl}amino]ethyl]benzamide
I-352	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}-2,2-dimethylpropyl)-4-methoxybenzamide
I-353	<i>N</i> -(1-{3-[(hydroxyamino)carbonyl]phenyl}ethyl)-1-methyl-1 <i>H</i> -indole-3-carboxamide
I-354	4-[(1 <i>R</i>)-1-{[1-adamantylamino]carbonyl}amino]-2-methylpropyl]- <i>N</i> -hydroxybenzamide
I-355	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}-2,2-dimethylpropyl)biphenyl-4-carboxamide
I-356	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-1-methyl-1 <i>H</i> -pyrrole-2-carboxamide
I-357	4-{1-[(2,3-dihydro-1 <i>H</i> -inden-2-ylacetyl)amino]ethyl}- <i>N</i> -hydroxybenzamide
I-358	4-[1-({[(3-acetylphenyl)amino]carbonyl}amino)ethyl]- <i>N</i> -hydroxybenzamide

I-359	4,5-dichloro- <i>N</i> -((1 <i>R</i>)-1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-1-methyl-1 <i>H</i> -pyrrole-2-carboxamide
I-360	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-1,3-benzothiazole-6-carboxamide
I-361	4-(1-{[(2-chlorophenyl)sulfonyl]amino}ethyl)- <i>N</i> -hydroxybenzamide
I-362	3-[1-({[3,5-bis(trifluoromethyl)phenyl]acetyl}amino)ethyl]- <i>N</i> -hydroxybenzamide
I-363	<i>N</i> -hydroxy-4-{1-[(quinolin-8-ylsulfonyl)amino]ethyl}benzamide
I-364	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}-2,2-dimethylpropyl)-1-methyl-1 <i>H</i> -indole-2-carboxamide
I-365	4-{(1 <i>R</i>)-1-[(2,2-dimethylpropanoyl)amino]butyl}- <i>N</i> -hydroxybenzamide
I-366	2,6-dichloro- <i>N</i> -(1-{3-[(hydroxyamino)carbonyl]phenyl}ethyl)benzamide
I-367	<i>N</i> -((1 <i>R</i>)-1-{4-[(hydroxyamino)carbonyl]phenyl}butyl)-3-methyl-1-benzofuran-2-carboxamide
I-368	4-((1 <i>R</i>)-1-{[(<i>tert</i> -butylamino)carbonyl]amino}-2-methylpropyl)- <i>N</i> -hydroxybenzamide
I-369	4-{1-[(1-benzothien-2-ylsulfonyl)amino]ethyl}- <i>N</i> -hydroxybenzamide
I-370	4-{1-[(cyclopentylacetyl)amino]ethyl}- <i>N</i> -hydroxybenzamide
I-371	<i>N</i> -hydroxy-4-{1-[(3-(trifluoromethyl)phenyl)amino]carbonyl}amino]ethyl}benzamide
I-372	<i>N</i> -hydroxy-4-(1-{[(2,2,3,3-tetramethylcyclopropyl)carbonyl]amino}ethyl)benzamide
I-373	4-{1-[(cyclopentylcarbonyl)amino]-2,2-dimethylpropyl}- <i>N</i> -hydroxybenzamide
I-374	4-[(1 <i>R</i>)-1-({[1-adamantylamino]carbonyl}amino)ethyl]- <i>N</i> -hydroxybenzamide
I-375	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)-2-oxo-6-phenyl-1,2-dihydropyridine-3-carboxamide
I-376	<i>N</i> -(1-{3-[(hydroxyamino)carbonyl]phenyl}ethyl)-3,5-dimethyl-1 <i>H</i> -indole-2-carboxamide
I-377	4- <i>tert</i> -butyl- <i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}-2,2-dimethylpropyl)benzamide
I-378	4-(1-{[2-(4-chlorophenyl)-2-methylpropanoyl]amino}ethyl)- <i>N</i> -hydroxybenzamide
I-379	4-{1-[(cyclopropylacetyl)amino]ethyl}- <i>N</i> -hydroxybenzamide
I-380	4-((1 <i>R</i>)-1-{[(<i>tert</i> -butylamino)carbonyl]amino}butyl)- <i>N</i> -hydroxybenzamide
I-381	4-[1-({[(4-ethylphenyl)amino]carbonyl}amino)ethyl]- <i>N</i> -hydroxybenzamide
I-382	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)cycloheptanecarboxamide
I-383	4-[1-({[(2,4-dimethylphenyl)amino]carbonyl}amino)ethyl]- <i>N</i> -hydroxybenzamide

I-384	4-(1-{[(biphenyl-2-ylamino)carbonyl]amino}ethyl)- <i>N</i> -hydroxybenzamide
I-385	4-[1-(benzoylamino)ethyl]- <i>N</i> -hydroxybenzamide
I-386	4,5-dichloro- <i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}-2,2-dimethylpropyl)-1-methyl-1 <i>H</i> -pyrrole-2-carboxamide
I-387	<i>N</i> -hydroxy-4-((1 <i>R</i>)-1-{[(1-methylcyclohexyl)carbonyl]amino}butyl)benzamide
I-388	4-[1-({[(3,5-dichlorophenyl)amino]carbonyl}amino)ethyl]- <i>N</i> -hydroxybenzamide
I-389	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)-1-methyl-1 <i>H</i> -pyrazole-3-carboxamide
I-390	<i>N</i> -(1-{3-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)-1-benzothiophene-2-carboxamide
I-391	<i>N</i> -hydroxy-4-[1-({[2-(trifluoromethyl)phenyl]sulfonyl}amino)ethyl]benzamide
I-392	<i>N</i> -(1-{4-[(hydroxyamino)carbonyl]phenyl}-2,2-dimethylpropyl)-4-methyl-2-phenyl-4 <i>H</i> -furo[3,2- <i>b</i>]pyrrole-5-carboxamide
I-393	<i>N</i> -((1 <i>S</i>)-1-{3-[(hydroxyamino)carbonyl]phenyl}ethyl)biphenyl-4-carboxamide
I-394	<i>N</i> -hydroxy-4-[1-({[(2-methylphenyl)amino]carbonyl}amino)ethyl]benzamide
I-395	4-(1-{[(cyclohexylamino)carbonyl]amino}ethyl)- <i>N</i> -hydroxybenzamide
I-396	4-{1-[(3,3-dimethylbutanoyl)amino]-2,2-dimethylpropyl}- <i>N</i> -hydroxybenzamide
I-397	4-[1-({[(3,5-dimethylphenyl)amino]carbonyl}amino)ethyl]- <i>N</i> -hydroxybenzamide
I-398	4-[1-({[(4-acetylphenyl)amino]carbonyl}amino)ethyl]- <i>N</i> -hydroxybenzamide
I-399	<i>N</i> -hydroxy-4-{1-({[4-(trifluoromethyl)phenyl]amino}carbonyl)amino}ethyl}benzamide
I-400	<i>N</i> -((1 <i>S</i>)-2,2,2-trifluoro-1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-1-benzofuran-2-carboxamide
I-401	<i>N</i> -(1-{3-[(hydroxyamino)carbonyl]phenyl}ethyl)-1-benzofuran-2-carboxamide
I-402	4-(1-{{[4-(2,4-difluorophenyl)acetyl]amino}ethyl}- <i>N</i> -hydroxybenzamide
I-403	<i>N</i> -hydroxy-3-[(1 <i>R</i>)-1-({[4-(trifluoromethyl)phenyl]sulfonyl}amino)ethyl]benzamide
I-404	6-((1 <i>S</i>)-1-[(1-benzothien-2-ylcarbonyl)amino]-2,2-dimethylpropyl)- <i>N</i> -hydroxynicotinamide
I-405	5-((1 <i>S</i>)-1-[(2,2-dimethylpropanoyl)amino]propyl)- <i>N</i> -hydroxynicotinamide
I-406	5-((1 <i>S</i>)-1-[(2,2-dimethylpropanoyl)amino]ethyl)- <i>N</i> -hydroxy-6-methoxynicotinamide
I-407	2-((1 <i>S</i>)-1-[(cyclopentylacetyl)amino]butyl)- <i>N</i> -hydroxyisonicotinamide

I-408	N-((1S)-1-{4-[(hydroxyamino)carbonyl]phenyl}propyl)-1-methylpiperidine-4-carboxamide
I-409	N-((1S)-1-{4-[(hydroxyamino)carbonyl]phenyl}propyl)-1-methyl-1H-indole-2-carboxamide
I-410	4-{(1R)-1-[(2,2-dimethylpropanoyl)amino]propyl}-N-hydroxy-3-methoxybenzamide
I-411	N-((1S)-1-{5-[(hydroxyamino)carbonyl]pyridin-2-yl}-2,2-dimethylpropyl)-1-methyl-1H-indole-2-carboxamide
I-412	6-{(1S)-1-[(2,2-dimethylpropanoyl)amino]-2,2-dimethylpropyl}-N-hydroxynicotinamide
I-413	N-((1S)-1-{4-[(hydroxyamino)carbonyl]pyridin-2-yl}butyl)-1-methyl-1H-indole-2-carboxamide
I-414	N-((1S)-1-{4-[(hydroxyamino)carbonyl]phenyl}-2,2-dimethylpropyl)-1-benzothiophene-2-carboxamide
I-415	N-hydroxy-2-[(1R)-1-({[4-(trifluoromethyl)phenyl]sulfonyl}amino)propyl]isonicotinamide
I-416	6-((1S)-2,2-dimethyl-1-{[(1-methyl-1H-pyrrol-2-yl)carbonyl]amino}propyl)-N-hydroxynicotinamide
I-417	6-((1S)-2,2-dimethyl-1-{[(1-methylpiperidin-4-yl)carbonyl]amino}propyl)-N-hydroxynicotinamide
I-418	4-{(1S)-1-[(2,2-dimethylpropanoyl)amino]-2,2-dimethylpropyl}-N-hydroxybenzamide
I-419	N-hydroxy-6-methoxy-5-((1S)-1-{[(1-methyl-1H-pyrrol-2-yl)carbonyl]amino}ethyl)nicotinamide
I-420	6-((1S)-1-{[(dimethylamino)acetyl]amino}-2,2-dimethylpropyl)-N-hydroxynicotinamide
I-421	6-((1S)-1-{[(dimethylamino)acetyl]amino}ethyl)-N-hydroxynicotinamide
I-422	4-{(1S)-1-[(cyclopentylacetyl)amino]propyl}-N-hydroxybenzamide
I-423	5-{(1S)-1-[(1-benzothien-2-ylcarbonyl)amino]propyl}-N-hydroxynicotinamide
I-424	5-{(1S)-1-[(cyclopentylacetyl)amino]ethyl}-N-hydroxy-6-methoxynicotinamide
I-425	N-hydroxy-5-((1S)-1-{[(1-methylpiperidin-4-yl)carbonyl]amino}propyl)nicotinamide
I-426	2-{(1S)-1-[(2,2-dimethylpropanoyl)amino]butyl}-N-hydroxyisonicotinamide
I-427	3-fluoro-N-hydroxy-4-[(1R)-1-({[4-(trifluoromethyl)phenyl]sulfonyl}amino)ethyl]benzamide
I-428	5-{(1S)-1-[(1-adamantylcarbonyl)amino]propyl}-N-hydroxynicotinamide
I-429	6-{(1S)-1-[(1-adamantylcarbonyl)amino]-2,2-dimethylpropyl}-N-hydroxynicotinamide
I-430	2-{(1S)-1-[(cyclopentylacetyl)amino]-2-methylpropyl}-N-hydroxypyrimidine-5-carboxamide
I-431	N-hydroxy-6-methoxy-5-((1S)-1-{[(1-methylpiperidin-4-yl)carbonyl]amino}ethyl)nicotinamide

I-432	6-((1S)-1-[(cyclopentylacetyl)amino]-2,2-dimethylpropyl)-N-hydroxynicotinamide
I-433	N-hydroxy-6-((1S)-1-{[(1-methylpiperidin-4-yl)carbonyl]amino}ethyl)nicotinamide
I-434	6-((1S)-1-[(biphenyl-4-ylcarbonyl)amino]ethyl)-N-hydroxynicotinamide
I-435	N-hydroxy-6-((1S)-1-{[(1-methyl-1H-pyrrol-2-yl)carbonyl]amino}ethyl)nicotinamide
I-436	2-((1S)-1-[(1-adamantylcarbonyl)amino]-2-methylpropyl)-N-hydroxypyrimidine-5-carboxamide
I-437	N-((1S)-1-{4-[(hydroxyamino)carbonyl]phenyl}-2,2-dimethylpropyl)-1-methylpiperidine-4-carboxamide
I-438	N-hydroxy-2-((1S)-1-{[(1-methyl-1H-pyrrol-2-yl)carbonyl]amino}butyl)isonicotinamide
I-439	N-((1R)-1-{2-fluoro-4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)biphenyl-4-carboxamide
I-440	N-hydroxy-2-[(1R)-1-({[4-(trifluoromethyl)phenyl]sulfonyl}amino)ethyl]pyrimidine-5-carboxamide
I-441	N-((1S)-1-{4-[(hydroxyamino)carbonyl]phenyl}propyl)-1-benzothiophene-2-carboxamide
I-442	5-((1S)-1-[(cyclopentylacetyl)amino]propyl)-N-hydroxynicotinamide
I-443	6-((1S)-1-[(biphenyl-4-ylcarbonyl)amino]-2,2-dimethylpropyl)-N-hydroxynicotinamide
I-444	N-((1S)-1-{5-[(hydroxyamino)carbonyl]-2-methoxypyridin-3-yl}ethyl)-1-methyl-1H-indole-2-carboxamide
I-445	6-((1S)-1-[(1-benzothien-2-ylcarbonyl)amino]ethyl)-N-hydroxynicotinamide
I-446	6-((1S)-1-[(2,2-dimethylpropanoyl)amino]ethyl)-N-hydroxynicotinamide
I-447	5-((1S)-1-{[(dimethylamino)acetyl]amino}ethyl)-N-hydroxy-6-methoxynicotinamide
I-448	2-((1S)-1-[(1-benzothien-2-ylcarbonyl)amino]-2-methylpropyl)-N-hydroxypyrimidine-5-carboxamide
I-449	2-((1S)-1-[(biphenyl-4-ylcarbonyl)amino]butyl)-N-hydroxyisonicotinamide
I-450	2-((1S)-1-[(biphenyl-4-ylcarbonyl)amino]-2-methylpropyl)-N-hydroxypyrimidine-5-carboxamide
I-451	2-((1S)-1-{[(dimethylamino)acetyl]amino}butyl)-N-hydroxyisonicotinamide
I-452	N-((1S)-1-{4-[(hydroxyamino)carbonyl]phenyl}-2,2-dimethylpropyl)-1-methyl-1H-indole-2-carboxamide
I-453	5-((1S)-1-{[(dimethylamino)acetyl]amino}propyl)-N-hydroxynicotinamide

I-454	N-hydroxy-2-[(1R)-2-methyl-1-({[4-(trifluoromethyl)phenyl]sulfonyl}amino)propyl]isonicotinamide
I-455	N-((1S)-1-{5-[(hydroxyamino)carbonyl]pyridin-3-yl}propyl)-1-methyl-1H-indole-2-carboxamide
I-456	2-((1S)-1-{[(dimethylamino)acetyl]amino}-2-methylpropyl)-N-hydroxypyrimidine-5-carboxamide
I-457	N-((1S)-1-{5-[(hydroxyamino)carbonyl]pyridin-2-yl}ethyl)-1-methyl-1H-indole-2-carboxamide
I-458	2-{(1S)-1-[(1-benzothien-2-ylcarbonyl)amino]butyl}-N-hydroxyisonicotinamide
I-459	4-{(1S)-1-[(cyclopentylacetyl)amino]-2,2-dimethylpropyl}-N-hydroxybenzamide
I-460	N-((1S)-1-{4-[(hydroxyamino)carbonyl]phenyl}propyl)-1-methyl-1H-pyrrole-2-carboxamide
I-461	N-hydroxy-5-((1S)-1-{[(1-methyl-1H-pyrrol-2-yl)carbonyl]amino}propyl)nicotinamide
I-462	N-((1S)-1-{4-[(hydroxyamino)carbonyl]phenyl}-2,2-dimethylpropyl)-1-methyl-1H-pyrrole-2-carboxamide
I-463	5-((1R)-1-{[(tert-butylamino)carbonyl]amino}propyl)-N-hydroxynicotinamide
I-464	5-{(1S)-1-[(biphenyl-4-ylcarbonyl)amino]ethyl}-N-hydroxy-6-methoxynicotinamide
I-465	2-{(1S)-1-[(1-adamantylcarbonyl)amino]butyl}-N-hydroxyisonicotinamide
I-466	N-((1S)-1-{5-[(hydroxyamino)carbonyl]pyrimidin-2-yl}-2-methylpropyl)-1-methyl-1H-indole-2-carboxamide
I-467	5-{(1S)-1-[(biphenyl-4-ylcarbonyl)amino]propyl}-N-hydroxynicotinamide
I-468	N-hydroxy-2-((1S)-1-{[(1-methylpiperidin-4-yl)carbonyl]amino}butyl)isonicotinamide
I-469	6-{(1S)-1-[(1-adamantylcarbonyl)amino]ethyl}-N-hydroxynicotinamide
I-470	4-((1S)-1-{[(dimethylamino)acetyl]amino}propyl)-N-hydroxybenzamide
I-471	N-((1S)-1-{4-[(hydroxyamino)carbonyl]phenyl}-2,2-dimethylpropyl)biphenyl-4-carboxamide
I-472	5-{(1S)-1-[(1-adamantylcarbonyl)amino]ethyl}-N-hydroxy-6-methoxynicotinamide
I-473	2-{(1S)-1-[(2,2-dimethylpropanoyl)amino]-2-methylpropyl}-N-hydroxypyrimidine-5-carboxamide
I-474	N-((1S)-1-{4-[(hydroxyamino)carbonyl]phenyl}propyl)biphenyl-4-carboxamide
I-475	4-{(1S)-1-[(2,2-dimethylpropanoyl)amino]propyl}-N-hydroxybenzamide
I-476	N-hydroxy-2-((1S)-2-methyl-1-{[(1-methyl-1H-pyrrol-2-yl)carbonyl]amino}propyl)pyrimidine-

	5-carboxamide
I-477	N-hydroxy-2-((1S)-2-methyl-1-[[[(1-methylpiperidin-4-yl)carbonyl]amino}propyl]pyrimidine-5-carboxamide
I-478	4-((1S)-1-[[[(dimethylamino)acetyl]amino}-2,2-dimethylpropyl]-N-hydroxybenzamide
I-479	5-{{(1S)-1-[(1-benzothien-2-ylcarbonyl)amino]ethyl}-N-hydroxy-6-methoxynicotinamide
I-480	N-(1-{4-[(hydroxyamino)carbonyl]-2-methoxyphenyl}ethyl)-1-benzothiophene-2-carboxamide
I-481	N-(1-{4-[(hydroxyamino)carbonyl]-2-methoxyphenyl}ethyl)-1-methyl-1H-pyrrole-2-carboxamide
I-482	4-((1R)-1-[[[(benzylamino)carbonyl]amino}ethyl]-N-hydroxybenzamide
I-483	N-(1-{4-[(hydroxyamino)carbonyl]-2-methoxyphenyl}ethyl)adamantane-1-carboxamide
I-484	4-{1-[(2,2-dimethylpropanoyl)amino]ethyl}-N-hydroxy-3-methoxybenzamide
I-485	N-(1-{4-[(hydroxyamino)carbonyl]-2-methylphenyl}ethyl)-1-benzothiophene-2-carboxamide
I-486	N-(1-{4-[(hydroxyamino)carbonyl]-2-methylphenyl}ethyl)-1-methyl-1H-pyrrole-2-carboxamide
I-487	N-((1R)-1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-4-methylpiperidine-4-carboxamide
I-488	N-hydroxy-4-[1-({4-(trifluoromethyl)phenyl}sulfonyl)amino]ethyl]benzamide
I-489	N-hydroxy-4-((1R)-1-[[[(1-methylcyclohexyl)methyl]amino}ethyl]benzamide
I-490	4-{1-[(2,2-dimethylpropanoyl)amino]ethyl}-N-hydroxy-3-methylbenzamide
I-491	N-(1-{4-[(hydroxyamino)carbonyl]-2-methylphenyl}ethyl)adamantane-1-carboxamide
I-492	N-hydroxy-4-[(1R)-2-methyl-1-({[(5-phenyl-2-thienyl)amino]carbonyl}amino)propyl]benzamide
I-493	4-((1R)-1-[[[(biphenyl-2-ylamino)carbonyl]amino}-2-methylpropyl]-N-hydroxybenzamide
I-494	4-((1R)-1-[[[(biphenyl-2-ylamino)carbonyl]amino}ethyl]-N-hydroxybenzamide
I-495	N-hydroxy-4-{{(1R)-2-methyl-1-[[[(1S)-1-phenylethyl]amino}carbonyl]amino}propyl}benzamide
I-496	4-((1R)-1-[[[(2,3-dihydro-1-benzofuran-5-ylamino)carbonyl]amino}ethyl]-N-hydroxybenzamide
I-497	4-[(1R)-1-({[(3,4-dimethylphenyl)amino]carbonyl}amino)-2-methylpropyl]-N-hydroxybenzamide
I-498	4-[(1R)-1-({[(4-cyanophenyl)amino]carbonyl}amino)-2-methylpropyl]-N-hydroxybenzamide
I-499	N-hydroxy-4-{{(1R)-1-[[[(1S)-1-phenylethyl]amino}carbonyl]amino}ethyl}benzamide

I-500	4-[(1R)-1-({[(3,4-dimethylphenyl)amino]carbonyl}amino)ethyl]-N-hydroxybenzamide
I-501	N-hydroxy-4-[(1R)-2-methyl-1-({[(2-phenylethyl)amino]carbonyl}amino)propyl]benzamide
I-502	N-hydroxy-4-[(1R)-1-({[(1R)-1-phenylethyl]amino}carbonyl)amino]ethyl]benzamide
I-503	N-hydroxy-4-[(1R)-1-({[(1-naphthylamino)carbonyl]amino}ethyl)benzamide
I-504	4-[(1R)-1-({[(4-cyanophenyl)amino]carbonyl}amino)ethyl]-N-hydroxybenzamide
I-505	4-[(1R)-1-({[(2,6-difluorophenyl)amino]carbonyl}amino)-2-methylpropyl]-N-hydroxybenzamide
I-506	N-hydroxy-4-[(1R)-1-({[(2-phenylethyl)amino]carbonyl}amino)ethyl]benzamide
I-507	N-hydroxy-4-[(1R)-2-methyl-1-({[(1R)-1-phenylethyl]amino}carbonyl)amino]propyl]benzamide
I-508	4-[(1R)-1-({[(2,6-difluorophenyl)amino]carbonyl}amino)ethyl]-N-hydroxybenzamide
I-509	4-[(1R)-1-({[(2,3-dihydro-1-benzofuran-5-ylamino)carbonyl]amino}-2-methylpropyl)-N-hydroxybenzamide
I-510	N-hydroxy-4-[(1R)-2-methyl-1-({[(1-naphthylamino)carbonyl]amino}propyl)benzamide
I-511	N-hydroxy-4-[(1R)-1-({[(5-phenyl-2-thienyl)amino]carbonyl}amino)ethyl]benzamide
I-512	4-[(1R)-1-({[(3,4-dimethylphenyl)amino]carbonyl}amino)-2-methylpropyl]-N-hydroxybenzamide
I-513	N-hydroxy-4-[(1R)-1-({[(1S)-1-phenylethyl]carbamoyl}amino)ethyl]benzamide
I-514	N-hydroxy-4-[(1R)-2-methyl-1-({[(1R)-1-phenylethyl]carbamoyl}amino)propyl]benzamide
I-515	4-[(1R)-1-({[(biphenyl-2-ylamino)carbonyl]amino}-2-methylpropyl)-N-hydroxybenzamide
I-516	N-hydroxy-4-[(1R)-2-methyl-1-({[(1S)-1-phenylethyl]amino}carbonyl)amino]propyl]benzamide
I-517	N-hydroxy-4-[(1R)-1-({[(1R)-1-phenylethyl]carbamoyl}amino)ethyl]benzamide
I-518	4-[(1R)-1-({[(2,6-difluorophenyl)amino]carbonyl}amino)ethyl]-N-hydroxybenzamide
I-519	N-hydroxy-4-[(1R)-2-methyl-1-({[4-(3-phenylisoxazol-5-yl)-1,3-thiazol-2-yl]amino}propyl)benzamide
I-520	4-[(1R)-1-({[(4-cyanophenyl)amino]carbonyl}amino)ethyl]-N-hydroxybenzamide
I-521	4-[(1R)-1-({[(2,6-difluorophenyl)amino]carbonyl}amino)-2-methylpropyl]-N-hydroxybenzamide
I-522	N-hydroxy-4-[(1R)-2-methyl-1-({[(2-phenylethyl)amino]carbonyl}amino)propyl]benzamide
I-523	4-[(1R)-1-({[(biphenyl-2-ylamino)carbonyl]amino}ethyl)-N-hydroxybenzamide

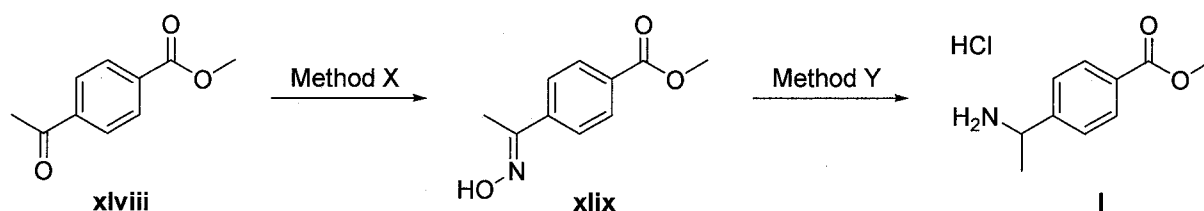
I-524	N-hydroxy-4-((1R)-2-methyl-1-{[(1-naphthylamino)carbonyl]amino}propyl)benzamide
I-525	4-[(1R)-1-({[(4-cyanophenyl)amino]carbonyl}amino)-2-methylpropyl]-N-hydroxybenzamide
I-526	4-((1R)-1-{{(2,3-dihydro-1-benzofuran-5-ylamino)carbonyl}amino}-2-methylpropyl)-N-hydroxybenzamide
I-527	N-hydroxy-4-((1R)-1-{{(1-naphthylamino)carbonyl}amino}ethyl)benzamide
I-528	4-((1R)-1-{{(2,3-dihydro-1-benzofuran-5-ylamino)carbonyl}amino}ethyl)-N-hydroxybenzamide
I-529	N-hydroxy-4-((1R)-2-methyl-1-{{4-(trifluoromethyl)-1,3-thiazol-2-yl}amino}propyl)benzamide
I-530	N-hydroxy-4-((1R)-1-{{(1-isopropylpiperidin-4-yl)methyl}amino}butyl)benzamide
I-531	3-{{(((1R)-1-{4-[(hydroxyamino)carbonyl]phenyl}butyl)amino)methyl}-N-pyrrolidin-3-yl)benzamide
I-532	N-(4-{{(((1R)-1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)amino)methyl}pyridin-2-yl)-4-methylpiperidine-4-carboxamide
I-533	N-(4-{{(((1R)-1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)amino)methyl}phenyl)-1-methylpiperidine-4-carboxamide
I-534	4-((1R)-1-{{(1-ethylpiperidin-4-yl)methyl}amino}ethyl)-N-hydroxybenzamide
I-535	N-(1-{4-[(hydroxyamino)carbonyl]phenyl}-2,2-dimethylpropyl)-2-(trifluoromethyl)benzamide
I-536	4-{{(1S)-1-[(2,2-dimethylpropanoyl)amino]butyl}-N-hydroxybenzamide

4. General Synthetic Methods and Intermediates

[00120] The compounds of the present invention can be prepared by methods known to one of ordinary skill in the art and / or by reference to the schemes shown below and the synthetic examples. Exemplary synthetic routes are set forth in Schemes below, and in the Examples.

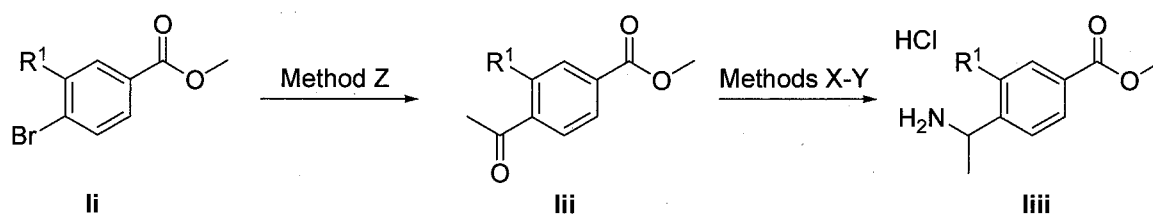
[00121] As shown in **Scheme 1** below, condensation of commercially available methyl 4-acetylbenzoate (**xlvi**) with hydroxylamine (Method X) affords the resulting oxime **xlvi** which can be reduced by catalytic hydrogenolysis in the presence of acid (Method Y) to generate racemic compound of formula **I**. The amine can be further elaborated according to Methods D, H or I, or those described in **Scheme 13**, followed by treatment with hydroxylamine hydrochloride in the presence of base to generate the corresponding substituted hydroxamate.

Scheme 1: General route to (±) methyl 4-(1-aminoethyl)benzoate hydrochloride



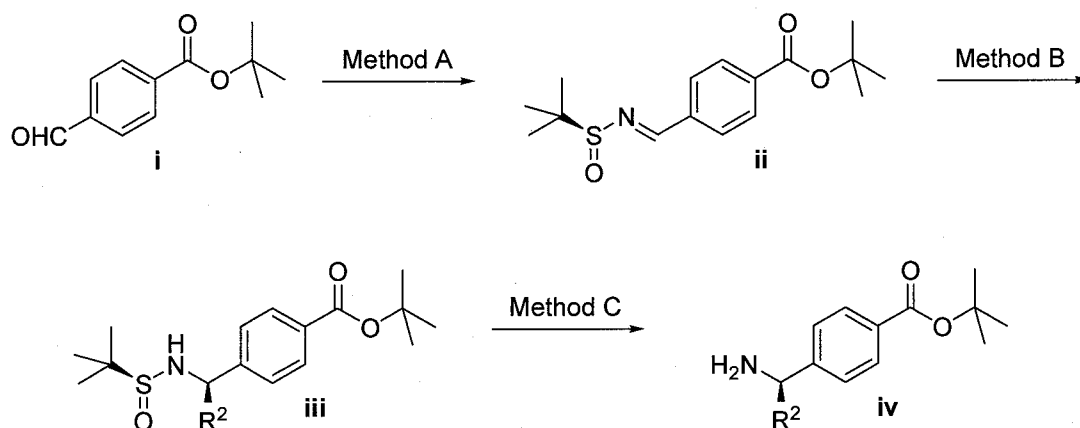
[00122] As shown in **Scheme 2**, aryl bromide **li** can be acylated via a Heck coupling (Method Z) to afford **lii**. Application of Methods X-Y as shown in **Scheme 1** provides **lii** which can then be further elaborated as described herein.

Scheme 2: General route to substituted (±)-methyl 4-(1-aminoethyl)-3-benzoate hydrochloride



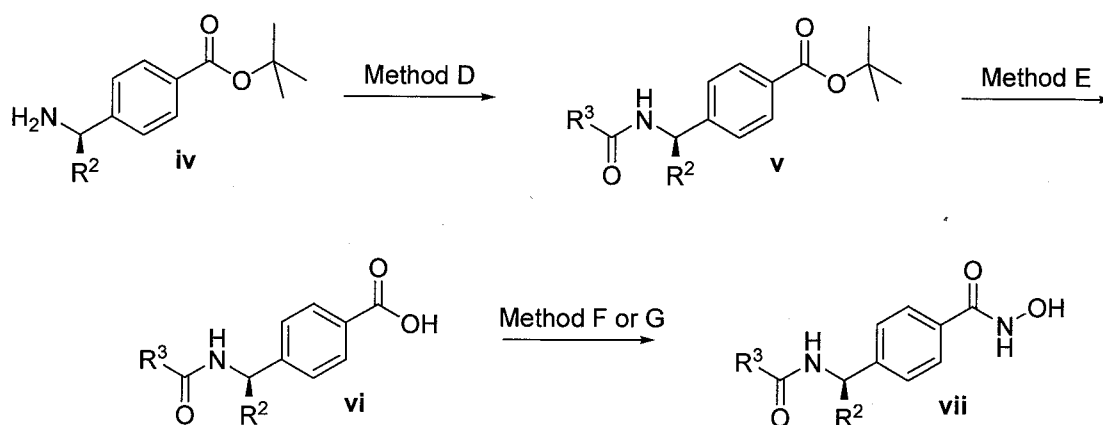
[00123] **Scheme 3** below shows a general route for the preparation of substituted aminomethyl benzoate compounds of formula **iv**. Conversion of tert-butyl 4-formylbenzoate **i** (prepared as described in Adlington *et al.*, *J. Med. Chem.* **2001**, 44:1491) to the *N*-(tert-butanefulfinyl)imine **ii** is carried out by reaction with one enantiomer of 2-methyl-2-propanesulfinamide under dehydrative conditions (Method A; Ti(OEt)₄ or Ti(O^{*i*}Pr)₄, DCM; Ellman *et al.*, *Acc. Chem. Res.* **2002**, 35:984; Ellman *et al.*, *J. Org. Chem.* **1999**, 64:1278; Ellman *et al.*, *J. Am. Chem. Soc.* **1999**, 121:268; Davis *et al.*, *J. Org. Chem.* **1999**, 64:1403). Diastereoselective addition of the R² group by the use of the appropriate Grignard reagent (Method B; as described by Liu *et al.*, *J. Am. Chem. Soc.* **1997**, 119:9913) provides α-branched sulfinamides **iii** in high diastereomeric ratios. Isolation of single diastereomers by chromatography followed by removal of the chiral auxiliary (1 equiv. HCl; Method C) provides enantiomerically pure amine **iv**. When R² is trifluoromethyl, tetra-*n*-butylammoniumdifluorotriphenylsilicate and (trifluoromethyl)trimethylsilane can be used instead of a Grignard reagent to introduce the trifluoromethyl group to the compound of formula **ii**, resulting in the compound of formula **iii** wherein R² is trifluoromethyl. The synthetic sequence can be repeated with the opposite enantiomer of the 2-methyl-2-propanesulfinamide to generate the other enantiomer of the compound of formula **iv**. It will also be appreciated that this method can be used to generate the meta-regioisomer of the compounds of formula **iv** starting from the appropriate starting materials.

[00124] The absolute stereochemistry of the chiral primary amines is established by comparison of the ¹H-NMR spectra of the corresponding Mosher amides as described by Priest *et al.*, *J. Chem. Ed.*, **2008**, 85:698.

Scheme 3: General route to single enantiomers of tert-butyl 4-(amino(alkyl)methyl)benzoates

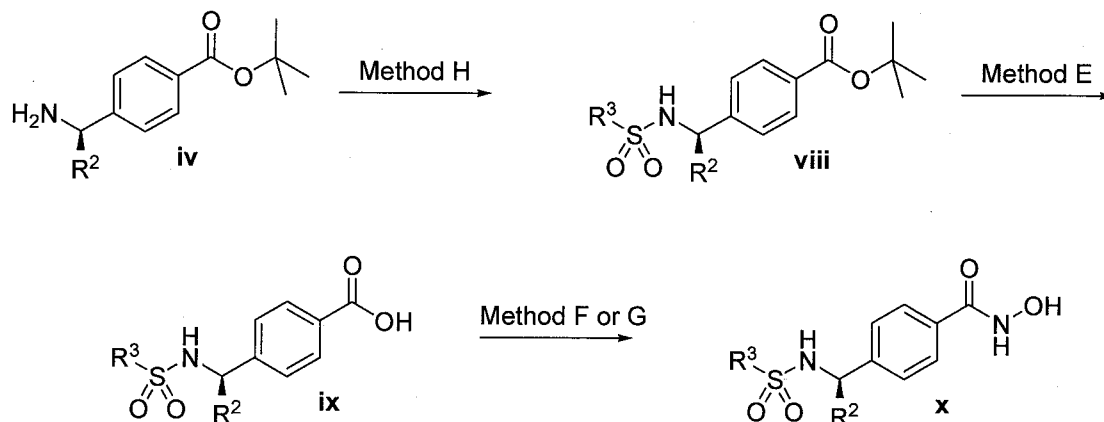
[00125] Scheme 4 shows a general route for the elaboration of compounds of formula **iv** to compounds of formula **vii**. The primary amine of **iv** is acylated with a carboxylic acid (R^3 -CO₂H) in the presence of a coupling agent (Method D). Suitable coupling agents include, but are not limited to, 2-(1H-benzotriazole-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate (HBTU), or O-(7-azabenzotriazol-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate (HATU). Suitable bases for Method D include, but are not limited to, triethylamine (Et₃N), *N,N'*-diisopropylethylamine (DIPEA) and *N*-methylmorpholine. Suitable solvents for Method D include, but are not limited to, dichloromethane (DCM), tetrahydrofuran (THF), *N,N'*-dimethylformamide (DMF), *N*-methylpyrrolidone (NMP) or *N,N'*-dimethylacetamide. Deprotection of the tert-butyl ester to give compounds of formula **vi** is achieved under acidic conditions, using for example, trifluoroacetic acid in DCM or dichloroethane (Method E). Conversion of the acid of formula **vi** to the corresponding hydroxamate of formula **vii** (Method F) is achieved by activation of the acid with a coupling reagent such as HATU, in the presence of base such as Et₃N, in a solvent such as DMF, followed by treatment with *O*-(tert-butyldimethylsilyl)hydroxylamine. The silyl protecting group can then be removed by treatment under acidic conditions such as 1% HCl in isopropyl alcohol. Alternatively, the hydroxamate can be introduced by treatment of the acid of formula **vi** with cyanuric chloride, base and catalytic DMAP followed by hydroxylamine hydrochloride (Method G; Giacomelli *et al.*, *Org. Lett.* **2003**, 5:2715).

Scheme 4: General route to 4-(substituted-carboxamido(alkyl)methyl)-*N*-hydroxybenzamide analogs



[00126] **Scheme 5** shows a route for the preparation of substituted aminomethyl benzoate compounds of formula **x**. The primary amine of formula **iv** is treated with the appropriate sulfonyl chloride, R³-SO₂Cl, and DMAP in DMF at ambient temperature to give compounds of formula **viii** (Method H). Method H may also be carried out in a solvent such as DCM or *N,N*-dimethylacetamide. Deprotection of the tert-butyl ester (Method E), and conversion of the acid to the corresponding hydroxamate (Method F or G) can be carried out as described in **Scheme 3** above to generate compounds of formula **x**.

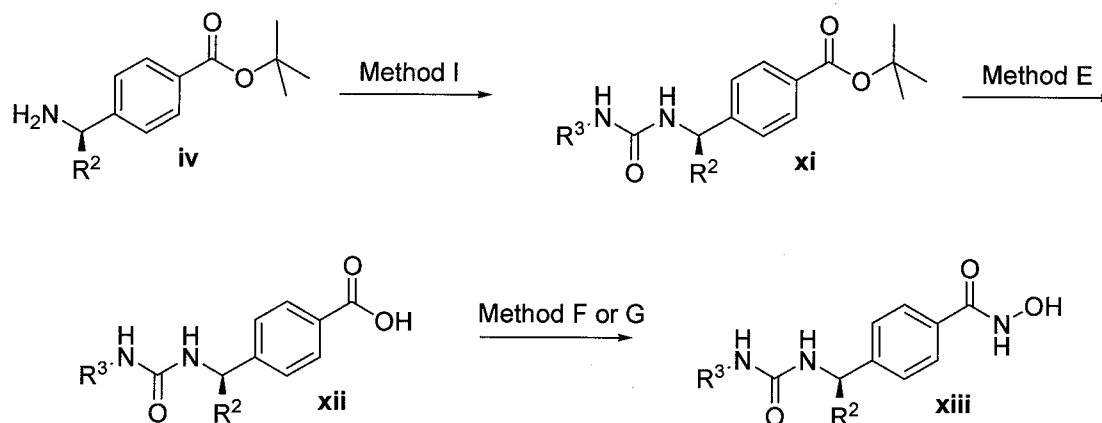
[00127] **Scheme 5: General route to 4-(substituted-sulfonamido(alkyl)methyl)-*N*-hydroxybenzamide analogs**



[00128] **Scheme 6** shows a route for the preparation of substituted aminomethyl benzoate compounds of formula **xiii**. The primary amine of formula **iv** is treated with the appropriate isocyanate, (R³-NCO), and base in solvent overnight at ambient or elevated temperature to afford compounds of formula **xi** (Method I). Suitable bases for Method I include, but are not limited to Et₃N, DIPEA, and *N*-methylmorpholine. Suitable solvents for Method I include, but are not limited to, DCM, THF, DMF, NMP or *N,N*-dimethylacetamide. Deprotection of the tert-butyl ester (Method E), and conversion of the

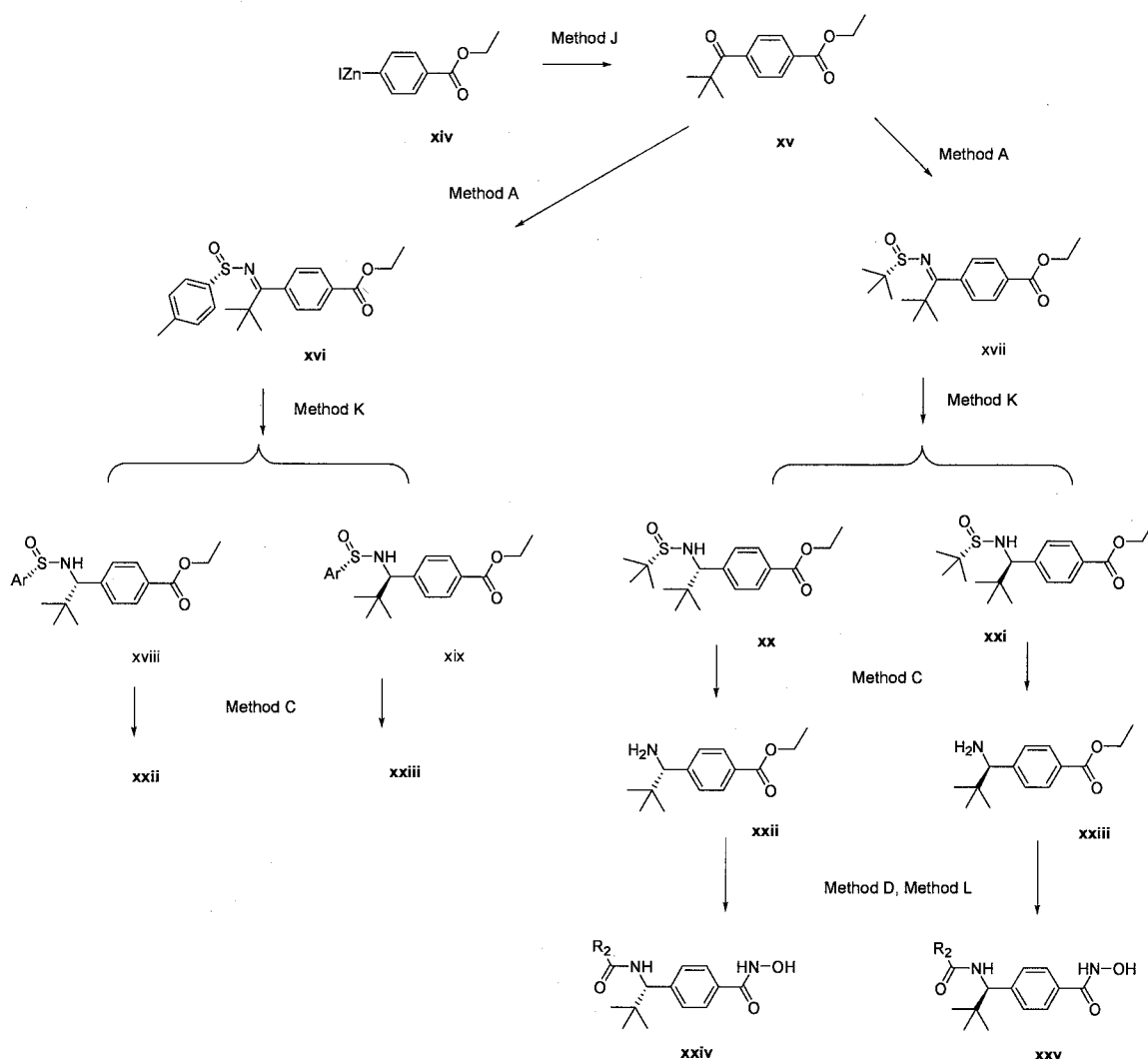
acid to the corresponding hydroxamate (Method F or G) can be carried out as described in **Scheme 4** above to give compounds of formula **xiii**. It will be appreciated that the methods described in **Schemes 4, 5 and 6** can be carried out on amines with different substitution at the R^2 position and differing ring A structures.

Scheme 6: General route to 4-((3-substituted-ureido)(alkyl)methyl)-N-hydroxybenzamide analogs



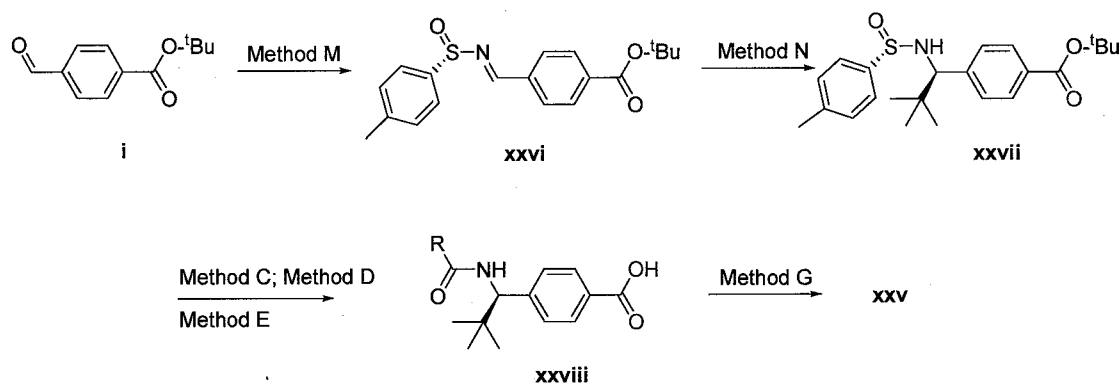
[00129] **Scheme 7** below shows a route for the preparation of tert-butyl substituted compounds of formula **xxiv** and **xxv**. Ketone **xv** is prepared by reaction of the arylzinc reagent **xiv** with pivaloyl chloride (Method J; WO 08/156721). Conversion of **xv** to the sufinimines **xvi** and **xvii** is carried out by reaction with the appropriate sulfinamide under dehydrative conditions (Method A; Ellman *et al.*, *Acc. Chem. Res.* **2002**, 35:984; Ellman *et al.*, *J. Org. Chem.* **1999**, 64:1278; Ellman *et al.*, *J. Am. Chem. Soc.* **1999**, 121:268; Davis *et al.*, *J. Org. Chem.* **1999**, 64:1403). Reduction using NaBH_4 (Method K; Ellman *et al.*, *Tetrahedron Lett.* **1999**, 40:6709; Coyler *et al.*, *J. Org. Chem.* **2006**, 71:6859) and subsequent separation of pairs of diastereomers **xviii** and **xix** or **xx** and **xxi** by normal phase chromatography is followed by removal of the chiral auxiliary (Method C) to give enantiomerically pure amines **xxii** and **xxiii**. Further elaboration of the compounds of formula **xxiv** and **xxv** is accomplished by reaction with a carboxylic acid as described above in **Scheme 4** (Method D), and then conversion to the hydroxamate by treatment with hydroxylamine hydrochloride (Method L; KOH, MeOH). Alternatively, the compounds of formula **xxii** and **xxiii** can be further elaborated as described in **Schemes 5, 6 or 13** followed by conversion to the corresponding hydroxamates.

Scheme 7: General route to enantiomerically pure 4-(substituted-carboxamido(tert-butyl)methyl)-N-hydroxybenzamide analogs



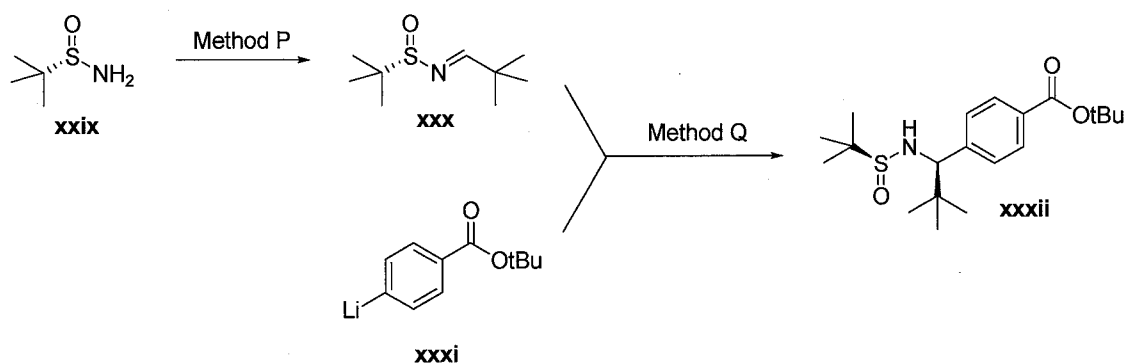
[00130] Alternatively, sulfinimine **xxvi** is prepared as shown in **Scheme 8** by condensation of the appropriate sulfinamide with tert-butyl 4-formylbenzoate **i** (Method M; Yim and Wong, *J. Org. Chem.* **2004**, 69:2892); treated with tert-butyllithium in THF (Method N) to give **xxvii** after separation of the resulting diastereomers. Removal of the chiral auxiliary (Method C) followed by elaboration of the resulting amine as described above in Scheme 2 (Method D), and removal of the tert-butyl ester using TFA (Method E) yields the compound of formula **xxviii**. The compound of formula **xxviii** is converted to the corresponding hydroxamate of formula **xxv** using cyanuric chloride, base and catalytic DMAP followed by hydroxylamine hydrochloride (Method G) (Giacomelli, G., *et. al. Org. Lett.* **2003**, 5, 2715). Alternatively, following removal of the chiral auxiliary the compound of formula **xxvii** can be further elaborated as described in **Schemes 5, 6** or **13** followed by conversion to the corresponding hydroxamates.

Scheme 8: General route to 4-(substituted-carboxamido(tert-butyl)methyl)-N-hydroxybenzamide analogs



[00131] Alternatively, as shown in **Scheme 9**, condensation of pivaloyl aldehyde with S-2-methyl-2-sulfinamide **xxix** (Method P) gives **xxx** which can be treated with the aryllithium reagent **xxxi** (Knochel, *Science of Synthesis* **2004**, 3:5-90) in THF at reflux to give compound **xxxii** (Method Q; Ellman et al *J. Am. Chem. Soc.* **1997**, 119:913; *J. Org. Chem.* **2001**, 66:8772; WO 02/070492; WO 07/145568). Compound **xxxii** can then be further elaborated as described above.

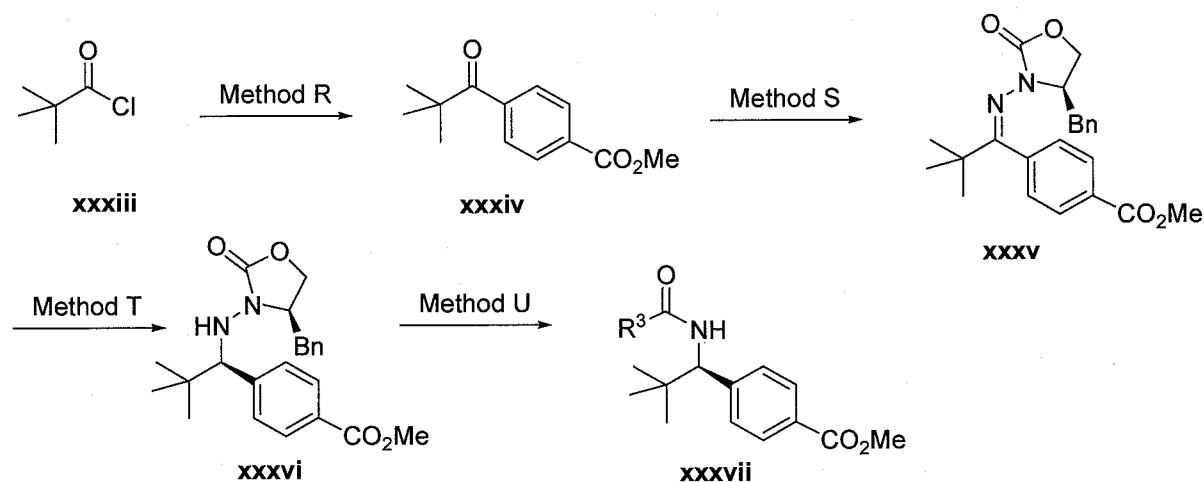
Scheme 9: General route to enantiomerically pure 4-(substituted-carboxamido(tert-butyl)methyl)-N-hydroxybenzamide analogs



[00132] **Scheme 10** shows another alternative route to enantiomerically pure tert-butyl derivatives. Treatment of pivaloyl chloride **xxxiii** with 4-carboxymethylphenylmagnesium iodide (prepared according to Wang *et al.*, *Org. Lett.* **2006**, 8:305) in the presence of vanadium chloride in DCM affords ketone **xxxiv** (Method R). Treatment with N-amino-4-benzyl-2-oxazolidinone, and TsOH affords acylhydrazone **xxxv** (Method S; Friestad *et al.*, *J. Am. Chem. Soc.* **2000**, 122:8329). The acylhydrazone is reduced using Bu_3SnH and BF_3 in DCM (Method T; Friestad *et al.*, *Tetrahedron* **2003**, 59: 6393) to give the compound of formula **xxxvi**. The compound of formula **xxxvi** is then acylated using $n\text{-BuLi}$, R^3COCl ; the chiral auxiliary is removed with SmI_2 and HMPA in THF (Method U; Friestad *et al.*, *J. Am. Chem. Soc.* **2000**,

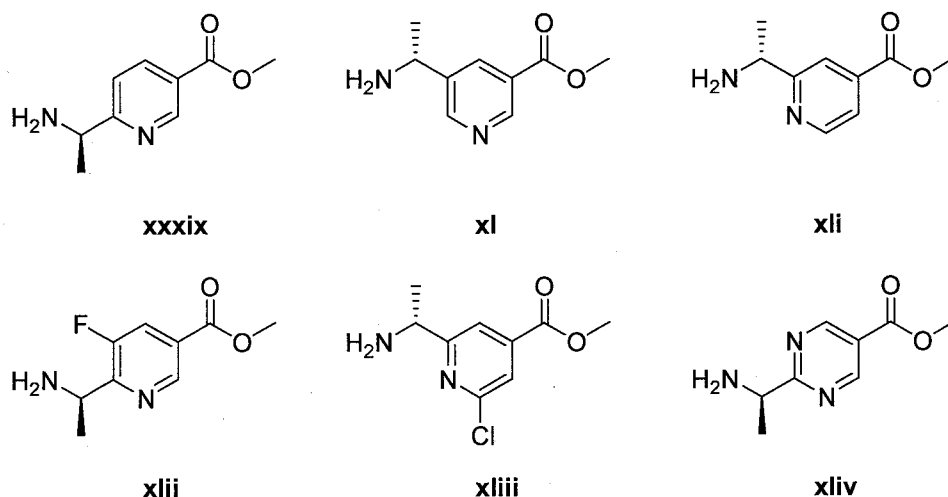
122:8329) to afford the compound of formula **xxxvii** which can then be transformed to the corresponding hydroxamate as described above.

Scheme 10: General route to enantiomerically pure 4-(substituted-carboxamido(tert-butyl)methyl)-N-hydroxybenzamide analogs



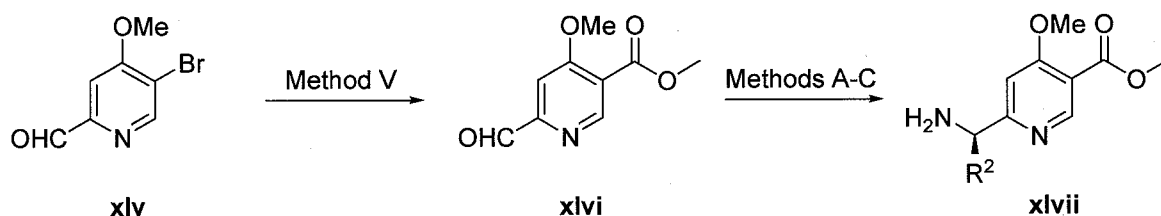
[00133] Compounds of formula **xxxix**, **xl** and **xli** can be prepared starting from the commercially available 6-formylnicotinic acid, 5-formylnicotinic acid, and 2-formylisonicotinic acid respectively as shown in **Figure 1** below. Elaboration using Methods A-C as outlined in **Scheme 3** provides access to the corresponding enantiomerically pure products **xxxix**, **xl** and **xli**. The compounds of formula **xlii** can be prepared starting from methyl 5-fluoro-6-formylnicotinate (as described by Locardi *et al.*, WO 09/036996). Elaboration using Methods A-C as outlined in **Scheme 3** provides access to enantiomerically pure **xlii**. Compounds of formula **xliii** can be prepared starting from methyl 2-chloro-6-formylisonicotinate (prepared as described in Augustine *et al.*, *Tetrahedron* **2008**, 64(4):688-695). Elaboration using Methods A-C as outlined in **Scheme 3** provides access to enantiomerically pure **xliii**. The compound of formula **xliv** can be prepared starting from methyl 2-formylpyrimidine-5-carboxylate (as described by Hunt *et al.* WO 08/156715). Elaboration using Methods A-C as outlined in **Scheme 3** provides access to enantiomerically pure **xliv**. It will be appreciated that the other optical isomer of each of the amines shown in Figure 1 will be isolated following column chromatography of the diastereomers prior to removal of the chiral auxiliary. The amines can be further elaborated according to Methods D, H or I, or those described in **Scheme 13**, followed by treatment with hydroxylamine hydrochloride in the presence of base to generate the substituted hydroxamate.

Figure 1: Examples of enantiomerically pure amines accessible via route outlined in Scheme 3



[00134] **Scheme 11** shows a general route for the elaboration of compounds of formula **xlvi** to compounds of formula **xlvi**. Carbonylation of **xlvi** employing carbon monoxide in the presence of a Pd catalyst, as described in WO 05/037214 (Method V) provides **xlvi**. Elaboration using methods A-C as outlined in **Scheme 3** provides access to enantiomerically pure **xlvi** which can be further elaborated according to Methods D, H or I, or those described in **Scheme 13** followed by treatment with hydroxylamine hydrochloride in the presence of base to generate corresponding substituted hydroxamates.

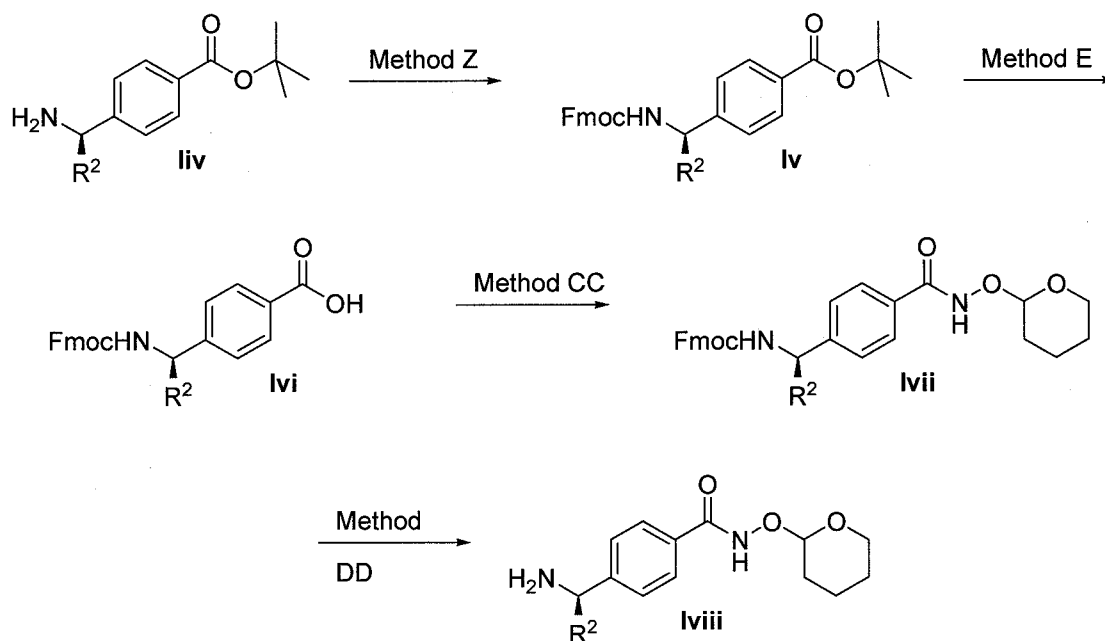
Scheme 11: General route to single enantiomers of substituted methyl 6-(aminomethyl)-4-methoxynicotinate.



[00135] **Scheme 12** shows a route for the preparation of substituted (aminomethyl)-N-(tetrahydro-2H-pyran-2-yloxy)benzamides represented by formula **lviii**. The primary nitrogen of **lv** can be orthogonally protected with a Fmoc group employing standard conditions using reagents such as Fmoc-Cl (Method Z). Removal of the *t*-butyl ester under acidic conditions (Method E) followed by coupling of the liberated acid of formula **lvi** with O-(tetrahydro-2H-pyran-2-yl)hydroxylamine in the presence of an appropriate coupling agent (Method CC) provides **lvii**. Removal of the Fmoc group is accomplished with piperidine in an appropriate solvent (Method DD) to give compound of formula **lviii**. The compound of

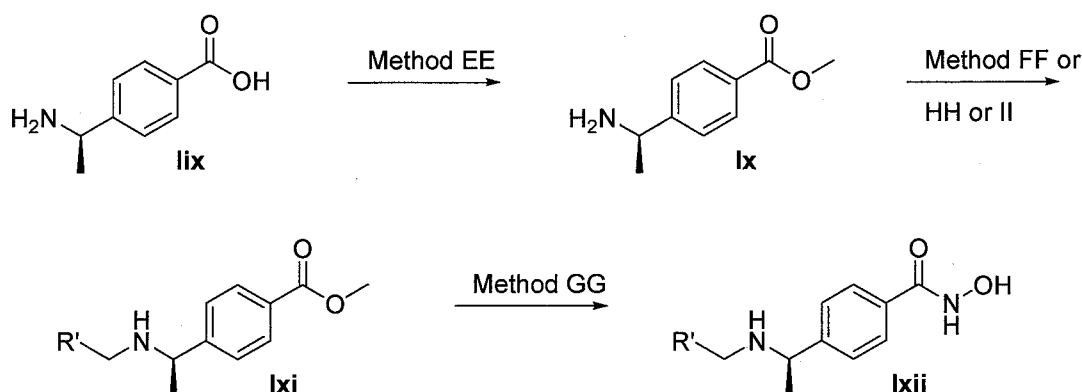
formula **lviii** can be further functionalized employing transformations such as described in Methods D, H or I or those described in **Scheme 13** followed by removal of the THP group under acidic conditons.

Scheme 12: General route to enantiomerically pure 4-((R)-amino(alkyl)methyl)-N-(tetrahydro-2H-pyran-2-yloxy)benzamides



[00136] **Scheme 13** shows a route for the preparation of substituted (R)-4-(1-ethylamino)-N-hydroxybenzamides represented by formula **lxii**. The compound of formula **lix** can be selectively converted to the corresponding ester using acid catalyzed Fisher esterification conditons (Method EE). Reductive alkylation resulting from the reaction of an aldehyde (R'CHO) in the presence of an appropriate borohydride such as, but not limited to, sodium cyanoborohydride (Method FF; Jones *et al.*, *Bioorg. & Med. Chem. Lett.* **2008**, 18(11):3456-3461) provides the compound of formula **lxi**. Amine **lx** may also be arylated using standard nucleophilic aromatic substitution of a suitable electrophile such as 2-chloro-nitropyridine, in the presence of suitable base, such as DIPEA at elevated temperatures (Method HH). Amine **lx** may also be N-arylated through a copper(II)-acetate mediated coupling with a suitable arylboronic acid (Method II; Chan *et al. Tetrahedron Lett.* **1998**, 39(19):2933). Reaction of the compound of formula **lxi** with the potassium salt of hydroxylamine (Method GG; Huang *et al.*, *J. Med. Chem.* 2009, 52(21):6757) leads to the formation of the corresponding hydroxamate **lxii**.

Scheme 13: General route to substituted (R)-4-(1-(ethylamino)alkyl)-N-hydroxybenzamides



4. Uses, Formulation and Administration

[00137] As discussed above, the present invention provides compounds and pharmaceutical compositions that are useful as inhibitors of HDAC enzymes, particularly HDAC6, and thus the present compounds are useful for treating proliferative, inflammatory, infectious, neurological or cardiovascular disorders.

[00138] The compounds and pharmaceutical compositions of the invention are particularly useful for the treatment of cancer. As used herein, the term "cancer" refers to a cellular disorder characterized by uncontrolled or dysregulated cell proliferation, decreased cellular differentiation, inappropriate ability to invade surrounding tissue, and/or ability to establish new growth at ectopic sites. The term "cancer" includes, but is not limited to, solid tumors and bloodborne tumors. The term "cancer" encompasses diseases of skin, tissues, organs, bone, cartilage, blood, and vessels. The term "cancer" further encompasses primary and metastatic cancers.

[00139] Non-limiting examples of solid tumors that can be treated with the disclosed inhibitors include pancreatic cancer; bladder cancer; colorectal cancer; breast cancer, including metastatic breast cancer; prostate cancer, including androgen-dependent and androgen-independent prostate cancer; renal cancer, including, e.g., metastatic renal cell carcinoma; hepatocellular cancer; lung cancer, including, e.g., non-small cell lung cancer (NSCLC), bronchioloalveolar carcinoma (BAC), and adenocarcinoma of the lung; ovarian cancer, including, e.g., progressive epithelial or primary peritoneal cancer; cervical cancer; gastric cancer; esophageal cancer; head and neck cancer, including, e.g., squamous cell carcinoma of the head and neck; melanoma; neuroendocrine cancer, including metastatic neuroendocrine tumors; brain

tumors, including, e.g., glioma, anaplastic oligodendroglioma, adult glioblastoma multiforme, and adult anaplastic astrocytoma; bone cancer; and soft tissue sarcoma.

[00140] Non-limiting examples of hematologic malignancies that can be treated with the disclosed inhibitors include acute myeloid leukemia (AML); chronic myelogenous leukemia (CML), including accelerated CML and CML blast phase (CML-BP); acute lymphoblastic leukemia (ALL); chronic lymphocytic leukemia (CLL); Hodgkin's disease (HD); non-Hodgkin's lymphoma (NHL), including follicular lymphoma and mantle cell lymphoma; B-cell lymphoma; T-cell lymphoma; multiple myeloma (MM); Waldenstrom's macroglobulinemia; myelodysplastic syndromes (MDS), including refractory anemia (RA), refractory anemia with ringed sideroblasts (RARS), (refractory anemia with excess blasts (RAEB), and RAEB in transformation (RAEB-T); and myeloproliferative syndromes.

[00141] In some embodiments, compounds of the invention are suitable for the treatment of breast cancer, lung cancer, ovarian cancer, multiple myeloma, acute myeloid leukemia or acute lymphoblastic leukemia.

[00142] In other embodiments, compounds of the invention are suitable for the treatment of inflammatory and cardiovascular disorders including, but not limited to, allergies/anaphylaxis, acute and chronic inflammation, rheumatoid arthritis; autoimmunity disorders, thrombosis, hypertension, cardiac hypertrophy, and heart failure.

[00143] Accordingly, in another aspect of the present invention, pharmaceutical compositions are provided, wherein these compositions comprise any of the compounds as described herein, and optionally comprise a pharmaceutically acceptable carrier, adjuvant or vehicle. In certain embodiments, these compositions optionally further comprise one or more additional therapeutic agents.

[00144] It will also be appreciated that certain of the compounds of present invention can exist in free form for treatment, or where appropriate, as a pharmaceutically acceptable derivative thereof. According to the present invention, a pharmaceutically acceptable derivative includes, but is not limited to, pharmaceutically acceptable prodrugs, salts, esters, salts of such esters, or any other adduct or derivative which upon administration to a patient in need is capable of providing, directly or indirectly, a compound as otherwise described herein, or a metabolite or residue thereof.

[00145] As used herein, the term "pharmaceutically acceptable salt" refers to those salts which are, within the scope of sound medical judgement, suitable for use in contact with the tissues of humans and lower animals without undue toxicity, irritation, allergic response and the like, and are commensurate with a reasonable benefit/risk ratio. A "pharmaceutically acceptable salt" means any non-toxic salt or salt of an ester of a compound of this invention that, upon administration to a recipient, is capable of providing, either directly or indirectly, a compound of this invention or an inhibitorily active metabolite

or residue thereof. As used herein, the term "inhibitorily active metabolite or residue thereof" means that a metabolite or residue thereof is also an inhibitor of HDAC6.

[00146] Pharmaceutically acceptable salts are well known in the art. For example, S. M. Berge *et al.*, describe pharmaceutically acceptable salts in detail in *J. Pharmaceutical Sciences*, **1977**, *66*, 1-19, incorporated herein by reference. Pharmaceutically acceptable salts of the compounds of this invention include those derived from suitable inorganic and organic acids and bases. Examples of pharmaceutically acceptable, nontoxic acid addition salts are salts of an amino group formed with inorganic acids such as hydrochloric acid, hydrobromic acid, phosphoric acid, sulfuric acid and perchloric acid or with organic acids such as acetic acid, oxalic acid, maleic acid, tartaric acid, citric acid, succinic acid or malonic acid or by using other methods used in the art such as ion exchange. Other pharmaceutically acceptable salts include adipate, alginate, ascorbate, aspartate, benzenesulfonate, benzoate, bisulfate, borate, butyrate, camphorate, camphorsulfonate, citrate, cyclopentanepropionate, digluconate, dodecylsulfate, ethanesulfonate, formate, fumarate, glucoheptonate, glycerophosphate, gluconate, hemisulfate, heptanoate, hexanoate, hydroiodide, 2-hydroxy-ethanesulfonate, lactobionate, lactate, laurate, lauryl sulfate, malate, maleate, malonate, methanesulfonate, 2-naphthalenesulfonate, nicotinate, nitrate, oleate, oxalate, palmitate, pamoate, pectinate, persulfate, 3-phenylpropionate, phosphate, picrate, pivalate, propionate, stearate, succinate, sulfate, tartrate, thiocyanate, p-toluenesulfonate, undecanoate, valerate salts, and the like. Salts derived from appropriate bases include alkali metal, alkaline earth metal, ammonium and $N^+(C_{1-4}alkyl)_4$ salts. This invention also envisions the quaternization of any basic nitrogen-containing groups of the compounds disclosed herein. Water or oil-soluble or dispersable products may be obtained by such quaternization. Representative alkali or alkaline earth metal salts include sodium, lithium, potassium, calcium, magnesium, and the like. Further pharmaceutically acceptable salts include, when appropriate, nontoxic ammonium, quaternary ammonium, and amine cations formed using counterions such as halide, hydroxide, carboxylate, sulfate, phosphate, nitrate, loweralkyl sulfonate and aryl sulfonate.

[00147] As described above, the pharmaceutically acceptable compositions of the present invention additionally comprise a pharmaceutically acceptable carrier, adjuvant, or vehicle, which, as used herein, includes any and all solvents, diluents, or other liquid vehicle, dispersion or suspension aids, surface active agents, isotonic agents, thickening or emulsifying agents, preservatives, solid binders, lubricants and the like, as suited to the particular dosage form desired. Remington's Pharmaceutical Sciences, Sixteenth Edition, E. W. Martin (Mack Publishing Co., Easton, Pa., 1980) discloses various carriers used in formulating pharmaceutically acceptable compositions and known techniques for the preparation thereof. Except insofar as any conventional carrier medium is incompatible with the compounds of the invention, such as by producing any undesirable biological effect or otherwise interacting in a deleterious

manner with any other component(s) of the pharmaceutically acceptable composition, its use is contemplated to be within the scope of this invention. Some examples of materials which can serve as pharmaceutically acceptable carriers include, but are not limited to, ion exchangers, alumina, aluminum stearate, lecithin, serum proteins, such as human serum albumin, buffer substances such as phosphates, glycine, sorbic acid, or potassium sorbate, partial glyceride mixtures of saturated vegetable fatty acids, water, salts or electrolytes, such as protamine sulfate, disodium hydrogen phosphate, potassium hydrogen phosphate, sodium chloride, zinc salts, colloidal silica, magnesium trisilicate, polyvinyl pyrrolidone, polyacrylates, waxes, polyethylene-polyoxypropylene-block polymers, wool fat, sugars such as lactose, glucose and sucrose; starches such as corn starch and potato starch; cellulose and its derivatives such as sodium carboxymethyl cellulose, ethyl cellulose and cellulose acetate; powdered tragacanth; malt; gelatin; talc; excipients such as cocoa butter and suppository waxes; oils such as peanut oil, cottonseed oil; safflower oil; sesame oil; olive oil; corn oil and soybean oil; glycols; such a propylene glycol or polyethylene glycol; esters such as ethyl oleate and ethyl laurate; agar; buffering agents such as magnesium hydroxide and aluminum hydroxide; alginic acid; pyrogen-free water; isotonic saline; Ringer's solution; ethyl alcohol, and phosphate buffer solutions, as well as other non-toxic compatible lubricants such as sodium lauryl sulfate and magnesium stearate, as well as coloring agents, releasing agents, coating agents, sweetening, flavoring and perfuming agents, preservatives and antioxidants can also be present in the composition, according to the judgment of the formulator.

[00148] In yet another aspect, a method for treating a proliferative, inflammatory, infectious, neurological or cardiovascular disorder is provided comprising administering an effective amount of a compound, or a pharmaceutical composition to a subject in need thereof. In certain embodiments of the present invention an "effective amount" of the compound or pharmaceutical composition is that amount effective for treating a proliferative, inflammatory, infectious, neurological or cardiovascular disorder, or is that amount effective for treating cancer. In other embodiments, an "effective amount" of a compound is an amount which inhibits binding of HDAC6, and thereby blocks the resulting signaling cascades that lead to the abnormal activity of growth factors, receptor tyrosine kinases, protein serine/threonine kinases, G protein coupled receptors and phospholipid kinases and phosphatases.

[00149] The compounds and compositions, according to the method of the present invention, may be administered using any amount and any route of administration effective for treating the disease. The exact amount required will vary from subject to subject, depending on the species, age, and general condition of the subject, the severity of the infection, the particular agent, its mode of administration, and the like. The compounds of the invention are preferably formulated in dosage unit form for ease of administration and uniformity of dosage. The expression "dosage unit form" as used herein refers to a physically discrete unit of agent appropriate for the patient to be treated. It will be understood, however,

that the total daily usage of the compounds and compositions of the present invention will be decided by the attending physician within the scope of sound medical judgment. The specific effective dose level for any particular patient or organism will depend upon a variety of factors including the disease being treated and the severity of the disease; the activity of the specific compound employed; the specific composition employed; the age, body weight, general health, sex and diet of the patient; the time of administration, route of administration, and rate of excretion of the specific compound employed; the duration of the treatment; drugs used in combination or coincidental with the specific compound employed, and like factors well known in the medical arts. The term "patient", as used herein, means an animal, preferably a mammal, and most preferably a human.

[00150] The pharmaceutically acceptable compositions of this invention can be administered to humans and other animals orally, rectally, parenterally, intracisternally, intravaginally, intraperitoneally, topically (as by powders, ointments, or drops), buccally, as an oral or nasal spray, or the like, depending on the severity of the infection being treated. In certain embodiments, the compounds of the invention may be administered orally or parenterally at dosage levels of about 0.01 mg/kg to about 50 mg/kg and preferably from about 1 mg/kg to about 25 mg/kg, of subject body weight per day, one or more times a day, to obtain the desired therapeutic effect.

[00151] Liquid dosage forms for oral administration include, but are not limited to, pharmaceutically acceptable emulsions, microemulsions, solutions, suspensions, syrups and elixirs. In addition to the active compounds, the liquid dosage forms may contain inert diluents commonly used in the art such as, for example, water or other solvents, solubilizing agents and emulsifiers such as ethyl alcohol, isopropyl alcohol, ethyl carbonate, ethyl acetate, benzyl alcohol, benzyl benzoate, propylene glycol, 1,3-butylene glycol, dimethylformamide, oils (in particular, cottonseed, groundnut, corn, germ, olive, castor, and sesame oils), glycerol, tetrahydrofurfuryl alcohol, polyethylene glycols and fatty acid esters of sorbitan, and mixtures thereof. Besides inert diluents, the oral compositions can also include adjuvants such as wetting agents, emulsifying and suspending agents, sweetening, flavoring, and perfuming agents.

[00152] Injectable preparations, for example, sterile injectable aqueous or oleaginous suspensions may be formulated according to the known art using suitable dispersing or wetting agents and suspending agents. The sterile injectable preparation may also be a sterile injectable solution, suspension or emulsion in a nontoxic parenterally acceptable diluent or solvent, for example, as a solution in 1,3-butanediol. Among the acceptable vehicles and solvents that may be employed are water, Ringer's solution, U.S.P. and isotonic sodium chloride solution. In addition, sterile, fixed oils are conventionally employed as a solvent or suspending medium. For this purpose any bland fixed oil can be employed including synthetic mono- or diglycerides. In addition, fatty acids such as oleic acid are used in the preparation of injectables.

[00153] The injectable formulations can be sterilized, for example, by filtration through a bacterial-retaining filter, or by incorporating sterilizing agents in the form of sterile solid compositions which can be dissolved or dispersed in sterile water or other sterile injectable medium prior to use.

[00154] In order to prolong the effect of a compound of the present invention, it is often desirable to slow the absorption of the compound from subcutaneous or intramuscular injection. This may be accomplished by the use of a liquid suspension of crystalline or amorphous material with poor water solubility. The rate of absorption of the compound then depends upon its rate of dissolution that, in turn, may depend upon crystal size and crystalline form. Alternatively, delayed absorption of a parenterally administered compound form is accomplished by dissolving or suspending the compound in an oil vehicle. Injectable depot forms are made by forming microencapsule matrices of the compound in biodegradable polymers such as polylactide-polyglycolide. Depending upon the ratio of compound to polymer and the nature of the particular polymer employed, the rate of compound release can be controlled. Examples of other biodegradable polymers include poly(orthoesters) and poly(anhydrides). Depot injectable formulations are also prepared by entrapping the compound in liposomes or microemulsions that are compatible with body tissues.

[00155] Compositions for rectal or vaginal administration are preferably suppositories which can be prepared by mixing the compounds of this invention with suitable non-irritating excipients or carriers such as cocoa butter, polyethylene glycol or a suppository wax which are solid at ambient temperature but liquid at body temperature and therefore melt in the rectum or vaginal cavity and release the active compound.

[00156] Solid dosage forms for oral administration include capsules, tablets, pills, powders, and granules. In such solid dosage forms, the active compound is mixed with at least one inert, pharmaceutically acceptable excipient or carrier such as sodium citrate or dicalcium phosphate and/or a) fillers or extenders such as starches, lactose, sucrose, glucose, mannitol, and silicic acid, b) binders such as, for example, carboxymethylcellulose, alginates, gelatin, polyvinylpyrrolidone, sucrose, and acacia, c) humectants such as glycerol, d) disintegrating agents such as agar--agar, calcium carbonate, potato or tapioca starch, alginic acid, certain silicates, and sodium carbonate, e) solution retarding agents such as paraffin, f) absorption accelerators such as quaternary ammonium compounds, g) wetting agents such as, for example, cetyl alcohol and glycerol monostearate, h) absorbents such as kaolin and bentonite clay, and i) lubricants such as talc, calcium stearate, magnesium stearate, solid polyethylene glycols, sodium lauryl sulfate, and mixtures thereof. In the case of capsules, tablets and pills, the dosage form may also comprise buffering agents.

[00157] Solid compositions of a similar type may also be employed as fillers in soft and hard-filled gelatin capsules using such excipients as lactose or milk sugar as well as high molecular weight

polyethylene glycols and the like. The solid dosage forms of tablets, dragees, capsules, pills, and granules can be prepared with coatings and shells such as enteric coatings and other coatings well known in the pharmaceutical formulating art. They may optionally contain opacifying agents and can also be of a composition that they release the active ingredient(s) only, or preferentially, in a certain part of the intestinal tract, optionally, in a delayed manner. Examples of embedding compositions that can be used include polymeric substances and waxes. Solid compositions of a similar type may also be employed as fillers in soft and hard-filled gelatin capsules using such excipients as lactose or milk sugar as well as high molecular weight polyethylene glycols and the like.

[00158] The active compounds can also be in micro-encapsulated form with one or more excipients as noted above. The solid dosage forms of tablets, dragees, capsules, pills, and granules can be prepared with coatings and shells such as enteric coatings, release controlling coatings and other coatings well known in the pharmaceutical formulating art. In such solid dosage forms the active compound may be admixed with at least one inert diluent such as sucrose, lactose or starch. Such dosage forms may also comprise, as is normal practice, additional substances other than inert diluents, e.g., tableting lubricants and other tableting aids such as magnesium stearate and microcrystalline cellulose. In the case of capsules, tablets and pills, the dosage forms may also comprise buffering agents. They may optionally contain opacifying agents and can also be of a composition that they release the active ingredient(s) only, or preferentially, in a certain part of the intestinal tract, optionally, in a delayed manner. Examples of embedding compositions that can be used include polymeric substances and waxes.

[00159] Dosage forms for topical or transdermal administration of a compound of this invention include ointments, pastes, creams, lotions, gels, powders, solutions, sprays, inhalants or patches. The active component is admixed under sterile conditions with a pharmaceutically acceptable carrier and any needed preservatives or buffers as may be required. Ophthalmic formulation, ear drops, and eye drops are also contemplated as being within the scope of this invention. Additionally, the present invention contemplates the use of transdermal patches, which have the added advantage of providing controlled delivery of a compound to the body. Such dosage forms can be made by dissolving or dispensing the compound in the proper medium. Absorption enhancers can also be used to increase the flux of the compound across the skin. The rate can be controlled by either providing a rate controlling membrane or by dispersing the compound in a polymer matrix or gel.

[00160] In some embodiments, a compound of formula (I) or a pharmaceutical composition thereof is administered in conjunction with an anticancer agent. As used herein, the term "anticancer agent" refers to any agent that is administered to a subject with cancer for purposes of treating the cancer. Combination therapy includes administration of the therapeutic agents concurrently or sequentially.

Alternatively, the therapeutic agents can be combined into one composition which is administered to the patient.

[00161] Non-limiting examples of DNA damaging chemotherapeutic agents include topoisomerase I inhibitors (e.g., irinotecan, topotecan, camptothecin and analogs or metabolites thereof, and doxorubicin); topoisomerase II inhibitors (e.g., etoposide, teniposide, and daunorubicin); alkylating agents (e.g., melphalan, chlorambucil, busulfan, thiopeta, ifosfamide, carmustine, lomustine, semustine, streptozocin, decarbazine, methotrexate, mitomycin C, and cyclophosphamide); DNA intercalators (e.g., cisplatin, oxaliplatin, and carboplatin); DNA intercalators and free radical generators such as bleomycin; and nucleoside mimetics (e.g., 5-fluorouracil, capecitabine, gemcitabine, fludarabine, cytarabine, mercaptopurine, thioguanine, pentostatin, and hydroxyurea).

[00162] Chemotherapeutic agents that disrupt cell replication include: paclitaxel, docetaxel, and related analogs; vincristine, vinblastin, and related analogs; thalidomide, lenalidomide, and related analogs (e.g., CC-5013 and CC-4047); protein tyrosine kinase inhibitors (e.g., imatinib mesylate and gefitinib); proteasome inhibitors (e.g., bortezomib); NF- κ B inhibitors, including inhibitors of I κ B kinase; antibodies which bind to proteins overexpressed in cancers and thereby downregulate cell replication (e.g., trastuzumab, rituximab, cetuximab, and bevacizumab); and other inhibitors of proteins or enzymes known to be upregulated, over-expressed or activated in cancers, the inhibition of which downregulates cell replication. In certain embodiments, a compound of the invention is administered in conjunction with a proteasome inhibitor.

[00163] Another aspect of the invention relates to inhibiting HDAC6, activity in a biological sample or a patient, which method comprises administering to the patient, or contacting said biological sample with a compound of formula (I), or a composition comprising said compound. The term "biological sample", as used herein, generally includes *in vivo*, *in vitro*, and *ex vivo* materials, and also includes, without limitation, cell cultures or extracts thereof; biopsied material obtained from a mammal or extracts thereof; and blood, saliva, urine, feces, semen, tears, or other body fluids or extracts thereof.

[00164] Still another aspect of this invention is to provide a kit comprising separate containers in a single package, wherein the inventive pharmaceutical compounds, compositions and/or salts thereof are used in combination with pharmaceutically acceptable carriers to treat disorders, symptoms and diseases where HDAC6 plays a role.

EXPERIMENTAL PROCEDURES

I. PREPARATION OF EXEMPLARY COMPOUNDS

[00165] Definitions

ATP

adenosine triphosphate

DCE	dichloroethane
DCM	dichloromethane
DIPEA	diisopropylethyl amine
DMF	<i>N, N</i> -dimethylformamide
DMFDMA	<i>N, N</i> -dimethylformamide dimethyl acetal
DMSO	dimethylsulfoxide
EDCI	<i>N</i> -(3-dimethylaminopropyl)- <i>N'</i> -ethylcarbodiimide hydrochloride
EDTA	ethylenediaminetetraacetic acid
EtOAc	ethyl acetate
EtOH	ethanol
FA	formic acid
FBS	fetal bovine serum
h	hours
HATU	<i>N, N, N', N'</i> -tetramethyl- <i>o</i> -(7-azabenzotriazole-1-yl)uronium hexafluorophosphate
HBTU	<i>o</i> -benzotriazol-1-yl- <i>N, N, N', N'</i> -tetramethyluronium hexafluorophosphate
HEPES	<i>N</i> -(2-Hydroxyethyl)piperazine- <i>N'</i> -(2-ethanesulfonic acid)
HOBT	1-hydroxybenztriazole hydrate
HRMS	high resolution mass spectrum
IPA	isopropyl alcohol
LAH	lithium aluminum hydride
LC-MS	liquid chromatography mass spectrum
<i>m/z</i>	mass to charge
Me	methyl
MEM	minimum essential media
MeOH	methanol
min	minutes
MS	mass spectrum
MWI	microwave irradiation
NMM	<i>N</i> -methyl morpholine
PBS	phosphate buffered saline
rt	room temperature
TEA	triethylamine
TFA	trifluoroacetic acid

TFAA trifluoroacetic anhydride
 THF tetrahydrofuran

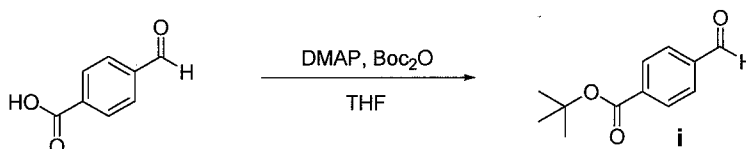
[00166] Analytical Methods

[00167] **NMR:** ^1H NMR spectra are run on a 400 MHz Bruker unless otherwise stated.

[00168] **LCMS:** LC-MS spectra are run using an Agilent 1100 LC interfaced to a micromass Waters® Micromass® Zspray™ Mass Detector (ZMD).

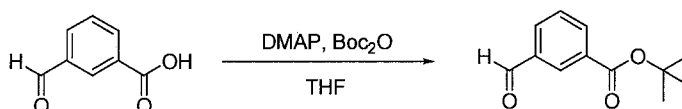
[00169] **HPLC:** Preparative HPLC are conducted using 18x150 mm Sunfire C-18 columns eluting with water-MeCN gradients using a Gilson instrument operated by 322 pumps with the UV/visible 155 detector triggered fraction collection set to between 200 nm and 400 nm. Mass gated fraction collection is conducted on an Agilent 1100 LC/MSD instrument.

Example 1: *tert*-Butyl 4-formylbenzoate

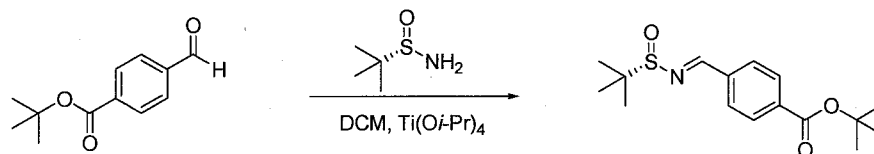


[00170] To a 250-mL round-bottom flask was added 4-formylbenzoic acid (5.0 g, 33 mmol), di-*tert*-butyldicarbonate (14.54 g, 66.6 mmol), *N,N*-dimethylaminopyridine (0.814 g, 6.66 mmol), and THF (100 mL). The mixture was stirred at rt for 16 h. The solvent was then removed to give a solid. To the residue was added EtOAc (150 mL), sat. NaHCO_3 solution (25 mL), and water (25 mL). After separation, the aqueous layer was extracted with EtOAc (2×100 mL). The combined organic phases were washed with brine (50 mL), dried (MgSO_4), and concentrated. Purification via flash chromatography (hexanes to 10% EtOAc-hexanes) afforded *tert*-butyl 4-formylbenzoate (1.90 g, 28%) as a white solid. ^1H NMR (CDCl_3 , 400 MHz) δ 10.10 (s, 1 H), 8.14 (d, $J = 8.3$ Hz, 2 H), 7.93 (d, $J = 8.5$ Hz, 2 H), 1.61 (s, 9 H).

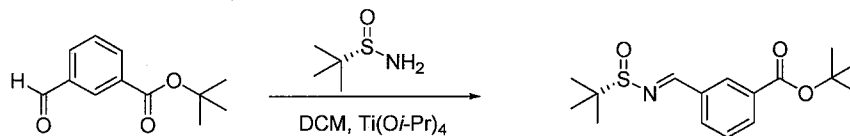
Example 2: *tert*-Butyl 3-formylbenzoate



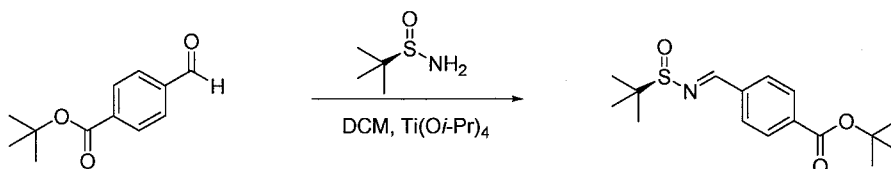
[00171] The title compound was prepared in an analogous fashion to that described in Example 1 starting from commercially available 3-formylbenzoic acid. Yield: 92.4%; ^1H NMR (CDCl_3 , 400 MHz) δ 10.08 (s, 1 H), 8.46 (d, $J = 1.8$ Hz, 1 H), 8.25 (dd, $J = 7.6, 1.5$ Hz, 1 H), 8.05 (dd, $J = 7.6, 1.5$ Hz, 1 H), 7.60 (t, $J = 7.8$ Hz, 1 H), 1.62 (s, 9 H).

Example 3: 4-[(*E*)-{[(*S*)-*tert*-butylsulfinyl]imino}methyl]benzoate

[00172] To a 500-mL round-bottom flask was added (*S*)-(-)-2-methyl-2-propanesulfinamide (1.41 g, 11.6 mmol), *tert*-butyl 4-formylbenzoate (2.00 g, 9.70 mmol) and DCM (90 mL). The mixture was cooled to 0 °C then titanium tetraisopropoxide (17.2 mL, 58.2 mmol) was added. After the solution was warmed to rt and stirred for 6 h, the reaction mixture was diluted with DCM (200 mL). To the flask was added water (17.2 mL) slowly. The mixture was vigorously stirred at rt for 30 min, then filtered through a pad of Celite. The filtrate was concentrated to give a solid. Purification via flash chromatography (hexanes to 10% EtOAc-hexanes) afforded 4-[(*E*)-{[(*S*)-*tert*-butylsulfinyl]imino}methyl]benzoate (2.42 g, 81%) as a white solid. $[\alpha]_D^{20} = +52.0$ ($c = 1.0$, CHCl₃); ¹H NMR (CDCl₃, 400 MHz) δ 8.63 (s, 1 H), 8.08 (d, $J = 8.5$ Hz, 2 H), 7.89 (d, $J = 8.5$ Hz, 2 H), 1.61 (s, 9 H), 1.28 (s, 9 H).

Example 4: 3-[(*E*)-{[(*S*)-*tert*-butylsulfinyl]imino}methyl]benzoate

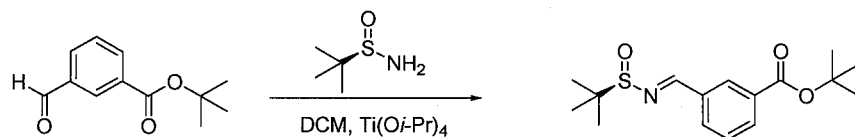
[00173] The title compound was prepared in an analogous fashion to that described in Example 3 starting from *tert*-butyl 3-formylbenzoate. Yield: 83%; ¹H NMR (CDCl₃, 400 MHz) δ 8.63 (s, 1 H), 8.43 (s, 1 H), 8.13 (d, $J = 7.8$ Hz, 1 H), 8.03 (dt, $J = 8.0, 3.0$ Hz, 1 H), 7.54 (t, $J = 7.8$ Hz, 1 H), 1.62 (s, 9 H), 1.28 (s, 9 H).

Example 5: 4-[(*E*)-{[(*R*)-*tert*-butylsulfinyl]imino}methyl]benzoate

[00174] To a 250-mL round-bottom flask was added (*R*)-(+)-2-methyl-2-propanesulfinamide (0.360 g, 2.97 mmol), *tert*-butyl 4-formylbenzoate (0.51 g, 2.47 mmol), DCM (20 mL). The mixture was cooled to 0 °C, then titanium tetraisopropoxide (4.40 mL, 14.8 mmol) was added. The solution was warmed to rt and stirred overnight. After the reaction was diluted with DCM (100 mL), water (4.4 mL) was added slowly. The mixture was vigorously stirred at rt for 30 min, filtered through a pad of Celite. The filtrate

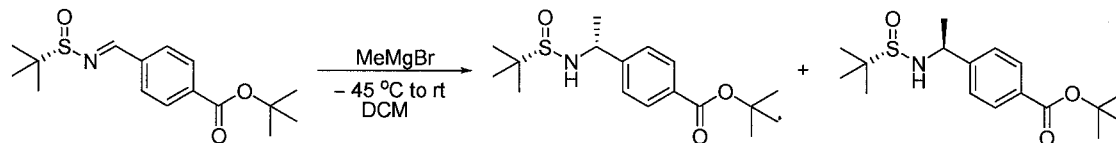
was concentrated to give a solid. Purification via flash chromatography (hexanes to 10% EtOAc-hexanes) afforded 4-[(*E*)-{[(*R*)-*tert*-butylsulfinyl]imino}methyl]benzoate (0.52 g, 68%) as a white solid. $[\alpha]_{\text{D}}^{20} = -49.6$ ($c = 1.0$, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz) δ 8.63 (s, 1 H), 8.08 (d, $J = 8.3$ Hz, 2 H), 7.89 (d, $J = 8.3$ Hz, 2 H), 1.61 (s, 9 H), 1.28 (s, 9 H).

Example 6: 4-[(*E*)-{[(*R*)-*tert*-butylsulfinyl]imino}methyl]benzoate

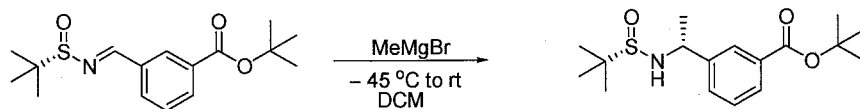


[00175] The title compound was prepared in an analogous fashion to that described in Example 5 starting from *tert*-butyl 3-formylbenzoate. Yield: 83%; $[\alpha]_{\text{D}}^{20} = -83.6$ ($c = 1.0$, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz) δ 8.63 (s, 1 H), 8.43 (s, 1 H), 8.13 (dd, $J = 8.0, 3.0$ Hz, 1 H), 8.03 (d, $J = 7.8$ Hz, 1 H), 7.54 (t, $J = 7.8$ Hz, 1 H), 1.57 (s, 9 H), 1.28 (s, 9 H).

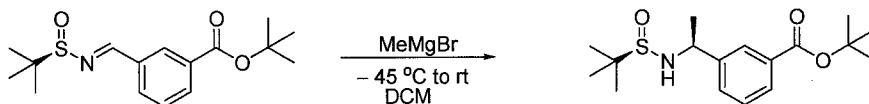
Example 7: *tert*-butyl 4-[(1*R*)-1-{[(*S*)-*tert*-butylsulfinyl]amino}ethyl]benzoate and *tert*-butyl 4-[(1*S*)-1-{[(*S*)-*tert*-butylsulfinyl]amino}ethyl]benzoate



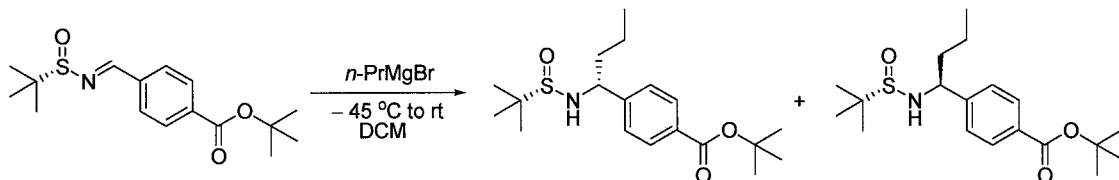
[00176] To an oven-dried 100-mL round-bottom flask was added 4-[(*E*)-{[(*S*)-*tert*-butylsulfinyl]imino} methyl]benzoate (0.83 g, 2.68 mmol), and DCM (13.4 mL). The solution was cooled to $-45\text{ }^{\circ}\text{C}$ then methylmagnesium bromide (1.78 mL, 5.35 mmol, 3.0 M in ether) was slowly added via syringe. The resulting reaction mixture was stirred at $-45\text{ }^{\circ}\text{C}$ for 4 h, then gradually warmed to rt and stirred for 16 h. To the reaction was added DCM (50 mL) and sat. NH_4Cl solution (10 mL). After separation, the aqueous layer was extracted with DCM (2×30 mL). The combined organic layers were washed with brine, dried (MgSO_4), and concentrated. Purification via flash chromatography (20% EtOAc-hexanes to 50% EtOAc-hexanes) afforded major diastereomer *tert*-butyl 4-[(1*R*)-1-{[(*S*)-*tert*-butylsulfinyl]amino}ethyl] benzoate (0.656 g, 75%) as a white solid. $[\alpha]_{\text{D}}^{20} = +86.1$ ($c = 1.0$, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz) δ 7.96 (d, $J = 8.3$ Hz, 2 H), 7.37 (d, $J = 8.3$ Hz, 2 H), 4.62 (m, 1 H), 3.33 (d, $J = 3.0$ Hz, 1 H), 1.58 (s, 9 H), 1.52 (d, $J = 6.8$ Hz, 3 H), 1.20 (s, 9 H). The minor diastereomer *tert*-butyl 4-[(1*S*)-1-{[(*S*)-*tert*-butylsulfinyl]amino}ethyl]benzoate (0.065 g, 7.5%) was isolated as a white solid.

Example 8: *tert*-butyl 3-[(1*R*)-1-[(*S*)-*tert*-butylsulfinyl]amino]ethyl] benzoate

[00177] The title compound was prepared in an analogous fashion to that described in Example 7 starting from 3-[(*E*)-{[(*S*)-*tert*-butylsulfinyl]imino}methyl]benzoate. Yield: 74% $[\alpha]_{\text{D}}^{20} = +90.9$ ($c = 1.0$, CHCl_3); $^1\text{H NMR}$ (CDCl_3 , 400 MHz) δ 7.96 (s, 1 H), 7.89 (d, $J = 7.8$ Hz, 1 H), 7.48 (d, $J = 7.8$, 1 H), 7.38 (t, $J = 7.8$ Hz, 1 H), 4.63 (m, 1 H), 3.35 (d, $J = 3.3$ Hz, 1 H), 1.58 (s, 9 H), 1.54 (d, $J = 6.8$ Hz, 3 H), 1.21 (s, 9 H).

Example 9: *tert*-butyl 3-[(1*S*)-1-[(*R*)-*tert*-butylsulfinyl]amino]ethyl]benzoate

[00178] The title compound was prepared in an analogous fashion to that described in Example 7 starting from 3-[(*E*)-{[(*R*)-*tert*-butylsulfinyl]imino}methyl]benzoate. Yield: 58%; $^1\text{H NMR}$ (CDCl_3 , 400 MHz) δ 7.95 (s, 1 H), 7.89 (d, $J = 7.8$ Hz, 1 H), 7.48 (d, $J = 7.8$ Hz, 1 H), 7.38 (t, $J = 7.8$ Hz, 1 H), 4.63 (m, 1 H), 3.35 (d, $J = 3.3$ Hz, 1 H), 1.58 (s, 9 H), 1.54 (d, $J = 6.8$ Hz, 3 H), 1.21 (s, 9 H).

Example 10: *tert*-butyl 4-[(*R*)-1-[(*S*)-1,1-dimethylethylsulfinamido]butyl]benzoate and *tert*-butyl 4-[(*S*)-1-[(*S*)-1,1-dimethylethylsulfinamido]butyl]benzoate

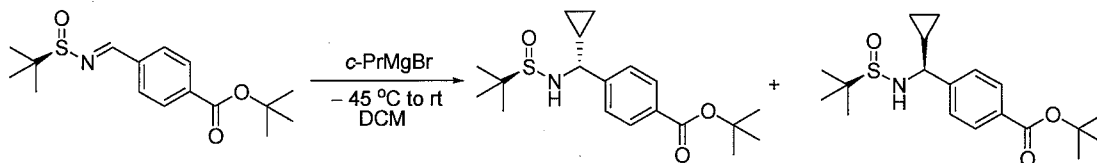
[00179] The title compounds were prepared in an analogous fashion to that described in Example 7 starting from 4-[(*E*)-{[(*S*)-*tert*-butylsulfinyl]imino}methyl]benzoate.

tert-butyl 4-[(*R*)-1-[(*S*)-1,1-dimethylethylsulfinamido]butyl]benzoate Yield: 39%; $[\alpha]_{\text{D}}^{20} = +75.2$ ($c = 1.0$, CHCl_3); $^1\text{H NMR}$ (CDCl_3 , 400 MHz) δ 7.95 (d, $J = 8.1$ Hz, 2 H), 7.34 (d, $J = 8.3$ Hz, 2 H), 4.43 (dt, $J = 7.1, 2.0$ Hz, 1 H), 3.38 (d, $J = 2.0$ Hz, 1 H), 1.77 (m, 2 H), 1.59 (s, 9 H), 1.26 (m, 2 H), 1.17 (s, 9 H), 0.88 (t, $J = 7.4$ Hz, 3 H).

tert-butyl 4-[(*S*)-1-[(*S*)-1,1-dimethylethylsulfinamido]butyl]benzoate Yield: 39%; $[\alpha]_{\text{D}}^{20} = +34.2$ ($c = 1.0$, CHCl_3); $^1\text{H NMR}$ (CDCl_3 , 400 MHz) δ 7.96 (d, $J = 8.4$ Hz, 2 H), 7.36 (d, $J = 8.1$ Hz, 2 H), 4.39 (m, 1 H),

3.37 (d, $J = 4.0$ Hz, 1 H), 2.00 (m, 1 H), 1.71 (m, 1 H), 1.58 (s, 9 H), 1.22 (s, 9 H), 1.17 (m, 2 H), 0.87 (t, $J = 7.4$ Hz, 3 H).

Example 11: *tert*-butyl-4-[(*R*)-{[(*R*)-*tert*-butylsulfinyl]amino}(cyclopropyl)methyl]benzoate and *tert*-butyl 4-[(*S*)-{[(*R*)-*tert*-butylsulfinyl]amino}(cyclopropyl) methyl]benzoate

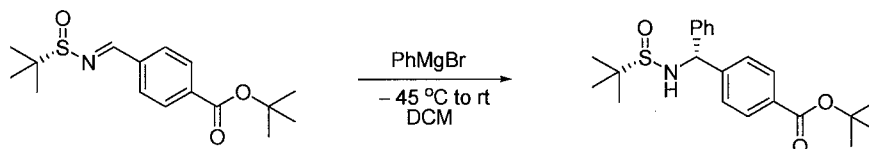


[00180] The title compounds were prepared in an analogous fashion to that described in Example 7 starting from 4-[(*E*)-{[(*R*)-*tert*-butylsulfinyl]imino}methyl]benzoate.

tert-butyl-4-[(*R*)-{[(*R*)-*tert*-butylsulfinyl]amino}(cyclopropyl)methyl]benzoate: Yield: 36%; ^1H NMR (CDCl_3 , 400 MHz) δ 7.97 (d, $J = 8.5$ Hz, 2 H), 7.42 (d, $J = 8.3$ Hz, 2 H), 3.72 (dd, $J = 8.8, 3.3$ Hz, 1 H), 3.54 (d, $J = 3.0$ Hz, 1 H), 1.58 (s, 9 H), 1.24 (s, 9 H), 1.14 (m, 1 H), 0.80 (m, 1 H), 0.64 (m, 1 H), 0.48 (m, 1 H), 0.23 (m, 1 H).

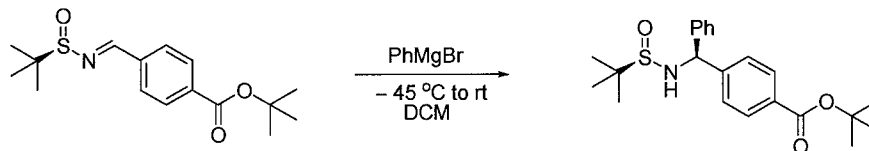
tert-butyl-4-[(*S*)-{[(*R*)-*tert*-butylsulfinyl]amino}(cyclopropyl)methyl]benzoate: Yield: 53%; ^1H NMR (CDCl_3 , 400 MHz) δ 7.96 (d, $J = 8.3$ Hz, 2 H), 7.38 (d, $J = 8.3$ Hz, 2 H), 3.61 (m, 1 H), 3.58 (d, $J = 1.8$ Hz, 1 H), 1.57 (s, 9 H), 1.20 (s, 9 H), 1.17 (m, 1 H), 0.67 (m, 1 H), 0.48 (m, 2 H), 0.38 (m, 1 H).

Example 12: *tert*-butyl 4-[(*R*)-{[(*S*)-*tert*-butylsulfinyl]amino}(phenyl)methyl]benzoate



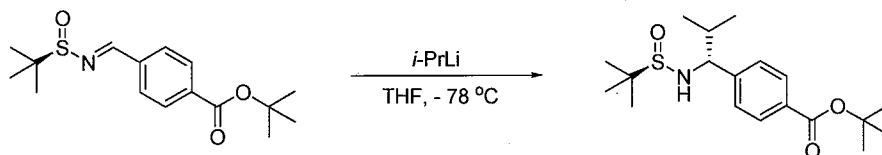
[00181] The title compound (dr, 6.0:1) was prepared in an analogous fashion to that described in Example 7 starting from 4-[(*E*)-{[(*S*)-*tert*-butylsulfinyl]imino}methyl]benzoate. Yield: 84%; ^1H NMR (CDCl_3 , 400 MHz) δ 7.96 (d, $J = 8.3$ Hz, 2 H), 7.48 (d, $J = 8.5$ Hz, 2 H), 7.37-7.27 (m, 5 H), 5.69 (d, $J = 2.3$ Hz, 1 H), 3.71 (d, $J = 2.3$ Hz, 1 H), 1.57 (s, 9 H), 1.27 (s, 9 H).

Example 13: *tert*-butyl 4-[(*S*)-{[(*R*)-*tert*-butylsulfinyl]amino}(phenyl)methyl]benzoate



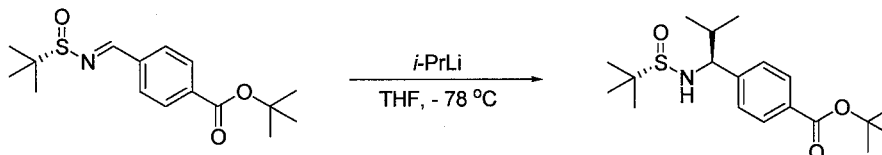
[00182] The title compound (dr, 6.3:1) was prepared in an analogous fashion to that described in Example 7 starting from 4-[(*E*)-{[(*R*)-*tert*-butylsulfinyl]imino}methyl]benzoate. Yield: 75%; ¹H NMR (CDCl₃, 400 MHz) δ 7.96 (d, *J* = 8.5 Hz, 2 H), 7.48 (d, *J* = 8.1 Hz, 2 H), 7.37-7.27 (m, 5 H), 5.69 (d, *J* = 2.3 Hz, 1 H), 3.72 (d, *J* = 2.3 Hz, 1 H), 1.57 (s, 9 H), 1.27 (s, 9 H).

Example 14: *tert*-butyl 4-[(1*R*)-1-{[(*R*)-*tert*-butylsulfinyl]amino}-2-methylpropyl]benzoate



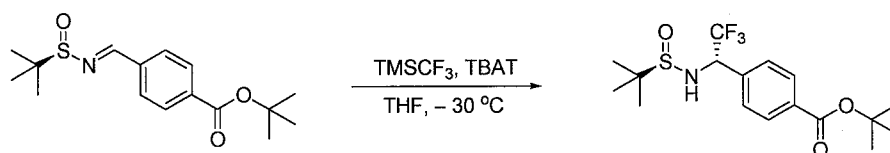
[00183] To an oven-dried 50-mL round-bottom flask was added *tert*-butyl 4-[(*E*)-{[(*R*)-*tert*-butylsulfinyl]imino}methyl]benzoate (3.00 g, 9.70 mmol) and THF (48 mL). The solution was cooled to -78 °C then isopropyllithium (55.4 mL, 38.8 mmol, 0.70 M of in pentane) was slowly added via a syringe pump over 15 min. The resulting reaction mixture was stirred at -78 °C. After 1 h, EtOAc (100 mL), sat. NH₄Cl solution (20 mL), and water (10 mL) were added to the flask at this temperature. After separation, the aqueous layer was extracted with EtOAc (2 × 60 mL). Combined organic layers were washed with brine (20 mL), dried (MgSO₄), and concentrated. Purification via flash chromatography (20% EtOAc-hexanes to 50% EtOAc-hexanes) afforded major diastereomer *tert*-butyl 4-[(1*R*)-1-{[(*R*)-*tert*-butylsulfinyl]amino}-2-methylpropyl]benzoate (1.59 g, 46%) as a white solid. $[\alpha]_D^{20} = -18.9$ (*c* = 1.0, CHCl₃); ¹H NMR (CDCl₃, 300 MHz) δ 7.96 (d, *J* = 8.5 Hz, 2 H), 7.31 (d, *J* = 8.1 Hz, 2 H), 4.18 (d, *J* = 6.0 Hz, 1 H), 3.45 (d, *J* = 6.0 Hz, 1 H), 2.22 (m, 1 H), 1.58 (s, 9 H), 1.24 (s, 9 H), 0.94 (d, *J* = 6.8 Hz, 3 H), 0.80 (d, *J* = 6.8 Hz, 3 H).

Example 15: *tert*-butyl 4-[(1*S*)-1-{[(*S*)-*tert*-butylsulfinyl]amino}-2-methylpropyl]benzoate



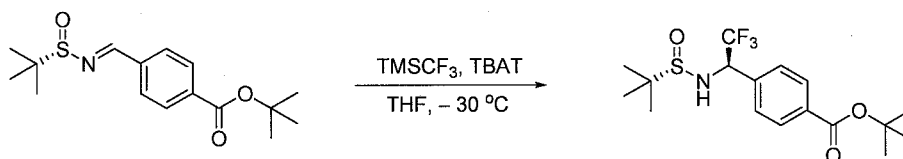
[00184] The title compound was prepared in an analogous fashion to that described in Example 14 starting from 4-[(*E*)-{[(*S*)-*tert*-butylsulfinyl]imino}methyl]benzoate. Yield: 47%; ¹H NMR (CDCl₃, 400 MHz) δ 7.96 (d, *J* = 8.3 Hz, 2 H), 7.31 (d, *J* = 8.3 Hz, 2 H), 4.18 (d, *J* = 6.0 Hz, 1 H), 3.45 (d, *J* = 5.8 Hz, 1 H), 2.22 (m, 1 H), 1.58 (s, 9 H), 1.24 (s, 9 H), 0.94 (d, *J* = 6.8 Hz, 3 H), 0.80 (d, *J* = 6.6 Hz, 3 H).

Example 16: *tert*-butyl 4-[(1*S*)-1-{[(*R*)-*tert*-butylsulfinyl]amino}-2,2,2-trifluoroethyl]benzoate



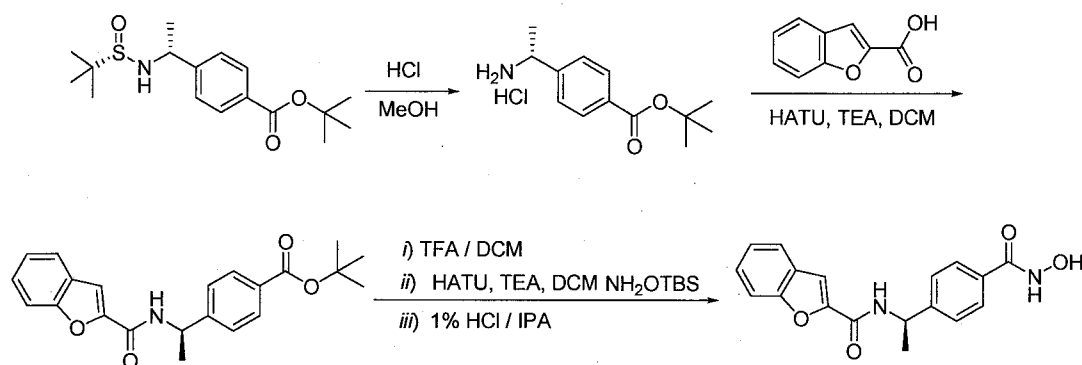
[00185] To a 50-mL oven-dried round-bottom flask charged with *tert*-butyl 4-[(*E*)-{[(*R*)-*tert*-butylsulfinyl]imino}methyl]benzoate (0.16 g, 0.5 mmol), tetra-*n*-butylammoniumdifluorotriphenylsilicate (0.30 g, 0.55 mmol), THF (8 mL) was slowly added (trifluoromethyl)trimethylsilane (0.94 mL, 0.60 mmol) in THF (2 mL) slowly at -45 °C. The mixture was stirred at this temperature for 2 h, then warmed to -30 °C and stirred for 1 h. The reaction was quenched with addition of sat. NH₄Cl (5 mL) and EtOAc (10 mL) at -30 °C. After warming to rt, the mixture was extracted with EtOAc (2 × 20 mL). The combined organic phases were washed with brine (10 mL), dried (MgSO₄), and concentrated. Purification via flash chromatography (10% EtOAc-hexanes to 20% EtOAc-hexanes) afforded *tert*-butyl 4-[(1*S*)-1-{[(*R*)-*tert*-butylsulfinyl]amino}-2,2,2-trifluoroethyl]benzoate (0.136 g, 72%) as a white solid. ¹H NMR (Methanol-*d*₄, 300 MHz) δ 7.98 (d, *J* = 8.5 Hz, 2 H), 7.65 (d, *J* = 8.3 Hz, 2 H), 5.15 (d, *J* = 7.9 Hz, 1 H), 1.59 (s, 9 H), 1.23 (s, 9 H).

Example 17: *tert*-butyl 4-[(1*R*)-1-{[(*S*)-*tert*-butylsulfinyl]amino}-2,2,2-trifluoroethyl]benzoate



[00186] The title compound was prepared in an analogous fashion to that described in Example 16 starting from 4-[(*E*)-{[(*S*)-*tert*-butylsulfinyl]imino}methyl]benzoate. Yield: 47%; [α]_D²⁰ = +49.3 (*c* = 1.0, CHCl₃); ¹H NMR (CDCl₃, 400 MHz) δ 8.03 (d, *J* = 8.3 Hz, 2 H), 7.49 (d, *J* = 8.3 Hz, 2 H), 4.88 (q, *J* = 7.0 Hz, 1 H), 3.67 (d, *J* = 6.5 Hz, 1 H), 1.59 (s, 9 H), 1.25 (s, 9 H).

**Example 18: *N*-((1*R*)-1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-1-benzofuran-2-carboxamide
Compound I-317**



Step 1: *tert*-butyl 4-[(1*R*)-1-aminoethyl]benzoate hydrochloride

[00187] To a 2-dram vial was added *tert*-butyl 4-[(1*R*)-1-[(*S*)-*tert*-butylsulfinyl]amino]ethyl benzoate (0.0586 g, 0.180 mmol), hydrochloric acid (0.14 mL, 0.54 mmol, 4.0 M in 1,4-dioxane), and methanol (2 mL). The mixture was stirred at rt for 2 h. The solvent was then completely removed to give *tert*-butyl 4-[(1*R*)-1-aminoethyl]benzoate hydrochloride as a white solid. LC-MS: (FA) ES+ 222.

Step 2: *tert*-butyl 4-[(1*R*)-1-[(1-benzofuran-2-ylcarbonyl)amino]ethyl]benzoate

[00188] To a 2-dram vial was added triethylamine (0.10 mL, 0.72 mmol), HATU (0.068 g, 0.18 mmol), benzofuran-2-carboxylic acid (0.029 g, 0.18 mmol), and DCM (2 mL). The solution was stirred at rt for 30 min then transferred to another 2-dram vial containing solid *tert*-butyl 4-[(1*R*)-1-aminoethyl]benzoate hydrochloride. The mixture was stirred at rt for 16 h. To the reaction was then added DCM (3 mL) and water (1 mL). After separation, the aqueous layer was extracted with DCM (2 × 3 mL). The combined organic phases were concentrated to dryness to give crude *tert*-butyl 4-[(1*R*)-1-[(1-benzofuran-2-ylcarbonyl)amino]ethyl]benzoate as a brown solid. LC-MS: (FA) ES+ 366.

Step 3: *N*-((1*R*)-1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-1-benzofuran-2-carboxamide

[00189] To a 2-dram vial containing *tert*-butyl 4-[(1*R*)-1-[(1-benzofuran-2-ylcarbonyl)amino]ethyl]benzoate was added DCM (2.5 mL), and trifluoroacetic acid (0.28 mL, 3.60 mmol). The mixture was stirred at rt for 6 h then evaporated to give an oil residue. To the residue was added HATU (0.10 g, 0.27 mmol), triethylamine (0.25 mL, 1.80 mmol), and DCM (2.5 mL). After stirring at rt for 30 min, *O*-(*tert*-butyldimethylsilyl)hydroxylamine (0.053 g, 0.360 mmol) was added. The mixture was stirred at rt for 2 h, then the solvent was completely removed to give a sticky brown oil. To this oil residue was added hydrochloric acid (4.0 mL, 1% v/v in IPA). After stirring at rt for 30 min, the solvent was evaporated to dryness to give a solid. To the solid was then added DMSO (1.1 mL). The solution was filtered and purified by Gilson prep-HPLC [25-50 % MeCN-H₂O] to give *N*-((1*R*)-1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-1-benzofuran-2-carboxamide (0.0148 g, 24%) as a white solid. LC-MS: (FA) ES+ 325; ¹H NMR (Methanol-*d*₄, 400 MHz) δ 7.71 (m, 3 H), 7.60 (d, *J* = 8.5 Hz, 1 H), 7.50

(m, 3 H), 7.45 (t, $J = 7.0$ Hz, 1 H), 7.31 (t, $J = 7.8$ Hz, 1 H), 5.30 (q, $J = 7.2$ Hz, 1 H), 1.61 (d, $J = 7.0$ Hz, 3 H).

Example 19: *N*-((1*R*)-1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-1-methyl-1*H*-pyrrole-2-carboxamide Compound I-102

[00190] The title compound was prepared in an analogous fashion to that described in Example 18 starting from *tert*-butyl 4-[(1*R*)-1-{[(*S*)-*tert*-butylsulfinyl]amino}ethyl] benzoate. Yield: 38%; LC-MS: (FA) ES+ 288; ^1H NMR (Methanol- d_4 , 400 MHz) δ 8.06 (s, 1 H), 7.70 (d, $J = 8.5$ Hz, 2 H), 7.46 (d, $J = 8.5$ Hz, 2 H), 6.86 (dd, $J = 4.0$, 1.8 Hz, 1 H), 6.80 (t, $J = 2.3$ Hz, 1 H), 6.05 (dd, $J = 4.0$, 2.8 Hz, 1 H), 5.17 (q, $J = 7.0$ Hz, 1 H), 3.82 (s, 3 H), 1.52 (d, $J = 7.3$ Hz, 3 H).

Example 20: *N*-((1*R*)-1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-1-benzothiophene-2-carboxamide Compound I-184

[00191] The title compound was prepared in an analogous fashion to that described in Example 18 starting from *tert*-butyl 4-[(1*R*)-1-{[(*S*)-*tert*-butylsulfinyl]amino}ethyl] benzoate. Yield: 38%; LC-MS: (FA) ES+ 341; ^1H NMR (Methanol- d_4 , 400 MHz) δ 8.04 (s, 1 H), 7.88 (m, 2 H), 7.73 (d, $J = 8.0$ Hz, 2 H), 7.50 (d, $J = 8.3$ Hz, 2 H), 7.42 (m, 2 H), 5.26 (q, $J = 7.3$ Hz, 1 H), 1.60 (d, $J = 7.3$ Hz, 3 H).

Example 21: *N*-hydroxy-4-((1*R*)-1-{[(1-methylcyclohexyl)carbonyl]amino}ethyl)benzamide Compound I-26

[00192] The title compound was prepared in an analogous fashion to that described in Example 18 starting from *tert*-butyl 4-[(1*R*)-1-{[(*S*)-*tert*-butylsulfinyl]amino}ethyl] benzoate. Yield: 27%; LC-MS: (FA) ES+ 305; ^1H NMR (Methanol- d_4 , 400 MHz) δ 7.81 (d, $J = 7.8$ Hz, 1 H), 7.69 (d, $J = 8.3$ Hz, 2 H), 7.41 (d, $J = 8.0$ Hz, 2 H), 5.08 (q, $J = 7.3$ Hz, 1 H), 2.02 (m, 2 H), 1.53 (m, 2 H), 1.47 (d, $J = 7.0$ Hz, 3 H), 1.30 (m, 6 H), 1.12 (s, 3 H).

Example 22: *N*-((1*R*)-1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)biphenyl-4-carboxamide Compound I-92

[00193] The title compound was prepared in an analogous fashion to that described in Example 18 starting from *tert*-butyl 4-[(1*R*)-1-{[(*S*)-*tert*-butylsulfinyl]amino}ethyl] benzoate. LC-MS: (FA) ES+ 361.

Example 23: *N*-((1*R*)-1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-3-methyl-1-benzothiophene-2-carboxamide Compound I-12

[00194] The title compound was prepared in an analogous fashion to that described in Example 18 starting from *tert*-butyl 4-[(1*R*)-1-{[(*S*)-*tert*-butylsulfinyl]amino}ethyl] benzoate. LC-MS: (FA) ES+ 355.

Example 24: 4,5-dichloro-*N*-((1*R*)-1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-1-methyl-1*H*-pyrrole-2-carboxamide Compound I-359

[00195] The title compound was prepared in an analogous fashion to that described in Example 18 starting from *tert*-butyl 4-[(1*R*)-1-{[(*S*)-*tert*-butylsulfinyl]amino}ethyl] benzoate. LC-MS: (FA) ES+ 356.

Example 25: *N*-((1*R*)-1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-4-methyl-2-phenyl-4*H*-furo[3,2-*b*]pyrrole-5-carboxamide Compound I-5

[00196] The title compound was prepared in an analogous fashion to that described in Example 18 starting from *tert*-butyl 4-[(1*R*)-1-{[(*S*)-*tert*-butylsulfinyl]amino}ethyl] benzoate. LC-MS: (FA) ES+ 404.

Example 26: *N*-((1*R*)-1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)adamantane-1-carboxamide Compound I-209

[00197] The title compound was prepared in an analogous fashion to that described in Example 18 starting from *tert*-butyl 4-[(1*R*)-1-{[(*S*)-*tert*-butylsulfinyl]amino}ethyl] benzoate. LC-MS: (FA) ES+ 343.

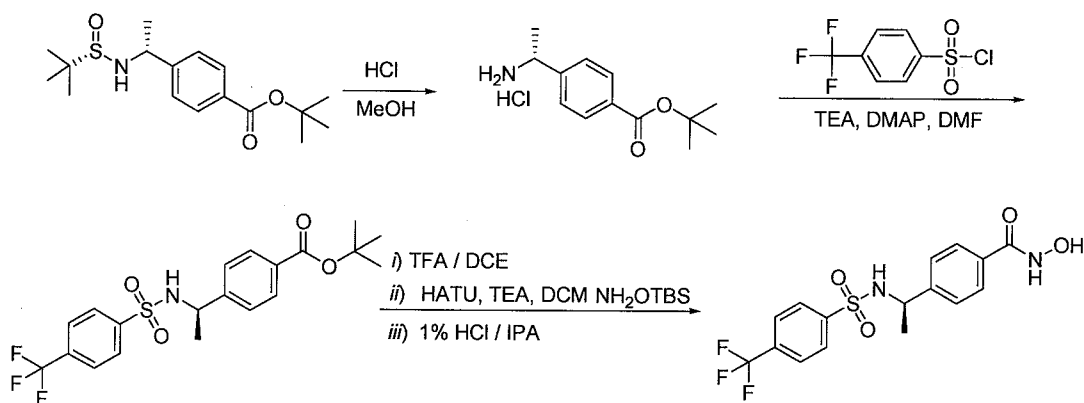
Example 27: *N*-((1*R*)-1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-3-methyl-1-benzofuran-2-carboxamide Compound I-237

[00198] The title compound was prepared in an analogous fashion to that described in Example 18 starting from *tert*-butyl 4-[(1*R*)-1-{[(*S*)-*tert*-butylsulfinyl]amino}ethyl] benzoate. LC-MS: (FA) ES+ 339.

Example 28: *N*-((1*R*)-1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-1-methyl-1*H*-indole-2-carboxamide Compound I-115

[00199] The title compound was prepared in an analogous fashion to that described in Example 18 starting from *tert*-butyl 4-[(1*R*)-1-{[(*S*)-*tert*-butylsulfinyl]amino}ethyl] benzoate. LC-MS: (FA) ES+ 338.

Example 29: *N*-hydroxy-4-[(1*R*)-1-({4-(trifluoromethyl)phenyl}sulfonyl)amino]ethyl]benzamide Compound I-351



Step 1: *tert*-butyl-4-[(1*R*)-1-aminoethyl]benzoate hydrochloride

[00200] To a microwave vial containing *tert*-butyl 4-[(1*R*)-1-[(*S*)-*tert*-butylsulfinyl]amino]ethyl]benzoate (0.052 g, 0.16 mmol) was added hydrochloric acid (0.08 mL, 0.32 mmol, 4.0 M of in 1,4-dioxane), and methanol (2 mL). This mixture was stirred at rt for 2 h, and then evaporated to dryness to afford *tert*-butyl-4-[(1*R*)-1-aminoethyl]benzoate hydrochloride as a white solid. LC-MS: (FA) ES+ 222.

Step 2: (*R*)-*tert*-butyl 4-(1-(4-(trifluoromethyl)phenyl)sulfonamido)ethyl]benzoate

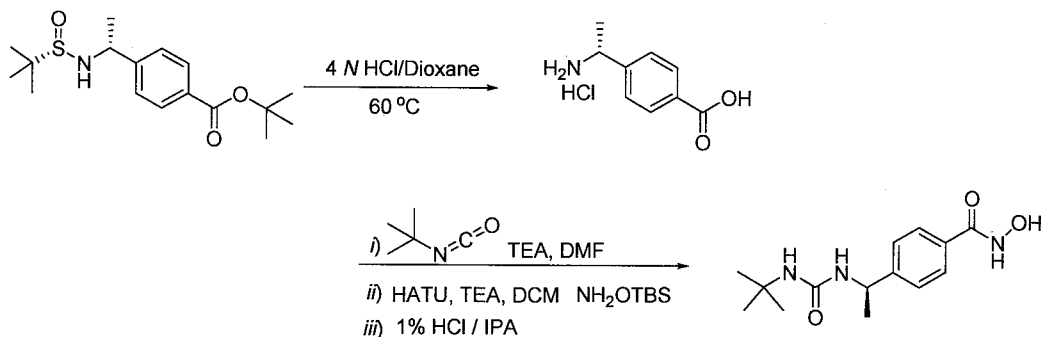
[00201] To a vial containing *tert*-butyl-4-[(1*R*)-1-aminoethyl]benzoate hydrochloride from Step 1 was added *N,N*-dimethylaminopyridine (3.91 mg, 0.032 mmol), 4-(trifluoromethyl)benzenesulfonyl chloride (0.059 g, 0.24 mmol), *N,N*-dimethylformamide (2 mL), and triethylamine (0.18 mL, 1.28 mmol). The mixture was stirred at rt for 16 h, after which the solvent was fully evaporated. To the residue was added 1,2-dichloroethane (3 mL), sat. NaHCO₃ solution (0.5 mL), and water (0.5 mL). After separation, the aqueous layer was extracted with 1,2-dichloroethane (2 × 3 mL). The combined organic phases were evaporated to dryness to give (*R*)-*tert*-butyl 4-(1-(4-(trifluoromethyl)phenyl)sulfonamido)ethyl]benzoate as a brown solid. LC-MS: (FA) ES+ 430.

Step 3: *N*-hydroxy-4-[(1*R*)-1-({4-(trifluoromethyl)phenyl}sulfonyl)amino]ethyl]benzamide

[00202] To a 2-dram vial containing (*R*)-*tert*-butyl 4-(1-(4-(trifluoromethyl)phenyl)sulfonamido)ethyl]benzoate was added 1,2-dichloroethane (2 mL), and trifluoroacetic acid (0.246 mL, 3.20 mmol). After shaking at rt for 4 h, the mixture was evaporated to dryness to give a residue which was azeotroped with toluene (2 × 5 mL). To the solid residue in another vial was added HATU (0.091 g, 0.24 mmol), *N,N*-dimethylformamide (1.5 mL), triethylamine (0.18 mL, 1.28 mmol). The mixture was stirred for 10 min then *O*-(*tert*-butyldimethylsilyl)hydroxylamine (0.047 g, 0.32 mmol) in DCM (0.5 mL) was added. The solution was shaken at rt for 2 h, after which the solvent was then completely removed to afford a brown oil. To this oil in another vial was added hydrochloric acid (3.5 mL, 1% in IPA). After shaking at rt for 30 min, solid NaHCO₃ was added to quench the excess acid, and the solvent was then removed. To the solid residue was added DMSO (1.2 mL). After filtration, the

DMSO solution was purified by Gilson prep-HPLC to give the title compound (0.091 g, 15%) as a white solid. LC-MS: (FA) ES- 387; ^1H NMR (Methanol- d_4 , 400 MHz) δ 7.79 (d, J = 8.3 Hz, 2 H), 7.66 (d, J = 8.3 Hz, 2 H), 7.51 (d, J = 8.5 Hz, 2 H), 7.19 (d, J = 8.5 Hz, 2 H), 4.53 (q, J = 7.0 Hz, 1 H), 1.36 (d, J = 7.0 Hz, 3 H).

Example 30: 4-((1R)-1-(((tert-butylamino)carbonyl)amino)ethyl)-N-hydroxybenzamide Compound I-14



Step 1: (R)-4-(1-aminoethyl)benzoic acid hydrochloride

[00203] To a vial containing *tert*-butyl 4-[(1*R*)-1-[(*S*)-*tert*-butylsulfinyl]amino]ethyl]benzoate (0.065 g, 0.20 mmol) was added hydrochloric acid (2.0 mL, 8.0 mmol, 4.0 M in 1,4-dioxane). This vial was capped and heated at 60 °C for 2 h, and then completely evaporated to afford (R)-4-(1-aminoethyl)benzoic acid hydrochloride as a white solid. LC-MS: (FA) ES+ 166.

Step 2: 4-((1R)-1-(((tert-butylamino)carbonyl)amino)ethyl)-N-hydroxybenzamide

[00204] To the vial containing (R)-4-(1-aminoethyl)benzoic acid hydrochloride was added *tert*-butyl isocyanate (0.023 mL, 0.198 mmol), *N,N* dimethylformamide (3.0 mL), and triethylamine (0.22 mL, 1.59 mmol). After the reaction was stirred at rt for 16 h, HATU (0.075 g, 0.198 mmol) in *N,N*-dimethylformamide (0.5 mL) was added, immediately followed by the addition of *O*-(*tert*-butyldimethylsilyl)hydroxylamine (0.044 g, 0.30 mmol) in DCM (1 mL). This mixture was shaken at rt for 1 hr, after which the mixture was evaporated to dryness. To the residue was added hydrochloric acid (4 mL, 1% in IPA). After shaking at rt for 30 min, solid NaHCO_3 was added to quench the excess acid, and the mixture was evaporated to dryness to give a solid residue. This solid was dissolved in DMSO (1.2 mL), and filtered; then purified via Gilson prep-HPLC [15-38% MeCN- H_2O] to give the title compound (0.026 g, 47%) as a white solid. LC-MS: (FA) ES+ 280; ^1H NMR (Methanol- d_4 , 400 MHz) δ 7.69 (d, J = 8.3 Hz, 2 H), 7.37 (d, J = 8.3 Hz, 2 H), 4.80 (q, J = 7.0 Hz, 1 H), 1.37 (d, J = 7.0 Hz, 3 H), 1.26 (s, 9 H).

Example 31: 4-[(1R)-1-([1-adamantylamino]carbonyl)amino]ethyl-N-hydroxybenzamide**Compound I-374**

[00205] The title compound was prepared in an analogous fashion to that described in Example 30 starting from *tert*-butyl 4-[(1R)-1-[(*S*)-*tert*-butylsulfinyl]amino]ethyl benzoate. LC-MS: (FA) ES+ 358.

Example 32: N-((1S)-1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-1-methyl-1H-pyrrole-2-carboxamide Compound I-25

[00206] The title compound was prepared in an analogous fashion to that described in Example 18 starting from *tert*-butyl 4-[(1S)-1-[(*R*)-*tert*-butylsulfinyl]amino]ethyl benzoate. Yield: 44.8%; LC-MS: (FA) ES+ 288; ¹H NMR (Methanol-*d*₄, 400 MHz) δ 7.70 (d, *J* = 8.3 Hz, 2 H), 7.46 (d, *J* = 8.0 Hz, 2 H), 6.86 (m, 1 H), 6.80 (m, 1 H), 6.05 (dd, *J* = 4.0, 2.7 Hz, 1 H), 5.17 (q, *J* = 7.0 Hz, 1 H), 3.82 (s, 3 H), 1.52 (d, *J* = 7.3 Hz, 3 H).

Example 33: N-((1S)-1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-1-benzothiophene-2-carboxamide Compound I-53

[00207] The title compound was prepared in an analogous fashion to that described in Example 18 starting from *tert*-butyl 4-[(1S)-1-[(*R*)-*tert*-butylsulfinyl]amino]ethyl benzoate. Yield: 42.5%; LC-MS: (FA) ES+ 341; ¹H NMR (Methanol-*d*₄, 400 MHz) δ 8.04 (s, 1 H), 7.88 (m, 2 H), 7.73 (d, *J* = 8.0 Hz, 2 H), 7.50 (d, *J* = 8.3 Hz, 2 H), 7.42 (m, 2 H), 5.26 (q, *J* = 7.3 Hz, 1 H), 1.60 (d, *J* = 7.3 Hz, 3 H).

Example 34: N-hydroxy-4-((1S)-1-[(1-methylcyclohexyl)carbonyl]amino)ethylbenzamide Compound I-273

[00208] The title compound was prepared in an analogous fashion to that described in Example 18 starting from *tert*-butyl 4-[(1S)-1-[(*R*)-*tert*-butylsulfinyl]amino]ethyl benzoate. Yield: 18.2 %; LC-MS: (FA) ES+ 305.

Example 35: N-((1R)-1-{4-[(hydroxyamino)carbonyl]phenyl}butyl)-1-methyl-1H-pyrrole-2-carboxamide Compound I-281

[00209] The title compound was prepared in an analogous fashion to that described in Example 18 starting from *tert*-butyl 4-[(*R*)-1-[(*S*)-1,1-dimethylethylsulfinamido]butyl]benzoate. LC-MS: (FA) ES+ 316.

Example 36: N-((1R)-1-{4-[(hydroxyamino)carbonyl]phenyl}butyl)-1-benzothiophene-2-carboxamide Compound I-299

[00210] The title compound was prepared in an analogous fashion to that described in Example 18 starting from *tert*-butyl 4-((*R*)-1-((*S*)-1,1-dimethylethylsulfinamido)butyl)benzoate. LC-MS: (FA) ES+ 369.

Example 37: 4-((1*R*)-1-[(2,2-dimethylpropanoyl)amino]butyl)-*N*-hydroxybenzamide Compound I-365

[00211] The title compound was prepared in an analogous fashion to that described in Example 18 starting from *tert*-butyl 4-((*R*)-1-((*S*)-1,1-dimethylethylsulfinamido)butyl)benzoate. LC-MS: (FA) ES+ 293; ¹H NMR (Methanol-*d*₄, 400 MHz) δ 7.75 (d, *J* = 8.0 Hz, 1 H), 7.69 (d, *J* = 8.5 Hz, 2 H), 7.39 (d, *J* = 8.3 Hz, 2 H), 4.91 (m, 1 H), 1.85-1.69 (m, 2 H), 1.45-1.27 (m, 2 H), 1.18 (s, 9 H), 0.94 (d, *J* = 7.5 Hz, 3 H).

Example 38: *N*-((1*R*)-1-{4-[(hydroxyamino)carbonyl]phenyl}butyl)-4-methyl-2-phenyl-4*H*-furo[3,2-*b*]pyrrole-5-carboxamide Compound I-222

[00212] The title compound was prepared in an analogous fashion to that described in Example 18 starting from *tert*-butyl 4-((*R*)-1-((*S*)-1,1-dimethylethylsulfinamido)butyl)benzoate. LC-MS: (FA) ES+ 432.

Example 39: *N*-((1*R*)-1-{4-[(hydroxyamino)carbonyl]phenyl}butyl)-3-methyl-1-benzothiophene-2-carboxamide Compound I-62

[00213] The title compound was prepared in an analogous fashion to that described in Example 18 starting from *tert*-butyl 4-((*R*)-1-((*S*)-1,1-dimethylethylsulfinamido)butyl)benzoate. LC-MS: (FA) ES+ 383.

Example 40: *N*-((1*R*)-1-{4-[(hydroxyamino)carbonyl]phenyl}butyl)biphenyl-4-carboxamide Compound I-274

[00214] The title compound was prepared in an analogous fashion to that described in Example 18 starting from *tert*-butyl 4-((*R*)-1-((*S*)-1,1-dimethylethylsulfinamido)butyl)benzoate. LC-MS: (FA) ES+ 389.

Example 41: *N*-((1*R*)-1-{4-[(hydroxyamino)carbonyl]phenyl}butyl)-4-methoxybenzamide Compound I-146

[00215] The title compound was prepared in an analogous fashion to that described in Example 18 starting from *tert*-butyl 4-((*R*)-1-((*S*)-1,1-dimethylethylsulfinamido)butyl)benzoate. LC-MS: (FA) ES+ 343.

Example 42: *N*-((1*R*)-1-{4-[(hydroxyamino)carbonyl]phenyl}butyl)-1-methyl-1*H*-indole-2-carboxamide Compound I-106

[00216] The title compound was prepared in an analogous fashion to that described in Example 18 starting from *tert*-butyl 4-((*R*)-1-((*S*)-1,1-dimethylethylsulfinamido)butyl)benzoate. LC-MS: (FA) ES+ 366.

Example 43: *N*-hydroxy-4-((1*R*)-1-{[(1-methylcyclohexyl)carbonyl]amino}butyl)benzamide Compound I-387

[00217] The title compound was prepared in an analogous fashion to that described in Example 18 starting from *tert*-butyl 4-((*R*)-1-((*S*)-1,1-dimethylethylsulfinamido)butyl)benzoate. LC-MS: (FA) ES+ 333.

Example 44: 4,5-dichloro-*N*-((1*R*)-1-{4-[(hydroxyamino)carbonyl]phenyl}butyl)-1-methyl-1*H*-pyrrole-2-carboxamide Compound I-245

[00218] The title compound was prepared in an analogous fashion to that described in Example 18 starting from *tert*-butyl 4-((*R*)-1-((*S*)-1,1-dimethylethylsulfinamido)butyl)benzoate. LC-MS: (FA) ES+ 384.

Example 45: *N*-((1*R*)-1-{4-[(hydroxyamino)carbonyl]phenyl}butyl)adamantane-1-carboxamide Compound I-15

[00219] The title compound was prepared in an analogous fashion to that described in Example 18 starting from *tert*-butyl 4-((*R*)-1-((*S*)-1,1-dimethylethylsulfinamido)butyl)benzoate. LC-MS: (FA) ES+ 371. ; ¹H NMR (Methanol-*d*₄, 400 MHz) δ 7.68 (d, *J* = 8.3 Hz, 2 H), 7.38 (d, *J* = 8.0 Hz, 2 H), 4.91 (m, 1 H), 2.01 (m, 3 H), 1.87 (m, 6 H), 1.75 (m, 6 H), 1.81-1.71 (m, 2 H), 1.45-1.27 (m, 2 H), 0.94 (d, *J* = 7.5 Hz, 3 H).

Example 46: *N*-((1*R*)-1-{4-[(hydroxyamino)carbonyl]phenyl}butyl)-3-methyl-1-benzofuran-2-carboxamide Compound I-367

[00220] The title compound was prepared in an analogous fashion to that described in Example 18 starting from *tert*-butyl 4-((*R*)-1-((*S*)-1,1-dimethylethylsulfinamido)butyl)benzoate. LC-MS: (FA) ES+ 367.

Example 47: *N*-((1*R*)-1-{4-[(hydroxyamino)carbonyl]phenyl}butyl)-1-benzofuran-2-carboxamide Compound I-79

[00221] The title compound was prepared in an analogous fashion to that described in Example 18 starting from *tert*-butyl 4-((*R*)-1-((*S*)-1,1-dimethylethylsulfinamido)butyl)benzoate. LC-MS: (FA) ES+ 353.

Example 48: *N*-hydroxy-4-[(1*R*)-1-({4-(trifluoromethyl)phenyl}sulfonyl)amino]butyl]benzamide Compound I-171

[00222] The title compound was prepared in an analogous fashion to that described in Example 29 starting from *tert*-butyl 4-((*R*)-1-((*S*)-1,1-dimethylethylsulfinamido)butyl)benzoate. LC-MS: (FA) ES- 415; ¹H NMR (Methanol-*d*₄, 400 MHz) δ 7.72 (d, *J* = 8.7 Hz, 2 H), 7.58 (d, *J* = 8.0 Hz, 2 H), 7.47 (d, *J* = 8.5 Hz, 2 H), 7.11 (d, *J* = 8.3 Hz, 2 H), 4.36 (m, 1 H), 1.71 (m, 1 H), 1.58 (m, 1 H), 1.32 (m, 1 H), 1.21 (m, 1 H), 0.85 (d, *J* = 7.5 Hz, 3 H).

Example 49: 4-((1*R*)-1-({(*tert*-butylamino)carbonyl}amino)butyl)-*N*-hydroxybenzamide Compound I-380

[00223] The title compound was prepared in an analogous fashion to that described in Example 30 starting from *tert*-butyl 4-((*R*)-1-((*S*)-1,1-dimethylethylsulfinamido)butyl)benzoate. LC-MS: (FA) ES+ 308.

Example 50: 4-[(1*R*)-1-({[(1*S*,3*R*,5*R*,7*S*)-1-adamantylamino]carbonyl}amino)butyl]-*N*-hydroxybenzamide Compound I-18

[00224] The title compound was prepared in an analogous fashion to that described in Example 30 starting from *tert*-butyl 4-((*R*)-1-((*S*)-1,1-dimethylethylsulfinamido)butyl)benzoate. LC-MS: (FA) ES+ 386.

Example 51: *N*-((1*R*)-1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)-1-benzothiophene-2-carboxamide Compound I-214

[00225] The title compound was prepared in an analogous fashion to that described in Example 18 starting from *tert*-butyl 4-[(1*R*)-1-{{(*R*)-*tert*-butylsulfinyl}amino}-2-methylpropyl]benzoate. Yield: 17%;

LC-MS: (FA) ES+ 369; ¹H NMR (Methanol-*d*₄, 400 MHz) δ 8.03 (s, 1 H), 7.89 (m, 2 H), 7.73 (d, *J* = 8.3 Hz, 2 H), 7.50 (d, *J* = 8.3 Hz, 2 H), 7.42 (m, 2 H), 4.73 (d, *J* = 10.0 Hz, 1 H), 2.25 (m, 1 H), 1.30 (t, *J* = 7.3 Hz, 1 H), 1.14 (d, *J* = 6.6 Hz, 3 H), 0.81 (d, *J* = 6.8 Hz, 3 H).

Example 52: *N*-((1*R*)-1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)adamantane-1-carboxamide Compound I-328

[00226] The title compound was prepared in an analogous fashion to that described in Example 18 starting from *tert*-butyl 4-[(1*R*)-1-{[(*R*)-*tert*-butylsulfinyl]amino}-2-methylpropyl]benzoate. Yield: 27.4%; LC-MS: (FA) ES+ 371.

Example 53: *N*-((1*R*)-1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)-1*H*-indole-2-carboxamide Compound I-68

[00227] The title compound was prepared in an analogous fashion to that described in Example 18 starting from *tert*-butyl 4-[(1*R*)-1-{[(*R*)-*tert*-butylsulfinyl]amino}-2-methylpropyl]benzoate. Yield: 15.0%; LC-MS: (FA) ES+ 352; ¹H NMR (Methanol-*d*₄, 400 MHz) δ 8.63 (d, *J* = 8.8 Hz, 1 H), 7.72 (d, *J* = 8.3 Hz, 2 H), 7.60 (d, *J* = 8.0 Hz, 1 H), 7.50 (d, *J* = 8.3 Hz, 2 H), 7.41 (d, *J* = 8.0 Hz, 1 H), 7.19 (m, 2 H), 7.04 (t, *J* = 7.3 Hz, 1 H), 4.77 (t, *J* = 9.3 Hz, 1 H), 2.23 (m, 1 H), 1.12 (d, *J* = 6.8 Hz, 3 H), 0.81 (d, *J* = 6.8 Hz, 3 H).

Example 54: *N*-((1*R*)-1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)-3-methyl-1-benzothiophene-2-carboxamide Compound I-307

[00228] The title compound was prepared in an analogous fashion to that described in Example 18 starting from *tert*-butyl 4-[(1*R*)-1-{[(*R*)-*tert*-butylsulfinyl]amino}-2-methylpropyl]benzoate. LC-MS: (FA) ES+ 383.

Example 55: 4-[(1*R*)-1-[(2,2-dimethylpropanoyl)amino]-2-methylpropyl]-*N*-hydroxybenzamide Compound I-287

[00229] The title compound was prepared in an analogous fashion to that described in Example 18 starting from *tert*-butyl 4-[(1*R*)-1-{[(*R*)-*tert*-butylsulfinyl]amino}-2-methylpropyl]benzoate. LC-MS: (FA) ES+ 293.

Example 56: *N*-((1*R*)-1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)-4-methyl-2-phenyl-4*H*-furo[3,2-*b*]pyrrole-5-carboxamide Compound I-332

[00230] The title compound was prepared in an analogous fashion to that described in Example 18 starting from *tert*-butyl 4-[(1*R*)-1-{[(*R*)-*tert*-butylsulfinyl]amino}-2-methylpropyl]benzoate. LC-MS: (FA) ES+ 432.

Example 57: *N*-((1*R*)-1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)-3-methyl-1-benzofuran-2-carboxamide Compound I-187

[00231] The title compound was prepared in an analogous fashion to that described in Example 18 starting from *tert*-butyl 4-[(1*R*)-1-{[(*R*)-*tert*-butylsulfinyl]amino}-2-methylpropyl]benzoate. LC-MS: (FA) ES+ 367.

Example 58: *N*-hydroxy-4-((1*R*)-2-methyl-1-[(1-methylcyclohexyl)carbonyl]amino)propyl)benzamide Compound I-126

[00232] The title compound was prepared in an analogous fashion to that described in Example 18 starting from *tert*-butyl 4-[(1*R*)-1-{[(*R*)-*tert*-butylsulfinyl]amino}-2-methylpropyl]benzoate. LC-MS: (FA) ES+ 333.

Example 59: 4,5-dichloro-*N*-((1*R*)-1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)-1-methyl-1*H*-pyrrole-2-carboxamide Compound I-96

[00233] The title compound was prepared in an analogous fashion to that described in Example 18 starting from *tert*-butyl 4-[(1*R*)-1-{[(*R*)-*tert*-butylsulfinyl]amino}-2-methylpropyl]benzoate. LC-MS: (FA) ES+ 385.

Example 60: *N*-((1*R*)-1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)-1-methyl-1*H*-indole-2-carboxamide Compound I-242

[00234] The title compound was prepared in an analogous fashion to that described in Example 18 starting from *tert*-butyl 4-[(1*R*)-1-{[(*R*)-*tert*-butylsulfinyl]amino}-2-methylpropyl]benzoate. LC-MS: (FA) ES+ 366.

Example 61: *N*-((1*R*)-1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)biphenyl-4-carboxamide Compound I-341

[00235] The title compound was prepared in an analogous fashion to that described in Example 18 starting from *tert*-butyl 4-[(1*R*)-1-{[(*R*)-*tert*-butylsulfinyl]amino}-2-methylpropyl]benzoate. LC-MS: (FA) ES+ 389.

Example 62: *N*-((1*R*)-1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)-4-methoxybenzamide Compound I-19

[00236] The title compound was prepared in an analogous fashion to that described in Example 18 starting from *tert*-butyl 4-[(1*R*)-1-{[(*R*)-*tert*-butylsulfinyl]amino}-2-methylpropyl]benzoate. LC-MS: (FA) ES+ 343.

Example 63: *N*-((1*R*)-1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)-1-methyl-1*H*-pyrrole-2-carboxamide Compound I-65

[00237] The title compound was prepared in an analogous fashion to that described in Example 18 starting from *tert*-butyl 4-[(1*R*)-1-{[(*R*)-*tert*-butylsulfinyl]amino}-2-methylpropyl]benzoate. LC-MS: (FA) ES+ 316.

Example 64: *N*-((1*R*)-1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)-1-benzofuran-2-carboxamide Compound I-22

[00238] The title compound was prepared in an analogous fashion to that described in Example 18 starting from *tert*-butyl 4-[(1*R*)-1-{[(*R*)-*tert*-butylsulfinyl]amino}-2-methylpropyl]benzoate. LC-MS: (FA) ES+ 353.

Example 65: *N*-hydroxy-4-[(1*R*)-2-methyl-1-({4-(trifluoromethyl)phenyl}sulfonyl)amino]propyl]benzamide Compound I-189

[00239] The title compound was prepared in an analogous fashion to that described in Example 29 starting from *tert*-butyl 4-[(1*R*)-1-{[(*R*)-*tert*-butylsulfinyl]amino}-2-methylpropyl]benzoate. LC-MS: (FA) ES- 415; ¹H NMR (Methanol-*d*₄, 400 MHz) δ 7.68 (d, *J* = 8.3 Hz, 2 H), 7.54 (d, *J* = 8.3 Hz, 2 H), 7.45 (d, *J* = 8.5 Hz, 2 H), 7.06 (d, *J* = 8.1 Hz, 2 H), 4.04 (d, *J* = 8.5 Hz, 1 H), 1.89 (m, 1 H), 1.02 (d, *J* = 6.8 Hz, 3 H), 0.69 (d, *J* = 6.8 Hz, 3 H).

Example 66: 4-((1*R*)-1-{[(*tert*-butylamino)carbonyl]amino}-2-methylpropyl)-*N*-hydroxybenzamide Compound I-368

[00240] The title compound was prepared in an analogous fashion to that described in Example 30 starting from *tert*-butyl 4-[(1*R*)-1-{[(*R*)-*tert*-butylsulfinyl]amino}-2-methylpropyl]benzoate. LC-MS: (FA) ES+ 308.

Example 67: 4-[(1*R*)-1-({1-adamantylamino}carbonyl)amino]-2-methylpropyl]-*N*-hydroxybenzamide Compound I-354

[00241] The title compound was prepared in an analogous fashion to that described in Example 30 starting from *tert*-butyl 4-[(1*R*)-1-{[(*R*)-*tert*-butylsulfinyl]amino}-2-methylpropyl]benzoate. LC-MS: (FA) ES+ 386.

Example 68: *N*-((1*S*)-1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)-1-benzothiophene-2-carboxamide Compound I-67

[00242] The title compound was prepared in an analogous fashion to that described in Example 18 starting from *tert*-butyl 4-[(1*S*)-1-{[(*S*)-*tert*-butylsulfinyl]amino}-2-methylpropyl]benzoate. Yield: 25.3%; LC-MS: (FA) ES+ 369; ¹H NMR (Methanol-*d*₄, 400 MHz) δ 8.03 (s, 1 H), 7.89 (m, 2 H), 7.73 (d, *J* = 8.3 Hz, 2 H), 7.50 (d, *J* = 8.3 Hz, 2 H), 7.42 (m, 2 H), 4.73 (d, *J* = 10.0 Hz, 1 H), 2.25 (m, 1 H), 1.30 (t, *J* = 7.3 Hz, 1 H), 1.14 (d, *J* = 6.6 Hz, 3 H), 0.81 (d, *J* = 6.8 Hz, 3 H).

Example 69: *N*-((1*S*)-1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)adamantane-1-carboxamide Compound I-157

[00243] The title compound was prepared in an analogous fashion to that described in Example 18 starting from *tert*-butyl 4-[(1*S*)-1-{[(*S*)-*tert*-butylsulfinyl]amino}-2-methylpropyl]benzoate. Yield: 33.4 %; LC-MS: (FA) ES+ 371.

Example 70: *N*-((1*S*)-1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)-1*H*-indole-2-carboxamide Compound I-279

[00244] The title compound was prepared in an analogous fashion to that described in Example 18 starting from *tert*-butyl 4-[(1*S*)-1-{[(*S*)-*tert*-butylsulfinyl]amino}-2-methylpropyl]benzoate. Yield: 11%; LC-MS: (FA) ES+ 352; ¹H NMR (Methanol-*d*₄, 300 MHz) δ 8.63 (d, *J* = 8.8 Hz, 1 H), 7.72 (d, *J* = 8.3 Hz, 2 H), 7.60 (d, *J* = 8.0 Hz, 1 H), 7.50 (d, *J* = 8.3 Hz, 2 H), 7.41 (d, *J* = 8.0 Hz, 1 H), 7.19 (m, 2 H), 7.04 (t, *J* = 7.3 Hz, 1 H), 4.77 (t, *J* = 9.3 Hz, 1 H), 2.23 (m, 1 H), 1.12 (d, *J* = 6.8 Hz, 3 H), 0.81 (d, *J* = 6.8 Hz, 3 H).

Example 71: *N*-((1*R*)-1-{3-[(hydroxyamino)carbonyl]phenyl}ethyl)-1-methyl-1*H*-indole-2-carboxamide Compound I-330

[00245] The title compound was prepared in an analogous fashion to that described in Example 18 starting from *tert*-butyl 3-[(1*R*)-1-{[(*S*)-*tert*-butylsulfinyl]amino}ethyl]benzoate. Yield: 31.3%; LC-MS: (FA) ES+ 338; ¹H NMR (Methanol-*d*₄, 300 MHz) δ 7.82 (s, 1 H), 7.61 (m, 3 H), 7.42 (m, 2 H), 7.27 (t, *J* = 7.8 Hz, 1 H), 7.11 (s, 1 H), 7.09 (d, *J* = 7.5 Hz, 1 H), 5.25 (q, *J* = 6.8 Hz, 1 H), 3.93 (s, 3 H), 1.59 (d, *J* = 7.0 Hz, 3 H).

Example 72: *N*-((1*R*)-1-{3-[(hydroxyamino)carbonyl]phenyl}ethyl)biphenyl-4-carboxamide**Compound I-121**

[00246] The title compound was prepared in an analogous fashion to that described in Example 18 starting from *tert*-butyl 3-[(1*R*)-1-{[(*S*)-*tert*-butylsulfinyl]amino}ethyl]benzoate. Yield: 43.9%; LC-MS: (FA) ES+ 361; ¹H NMR (Methanol-*d*₄, 400 MHz) δ 7.93 (d, *J* = 8.0 Hz, 2 H), 7.82 (s, 1 H), 7.71 (d, *J* = 8.3 Hz, 2 H), 7.65 (d, *J* = 8.3 Hz, 2 H), 7.61 (t, *J* = 7.3 Hz, 2 H), 7.45 (q, *J* = 7.8 Hz, 2 H), 7.37 (t, *J* = 7.8 Hz, 2 H), 5.29 (q, *J* = 6.8 Hz, 1 H), 1.61 (d, *J* = 7.0 Hz, 3 H).

Example 73: *N*-((1*R*)-1-{3-[(hydroxyamino)carbonyl]phenyl}ethyl)-1-benzothiophene-2-carboxamide Compound I-321

[00247] The title compound was prepared in an analogous fashion to that described in Example 18 starting from *tert*-butyl 3-[(1*R*)-1-{[(*S*)-*tert*-butylsulfinyl]amino}ethyl]benzoate. Yield: 40.9%; LC-MS: (FA) ES+ 341.

Example 74: 3-{(1*R*)-1-[(2,2-dimethylpropanoyl)amino]ethyl}-*N*-hydroxybenzamide Compound I-177

[00248] The title compound was prepared in an analogous fashion to that described in Example 18 starting from *tert*-butyl 3-[(1*R*)-1-{[(*S*)-*tert*-butylsulfinyl]amino}ethyl]benzoate. LC-MS: (FA) ES+ 265.

Example 75: *N*-hydroxy-3-((1*R*)-1-{[(1-methylcyclohexyl)carbonyl]amino}ethyl)benzamide Compound I-283

[00249] The title compound was prepared in an analogous fashion to that described in Example 18 starting from *tert*-butyl 3-[(1*R*)-1-{[(*S*)-*tert*-butylsulfinyl]amino}ethyl]benzoate. LC-MS: (FA) ES+ 305.

Example 76: *N*-((1*R*)-1-{3-[(hydroxyamino)carbonyl]phenyl}ethyl)-3-methyl-1-benzofuran-2-carboxamide Compound I-169

[00250] The title compound was prepared in an analogous fashion to that described in Example 18 starting from *tert*-butyl 3-[(1*R*)-1-{[(*S*)-*tert*-butylsulfinyl]amino}ethyl]benzoate. LC-MS: (FA) ES+ 339.

Example 77: *N*-((1*R*)-1-{3-[(hydroxyamino)carbonyl]phenyl}ethyl)-3-methyl-1-benzothiophene-2-carboxamide Compound I-113

[00251] The title compound was prepared in an analogous fashion to that described in Example 18 starting from *tert*-butyl 3-[(1*R*)-1-{[(*S*)-*tert*-butylsulfinyl]amino}ethyl]benzoate. LC-MS: (FA) ES+ 355.

Example 78: *N*-((1*R*)-1-{3-[(hydroxyamino)carbonyl]phenyl}ethyl)-1-methyl-1*H*-pyrrole-2-carboxamide Compound I-271

[00252] The title compound was prepared in an analogous fashion to that described in Example 18 starting from *tert*-butyl 3-[(1*R*)-1-{[(*S*)-*tert*-butylsulfinyl]amino}ethyl]benzoate. LC-MS: (FA) ES+ 288.

Example 79: *N*-((1*R*)-1-{3-[(hydroxyamino)carbonyl]phenyl}ethyl)-1-benzofuran-2-carboxamide Compound I-201

[00253] The title compound was prepared in an analogous fashion to that described in Example 18 starting from *tert*-butyl 3-[(1*R*)-1-{[(*S*)-*tert*-butylsulfinyl]amino}ethyl]benzoate. LC-MS: (FA) ES+ 325.

Example 80: *N*-((1*R*)-1-{3-[(hydroxyamino)carbonyl]phenyl}ethyl)adamantane-1-carboxamide Compound I-312

[00254] The title compound was prepared in an analogous fashion to that described in Example 18 starting from *tert*-butyl 3-[(1*R*)-1-{[(*S*)-*tert*-butylsulfinyl]amino}ethyl] benzoate. LC-MS: (FA) ES+ 343.

Example 81: *N*-((1*R*)-1-{3-[(hydroxyamino)carbonyl]phenyl}ethyl)-4-methyl-2-phenyl-4*H*-furo[3,2-*b*]pyrrole-5-carboxamide Compound I-16

[00255] The title compound was prepared in an analogous fashion to that described in Example 8 starting from *tert*-butyl 3-[(1*R*)-1-{[(*S*)-*tert*-butylsulfinyl]amino}ethyl] benzoate. LC-MS: (FA) ES+ 404.

Example 82: 4,5-dichloro-*N*-((1*R*)-1-{3-[(hydroxyamino)carbonyl]phenyl}ethyl)-1-methyl-1*H*-pyrrole-2-carboxamide Compound I-301

[00256] The title compound was prepared in an analogous fashion to that described in Example 18 starting from *tert*-butyl 3-[(1*R*)-1-{[(*S*)-*tert*-butylsulfinyl]amino}ethyl] benzoate. LC-MS: (FA) ES+ 356.

Example 83: *N*-hydroxy-3-{(1*R*)-1-[(4-methoxybenzoyl)amino]ethyl}benzamide Compound I-193

[00257] The title compound was prepared in an analogous fashion to that described in Example 18 starting from *tert*-butyl 3-[(1*R*)-1-{[(*S*)-*tert*-butylsulfinyl]amino}ethyl] benzoate. LC-MS: (FA) ES+ 315.

Example 84: *N*-hydroxy-3-[(1*R*)-1-([4-(trifluoromethyl)phenyl]sulfonyl)amino]ethyl]benzamide Compound I-403

[00258] The title compound was prepared in an analogous fashion to that described in Example 29 starting from *tert*-butyl 3-[(1*R*)-1-[[*(S)*-*tert*-butylsulfinyl]amino]-2-methylpropyl]benzoate. LC-MS: (FA) ES- 387.

Example 85: 3-((1*R*)-1-[(*tert*-butylamino)carbonyl]amino)ethyl)-*N*-hydroxybenzamide Compound I-320

[00259] The title compound was prepared in an analogous fashion to that described in Example 30 starting from *tert*-butyl 3-[(1*R*)-1-[[*(S)*-*tert*-butylsulfinyl]amino]-2-methylpropyl]benzoate. LC-MS: (FA) ES+ 280.

Example 86: 3-[(1*R*)-1-[[1-adamantylamino]carbonyl]amino)ethyl]-*N*-hydroxybenzamide Compound I-343

[00260] The title compound was prepared in an analogous fashion to that described in Example 30 starting from *tert*-butyl 3-[(1*R*)-1-[[*(S)*-*tert*-butylsulfinyl]amino]-2-methylpropyl]benzoate. LC-MS: (FA) ES+ 358.

Example 87: *N*-((1*S*)-1-{3-[(hydroxyamino)carbonyl]phenyl}ethyl)-1-methyl-1*H*-indole-2-carboxamide Compound I-294

[00261] The title compound was prepared in an analogous fashion to that described in Example 18 starting from *tert*-butyl 3-[(1*S*)-1-[[*(R)*-*tert*-butylsulfinyl]amino]ethyl] benzoate. Yield: 22.7%; LC-MS: (FA) ES+ 338; ¹H NMR (Methanol-*d*₄, 300 MHz) δ 7.82 (s, 1 H), 7.61 (m, 3 H), 7.42 (m, 2 H), 7.27 (t, *J* = 7.8 Hz, 1 H), 7.11 (s, 1 H), 7.09 (d, *J* = 7.5 Hz, 1 H), 5.25 (q, *J* = 6.8 Hz, 1 H), 3.93 (s, 3 H), 1.59 (d, *J* = 7.0 Hz, 3 H).

Example 88: *N*-((1*S*)-1-{3-[(hydroxyamino)carbonyl]phenyl}ethyl)biphenyl-4-carboxamide Compound I-393

[00262] The title compound was prepared in an analogous fashion to that described in Example 18 starting from *tert*-butyl 3-[(1*S*)-1-[[*(R)*-*tert*-butylsulfinyl]amino]ethyl]benzoate. Yield: 40.4%; LC-MS: (FA) ES+ 361; ¹H NMR (Methanol-*d*₄, 300 MHz) δ 7.93 (d, *J* = 8.0 Hz, 2 H), 7.82 (s, 1 H), 7.71 (d, *J* = 8.3 Hz, 2 H), 7.65 (d, *J* = 8.3 Hz, 2 H), 7.61 (t, *J* = 7.3 Hz, 2 H), 7.45 (q, *J* = 7.8 Hz, 2 H), 7.37 (t, *J* = 7.8 Hz, 2 H), 5.29 (q, *J* = 6.8 Hz, 1 H), 1.61 (d, *J* = 7.0 Hz, 3 H).

Example 89: *N*-((1*S*)-1-{3-[(hydroxyamino)carbonyl]phenyl}ethyl)-1-benzothiophene-2-carboxamide Compound I-240

[00263] The title compound was prepared in an analogous fashion to that described in Example 18 starting from *tert*-butyl 3-[(1*S*)-1-{[(*R*)-*tert*-butylsulfinyl]amino}ethyl]benzoate. Yield: 48.1%; LC-MS: (FA) ES+ 341; ¹H NMR (Methanol-*d*₄, 300 MHz) δ 8.04 (s, 1 H), 7.88 (m, 2 H), 7.82 (s, 1 H), 7.60 (m, 2 H), 7.46-7.38 (m, 3 H), 5.26 (q, *J* = 7.2 Hz, 1 H), 1.61 (d, *J* = 7.2 Hz, 3 H).

Example 90: *N*-((1*S*)-2,2,2-trifluoro-1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)biphenyl-4-carboxamide Compound I-296

[00264] The title compound was prepared in an analogous fashion to that described in Example 18 starting from *tert*-butyl 4-[(1*S*)-1-{[(*R*)-*tert*-butylsulfinyl]amino}-2,2,2-trifluoroethyl]benzoate. LC-MS: (FA) ES- 413; ¹H NMR (DMSO-*d*₆, 400 MHz) δ 11.26 (s, 1 H), 9.59 (d, *J* = 9.5 Hz, 1 H), 9.10 (s, 1 H), 8.01 (d, *J* = 8.5 Hz, 2 H), 7.82-7.75 (m, 4 H), 7.73 (m, 2 H), 7.50 (m, 2 H), 7.41 (m, 1 H), 6.15 (d, *J* = 9.2 Hz, 1 H).

Example 91: *N*-((1*S*)-2,2,2-trifluoro-1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-1-benzofuran-2-carboxamide Compound I-400

[00265] The title compound was prepared in an analogous fashion to that described in Example 18 starting from *tert*-butyl 4-[(1*S*)-1-{[(*R*)-*tert*-butylsulfinyl]amino}-2,2,2-trifluoroethyl]benzoate. LC-MS: (FA) ES- 377.

Example 92: 4,5-dichloro-1-methyl-*N*-((1*S*)-2,2,2-trifluoro-1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-1*H*-pyrrole-2-carboxamide Compound I-108

[00266] The title compound was prepared in an analogous fashion to that described in Example 18 starting from *tert*-butyl 4-[(1*S*)-1-{[(*R*)-*tert*-butylsulfinyl]amino}-2,2,2-trifluoroethyl]benzoate. LC-MS: (FA) ES- 409.

Example 93: 4-methyl-2-phenyl-*N*-((1*S*)-2,2,2-trifluoro-1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-4*H*-furo[3,2-*b*]pyrrole-5-carboxamide Compound I-231

[00267] The title compound was prepared in an analogous fashion to that described in Example 18 starting from *tert*-butyl 4-[(1*S*)-1-{[(*R*)-*tert*-butylsulfinyl]amino}-2,2,2-trifluoroethyl]benzoate. LC-MS: (FA) ES- 456.

Example 94: 4-methoxy-*N*-((1*S*)-2,2,2-trifluoro-1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)benzamide Compound I-122

[00268] The title compound was prepared in an analogous fashion to that described in Example 18 starting from *tert*-butyl 4-[(1*S*)-1-[[*(R)*-*tert*-butylsulfinyl]amino]-2,2,2-trifluoroethyl]benzoate. LC-MS: (FA) ES– 367.

Example 95: 3-methyl-*N*-((1*S*)-2,2,2-trifluoro-1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-1-benzofuran-2-carboxamide Compound I-304

[00269] The title compound was prepared in an analogous fashion to that described in Example 18 starting from *tert*-butyl 4-[(1*S*)-1-[[*(R)*-*tert*-butylsulfinyl]amino]-2,2,2-trifluoroethyl]benzoate. LC-MS: (FA) ES– 391.

Example 96: 4-[(1*R*)-1-[(2,2-dimethylpropanoyl)amino]-2,2,2-trifluoroethyl]-*N*-hydroxybenzamide Compound I-50

[00270] The title compound was prepared in an analogous fashion to that described in Example 18 starting from *tert*-butyl 4-[(1*R*)-1-[[*(S)*-*tert*-butylsulfinyl]amino]-2,2,2-trifluoroethyl]benzoate. LC-MS: (FA) ES– 317.

Example 97: 1-methyl-*N*-((1*R*)-2,2,2-trifluoro-1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-1*H*-pyrrole-2-carboxamide Compound I-119

[00271] The title compound was prepared in an analogous fashion to that described in Example 18 starting from *tert*-butyl 4-[(1*R*)-1-[[*(S)*-*tert*-butylsulfinyl]amino]-2,2,2-trifluoroethyl]benzoate. LC-MS: (FA) ES– 340.

Example 98: 1-methyl-*N*-((1*R*)-2,2,2-trifluoro-1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-1*H*-indole-2-carboxamide Compound I-276

[00272] The title compound was prepared in an analogous fashion to that described in Example 18 starting from *tert*-butyl 4-[(1*R*)-1-[[*(S)*-*tert*-butylsulfinyl]amino]-2,2,2-trifluoroethyl]benzoate. LC-MS: (FA) ES– 390.

Example 99: 4-[(1*R*)-1-[(*tert*-butylamino)carbonyl]amino]-2,2,2-trifluoroethyl)-*N*-hydroxybenzamide Compound I-290

[00273] The title compound was prepared in an analogous fashion to that described in Example 30 starting from *tert*-butyl 4-[(1*R*)-1-[[*(S)*-*tert*-butylsulfinyl]amino]-2,2,2-trifluoroethyl]benzoate. LC-MS: (FA) ES– 332.

Example 100: 4-((1*R*)-1-[[1-(adamantylamino)carbonyl]amino]-2,2,2-trifluoroethyl)-*N*-hydroxybenzamide Compound I-105

[00274] The title compound was prepared in an analogous fashion to that described in Example 30 starting from *tert*-butyl 4-[(1*R*)-1-[[*(S)*-*tert*-butylsulfinyl]amino]-2,2,2-trifluoroethyl]benzoate. LC-MS: (FA) ES- 410.

Example 101: *N*-((*R*)-cyclopropyl{4-[(hydroxyamino)carbonyl]phenyl}methyl)-1-benzothiophene-2-carboxamide Compound I-229

[00275] The title compound was prepared in an analogous fashion to that described in Example 18 starting from *tert*-butyl-4-[(*R*)-{[(*R*)-*tert*-butylsulfinyl]amino}(cyclopropyl)methyl]benzoate. Yield: 26.8%; LC-MS: (FA) ES+ 367.

Example 102: *N*-((*R*)-cyclopropyl{4-[(hydroxyamino)carbonyl]phenyl}methyl)adamantane-1-carboxamide Compound I-46

[00276] The title compound was prepared in an analogous fashion to that described in Example 18 starting from *tert*-butyl-4-[(*R*)-{[(*R*)-*tert*-butylsulfinyl]amino}(cyclopropyl)methyl]benzoate. Yield: 29.6%; LC-MS: (FA) ES+ 369.

Example 103: *N*-((*S*)-cyclopropyl{4-[(hydroxyamino)carbonyl]phenyl}methyl)-1-benzothiophene-2-carboxamide Compound I-249

[00277] The title compound was prepared in an analogous fashion to that described in Example 18 starting from *tert*-butyl-4-[(*S*)-{[(*R*)-*tert*-butylsulfinyl]amino}(cyclopropyl)methyl]benzoate. Yield: 27.8%; LC-MS: (FA) ES+ 367; ¹H NMR (Methanol-*d*₄, 300 MHz) δ 8.06 (s, 1 H), 7.89 (m, 2 H), 7.73 (d, *J* = 8.3 Hz, 2 H), 7.56 (d, *J* = 8.3 Hz, 2 H), 7.42 (m, 2 H), 4.42 (m, 1 H), 1.39 (m, 1 H), 0.68 (d, *J* = 7.7 Hz, 2 H), 0.49 (t, *J* = 4.5 Hz, 2 H).

Example 104: *N*-((*S*)-cyclopropyl{4-[(hydroxyamino)carbonyl]phenyl}methyl)adamantane-1-carboxamide Compound I-322

[00278] The title compound was prepared in an analogous fashion to that described in Example 18 starting from *tert*-butyl-4-[(*S*)-{[(*R*)-*tert*-butylsulfinyl]amino}(cyclopropyl)methyl]benzoate. Yield: 48.1%; LC-MS: (FA) ES+ 369; ¹H NMR (Methanol-*d*₄, 300 MHz) δ 7.69 (d, *J* = 8.3 Hz, 2 H), 7.45 (d, *J* = 8.3 Hz, 2 H), 4.21 (m, 1 H), 2.02 (m, 3 H), 1.89 (m, 6 H), 1.76 (m, 6 H), 1.26 (m, 1 H), 0.61 (d, *J* = 7.9 Hz, 2 H), 0.38 (t, *J* = 4.4 Hz, 2 H)..

Example 105: N-[(R)-{4-[(hydroxyamino)carbonyl]phenyl}(phenyl)methyl]-1-benzothiophene-2-carboxamide Compound I-99

[00279] The title compound (er, 6.0:1) was prepared in an analogous fashion to that described in Example 18 starting from *tert*-butyl 4-[(R)-{[(S)-*tert*-butylsulfinyl]amino}(phenyl)methyl]benzoate. Yield: 32.4%; LC-MS: (FA) ES+ 403.

Example 106: N-[(R)-{4-[(hydroxyamino)carbonyl]phenyl}(phenyl)methyl]adamantane-1-carboxamide Compound I-336

[00280] The title compound (er, 6.0:1) was prepared in an analogous fashion to that described in Example 18 starting from *tert*-butyl 4-[(R)-{[(S)-*tert*-butylsulfinyl]amino}(phenyl)methyl]benzoate. Yield: 57.7%; LC-MS: (FA) ES+ 405.

Example 107: N-[(S)-{4-[(hydroxyamino)carbonyl]phenyl}(phenyl)methyl]-1-benzothiophene-2-carboxamide Compound I-124

[00281] The title compound (er, 6.3:1) was prepared in an analogous fashion to that described in Example 18 starting from *tert*-butyl 4-[(S)-{[(R)-*tert*-butylsulfinyl]amino}(cyclopropyl)methyl]benzoate. Yield: 31.0%; LC-MS: (FA) ES+ 403; ¹H NMR (Methanol-*d*₄, 300 MHz) δ 8.09 (s, 1 H), 7.89 (m, 2 H), 7.74 (d, *J* = 7.9 Hz, 2 H), 7.47-7.25 (m, 9 H), 6.48 (d, *J* = 8.5 Hz, 1 H).

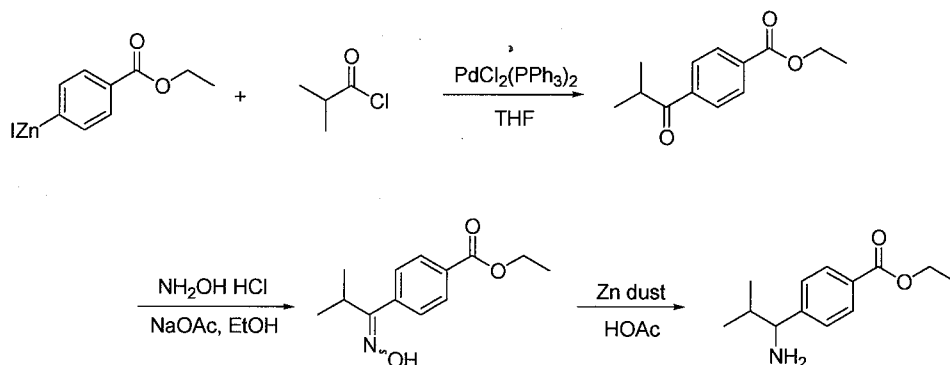
Example 108: N-[(S)-{4-[(hydroxyamino)carbonyl]phenyl}(phenyl)methyl]adamantane-1-carboxamide Compound I-259

[00282] The title compound (er, 6.3:1) was prepared in an analogous fashion to that described in Example 18 starting from *tert*-butyl 4-[(S)-{[(R)-*tert*-butylsulfinyl]amino}(cyclopropyl)methyl]benzoate. Yield: 29.9%; LC-MS: (FA) ES+ 405; ¹H NMR (Methanol-*d*₄, 300 MHz) δ 8.01 (d, *J* = 8.1 Hz, 1 H), 7.70 (d, *J* = 8.3 Hz, 2 H), 7.36-7.18 (m, 6 H), 6.27 (d, *J* = 8.1 Hz, 1 H), 2.01 (m, 3 H), 1.91 (m, 6 H), 1.76 (m, 6 H).

Example 109: 4-[(1R)-1-[(2,2-dimethylpropanoyl)amino]ethyl]-N-hydroxybenzamide Compound I-73

[00283] The title compound was prepared in an analogous fashion to that described in Example 18 starting from *tert*-butyl 4-[(1R)-1-{[(S)-*tert*-butylsulfinyl]amino}ethyl] benzoate. LC-MS: (FA) ES+ 265.

Example 110: ethyl 4-(1-amino-2-methylpropyl)benzoate



Step 1: ethyl 4-isobutyrylbenzoate

[00284] To a 100-mL round-bottom flask was added THF (25 mL). The solvent was bubbled with nitrogen for a few minutes then cooled to 0 °C and added bis(triphenylphosphine)palladium(II) chloride (0.44 g, 0.63 mmol) followed by 4-(ethoxycarbonyl)phenylzinciodide (25.0 mL, 12.5 mmol; 0.50 M in THF). After stirred at 0 °C for 15 min, isobutyryl chloride (1.32 mL, 12.5 mmol) was added and the resulting mixture was stirred at 0 °C for 2 h. The reaction was quenched with slow addition of 1 N HCl and extracted with EtOAc (3 × 100 mL). After separation, combined organic extracts were washed with sat. NaHCO₃, water, brine, dried (MgSO₄), and concentrated. Flash column chromatography (EtOAc:hexanes, 0:1 to 1:9) afforded ethyl 4-isobutyrylbenzoate (2.49 g, 90%) as a slight-brown oil. LC-MS: (FA) ES+ 221; ¹H NMR (CDCl₃, 400 MHz) δ 8.13 (d, *J* = 8.5 Hz, 2 H), 7.99 (d, *J* = 8.5 Hz, 2 H), 4.40 (q, *J* = 7.2 Hz, 2 H), 3.56 (m, 1 H), 1.42 (t, *J* = 7.2 Hz, 3 H), 1.23 (d, *J* = 7.2 Hz, 6 H).

Step 2: ethyl 4-(1-(hydroxyimino)-2-methylpropyl)benzoate

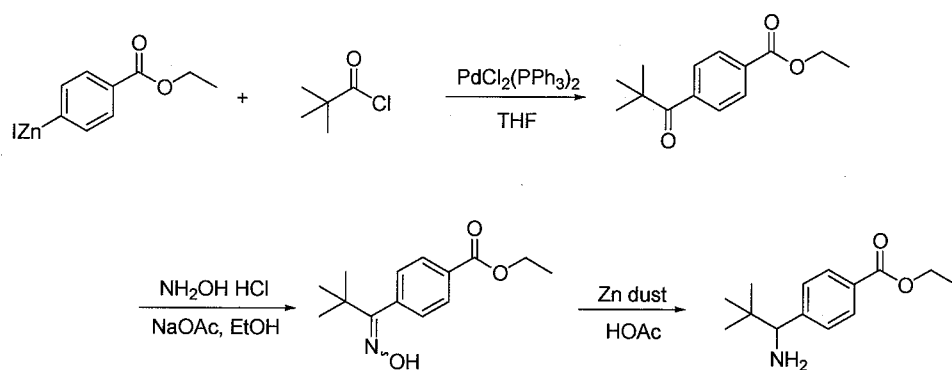
[00285] A mixture of ethyl 4-isobutyrylbenzoate (0.56 g, 2.54 mmol), hydroxylamine hydrochloride (1.06 g, 15.2 mmol), and sodium acetate (1.25 g, 15.2 mmol) in ethanol (36 mL) was heated to 36 °C for 2 h. The reaction was then concentrated and the residue was dissolved in EtOAc (200 mL). The organic phase was washed with water (2 × 20 mL), brine, dried (MgSO₄), and concentrated to give crude ethyl 4-(1-(hydroxyimino)-2-methylpropyl)benzoate as a slight-yellow solid. LC-MS: (FA) ES+ 236.

Step 3: ethyl 4-(1-amino-2-methylpropyl)benzoate

[00286] To the crude ethyl 4-(1-(hydroxyimino)-2-methylpropyl)benzoate in a 100-mL round-bottom flask was added acetic acid (8 mL) and zinc dust (1.33 g, 20.3 mmol). The mixture was stirred at rt for 1 h, then filtered through a pad of Celite. The pad was rinsed with ethanol (50 mL). Combined filtrate was concentrated to give a solid. To the solid residue was added ammonium hydroxide (20 mL) and DCM (50 mL). The solution was stirred at rt for 10 min. After separation, the aqueous layer was extracted with DCM (2 × 50 mL). Combined organic phases were washed with brine, dried (MgSO₄), and concentrated to give an oil. Flash column chromatography (EtOAc:hexanes:TEA, 20:80:2 to 100:0:2) afforded ethyl 4-(1-amino-2-methylpropyl)benzoate (0.563 g, 55%) as a clear oil. LC-MS: (FA) ES+

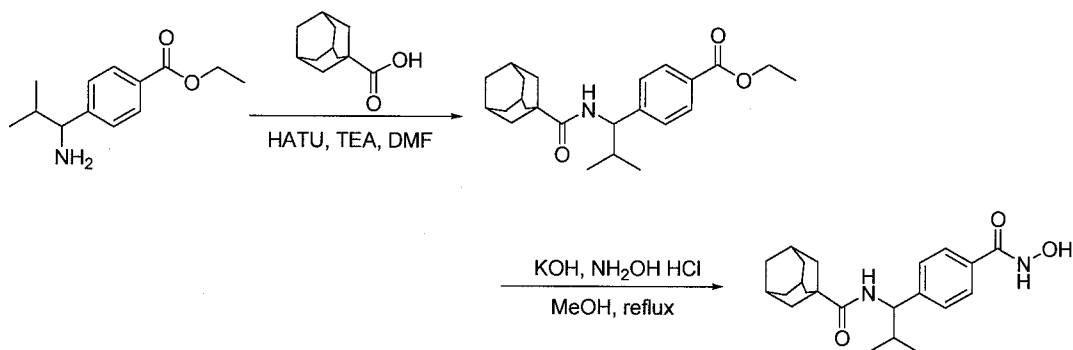
222; ^1H NMR (CDCl_3 , 300 MHz) δ 7.99 (d, $J = 8.3$ Hz, 2 H), 7.36 (d, $J = 8.5$ Hz, 2 H), 4.37 (q, $J = 7.2$ Hz, 2 H), 3.68 (d, $J = 7.0$ Hz, 1 H), 1.86 (m, 1 H), 1.39 (t, $J = 7.0$ Hz, 3 H), 0.96 (d, $J = 7.0$ Hz, 3 H), 0.77 (d, $J = 7.0$ Hz, 3 H).

Example 111: ethyl 4-(1-amino-2,2-dimethylpropyl)benzoate



[00287] The title compound was prepared in an analogous fashion to that described in Example 110 starting from (4-(ethoxycarbonyl)phenyl)zinc(II) iodide and pivaloyl chloride. Yield: 63%; LC-MS: (FA) ES+ 236; ^1H NMR (CDCl_3 , 300 MHz) δ 7.97 (d, $J = 8.3$ Hz, 2 H), 7.37 (d, $J = 8.3$ Hz, 2 H), 4.37 (q, $J = 7.0$ Hz, 2 H), 3.77 (s, 1 H), 1.86 (m, 1 H), 1.39 (t, $J = 7.3$ Hz, 3 H), 0.90 (s, 9 H).

Example 112: N-(1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)adamantane-1-carboxamide Compound I-58



Step 1: ethyl 4-{1-[(adamantan-1-ylcarbonyl)amino]-2-methylpropyl}benzoate

[00288] To a vial charged with 1-adamantanecarboxylic acid (0.031 g, 0.17 mmol) was added HATU (64.6 mg, 0.17 mmol), triethylamine (0.14 mL, 1.02 mmol) and DMF (1 mL). The solution was shaken at rt for 1 h then ethyl 4-(1-amino-2-methylpropyl)benzoate (0.038 g, 0.17 mmol) in DMF (1 mL) was added. The resulting mixture was shaken at rt for 16 h. Solvent was then evaporated. To the residue was added DCE (3 mL) and sat. NaHCO_3 solution (1.5 mL). After separation, the aqueous layer was

extracted with DCE twice. Combined organic layers were concentrated to give crude ethyl 4-{1-[(adamantan-1-ylcarbonyl)amino]-2-methylpropyl}benzoate as a solid.

Step 2: N-(1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)adamantane-1-carboxamide

[00289] To the crude ethyl 4-{1-[(adamantan-1-ylcarbonyl)amino]-2-methylpropyl}benzoate in a vial was added potassium hydroxide (0.11 g, 1.87 mmol), hydroxylamine hydrochloride (0.047 g, 0.68 mmol), and methanol (2 mL). The reaction was capped and heated at 80 °C for 1 h. After cooled to rt, acetic acid (0.097 mL, 1.7 mmol) was added to neutralize the excess base. The solvent was then completely evaporated. To the solid was added DMSO (1.3 mL). The solution was then filtered and purified by prep-HPLC purification to give the title compound (0.009 g, 15%) as a white solid. LC-MS: (FA) ES+ 371.

Example 113: 5-chloro-N-(1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)-1-benzofuran-2-carboxamide Compound I-130

[00290] The title compound was prepared in an analogous fashion to that described in Example 112 starting from ethyl 4-(1-amino-2-methylpropyl)benzoate. LC-MS: (FA) ES+ 387.

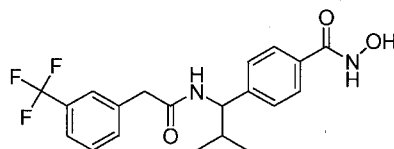
Example 114: N-(1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)pyrazine-2-carboxamide Compound I-203

[00291] The title compound was prepared in an analogous fashion to that described in Example 112 starting from ethyl 4-(1-amino-2-methylpropyl)benzoate. LC-MS: (FA) ES+ 315.

Example 115: N-(1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)-5-methyl-1H-indole-2-carboxamide Compound I-69

[00292] The title compound was prepared in an analogous fashion to that described in Example 112 starting from ethyl 4-(1-amino-2-methylpropyl)benzoate. LC-MS: (FA) ES+ 366.

Example 116: N-hydroxy-4-[2-methyl-1-({3-(trifluoromethyl)phenyl}acetyl)amino]propyl]benzamide Compound I-195



[00293] The title compound was prepared in an analogous fashion to that described in Example 111 starting from ethyl 4-(1-amino-2-methylpropyl)benzoate. LC-MS: (FA) ES- 393.

Example 117: *N*-(1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)quinoxaline-2-carboxamide Compound I-190

[00294] The title compound was prepared in an analogous fashion to that described in Example 112 starting from ethyl 4-(1-amino-2-methylpropyl)benzoate. LC-MS: (FA) ES+ 365.

Example 118: *N*-(1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)-2,1,3-benzothiadiazole-5-carboxamide Compound I-135

[00295] The title compound was prepared in an analogous fashion to that described in Example 112 starting from ethyl 4-(1-amino-2-methylpropyl)benzoate. LC-MS: (FA) ES+ 371.

Example 119: 4'-fluoro-*N*-(1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)biphenyl-4-carboxamide Compound I-143

[00296] The title compound was prepared in an analogous fashion to that described in Example 112 starting from ethyl 4-(1-amino-2-methylpropyl)benzoate. LC-MS: (FA) ES- 405.

Example 120: 2,4,5-trifluoro-*N*-(1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)benzamide Compound I-116

[00297] The title compound was prepared in an analogous fashion to that described in Example 112 starting from ethyl 4-(1-amino-2-methylpropyl)benzoate. LC-MS: (FA) ES- 365.

Example 121: *N*-(1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)-1-benzofuran-2-carboxamide Compound I-32

[00298] The title compound was prepared in an analogous fashion to that described in Example 112 starting from ethyl 4-(1-amino-2-methylpropyl)benzoate. LC-MS: (FA) ES+ 353.

Example 122: *N*-(1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)-4-methyl-2-phenylpyrimidine-5-carboxamide Compound I-17

[00299] The title compound was prepared in an analogous fashion to that described in Example 112 starting from ethyl 4-(1-amino-2-methylpropyl)benzoate. LC-MS: (FA) ES+ 405.

Example 123: *N*-(1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)cycloheptanecarboxamide Compound I-382

[00300] The title compound was prepared in an analogous fashion to that described in Example 112 starting from ethyl 4-(1-amino-2-methylpropyl)benzoate. LC-MS: (FA) ES+ 333.

Example 124: *N*-(1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)-1,3-benzothiazole-6-carboxamide Compound I-43

[00301] The title compound was prepared in an analogous fashion to that described in Example 112 starting from ethyl 4-(1-amino-2-methylpropyl)benzoate. LC-MS: (FA) ES+ 370.

Example 125: *N*-(1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)-3,5-dimethylisoxazole-4-carboxamide Compound I-238

[00302] The title compound was prepared in an analogous fashion to that described in Example 112 starting from ethyl 4-(1-amino-2-methylpropyl)benzoate. LC-MS: (FA) ES+ 332.

Example 126: *N*-(1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)-1,3-benzothiazole-2-carboxamide Compound I-191

[00303] The title compound was prepared in an analogous fashion to that described in Example 112 starting from ethyl 4-(1-amino-2-methylpropyl)benzoate. LC-MS: (FA) ES+ 370.

Example 127: *N*-(1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)-1-naphthamide Compound I-331

[00304] The title compound was prepared in an analogous fashion to that described in Example 112 starting from ethyl 4-(1-amino-2-methylpropyl)benzoate. LC-MS: (FA) ES+ 363.

Example 128: *N*-hydroxy-4-(2-methyl-1-[(5-methyl-2-phenyl-1,3-oxazol-4-yl)acetyl]amino)propyl)benzamide Compound I-48

[00305] The title compound was prepared in an analogous fashion to that described in Example 112 starting from ethyl 4-(1-amino-2-methylpropyl)benzoate. LC-MS: (FA) ES+ 408.

Example 129: 4-[1-({1-(4-chlorophenyl)cyclopropyl}carbonyl)amino]-2-methylpropyl]-*N*-hydroxybenzamide Compound I-300

[00306] The title compound was prepared in an analogous fashion to that described in Example 112 starting from ethyl 4-(1-amino-2-methylpropyl)benzoate. LC-MS: (FA) ES+ 387.

Example 130: *N*-(1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)thiophene-2-carboxamide Compound I-112

[00307] The title compound was prepared in an analogous fashion to that described in Example 112 starting from ethyl 4-(1-amino-2-methylpropyl)benzoate. LC-MS: (FA) ES+ 319.

Example 131: 5-chloro-*N*-(1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)-1*H*-indole-2-carboxamide Compound I-247

[00308] The title compound was prepared in an analogous fashion to that described in Example 112 starting from ethyl 4-(1-amino-2-methylpropyl)benzoate. LC-MS: (FA) ES+ 386.

Example 132: *N*-(1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)-1-benzofuran-5-carboxamide Compound I-194

[00309] The title compound was prepared in an analogous fashion to that described in Example 112 starting from ethyl 4-(1-amino-2-methylpropyl)benzoate. LC-MS: (FA) ES+ 353.

Example 133: 4-{1-[(cyclohexylcarbonyl)amino]-2-methylpropyl}-*N*-hydroxybenzamide Compound I-344

[00310] The title compound was prepared in an analogous fashion to that described in Example 112 starting from ethyl 4-(1-amino-2-methylpropyl)benzoate. LC-MS: (FA) ES+ 319.

Example 134: *N*-(1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)quinoline-4-carboxamide Compound I-246

[00311] The title compound was prepared in an analogous fashion to that described in Example 112 starting from ethyl 4-(1-amino-2-methylpropyl)benzoate. LC-MS: (FA) ES+ 364.

Example 135: *N*-(1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)biphenyl-4-carboxamide Compound I-11

[00312] The title compound was prepared in an analogous fashion to that described in Example 112 starting from ethyl 4-(1-amino-2-methylpropyl)benzoate. LC-MS: (FA) ES+ 389.

Example 136: *N*-(1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)-2,5-bis(trifluoromethyl)benzamide Compound I-155

[00313] The title compound was prepared in an analogous fashion to that described in Example 112 starting from ethyl 4-(1-amino-2-methylpropyl)benzoate. LC-MS: (FA) ES- 447.

Example 137: *N*-(1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)-7-methoxy-1-benzofuran-2-carboxamide Compound I-306

[00314] The title compound was prepared in an analogous fashion to that described in Example 112 starting from ethyl 4-(1-amino-2-methylpropyl)benzoate. LC-MS: (FA) ES+ 383.

Example 138: *N*-(1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)-3,5-bis(trifluoromethyl)benzamide Compound I-173

[00315] The title compound was prepared in an analogous fashion to that described in Example 112 starting from ethyl 4-(1-amino-2-methylpropyl)benzoate. LC-MS: (FA) ES- 447.

Example 139: 4-{1-[(diphenylacetyl)amino]-2-methylpropyl}-*N*-hydroxybenzamide Compound I-204

[00316] The title compound was prepared in an analogous fashion to that described in Example 112 starting from ethyl 4-(1-amino-2-methylpropyl)benzoate. LC-MS: (FA) ES+ 403.

Example 140: 4-*tert*-butyl-*N*-(1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)benzamide Compound I-192

[00317] The title compound was prepared in an analogous fashion to that described in Example 112 starting from ethyl 4-(1-amino-2-methylpropyl)benzoate. LC-MS: (FA) ES+ 369.

Example 141: 3,5-bis(acetylamino)-*N*-(1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)benzamide Compound I-282

[00318] The title compound was prepared in an analogous fashion to that described in Example 112 starting from ethyl 4-(1-amino-2-methylpropyl)benzoate. LC-MS: (FA) ES+ 427.

Example 142: *N*-hydroxy-4-{2-methyl-1-[(3-methyl-2-phenylbutanoyl)amino]propyl}benzamide Compound I-289

[00319] The title compound was prepared in an analogous fashion to that described in Example 112 starting from ethyl 4-(1-amino-2-methylpropyl)benzoate. LC-MS: (FA) ES+ 369.

Example 143: *N*-(1-(4-(hydroxycarbamoyl)phenyl)-2-methylpropyl)-2,5-dimethylfuran-3-carboxamide Compound I-252

[00320] The title compound was prepared in an analogous fashion to that described in Example 112 starting from ethyl 4-(1-amino-2-methylpropyl)benzoate. LC-MS: (FA) ES+ 331.

Example 144: *N*-hydroxy-4-(2-methyl-1-(2-(2,4,7-trimethyl-1*H*-indol-3-yl)acetamido)propyl)benzamide Compound I-220

[00321] The title compound was prepared in an analogous fashion to that described in Example 112 starting from ethyl 4-(1-amino-2-methylpropyl)benzoate. LC-MS: (FA) ES+ 408.

Example 145: *N*-hydroxy-4-(1-(4-methoxybenzamido)-2-methylpropyl)benzamide Compound I-346

[00322] The title compound was prepared in an analogous fashion to that described in Example 112 starting from ethyl 4-(1-amino-2-methylpropyl)benzoate. LC-MS: (FA) ES+ 343.

Example 146: *N*-(1-(4-(hydroxycarbamoyl)phenyl)-2-methylpropyl)-2-methyl-4-(trifluoromethyl)thiazole-5-carboxamide Compound I-139

[00323] The title compound was prepared in an analogous fashion to that described in Example 112 starting from ethyl 4-(1-amino-2-methylpropyl)benzoate. LC-MS: (FA) ES- 400.

Example 147: *N*-(1-(4-(hydroxycarbamoyl)phenyl)-2-methylpropyl)-2-phenylthiazole-4-carboxamide Compound I-172

[00324] The title compound was prepared in an analogous fashion to that described in Example 112 starting from ethyl 4-(1-amino-2-methylpropyl)benzoate. LC-MS: (FA) ES+ 396.

Example 148: 1-benzyl-3-*tert*-butyl-*N*-(1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)-1*H*-pyrazole-5-carboxamide Compound I-77

[00325] The title compound was prepared in an analogous fashion to that described in Example 112 starting from ethyl 4-(1-amino-2-methylpropyl)benzoate. LC-MS: (FA) ES+ 449.

Example 149: *N*-hydroxy-4-{1-[(mesitylacetyl)amino]-2-methylpropyl}benzamide Compound I-28

[00326] The title compound was prepared in an analogous fashion to that described in Example 112 starting from ethyl 4-(1-amino-2-methylpropyl)benzoate. LC-MS: (FA) ES+ 369.

Example 150: *N*-(1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)-2-oxo-6-phenyl-1,2-dihydropyridine-3-carboxamide Compound I-375

[00327] The title compound was prepared in an analogous fashion to that described in Example 112 starting from ethyl 4-(1-amino-2-methylpropyl)benzoate. LC-MS: (FA) ES+ 406.

Example 151: *N*-(1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)-1-methyl-1*H*-pyrazole-3-carboxamide Compound I-389

[00328] The title compound was prepared in an analogous fashion to that described in Example 112 starting from ethyl 4-(1-amino-2-methylpropyl)benzoate. LC-MS: (FA) ES+ 317.

Example 152: 4-[1-({[3,5-bis(trifluoromethyl)phenyl]acetyl}amino)-2-methylpropyl]-*N*-hydroxybenzamide Compound I-250

[00329] The title compound was prepared in an analogous fashion to that described in Example 112 starting from ethyl 4-(1-amino-2-methylpropyl)benzoate. LC-MS: (FA) ES+ 461.

Example 153: *N*-(1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)-1-benzothiophene-2-carboxamide Compound I-94

[00330] The title compound was prepared in an analogous fashion to that described in Example 112 starting from ethyl 4-(1-amino-2-methylpropyl)benzoate. LC-MS: (FA) ES+ 369.

Example 154: 4-{1-[(cyclopentylcarbonyl)amino]-2-methylpropyl}-*N*-hydroxybenzamide Compound I-255

[00331] The title compound was prepared in an analogous fashion to that described in Example 112 starting from ethyl 4-(1-amino-2-methylpropyl)benzoate. LC-MS: (FA) ES+ 305.

Example 155: *N*-hydroxy-4-(2-methyl-1-{{(1-phenylcyclopentyl)carbonyl}amino}propyl)benzamide Compound I-258

[00332] The title compound was prepared in an analogous fashion to that described in Example 112 starting from ethyl 4-(1-amino-2-methylpropyl)benzoate. LC-MS: (FA) ES+ 381.

Example 156: *N*-hydroxy-4-(2-methyl-1-{{(2-methyl-1*H*-indol-3-yl)acetyl}amino}propyl)benzamide Compound I-174

[00333] The title compound was prepared in an analogous fashion to that described in Example 112 starting from ethyl 4-(1-amino-2-methylpropyl)benzoate. LC-MS: (FA) ES+ 380.

Example 157: 4-(1-{{(5-chloro-1-benzothien-3-yl)acetyl}amino}-2-methylpropyl)-*N*-hydroxybenzamide Compound I-206

[00334] The title compound was prepared in an analogous fashion to that described in Example 112 starting from ethyl 4-(1-amino-2-methylpropyl)benzoate. LC-MS: (FA) ES+ 417.

Example 158: 4-fluoro-*N*-(1-{4-[(hydroxyamino)carbonyl]phenyl}-2-methylpropyl)benzamide Compound I-40

[00335] The title compound was prepared in an analogous fashion to that described in Example 112 starting from ethyl 4-(1-amino-2-methylpropyl)benzoate. LC-MS: (FA) ES- 329.

Example 159: *N*-(1-{4-[(hydroxyamino)carbonyl]phenyl}-2,2-dimethylpropyl)adamantane-1-carboxamide Compound I-162

[00336] The title compound was prepared in an analogous fashion to that described in Example 112 starting from ethyl 4-(1-amino-2,2-dimethylpropyl)benzoate. LC-MS: (FA) ES+ 385.

Example 160: *N*-(1-{4-[(hydroxyamino)carbonyl]phenyl}-2,2-dimethylpropyl)-1-methyl-1H-pyrazole-3-carboxamide Compound I-66

[00337] The title compound was prepared in an analogous fashion to that described in Example 112 starting from ethyl 4-(1-amino-2,2-dimethylpropyl)benzoate. LC-MS: (FA) ES+ 331.

Example 161: *N*-(1-{4-[(hydroxyamino)carbonyl]phenyl}-2,2-dimethylpropyl)-1-benzothiophene-2-carboxamide Compound I-308

[00338] The title compound was prepared in an analogous fashion to that described in Example 112 starting from ethyl 4-(1-amino-2,2-dimethylpropyl)benzoate. LC-MS: (FA) ES+ 383.

Example 162: 4-(1-{[(5-chloro-1-benzothien-3-yl)acetyl]amino}-2,2-dimethylpropyl)-*N*-hydroxybenzamide Compound I-345

[00339] The title compound was prepared in an analogous fashion to that described in Example 112 starting from ethyl 4-(1-amino-2,2-dimethylpropyl)benzoate. LC-MS: (FA) ES+ 431.

Example 163: 5-chloro-*N*-(1-{4-[(hydroxyamino)carbonyl]phenyl}-2,2-dimethylpropyl)-1-benzofuran-2-carboxamide Compound I-270

[00340] The title compound was prepared in an analogous fashion to that described in Example 112 starting from ethyl 4-(1-amino-2,2-dimethylpropyl)benzoate. LC-MS: (FA) ES+ 401.

Example 164: *N*-(1-{4-[(hydroxyamino)carbonyl]phenyl}-2,2-dimethylpropyl)-4-methoxybenzamide Compound I-352

[00341] The title compound was prepared in an analogous fashion to that described in Example 112 starting from ethyl 4-(1-amino-2,2-dimethylpropyl)benzoate. LC-MS: (FA) ES+ 357.

Example 165: 4-(2,2-dimethyl-1-[[4-(trifluoromethyl)benzoyl]amino]propyl)-*N*-hydroxybenzamide Compound I-303

[00342] The title compound was prepared in an analogous fashion to that described in Example 112 starting from ethyl 4-(1-amino-2,2-dimethylpropyl)benzoate. LC-MS: (FA) ES- 393.

Example 166: 3-ethyl-*N*-(1-{4-[(hydroxyamino)carbonyl]phenyl}-2,2-dimethylpropyl)-1-methyl-1*H*-pyrazole-5-carboxamide Compound I-318

[00343] The title compound was prepared in an analogous fashion to that described in Example 112 starting from ethyl 4-(1-amino-2,2-dimethylpropyl)benzoate. LC-MS: (FA) ES+ 359.

Example 167: *N*-(1-{4-[(hydroxyamino)carbonyl]phenyl}-2,2-dimethylpropyl)-1-methyl-1*H*-pyrrole-2-carboxamide Compound I-133

[00344] The title compound was prepared in an analogous fashion to that described in Example 112 starting from ethyl 4-(1-amino-2,2-dimethylpropyl)benzoate. LC-MS: (FA) ES+ 330.

Example 168: *N*-(1-{4-[(hydroxyamino)carbonyl]phenyl}-2,2-dimethylpropyl)-1,3-dimethyl-1*H*-pyrazole-4-carboxamide Compound I-86

[00345] The title compound was prepared in an analogous fashion to that described in Example 112 starting from ethyl 4-(1-amino-2,2-dimethylpropyl)benzoate. LC-MS: (FA) ES+ 345.

Example 169: 4-[1-([1-(4-chlorophenyl)cyclopropyl]carbonyl)amino]-2,2-dimethylpropyl]-*N*-hydroxybenzamide Compound I-41

[00346] The title compound was prepared in an analogous fashion to that described in Example 112 starting from ethyl 4-(1-amino-2,2-dimethylpropyl)benzoate. LC-MS: (FA) ES+ 401.

Example 170: *N*-(1-{4-[(hydroxyamino)carbonyl]phenyl}-2,2-dimethylpropyl)-3,5-dimethyl-1*H*-pyrrole-2-carboxamide Compound I-262

[00347] The title compound was prepared in an analogous fashion to that described in Example 112 starting from ethyl 4-(1-amino-2,2-dimethylpropyl)benzoate. LC-MS: (FA) ES+ 344.

Example 171: *N*-(1-{4-[(hydroxyamino)carbonyl]phenyl}-2,2-dimethylpropyl)-1-methyl-1*H*-indole-2-carboxamide Compound I-364

[00348] The title compound was prepared in an analogous fashion to that described in Example 112 starting from ethyl 4-(1-amino-2,2-dimethylpropyl)benzoate. LC-MS: (FA) ES+ 385.

Example 172: *N*-(1-{4-[(hydroxyamino)carbonyl]phenyl}-2,2-dimethylpropyl)pyrazine-2-carboxamide Compound I-87

[00349] The title compound was prepared in an analogous fashion to that described in Example 112 starting from ethyl 4-(1-amino-2,2-dimethylpropyl)benzoate. LC-MS: (FA) ES+ 329.

Example 173: *N*-(1-{4-[(hydroxyamino)carbonyl]phenyl}-2,2-dimethylpropyl)-2-methyl-4,5,6,7-tetrahydro-2*H*-indazole-3-carboxamide Compound I-211

[00350] The title compound was prepared in an analogous fashion to that described in Example 112 starting from ethyl 4-(1-amino-2,2-dimethylpropyl)benzoate. LC-MS: (FA) ES+ 385.

Example 174: *N*-(1-(4-(hydroxycarbamoyl)phenyl)-2,2-dimethylpropyl)-2-(trifluoromethyl)benzamide Compound I-535

[00351] The title compound was prepared in an analogous fashion to that described in Example 112 starting from ethyl 4-(1-amino-2,2-dimethylpropyl)benzoate. LC-MS: (FA) ES- 393.

Example 175: 4-(2,2-dimethyl-1-[(5-methyl-2-phenyl-1,3-oxazol-4-yl)acetyl]amino)propyl)-*N*-hydroxybenzamide Compound I-80

[00352] The title compound was prepared in an analogous fashion to that described in Example 111 starting from ethyl 4-(1-amino-2,2-dimethylpropyl)benzoate. LC-MS: (FA) ES+ 422.

Example 176: 3,5-difluoro-*N*-(1-{4-[(hydroxyamino)carbonyl]phenyl}-2,2-dimethylpropyl)benzamide Compound I-251

[00353] The title compound was prepared in an analogous fashion to that described in Example 112 starting from ethyl 4-(1-amino-2,2-dimethylpropyl)benzoate. LC-MS: (FA) ES- 361.

Example 177: *N*-(1-{4-[(hydroxyamino)carbonyl]phenyl}-2,2-dimethylpropyl)-2,5-dimethyl-3-furamide Compound I-9

[00354] The title compound was prepared in an analogous fashion to that described in Example 112 starting from ethyl 4-(1-amino-2,2-dimethylpropyl)benzoate. LC-MS: (FA) ES+ 345.

Example 178: *N*-(1-{4-[(hydroxyamino)carbonyl]phenyl}-2,2-dimethylpropyl)-2,5-dimethyl-1*H*-pyrrole-3-carboxamide Compound I-310

[00355] The title compound was prepared in an analogous fashion to that described in Example 112 starting from ethyl 4-(1-amino-2,2-dimethylpropyl)benzoate. LC-MS: (FA) ES+ 344.

Example 179: *N*-(1-{4-[(hydroxyamino)carbonyl]phenyl}-2,2-dimethylpropyl)thiophene-2-carboxamide Compound I-215

[00356] The title compound was prepared in an analogous fashion to that described in Example 112 starting from ethyl 4-(1-amino-2,2-dimethylpropyl)benzoate. LC-MS: (FA) ES+ 333.

Example 180: *N*-(1-{4-[(hydroxyamino)carbonyl]phenyl}-2,2-dimethylpropyl)-1-benzothiophene-3-carboxamide Compound I-158

[00357] The title compound was prepared in an analogous fashion to that described in Example 112 starting from ethyl 4-(1-amino-2,2-dimethylpropyl)benzoate. LC-MS: (FA) ES+ 383.

Example 181: 4-*tert*-butyl-*N*-(1-{4-[(hydroxyamino)carbonyl]phenyl}-2,2-dimethylpropyl)benzamide Compound I-377

[00358] The title compound was prepared in an analogous fashion to that described in Example 112 starting from ethyl 4-(1-amino-2,2-dimethylpropyl)benzoate. LC-MS: (FA) ES+ 383.

Example 182: *N*-(1-{4-[(hydroxyamino)carbonyl]phenyl}-2,2-dimethylpropyl)-3,5-dimethyl-1*H*-indole-2-carboxamide Compound I-329

[00359] The title compound was prepared in an analogous fashion to that described in Example 112 starting from ethyl 4-(1-amino-2,2-dimethylpropyl)benzoate. LC-MS: (FA) ES+ 394.

Example 183: *N*-(1-{4-[(hydroxyamino)carbonyl]phenyl}-2,2-dimethylpropyl)-1,5-dimethyl-1*H*-pyrazole-3-carboxamide Compound I-260

[00360] The title compound was prepared in an analogous fashion to that described in Example 112 starting from ethyl 4-(1-amino-2,2-dimethylpropyl)benzoate. LC-MS: (FA) ES+ 345.

Example 184: 4-{1-[(3,3-dimethylbutanoyl)amino]-2,2-dimethylpropyl}-*N*-hydroxybenzamide Compound I-396

[00361] The title compound was prepared in an analogous fashion to that described in Example 112 starting from ethyl 4-(1-amino-2,2-dimethylpropyl)benzoate. LC-MS: (FA) ES+ 307.

Example 185: *N*-(1-{4-[(hydroxyamino)carbonyl]phenyl}-2,2-dimethylpropyl)-1*H*-indole-3-carboxamide Compound I-319

[00362] The title compound was prepared in an analogous fashion to that described in Example 112 starting from ethyl 4-(1-amino-2,2-dimethylpropyl)benzoate. LC-MS: (FA) ES+ 366.

Example 186: 3-*tert*-butyl-*N*-(1-{4-[(hydroxyamino)carbonyl]phenyl}-2,2-dimethylpropyl)-1-methyl-1*H*-pyrazole-5-carboxamide Compound I-291

[00363] The title compound was prepared in an analogous fashion to that described in Example 112 starting from ethyl 4-(1-amino-2,2-dimethylpropyl)benzoate. LC-MS: (FA) ES+ 387.

Example 187: *N*-(1-{4-[(hydroxyamino)carbonyl]phenyl}-2,2-dimethylpropyl)-1-benzofuran-2-carboxamide Compound I-4

[00364] The title compound was prepared in an analogous fashion to that described in Example 112 starting from ethyl 4-(1-amino-2,2-dimethylpropyl)benzoate. LC-MS: (FA) ES+ 367.

Example 188: *N*-(1-{4-[(hydroxyamino)carbonyl]phenyl}-2,2-dimethylpropyl)-3,5-dimethylisoxazole-4-carboxamide Compound I-200

[00365] The title compound was prepared in an analogous fashion to that described in Example 112 starting from ethyl 4-(1-amino-2,2-dimethylpropyl)benzoate. LC-MS: (FA) ES+ 346.

Example 189: *N*-(1-{4-[(hydroxyamino)carbonyl]phenyl}-2,2-dimethylpropyl)-5-methyl-1*H*-indole-2-carboxamide Compound I-129

[00366] The title compound was prepared in an analogous fashion to that described in Example 112 starting from ethyl 4-(1-amino-2,2-dimethylpropyl)benzoate. LC-MS: (FA) ES+ 380.

Example 190: *N*-(1-{4-[(hydroxyamino)carbonyl]phenyl}-2,2-dimethylpropyl)biphenyl-4-carboxamide Compound I-355

[00367] The title compound was prepared in an analogous fashion to that described in Example 112 starting from ethyl 4-(1-amino-2,2-dimethylpropyl)benzoate. LC-MS: (FA) ES+ 403.

Example 191: *N*-(1-{4-[(hydroxyamino)carbonyl]phenyl}-2,2-dimethylpropyl)-1-methyl-1*H*-indole-5-carboxamide Compound I-145

[00368] The title compound was prepared in an analogous fashion to that described in Example 112 starting from ethyl 4-(1-amino-2,2-dimethylpropyl)benzoate. LC-MS: (FA) ES+ 380.

Example 192: *N*-(1-{4-[(hydroxyamino)carbonyl]phenyl}-2,2-dimethylpropyl)-1,3-thiazole-4-carboxamide Compound I-123

[00369] The title compound was prepared in an analogous fashion to that described in Example 112 starting from ethyl 4-(1-amino-2,2-dimethylpropyl)benzoate. LC-MS: (FA) ES+ 334.

Example 193: 4-{1-[(cyclohexylcarbonyl)amino]-2,2-dimethylpropyl}-*N*-hydroxybenzamide Compound I-265

[00370] The title compound was prepared in an analogous fashion to that described in Example 112 starting from ethyl 4-(1-amino-2,2-dimethylpropyl)benzoate. LC-MS: (FA) ES+ 333.

Example 194: *N*-(1-{4-[(hydroxyamino)carbonyl]phenyl}-2,2-dimethylpropyl)-2-methyl-1,3-thiazole-4-carboxamide Compound I-42

[00371] The title compound was prepared in an analogous fashion to that described in Example 112 starting from ethyl 4-(1-amino-2,2-dimethylpropyl)benzoate. LC-MS: (FA) ES+ 348.

Example 195: *N*-(1-{4-[(hydroxyamino)carbonyl]phenyl}-2,2-dimethylpropyl)-5-methyl-1-phenyl-1*H*-pyrazole-4-carboxamide Compound I-182

[00372] The title compound was prepared in an analogous fashion to that described in Example 112 starting from ethyl 4-(1-amino-2,2-dimethylpropyl)benzoate. LC-MS: (FA) ES+ 407.

Example 196: *N*-(1-{4-[(hydroxyamino)carbonyl]phenyl}-2,2-dimethylpropyl)-1-methyl-1*H*-indole-3-carboxamide Compound I-107

[00373] The title compound was prepared in an analogous fashion to that described in Example 112. starting from ethyl 4-(1-amino-2,2-dimethylpropyl)benzoate. LC-MS: (FA) ES+ 380.

Example 197: *N*-(1-{4-[(hydroxyamino)carbonyl]phenyl}-2,2-dimethylpropyl)-1*H*-indole-2-carboxamide Compound I-127

[00374] The title compound was prepared in an analogous fashion to that described in Example 112 starting from ethyl 4-(1-amino-2,2-dimethylpropyl)benzoate. LC-MS: (FA) ES+ 366.

Example 198: 4-{1-[(cyclopentylcarbonyl)amino]-2,2-dimethylpropyl}-*N*-hydroxybenzamide**Compound I-373**

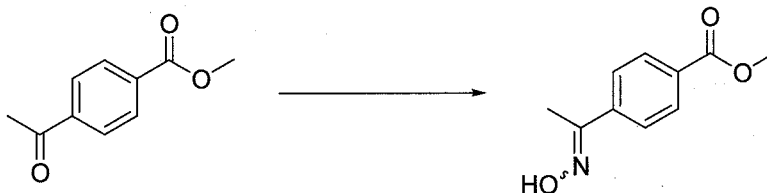
[00375] The title compound was prepared in an analogous fashion to that described in Example 112 starting from ethyl 4-(1-amino-2,2-dimethylpropyl)benzoate. LC-MS: (FA) ES+ 319.

Example 199: *N*-(1-{4-[(hydroxyamino)carbonyl]phenyl}-2,2-dimethylpropyl)-3,5-bis(trifluoromethyl)benzamide Compound I-52

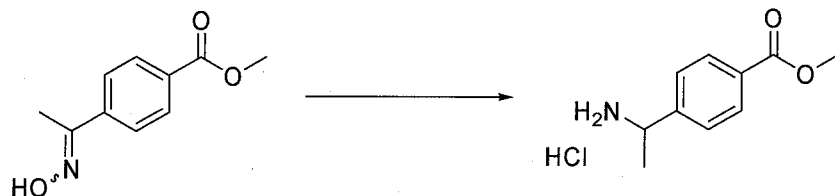
[00376] The title compound was prepared in an analogous fashion to that described in Example 112 starting from ethyl 4-(1-amino-2,2-dimethylpropyl)benzoate. LC-MS: (FA) ES- 461.

Example 200: *N*-(1-{4-[(hydroxyamino)carbonyl]phenyl}-2,2-dimethylpropyl)-3-(methylsulfonyl)benzamide Compound I-75

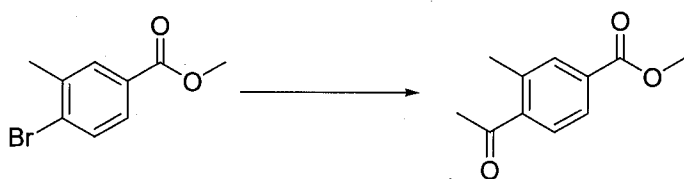
[00377] The title compound was prepared in an analogous fashion to that described in Example 112 starting from ethyl 4-(1-amino-2,2-dimethylpropyl)benzoate. LC-MS: (FA) ES+ 405.

Example 201: methyl 4-(1-(hydroxyimino)ethyl)benzoate

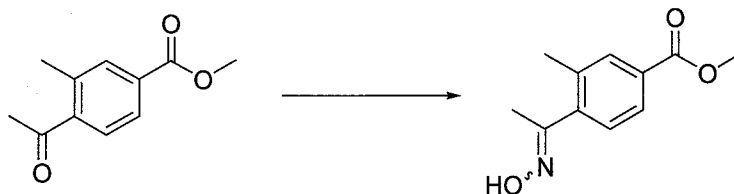
[00378] A mixture of 4-acetylbenzoic acid methyl ester (1.0 g, 5.6 mmol), hydroxylamine hydrochloride (3.1 g, 45 mmol) and sodium acetate (3.7 g, 45 mmol) in methanol (50 mL) was heated at 40 °C for 2 hours. The mixture was evaporated to dryness and the residue partitioned between EtOAc (40 mL) and water (40 mL). The organic layer was washed with brine (40 mL), dried over anhydrous MgSO₄ and evaporated to dryness to afford the title compound as a white solid (1.04g, 96%). LC-MS: (FA) ES+ 194; ¹H NMR (400 MHz, MeOD) δ 8.02 – 7.98 (m, 2H), 7.78 – 7.75 (m, 2H), 3.90 (s, 3H), 2.24 (s, 3H).

Example 202: methyl 4-(1-aminoethyl)benzoate hydrochloride

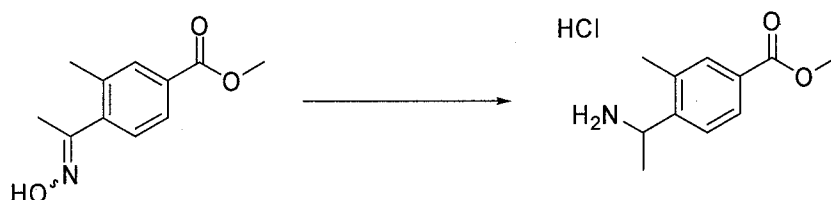
[00379] To a degassed solution of methyl 4-(1-(hydroxyimino)ethyl)benzoate (1.1 g, 5.6 mmol) and 12.0 M of hydrochloric acid in water (0.6 mL, 7.3 mmol) in methanol (50 mL) was added 10% palladium on carbon (0.20 g, 0.18 mmol). The reaction mixture was stirred overnight at room temperature. All insolubles were removed via filtration through celite and subsequent evaporation of the filtrate to dryness afforded the title compound as a white solid (1.12g, 83%). LC-MS: (FA) ES+ 180; ¹H NMR (400 MHz, MeOD) δ 8.09 (d, *J* = 8.4 Hz, 1H), 7.58 (d, *J* = 8.4 Hz, 1H), 4.55 (q, *J* = 6.8 Hz, 1H), 3.91 (s, 3H), 1.65 (d, *J* = 6.9 Hz, 3H).

Example 203: methyl 4-acetyl-3-methylbenzoate

[00380] Methyl 4-bromo-methylbenzoate (2.146 g, 9.368 mmol), 1,3-bis(diphenylphosphino)propane (0.21 g, 0.52 mmol), sodium carbonate (2.19 g, 20.6 mmol) and palladium (II) acetate (0.10 g, 0.47 mmol) were combined in a vial and purged with argon. Methanol (10.7 mL, 265 mmol) and n-butyl vinyl ether (4.83 mL, 37.5 mmol) were added by syringe. The resulting mixture was further sonicated under argon flow for several minutes then heated at 90 °C overnight. Upon cooling to room temperature, the reaction was diluted with methanol (10 mL). Celite (2 g) was added, the mixture thoroughly homogenized and filtered. The filter cake was washed with several mL of methanol. To the red/brown methanolic filtrate was added 6M aqueous HCl (6.5 mL). The solution turned yellow and then turbid white over stirring at room temperature (0.3 h). The solvent was removed under reduced pressure and the residue obtained was partitioned between ethyl acetate (75 mL) and water (30 mL). The aqueous phase was extracted with ethyl acetate (30 mL). The extracts were combined, washed with saturated aqueous sodium bicarbonate then brine, dried over sodium sulfate, filtered and concentrated under reduced pressure. The crude residue was dried in vacuo to remove butanol. The residue was purified by silica gel chromatography (5-20% EtOAc/hexanes gradient) to afford the title compound as an off-white solid (1.49g, 83%). LC-MS: (FA) ES+ 193; ¹H NMR (400 MHz, DMSO) δ 7.89 – 7.83 (m, 3H), 3.86 (s, 3H), 2.57 (s, 3H), 2.44 (s, 3H).

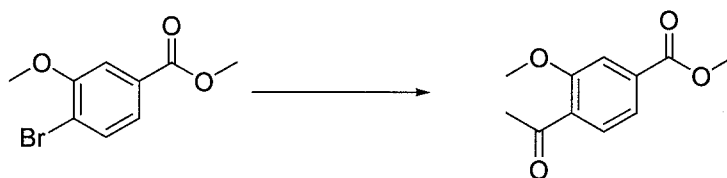
Example 204: methyl 4-(1-(hydroxyimino)ethyl)-3-methylbenzoate

[00381] Methyl 4-acetyl-3-methylbenzoate (1.49 g, 7.76 mmol), hydroxylamine hydrochloride (4.18 g, 60.1 mmol), and sodium acetate (4.93 g, 60.1 mmol) were suspended in methanol (40 mL) and the reaction mixture heated at 40 °C for 2h. Upon cooling to room temperature the solvent was removed under reduced pressure. The residue obtained was partitioned between ethyl acetate (75 mL) and water (30 mL). The organic extract was washed with water (20 mL) and brine. The washed extract was dried over sodium sulfate, filtered and concentrated under reduced pressure to afford the title compound as a solid (1.61 g, 100%). LC-MS: (FA) ES+ 208; ¹H NMR (300 MHz, MeOD) δ 7.91 – 7.77 (m, 2H), 7.31 (d, *J* = 8.0 Hz, 0.7H), 7.16 (d, *J* = 7.9 Hz, 0.3H), 3.89 (s, 3H), 2.37 (s, 2H), 2.28 (s, 1H), 2.17 (s, 2H), 2.10 (s, 1H).

Example 205: methyl 4-(1-aminoethyl)-3-methylbenzoate hydrochloride

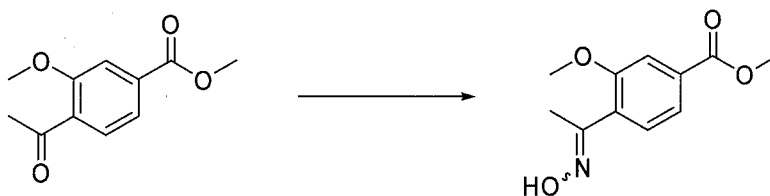
[00382] To a degassed solution of methyl 4-[N-hydroxyethanimidoyl]-3-methylbenzoate (0.348 g, 1.68 mmol) and 12.0 M aqueous hydrochloric acid (0.35 mL, 4.20 mmol) in methanol (15 mL) was added 10% palladium on carbon (0.11 g, 0.101 mmol). The reaction mixture was stirred under a balloon atmosphere of H₂ overnight. All insolubles were then removed via filtration through celite and the filtrate was evaporated to dryness. The residue was redissolved in methanol/toluene and concentrated under reduced pressure to afford a white solid (0.385 g, 100%). LC-MS: (FA) ES+ 195; ¹H NMR (300 MHz, DMSO) δ 7.15 (m Hz, 2H), 6.73 (d, *J* = 8.1 Hz, 1H), 6.45 – 6.26 (m, 1H), 3.96 (dd, *J* = 13.7, 6.9 Hz, 1H), 3.10 (s, 3H), 1.67 (s, 3H), 0.80 (d, *J* = 6.8 Hz, 3H).

Example 206: methyl 4-acetyl-3-methoxybenzoate

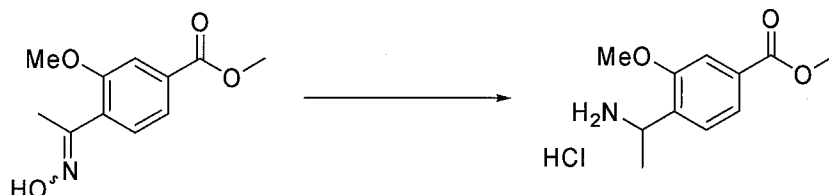


[00383] Methyl 4-bromo-3-methoxybenzoate (0.53 g, 2.2 mmol), 1,3-bis(diphenylphosphino)propane (0.050 g, 0.12 mmol), sodium carbonate (0.510 g, 4.81 mmol) and palladium (II) acetate (0.024 g, 0.11 mmol) were combined in a 5 mL microwave vial. The vial was sealed and purged with argon. Methanol (2.50 mL, 61.7 mmol) and n-butyl vinyl ether (1.12 mL, 8.74 mmol) were added by syringe, and the mixture was sonicated under argon flow for several minutes, then heated to 90 °C over night. Upon cooling to room temperature, celite (1 g) was added. The mixture was diluted with methanol (5 mL) and the slurry was then filtered. The filter cake was washed with methanol and to the pale red/brown methanolic filtrate was added 6M aqueous HCl (2.5 mL). The solution turned yellow and then turbid white over stirring at room temperature (0.5h). The solvent was removed under reduced pressure and the residue obtained was partitioned between ethyl acetate (50 mL) and half-saturated aqueous sodium bicarbonate solution (25 mL). The aqueous phase was extracted with ethyl acetate (30 mL). The organic extracts were combined, washed with brine, dried over sodium sulfate, filtered and concentrated under reduced pressure. The residue was purified by silica gel chromatography (15-85% EtOAc/hexanes gradient) to afford the title compound (0.396 g, 87%). LC-MS: (FA) ES+ 209; ¹H NMR (300 MHz, DMSO) δ 7.69 – 7.53 (m, 3H), 3.94 (s, 3H), 3.88 (s, 3H), 2.54 (s, 3H).

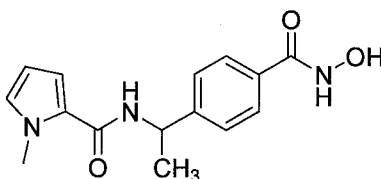
Example 207: methyl 4-(1-(hydroxyimino)ethyl)-3-methoxybenzoate



[00384] Methyl 4-acetyl-3-methoxybenzoate (0.396 g, 1.90 mmol), hydroxylamine hydrochloride (1.02 g, 14.7 mmol), and sodium acetate (1.21 g, 14.7 mmol) were suspended in methanol (10 mL) and the reaction mixture heated at 40 °C for 4h. Upon cooling to room temperature the solvent was removed under reduced pressure. The residue obtained was partitioned between ethyl acetate (80 mL) and water (30 mL). The organic extract was washed with water (25 mL) and brine. The washed extract was dried over sodium sulfate, filtered and concentrated under reduced pressure to afford the title compound as a solid (0.417g, 98%). LC-MS: (FA) ES+ 224; ¹H NMR (400 MHz, DMSO) δ 11.22 (s, 1H), 7.61 – 7.49 (m, 2H), 7.34 (d, *J* = 7.7 Hz, 1H), 3.86 (s, 6H), 2.05 (s, 3H).

Example 208: methyl 4-(1-aminoethyl)-3-methoxybenzoate hydrochloride

[00385] To a degassed solution of methyl 4-(1-(hydroxyimino)ethyl)-3-methoxybenzoate (0.417 g, 1.87 mmol) in methanol (17 mL) was added 12.0 M aqueous hydrochloric acid (0.389 mL, 4.67 mmol) and 10% palladium on carbon (0.120 g, 0.113 mmol). The reaction mixture was stirred under a balloon atmosphere of H₂ overnight. The catalyst was removed via filtration through celite and evaporation of the filtrate to dryness afforded the title compound (0.471g, 100%). LC-MS: (FA) ES+ 209; ¹H NMR (300 MHz, DMSO) δ 8.20 (s, 3H), 7.64 (m, 1H), 7.55 (s, 2H), 4.60 (m, 1H), 3.91 (s, 3H), 3.86 (s, 3H), 1.46 (d, *J* = 6.9 Hz, 3H).

Example 209: *N*-(1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-1-methyl-1*H*-pyrrole-2-carboxamide Compound I-356

[00386] To a solution of *N*-methylpyrrole-2-carboxylic acid (0.032 g, 0.26 mmol) and methyl 4-(1-aminoethyl)benzoate hydrochloride (50 mg, 0.23 mmol) in methylene chloride (2 mL) was added *N,N,N',N'*-tetramethyl-*O*-(7-azabenzotriazol-1-yl)uronium hexafluorophosphate (0.106 g, 0.278 mmol) and *N*-methylmorpholine (0.0586 g, 0.58 mmol) respectively. The resulting mixture was stirred at room temperature overnight. The reaction was evaporated to dryness and the residue obtained was partitioned between DCE (3 mL) and saturated aqueous NaHCO₃ (1 mL). The layers were separated and the aqueous layer was washed with additional DCE (3 mL). The combined organic layers were concentrated. The residue was taken up in anhydrous methanol (2 mL) to which was added potassium hydroxide (0.10 g, 1.8 mmol) and hydroxylamine hydrochloride (0.0805 g, 1.16 mmol). The mixture was stirred at room temperature for 30 minutes then heated to 80 °C for 5 hours. The reaction was neutralized by the addition of formic acid (0.0673 mL, 1.78 mmol) and the solution purified using prep-HPLC. Concentration of fractions containing desired product afforded the title compound as a white solid (11.3 mg, 17%). LC-MS: (FA) ES+ 288; ¹H NMR (400 MHz, DMSO) δ 11.10 (s, 1H), 9.00 (s, 1H), 8.31 (d, *J* = 8.0 Hz, 1H),

7.68 (d, $J = 8.3$ Hz, 2H), 7.41 (d, $J = 8.2$ Hz, 2H), 6.92 (dd, $J = 3.9, 1.7$ Hz, 1H), 6.88 (t, $J = 2.1$ Hz, 1H), 6.01 (dd, $J = 3.9, 2.5$ Hz, 1H), 3.77 (s, 3H), 1.43 (d, $J = 7.1$ Hz, 3H).

[00387] The following compounds were prepared in an analogous fashion to Example 209.

4-{1-[(2,2-dimethylpropanoyl)amino]ethyl}-*N*-hydroxybenzamide Compound I-59: LCMS: (FA) ES+ 265

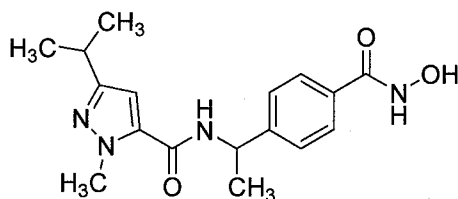
6-chloro-*N*-(1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)imidazo[1,2-*a*]pyridine-2-carboxamide Compound I-35: LCMS: (FA) ES+ 360

4-[1-({1-(4-chlorophenyl)cyclobutyl}carbonyl)amino]ethyl)-*N*-hydroxybenzamide Compound I-110: LCMS: (FA) ES+ 374

***N*-(1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-3-phenyl-1*H*-pyrazole-5-carboxamide Compound I-109:** LCMS: (FA) ES+ 351

***N*-hydroxy-4-{1-[(3-phenylpropanoyl)amino]ethyl}benzamide Compound I-45:** LCMS: (FA) ES+ 313

Example 210: *N*-(1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-3-isopropyl-1-methyl-1*H*-pyrazole-5-carboxamide Compound I-186



[00388] A solution of *N,N,N',N'*-tetramethyl-*O*-(7-azabenzotriazol-1-yl)uronium hexafluorophosphate (41.8 mg, 0.110 mmol), 3-isopropyl-1-methyl-1*H*-pyrazole-5-carboxylic acid (20.2 mg, 0.12 mmol) and *N,N*-diisopropylethylamine (52.2 μ L, 0.3 mmol) in DMF (1.0 mL, 13 mmol) was stirred at room temperature for 30 minutes. Methyl 4-(1-aminoethyl)benzoate hydrochloride (21.6 mg, 0.10 mmol) and *N,N*-diisopropylethylamine (17.4 μ L, 0.10 mmol) in DMF (1 mL) was then added and the reaction solution was stirred at room temperature overnight. The solution was evaporated to dryness and the residue obtained was partitioned between DCE (2 mL) and half-saturated aqueous sodium bicarbonate solution (2 mL). The aqueous layer was washed with additional DCE (2 mL) and the combined organic layers concentrated. The residue was dissolved in a mixture of MeOH (0.5 mL) and THF (2 mL); 1.0M aqueous NaOH (0.5 mL) was added and the solution heated to 40 °C overnight. Upon cooling to room temperature, the solution was neutralized by the addition of 1.0M aqueous HCl (0.5 mL) and evaporated to dryness. The residue obtained was taken up in DMF (2.0 mL) and to the solution was added *N,N,N',N'*-tetramethyl-*O*-(7-azabenzotriazol-1-yl)uronium hexafluorophosphate (41.8 mg, 0.11 mmol),

O-(tetrahydropyran-2-yl)hydroxylamine (14.0 mg, 0.120 mmol) and N,N-diisopropylethylamine (52 µL, 0.3 mmol). The reaction solution was stirred at room temperature overnight. The solution was evaporated to dryness and the residue obtained was partitioned between DCE (2 mL) and half-saturated aqueous sodium bicarbonate solution (2 mL). The aqueous layer was washed with additional DCE (2 mL) and the combined organic layers concentrated. The material obtained was dissolved in MeOH (1 mL), 2.0 M HCl in dioxane (52.2 uL, 0.30 mmol) was added and the solution stirred at room temperature for 1 hour. The solvents were evaporated and the resulting material was dissolved in DMSO and purified on Agilent 1100 LC/MSD instrument to afford the title compound as a white solid (5.3 mg, 16%). LC-MS: (FA) ES+ 331.

[00389] The following compounds were prepared in an analogous fashion to Example 210.

4-(1-[(2-chlorophenyl)acetyl]amino)ethyl)-N-hydroxybenzamide Compound I-292: LCMS: (FA) ES+ 334;

N-hydroxy-4-(1-[(1-phenylcyclopentyl)carbonyl]amino)ethyl)benzamide Compound I-198: LCMS: (FA) ES+ 353;

N-(1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-2-methyl-4,5,6,7-tetrahydro-2H-indazole-3-carboxamide Compound I-114: LCMS: (FA) ES+ 343;

N-(1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-5-isobutylisoxazole-3-carboxamide Compound I-286: LCMS: (FA) ES+ 332;

N-(1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-1-benzothiophene-3-carboxamide Compound I-244: LCMS: (FA) ES+ 341;

4-{1-[(2,3-dihydro-1H-inden-2-ylacetyl)amino]ethyl)-N-hydroxybenzamide Compound I-357: LCMS: (FA) ES+ 339;

N-hydroxy-4-(1-[(4-isopropylphenyl)acetyl]amino)ethyl)benzamide Compound I-285: LCMS: (FA) ES+ 341;

N-(1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)cinnoline-4-carboxamide Compound I-56: LCMS: (FA) ES+ 337;

N-hydroxy-4-(1-{4-(4-methoxyphenyl)butanoyl]amino}ethyl)benzamide Compound I-70: LCMS: (FA) ES+ 357;

4-(1-[(2,5-dimethyl-1,3-thiazol-4-yl)acetyl]amino)ethyl)-N-hydroxybenzamide Compound I-217: LCMS: (FA) ES+ 334;

N-(1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-4-(1H-pyrazol-1-yl)benzamide Compound I-185: LCMS: (FA) ES+ 351;

4-tert-butyl-N-(1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)benzamide Compound I-350: LCMS: (FA) ES+ 341;

N-(1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-2-naphthamide Compound I-327: LCMS: (FA) ES+ 335;

4-{1-[(1,3-benzodioxol-5-ylacetyl)amino]ethyl}-*N*-hydroxybenzamide Compound I-280: LCMS: (FA) ES+ 343;

N-hydroxy-4-[1-({1-(4-methylphenyl)cyclopropyl}carbonyl)amino]ethyl]benzamide Compound I-264: LCMS: (FA) ES+ 339;

N-(1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-3-methyl-1-benzofuran-2-carboxamide Compound I-7: LCMS: (FA) ES+ 339;

N-(1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-2*H*-chromene-3-carboxamide Compound I-224: LCMS: (FA) ES+ 339;

4-(1-{[(2,4-difluorophenyl)acetyl]amino}ethyl)-*N*-hydroxybenzamide Compound I-402: LCMS: (FA) ES+ 335;

N-(1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)quinoline-2-carboxamide Compound I-128: LCMS: (FA) ES+ 336;

N-(1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-2,1,3-benzothiadiazole-5-carboxamide Compound I-233: LCMS: (FA) ES+ 343;

N-(1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-4-(1,3-oxazol-5-yl)benzamide Compound I-138: LCMS: (FA) ES+ 352;

N-(1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-4-isopropoxybenzamide Compound I-38: LCMS: (FA) ES+ 343;

N-(1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-5,7-dimethylpyrazolo[1,5-*a*]pyrimidine-2-carboxamide Compound I-160: LCMS: (FA) ES+ 354;

4-(1-{[(2-chloro-6-fluorophenyl)acetyl]amino}ethyl)-*N*-hydroxybenzamide Compound I-24: LCMS: (FA) ES+ 352;

N-(1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)adamantane-1-carboxamide Compound I-3: LCMS: (FA) ES+ 343;

4-fluoro-*N*-(1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-3-methoxybenzamide Compound I-164: LCMS: (FA) ES+ 333;

N-(1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-1-methyl-1*H*-indole-2-carboxamide Compound I-98: LCMS: (FA) ES+ 338;

N-(1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-3-(1*H*-pyrrol-1-yl)thiophene-2-carboxamide Compound I-228: LCMS: (FA) ES+ 356;

4-(1-{[2-(4-chlorophenyl)-2-methylpropanoyl]amino}ethyl)-*N*-hydroxybenzamide Compound I-378: LCMS: (FA) ES+ 362;

N-(1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-2-methyl-1,3-benzothiazole-5-carboxamide

Compound I-230: LCMS: (FA) ES+ 356;

4-(1-{1-adamantylacetyl}amino)ethyl)-*N*-hydroxybenzamide **Compound I-212:** LCMS: (FA) ES+ 357;

N-(1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-4-(1*H*-pyrrol-1-yl)benzamide **Compound I-63:**

LCMS: (FA) ES+ 350;

N-(1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-1,3-benzothiazole-6-carboxamide **Compound I-**

360: LCMS: (FA) ES+ 342;

N-(1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)imidazo[1,2-*a*]pyridine-2-carboxamide **Compound**

I-125: LCMS: (FA) ES+ 325;

4-{1-[(cyclopropylcarbonyl)amino]ethyl}-*N*-hydroxybenzamide **Compound I-239:** LCMS: (FA) ES+ 249;

4-{1-[(cyclopropylacetyl)amino]ethyl}-*N*-hydroxybenzamide **Compound I-379:** LCMS: (FA) ES+ 263;

N-hydroxy-4-(1-{[(2-methoxyphenyl)acetyl]amino}ethyl)benzamide **Compound I-34:** LCMS: (FA) ES+ 329;

N-(1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-2,3-dihydro-1-benzofuran-7-carboxamide

Compound I-134: LCMS: (FA) ES+ 327;

N-(1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-1,3-dimethyl-1*H*-pyrazole-5-carboxamide

Compound I-288: LCMS: (FA) ES+ 303;

4-chloro-*N*-(1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)benzamide **Compound I-136:** LCMS: (FA) ES+ 320;

N-(1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-2-methyl-1,3-thiazole-4-carboxamide **Compound**

I-278: LCMS: (FA) ES+ 306;

N-(1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-1,3-benzodioxole-5-carboxamide **Compound I-297:**

LCMS: (FA) ES+ 329;

2-chloro-*N*-(1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)benzamide **Compound I-269:** LCMS: (FA) ES+ 320;

4-[1-(butyrylamino)ethyl]-*N*-hydroxybenzamide **Compound I-243:** LCMS: (FA) ES+ 251;

N-hydroxy-4-(1-{[(4-methoxyphenyl)acetyl]amino}ethyl)benzamide **Compound I-159:** LCMS: (FA) ES+ 329;

N-(1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-1,5-dimethyl-1*H*-pyrazole-3-carboxamide

Compound I-241: LCMS: (FA) ES+ 303;

N-(1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-1-benzofuran-5-carboxamide Compound I-349:

LCMS: (FA) ES+ 325;

N-(1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-3,5-dimethylisoxazole-4-carboxamide Compound

I-326: LCMS: (FA) ES+ 304;

4-{1-[(cyclopentylcarbonyl)amino]ethyl}-*N*-hydroxybenzamide Compound I-88: LCMS: (FA) ES+ 277;

4-{1-[(cyclobutylcarbonyl)amino]ethyl}-*N*-hydroxybenzamide Compound I-21: LCMS: (FA) ES+ 263;

N-(1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-5-methylthiophene-2-carboxamide Compound I-147: LCMS: (FA) ES+ 305;

4-{1-[(3,3-dimethylbutanoyl)amino]ethyl}-*N*-hydroxybenzamide Compound I-144: LCMS: (FA) ES+ 279;

N-(1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-1-benzofuran-2-carboxamide Compound I-207:

LCMS: (FA) ES+ 325;

N-(1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-3-methylbenzamide Compound I-295: LCMS: (FA) ES+ 299;

4-{1-[(cyclohexylcarbonyl)amino]ethyl}-*N*-hydroxybenzamide Compound I-208: LCMS: (FA) ES+ 291;

N-hydroxy-4-[1-(isobutyrylamino)ethyl]benzamide Compound I-36: LCMS: (FA) ES+ 251;

N-hydroxy-4-{1-[(tetrahydro-2*H*-pyran-4-ylacetyl)amino]ethyl}benzamide Compound I-313:

LCMS: (FA) ES+ 307;

N-hydroxy-4-(1-[(2,2,3,3-tetramethylcyclopropyl)carbonyl]amino)ethylbenzamide

Compound I-372: LCMS: (FA) ES+ 305;

4-{1-[(cyclohex-3-en-1-ylcarbonyl)amino]ethyl}-*N*-hydroxybenzamide Compound I-348: LCMS: (FA) ES+ 289;

4-{1-[(cyclopentylacetyl)amino]ethyl}-*N*-hydroxybenzamide Compound I-370: LCMS: (FA) ES+ 291;

2-fluoro-*N*-(1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-5-methylbenzamide Compound I-8:

LCMS: (FA) ES+ 317;

N-(1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)cycloheptanecarboxamide Compound I-213:

LCMS: (FA) ES+ 305;

N-hydroxy-4-{1-[(3-methylbutanoyl)amino]ethyl}benzamide Compound I-111: LCMS: (FA) ES+ 265;

***N*-hydroxy-4-(1-([(1-methylcyclohexyl)carbonyl]amino)ethyl)benzamide Compound I-132:** LCMS: (FA) ES+ 305;

N-hydroxy-4-(1-([(1-methylcyclopropyl)carbonyl]amino)ethyl)benzamide Compound I-154: LCMS: (FA) ES+ 263;

4-[1-(benzoylamino)ethyl]-*N*-hydroxybenzamide Compound I-385: LCMS: (FA) ES+ 285;

***N*-(1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-3-methoxybenzamide Compound I-225:** LCMS: (FA) ES+ 315;

[00390] The following compounds were prepared in an analogous fashion to Example 210 using methyl 4-(1-aminoethyl)-3-methoxybenzoate hydrochloride as the starting material:

***N*-(1-{4-[(hydroxyamino)carbonyl]-2-methoxyphenyl}ethyl)-1-methyl-1*H*-pyrrole-2-carboxamide Compound I-481:** LCMS: (FA) ES+ 318;

4-{1-[(2,2-dimethylpropanoyl)amino]ethyl}-*N*-hydroxy-3-methoxybenzamide Compound I-484: LCMS: (FA) ES+ 295;

***N*-(1-{4-[(hydroxyamino)carbonyl]-2-methoxyphenyl}ethyl)adamantane-1-carboxamide Compound I-483:** LCMS: (FA) ES+ 373;

***N*-(1-{4-[(hydroxyamino)carbonyl]-2-methoxyphenyl}ethyl)-1-benzothiophene-2-carboxamide Compound I-480:** LCMS: (FA) ES+ 371.

[00391] The following compounds were prepared in an analogous fashion to Example 210 using methyl 4-(1-aminoethyl)-3-methylbenzoate hydrochloride as the starting material:

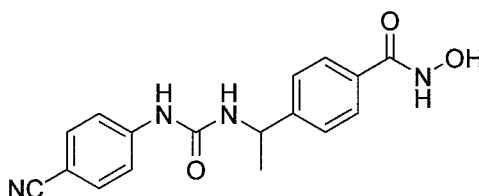
***N*-(1-{4-[(hydroxyamino)carbonyl]-2-methylphenyl}ethyl)-1-benzothiophene-2-carboxamide Compound I-485:** LCMS: (FA) ES+ 355;

***N*-(1-{4-[(hydroxyamino)carbonyl]-2-methylphenyl}ethyl)-1-methyl-1*H*-pyrrole-2-carboxamide Compound I-486:** LCMS: (FA) ES+ 302;

4-{1-[(2,2-dimethylpropanoyl)amino]ethyl}-*N*-hydroxy-3-methylbenzamide Compound I-490: LCMS: (FA) ES+ 279;

***N*-(1-{4-[(hydroxyamino)carbonyl]-2-methylphenyl}ethyl)adamantane-1-carboxamide Compound I-491:** LCMS: (FA) ES+ 357.

Example 211: 4-[1-([(4-cyanophenyl)amino]carbonyl)amino]ethyl)-*N*-hydroxybenzamide Compound I-236



[00392] To a solution of methyl 4-(1-aminoethyl)benzoate hydrochloride (32.4 mg, 0.15 mmol) and N,N-diisopropylethylamine (125 μ L, 0.718 mmol) in 1,2-dichloroethane (1 mL) was added 4-isocyanatobenzonitrile (32.4 g, 0.23 mmol). The reaction solution was stirred at room temperature overnight. The solution was evaporated to dryness and the residue was partitioned between DCE (2 mL) and half-saturated aqueous sodium bicarbonate solution (2 mL). The aqueous layer was washed with additional DCE (2 mL) and the combined organic layers concentrated. The material thus obtained was dissolved in a mixture of MeOH (0.5 mL) and THF (2 mL); 1.0M aqueous NaOH (0.5 mL) was added and the solution heated at 40 °C overnight. Upon cooling to room temperature, the solution was neutralized by the addition of 1.0M aqueous HCl (0.5 mL) and evaporated to dryness. The residue was taken up in DMF (2 mL) and to the solution was added N,N,N',N'-tetramethyl-O-(7-azabenzotriazol-1-yl)uronium hexafluorophosphate (62.7 mg, 0.165 mmol), O-(tetrahydropyran-2-yl)hydroxylamine (14 mg, 0.12 mmol) and N,N-diisopropylethylamine (104 μ L, 0.6 mmol). The reaction solution was heated at 45 °C overnight. The reaction mixture was then evaporated to dryness and the residue obtained was partitioned between DCE (2 mL) and half-saturated aqueous sodium bicarbonate solution (2 mL). The aqueous layer was washed with additional DCE (2 mL) and the combined organic layers concentrated. The residue obtained was dissolved in MeOH (1 mL), and 2.0 M HCl in dioxane (52.2 μ L, 0.30 mmol) was added and the solution stirred at room temperature for 1 hour. The solvent was evaporated and the resulting material was dissolved in DMSO and purified using an Agilent 1100 LC/MSD instrument to afford the title compound as a white solid (8.1 mg, 25%). LC-MS: (FA) ES+ 325.

[00393] The following compounds were prepared in an analogous fashion to Example 211.

4-[1-({[(3-fluoro-4-methylphenyl)amino]carbonyl}amino)ethyl]-N-hydroxybenzamide Compound I-120: LCMS: (FA) ES+ 332;

4-[1-({[(3-chloro-4-methylphenyl)amino]carbonyl}amino)ethyl]-N-hydroxybenzamide Compound I-103: LCMS: (FA) ES+ 349;

N-hydroxy-4-[1-({[(4-phenoxyphenyl)amino]carbonyl}amino)ethyl]benzamide Compound I-20: LCMS: (FA) ES+ 392;

4-[1-({[(2,4-dimethylphenyl)amino]carbonyl}amino)ethyl]-N-hydroxybenzamide Compound I-383: LCMS: (FA) ES+ 328;

4-[1-({[(3,4-dimethylphenyl)amino]carbonyl}amino)ethyl]-N-hydroxybenzamide Compound I-55: LCMS: (FA) ES+ 328;

4-[1-({[(3-acetylphenyl)amino]carbonyl}amino)ethyl]-N-hydroxybenzamide Compound I-358: LCMS: (FA) ES+ 342;

4-(1-({[(biphenyl-2-ylamino)carbonyl]amino}ethyl)-N-hydroxybenzamide Compound I-384: LCMS: (FA) ES+ 376;

***N*-hydroxy-4-[1-(((2-methylbenzyl)amino)carbonyl)amino]ethyl]benzamide Compound I-76:**

LCMS: (FA) ES+ 328;

4-[1-(((2,1,3-benzothiadiazol-4-ylamino)carbonyl)amino)ethyl]-*N*-hydroxybenzamide Compound I-

293: LCMS: (FA) ES+ 358;

***N*-hydroxy-4-[1-(((2-phenoxyphenyl)amino)carbonyl)amino]ethyl]benzamide Compound I-31:**

LCMS: (FA) ES+ 392;

4-{1-(((2-fluoro-5-(trifluoromethyl)phenyl)amino)carbonyl)amino]ethyl}-*N*-hydroxybenzamide

Compound I-334: LCMS: (FA) ES+ 386;

4-[1-(((2,3-dimethylphenyl)amino)carbonyl)amino]ethyl]-*N*-hydroxybenzamide Compound I-175:

LCMS: (FA) ES+ 328;

***N*-hydroxy-4-{1-(((4-(trifluoromethyl)phenyl)amino)carbonyl)amino]ethyl}benzamide Compound**

I-399: LCMS: (FA) ES+ 368;

***N*-hydroxy-4-[1-(((2-methoxy-5-methylphenyl)amino)carbonyl)amino]ethyl]benzamide Compound**

I-253: LCMS: (FA) ES+ 344

4-{1-(((2-chloro-4-(trifluoromethyl)phenyl)amino)carbonyl)amino]ethyl}-*N*-hydroxybenzamide

Compound I-163: LCMS: (FA) ES+ 403;

4-[1-(((2,6-dimethylphenyl)amino)carbonyl)amino]ethyl]-*N*-hydroxybenzamide Compound I-156:

LCMS: (FA) ES+ 328

4-[1-(((2,6-difluorophenyl)amino)carbonyl)amino]ethyl]-*N*-hydroxybenzamide Compound I-261:

LCMS: (FA) ES+ 336

***N*-hydroxy-4-[1-(((3-methylbenzyl)amino)carbonyl)amino]ethyl]benzamide Compound I-316:**

LCMS: (FA) ES+ 328

4-[1-(((4-ethylphenyl)amino)carbonyl)amino]ethyl]-*N*-hydroxybenzamide Compound I-381:

LCMS: (FA) ES+ 328

***N*-hydroxy-4-[1-(((2-phenylethyl)amino)carbonyl)amino]ethyl]benzamide Compound I-210:**

LCMS: (FA) ES+ 328

4-{1-(((4-(difluoromethoxy)phenyl)amino)carbonyl)amino]ethyl}-*N*-hydroxybenzamide

Compound I-150: LCMS: (FA) ES+ 366

4-[1-(((2,5-dichlorophenyl)amino)carbonyl)amino]ethyl]-*N*-hydroxybenzamide Compound I-89:

LCMS: (FA) ES+ 369

***N*-hydroxy-4-(1-(((1-naphthylamino)carbonyl)amino)ethyl)benzamide Compound I-6:** LCMS: (FA)

ES+ 350

4-(1-(((1,3-benzodioxol-5-ylamino)carbonyl)amino)ethyl)-*N*-hydroxybenzamide Compound I-71:

LCMS: (FA) ES+ 344

4-[1-(((2,4-dimethoxyphenyl)amino)carbonyl)amino)ethyl]-N-hydroxybenzamide Compound I-44:

LCMS: (FA) ES+ 360

4-[1-(((4-fluorophenyl)amino)carbonyl)amino)ethyl]-N-hydroxybenzamide Compound I-37:

LCMS: (FA) ES+ 318

4-[1-(((4-*tert*-butylphenyl)amino)carbonyl)amino)ethyl]-N-hydroxybenzamide Compound I-140:

LCMS: (FA) ES+ 356

4-(1-(((2,3-dihydro-1-benzofuran-5-ylamino)carbonyl)amino)ethyl)-N-hydroxybenzamide

Compound I-148: LCMS: (FA) ES+ 342

4-[1-(((2-fluorophenyl)amino)carbonyl)amino)ethyl]-N-hydroxybenzamide Compound I-74:

LCMS: (FA) ES+ 318

N-hydroxy-4-[1-(((3-methylphenyl)amino)carbonyl)amino)ethyl]benzamide Compound I-85:

LCMS: (FA) ES+ 314

4-[1-(((3,4-difluorophenyl)amino)carbonyl)amino)ethyl]-N-hydroxybenzamide Compound I-275:

LCMS: (FA) ES+ 336

4-[1-(((3,5-dimethylphenyl)amino)carbonyl)amino)ethyl]-N-hydroxybenzamide Compound I-397:

LCMS: (FA) ES+ 328

N-hydroxy-4-[1-(((4-methylbenzyl)amino)carbonyl)amino)ethyl]benzamide Compound I-277:

LCMS: (FA) ES+ 328

4-[1-(((3,5-dichlorophenyl)amino)carbonyl)amino)ethyl]-N-hydroxybenzamide Compound I-388:

LCMS: (FA) ES+ 369

N-hydroxy-4-{1-[[[3-(trifluoromethyl)phenyl]amino]carbonyl]amino}ethyl}benzamide Compound

I-371: LCMS: (FA) ES+ 368

N-hydroxy-4-[1-(((3-methyl-5-phenylisoxazol-4-yl)amino)carbonyl)amino)ethyl]benzamide

Compound I-168: LCMS: (FA) ES+ 381

N-hydroxy-4-{1-[[[4-(trifluoromethoxy)phenyl]amino]carbonyl]amino}ethyl}benzamide

Compound I-141: LCMS: (FA) ES+ 384

4-[1-(((4-acetylphenyl)amino)carbonyl)amino)ethyl]-N-hydroxybenzamide Compound I-398:

LCMS: (FA) ES+ 342

N-hydroxy-4-[1-(((5-methyl-3-phenylisoxazol-4-yl)amino)carbonyl)amino)ethyl]benzamide

Compound I-305: LCMS: (FA) ES+ 381

4-{1-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino}ethyl}-N-hydroxybenzamide

Compound I-325: LCMS: (FA) ES+ 403

N-hydroxy-4-[1-(((1-phenylethyl)amino)carbonyl)amino)ethyl]benzamide Compound I-196:

LCMS: (FA) ES+ 328

***N*-hydroxy-4-[1-({(2-methylphenyl)amino}carbonyl)amino]ethyl]benzamide Compound I-394:**

LCMS: (FA) ES+ 314

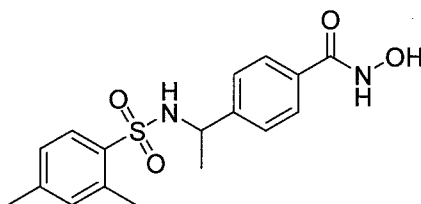
4-(1-{{(cyclohexylamino)carbonyl}amino}ethyl)-*N*-hydroxybenzamide Compound I-395: LCMS:

(FA) ES+ 306

4-[1-({(3-fluorophenyl)amino}carbonyl)amino]ethyl]-*N*-hydroxybenzamide Compound I-27:

LCMS: (FA) ES+ 318.

Example 212: 4-(1-{{(2,4-dimethylphenyl)sulfonyl}amino}ethyl)-*N*-hydroxybenzamide Compound I-78



[00394] To a solution of methyl 4-(1-aminoethyl)benzoate hydrochloride (32.4 mg, 0.15 mmol) and *N,N*-diisopropylethylamine (125 μ L, 0.72 mmol) in 1,2-dichloroethane (1 mL) was added 2,4-dimethylbenzenesulfonyl chloride (46 mg, 0.23 mmol). The reaction was stirred at room temperature overnight. The solution was evaporated to dryness and the residue was partitioned between DCE (2 mL) and half-saturated aqueous sodium bicarbonate solution (2 mL). The aqueous layer was washed with additional DCE (2 mL) and the combined organic layers concentrated. The residue was dissolved in a mixture of MeOH (0.5 mL) and THF (2 mL); then 1.0M aqueous NaOH (0.5 mL) was added and the solution heated at 40 °C overnight. Upon cooling to room temperature, the solution was neutralized with 1.0M aqueous HCl (0.5 mL) and evaporated to dryness. The resulting solid was taken up in DMF (2 mL) and to the resulting solution was added *N,N,N',N'*-tetramethyl-O-(7-azabenzotriazol-1-yl)uronium hexafluorophosphate (62.7 mg, 0.165 mmol), O-(tetrahydropyran-2-yl)hydroxylamine (19.3 mg, 0.165 mmol) and *N,N*-diisopropylethylamine (104 μ L, 0.60 mmol). The reaction solution was stirred at 45 °C overnight. The reaction mixture was evaporated to dryness and the residue obtained was partitioned between DCE (2 mL) and half-saturated aqueous sodium bicarbonate solution (2 mL). The aqueous layer was washed with additional DCE (2 mL) and the combined organic layers concentrated. The residue obtained was dissolved in MeOH (1 mL), 2.0 M HCl in dioxane (52 μ L, 0.3 mmol) was added and the solution stirred at room temperature for 1 hour. The solvent was evaporated and the resulting material was dissolved in DMSO and purified using an Agilent 1100 LC/MSD instrument to afford the title compounds as a white solid (23.3mg, 45%). LC-MS: (FA) ES+ 349.

[00395] The following compounds were prepared in an analogous fashion to Example 212.

N-hydroxy-4-{1-[(propylsulfonyl)amino]ethyl}benzamide Compound I-33: LCMS: (FA) ES+ 287;
4-{1-[(ethylsulfonyl)amino]ethyl}-N-hydroxybenzamide Compound I-1: LCMS: (FA) ES+ 273;
4-{1-[(benzylsulfonyl)amino]ethyl}-N-hydroxybenzamide Compound I-338: LCMS: (FA) ES+ 335;
4-(1-{[(4-fluorophenyl)sulfonyl]amino}ethyl)-N-hydroxybenzamide Compound I-2: LCMS: (FA) ES+ 339;
N-hydroxy-4-(1-{[(4-methylphenyl)sulfonyl]amino}ethyl)benzamide Compound I-266: LCMS: (FA) ES+ 335;
N-hydroxy-4-(1-{[(2-methylphenyl)sulfonyl]amino}ethyl)benzamide Compound I-232: LCMS: (FA) ES+ 335;
N-hydroxy-4-(1-{[(1-methyl-1H-imidazol-4-yl)sulfonyl]amino}ethyl)benzamide Compound I-335: LCMS: (FA) ES+ 325;
N-hydroxy-4-{1-[(phenylsulfonyl)amino]ethyl}benzamide Compound I-315: LCMS: (FA) ES+ 321;
N-hydroxy-4-[1-({[4-(trifluoromethyl)phenyl]sulfonyl}amino)ethyl]benzamide Compound I-488: LCMS: (FA) ES+ 389;
4-(1-{[(*tert*-butylamino)carbonyl]amino}ethyl)-N-hydroxybenzamide Compound I-339: LCMS: (FA) ES+ 280;
N-hydroxy-4-{1-[(mesitylsulfonyl)amino]ethyl}benzamide Compound I-176: LCMS: (FA) ES+ 363;
N-hydroxy-4-[1-({[3-(trifluoromethyl)phenyl]sulfonyl}amino)ethyl]benzamide Compound I-166: LCMS: (FA) ES+ 389;
N-hydroxy-4-[1-({[4-(1,3-oxazol-5-yl)phenyl]sulfonyl}amino)ethyl]benzamide Compound I-178: LCMS: (FA) ES+ 388;
4-(1-{[(5-fluoro-2-methylphenyl)sulfonyl]amino}ethyl)-N-hydroxybenzamide Compound I-205: LCMS: (FA) ES+ 353;
4-{1-[(1-benzothien-2-ylsulfonyl)amino]ethyl}-N-hydroxybenzamide Compound I-369: LCMS: (FA) ES+ 377;
4-(1-{[(2-cyanophenyl)sulfonyl]amino}ethyl)-N-hydroxybenzamide Compound I-340: LCMS: (FA) ES+ 346;
N-hydroxy-4-(1-{[(4-isopropylphenyl)sulfonyl]amino}ethyl)benzamide Compound I-221: LCMS: (FA) ES+ 363;
4-(1-{[(2,5-difluorophenyl)sulfonyl]amino}ethyl)-N-hydroxybenzamide Compound I-152: LCMS: (FA) ES+ 357;
4-(1-{[(2,5-dimethyl-3-thienyl)sulfonyl]amino}ethyl)-N-hydroxybenzamide Compound I-256: LCMS: (FA) ES+ 355;

4-(1-{{(3-chlorophenyl)sulfonyl}amino}ethyl)-*N*-hydroxybenzamide Compound I-197: LCMS: (FA) ES+ 356;

4-(1-{{(2-chloro-4-fluorophenyl)sulfonyl}amino}ethyl)-*N*-hydroxybenzamide Compound I-235: LCMS: (FA) ES+ 374;

4-{1-[(2,3-dihydro-1,4-benzodioxin-6-ylsulfonyl)amino]ethyl}-*N*-hydroxybenzamide Compound I-82: LCMS: (FA) ES+ 379;

N-hydroxy-4-(1-{{(2-oxo-2*H*-chromen-6-yl)sulfonyl}amino}ethyl)benzamide Compound I-49: LCMS: (FA) ES+ 389;

4-(1-{{(5-chloro-2-methoxyphenyl)sulfonyl}amino}ethyl)-*N*-hydroxybenzamide Compound I-347: LCMS: (FA) ES+ 386;

4-(1-{{(4-chlorophenyl)sulfonyl}amino}ethyl)-*N*-hydroxybenzamide Compound I-302: LCMS: (FA) ES+ 356;

N-hydroxy-4-{1-[(isoquinolin-5-ylsulfonyl)amino]ethyl}benzamide Compound I-170: LCMS: (FA) ES+ 372;

N-hydroxy-4-(1-{{(3-methoxyphenyl)sulfonyl}amino}ethyl)benzamide Compound I-23: LCMS: (FA) ES+ 351;

N-hydroxy-4-{1-[(1-naphthylsulfonyl)amino]ethyl}benzamide Compound I-95: LCMS: (FA) ES+ 371;

4-(1-{{(1,2-dimethyl-1*H*-imidazol-4-yl)sulfonyl}amino}ethyl)-*N*-hydroxybenzamide Compound I-54: LCMS: (FA) ES+ 339;

4-(1-{{(2-chloro-4-cyanophenyl)sulfonyl}amino}ethyl)-*N*-hydroxybenzamide Compound I-254: LCMS: (FA) ES+ 381;

N-hydroxy-4-(1-{{(1,3,5-trimethyl-1*H*-pyrazol-4-yl)sulfonyl}amino}ethyl)benzamide Compound I-60: LCMS: (FA) ES+ 353;

4-(1-{{(3,4-difluorophenyl)sulfonyl}amino}ethyl)-*N*-hydroxybenzamide Compound I-90: LCMS: (FA) ES+ 357;

4-(1-{{(3-chloro-4-methylphenyl)sulfonyl}amino}ethyl)-*N*-hydroxybenzamide Compound I-118: LCMS: (FA) ES+ 370;

4-(1-{{(4-*tert*-butylphenyl)sulfonyl}amino}ethyl)-*N*-hydroxybenzamide Compound I-131: LCMS: (FA) ES+ 377;

4-(1-{{(2-chlorophenyl)sulfonyl}amino}ethyl)-*N*-hydroxybenzamide Compound I-361: LCMS: (FA) ES+ 356;

N-hydroxy-4-{1-[(quinolin-8-ylsulfonyl)amino]ethyl}benzamide Compound I-363: LCMS: (FA) ES+ 372;

4-{1-[(2,1,3-benzoxadiazol-4-ylsulfonyl)amino]ethyl}-N-hydroxybenzamide Compound I-161:

LCMS: (FA) ES+ 363;

4-(1-[(4-chlorobenzyl)sulfonyl]amino)ethyl)-N-hydroxybenzamide Compound I-64: LCMS: (FA)

ES+ 370;

4-{1-[(2,1,3-benzothiadiazol-5-ylsulfonyl)amino]ethyl}-N-hydroxybenzamide Compound I-272:

LCMS: (FA) ES+ 379;

4-(1-[(4-fluoro-2-methylphenyl)sulfonyl]amino)ethyl)-N-hydroxybenzamide Compound I-61:

LCMS: (FA) ES+ 353;

4-(1-[(3-fluoro-4-methoxyphenyl)sulfonyl]amino)ethyl)-N-hydroxybenzamide Compound I-153:

LCMS: (FA) ES+ 369;

4-(1-[(2-chloro-6-methylphenyl)sulfonyl]amino)ethyl)-N-hydroxybenzamide Compound I-188:

LCMS: (FA) ES+ 370;

N-hydroxy-4-[1-({2-(trifluoromethyl)phenyl}sulfonyl)amino]ethyl]benzamide Compound I-391:

LCMS: (FA) ES+ 389;

4-(1-[(4-fluorobenzyl)sulfonyl]amino)ethyl)-N-hydroxybenzamide Compound I-198: LCMS: (FA)

ES+ 353;

N-hydroxy-4-(1-[(4-methoxyphenyl)sulfonyl]amino)ethyl)benzamide Compound I-47: LCMS: (FA)

ES+ 351;

N-hydroxy-4-(1-[(2,3,4-trifluorophenyl)sulfonyl]amino)ethyl)benzamide Compound I-284: LCMS:

(FA) ES+ 375;

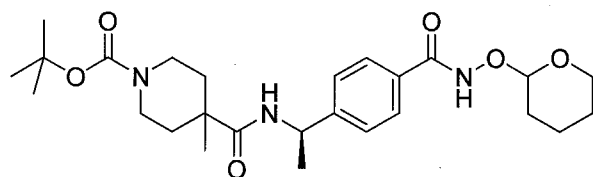
4-(1-[(2,5-dimethylphenyl)sulfonyl]amino)ethyl)-N-hydroxybenzamide Compound I-51: LCMS:

(FA) ES+ 349;

4-(1-[(2,4-dimethylphenyl)sulfonyl]amino)ethyl)-N-hydroxybenzamide Compound I-78: LCMS:

(FA) ES+ 349.

Example 213: tert-butyl 4-methyl-4-({[(1R)-1-(4-{[(tetrahydro-2H-pyran-2-yloxy)amino]carbonyl}phenyl)ethyl]amino}carbonyl)piperidine-1-carboxylate

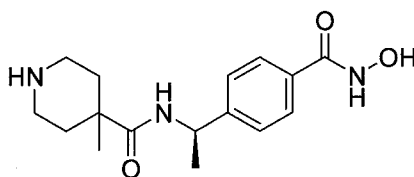


[00396] To a solution of 4-methyl-4-carboxy-1-N-butoxycarbonyl-piperidine (0.250 g, 1.03 mmol) in N,N-dimethylformamide (1.85 mL) was added N,N-diisopropylethylamine (0.537 mL, 3.08 mmol) and

fluoro-N,N,N',N'-tetramethylformamidinium hexafluorophosphate (0.298 g, 1.13 mmol). The reaction mixture was stirred for 15 minutes whereupon (R)-4-(1-amino-ethyl)-benzoic acid hydrochloride (0.200 g, 0.99 mmol) was added and further stirred at room temperature overnight. Water was added and the mixture extracted into ethyl acetate. Upon separation of the layers, the organic layer was dried over anhydrous MgSO₄ and evaporated to dryness. LC-MS: (FA) ES+ 391.

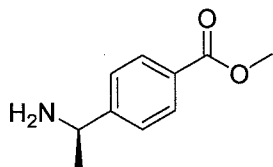
[00397] To a mixture of this material and N,N-diisopropylethylamine (0.518 mL, 2.97 mmol) in N,N-dimethylformamide (2 mL) was added fluoro-N,N,N',N'-tetramethylformamidinium hexafluorophosphate (0.288 g, 1.09 mmol) and O-(tetrahydropyran-2-yl)hydroxylamine (0.139 g, 1.19 mmol). The resulting solution was stirred at room temperature overnight. Upon quenching the reaction with the addition of water, the solution was extracted into ethyl acetate, the organic layer washed with brine and the solvent evaporated to dryness. The residue obtained was purified via silica chromatography (0-5% MeOH/DCM) to afford the title compound as a white solid (86.0 mg, 18%). LC-MS: (FA) ES+ 490.

Example 214: N-((1R)-1-{4-[(hydroxyamino)carbonyl]phenyl}ethyl)-4-methylpiperidine-4-carboxamide Compound I-487



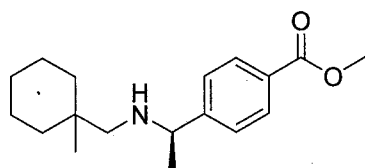
[00398] To a solution of tert-butyl 4-methyl-4-({[(1R)-1-(4-{[(tetrahydro-2H-pyran-2-yloxy)amino]carbonyl}phenyl)ethyl]amino}carbonyl)piperidine-1-carboxylate (0.082 g, 0.17 mmol) in methylene chloride (2 mL) was added 4.0 M hydrochloric acid in 1,4-dioxane (1 mL). The reaction mixture was stirred at room temperature for 4 hours. The reaction was concentrated to dryness. Acetic acid (1.0 mL, 18 mmol), tetrahydrofuran (1 mL), water (0.50 mL) were added and the resulting mixture was heated at 60 °C for 3h. The reaction mixture was concentrated to dryness and co-evaporated with toluene. The crude compound was purified on a BioCAC 700E HPLC instrument using a Waters Symmetry (21mm x 300mm) column to afford the title compound (22 mg, 43%). ¹H NMR (300 MHz, DMSO) δ 8.38 (s, 1H), 8.07 (d, *J* = 7.8 Hz, 1H), 7.67 (d, *J* = 8.3 Hz, 2H), 7.34 (d, *J* = 8.2 Hz, 2H), 4.97 (dd, *J* = 14.4, 7.1 Hz, 1H), 2.97 (d, *J* = 13.1 Hz, 2H), 2.66 (dd, *J* = 20.6, 10.7 Hz, 2H), 2.08 (s, 2H), 1.52 – 1.39 (m, 2H), 1.36 (d, *J* = 7.1 Hz, 3H), 1.12 (s, 3H). LC-MS: (FA) ES+ 306.

Example 215: (R)-methyl 4-(1-aminoethyl)benzoate



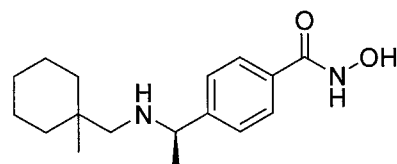
[00399] To a solution of (R)-4-(1-amino-ethyl)-benzoic acid hydrochloride (0.20 g, 0.99 mmol) in methanol (3.2 mL) was added sulfuric acid (5.29 μ L, 0.0992 mmol). The resulting solution was heated at reflux overnight. The methanol was removed under reduced pressure leaving a light brown oil which was partitioned between half-saturated sodium bicarbonate solution (50 mL) and ethyl acetate (75 mL). The aqueous phase was extracted with additional ethyl acetate (50 mL). The extracts were combined, washed with saturated aqueous sodium bicarbonate and brine, dried over sodium sulfate, filtered and concentrated under reduced pressure. Purification via silica chromatography (0-50% EtOAc/hexane) afforded product as a white solid (0.124g, 70%). LC-MS: (FA) ES+ 180.

Example 216: (R)-methyl 4-(1-((1-methylcyclohexyl)methylamino)ethyl)benzoate



[00400] To a solution of (R)-methyl 4-(1-aminoethyl)benzoate (0.12 g, 0.67 mmol) in methanol (2.97 mL, 73.33 mmol) was added 1-methylcyclohexane-1-carboxaldehyde (0.093 g, 0.74 mmol) and acetic acid (0.152 mL, 2.67 mmol). The reaction was stirred for 1 hour at room temperature whereupon sodium cyanoborohydride (63.1 mg, 1.00 mmol) was added and the mixture further stirred at room temperature overnight. The solvent was evaporated and the residual sodium cyanoborohydride quenched with saturated aqueous NaHCO_3 . The mixture was extracted into ethyl acetate, the organic layer washed with brine and the solvent evaporated to dryness. The residue obtained was purified via silica chromatography (0-5% MeOH/DCM) to afford the title compound as a colorless oil (123.0 mg, 63%). LC-MS: (FA) ES+ 290.

Example 217: N-hydroxy-4-((1R)-1-[(1-methylcyclohexyl)methyl]amino)ethyl)benzamide
Compound I-489



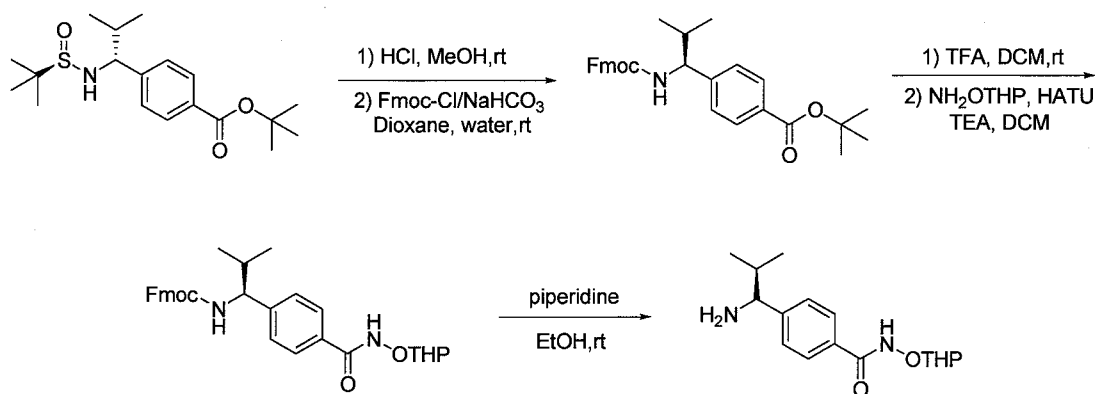
[00401] To a solution of methyl 4-((1R)-1-[[1-(1-methylcyclohexyl)methyl]amino]ethyl)benzoate (0.12 g, 0.415 mmol) in methanol (1 mL) was added 1.7 M of hydroxylamine potassium salt in methanol (2.46 mL, 4.19 mmol – prepared as described in *J. Med. Chem.* **2009**, 52(21):6757-6767). The reaction mixture was stirred at room temperature for 1 hour. The reaction was neutralized with the addition of acetic acid (0.24 mL, 4.15 mmol) and was concentrated to dryness. The residue was co-evaporated with toluene (2x). The crude product was purified on a BioCAD 700E HPLC instrument using a Phenomenex (C18) Luna (21.2 mm x 250mm) column to afford product (85 mg, 70%). ¹H NMR (400 MHz, DMSO) δ 11.13 (s, 1H), 8.17 (s, 1H), 7.67 (d, *J* = 8.2 Hz, 2H), 7.39 (d, *J* = 8.2 Hz, 2H), 3.69 (q, *J* = 6.5 Hz, 1H), 2.19 (d, *J* = 11.5 Hz, 1H), 2.03 (d, *J* = 11.5 Hz, 1H), 1.41 – 1.09 (m, 13H), 0.83 (s, 3H). LC-MS: (FA) ES+ 291

Example 218

[00402] The following compounds were prepared in an analogous fashion to that described in Example 211 starting from appropriate chiral benzyl amine starting material.

Compound No	LC-MS (FA)
I-520	ES+ 325
I-523	ES+ 376
I-527	ES+ 350
I-528	ES+ 342
I-513	ES+ 328
I-518	ES+ 336
I-517	ES+ 328
I-512	ES+ 356
I-525	ES+ 353
I-515	ES+ 404
I-524	ES+ 378
I-526	ES+ 370
I-516	ES+ 356
I-521	ES+ 364
I-514	ES+ 356
I-522	ES+ 356

Example 219: 4-((*R*)-1-amino-2-methylpropyl)-*N*-(tetrahydro-2*H*-pyran-2-yloxy)benzamide



Step 1: (S)-tert-butyl 4-(1-(((9-fluoren-9-yl)methoxy)carbonylamino)-2-methylpropyl)benzoate

[00403] To a 2-L round-bottom flask charged with *tert*-butyl 4-((*R*)-1-((*R*)-1,1-dimethylethylsulfonamido)-2-methylpropyl)benzoate (13.0 g, 0.0368 mol) was added MeOH (650 mL) and hydrochloric acid (650 mL, 4.0 M in 1,4-dioxane). The mixture was stirred at rt for 2 h. The solvent was then evaporated to give a slightly yellow solid. To the solid was added 1,4-dioxane (650 mL), sat. NaHCO₃ solution (650 mL), followed by (9*H*-fluoren-9-yl)methyl carbonochloridate (10.4 g, 0.0405 mol). The mixture was stirred at rt for 2 h. The reaction was quenched with EtOAc (800 mL) and water (200 mL). After separation, the aqueous phase was extracted with EtOAc (2 × 600 mL). Combined organic phases were washed with brine, dried (Na₂SO₄), and concentrated. Flash column chromatography gave (S)-*tert*-butyl 4-(1-(((9-fluoren-9-yl)methoxy)carbonylamino)-2-methylpropyl)benzoate (6.5 g, 38%).

Step 2: (9*H*-fluoren-9-yl)methyl (1*R*)-2-methyl-1-(4-(tetrahydro-2*H*-pyran-2-yloxy)carbonyl)phenylpropylcarbamate

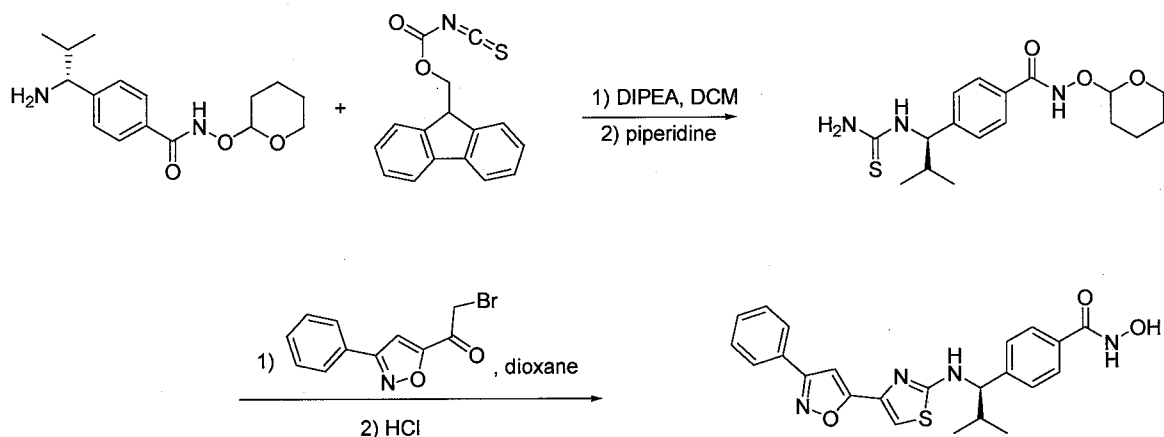
[00404] To a 1-L round-bottom flask was added (S)-*tert*-butyl 4-(1-(((9-fluoren-9-yl)methoxy)carbonylamino)-2-methylpropyl)benzoate (6.0 g, 12.7 mmol), DCM (260 mL), and trifluoroacetic acid (28.9 g, 254 mmol). The solution was stirred at rt for 16 h. The solvent were evaporated to give an oil. To this oil in a 500-mL round-bottom flask was added diisopropylethyl amine (20.0 g, 155 mmol), DCM (100 mL), *O*-(tetrahydro-2*H*-pyran-2-yl)hydroxylamine (1.78 g, 15.24 mmol), and HBTU (5.79 g, 15.2 mmol). The mixture was stirred at rt for 4 h, then diluted with DCM (500 mL), and washed with water (2 × 100 mL), dried (Na₂SO₄), and concentrated. Flash column chromatography gave (9*H*-fluoren-9-yl)methyl (1*R*)-2-methyl-1-(4-(tetrahydro-2*H*-pyran-2-yloxy)carbonyl)phenylpropylcarbamate (4.0 g, 62%).

Step 3: 4-((*R*)-1-amino-2-methylpropyl)-*N*-(tetrahydro-2*H*-pyran-2-yloxy) benzamide

[00405] To a 1-L round-bottom flask was added (9*H*-fluoren-9-yl)methyl (1*R*)-2-methyl-1-(4-(tetrahydro-2*H*-pyran-2-yloxy)carbonyl)phenylpropylcarbamate (10.0 g, 0.0195 mol), ethanol (588 mL), and piperidine (51.7 mL). The solution was stirred at rt for 16 h, then concentrated to give a solid.

Flash column chromatography gave 4-((*R*)-1-amino-2-methylpropyl)-*N*-(tetrahydro-2*H*-pyran-2-yloxy) benzamide (2.3 g, 41%). ¹H NMR (CDCl₃, 400 MHz) δ 7.59 (d, *J* = 8.0 Hz, 2 H), 7.23 (d, *J* = 8.0 Hz, 2 H), 5.00 (m, 1 H), 3.95 (m, 1 H), 3.59 (m, 2 H), 1.83 (m, 4 H), 1.57 (m, 3 H), 1.20 (m, 1 H), 0.90 (t, *J* = 6.8 Hz, 3 H), 0.67 (t, *J* = 6.8 Hz, 3 H).

Example 220: (*R*)-*N*-hydroxy-4-(2-methyl-1-(4-(3-phenylisoxazol-5-yl)thiazol-2-ylamino)propyl)benzamide Compound I-519



Step 1: 4-((*R*)-2-methyl-1-thioureidopropyl)-*N*-(tetrahydro-2*H*-pyran-2-yloxy) benzamide

[00406] A solution of 4-((*R*)-1-amino-2-methylpropyl)-*N*-(tetrahydro-2*H*-pyran-2-yloxy)benzamide (0.1643 g, 0.562 mmol) and *N,N*-diisopropylethylamine (0.1 mL, 0.6 mmol) in DCM (2.5 mL) was cooled in an ice bath and added to a solution of Fmoc-isothiocyanate (0.173 g, 0.616 mmol) in DCM (2.5 mL, 38 mmol) cooled at 0 °C in an ice bath. The reaction solution was stirred at rt for 1 h. Piperidine (1.0 mL, 2.0 mmol, 2.0 M in MeOH) was then added and the reaction stirred at rt for an additional 2 h. The reaction was concentrated and the residue was purified by flash chromatography (EtOAc:hex, 7:3 to 1:0) to afford 4-((*R*)-2-methyl-1-thioureidopropyl)-*N*-(tetrahydro-2*H*-pyran-2-yloxy) benzamide as a white solid. LC-MS: (FA) ES+ 352.

Step 2: (*R*)-*N*-hydroxy-4-(2-methyl-1-(4-(3-phenylisoxazol-5-yl)thiazol-2-ylamino)propyl)benzamide

[00407] A mixture of 4-((*R*)-2-methyl-1-thioureidopropyl)-*N*-(tetrahydro-2*H*-pyran-2-yloxy) benzamide (0.0252 g, 0.0717 mmol) and 5-(bromoacetyl)-3-phenylisoxazole (0.0191 g, 0.0717 mmol) in 1,4-dioxane (0.50 mL) was heated at 40 °C for 1 h. The solution was diluted with DCM (0.50 mL) and hydrochloric acid (0.20 mL, 0.80 mmol, 4.00 M of in 1,4-dioxane) was added. The reaction was stirred at rt for 3 h. The mixture was evaporated to dryness, the residue dissolved in DMSO and the solution purified on prep-HPLC to give (*R*)-*N*-hydroxy-4-(2-methyl-1-(4-(3-phenylisoxazol-5-yl)thiazol-2-ylamino)propyl)benzamide as a white solid (0.0173 g, 56%). LC-MS: (FA) ES+ 435. ¹H NMR (dms-*d*₆, 400 MHz) δ 11.13 (s, 1 H), 9.00 (s, 1 H), 8.52 (d, *J* = 8.6 Hz, 1 H), 7.90 (m, 2 H), 7.70 (d, *J* = 8.3 Hz,

2 H), 7.51 (dd, $J = 5.1, 1.9$ Hz, 3 H), 7.44 (d, $J = 8.3$ Hz, 2 H), 7.26 (s, 1 H), 7.09 (s, 1 H), 4.48 (t, $J = 8.1$ Hz, 1 H), 2.10 (m, 1 H), 1.00 (d, $J = 6.6$ Hz, 3 H), 0.78 (d, $J = 6.7$ Hz, 3 H).

Example 221: (R)-N-hydroxy-4-(2-methyl-1-(4-(trifluoromethyl) thiazol-2-ylamino)propyl)benzamide Compound I-529

[00408] The title compound was prepared in an analogous fashion to that described in Example 3 starting from appropriate starting materials. LC-MS: (FA) ES+ 360. ^1H NMR (dmso- d_6 , 400 MHz) δ 11.13 (s, 1 H), 9.03 (s, 1 H), 8.64 (d, $J = 8.5$ Hz, 1H), 7.69 (d, $J = 8.3$ Hz, 2 H), 7.39 (d, $J = 8.3$ Hz, 2 H), 7.27 (d, $J = 0.9$ Hz, 1 H), 4.39 (t, $J = 8.0$ Hz, 1 H), 2.00 (m, 1 H), 0.95 (d, $J = 6.7$ Hz, 3 H), 0.76 (d, $J = 6.7$ Hz, 3 H).

II. BIOLOGICAL DATA

Example 222: HDAC6 enzyme assay

[00409] To measure the inhibition of HDAC6 activity, purified human HDAC6 (BPS Bioscience; Cat. No. 5006) is incubated with substrate Ac-Arg-Gly-Lys(Ac)-AMC peptide (Bachem Biosciences; Cat. No. I-1925) for 1 hour at 30 °C in the presence of test compounds or vehicle DMSO control. The reaction is stopped with the HDAC inhibitor trichostatin A (Sigma; Cat. No. T8552) and the amount of Arg-Gly-Lys-AMC generated is quantitated by digestion with trypsin (Sigma; Cat. No. T1426) and subsequent measurement of the amount of AMC released using a fluorescent plate reader (Pherastar; BMG Technologies) set at Ex 340nm and Em 460nm. Concentration response curves are generated by calculating the fluorescence increase in test compound-treated samples relative to DMSO-treated controls, and enzyme inhibition (IC_{50}) values are determined from those curves.

Example 223: Nuclear extract HDAC assay

[00410] As a screen against Class I HDAC enzymes, HeLa nuclear extract (BIOMOL; Cat. No. KI-140) is incubated with Ac-Arg-Gly-Lys(Ac)-AMC peptide (Bachem Biosciences; Cat. No. I-1925) in the presence of test compounds or vehicle DMSO control. The HeLa nuclear extract is enriched for Class I enzymes HDAC1, -2 and -3. The reaction is stopped with the HDAC inhibitor Trichostatin A (Sigma; Cat. No. T8552) and the amount of Arg-Gly-Lys-AMC generated is quantitated by digestion with trypsin (Sigma; Cat. No. T1426) and subsequent measurement of the amount of AMC released using a fluorescent plate reader (Pherastar; BMG Technologies) set at Ex 340nm and Em 460nm. Concentration response curves are generated by calculating the fluorescence increase in test compound-treated samples relative to DMSO-treated controls, and enzyme inhibition (IC_{50}) values are determined from those curves.

Example 224: Western Blot and Immunofluorescence Assays

[00411] Cellular potency and selectivity of compounds are determined using a published assay (Haggarty *et al.*, *Proc. Natl. Acad. Sci. USA* **2003**, 100 (8): 4389-4394) using Hela cells (ATCC cat# CCL-2™) which are maintained in MEM medium (Invitrogen) supplemented with 10% FBS; or multiple myeloma cells RPMI-8226 (ATCC cat# CCL-155™) which are maintained in RPMI 1640 medium (Invitrogen) supplemented with 10% FBS. Briefly, cells are treated with inhibitors for 6 or 24 h and either lysed for Western blotting, or fixed for immunofluorescence analyses. HDAC6 potency is determined by measuring K40 hyperacetylation of alpha-tubulin with an acetylation selective monoclonal antibody (Sigma cat# T7451) in IC50 experiments. Selectivity against Class I HDAC activity is determined similarly using an antibody that recognizes hyperacetylation of histone H4 (Upstate cat# 06-866) in the Western blotting assay or nuclear acetylation (Abcam cat# ab21623) in the immunofluorescence assay.

Example 225: In vivo Tumor Efficacy Model

[00412] Female NCr-Nude mice (age 6-8 weeks, Charles River Labs) are aseptically injected into the subcutaneous space in the right dorsal flank with $1.0\text{-}5.0 \times 10^6$ cells (SKOV-3, HCT-116, BxPC3) in 100 μL of a 1:1 ratio of serum-free culture media (Sigma Aldrich) and BD Matrigel™ (BD Biosciences) using a 1 mL 26 3/8 gauge needle (Becton Dickinson Ref#309625). Alternatively, some xenograft models require the use of more immunocompromised strains of mice such as CB-17 SCID (Charles River Labs) or NOD-SCID (Jackson Laboratory). Furthermore, some xenograft models require serial passaging of tumor fragments in which small fragments of tumor tissue (approximately 1 mm^3) are implanted subcutaneously in the right dorsal flank of anesthetized (3-5% isoflourane/oxygen mixture) NCr-Nude, CB-17 SCID or NOD-SCID mice (age 5-8 weeks, Charles River Labs or Jackson Laboratory) via a 13-ga trocar needle (Popper & Sons 7927). Tumor volume is monitored twice weekly with Vernier calipers. The mean tumor volume is calculated using the formula $V = W^2 \times L / 2$. When the mean tumor volume is approximately 200 mm^3 , the animals are randomized into treatment groups of ten animals each. Drug treatment typically includes the test compound as a single agent, and may include combinations of the test compound and other anticancer agents. Dosing and schedules are determined for each experiment based on previous results obtained from pharmacokinetic/pharmacodynamic and maximum tolerated dose studies. The control group will receive vehicle without any drug. Typically, test compound (100-200 μL) is administered via intravenous (27-ga needle), oral (20-ga gavage needle) or subcutaneous (27-ga needle) routes at various doses and schedules. Tumor size and body weight are measured twice a week and the study is terminated when the control tumors reach approximately 2000 mm^3 , and/or if tumor volume exceeds 10% of the animal body weight or if the body weight loss exceeds 20%.

[00413] The differences in tumor growth trends over time between pairs of treatment groups are assessed using linear mixed effects regression models. These models account for the fact that each animal is measured at multiple time points. A separate model is fit for each comparison, and the areas under the

curve (AUC) for each treatment group are calculated using the predicted values from the model. The percent decrease in AUC (dAUC) relative to the reference group is then calculated. A statistically significant *P* value suggests that the trends over time for the two treatment groups are different.

[00414] The tumor measurements observed on a date pre-specified by the researcher (typically the last day of treatment) are analyzed to assess tumor growth inhibition. For this analysis, a T/C ratio is calculated for each animal by dividing the tumor measurement for the given animal by the mean tumor measurement across all control animals. The T/C ratios across a treatment group are compared to the T/C ratios of the control group using a two-tailed Welch's *t*-test. To adjust for multiplicity, a False Discovery Rate (FDR) is calculated for each comparison using the approach described by Benjamini and Hochberg, *J.R. Stat. Soc. B* **1995**, 57:289-300.

[00415] As detailed above, compounds of the invention inhibit HDAC6. In certain embodiments, compounds of the invention inhibit HDAC6 with an IC₅₀ value of less than 100 nM including compounds: I-3, I-4, I-5, I-6, I-7, I-8, I-11, I-12, I-15, I-18, I-19, I-22, I-25, I-26, I-30, I-31, I-32, I-35, I-37, I-38, I-44, I-45, I-53, I-55, I-58, I-59, I-62, I-63, I-65, I-68, I-69, I-71, I-73, I-74, I-79, I-85, I-88, I-89, I-92, I-94, I-96, I-98, I-99, I-102, I-103, I-106, I-107, I-109, I-110, I-112, I-115, I-116, I-120, I-122, I-124, I-125, I-127, I-128, I-129, I-130, I-132, I-134, I-135, I-136, I-138, I-140, I-141, I-143, I-145, I-146, I-147, I-148, I-150, I-154, I-160, I-163, I-164, I-172, I-175, I-184, I-185, I-186, I-187, I-190, I-191, I-194, I-207, I-208, I-209, I-210, I-213, I-214, I-222, I-223, I-224, I-225, I-228, I-229, I-230, I-233, I-236, I-237, I-242, I-243, I-245, I-247, I-253, I-261, I-264, I-269, I-274, I-275, I-278, I-281, I-282, I-286, I-287, I-288, I-293, I-295, I-296, I-297, I-299, I-304, I-306, I-307, I-308, I-317, I-319, I-321, I-327, I-328, I-329, I-332, I-334, I-341, I-346, I-348, I-349, I-350, I-354, I-356, I-357, I-358, I-359, I-360, I-365, I-367, I-371, I-374, I-375, I-378, I-381, I-383, I-384, I-385, I-387, I-389, I-397, I-399, I-400, I-512, I-513, I-514, I-515, I-516, I-518, I-519, I-521, I-522, I-523, I-524, I-525, I-526, I-527, I-528, I-529.

[00416] In certain embodiments, compounds of the invention inhibit HDAC6 with an IC₅₀ value of greater than 100 nM and less than 500 nM including compounds: I-1, I-2, I-10, I-16, I-17, I-20, I-21, I-23, I-40, I-42, I-43, I-46, I-47, I-48, I-66, I-67, I-76, I-77, I-78, I-84, I-86, I-87, I-97, I-105, I-113, I-114, I-117, I-121, I-123, I-126, I-133, I-142, I-156, I-158, I-173, I-174, I-176, I-178, I-182, I-192, I-193, I-196, I-201, I-202, I-203, I-206, I-215, I-219, I-220, I-226, I-227, I-232, I-239, I-240, I-249, I-252, I-255, I-258, I-260, I-262, I-266, I-267, I-270, I-277, I-279, I-290, I-291, I-294, I-298, I-300, I-301, I-302, I-305, I-310, I-315, I-316, I-318, I-330, I-331, I-336, I-338, I-342, I-344, I-352, I-353, I-355, I-363, I-364, I-368, I-369, I-372, I-376, I-377, I-380, I-382, I-388, I-395, I-401, I-480, I-485, I-487, I-489, I-488, I-517.

[00417] In certain embodiments, compounds of the invention inhibit HDAC6 with an IC₅₀ value of greater than 500 nM and less than 1 μ M including compounds: I-9, I-13, I-28, I-29, I-41, I-52, I-75, I-81, I-91, I-101, I-108, I-137, I-139, I-151, I-179, I-181, I-183, I-195, I-199, I-204, I-216, I-246, I-251, I-259, I-268, I-271, I-272, I-273, I-303, I-309, I-339, I-351, I-393, I-536.

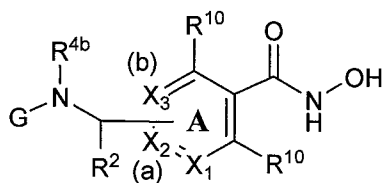
[00418] In certain embodiments, compounds of the invention inhibit HDAC6 with an IC₅₀ value of greater than 1 μ M including compounds: I-24, I-34, I-36, I-39, I-56, I-57, I-70, I-72, I-80, I-83, I-93, I-100, I-104, I-111, I-144, I-149, I-155, I-157, I-159, I-162, I-165, I-167, I-169, I-171, I-177, I-180, I-189, I-200, I-211, I-212, I-217, I-218, I-231, I-234, I-238, I-241, I-244, I-248, I-250, I-257, I-263, I-265, I-280, I-283, I-285, I-289, I-292, I-311, I-312, I-313, I-314, I-320, I-322, I-323, I-324, I-326, I-333, I-337, I-343, I-345, I-362, I-366, I-370, I-373, I-379, I-386, I-390, I-392, I-396, I-402, I-403, I-481, I-483, I-484, I-486, I-488, I-491, I-490.

[00419] As detailed above, compounds of the invention are selective for HDAC6 over other Class I HDAC enzymes. In certain embodiments, the ratio of HDAC IC₅₀ (as obtained in the nuclear extract assay described above) to HDAC6 IC₅₀ is less than 5 (HDAC IC₅₀/HDAC6 IC₅₀). In certain embodiments, the ratio of HDAC IC₅₀ to HDAC6 IC₅₀ is between 5 and 10. In certain embodiments, the ratio of HDAC IC₅₀ to HDAC6 IC₅₀ is between 10 and 100.

[00420] While we have described a number of embodiments of this invention, it is apparent that our basic examples may be altered to provide other embodiments, which utilize the compounds and methods of this invention. Therefore, it will be appreciated that the scope of this invention is to be defined by the appended claims rather than by the specific embodiments, which have been represented by way of examples.

WHAT IS CLAIMED IS:

1. A compound of formula (I):



(I);

or a pharmaceutically acceptable salt thereof; wherein:

ring A is an aromatic 6-membered ring connected through one of positions (a) or (b);

X_1 is CR^1 or N;

(i) when ring A is connected through position (a), X_2 is C; and X_3 is CR^1 or N; or

(ii) when ring A is connected through position (b), X_3 is C; and X_2 is CR^1 or N;

each occurrence of R^1 is independently hydrogen, halogen, C_{1-4} alkyl, C_{1-3} fluoroalkyl, $-O-C_{1-3}$ alkyl, $-O-C_{1-3}$ fluoroalkyl, cyano, hydroxy, $-NHC(O)C_{1-3}$ alkyl, $-C(O)NHC_{1-3}$ alkyl, $-NHC(O)NHC_{1-3}$ alkyl, or $-NHS(O)_2C_{1-3}$ alkyl.

each occurrence of R^{10} is independently hydrogen, halogen, hydroxy, $-O-C_{1-3}$ alkyl, or $-O-C_{1-3}$ fluoroalkyl;

R^2 is C_{1-6} aliphatic, C_{1-6} fluoroaliphatic, or unsubstituted or substituted 6-10-membered aryl;

R^{4b} is hydrogen, or C_{1-4} aliphatic;

G is $-R^3$, $-V_1-R^3$, $-V_1-L_1-R^3$, $-L_2-V_1-R^3$, $-L_2-V_2-R^3$, or $-L_1-R^3$;

L_1 is an unsubstituted or substituted C_{1-3} alkylene chain;

L_2 is an unsubstituted or substituted C_{2-3} alkylene chain;

V_1 is $-C(O)-$, $-C(O)-CR^A=CR^A-$, $-C(O)-N(R^{4a})-$, $-C(O)-O-$, or $-S(O)_2-$;

V_2 is $-C(S)-$, $-N(R^{4a})-$, $-N(R^{4a})-C(O)-$, $-SO_2-N(R^{4a})-$, $-N(R^{4a})-SO_2-$, $-O-$, $-S-$, $-S(O)-$, $-N(R^{4a})-C(O)-N(R^{4a})-$, $-N(R^{4a})-C(O)-O-$, $-O-C(O)-N(R^{4a})-$, or $-N(R^{4a})-SO_2-N(R^{4a})-$;

R^3 is unsubstituted or substituted C_{1-6} aliphatic, unsubstituted or substituted 3-10-membered cycloaliphatic, unsubstituted or substituted 4-10-membered heterocyclyl having 1-5 heteroatoms independently selected from nitrogen, oxygen, and sulfur, unsubstituted or substituted 6-10-membered aryl, or unsubstituted or substituted 5-10-membered heteroaryl having 1-5 heteroatoms independently selected from nitrogen, oxygen, and sulfur;

each occurrence of R^A is independently hydrogen, fluoro, or unsubstituted or substituted C_{1-4} aliphatic; and

each occurrence of R^{4a} is independently hydrogen, or unsubstituted or substituted C_{1-4} aliphatic.

2. The compound of claim 1, wherein:

X_1 is CR^1 ; and

(i) when ring A is connected through position (a), X_2 is C; and X_3 is CR^1 ; or

(ii) when ring A is connected through position (b), X_3 is C; and X_2 is CR^1 .

3. The compound of claim 1, wherein:

R^{4b} is H; and

R^2 is methyl, ethyl, isopropyl, n-propyl, trifluoromethyl, tert-butyl, cyclopropyl, or phenyl.

4. The compound of claim 1, wherein:

G is $-V_1-R^3$; and

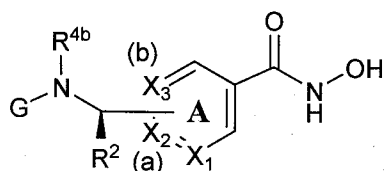
V_1 is $-C(O)-$, $-C(O)-N(R^{4a})-$, or $-S(O)_2-$.

5. The compound of claim 1, wherein:

R^1 is hydrogen, chloro, fluoro, hydroxy, methoxy, ethoxy, n-propoxy, isopropoxy, cyano, trifluoromethyl, methyl, ethyl, isopropyl, n-propyl, or tert-butyl; and

R^{10} is hydrogen.

6. The compound of claim 1, represented by formula (II-a):



(II-a):

wherein

ring A is an aromatic 6-membered ring connected through one of positions (a) or (b);

X_1 is CR^1 or N;

(i) when ring A is connected through position (a), X_2 is C; and X_3 is CR^1 or N; or

(ii) when ring A is connected through position (b), X_3 is C; and X_2 is CR^1 or N;

each occurrence of R^1 is independently hydrogen, halogen, C_{1-4} alkyl, C_{1-3} fluoroalkyl, -O- C_{1-3} alkyl, -O- C_{1-3} fluoroalkyl, cyano, hydroxy, -NHC(O) C_{1-3} alkyl, -C(O)NHC C_{1-3} alkyl, -NHC(O)NHC C_{1-3} alkyl, or -NHS(O) C_{1-3} alkyl.

each occurrence of R^{10} is independently hydrogen, halogen, hydroxy, -O- C_{1-3} alkyl, or -O- C_{1-3} fluoroalkyl;

R^2 is C_{1-6} aliphatic, C_{1-6} fluoroaliphatic, or unsubstituted or substituted 6-10-membered aryl;

R^{4b} is hydrogen, or C_{1-4} aliphatic;

G is $-R^3$, $-V_1-R^3$, $-V_1-L_1-R^3$, $-L_2-V_1-R^3$, $-L_2-V_2-R^3$, or $-L_1-R^3$;

L_1 is an unsubstituted or substituted C_{1-3} alkylene chain;

L_2 is an unsubstituted or substituted C_{2-3} alkylene chain;

V_1 is -C(O)-, -C(O)- $CR^A=CR^A$ -, -C(O)-N(R^{4a})-, -C(O)-O-, or -S(O) $_2$ -;

V_2 is -C(S)-, -N(R^{4a})-, -N(R^{4a})-C(O)-, -SO $_2$ -N(R^{4a})-, -N(R^{4a})-SO $_2$ -, -O-, -S-, -S(O)-, -N(R^{4a})-C(O)-N(R^{4a})-, -N(R^{4a})-C(O)-O-, -O-C(O)-N(R^{4a})-, or -N(R^{4a})-SO $_2$ -N(R^{4a})-;

R^3 is unsubstituted or substituted C_{1-6} aliphatic, unsubstituted or substituted 3-10-membered cycloaliphatic, unsubstituted or substituted 4-10-membered heterocyclyl having 1-5 heteroatoms independently selected from nitrogen, oxygen, and sulfur, unsubstituted or substituted 6-10-membered

aryl, or unsubstituted or substituted 5-10-membered heteroaryl having 1-5 heteroatoms independently selected from nitrogen, oxygen, and sulfur;

each occurrence of R^A is independently hydrogen, fluoro, or unsubstituted or substituted C_{1-4} aliphatic; and

each occurrence of R^{4a} is independently hydrogen, or unsubstituted or substituted C_{1-4} aliphatic.

7. The compound of claim 6, wherein:

X_1 is CR^1 ; and

(i) when ring A is connected through position (a), X_2 is C; and X_3 is CR^1 ; or

(ii) when ring A is connected through position (b), X_3 is C; and X_2 is CR^1 .

8. The compound of claim 6, wherein:

R^{4b} is H; and

R^2 is methyl, ethyl, isopropyl, n-propyl, trifluoromethyl, tert-butyl, cyclopropyl, or phenyl.

9. The compound of claim 6, wherein:

G is $-V_1-R^3$; and

V_1 is $-C(O)-$, $-C(O)-N(R^{4a})-$, or $-S(O)_2-$.

10. The compound of claim 6, wherein:

R^1 is hydrogen, chloro, fluoro, hydroxy, methoxy, ethoxy, n-propoxy, isopropoxy, cyano, trifluoromethyl, methyl, ethyl, isopropyl, n-propyl, or tert-butyl; and

R^{10} is hydrogen.

11. The compound of claim 6, wherein:

each substitutable carbon chain atom in R^3 is unsubstituted or substituted with 1-2 occurrences of

$-R^{5dd}$,

each substitutable saturated ring carbon atom in R^3 is unsubstituted or substituted with $=O$, $=S$, $=C(R^5)_2$, $=N-N(R^4)_2$, $=N-OR^5$, $=N-NHC(O)R^5$, $=N-NHCO_2R^6$, $=N-NHSO_2R^6$, $=N-R^5$ or

$-R^{5a}$,

each substitutable unsaturated ring carbon atom in R^3 is unsubstituted or is substituted with $-R^{5a}$;

each substitutable ring nitrogen atom in R^3 is unsubstituted or substituted with $-R^{9b}$;

each R^{5a} is independently halogen, $-NO_2$, $-CN$, $-C(R^5)=C(R^5)_2$,

$-C(R^5)=C(R^5)(R^{10})$, $-C\equiv C-R^5$, $-OR^5$, $-SR^6$, $-S(O)R^6$, $-SO_2R^6$, $-SO_2N(R^4)_2$, $-N(R^4)_2$,

$-NR^4C(O)R^5$, $-NR^4C(O)N(R^4)_2$, $-NR^4CO_2R^6$, $-OC(O)N(R^4)_2$, $-C(O)-C(O)R^5$, $-C(O)R^5$,

$-C(O)N(R^4)_2$, $-C(=NR^4)-N(R^4)_2$, $-C(=NR^4)-OR^5$, $-N(R^4)-N(R^4)_2$, $-N(R^4)C(=NR^4)-N(R^4)_2$,

$-N(R^4)SO_2R^6$, $-N(R^4)SO_2N(R^4)_2$, $-P(O)(R^5)_2$, $-P(O)(OR^5)_2$, unsubstituted or substituted C_{1-6}

aliphatic, unsubstituted or substituted 3-10-membered cycloaliphatic, unsubstituted or substituted 4-10-membered heterocyclyl having 1-5 heteroatoms independently selected from nitrogen,

oxygen, and sulfur, unsubstituted or substituted 6-10-membered aryl, or unsubstituted or

substituted 5-10-membered heteroaryl having 1-5 heteroatoms independently selected from

nitrogen, oxygen, and sulfur; or two adjacent R^{5a} , taken together with the intervening ring atoms,

form an unsubstituted or substituted fused aromatic ring or an unsubstituted or substituted non-

aromatic ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, and sulfur;

each occurrence of R^{5dd} is independently halogen, $-OH$, $-O(C_{1-3} \text{ alkyl})$, $-CN$, $-N(R^4)_2$,

$-C(O)(C_{1-3} \text{ alkyl})$, $-CO_2H$, $-CO_2(C_{1-3} \text{ alkyl})$, $-C(O)NH_2$, or $-C(O)NH(C_{1-3} \text{ alkyl})$;

each R^4 is independently hydrogen, unsubstituted or substituted 3-10-membered

cycloaliphatic, unsubstituted or substituted 4-10-membered heterocyclyl having 1-5 heteroatoms independently selected from nitrogen, oxygen, and sulfur, unsubstituted or substituted 6-10-

membered aryl, or unsubstituted or substituted 5-10-membered heteroaryl having 1-5 heteroatoms

independently selected from nitrogen, oxygen, and sulfur; or two R^4 on the same nitrogen atom,

taken together with the nitrogen atom, form an unsubstituted or substituted 5- to 6-membered

heteroaryl or an unsubstituted or substituted 4- to 8-membered heterocyclyl having, in addition to the nitrogen atom, 0-2 ring heteroatoms selected from nitrogen, oxygen, and sulfur;

each R^5 is independently hydrogen, unsubstituted or substituted C_{1-6} aliphatic,

unsubstituted or substituted 3-10-membered cycloaliphatic, unsubstituted or substituted 4-10-

membered heterocyclyl having 1-5 heteroatoms independently selected from nitrogen, oxygen, and sulfur, unsubstituted or substituted 6-10-membered aryl, or unsubstituted or substituted 5-10-membered heteroaryl having 1-5 heteroatoms independently selected from nitrogen, oxygen, and sulfur.

each R^6 is independently unsubstituted or substituted C_{1-6} aliphatic, or unsubstituted or substituted 6-10-membered aryl;

each R^7 is independently unsubstituted or substituted 4-10-membered heterocyclyl having 1-5 heteroatoms independently selected from nitrogen, oxygen, and sulfur, unsubstituted or substituted 6-10-membered aryl, or unsubstituted or substituted 5-10-membered heteroaryl having 1-5 heteroatoms independently selected from nitrogen, oxygen, and sulfur;

each R^{9b} is independently $-C(O)R^5$, $-C(O)N(R^4)_2$, $-CO_2R^6$, $-SO_2R^6$, $-SO_2N(R^4)_2$, unsubstituted C_{1-4} aliphatic, or C_{1-4} aliphatic substituted with 1-2 occurrences of R^7 or R^8 ; and

each R^8 is independently halogen, $-OH$, $-O(C_{1-3} \text{ alkyl})$, $-CN$, $-N(R^4)_2$, $-C(O)(C_{1-3} \text{ alkyl})$, $-CO_2H$, $-CO_2(C_{1-3} \text{ alkyl})$, $-C(O)NH_2$, or $-C(O)NH(C_{1-3} \text{ alkyl})$.

12. The compound of claim 11, wherein:

each substitutable saturated ring carbon atom in R^3 is unsubstituted or substituted with $-R^{5a}$;

the total number of R^{5a} substituents is p;

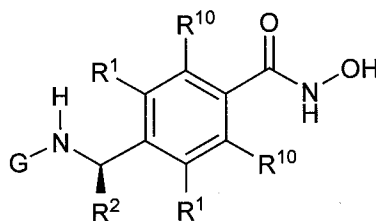
p is 1-2;

each R^{5a} is independently halogen, $-CN$, $-OH$, C_{1-4} alkyl, C_{1-3} fluoroalkyl, $-O-C_{1-3}$ alkyl, $-O-C_{1-3}$ fluoroalkyl, $-NHC(O)C_{1-3}$ alkyl, $-NHC(O)NHC_{1-3}$ alkyl, $-NHS(O)_2C_{1-3}$ alkyl, $-NHC_{1-3}$ alkyl, $-N(C_{1-3} \text{ alkyl})_2$, 3-10-membered cycloaliphatic substituted with 0-2 occurrences of $-R^{7a}$, 4-10-membered heterocyclyl having 1-5 heteroatoms independently selected from nitrogen, oxygen, and sulfur substituted with 0-2 occurrences of $-R^{7a}$, 6-10-membered aryl substituted with 0-2 occurrences of $-R^{7a}$, or 5-10-membered heteroaryl having 1-5 heteroatoms independently selected from nitrogen, oxygen, and sulfur substituted with 0-2 occurrences of $-R^{7a}$; and

each occurrence of R^{7a} is independently halogen, C_{1-3} alkyl, C_{1-3} fluoroalkyl, $-O-C_{1-3}$ alkyl, $-O-C_{1-3}$ fluoroalkyl, $-NHC(O)C_{1-3}$ alkyl, $-C(O)NHC_{1-3}$ alkyl,

-NHC(O)NHC₁₋₃ alkyl, or -NHS(O)₂C₁₋₃ alkyl.

13. The compound of claim 11, represented by formula (*III-a-i*):



(*III-a-i*);

wherein:

each occurrence of R¹ is independently hydrogen, chloro, fluoro, hydroxy, trifluoromethyl, or methyl;

R¹⁰ is hydrogen;

G is -V₁-R³; and

V₁ is -C(O)-, -C(O)-N(R^{4a})- or -S(O)₂-.

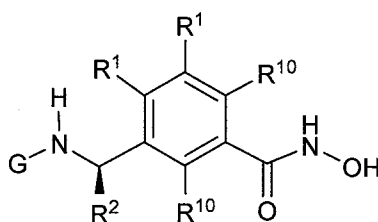
14. The compound of claim 13, wherein R¹ is hydrogen.
15. The compound of claim 13, wherein R² is methyl, ethyl, isopropyl, n-propyl, trifluoromethyl, tert-butyl, cyclopropyl, or phenyl.
16. The compound of claim 13, wherein R² is methyl, ethyl, isopropyl, or n-propyl.
17. The compound of claim 13, wherein:
- each substitutable saturated ring carbon atom in R³ is unsubstituted or substituted with -R^{5a};
- the total number of R^{5a} substituents is p;

p is 1-2;

each R^{5a} is independently halogen, -CN, -OH, C_{1-4} alkyl, C_{1-3} fluoroalkyl, -O- C_{1-3} alkyl, -O- C_{1-3} fluoroalkyl, -NHC(O) C_{1-3} alkyl, -C(O)NHC $_{1-3}$ alkyl, -NHC(O)NHC $_{1-3}$ alkyl, -NHS(O) $_2C_{1-3}$ alkyl, 3-10-membered cycloaliphatic substituted with 0-2 occurrences of $-R^{7a}$, 4-10-membered heterocyclyl having 1-5 heteroatoms independently selected from nitrogen, oxygen, and sulfur substituted with 0-2 occurrences of $-R^{7a}$, 6-10-membered aryl substituted with 0-2 occurrences of $-R^{7a}$, or 5-10-membered heteroaryl having 1-5 heteroatoms independently selected from nitrogen, oxygen, and sulfur substituted with 0-2 occurrences of $-R^{7a}$; and

each occurrence of R^{7a} is independently halogen, C_{1-3} alkyl, C_{1-3} fluoroalkyl, -O- C_{1-3} alkyl, -O- C_{1-3} fluoroalkyl, -NHC(O) C_{1-3} alkyl, -C(O)NHC $_{1-3}$ alkyl, -NHC(O)NHC $_{1-3}$ alkyl, or -NHS(O) $_2C_{1-3}$ alkyl.

18. The compound of claim 11, represented by formula (III-a-v):



(III-a-v);

wherein:

each occurrence of R^1 is independently hydrogen, chloro, fluoro, hydroxy, trifluoromethyl, or methyl;

R^{10} is hydrogen;

G is $-V_1-R^3$; and

V_1 is -C(O)-, -C(O)-N(R^{4a})- or -S(O) $_2$ -.

19. The compound of claim 18, wherein R^1 is hydrogen.

20. The compound of claim 18, wherein R^2 is methyl, ethyl, isopropyl, n-propyl, trifluoromethyl, tert-butyl, cyclopropyl, or phenyl.
21. The compound of claim 18, wherein R^2 is methyl, ethyl, isopropyl, or n-propyl.
22. The compound of claim 18, wherein:
each substitutable saturated ring carbon atom in R^3 is unsubstituted or substituted with $-R^{5a}$;
the total number of R^{5a} substituents is p;
p is 1-2;
each R^{5a} is independently halogen, -CN, -OH, C_{1-4} alkyl, C_{1-3} fluoroalkyl, -O- C_{1-3} alkyl, -O- C_{1-3} fluoroalkyl, -NHC(O) C_{1-3} alkyl, -C(O)NHC $_{1-3}$ alkyl, -NHC(O)NHC $_{1-3}$ alkyl, -NHS(O) $_2C_{1-3}$ alkyl, 3-10-membered cycloaliphatic substituted with 0-2 occurrences of $-R^{7a}$, 4-10-membered heterocyclyl having 1-5 heteroatoms independently selected from nitrogen, oxygen, and sulfur substituted with 0-2 occurrences of $-R^{7a}$, 6-10-membered aryl substituted with 0-2 occurrences of $-R^{7a}$, or 5-10-membered heteroaryl having 1-5 heteroatoms independently selected from nitrogen, oxygen, and sulfur substituted with 0-2 occurrences of $-R^{7a}$; and
each occurrence of R^{7a} is independently halogen, C_{1-3} alkyl, C_{1-3} fluoroalkyl, -O- C_{1-3} alkyl, -O- C_{1-3} fluoroalkyl, -NHC(O) C_{1-3} alkyl, -C(O)NHC $_{1-3}$ alkyl, -NHC(O)NHC $_{1-3}$ alkyl, or -NHS(O) $_2C_{1-3}$ alkyl.
23. A pharmaceutical composition comprising a compound of any of claims 1-22, and a pharmaceutically acceptable carrier.
24. A method of treating a proliferative disorder in a patient comprising administering to said patient a therapeutically effective amount of a compound of any of claims 1-22.
25. The method of claim 24, wherein the proliferative disorder is breast cancer, lung cancer, ovarian cancer, multiple myeloma, acute myeloid leukemia, or acute lymphoblastic leukemia.

26. A compound or a pharmaceutically acceptable salt of any of claims 1-22 or a pharmaceutical composition thereof for use in treating a proliferative disorder in a patient in need thereof.
27. The compound or pharmaceutically acceptable salt or pharmaceutical composition thereof according to claim 26, wherein the proliferative disorder is breast cancer, lung cancer, ovarian cancer, multiple myeloma, acute myeloid leukemia, or acute lymphoblastic leukemia.
28. A pharmaceutical composition for the treatment of a proliferative disorder in a patient in need thereof comprising a compound or a pharmaceutically acceptable salt of any of claims 1-22 as the active ingredient, and a pharmaceutically acceptable carrier.
29. The pharmaceutical composition according to claim 28, wherein the proliferative disorder is breast cancer, lung cancer, ovarian cancer, multiple myeloma, acute myeloid leukemia, or acute lymphoblastic leukemia.
30. Use of a compound or a pharmaceutically acceptable salt of any of claims 1-22 for the preparation of a pharmaceutical composition for the treatment of a proliferative disorder.
31. The use according to claim 30, wherein the proliferative disorder is breast cancer, lung cancer, ovarian cancer, multiple myeloma, acute myeloid leukemia, or acute lymphoblastic leukemia.
32. Use of an effective amount of a compound or a pharmaceutically acceptable salt of any of claims 1-22 or a pharmaceutical composition thereof for the treatment of a proliferative disorder in a patient in need thereof.
33. The use according to claim 32, wherein the proliferative disorder is breast cancer, lung cancer, ovarian cancer, multiple myeloma, acute myeloid leukemia, or acute lymphoblastic leukemia.
34. Use of a compound or a pharmaceutically acceptable salt according to any of claims 1-22 in the manufacture of a medicament for treating a proliferative disorder.
35. The use according to claim 34, wherein the proliferative disorder is breast cancer, lung cancer, ovarian cancer, multiple myeloma, acute myeloid leukemia, or acute lymphoblastic leukemia.

36. A method for inhibiting HDAC6 activity in a patient comprising administering a pharmaceutical composition comprising an amount of a compound of any of claims 1-22 effective to inhibit HDAC6 activity in the patient.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 11/26224

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - A01N 37/28; A61K 31/19, 31/185 (2011.01)

USPC - 514/575-577

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

USPC: 514/575-577

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
USPC: 514/507 (see search terms below)

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

Electronic Database Searched: PUBWEST (PGPUB, EPAB, JPAB, USPT), Google. Search Terms Used Hydroxamic acid, breast cancer, lung cancer, ovarian cancer, multiple myeloma, acute myeloid leukemia, proliferative disorder

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2009/0137679 A1 (Chen et al.) 28 May 2009 (28.05.2009) entire document especially fig 2; para [0007], [0009]-[0018], [0143]-[0144], [0191], [0215]	1-36
A	US 2006/0100285 A1 (Pinori et al.) 11 May 2006 (11.05.2006) entire document	1-36
A	US 5,442,110 A (Isomura et al.) 15 August 1995 (15.08.1995) entire document	1-36
A	US 2006/0252834 A1 (Rho et al.) 09 November 2006 (09.11.2006) entire document	1-36

☐ Further documents are listed in the continuation of Box C.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

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"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

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"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

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03 April 2011 (03.04.2011)

Date of mailing of the international search report

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Name and mailing address of the ISA/US

Mail Stop PCT, Attn: ISA/US, Commissioner for Patents
P.O. Box 1450, Alexandria, Virginia 22313-1450

Facsimile No. 571-273-3201

Authorized officer:

Lee W. Young

PCT Helpdesk: 571-272-4300
PCT OSP: 571-272-7774