Innovation, Sciences et Développement économique Canada
Office de la Propriété Intellectuelle du Canada

Innovation, Science and Economic Development Canada
Canadian Intellectual Property Office

CA 3015702 A1 2017/03/09

(21) 3 015 702

(12) DEMANDE DE BREVET CANADIEN
CANADIAN PATENT APPLICATION

(13) A1

(86) Date de dépôt PCT/PCT Filing Date: 2016/08/30
(87) Date publication PCT/PCT Publication Date: 2017/03/09
(85) Entrée phase nationale/National Entry: 2018/02/20
(86) N° demande PCT/PCT Application No.: US 2016/049526
(87) N° publication PCT/PCT Publication No.: 2017/040545
(30) Priorité/Priority: 2015/09/02 (US62/213,203)

(51) Cl.Int./Int.Cl. *A61K 31/445* (2006.01), *A61P 25/00* (2006.01), *C07D 211/00* (2006.01)

(71) Demandeur/Applicant:
TREVENA, INC., US

(72) Inventeurs/Inventors:
SPEERSCHNEIDER, AIMEE CROMBIE, US;
YAMASHITA, DENNIS SHINJI, US;
PITIS, PHILIP MICHAEL, US;
HAWKINS, MICHAEL JOHN, US;
LIU, GUODONG, US;
MISKOWSKI DAUBERT, TAMARA ANN, US;
...

(74) Agent: RIDOUT & MAYBEE LLP

(54) Titre : AZA-HETEROCYCLIQUE A 6 ELEMENTS CONTENANT DES COMPOSES MODULATEURS DE RECEPTEURS OPIOIDES DELTA, ET LEURS PROCEDES DE FABRICATION ET D'UTILISATION

(54) Title: 6-MEMBERED AZA-HETEROCYCLIC CONTAINING DELTA-OPIOID RECEPTOR MODULATING COMPOUNDS, METHODS OF USING AND MAKING THE SAME

(57) Abrégé/Abstract:
The present embodiments are directed, in part, to compounds, or pharmaceutically acceptable salts thereof, or pharmaceutical compositions thereof for modulating the activity of delta opioid receptor, biased and/or unbiased, and/or methods for treating pain, migraines, headaches, depression, Parkinsons Disease, anxiety, and/or overactive bladder, and other disorders and conditions described herein or any combination thereof.

CA 3015702 A1 2017/03/09

(21) 3 015 702

(13) A1

(72) Inventeurs(suite)/Inventors(continued): YUAN, CATHERINE C.K., US; BORBO KARGBO, ROBERT, US; HERR, ROBERT JASON, US; ROMERO, DONNA, US; PACOFSKY, GREGORY J., US

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
9 March 2017 (09.03.2017)

WIPO | PCT

(10) International Publication Number
WO 2017/040545 A1

(51) **International Patent Classification**:
A61K 31/445 (2006.01) *A61P 25/00* (2006.01)
C07D 211/00 (2006.01)

(21) **International Application Number**:
PCT/US2016/049526

(22) **International Filing Date**:
30 August 2016 (30.08.2016)

(25) **Filing Language**: English

(26) **Publication Language**: English

(30) **Priority Data**:
62/213,203 2 September 2015 (02.09.2015) US

(71) **Applicant**: **TREVENA, INC.** [US/US]; 1018 West 8th Avenue, Suite A, King of Prussia, Pennsylvania 19406 (US).

(72) **Inventors**: **SPEERSCHNEIDER, Aimee Crombie**; 1018 West 8th Avenue, Suite A, King of Prussia, Pennsylvania 19406 (US). **YAMASHITA, Dennis Shinji**; 1018 West 8th Avenue, Suite A, King of Prussia, Pennsylvania 19406 (US). **PITIS, Philip Michael**; 1018 West 8th Avenue, Suite A, King of Prussia, Pennsylvania 19406 (US). **HAWKINS, Michael John**; 1018 West 8th Avenue, Suite A, King of Prussia, Pennsylvania 19406 (US). **LIU, Guodong**; 1018 West 8th Avenue, Suite A, King of Prussia, Pennsylvania 19406 (US). **MISKOWSKI DAUBERT, Tamara Ann**; 1018 West 8th Avenue, Suite A, King of Prussia, Pennsylvania 19406 (US). **YUAN, Catherine C.K.**; 1018 West 8th Avenue, Suite A, King of Prussia, Pennsylvania 19406 (US). **BORBO KARGBO, Robert**; 1018 West 8th Avenue, Suite A, King of Prussia, Pennsylvania 19406 (US). **HERR, Robert Jason**; 1018 West 8th Avenue, Suite A, King of Prussia, Pennsylvania 19406 (US). **ROMERO, Donna**; 1018 West 8th Avenue, Suite A, King of Prussia, Pennsylvania 19406 (US). **PACOFSKY, Gregory J.**; 1018 West 8th Avenue, Suite A, King of Prussia, Pennsylvania 19406 (US).

(74) **Agent**: **SCOLNICK, Daniel M.**; Pepper Hamilton LLP, 400 Berwyn Park, 899 Cassatt Road, Berwyn, Pennsylvania 19312 (US).

(81) **Designated States** *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) **Designated States** *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Published:

— *with international search report (Art. 21(3))*

— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))*

WO 2017/040545 A1

(54) **Title**: 6-MEMBERED AZA-HETEROCYCLIC CONTAINING DELTA-OPIOID RECEPTOR MODULATING COMPOUNDS, METHODS OF USING AND MAKING THE SAME

(57) **Abstract**: The present embodiments are directed, in part, to compounds, or pharmaceutically acceptable salts thereof, or pharmaceutical compositions thereof for modulating the activity of delta opioid receptor, biased and/or unbiased, and/or methods for treating pain, migraines, headaches, depression, Parkinsons Disease, anxiety, and/or overactive bladder, and other disorders and conditions described herein or any combination thereof.

6-MEMBERED AZA-HETEROCYCLIC CONTAINING DELTA-OPIOID RECEPTOR MODULATING COMPOUNDS, METHODS OF USING AND MAKING THE SAME

Cross-Reference to Related Applications

The present application claims priority to U.S. Provisional Application No. 62/213,203, filed September 2, 2015, which is hereby incorporated by reference in its entirety.

Reference To Government Grants

The present invention was supported by funds from the U.S. Government (NIH Grant Nos. 5U01NS074480-02 and 1RC2MH090877-01) and the U.S. Government may therefore have certain rights in the invention.

Field

Embodiments disclosed herein are directed, in part, to compounds, or pharmaceutically acceptable salts thereof, for modulating the activity of delta opioid receptor and/or methods for treating pain, (*e.g.*, neuropathic pain), migraines (*e.g.* episodic, chronic or acute), headaches (*e.g.*, episodic, chronic, or acute), depression, Parkinsons Disease, PTSD, anxiety, and/or overactive bladder, or any combination thereof.

Background

Opioid receptors (ORs) mediate the actions of morphine and morphine-like opioids, including most clinical analgesics. Three molecularly and pharmacologically distinct opioid receptor types have been described: δ, κ and μ. Furthermore, each type is believed to have sub-types. All three of these opioid receptor types appear to share the same functional mechanisms at a cellular level. For example, certain activation of the opioid receptors causes inhibition of adenylate cyclase, and recruits β-arrestin.

The delta opioid receptor (DOR) has long been of interest as a target for potentially non-addictive treatments for a variety of CNS disorders. Recent evidence suggests that DOR activation may be beneficial in the treatment of migraine, neuropathic pain, Parkinson's disease, depression, anxiety and several other indications. However, some DOR agonists have caused seizure in preclinical species, hindering the development of selective drugs targeting the DOR. Thus there is a need to identify a DOR modulator for the treatment of these and other conditions. The present embodiments described herein fulfill these needs and others.

Summary Of The Embodiments

In some embodiments, the present invention provides a compound as described herein or a compound of a formula described herein or a pharmaceutically acceptable salt thereof of.

In some embodiments, the present invention provides pharmaceutical compositions comprising one or more compounds described herein or a pharmaceutically acceptable salt thereof of.

In some embodiments, a compound, or a pharmaceutically acceptable salt thereof, selected from the group consisting of: B1049, B0704, B0707, B0720, B0876, B1079, B1145, B1194, B1205, B1211, B1365, and B1401 is provided. In some embodiments, the opposite stereochemistry is provided. In some embodiments, the racemic mixture is provided.

In some embodiments, the present embodiments provide methods of treating pain, migraines (*e.g.* episodic, chronic or acute), headaches (*e.g.*, episodic, chronic, or acute),depression, anxiety, and/or overactive bladder in a subject are provided. In some embodiments, the methods comprise administering to the subject one or more compounds described herein, or a salt thereof or a pharmaceutical composition comprising one or more compounds, or salt thereof of a compound described herein. In some embodiments, methods of preventing the conditions described herein are provided. In some embodiments, methods for treating and/or preventing major depressive disorder, treatment resistant anxiety, post traumatic stress disorder, neuropathic pain, including, diabetic peripheral neuropathy, post-herpetic neuralgia, chemotherapy induced neuropathic pain, prevention of chemotherapy-induced neuropathy, prevention of chemotherapy-induced neuropathic pain, trigeminal neuralgia, inflammatory pain, including, osteoarthritis, rheumatoid arthritis, Rett Syndrome, Autism spectrum disorders, migraine, cluster headaches, acute abortive treatment, prophylaxis of acute intermittent migraine, prophylaxis of chronic migraine, treatment of episodic and chronic cluster headache, treatment or prevention of episodic and chronic cluster headache, Charcot-Marie Tooth disease, Traumatic brain injury, fibromyalgia, stroke, acute ischemic syndrome, ischemia/reperfusion injury, substance abuse intervention, and/or treatment of alcohol abuse in a subject are provided. In some embodiments, the methods comprise administering to the subject one or more compounds described herein, or a salt thereof or a pharmaceutical composition comprising one or more compounds, or salt thereof of a compound described herein. In some embodiments the subject is a mammal. In some embodiments, the subject is a subject in need thereof.

Brief Description of the Drawings

Figure 1 illustrates compounds prepared according to the examples, which includes the LCMS data.

Figure 2 illustrates the *in vitro* data for the compounds described herein and as referenced in the examples.

Figure 3 illustrates that the compounds of the present disclosure are effective in treating medication overuse headache and

Figure 4 illustrates that the compounds of the present disclosure are effective in treating opioid-induced hyperalgesia.

Figure 5 illustrates that the compounds of the present disclosure do not lead to medication overuse headache.

Description Of Embodiments

Unless defined otherwise, all technical and scientific terms have the same meaning as is commonly understood by one of ordinary skill in the art to which the embodiments disclosed belongs.

As used herein, the terms "a" or "an" means that "at least one" or "one or more" unless the context clearly indicates otherwise.

As used herein, the term "about" means that the numerical value is approximate and small variations would not significantly affect the practice of the disclosed embodiments. Where a numerical limitation is used, unless indicated otherwise by the context, "about" means the numerical value can vary by ±10% and remain within the scope of the disclosed embodiments.

As used herein, the term "acylamino" means an amino group substituted by an acyl group (e.g., -O-C(=O)-H or -O-C(=O)-alkyl). An example of an acylamino is -NHC(=O)H or $-NHC(=O)CH_3$. The term "lower acylamino" refers to an amino group substituted by a loweracyl group (e.g., -O-C(=O)-H or $-O-C(=O)-C_{1-6}$alkyl). An example of a lower acylamino is -NHC(=O)H or $-NHC(=O)CH_3$.

As used herein, the term "alkenyl" means a straight or branched alkyl group having one or more double carbon-carbon bonds and 2-20 carbon atoms, including, but not limited to, ethenyl, 1-propenyl, 2-propenyl, 2-methyl-1-propenyl, 1-butenyl, 2-butenyl, and the like. In some embodiments, the alkenyl chain is from 2 to 10 carbon atoms in length, from 2 to 8 carbon atoms in length, from 2 to 6 carbon atoms in length, or from 2 to 4 carbon atoms in length.

The terms "alkoxy", "phenyloxy", "benzoxy" and "pyrimidinyloxy" refer to an alkyl group, phenyl group, benzyl group, or pyrimidinyl group, respectively, each optionally substituted, that is bonded through an oxygen atom. For example, the term "alkoxy" means a straight or branched -O-alkyl group of 1 to 20 carbon atoms, including, but not limited to, methoxy, ethoxy, n-propoxy, isopropoxy, t-butoxy, and the like. In some embodiments, the alkoxy chain is from 1 to 10 carbon atoms in length, from 1 to 8 carbon atoms in length, from 1 to 6 carbon atoms in length, from 1 to 4 carbon atoms in length, from 2 to 10 carbon atoms in length, from 2 to 8 carbon atoms in length, from 2 to 6 carbon atoms in length, or from 2 to 4 carbon atoms in length.

As used herein, the term "alkyl" means a saturated hydrocarbon group which is straight-chained or branched. An alkyl group can contain from 1 to 20, from 2 to 20, from 1 to 10, from 2 to 10, from 1 to 8, from 2 to 8, from 1 to 6, from 2 to 6, from 1 to 4, from 2 to 4, from 1 to 3, or 2 or 3 carbon atoms. Examples of alkyl groups include, but are not limited to, methyl (Me), ethyl (Et), propyl (e.g., n-propyl and isopropyl), butyl (e.g., n-butyl, t-butyl, isobutyl), pentyl (e.g., n-pentyl, isopentyl, neopentyl), hexyl, isohexyl, heptyl, 4,4-dimethylpentyl, octyl, 2,2,4-trimethylpentyl, nonyl, decyl, undecyl, dodecyl, 2-methyl-1-propyl, 2-methyl-2-propyl, 2-methyl-1-butyl, 3-methyl-1-butyl, 2-methyl-3-butyl, 2-methyl-1-pentyl, 2,2-dimethyl-1-propyl, 3-methyl-1-pentyl, 4-methyl-1-pentyl, 2-methyl-2-pentyl, 3-methyl-2-pentyl, 4-methyl-2-pentyl, 2,2-dimethyl-1-butyl, 3,3-dimethyl-1-butyl, 2-ethyl-1-butyl, and the like.

As used herein, the term "alkylamino" means an amino group substituted by an alkyl group having from 1 to 6 carbon atoms. An example of an alkylamino is $-NHCH_2CH_3$.

As used herein, the term "alkylene" or "alkylenyl" means a divalent alkyl linking group. An example of an alkylene (or alkylenyl) is methylene or methylenyl ($-CH_2-$).

As used herein, the term "alkylthio" means an -S-alkyl group having from 1 to 6 carbon atoms. An example of an alkylthio group is $-SCH_2CH_3$.

As used herein, the term "alkynyl" means a straight or branched alkyl group having one or more triple carbon-carbon bonds and 2-20 carbon atoms, including, but not limited to, acetylene, 1-propylene, 2-propylene, and the like. In some embodiments, the alkynyl chain is 2 to 10 carbon atoms in length, from 2 to 8 carbon atoms in length, from 2 to 6 carbon atoms in length, or from 2 to 4 carbon atoms in length.

As used herein, the term "amidino" means $-C(=NH)NH_2$.

As used herein, the term "amino" means $-NH_2$.

As used herein, the term "aminoalkoxy" means an alkoxy group substituted by an amino group. An example of an aminoalkoxy is $-OCH_2CH_2NH_2$.

As used herein, the term "aminoalkyl" means an alkyl group substituted by an amino group. An example of an aminoalkyl is $-CH_2CH_2NH_2$.

As used herein, the term "aminosulfonyl" means $-S(=O)_2NH_2$.

As used herein, the term "aminoalkylthio" means an alkylthio group substituted by an amino group. An example of an aminoalkylthio is $-SCH_2CH_2NH_2$.

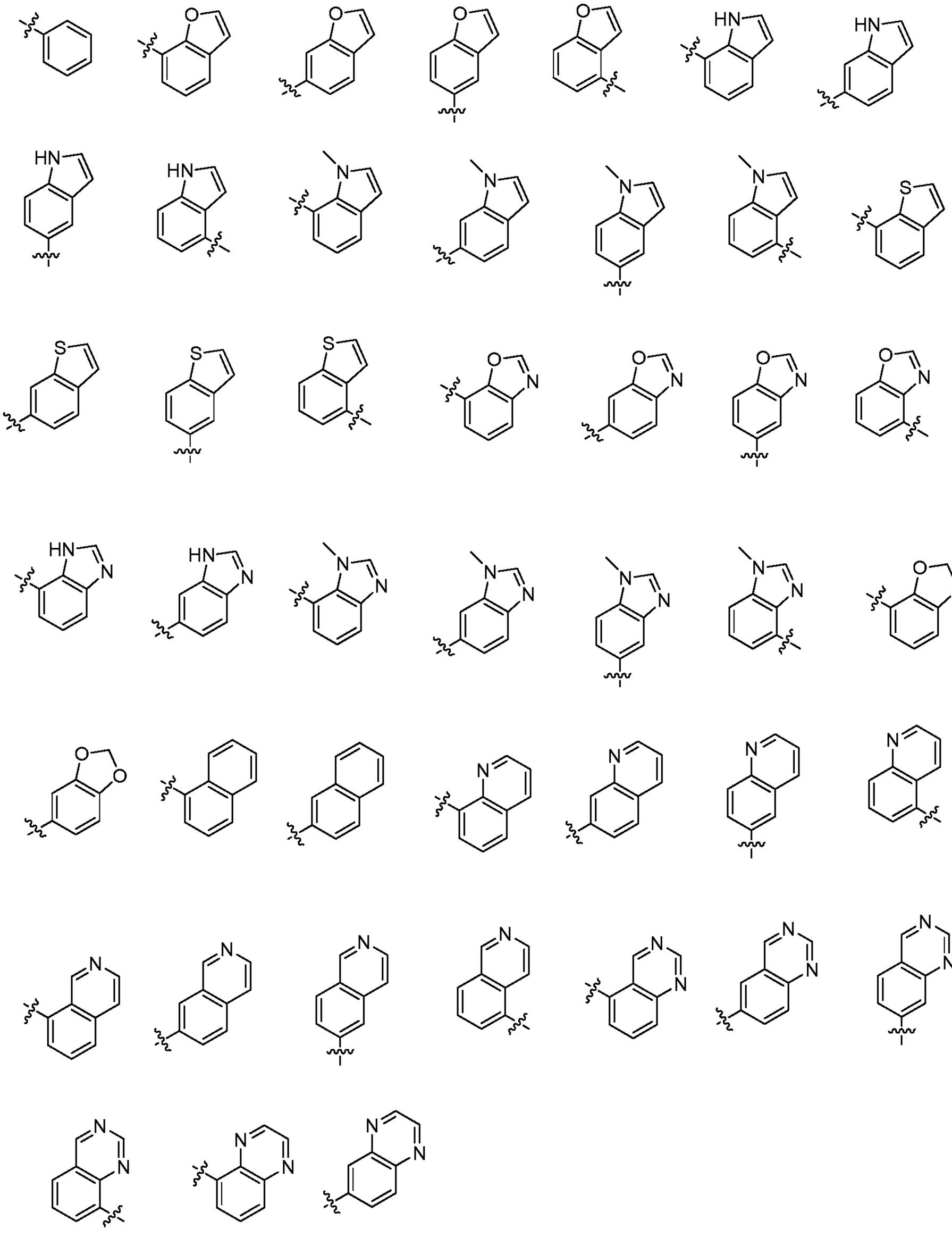
As used herein, the term "amphiphilic" means a three-dimensional structure having discrete hydrophobic and hydrophilic regions. An amphiphilic compound suitably has the presence of both hydrophobic and hydrophilic elements.

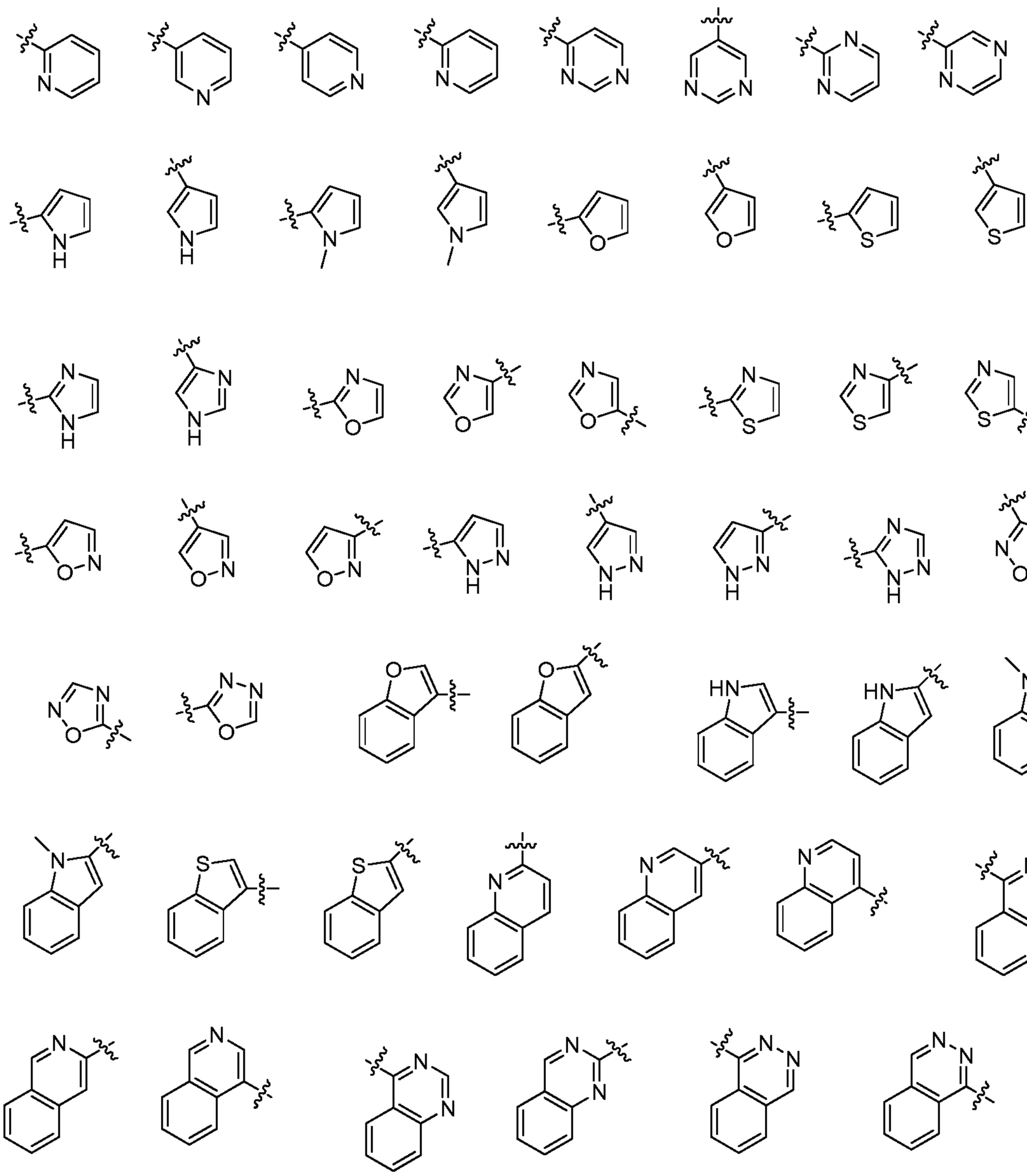
As used herein, the term "animal" includes, but is not limited to, humans and non-human vertebrates such as wild, domestic, and farm animals.

As used herein, the term "antagonize" or "antagonizing" means reducing or completely eliminating an effect, such as an activity of the delta opioid recetpor.

As used herein, the phrase "anti-recetpor effective amount" of a compound can be measured by the anti-receptor effectiveness of the compound. In some embodiments, an anti-receptor effective amount inhibits an activity of the receptor by at least 10%, by at least 20%, by at least 30%, by at least 40%, by at least 50%, by at least 60%, by at least 70%, by at least 80%, by at least 90%, or by at least 95%. In some embodiments, an "anti-recetpor effective amount" is also a "therapeutically effective amount" whereby the compound reduces or eliminates at least one effect of a delta opioid recetpor. In some embodiments, the effect is the beta-arrestin effect. In some embodiments, the effect is the G-protein mediated effect.

As used herein, the term "aryl" means a monocyclic, bicyclic, or polycyclic (e.g., having 2, 3 or 4 fused rings) aromatic hydrocarbons. In some embodiments, aryl groups have from 6 to 20 carbon atoms or from 6 to 10 carbon atoms. Examples of aryl groups include, but are not limited to, phenyl, naphthyl, anthracenyl, phenanthrenyl, indanyl, indenyl, tetrahydronaphthyl, and the like. Examples of aryl groups include, but are not limited to:





As used herein, the term "arylalkyl" means a C_{1-6}alkyl substituted by aryl.

As used herein, the term "arylamino" means an amino group substituted by an aryl group. An example of an arylamino is -NH(phenyl).

As used herein, the term "arylene" means an aryl linking group, i.e., an aryl group that links one group to another group in a molecule.

As used herein, the term "cancer" means a spectrum of pathological symptoms associated with the initiation or progression, as well as metastasis, of malignant tumors.

As used herein, the term "carbamoyl" means $-C(=O)-NH_2$.

As used herein, the term "carbocycle" means a 5- or 6-membered, saturated or unsaturated cyclic ring, optionally containing O, S, or N atoms as part of the ring. Examples

of carbocycles include, but are not limited to, cyclopentyl, cyclohexyl, cyclopenta-1,3-diene, phenyl, and any of the heterocycles recited above.

As used herein, the term "carrier" means a diluent, adjuvant, or excipient with which a compound is administered. Pharmaceutical carriers can be liquids, such as water and oils, including those of petroleum, animal, vegetable or synthetic origin, such as peanut oil, soybean oil, mineral oil, sesame oil and the like. The pharmaceutical carriers can also be saline, gum acacia, gelatin, starch paste, talc, keratin, colloidal silica, urea, and the like. In addition, auxiliary, stabilizing, thickening, lubricating and coloring agents can be used.

As used herein, the term, "compound" means all stereoisomers, tautomers, and isotopes of the compounds described herein.

As used herein, the terms "comprising" (and any form of comprising, such as "comprise", "comprises", and "comprised"), "having" (and any form of having, such as "have" and "has"), "including" (and any form of including, such as "includes" and "include"), or "containing" (and any form of containing, such as "contains" and "contain"), are inclusive or open-ended and do not exclude additional, unrecited elements or method steps.

As used herein, the term "contacting" means bringing together of two elements in an *in vitro* system or an *in vivo* system. For example, "contacting" a δ-opioid compound with a δ-opioid receptor with an individual or patient or cell includes the administration of the compound to an individual or patient, such as a human, as well as, for example, introducing a compound into a sample containing a cellular or purified preparation containing the δ-opioid receptor.

As used herein, the term "cyano" means -CN.

As used herein, the term "cycloalkyl" means non-aromatic cyclic hydrocarbons including cyclized alkyl, alkenyl, and alkynyl groups that contain up to 20 ring-forming carbon atoms. Cycloalkyl groups can include mono- or polycyclic ring systems such as fused ring systems, bridged ring systems, and spiro ring systems. In some embodiments, polycyclic ring systems include 2, 3, or 4 fused rings. A cycloalkyl group can contain from 3 to 15, from 3 to 10, from 3 to 8, from 3 to 6, from 4 to 6, from 3 to 5, or 5 or 6 ring-forming carbon atoms. Ring-forming carbon atoms of a cycloalkyl group can be optionally substituted by oxo or sulfido. Examples of cycloalkyl groups include, but are not limited to, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, cyclooctyl, cyclononyl, cyclopentenyl, cyclohexenyl, cyclohexadienyl, cycloheptatrienyl, norbornyl, norpinyl, norcarnyl, adamantyl,

and the like. Also included in the definition of cycloalkyl are moieties that have one or more aromatic rings fused (having a bond in common with) to the cycloalkyl ring, for example, benzo or thienyl derivatives of pentane, pentene, hexane, and the like (e.g., 2,3-dihydro-1H-indene-1-yl, or 1H-inden-2(3H)-one-1-yl).

As used herein, the term "cycloalkylalkyl" means a C_{1-6}alkyl substituted by cycloalkyl.

As used herein, the term "dialkylamino" means an amino group substituted by two alkyl groups, each having from 1 to 6 carbon atoms.

As used herein, the term "diazamino" means $-N(NH_2)_2$.

As used herein, the term "facially amphiphilic" or "facial amphiphilicity" means compounds with polar (hydrophilic) and nonpolar (hydrophobic) side chains that adopt conformation(s) leading to segregation of polar and nonpolar side chains to opposite faces or separate regions of the structure or molecule.

As used herein, the term "guanidino" means $-NH(=NH)NH_2$.

As used herein, the term "halo" means halogen groups including, but not limited to fluoro, chloro, bromo, and iodo.

As used herein, the term "haloalkoxy" means an -O-haloalkyl group. An example of an haloalkoxy group is OCF_3.

As used herein, the term "haloalkyl" means a C_{1-6}alkyl group having one or more halogen substituents. Examples of haloalkyl groups include, but are not limited to, CF_3, C_2F_5, CH_2F, CHF_2, CCl_3, $CHCl_2$, CH_2CF_3, and the like.

As used herein, the term "heteroaryl" means an aromatic heterocycle having up to 20 ring-forming atoms (e.g., C) and having at least one heteroatom ring member (ring-forming atom) such as sulfur, oxygen, or nitrogen. In some embodiments, the heteroaryl group has at least one or more heteroatom ring-forming atoms, each of which are, independently, sulfur, oxygen, or nitrogen. In some embodiments, the heteroaryl group has from 3 to 20 ring-forming atoms, from 3 to 10 ring-forming atoms, from 3 to 6 ring-forming atoms, or from 3 to 5 ring-forming atoms. In some embodiments, the heteroaryl group contains 2 to 14 carbon atoms, from 2 to 7 carbon atoms, or 5 or 6 carbon atoms. In some embodiments, the heteroaryl group has 1 to 4 heteroatoms, 1 to 3 heteroatoms, or 1 or 2 heteroatoms. Heteroaryl groups include monocyclic and polycyclic (e.g., having 2, 3 or 4 fused rings) systems. Examples of heteroaryl groups include, but are not limited to, pyridyl, pyrimidinyl, pyrazinyl, pyridazinyl, triazinyl, furyl, quinolyl, isoquinolyl, thienyl, imidazolyl,

thiazolyl, indolyl (such as indol-3-yl), pyrroyl, oxazolyl, benzofuryl, benzothienyl, benzthiazolyl, isoxazolyl, pyrazolyl, triazolyl, tetrazolyl, indazolyl, 1,2,4-thiadiazolyl, isothiazolyl, benzothienyl, purinyl, carbazolyl, benzimidazolyl, indolinyl, pyranyl, oxadiazolyl, isoxazolyl, triazolyl, thianthrenyl, pyrazolyl, indolizinyl, isoindolyl, isobenzofuranyl, benzoxazolyl, xanthenyl, 2H-pyrrolyl, pyrrolyl, 3H-indolyl, 4H-quinolizinyl, phthalazinyl, naphthyridinyl, quinazolinyl, phenanthridinyl, acridinyl, perimidinyl, phenanthrolinyl, phenazinyl, isothiazolyl, phenothiazinyl, isoxazolyl, furanyl, phenoxazinyl groups, and the like. Suitable heteroaryl groups include 1,2,3-triazole, 1,2,4-triazole, 5-amino-1,2,4-triazole, imidazole, oxazole, isoxazole, 1,2,3-oxadiazole, 1,2,4-oxadiazole, 3-amino-1,2,4-oxadiazole, 1,2,5-oxadiazole, 1,3,4-oxadiazole, pyridine, and 2-aminopyridine.

As used herein, the term "heteroarylalkyl" means a C_{1-6}alkyl group substituted by a heteroaryl group.

As used herein, the term "heteroarylamino" means an amino group substituted by a heteroaryl group. An example of a heteroarylamino is -NH-(2-pyridyl).

As used herein, the term "heteroarylene" means a heteroaryl linking group, i.e., a heteroaryl group that links one group to another group in a molecule.

As used herein, the term "heterocycle" or "heterocyclic ring" means a 5- to 7-membered mono- or bicyclic or 7- to 10-membered bicyclic heterocyclic ring system any ring of which may be saturated or unsaturated, and which consists of carbon atoms and from one to three heteroatoms chosen from N, O and S, and wherein the N and S heteroatoms may optionally be oxidized, and the N heteroatom may optionally be quaternized, and including any bicyclic group in which any of the above-defined heterocyclic rings is fused to a benzene ring. Particularly useful are rings containing one oxygen or sulfur, one to three nitrogen atoms, or one oxygen or sulfur combined with one or two nitrogen atoms. The heterocyclic ring may be attached at any heteroatom or carbon atom which results in the creation of a stable structure. Examples of heterocyclic groups include, but are not limited to, piperidinyl, piperazinyl, 2-oxopiperazinyl, 2-oxopiperidinyl, 2-oxopyrrolodinyl, 2-oxoazepinyl, azepinyl, pyrrolyl, 4-piperidonyl, pyrrolidinyl, pyrazolyl, pyrazolidinyl, imidazolyl, imidazolinyl, imidazolidinyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, oxazolyl, oxazolidinyl, isoxazolyl, isoxazolidinyl, morpholinyl, thiazolyl, thiazolidinyl, isothiazolyl, quinuclidinyl, isothiazolidinyl, indolyl, quinolinyl, isoquinolinyl, benzimidazolyl, thiadiazoyl, benzopyranyl, benzothiazolyl, benzoxazolyl, furyl, tetrahydrofuryl, tetrahydropyranyl,

thienyl, benzothienyl, thiamorpholinyl, thiamorpholinyl sulfoxide, thiamorpholinyl sulfone, and oxadiazolyl. Morpholino is the same as morpholinyl.

As used herein, the term "heterocycloalkyl" means non-aromatic heterocycles having up to 20 ring-forming atoms including cyclized alkyl, alkenyl, and alkynyl groups, where one or more of the ring-forming carbon atoms is replaced by a heteroatom such as an O, N, or S atom. Hetercycloalkyl groups can be mono or polycyclic (e.g., fused, bridged, or spiro systems). In some embodiments, the heterocycloalkyl group has from 1 to 20 carbon atoms, or from 3 to 20 carbon atoms. In some embodiments, the heterocycloalkyl group contains 3 to 14 ring-forming atoms, 3 to 7 ring-forming atoms, or 5 or 6 ring-forming atoms. In some embodiments, the heterocycloalkyl group has 1 to 4 heteroatoms, 1 to 3 heteroatoms, or 1 or 2 heteroatoms. In some embodiments, the heterocycloalkyl group contains 0 to 3 double bonds. In some embodiments, the heterocycloalkyl group contains 0 to 2 triple bonds. Examples of heterocycloalkyl groups include, but are not limited to, morpholino, thiomorpholino, piperazinyl, tetrahydrofuranyl, tetrahydrothienyl, 2,3-dihydrobenzofuryl, 1,3-benzodioxole, benzo-1,4-dioxane, piperidinyl, pyrrolidinyl, isoxazolidinyl, oxazolidinyl, isothiazolidinyl, pyrazolidinyl, thiazolidinyl, imidazolidinyl, pyrrolidin-2-one-3-yl, and the like. In addition, ring-forming carbon atoms and heteroatoms of a heterocycloalkyl group can be optionally substituted by oxo or sulfido. For example, a ring-forming S atom can be substituted by 1 or 2 oxo (form a S(O) or $S(O)_2$). For another example, a ring-forming C atom can be substituted by oxo (form carbonyl). Also included in the definition of heterocycloalkyl are moieties that have one or more aromatic rings fused (having a bond in common with) to the nonaromatic heterocyclic ring including, but not limited to, pyridinyl, thiophenyl, phthalimidyl, naphthalimidyl, and benzo derivatives of heterocycles such as indolene, isoindolene, 4,5,6,7-tetrahydrothieno[2,3-c]pyridine-5-yl, 5,6-dihydrothieno[2,3-c]pyridin-7(4H)-one-5-yl, isoindolin-1-one-3-yl, and 3,4-dihydroisoquinolin-1(2H)-one-3yl groups. Ring-forming carbon atoms and heteroatoms of the heterocycloalkyl group can be optionally substituted by oxo or sulfido.

As used herein, the term "heterocycloalkylalkyl" refers to a C_{1-6}alkyl substituted by heterocycloalkyl.

As used herein, the term "hydoxy" or "hydroxyl" means an -OH group.

As used herein, the term "hydroxyalkyl" or "hydroxylalkyl" means an alkyl group substituted by a hydroxyl group. Examples of a hydroxylalkyl include, but are not limited to, $-CH_2OH$ and $-CH_2CH_2OH$.

As used herein, the term "individual" or "patient," used interchangeably, means any animal, including mammals, such as mice, rats, other rodents, rabbits, dogs, cats, swine, cattle, sheep, horses, or primates, such as humans.

As used herein, the phrase "inhibiting activity," such as enzymatic or receptor activity means reducing by any measurable amount the acitivty of an enzyme or receptor, such as the δ-opioid receptor.

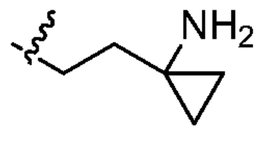
As used herein, the phrase "in need thereof" means that the animal or mammal has been identified as having a need for the particular method or treatment. In some embodiments, the identification can be by any means of diagnosis. In any of the methods and treatments described herein, the animal or mammal can be in need thereof. In some embodiments, the animal or mammal is in an environment or will be traveling to an environment in which a particular disease, disorder, or condition is prevelant.

As used herein, the phrase "*in situ* gellable" means embracing not only liquids of low viscosity that form gels upon contact with the eye or with lacrimal fluid in the exterior of the eye, but also more viscous liquids such as semi-fluid and thixotropic gels that exhibit substantially increased viscosity or gel stiffness upon administration to the eye.

As used herein, the phrase "integer from X to Y" means any integer that includes the endpoints. For example, the phrase "integer from X to Y" means 1, 2, 3, 4, or 5.

As used herein, the term "isolated" means that the compounds described herein are separated from other components of either (a) a natural source, such as a plant or cell, or (b) a synthetic organic chemical reaction mixture, such as by conventional techniques.

As used herein, the term "mammal" means a rodent (i.e., a mouse, a rat, or a guinea pig), a monkey, a cat, a dog, a cow, a horse, a pig, or a human. In some embodiments, the mammal is a human.

As used herein, the term "N-alkyl" refers to a alkyl chain that is substituted with an amine group. Non-limiting examples, include, but are not limited to  and the like. The alkyl chain can be linear, branched, cyclic, or any combination thereof. In some embodiments, the alkyl comprises 1-10, 1-9, 1-8, 1-7, 1-6, 1-5, 1-4, 1-3, or 1-2 carbons.

As used herein, the term "nitro" means $-NO_2$.

As used herein, the term "n-membered", where n is an integer, typically describes the number of ring-forming atoms in a moiety, where the number of ring-forming atoms is n.

For example, pyridine is an example of a 6-membered heteroaryl ring and thiophene is an example of a 5-membered heteroaryl ring.

As used herein, the phrase "ophthalmically acceptable" means having no persistent detrimental effect on the treated eye or the functioning thereof, or on the general health of the subject being treated. However, it will be recognized that transient effects such as minor irritation or a "stinging" sensation are common with topical ophthalmic administration of drugs and the existence of such transient effects is not inconsistent with the composition, formulation, or ingredient (e.g., excipient) in question being "ophthalmically acceptable" as herein defined.

As used used herein, the phrase "optionally substituted" means that substitution is optional and therefore includes both unsubstituted and substituted atoms and moieties. A "substituted" atom or moiety indicates that any hydrogen on the designated atom or moiety can be replaced with a selection from the indicated substituent groups, provided that the normal valency of the designated atom or moiety is not exceeded, and that the substitution results in a stable compound. For example, if a methyl group is optionally substituted, then 3 hydrogen atoms on the carbon atom can be replaced with substituent groups.

As used herein, the phrase "pharmaceutically acceptable" means those compounds, materials, compositions, and/or dosage forms which are, within the scope of sound medical judgment, suitable for use in contact with tissues of humans and animals. In some embodiments, "pharmaceutically acceptable" means approved by a regulatory agency of the Federal or a state government or listed in the U.S. Pharmacopeia or other generally recognized pharmacopeia for use in animals, and more particularly in humans.

In some embodiments, the salt of a compound described herein is a pharmaceutically acceptable salt thereof. As used herein, the phrase "pharmaceutically acceptable salt(s)," includes, but is not limited to, salts of acidic or basic groups. Compounds that are basic in nature are capable of forming a wide variety of salts with various inorganic and organic acids. Acids that may be used to prepare pharmaceutically acceptable acid addition salts of such basic compounds are those that form non-toxic acid addition salts, i.e., salts containing pharmacologically acceptable anions including, but not limited to, sulfuric, thiosulfuric, citric, maleic, acetic, oxalic, hydrochloride, hydrobromide, hydroiodide, nitrate, sulfate, bisulfate, bisulfite, phosphate, acid phosphate, isonicotinate, borate, acetate, lactate, salicylate, citrate, acid citrate, tartrate, oleate, tannate, pantothenate, bitartrate, ascorbate, succinate, maleate, gentisinate, fumarate, gluconate, glucaronate, saccharate, formate,

benzoate, glutamate, methanesulfonate, ethanesulfonate, benzenesulfonate, p-toluenesulfonate, bicarbonate, malonate, mesylate, esylate, napsydisylate, tosylate, besylate, orthophoshate, trifluoroacetate, and pamoate (i.e., 1,1′-methylene-bis-(2-hydroxy-3-naphthoate)) salts. Compounds that include an amino moiety may form pharmaceutically acceptable salts with various amino acids, in addition to the acids mentioned above. Compounds that are acidic in nature are capable of forming base salts with various pharmacologically acceptable cations. Examples of such salts include, but are not limited to, alkali metal or alkaline earth metal salts and, particularly, calcium, magnesium, ammonium, sodium, lithium, zinc, potassium, and iron salts. The present invention also includes quaternary ammonium salts of the compounds described herein, where the compounds have one or more tertiary amine moiety.

As used herein, the term "phenyl" means $-C_6H_5$. A phenyl group can be unsubstituted or substituted with one, two, or three suitable substituents.

As used herein, the term "prodrug" means a derivative of a known direct acting drug, which derivative has enhanced delivery characteristics and therapeutic value as compared to the drug, and is transformed into the active drug by an enzymatic or chemical process.

As used herein, the term "purified" means that when isolated, the isolate contains at least 90%, at least 95%, at least 98%, or at least 99% of a compound described herein by weight of the isolate.

As used herein, the phrase "quaternary ammonium salts" means derivatives of the disclosed compounds with one or more tertiary amine moieties wherein at least one of the tertiary amine moieties in the parent compound is modified by converting the tertiary amine moiety to a quaternary ammonium cation via alkylation (and the cations are balanced by anions such as Cl^-, CH_3COO^-, and CF_3COO^-), for example methylation or ethylation.

As used herein, the term "semicarbazone" means $=NNHC(=O)NH_2$.

As used herein, the phrase "solubilizing agent" means agents that result in formation of a micellar solution or a true solution of the drug.

As used herein, the term "solution/suspension" means a liquid composition wherein a first portion of the active agent is present in solution and a second portion of the active agent is present in particulate form, in suspension in a liquid matrix.

As used herein, the phrase "substantially isolated" means a compound that is at least partially or substantially separated from the environment in which it is formed or detected.

As used herein, the phrase "suitable substituent" or "substituent" means a group that does not nullify the synthetic or pharmaceutical utility of the compounds described herein or the intermediates useful for preparing them. Examples of suitable substituents include, but are not limited to: C_1-C_6alkyl, C_1-C_6alkenyl, C_1-C_6alkynyl, C_5-C_6aryl, C_1-C_6alkoxy, C_3-C_5heteroaryl, C_3-C_6cycloalkyl, C_5-C_6aryloxy, -CN, -OH, oxo, halo, haloalkyl, -NO_2, -CO_2H, -NH_2, -NH(C_1-C_8alkyl), -N(C_1-C_8alkyl)$_2$, -NH(C_6aryl), -N(C_5-C_6aryl)$_2$, -CHO, -CO(C_1-C_6alkyl), -CO((C_5-C_6)aryl), -CO_2((C_1-C_6)alkyl), and -CO_2((C_5-C_6)aryl). One of skill in art can readily choose a suitable substituent based on the stability and pharmacological and synthetic activity of the compounds described herein.

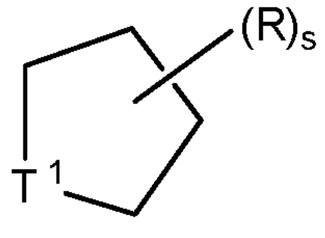
As used herein, the phrase "therapeutically effective amount" means the amount of active compound or pharmaceutical agent that elicits the biological or medicinal response that is being sought in a tissue, system, animal, individual or human by a researcher, veterinarian, medical doctor or other clinician. The therapeutic effect is dependent upon the disorder being treated or the biological effect desired. As such, the therapeutic effect can be a decrease in the severity of symptoms associated with the disorder and/or inhibition (partial or complete) of progression of the disorder, or improved treatment, healing, prevention or elimination of a disorder, or side-effects. The amount needed to elicit the therapeutic response can be determined based on the age, health, size and sex of the subject. Optimal amounts can also be determined based on monitoring of the subject's response to treatment.

As used herein, the terms "treat," "treated," or "treating" mean both therapeutic treatment and prophylactic measures wherein the object is to slow down (lessen) an undesired physiological condition, disorder or disease, or obtain beneficial or desired clinical results. For purposes of this invention, beneficial or desired clinical results include, but are not limited to, alleviation of symptoms; diminishment of extent of condition, disorder or disease; stabilized (i.e., not worsening) state of condition, disorder or disease; delay in onset or slowing of condition, disorder or disease progression; amelioration of the condition, disorder or disease state or remission (whether partial or total), whether detectable or undetectable; an amelioration of at least one measurable physical parameter, not necessarily discernible by the patient; or enhancement or improvement of condition, disorder or disease. Treatment includes eliciting a clinically significant response without excessive levels of side effects. Treatment also includes prolonging survival as compared to expected survival if not receiving treatment. Thus, "treatment of pain" or "treating pain" means an activity that

alleviates or ameliorates any of the primary phenomena or secondary symptoms associated with the pain or other condition described herein.

As used herein, the term "ureido" means -NHC(=O)-NH_2.

At various places in the present specification, substituents of compounds may be disclosed in groups or in ranges. It is specifically intended that embodiments include each and every individual subcombination of the members of such groups and ranges. For example, the term "C_{1-6}alkyl" is specifically intended to individually disclose methyl, ethyl, propyl, C_4alkyl, C_5alkyl, and C_6alkyl.

For compounds in which a variable appears more than once, each variable can be a different moiety selected from the Markush group defining the variable. For example, where a structure is described having two R groups that are simultaneously present on the same compound, the two R groups can represent different moieties selected from the Markush groups defined for R. In another example, when an optionally multiple substituent is designated in the form, for example, 

, then it is understood that substituent R can occur s number of times on the ring, and R can be a different moiety at each occurrence. Further, in the above example, where the variable T^1 is defined to include hydrogens, such as when T^1 is CH_2, NH, etc., any H can be replaced with a substituent.

It is further appreciated that certain features described herein, which are, for clarity, described in the context of separate embodiments, can also be provided in combination in a single embodiment. Conversely, various features which are, for brevity, described in the context of a single embodiment, can also be provided separately or in any suitable subcombination.

It is understood that the present invention encompasses the use, where applicable, of stereoisomers, diastereomers and optical stereoisomers of the compounds of the invention, as well as mixtures thereof. Additionally, it is understood that stereoisomers, diastereomers, and optical stereoisomers of the compounds of the invention, and mixtures thereof, are within the scope of the invention. By way of non-limiting example, the mixture may be a racemate or the mixture may comprise unequal proportions of one particular stereoisomer over the other. Additionally, the compounds can be provided as a substantially pure stereoisomers, diastereomers and optical stereoisomers (such as epimers).

The compounds described herein can be asymmetric (e.g., having one or more stereocenters). All stereoisomers, such as enantiomers and diastereomers, are intended to be included within the scope of the invention unless otherwise indicated. Compounds that contain asymmetrically substituted carbon atoms can be isolated in optically active or racemic forms. Methods of preparation of optically active forms from optically active starting materials are known in the art, such as by resolution of racemic mixtures or by stereoselective synthesis. Many geometric isomers of olefins, C=N double bonds, and the like can also be present in the compounds described herein, and all such stable isomers are contemplated in the present invention. *Cis* and *trans* geometric isomers of the compounds are also included within the scope of the invention and can be isolated as a mixture of isomers or as separated isomeric forms. Where a compound capable of stereoisomerism or geometric isomerism is designated in its structure or name without reference to specific R/S or cis/trans configurations, it is intended that all such isomers are contemplated.

Resolution of racemic mixtures of compounds can be carried out by any of numerous methods known in the art, including, for example, chiral HPLC, fractional recrystallizaion using a chiral resolving acid which is an optically active, salt-forming organic acid. Suitable resolving agents for fractional recrystallization methods include, but are not limited to, optically active acids, such as the D and L forms of tartaric acid, diacetyltartaric acid, dibenzoyltartaric acid, mandelic acid, malic acid, lactic acid, and the various optically active camphorsulfonic acids such as β-camphorsulfonic acid. Other resolving agents suitable for fractional crystallization methods include, but are not limited to, stereoisomerically pure forms of α-methylbenzylamine (e.g., *S* and *R* forms, or diastereomerically pure forms),
2-phenylglycinol, norephedrine, ephedrine, N-methylephedrine, cyclohexylethylamine, 1,2-diaminocyclohexane, and the like. Resolution of racemic mixtures can also be carried out by elution on a column packed with an optically active resolving agent (e.g., dinitrobenzoylphenylglycine). Suitable elution solvent compositions can be determined by one skilled in the art.

Compounds may also include tautomeric forms. Tautomeric forms result from the swapping of a single bond with an adjacent double bond together with the concomitant migration of a proton. Tautomeric forms include prototropic tautomers which are isomeric protonation states having the same empirical formula and total charge. Examples of prototropic tautomers include, but are not limited to, ketone-enol pairs, amide-imidic acid

pairs, lactam-lactim pairs, amide-imidic acid pairs, enamine-imine pairs, and annular forms where a proton can occupy two or more positions of a heterocyclic system including, but not limited to, 1H- and 3H-imidazole, 1H-, 2H- and 4H-1,2,4-triazole, 1H- and 2H- isoindole, and 1H- and 2H-pyrazole. Tautomeric forms can be in equilibrium or sterically locked into one form by appropriate substitution.

Compounds also include hydrates and solvates, as well as anhydrous and non-solvated forms.

Compounds can also include all isotopes of atoms occurring in the intermediates or final compounds. Isotopes include those atoms having the same atomic number but different mass numbers. For example, isotopes of hydrogen include tritium and deuterium.

In some embodiments, the compounds, or salts thereof, are substantially isolated. Partial separation can include, for example, a composition enriched in the compound of the invention. Substantial separation can include compositions containing at least about 50%, at least about 60%, at least about 70%, at least about 80%, at least about 90%, at least about 95%, at least about 97%, or at least about 99% by weight of the compound of the invention, or salt thereof. Methods for isolating compounds and their salts are routine in the art.

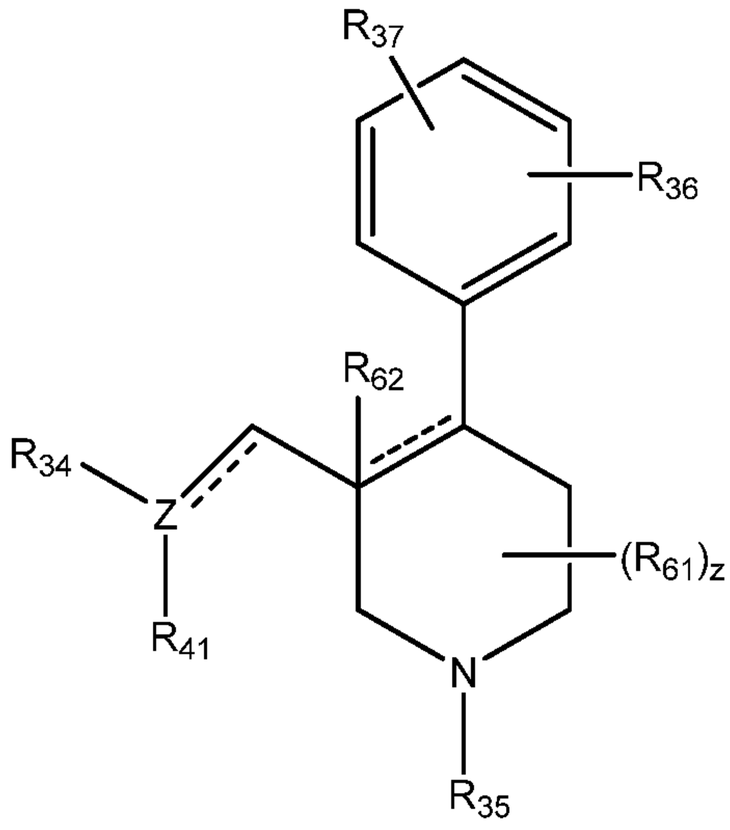
Although the disclosed compounds are suitable, other functional groups can be incorporated into the compound with an expectation of similar results. In particular, thioamides and thioesters are anticipated to have very similar properties. The distance between aromatic rings can impact the geometrical pattern of the compound and this distance can be altered by incorporating aliphatic chains of varying length, which can be optionally substituted or can comprise an amino acid, a dicarboxylic acid or a diamine. The distance between and the relative orientation of monomers within the compounds can also be altered by replacing the amide bond with a surrogate having additional atoms. Thus, replacing a carbonyl group with a dicarbonyl alters the distance between the monomers and the propensity of dicarbonyl unit to adopt an anti arrangement of the two carbonyl moiety and alter the periodicity of the compound. Pyromellitic anhydride represents still another alternative to simple amide linkages which can alter the conformation and physical properties of the compound. Modern methods of solid phase organic chemistry (E. Atherton and R. C. Sheppard, Solid Phase Peptide Synthesis A Practical Approach IRL Press Oxford 1989) now allow the synthesis of homodisperse compounds with molecular weights approaching 5,000 Daltons. Other substitution patterns are equally effective.

The compounds also include derivatives referred to as prodrugs.

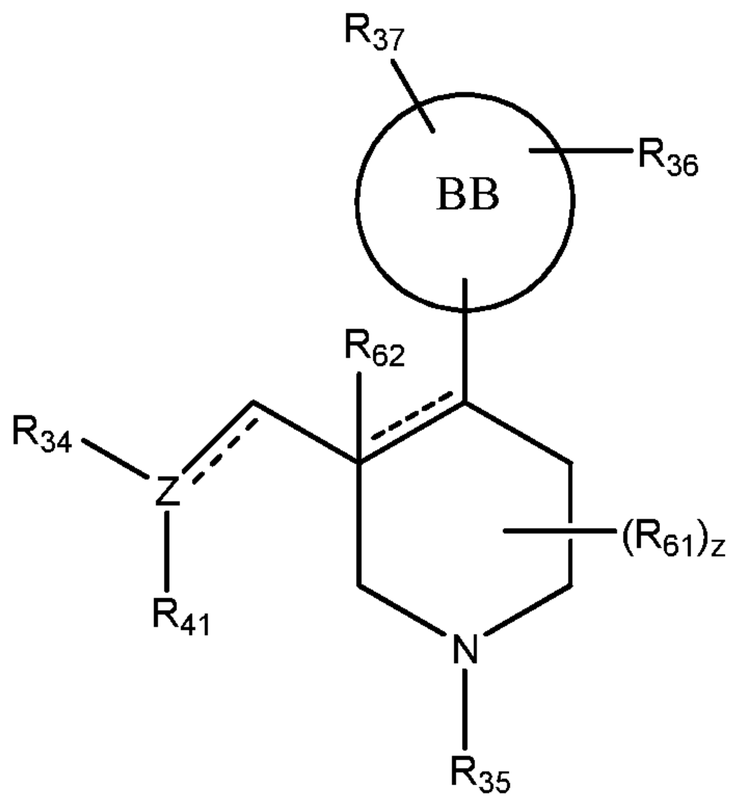
Compounds containing an amine function can also form N-oxides. A reference herein to a compound that contains an amine function also includes the N-oxide. Where a compound contains several amine functions, one or more than one nitrogen atom can be oxidized to form an N-oxide. Examples of N-oxides include N-oxides of a tertiary amine or a nitrogen atom of a nitrogen-containing heterocycle. N-Oxides can be formed by treatment of the corresponding amine with an oxidizing agent such as hydrogen peroxide or a per-acid (e.g., a peroxycarboxylic acid) (see, Advanced Organic Chemistry, by Jerry March, 4th Edition, Wiley Interscience).

Embodiments of various compounds and salts thereof are provided. Where a variable is not specifically recited, the variable can be any option described herein, except as otherwise noted or dictated by context.

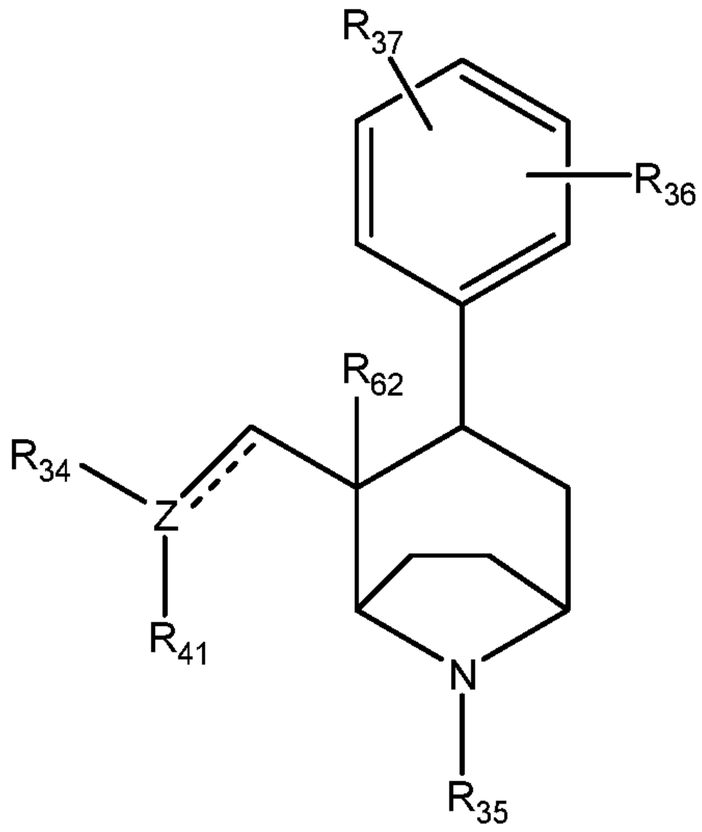
In some embodiments, compounds having Formula I, I-1, I-a, I-a1 or I-b, Ib-1, or Ib-2or pharmaceutically acceptable salt thereof are provided:



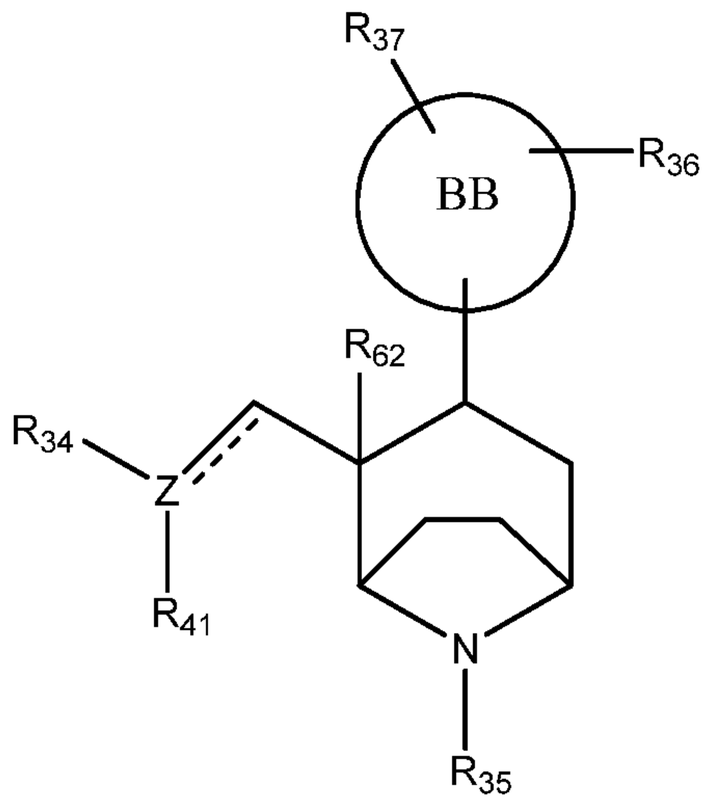
I



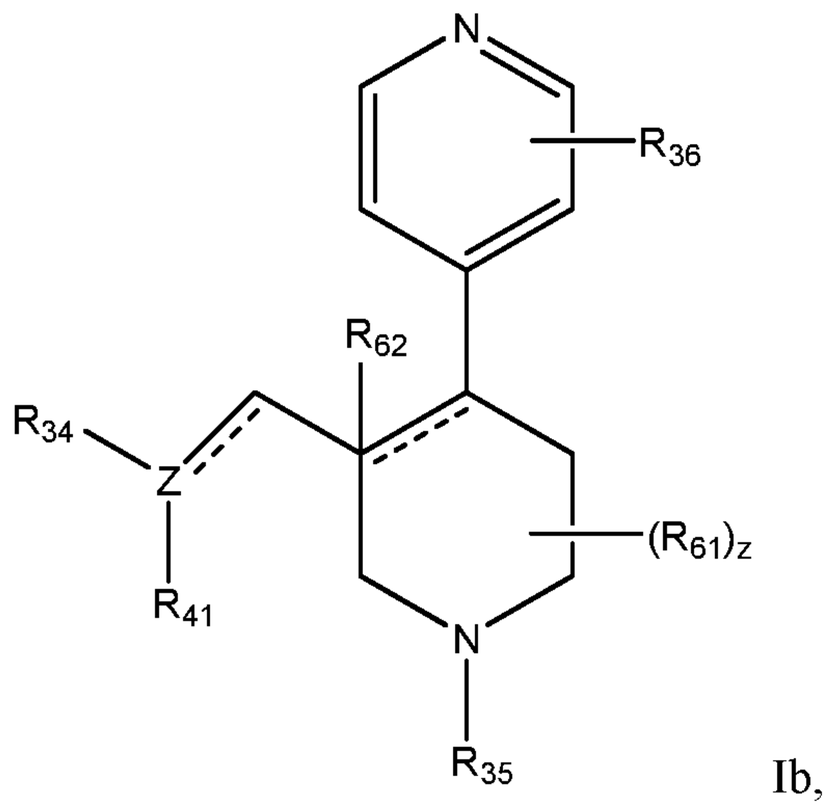
I-1



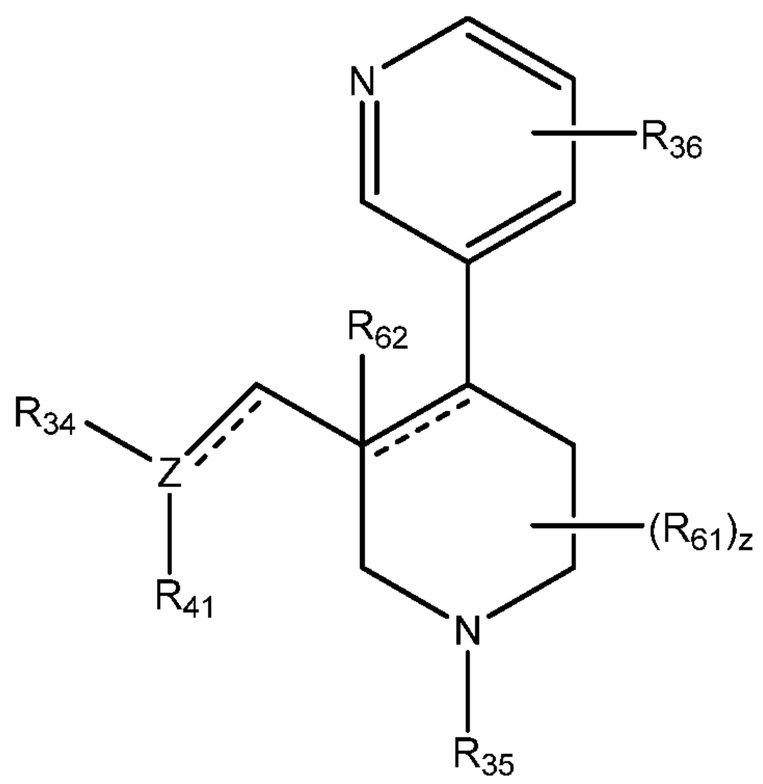
Ia, ,



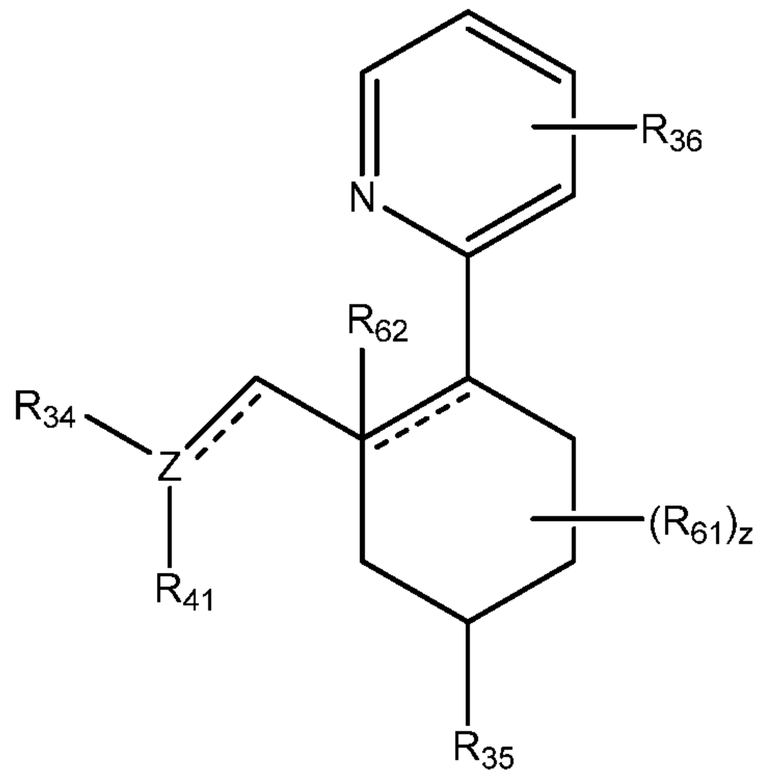
Ia-1



Ib,



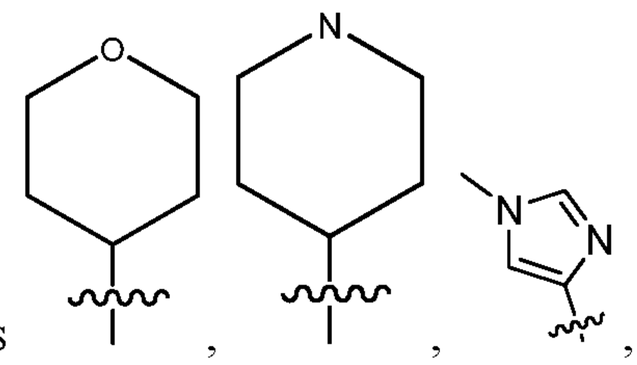
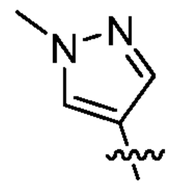
Ib-1, or



Ib-2

or pharmaceutically acceptable salt thereof, wherein:

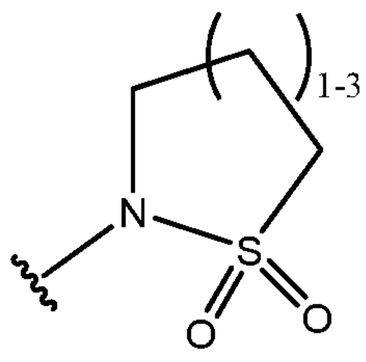
wherein

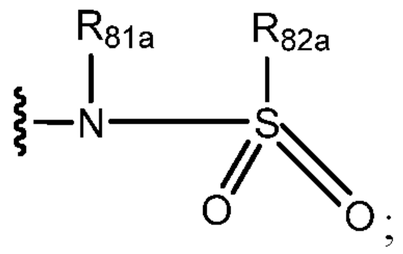
BB is cycloalkyl, heterocycle, imidazole, such as  , ,or  ;

Z is C, S, N, $S(O)_2$ or O;

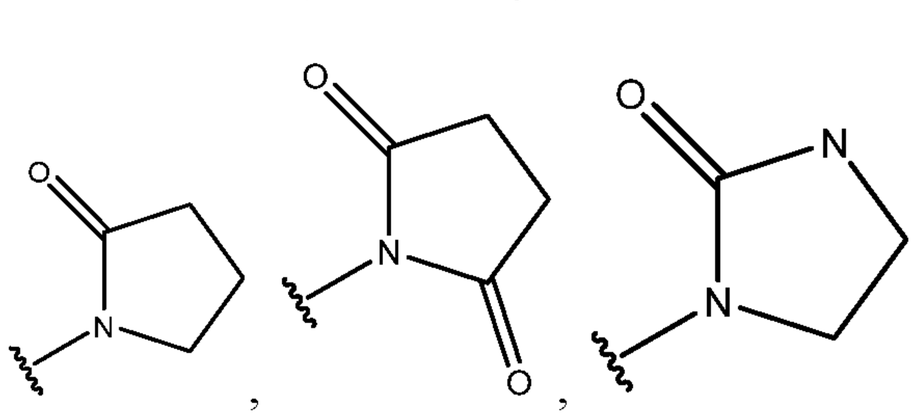
R_{35} is a protecting group, $C(=O)OR_{81b}$, H, optionally substituted aryl, optionally substituted C_1-C_6 haloalkyl, -$R_{63}R_{64}$, optionally substituted C_1-C_6 branched or unbranched alkyl, optionally substituted C_2-C_6 alkenyl, optionally substituted C_2-C_6 haloalkenyl – (CH2)nR_{65}, optionally substituted heterocycle, optionally substituted C_1-C_6 ester, optionally substituted cycloalkyl, optionally substituted C_1-C_6 alkoxy, optionally substituted pyrrolinyl, optionally substituted morpholinyl, , optionally substituted C_3-C_6 cyclic ether, or optionally substituted piperidyl;

R_{36} is null, H, halo, optionally substituted C_1-C_6 haloalkyl, -SO_2C_1-C_6alkyl, -OCF_3, optionally substituted C_1-C_6 alkyl, or -OR_{75}; wherein R_{75} is H or optionally substituted C_1-C_6 alkyl;

R_{37} is, null, H, halo, optionally substituted C_1-C_6 haloalkyl, -SO_2C_1-C_6alkyl, -OCF3, optionally substituted sulfonamide, optionally substituted cyclic sulfonamide, -(CH2)q-R38, -NH-(CH2)q-R38, -S-(CH2)q-R38, -C(=O)R38, or -O-(CH2)q-R38, 

,or 

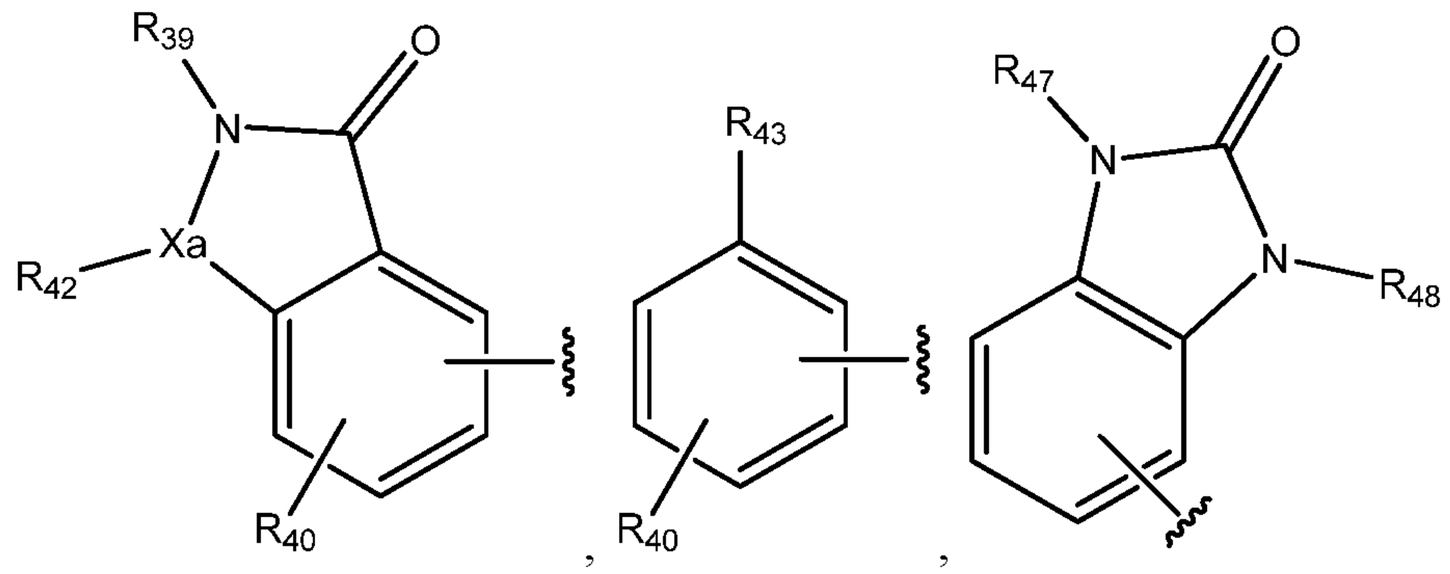
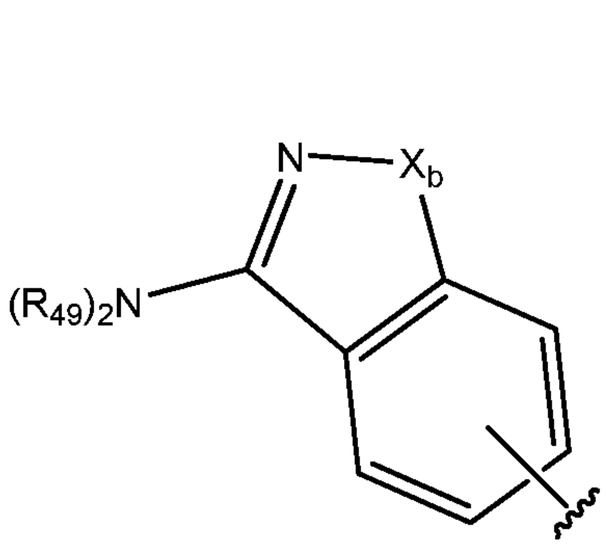
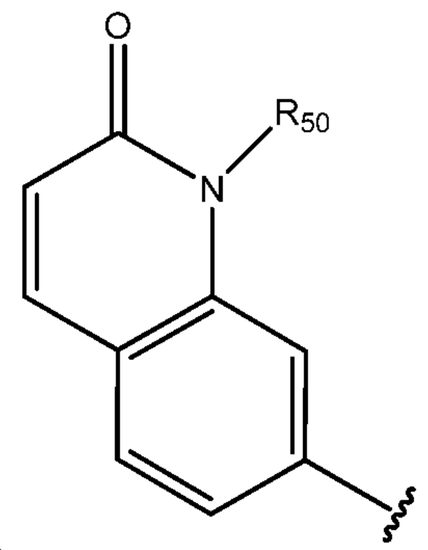
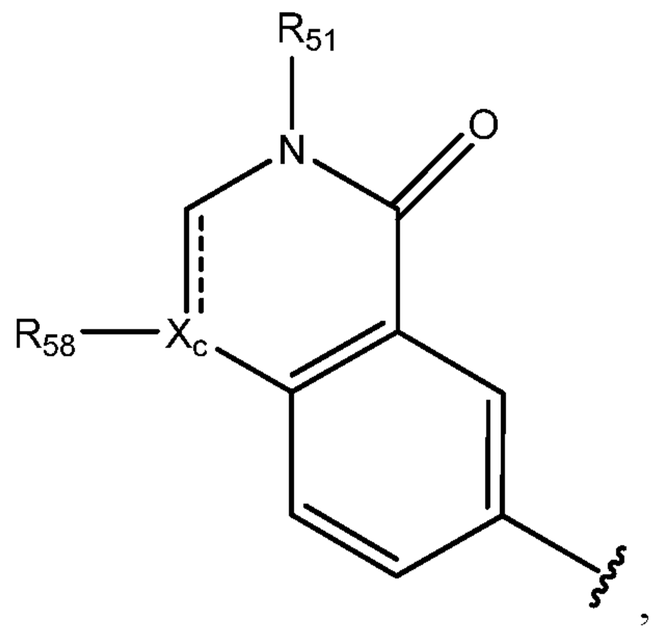
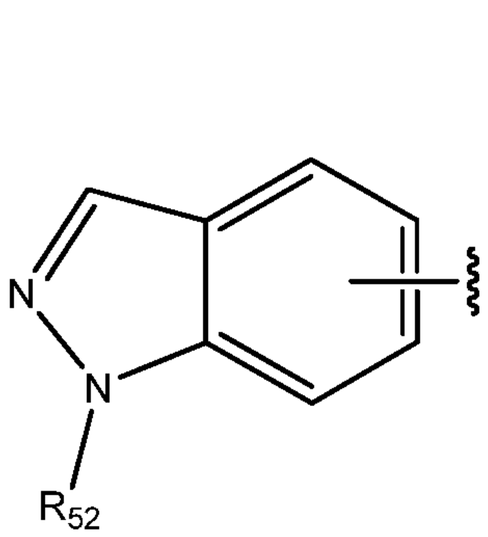
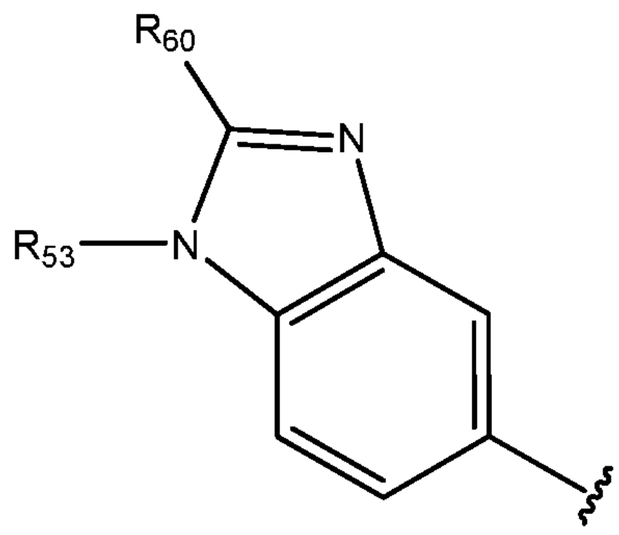
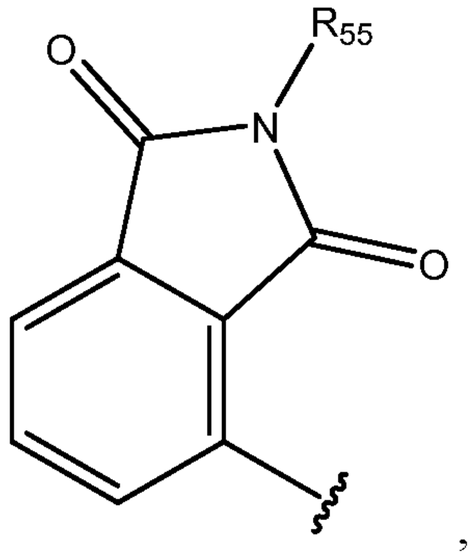
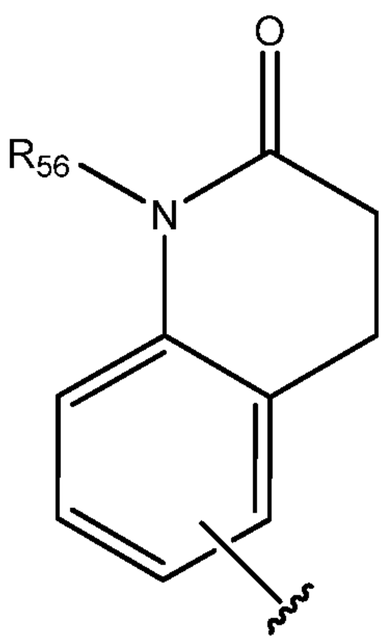
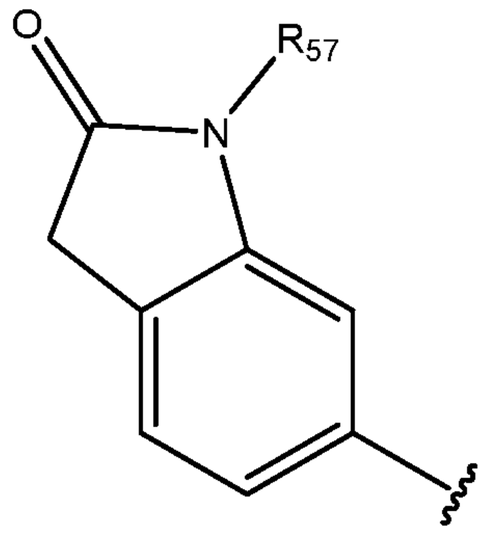
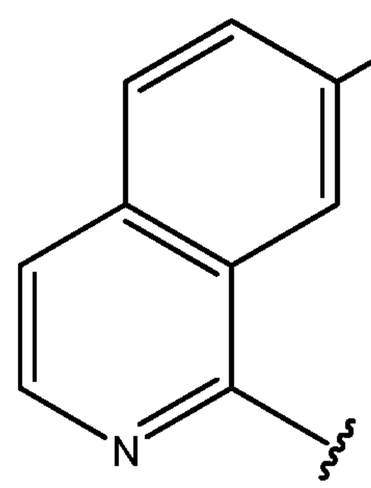
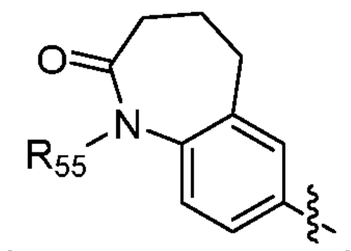
;

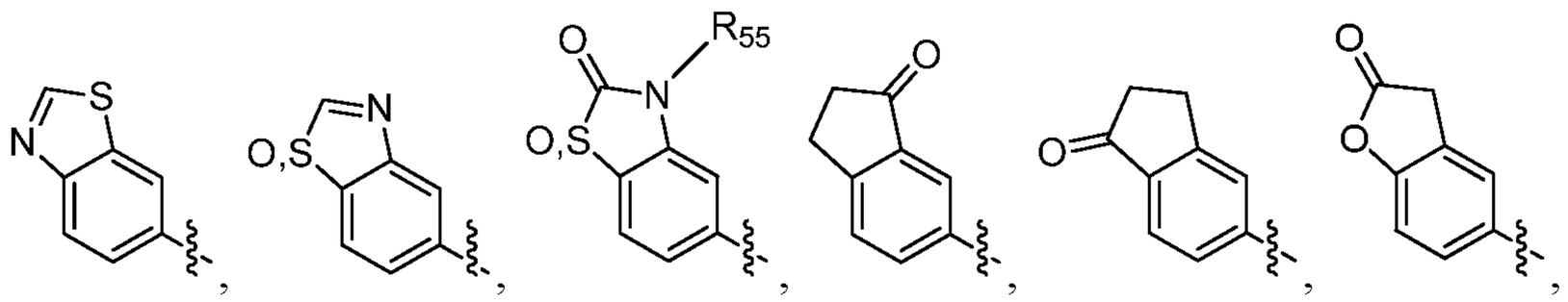
R_{38} is H, C_1-C_6 alkyl, halo, C_1-C_6 haloalkyl, -C(=O)C_1-C_6 alkyl, –OR_{66}, $S(O)_2R_{67}$ 

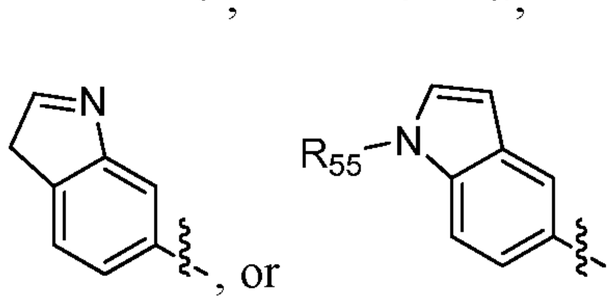
, optionally substituted cycloalkyl, -$(CH_2)_pR_{65}$, or optionally substituted heterocycle;

or R_{37} is-(CH2)q-R_{38} or R_{36} and R_{37} form a heterocycle that is fused to the phenyl ring;

R_{41} is absent, H, or C_1-C_6 alkyl provided that when Z is S, O or $S(O)_2$, R_{41} is absent; or when Z is C, the bond connecting Z to the adjacent carbon is a double bond and R_{41} is H,

R_{34} is  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,





, or

wherein,

R_{39} is H or C_1-C_6 alkyl;

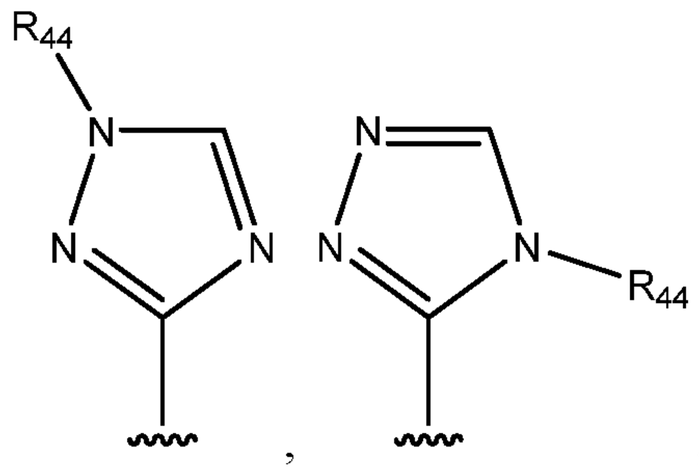
R_{40} is H, C_1-C_6 alkyl, halo, or alkoxy;

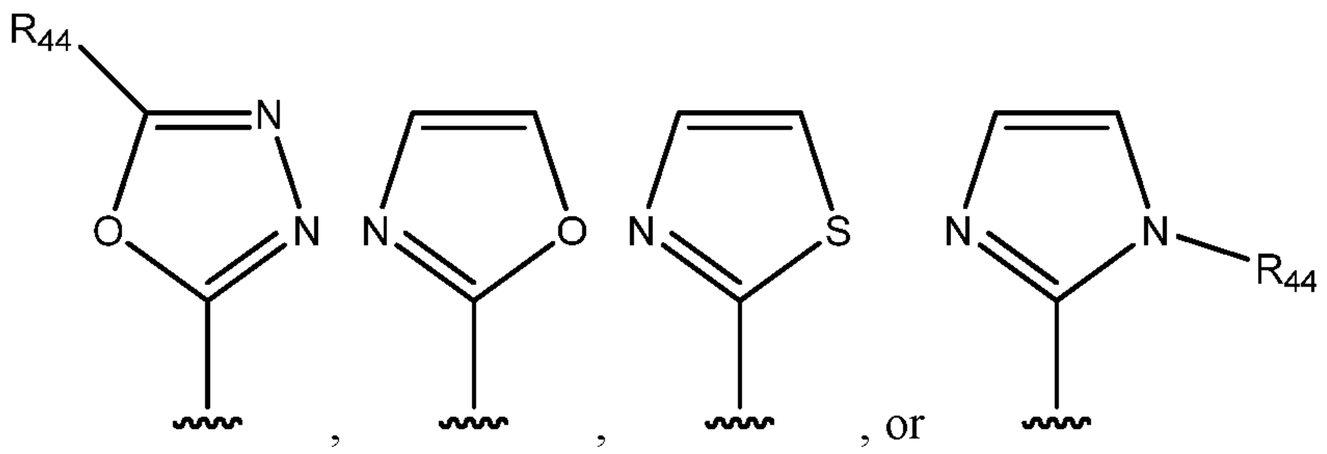
R_{42} is absent, H, C_1-C_6 alkyl, a member of a carbocyle that includes the atom to which it is attached, or =O;

X_a is C or O, provided that when X_a is O, R_{42} is absent;

X_b is S or O;

X_c is C or N;

R_{43} is -OH, -CN, -C(=O)$NR_{45}R_{46}$, 



wherein: R_{44} is H or C_1-C_6 alkyl; R_{45} is H or C_1-C_6 alkyl; and R_{46} is H or C_1-C_6 alkyl;

R_{47} is H or C_1-C_6 alkyl;

R_{48} is H or C_1-C_6 alkyl;

each R_{49} is, independently, H or C_1-C_6 alkyl;

R_{50} is H or C_1-C_6 alkyl;

R_{51} is H or C_1-C_6 alkyl;

R_{52} is H or C_1-C_6 alkyl;

R_{53} is H or C_1-C_6 alkyl;

R_{55} is H or C_1-C_6 alkyl;

R_{56} is H or C_1-C_6 alkyl;

R_{57} is H or C_1-C_6 alkyl;

R_{58} is absent or H;

R_{59} is H or OH;

R_{60} is H or $N(R_{54})_2$;

each R_{54} is, independently, H or C_1-C_6 alkyl;

R_{61} is H, C_1-C_6 alkyl, optionally substituted C_1-C_6 haloalkyl, gem-dimethyl, cyclopropyl spirocycle, or CF_3;

R_{62} is absent, H, or C_1-C_6 alkyl;

each R_{63} and R_{64} are, independently, H, optionally substituted aryl, optionally substituted C_1-C_6 haloalkyl, optionally substituted C_1-C_6 branched or unbranched alkyl, optionally substituted C_2-C_6 alkenyl, $-(CH_2)_vR_{65}$, optionally substituted cycloalkyl, -OH, optionally substituted alkoxy, optionally substituted pyrrolinyl, optionally substituted morpholinyl, or optionally substituted piperidyl; or R_{63} and R_{64} together form a 5-10 membered optionally substituted heterocycle or a 5-10 membered optionally substituted heteroaryl with the atom to which R_{63} and R_{64} are bonded to;

each R_{65} is, independently, H, $-C(=O)R_{65A}$, optionally substituted C_1-C_6 haloalkyl, optionally substituted nitrogen, optionally substituted C_1-C_6 branched or unbranched alkyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted C_2-C_6 alkenyl, optionally substituted cycloalkyl, optionally substituted heterocycle, -OH, optionally substituted alkoxy, optionally substituted pyrrolinyl, optionally substituted phenyl, optionally substituted pyrrolidinyl, optionally substituted imidazolidinyl, optionally substituted morpholinyl, or optionally substituted piperidyl;

R_{65A} is phenyl or C_1-C_6 branched or unbranched alkyl;

R_{66} is H, optionally substituted aryl, optionally substituted C_1-C_6 haloalkyl, $-NR_{63}R_{64}$, optionally substituted C_1-C_6 branched or unbranched alkyl, optionally substituted C_2-C_6 alkenyl, $-(CH_2)_wR_{65}$, optionally substituted cycloalkyl, -OH, optionally substituted alkoxy,

optionally substituted pyrrolinyl, optionally substituted morpholinyl, or optionally substituted piperidyl;

R_{67} is optionally substituted C_1-C_6 branched or unbranched alkyl, optionally substituted C_1-C_6 haloalkyl;

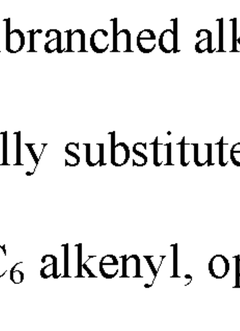
R_{81a} and R_{82a} are each independently H or optionally substituted C_1-C_6 alkyl;

R_{81b} is H or optionally substituted branched or unbranched C_1-C_6 alkyl;

z is 1 or 2,

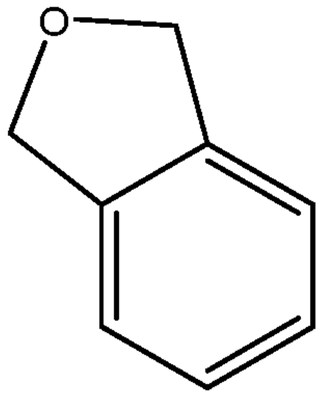
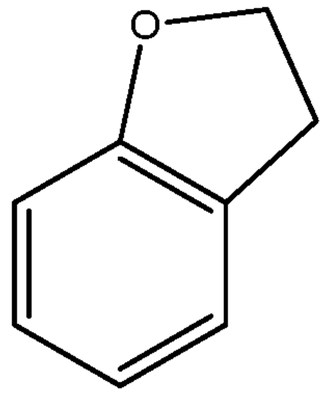
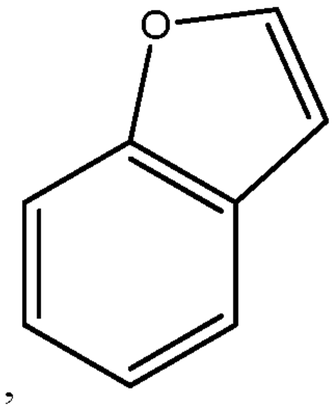
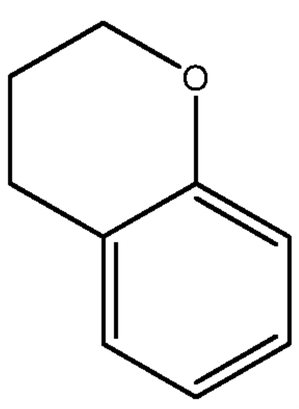
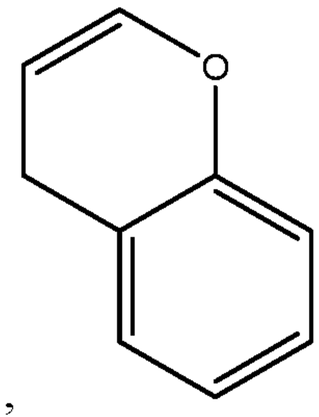
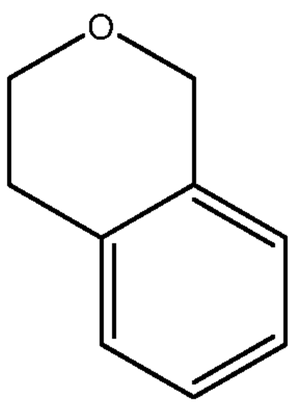
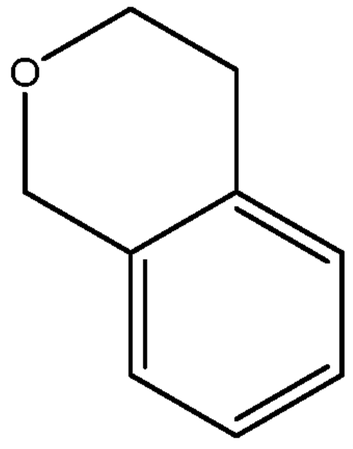
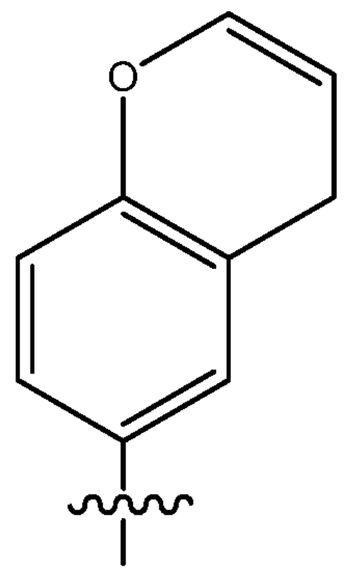
each n, p, v, w, and q is, independently, an integer from 0-6.

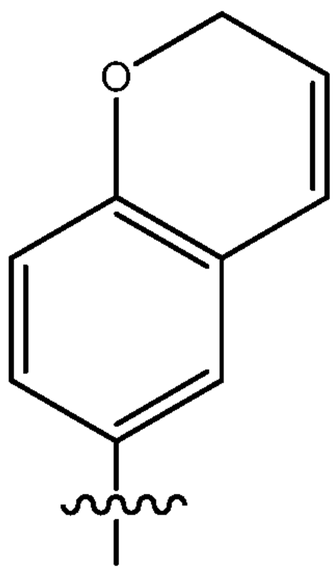
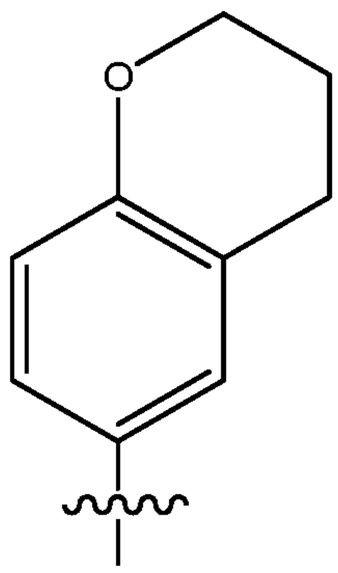
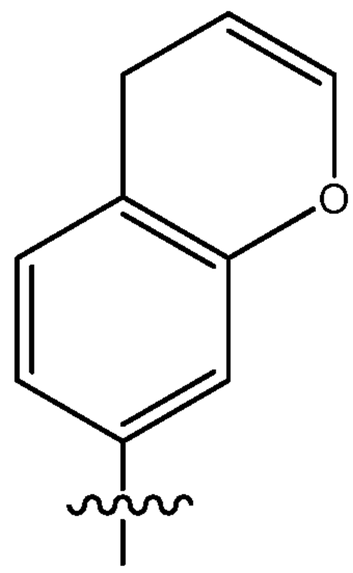
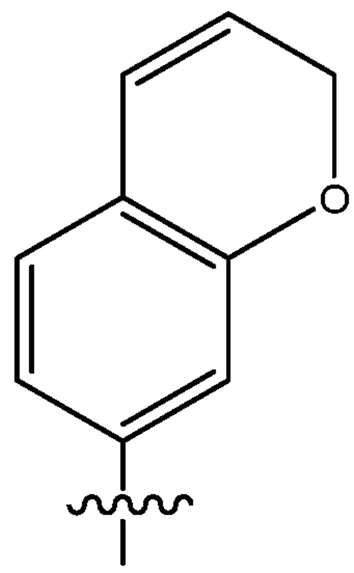
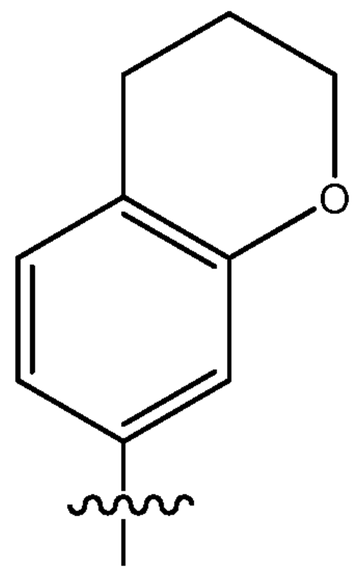
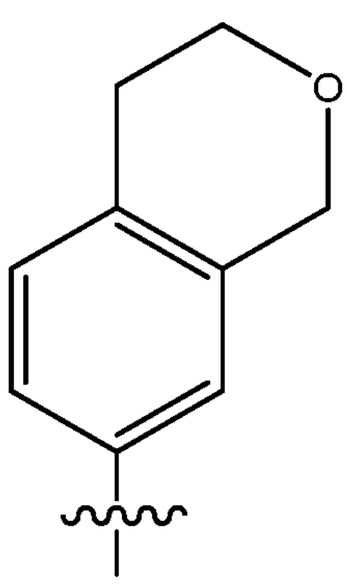
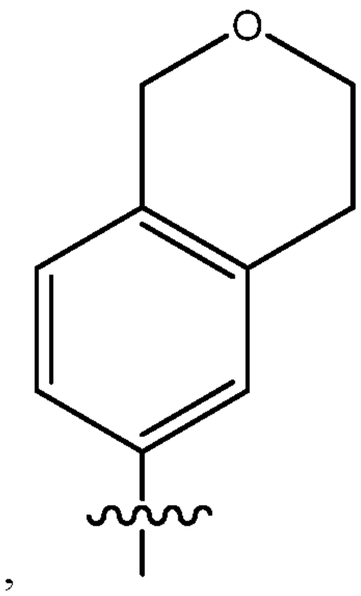
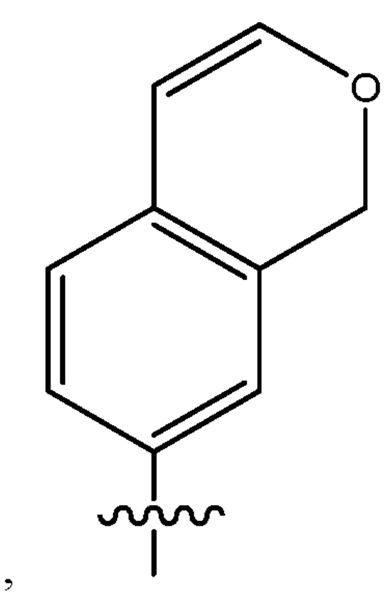
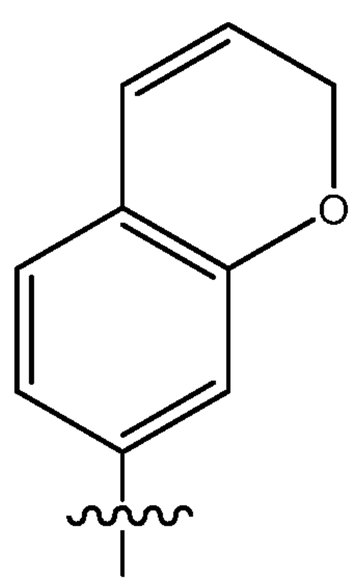
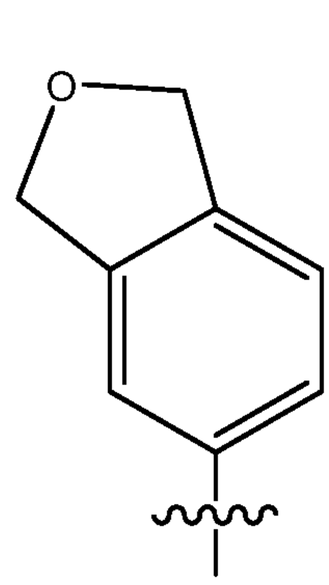
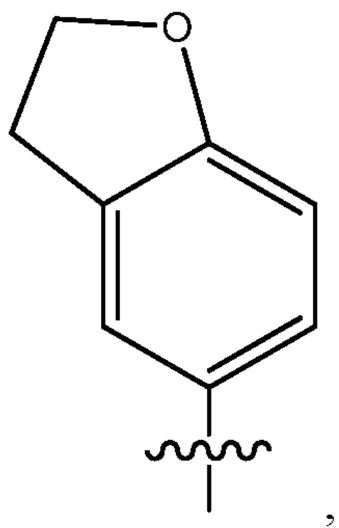
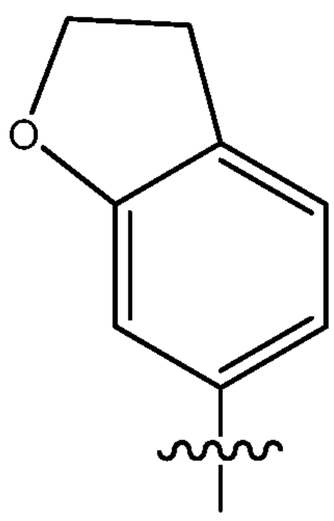
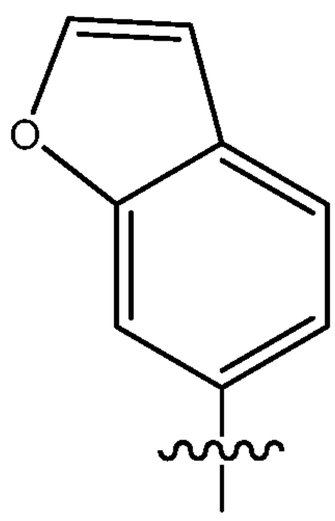
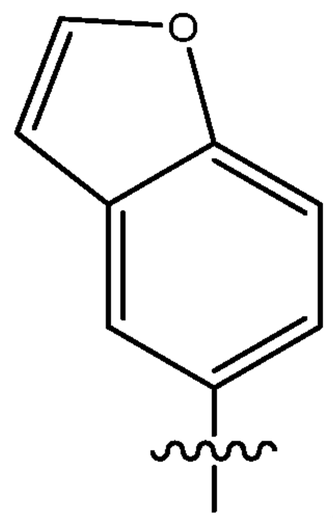
In some embodiments, R_{81b} is is t-butyl. In some embodimens, z is 1. In some embodiments z is 2. In some embodiments, when z is 2, one of R_{61} is H. In some embodiments, when z is 2, one of R_{61} is methyl. In some embodiments, when z is 2, each of R_{61} is independently, methyl or gem-dimethyl. In some embodiments, each R_{61} is the same.

In some embodiments, R_{35} is $-CH_2CH_2R_{76}$, wherein R_{76} is an optionally substituted aryl, heteroaryl or heterocycle. In some embodiments, R_{76} is phenyl. In some embodiments, R_{35} is optionally substituted C_1-C_6 branched or unbranched alkyl, $–CH_2R_{76}$ or$–CH_2CH_2R_{76}$, wherein R_{76} is optionally substituted aryl, optionally substituted ketone, optionally substituted cycloalkyl, optionally substituted C_2-C_6 alkenyl, optionally substituted C_2-C_6 haloalkenyl, or optionally substituted heteroaryl. In some embodiments, R_{76} is optionally substituted cyclopropyl. In some embodiments, R_{76} is diflourocyclopropyl. In some embodiments, R_{76} is 2,2-diflourocyclopropyl. In some embodiments R_{76} is C_2 halo-substitued alkenyl. The substitution can be mono- or di-substituted. In some embodiments, R_{76} is $–C=CF_2$. In some embodimens, R_{76} is optionally substituted pyrrole or optionally substituted alkenyl. In some embodiments, R_{76} is 

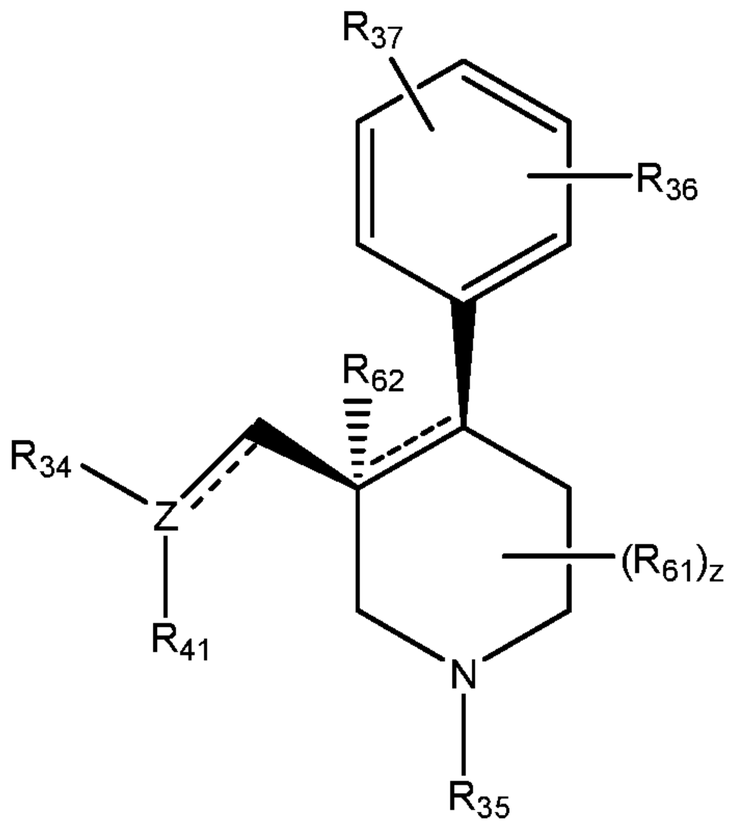
. In some embodiments, R_{76} is

cyclopropyl, halo substituted cylcopropyl, phenyl, -C(=O)R_{XA}, wherein R_{XA} is optionally substituted phenyl or optionally substituted C_1-C_6 branched or unbranched alkyl.

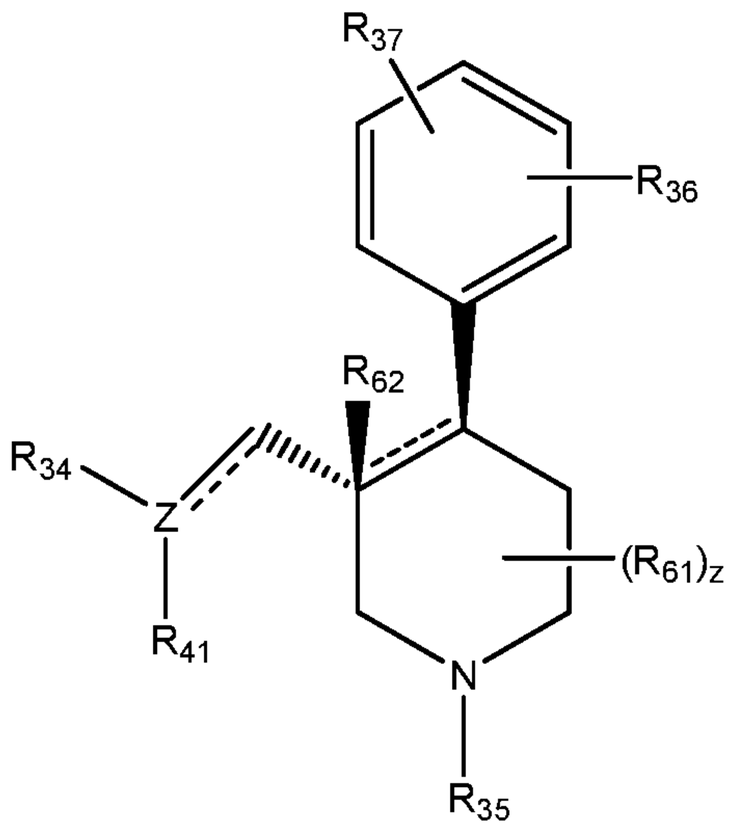
As used herein, the phrase "R_{36} and R_{37} form a heterocycle that is fused to the phenyl ring" refers to a structure that results in a fused ring structure. Non-limiting examples of such a structure include  ,  ,  and the like. In some embodiments, the fused ring is a 6 membered ring with or without the oxygen shown here. In some embodiments, the fused ring is aromatic. In some embodiments, the fused ring is not aromatic. For example, the fused ring can form a structure including, but not limited to,  ,  ,  ,  . Other non-limiting examples include benzofuran and benzopyran. The structure can also be represented using the following formula in context with the remaining compound:  ,


,

,

,

,

,

,

,

,

,

,

,

,

, or

. These are non-limiting examples. Examples of such structures are also shown in Figure 1. The location of the fusion can change as can the heteroatom. For example, the oxygen atom shown in this example can also be a nitrogen. Additionally, the ring structures can be substituted.

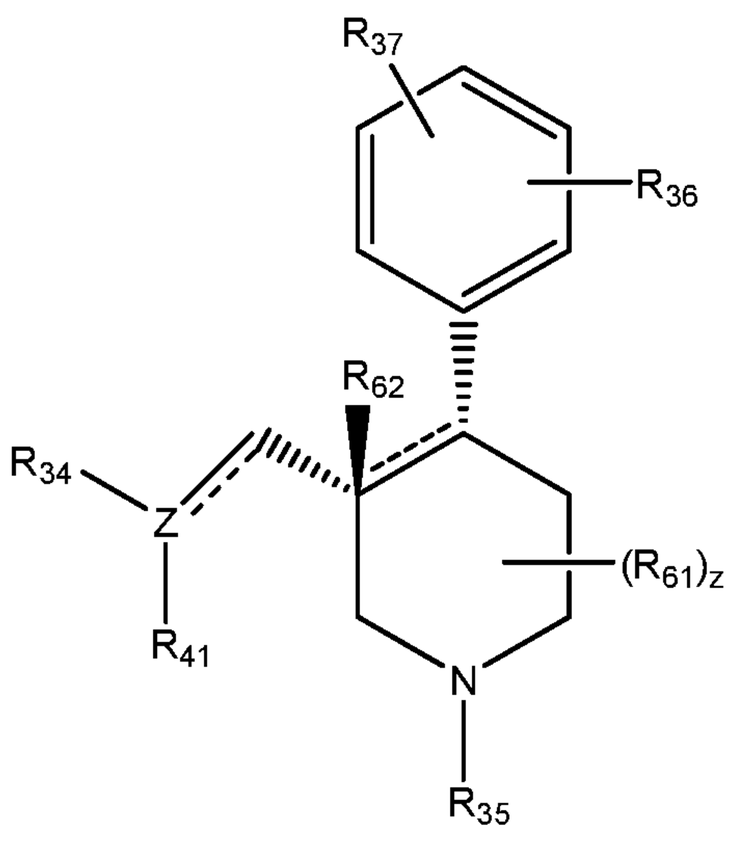
In some embodiments, the compounds of Formula I, Ia or Ib, or pharmaceutically acceptable salt thereof, have a formula of Formula II, III, IV, and V:


R37
R36
R62
R34
Z
R41
(R61)z
N
R35

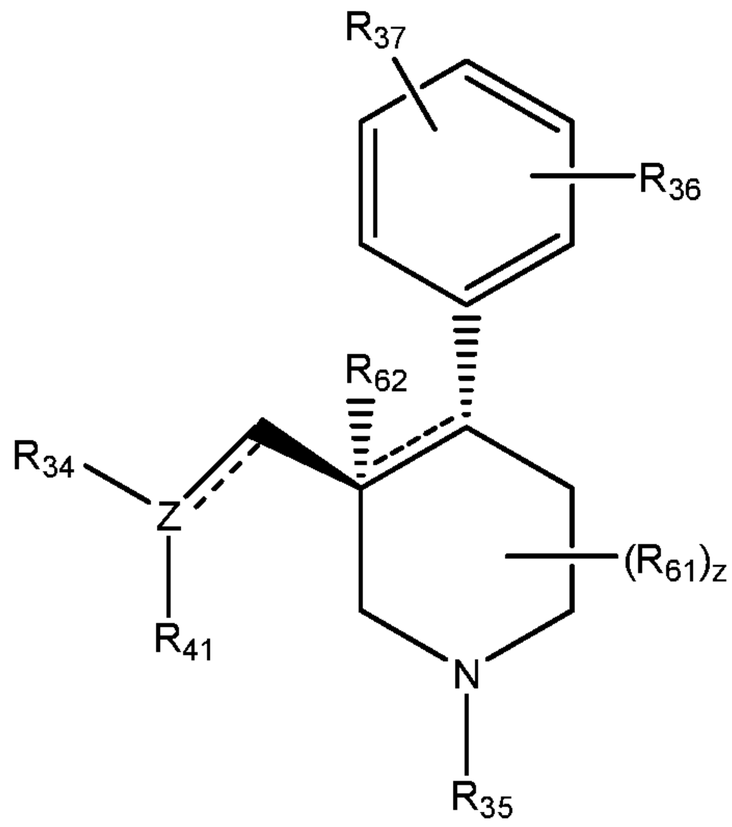
II


R37
R36
R62
R34
Z
R41
(R61)z
N
R35

III

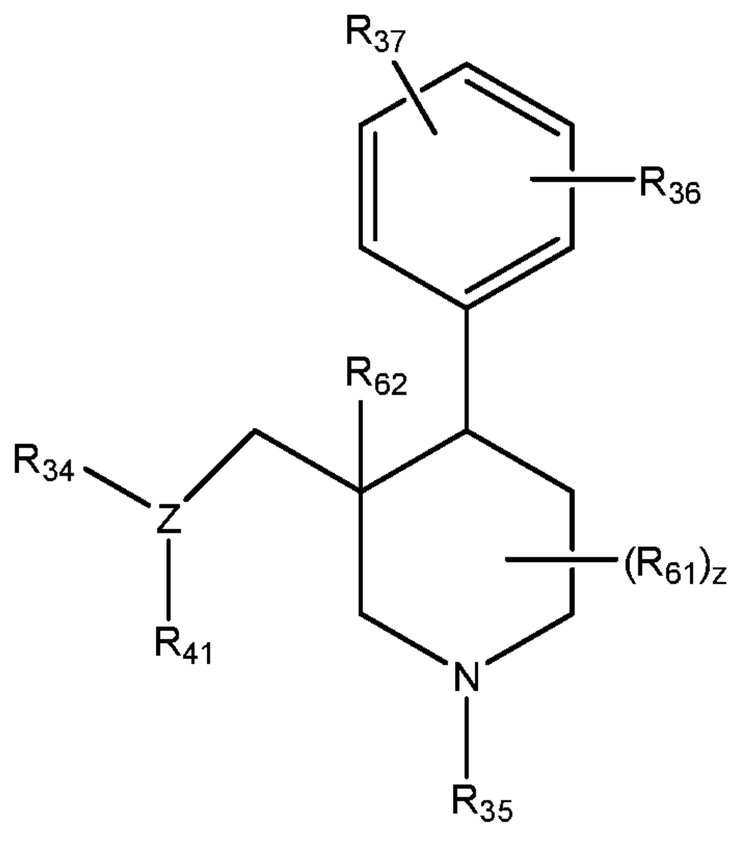

R37
R36
R62
R34
Z
R41
(R61)z
N
R35

IV,



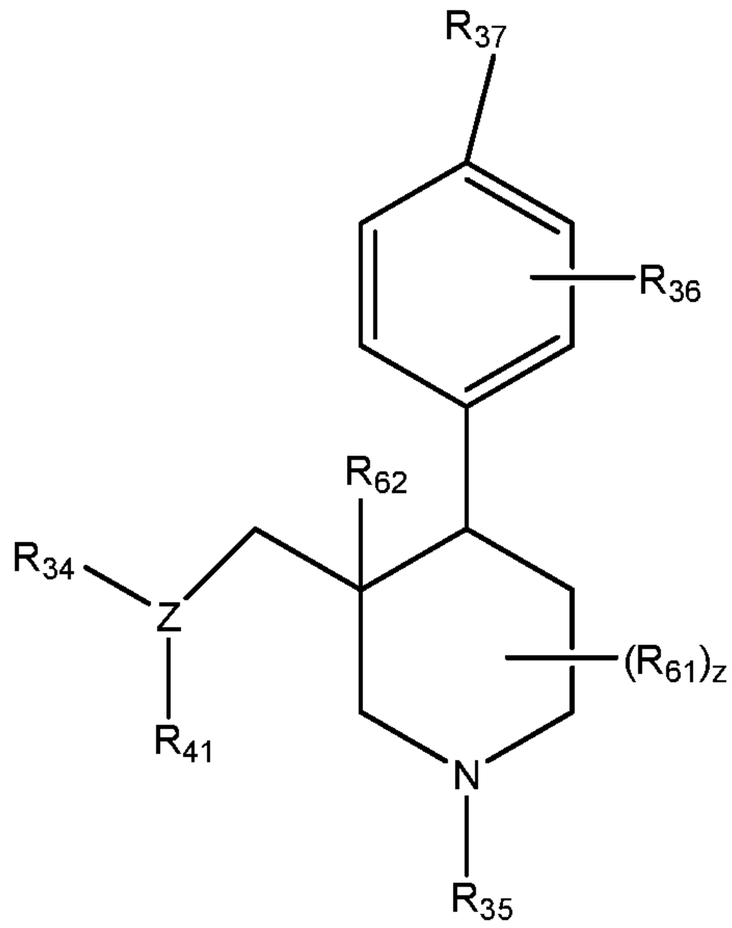
V.

In some embodiments, the compounds of Formula I, Ia or Ib, or pharmaceutically acceptable salt thereof, have a formula of VI:

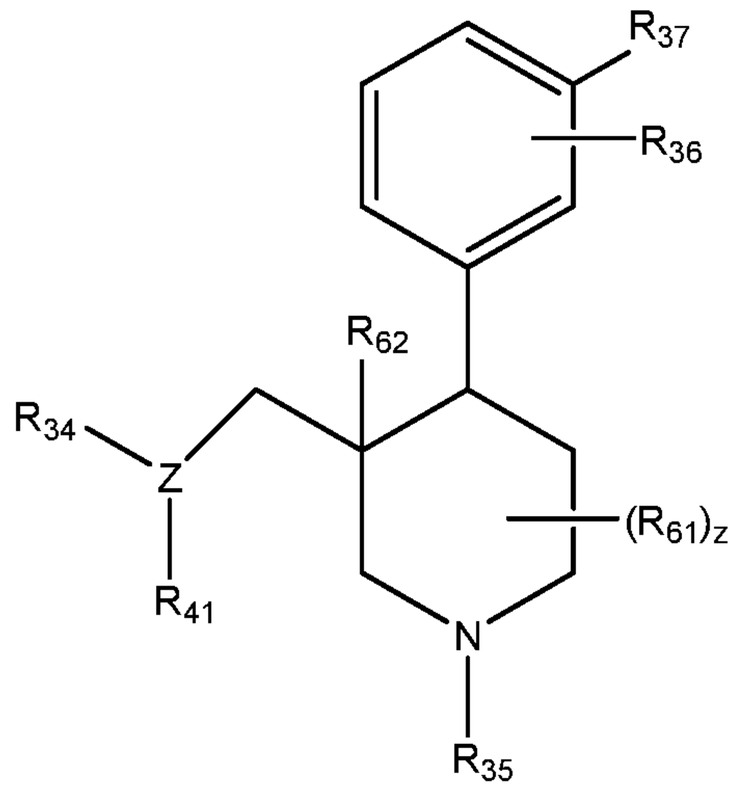


VI.

In some embodiments, the compounds of Formula I, Ia or Ib, or pharmaceutically acceptable salt thereof, have a formula of Formula VII or VIIa:



VII

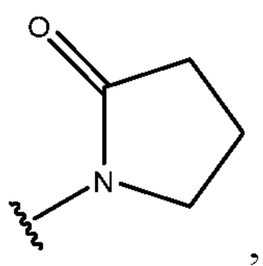


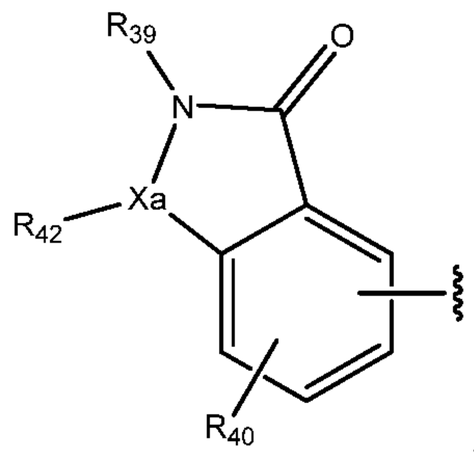
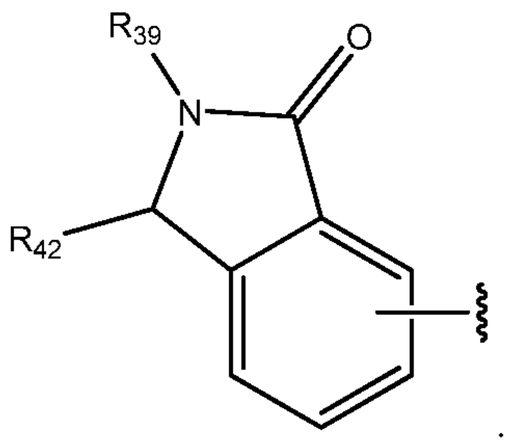
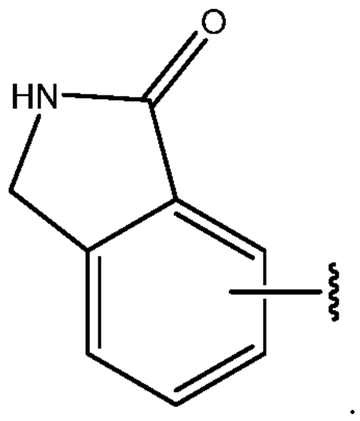
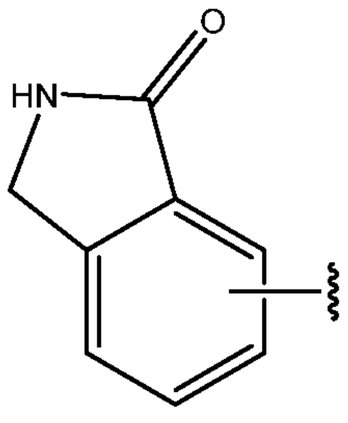
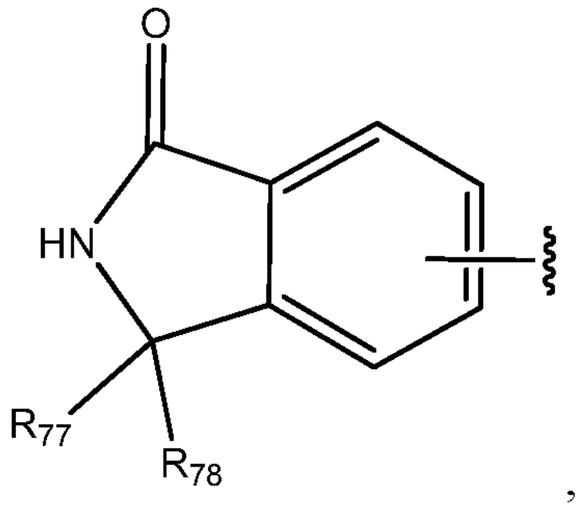
VIIa.

In some embodiments of compounds of Formula I, Ia or Ib, II, III, IV, V, VI, VII, VIIA, Z is O. In some embodiments, Z is C or N. In some embodiments, Z is O and R_{41} is absent.

In some embodiments, In some embodiments of compounds of Formula I, Ia or Ib, II, III, IV, V, VI, VII, or VIIa R_{37} is halo. In some embodiments, R_{37} is absent. In some embodiments, when R_{37} is halo, Z is O and R_{41} is absent. In some embodiments R_{37} is alkoxy, which can be optionally substituted. In some embodiments, z is 1.

In some embodiments, In some embodiments of compounds of Formula I, Ia or Ib, II, III, IV, V, VI, VII, or VIIa q is 0. In some embodiments, q is 1-4.

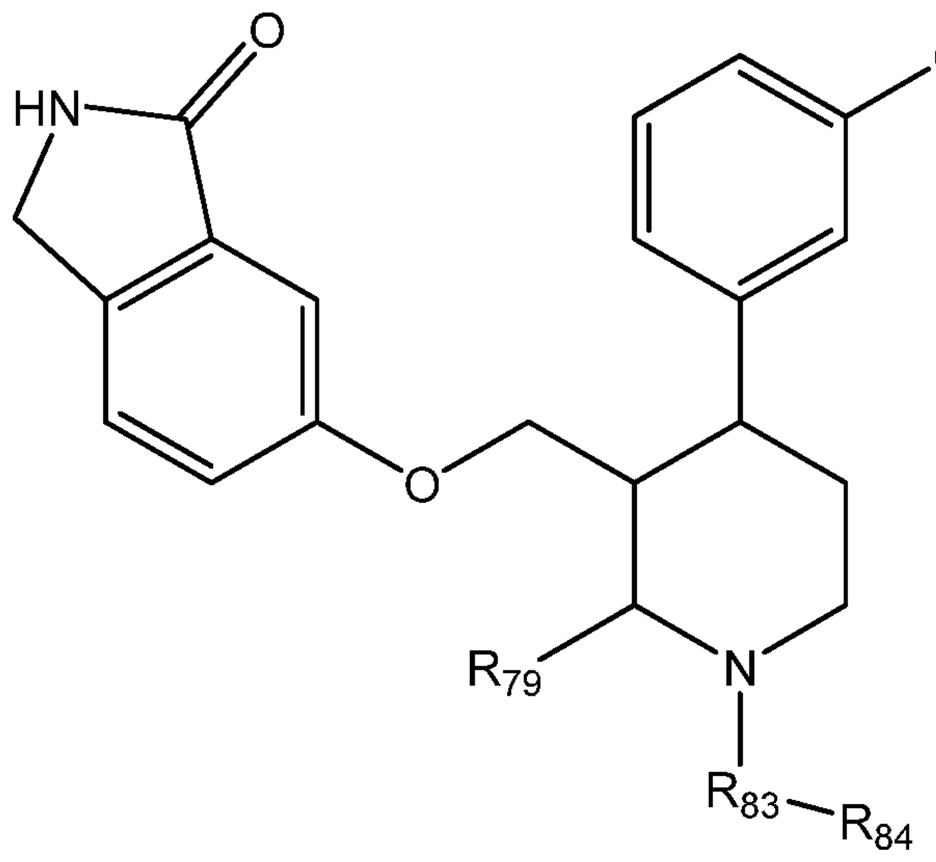
In some embodiments, In some embodiments of compounds of Formula I, Ia or Ib, II, III, IV, V, VI, VII, or VIIa R_{38} is absent or H. In some embodiments, R_{38} is haloalkyl. In some embodiments, R_{38} is $-C(=O)C_1$-C_6 alkyl. In some embodiments, R_{38} is OR_{66}, $S(O)_2$ R_{67},  , optionally substituted cycloalkyl, $-(CH_2)_pR_{65}$, or optionally substituted heterocycle.

In some embodiments, In some embodiments of compounds of Formula I, Ia or Ib, II, III, IV, V, VI, VII, or VIIa R_{34} is  . In some embodiments, R_{34} is  . In some embodiments, R_{34} is  . In some embodiments, when R_{34} is  , Z is O. In some embodiments, R_{34} is is  ,

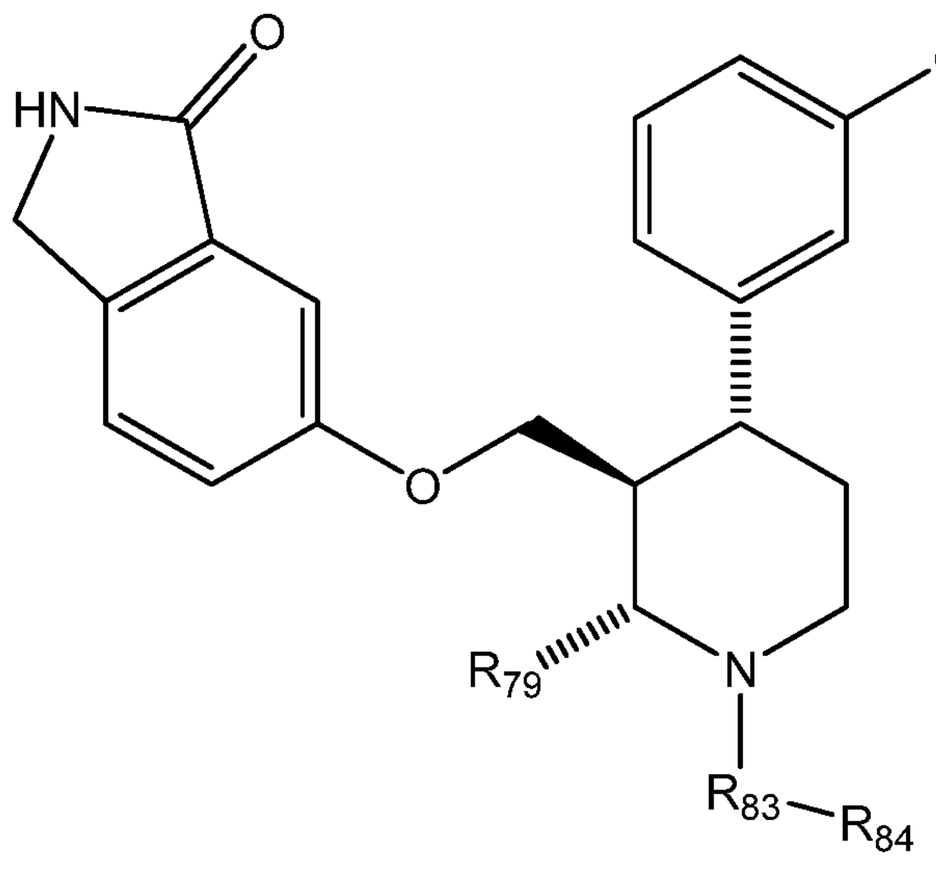
wherein R_{77} and R_{78} are each independently H or C_1-C_6 alkyl, or R_{77} and R_{78} form a C_3-C_6 cycloalkyl including the carbon that R_{77} and R_{78} are bound to.

In some embodiments of compounds, or pharmaceutically acceptable salts thereof, of Formula I, Ia or Ib, II, III, IV, V, VI, VII, VIIa, or any other formula described herein, the compound is selected from the group consisting of a compound described herein.

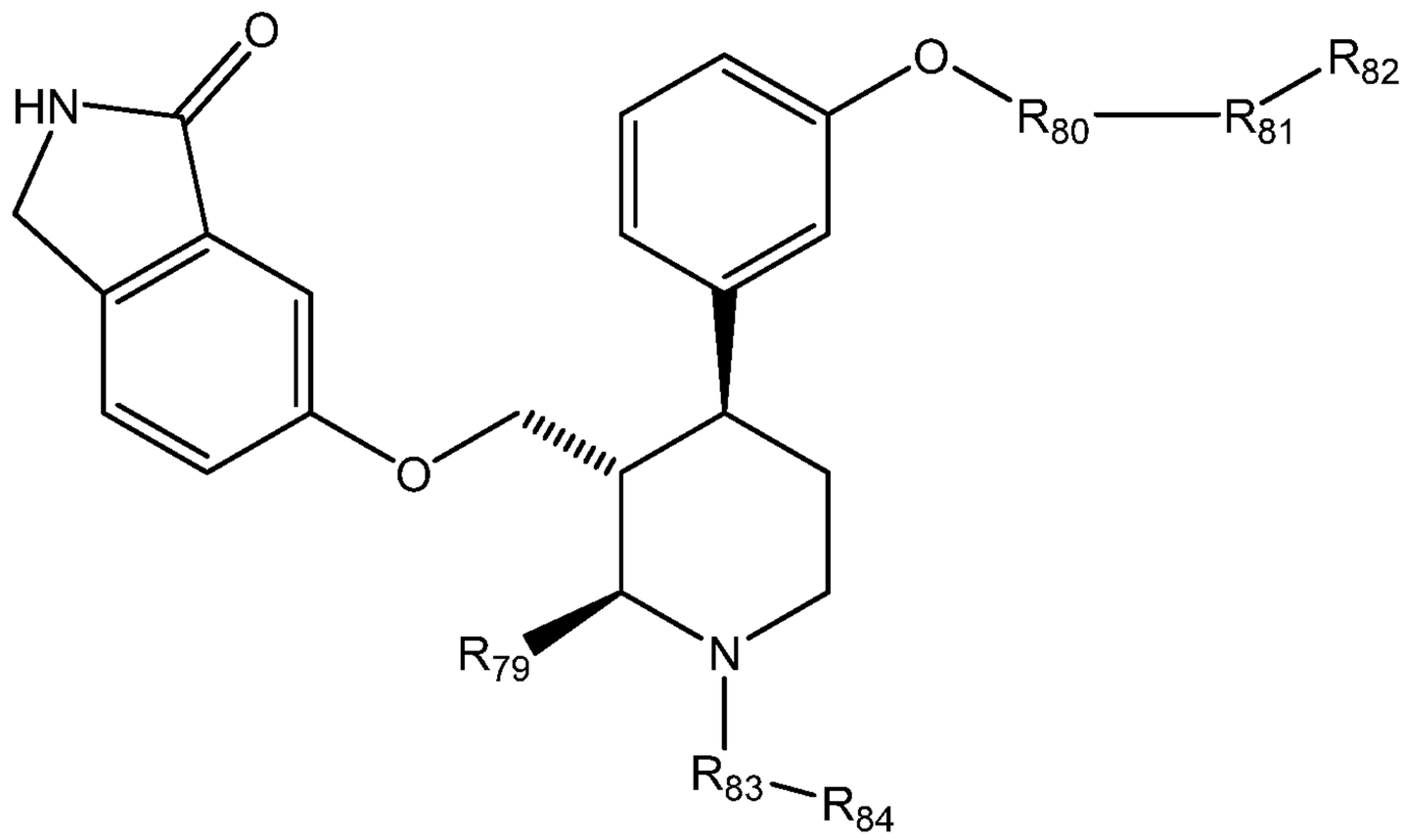
In some emodimemts, a compound is provided, or pharmaceutically acceptable salt thereof, having a formula of Formula VIII, VIII-a, or VIII-b:



VIII,



VIII-a, or



VIII-b

wherein:

R_{79} is optionally substituted C_1-C_6 alkyl;

R_{80} is optionally substituted C_1-C_6 alkyl;

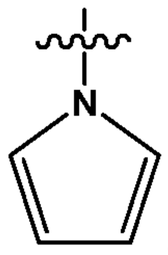
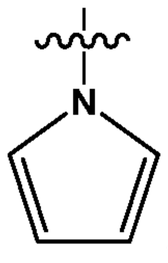
R_{81} is O, NH, S, or CH_2;

R_{82} is optionally substituted C_1-C_6 alkyl;

R_{83} is optionally substituted C_1-C_6 alkyl; and

R_{84} is optionally substituted aryl or heteroaryl.

In some embodiments of a compound, or or pharmaceutically acceptable salt thereof, having a formula of Formula VIII, VIII-a, or VIII-b, R_{79} is methyl or ethyl, with the other variables as described. In some embodiments of a compound, or or pharmaceutically acceptable salt thereof, having a formula of Formula VIII, VIII-a, or VIII-b, R_{80} is C_2, C_3, or C_4 alkyl with the other variables as described. In some embodiments of a compound, or or pharmaceutically acceptable salt thereof, having a formula of Formula VIII, VIII-a, or VIII-b, R_{81} is O or S with the other variables as described. In some embodiments of a compound, or or pharmaceutically acceptable salt thereof, having a formula of Formula VIII, VIII-a, or VIII-b, R_{82} is methyl or ethyl, with the other variables as described. In some embodiments of a compound, or or pharmaceutically acceptable salt thereof, having a formula of Formula

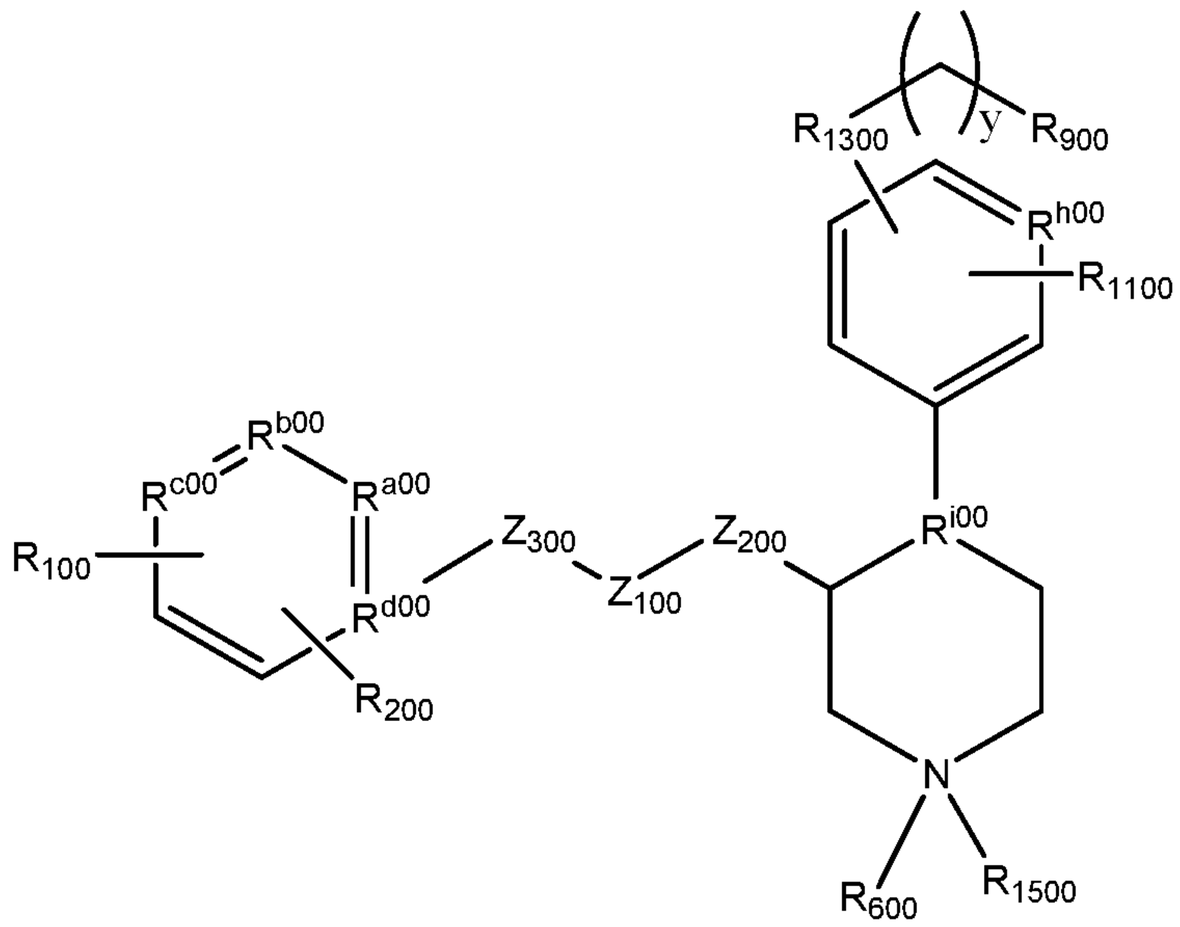
VIII, VIII-a, or VIII-b, R_{83} is C_2 alkyl with the other variables as described. In some embodiments of a compound, or or pharmaceutically acceptable salt thereof, having a formula of Formula VIII, VIII-a, or VIII-b, R_{84} is an optionally subsitutted phenyl, optionally subsitutted pyrrole, or optionally subsitutted pyrrolidine, with the other variables as described herein. In some embodiments, R_{84} is  . In some embodiments of a compound, or or pharmaceutically acceptable salt thereof, having a formula of Formula VIII, VIII-a, or VIII-b, R_{79} is methyl, R_{80} is C_2 alkyl, R_{81} is O, R_{82} is methyl, R_{83} is C_2 alkyl, and R_{84} is  .

The compounds described herein can be prepared according to any method.

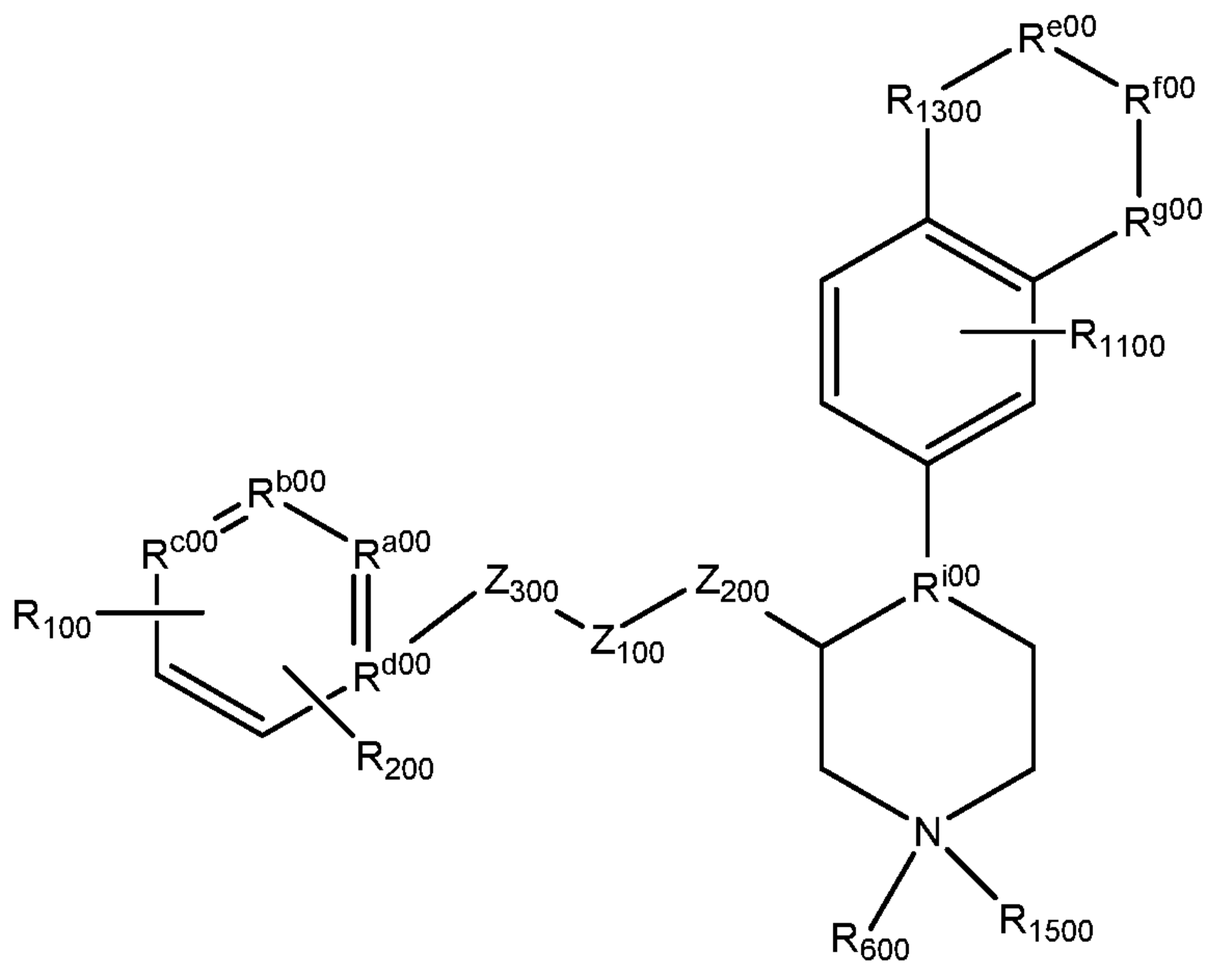
Examples of methods used to prepare the compounds described herein are provided herein. One of skill in the art can modify the procedures to yield compounds not specifically exemplified in the present disclosure without undue experimentation.

In some embodiments, a compound or salt thereof is chosen from a compound illustrated and exemplified in Figure 1 and as described herein or in the tables in the Examples section of the present disclosure. The compounds described herein can be synthesized according to the schemes described herein. The schemes can also be readily modified, if necessary, to prepare a compound described herein.

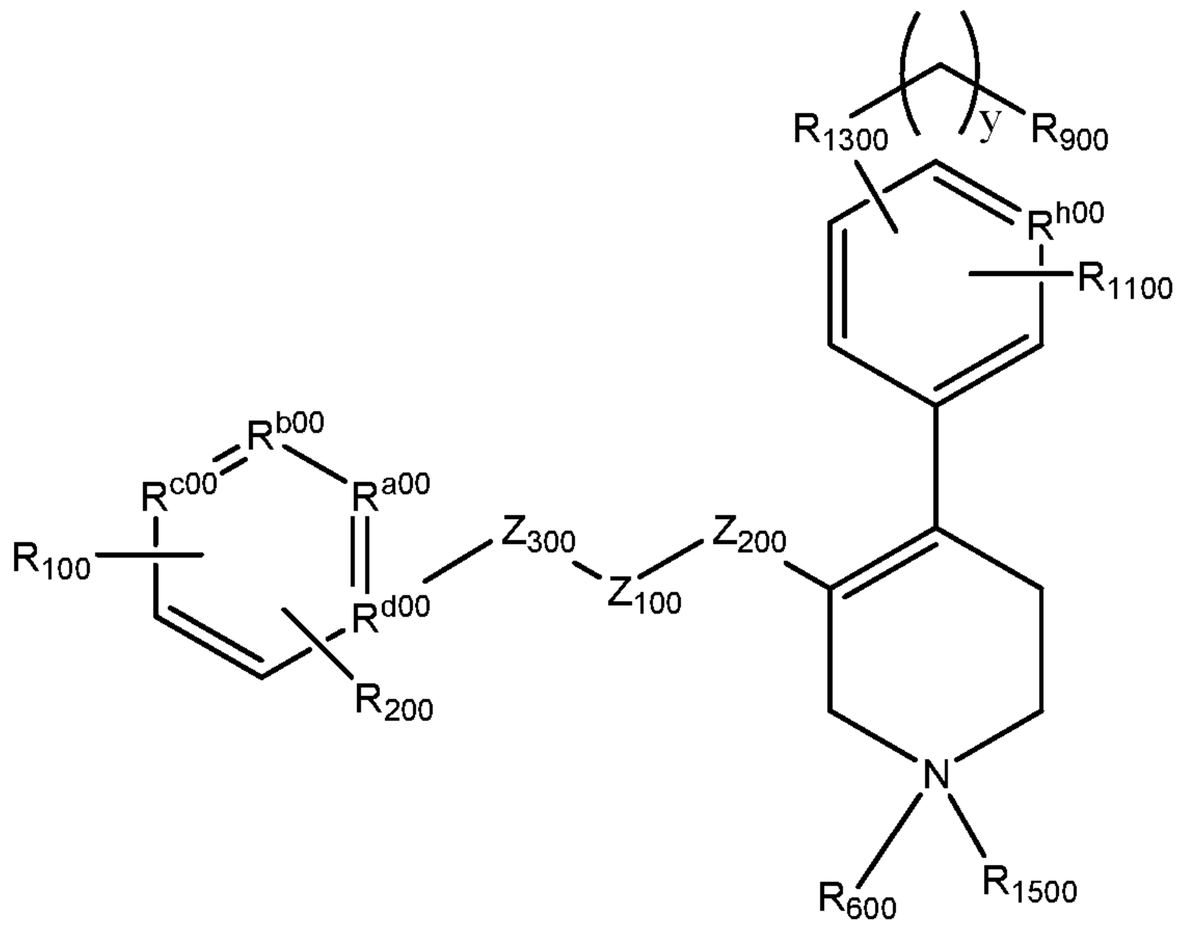
In some embodiments, the present invention provides a compound having Formula I00, Formula I00A, Formula I00B, or Formula I00C, or pharmaceutically acceptable salt thereof:


R1300
y
R900
Rh00
R1100
Rb00
Rc00
Ra00
R100
Z300
Z200
Ri00
Z100
Rd00
R200
N
R600
R1500

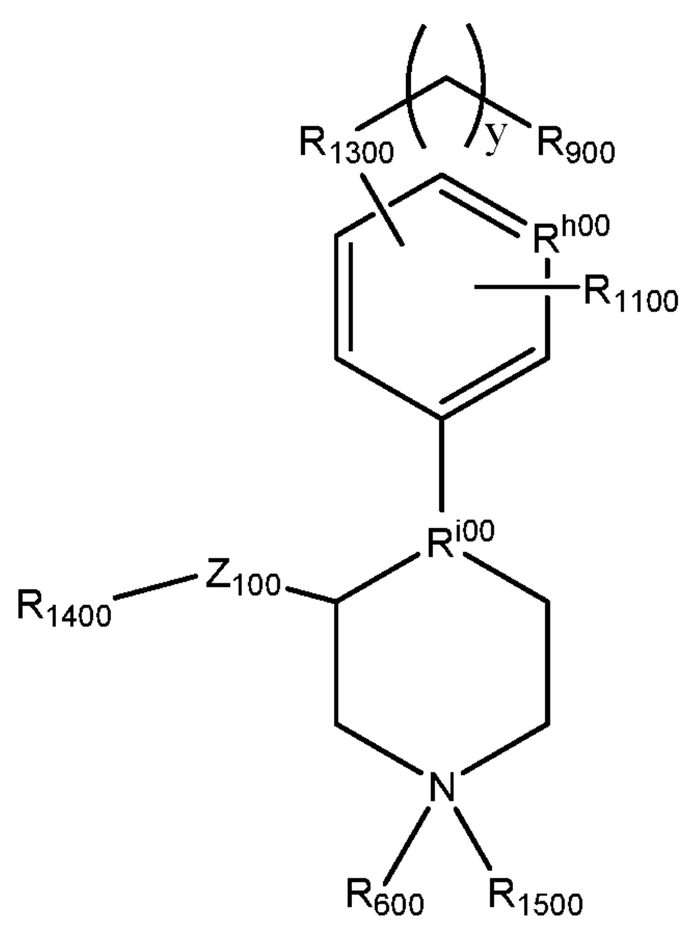
I


Re00
R1300
Rf00
Rg00
R1100
Rb00
Rc00
Ra00
R100
Z300
Z200
Ri00
Z100
Rd00
R200
N
R600
R1500

I00A



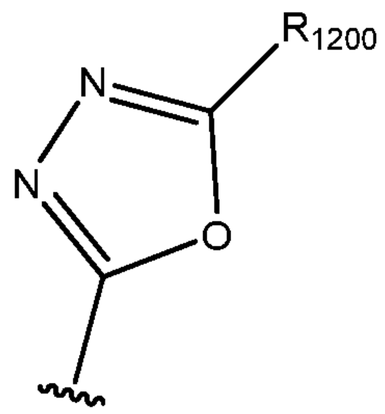
I00B



I00C.

In some embodiments, R_{100}, R_{200}, and R_{1400} are each, independently, H, cyano, optionally substituted C_1-C_6 branched or unbranched alkyl, optionally substituted C_1-C_6 alkoxy, optionally substituted C_1-C_6 haloalkyl, optionally substituted C_2-C_6 alkenyl, optionally substituted pyrimidine, optionally substituted pyridyl, optionally substituted pyrazole, optionally substituted isoxazole, optionally substituted pyridinone, optionally substituted $-CH_2$-pyridinone, optionally substituted aryl, halo,-$NC(=O)R_{300}$, -

$C(=O)NR_{300}R_{400}$, $-C(=O)OR_{300}$, $S(=O)_2NR_{300}R_{400}$, $-C(=O)R_{300}$, $-OR_{300}$, $-(CH_2)_nR_{500}$, $=O$, or



In some embodiments, R_{1500} is absent, C_2-C_6 alkenyl, a protecting group, or $C(=O)OR_{81b}$, wherein $R81_b$ is H or optionally substituted branched or unbranched C_1-C_6 alkyl. In some embodiments, R_{81b} is is t-butyl.

In some embodiments, when R_{1500} is absent, R_{600} is H, optionally substituted aryl, optionally substituted C_1-C_6 haloalkyl, $-R_{700}R_{800}$, optionally substituted C_1-C_6 branched or unbranched alkyl, optionally substituted C_2-C_6 alkenyl, $-(CH_2)_nR_{500}$, optionally substituted cycloalkyl, -OH, optionally substituted C_1-C_6 alkoxy, optionally substituted pyrrolinyl, optionally substituted morpholinyl, or optionally substituted piperldyl.

In some embodiments, when R_{1500} is C_2-C_6 alkenyl, R_{600} is C_2-C_6 alkenyl.

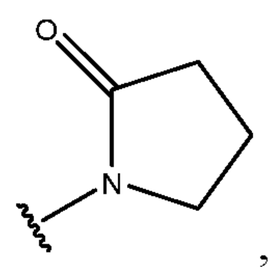
In some embodiments, R_{300} and R_{400} are each, independently, H, optionally substituted aryl, optionally substituted C_1-C_6 haloalkyl, $-R_{700}R_{800}$, optionally substituted C_1-C_6 branched or unbranched alkyl, optionally substituted C_2-C_6 alkenyl, $-(CH_2)_nR_{500}$, optionally substituted cycloalkyl, -OH, optionally substituted alkoxy, optionally substituted pyrrolinyl, optionally substituted morpholinyl, or optionally substituted piperldyl; or R_{300} and R_{400} together form a 5-10 membered optionally substituted heterocycle or 5-10 membered optionally substituted heteroaryl with the atom to which R_{300} and R_{400} are bonded.

In some embodiments R_{1200} is, independently, H, optionally substituted aryl, optionally substituted C_1-C_6 haloalkyl, $-R_{700}R_{800}$, optionally substituted C_1-C_6 branched or unbranched alkyl, optionally substituted C_2-C_6 alkenyl, $-(CH_2)_nR_{500}$, optionally substituted cycloalkyl, -OH, optionally substituted alkoxy, optionally substituted pyrrolinyl, optionally

substituted morpholinyl, or optionally substituted piperldyl; or R_{300} and R_{400} together form a 5-10 membered optionally substituted heterocycle or 5-10 membered optionally substituted heteroaryl with the atom to which R_{300} and R_{400} are bonded.

In some embodiments, each R_{500} is, independently, H, optionally substituted C_1-C_6 haloalkyl, $-NR_{700}R_{800}$, optionally substituted C_1-C_6 branched or unbranched alkyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted C_2-C_6 alkenyl, optionally substituted cycloalkyl, optionally substituted heterocycle, -OH, optionally substituted alkoxy, optionally substituted pyrrolinyl, optionally substituted morpholinyl, or optionally substituted piperldyl.

In some embodiments, R_{700} and R_{800} are, each, independently, H, optionally substituted aryl, optionally substituted C_1-C_6 haloalkyl, optionally substituted C_1-C_6 branched or unbranched alkyl, optionally substituted C_2-C_6 alkenyl, $-(CH_2)_nR_{500}$, optionally substituted cycloalkyl, -OH, optionally substituted alkoxy, optionally substituted pyrrolinyl, optionally substituted morpholinyl, or optionally substituted piperldyl; or R_{700} and R_{800} together form a 5-10 membered optionally substituted heterocycle or 5-10 membered optionally substituted heteroaryl with the atom to which R_{700} and R_{800} are bonded to.

In some embodiments, R_{900} is absent, H, haloalkyl, $-OR_{300}$, or  , optionally substituted cycloalkyl, $-(CH_2)_pR_{500}$, or optionally substituted heterocycle.

In some embodiments, R_{1100} is H, halo, or optionally substituted C_1-C_6 alkyl.

In some embodiments, R_{1300} is a bond, C, N, S, or O.

In some embodiments, R_{1400} is an optionally substituted pyridinone or optionally substituted $-CH_2$-pyridinone.

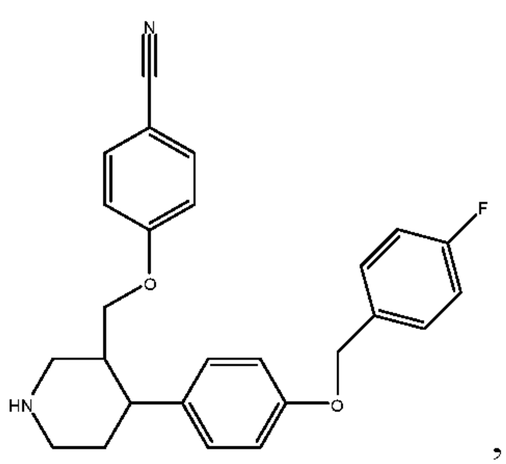
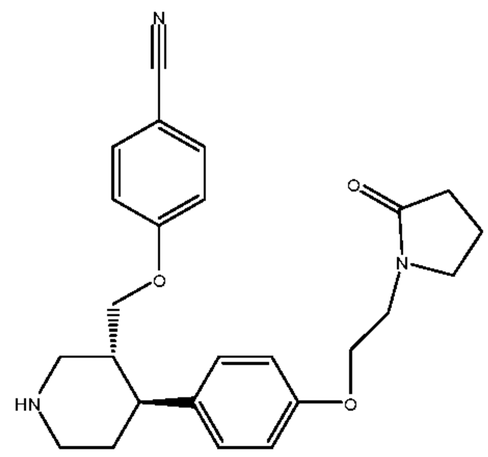
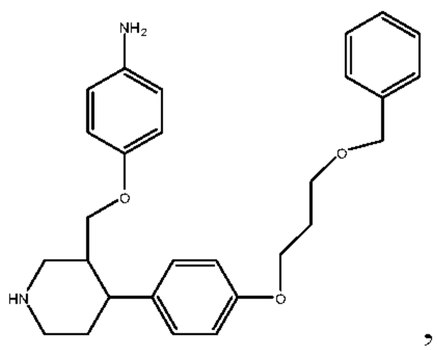
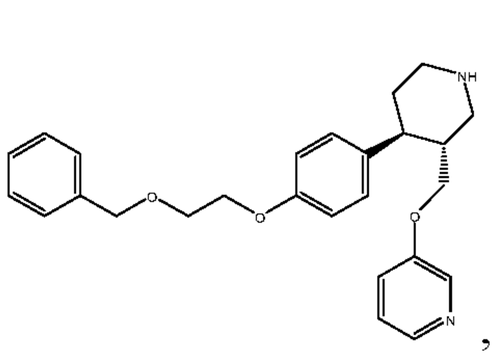
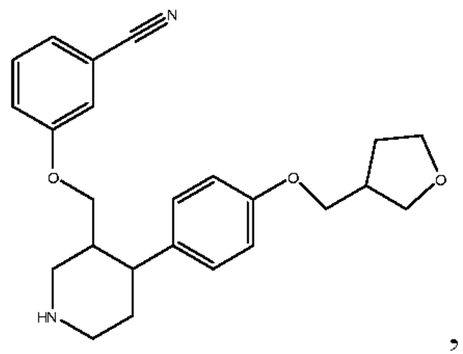
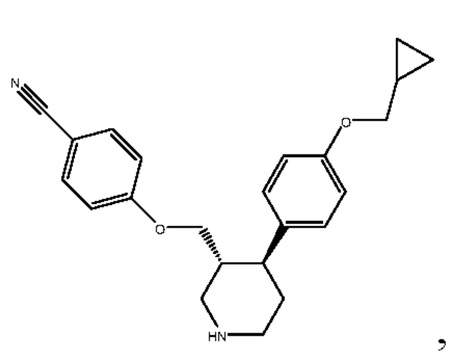
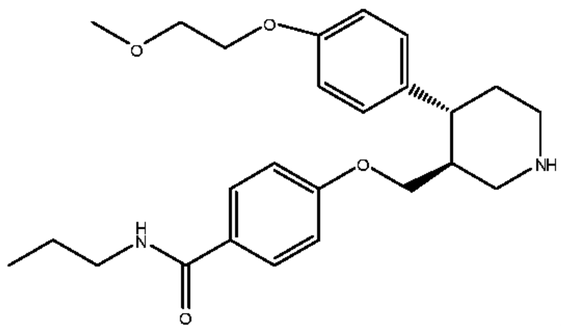
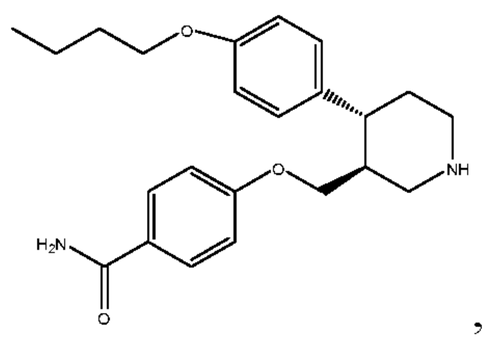
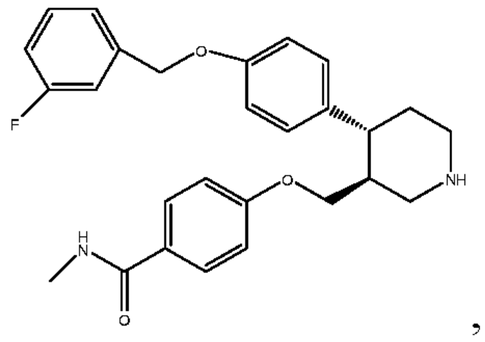
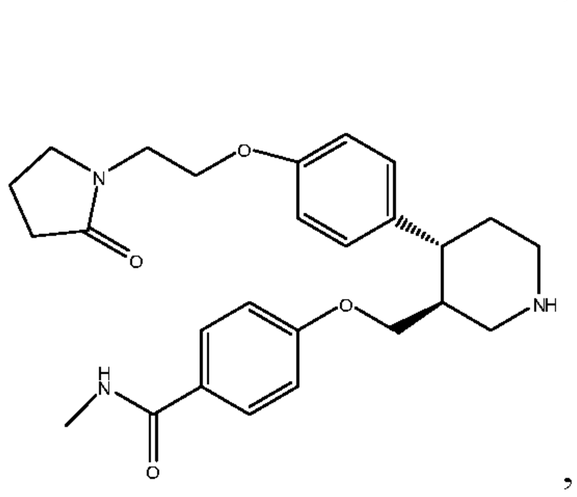
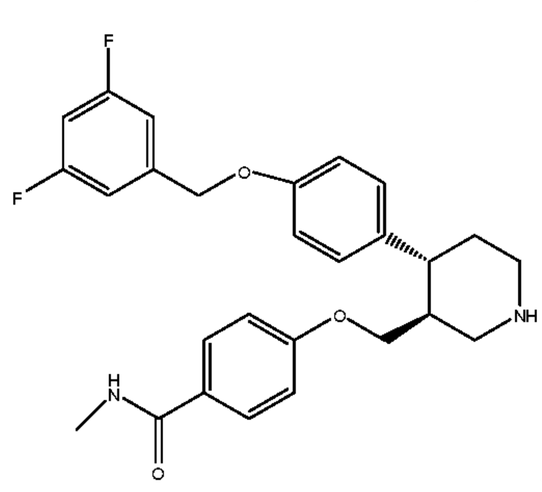
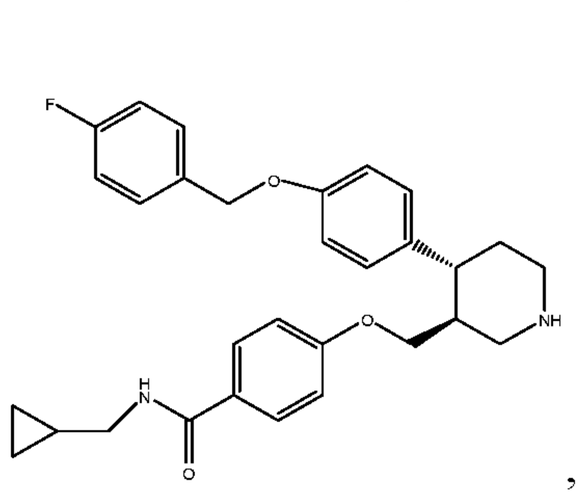
In some embodiments, each n, p, and y is independently, an integer from 0-6.

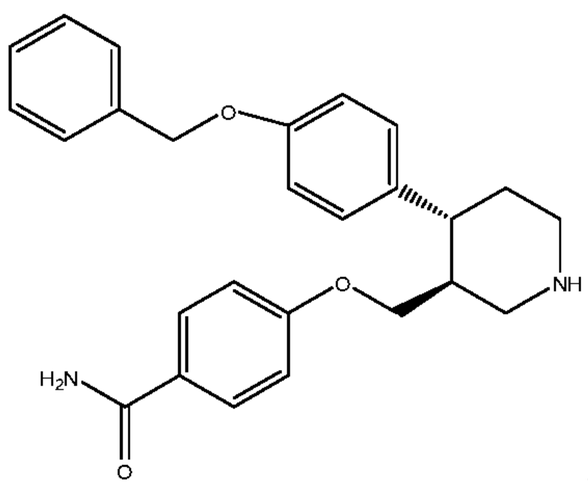
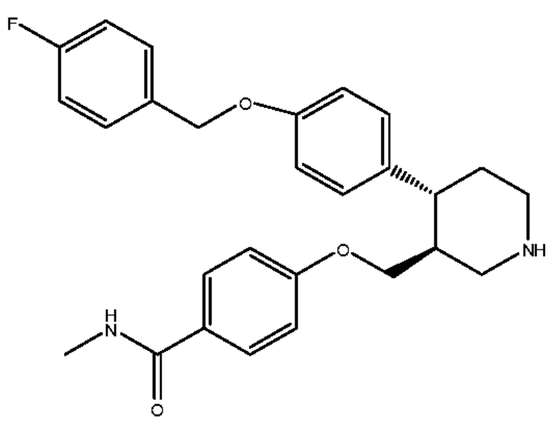
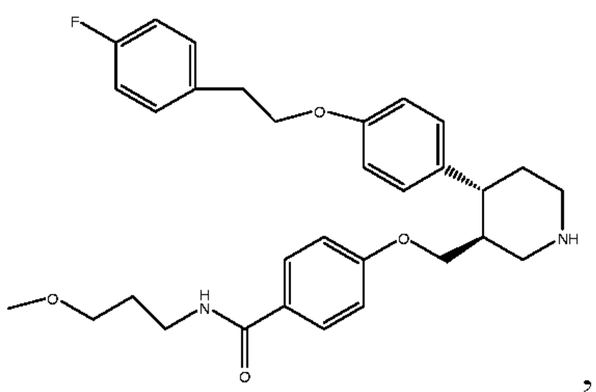
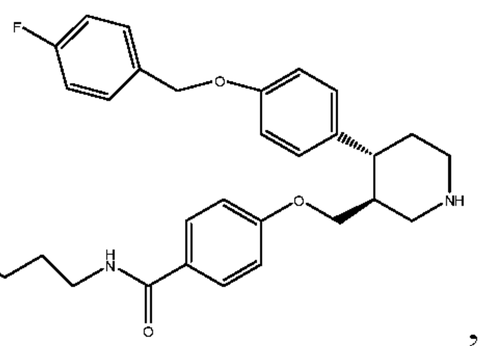
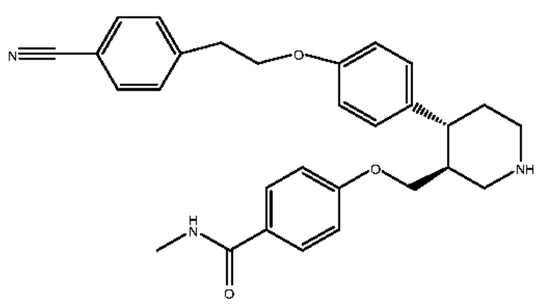
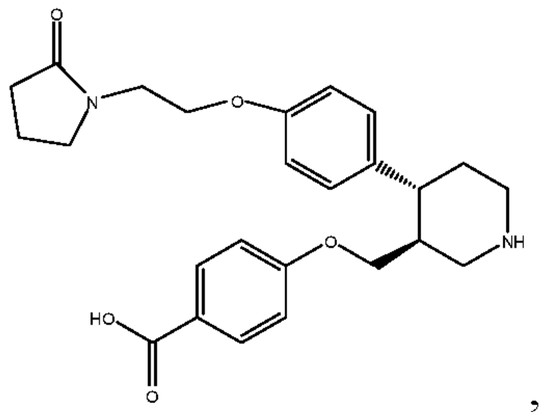
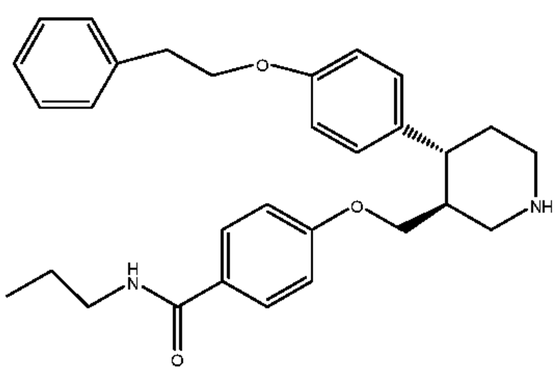
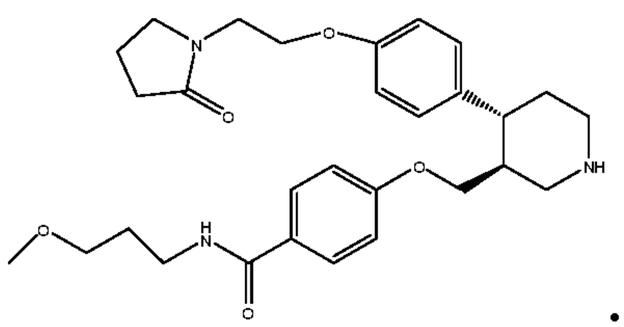
In some embodiments, each R^{a00}, R^{b00}, R^{c00}, R^{d00}, R^{h00}, and R^{i00}, is, independently, C, N, or O.

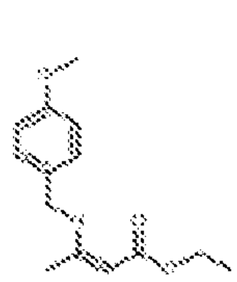
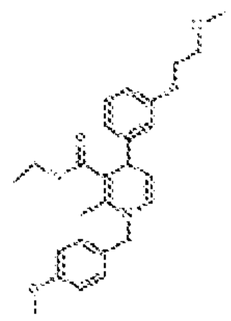
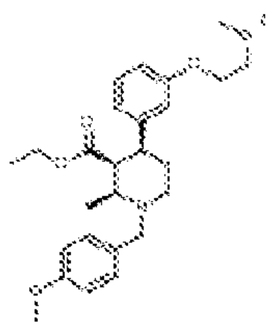
In some embodiments,each R^{e00}, R^{f00}, and R^{g00}, is, independently, C, N, S, O, or absent.

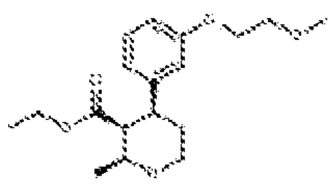
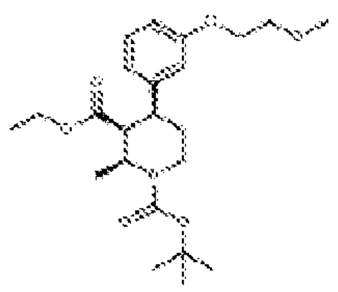
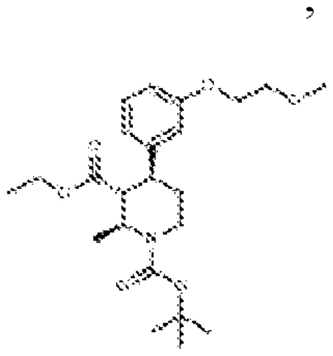
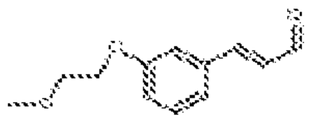
In some embodiments, each Z_{100}, Z_{200}, and Z_{300}, is, independently, a bond, C(=O), C, N, S, or O.

In some embodiments, provided that The compound or a pharmaceutically acceptable salt thereof is not


,

,

,

,

,

,

,

,

,

,

,

,

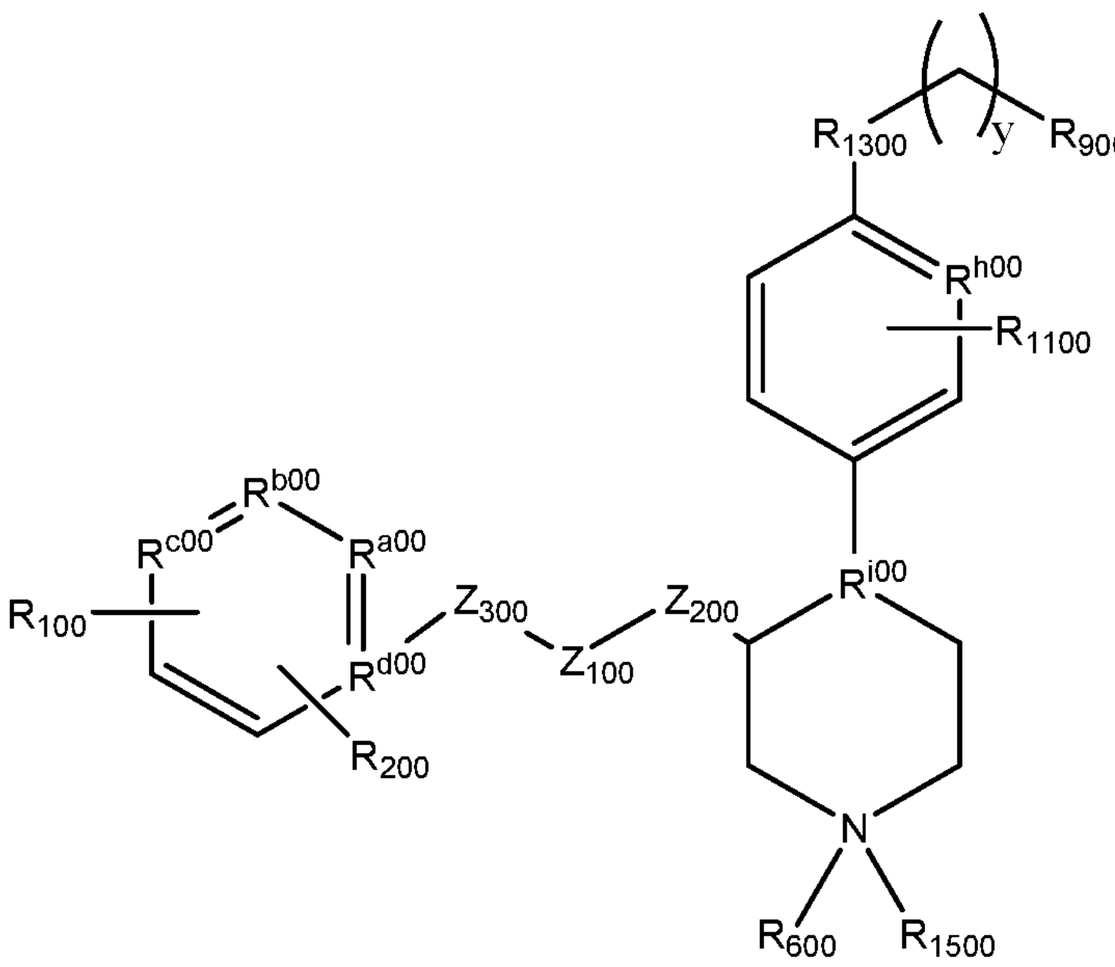

,

,

,

,

,

,

, or

.

In some embodiments, a compound, or pharmaceutically acceptable salt thereof, is selected from the group consisting of:

,

,

,

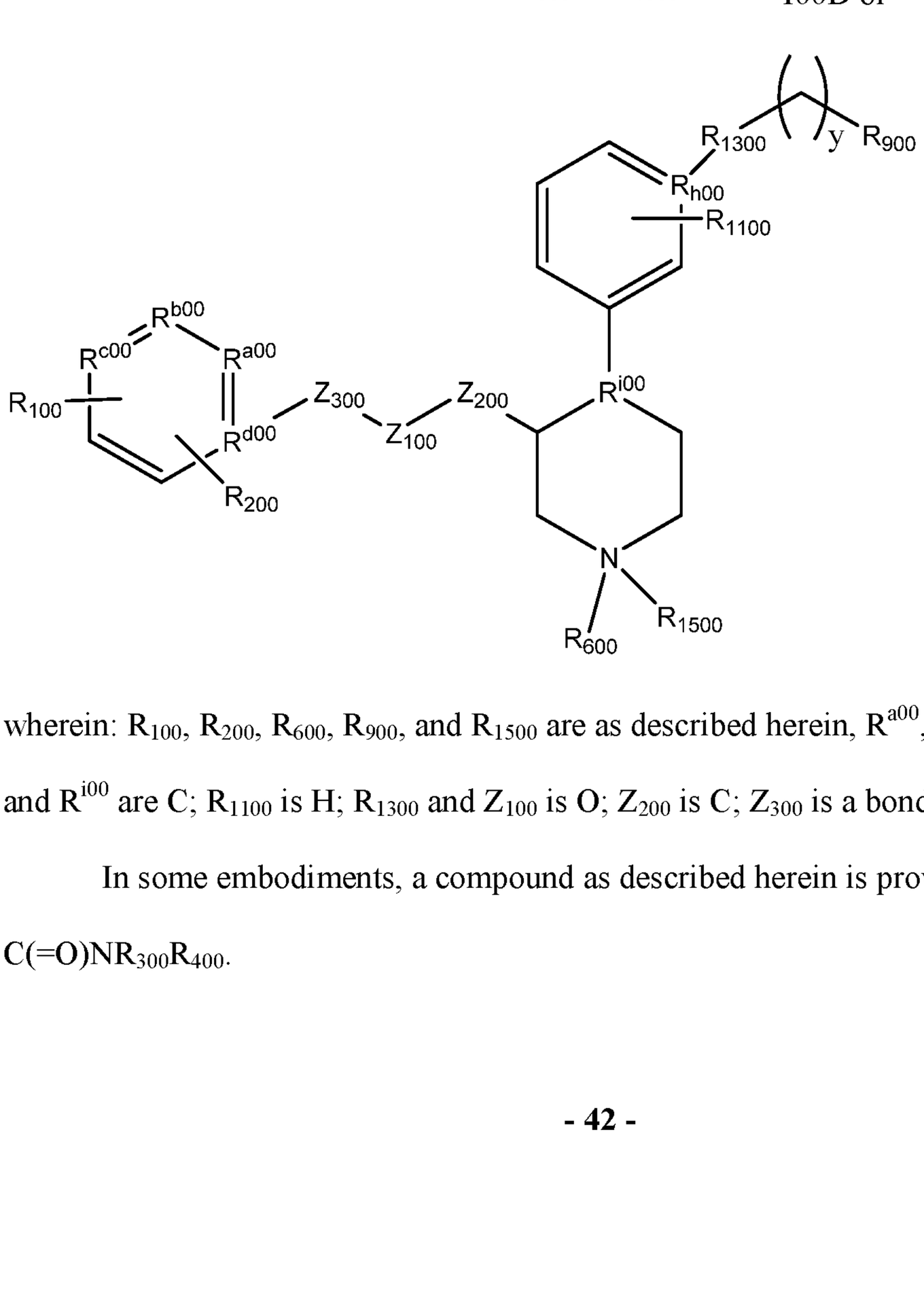
,

,

,


, and

. The compounds can be used, in some embodiments, to prepare other compounds described herein.

In some embodiments, the present invention provides a compound or salt thereof having Formula I00D or Formula I00E:



I00D or

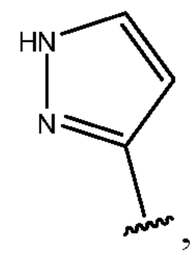


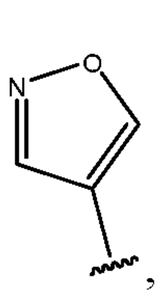
I00E

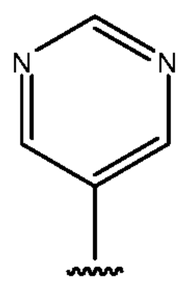
wherein: R_{100}, R_{200}, R_{600}, R_{900}, and R_{1500} are as described herein, R^{a00}, R^{b00}, R^{c00}, R^{d00}, R^{h00}, and R^{i00} are C; R_{1100} is H; R_{1300} and Z_{100} is O; Z_{200} is C; Z_{300} is a bond; and y=2.

In some embodiments, a compound as described herein is provided wherein R_{100} is –C(=O)$NR_{300}R_{400}$.

In some embodiments, a compound or salt thereof as described herein is provided wherein each of R_{300} and R_{400} is, independently, H, halo, optionally substituted C_1-C_6 haloalkyl, or optionally substituted C_1-C_6 alkyl.

In some embodiments, a compound or salt thereof is provided, wherein R_{100} is H, halo, $-C(=O)NH_2$, $-C(=O)NHCH_3$, $-C(=O)N(CH_3)_2$ -COOH, $-C(=O)OCH_3$, cyano, $S(=O)_2NH_2$, optionally substituted alkoxy, $-OCF_3$, CF_3, $-NC(=O)CH_3$, pyridyl, 

, 

, or 

.

In some embodiments, a compound or salt thereof is provided, wherein R_{100} and R_{200} is each, independently, H, halo, or optionally substituted C_1-C_6 haloalkyl.

In some embodiments, a compound or salt thereof is provided, wherein R_{100} and R_{200} are independently halo.

In some embodiments, a compound or salt thereof is provided, the optionally substituted C_1-C_6 haloalkyl is trifluoromethyl.

In some embodiments,a compound or salt thereof is provided, wherein R_{100} is fluoro and R_{200} is trifluoromethyl.

In some embodiments, a compound or salt thereof is provided, wherein R_{100} and R_{200} are attached to different ring atoms.

In some embodiments, a compound or salt thereof is provided, wherein wherein R_{200} is H.

In some embodiments, a compound or salt thereof is provided, wherein: R_{600} is H, optionally substituted C_1-C_6 alkyl, or –C(=O)OR_{300}; and R_{300} is an optionally substituted C_1-C_6 branched or unbranched alkyl.

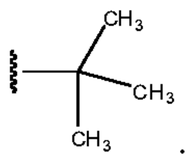
In some embodiments, a compound or salt thereof is provided, wherein: R_{100} is -C(=O)NH_2 and R_{600} is H or optionally substituted C_1-C_6 alkyl; or R_{100} is -C(=O)$NR_{300}R_{400}$, wherein R_{300} is H and R_{400} is optionally substituted branched or unbranched C_1-C_6 alkyl or optionally substituted branched or unbranched C_2-C_6 alkenyl and R_{600} is H or optionally substituted C_1-C_6 alkyl; or R_{100} is -C(=O)$NR_{300}R_{400}$, wherein R_{300} and R_{400} are each, independently, optionally substituted branched or unbranched C_1-C_6 alkyl, and R_{600} is H, optionally substituted C_1-C_6 alkyl, or optionally substituted alkaryl.

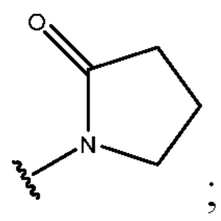
In some embodiments, a compound or salt thereof is provided, wherein R_{100} is -C(=O)$NR_{300}R_{400}$, wherein: R_{300} and R_{400} are H; R_{300} is H and R_{400} is optionally substituted C_1-C_6 unbranched or branched alkyl; or R_{300} is H and R_{400} is optionally substituted C_2-C_6 unbranched or branched alkenyl; or R_{300} is H and R_{400} is optionally substituted C_1-C_6 cycloalkyl; or R_{300} is H and R_{400} is –$(CH_2)_nR_{500}$; wherein n is 1-6 and R_{500} is an optionally substituted cycloalkyl; or R_{300} is H and R_{400} is –$(CH_2)_nR_{500}$, wherein n is 1-6 and R_{500} is an optionally substituted alkoxy; or R_{300} and R_{400} are each, independently, optionally substituted C_1-C_6 alkyl.

In some embodiments, a compound or salt thereof is provided, wherein R_{100} is –C(=O)$NR_{300}R_{400}$, wherein R_{300} and R_{400} together form a 5-10 membered optionally substituted heterocycle or 5-10 membered optionally substituted heteroaryl with the atom to which R_{300} and R_{400} are bonded.

In some embodiments, a compound or salt thereof is provided, wherein R^{b00} is N. In some embodiments, a compound or salt thereof is provided, wherein R^{a00} is N. In some embodiments, a compound or salt thereof is provided, wherein R^{c00} is N. In some

embodiments, a compound or salt thereof is provided, wherein R^{d00} is N. In some embodiments, a compound or salt thereof is provided, wherein R_{1100} is H, R_{1300} is O, R^{i00} is C, Z_{100} is O, Z_{200} is C, Z_{300} is a bond, and y=2. In some embodiments, R_{100}, R_{200}, and R_{600} are each H and Z is O. In some embodiments, R_{100} is =O and R_{200} is H.

In some embodiments, a compound or salt thereof is provided, wherein R_{100} is –$C(=O)NR_{300}R_{400;}$ and R_{600} is H, C_1-C_6 alkyl, or –$C(=O)OR_3$, wherein R_{300} is an optionally substituted C_1-C_6 branched or unbranched alkyl. In some embodiments, R_{300} is  .

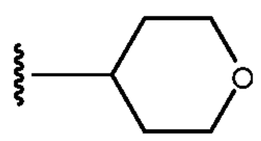
In some embodiments, a compound or salt thereof is provided wherein R_{600} is H, optionally substituted C_1-C_6 alkyl, optionally substituted C_2-C_6 alkenyl, -OR_3, or $(CH_2)_n$-aryl, n is an integer from 0-6; R_{900} is  ; R_{1100} is H or halo; R_{1300} is O; R^{i00} is C; y=2; and optionally R_{1500} is optionally substituted C_2-C_6 alkenyl when R_{600} is optionally substituted C_2-C_6 alkenyl.

In some embodiments, a compound or salt thereof is provided wherein R_{1100} is fluoro.

In some embodiments, a compound or salt thereof is provided, wherein R_{100} is –$C(=O)NH_2$.

In some embodiments, a compound or salt thereof is provided, wherein R_{100} is cyano.

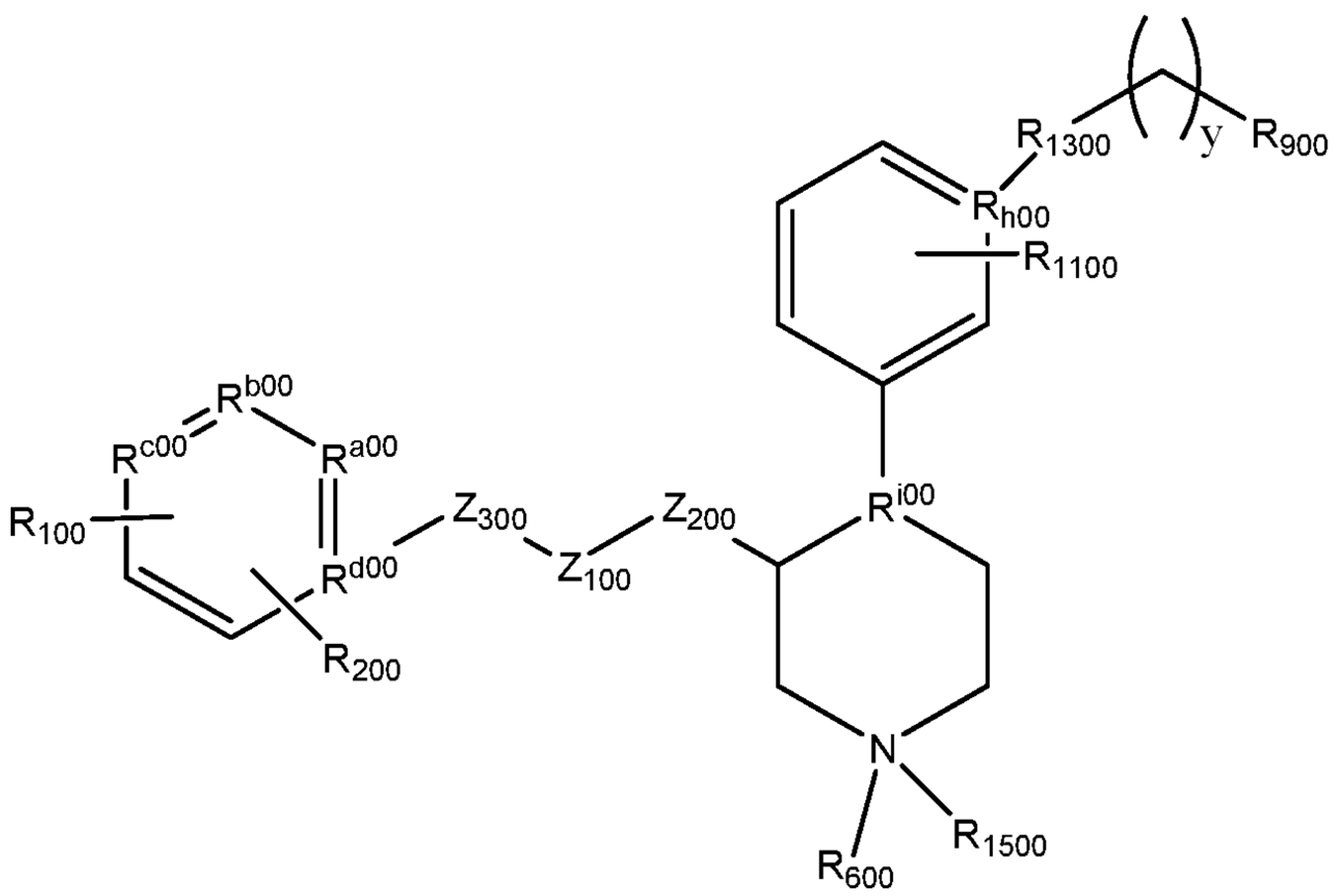
In some embodiments, a compound or salt thereof is provided, wherein: R^{a00}, R^{b00}, R^{c00}, R^{d00}, R^{h00}, and R^{i00} are C; Z_{100} is O, Z_{200} is C, Z_{300} is a bond; y=0; R_{900} is branched or unbranched optionally substituted C_1-C_6 alkyl, optionally substituted haloalkyl, optionally substituted cycloalkyl, or optionally substituted heterocycle; and R_{1300} is O. In some embodiments, R_{600} is H or optionally substituted branched or unbranched C_1-C_6 alkyl. In some embodiments,

R_{900} is  . In some embodiments, R_{100} is $-C(=O)NR_{300}R_{400}$ or cyano. In some embodiments, R_{200} is H. In some embodiments, R_{1100} is H.

In some embodiments, a compound or salt thereof is provided, wherein one of R^{a00}, R^{b00}, R^{c00}, and R^{d00} is N; Z_{100} is a bond or O; Z_{200} is C, Z_{300} is a bond, and y=0; R^{h00} and R^{i00} are C; R_{100} is H, -C(=O)$NR_{300}R_{400}$ or =O; R_{200} is H; R_{600} is H, C_1-C_6 alkyl, or C_2-C_6 alkenyl; R_{900} is C_1-C_6 alkyl, haloalkyl, or cycloalkyl; R_{1100} is H; and R_{1300} is O. In some embodiments, Z_{100} is a bond and R_{100} is =O. In some embodiments, R_{400} is H. In some embodiments, R^{d00} is N and R_{100} is =O.

In some embodiments, a compound or salt thereof is provided, wherein R^{a00}, R^{b00}, R^{c00}, and R^{d00} are C; R^{h00} and R^{i00} are C; Z_{100} is O, Z_{200} is C, Z_{300} is a bond; R_{1100} is halo or C_1-C_6 alkyl; y=0; R_{900} is H, haloalkyl or C_1-C_6 alkyl; R_{1300} is O; R_{600} is H, C_1-C_6 alkyl, or C_2-C_6 alkenyl; and R_{200} is H. In some embodiments, R_{100} is H, cyano or –$C(=O)NR_{300}R_{400}$.

In some embdoimets, a compound or salt thereof is provided having Formula I00E.



I00E

wherein R_{100}, R_{200}. R_{600}. and R_{900} are as defined as described herein, R^{a00}, R^{b00}, R^{c00}, R^{d00}, R^{h00} and R^{i00} are C; R_{1300} is O; Z_{100} is O, Z_{200} is C, Z_{300} is a bond; and y=0. In some embodiments, R_{900} is H, haloalkyl, or C_1-C_6 alkyl. In some embodiments, R_{200} is H. In some embodiments, R_{1100} is H. In some embodiments, R_{600} is H, C_1-C_6 alkyl, or C_2-C_6 alkenyl. In some embodiments, R_{100} is H, cyano, or $-C(=O)NR_{300}R_{400}$. In some embodiments, R_{900} is H or C_1-C_6 alkyl.

In some embodiments, a compound of salt thereof is provided having the structure of of Formula I00A of claim 1, wherein R^{a00}, R^{b00}, R^{c00}, R^{d00}, R^{e00}, and R^{i00} are C, R^{g00} is C or O; R^{f00} is absent; R_{1300} is O; and Z_{100} is O, Z_{200} is C, and Z_{300} is a bond. In some embodiments, R_{200} is H. In some embodiments, R_{1100} is H. In some embodiments, R_{600} is H, optionally substituted C_1-C_6 alkyl or optionally substituted C_2-C_6 alkenyl. In some embodiments, R_{100} is H, cyano, $-C(=O)NR_{300}R_{400}$, or C_1-C_6 alkyl. In some embodiments, R^{g00} is O.

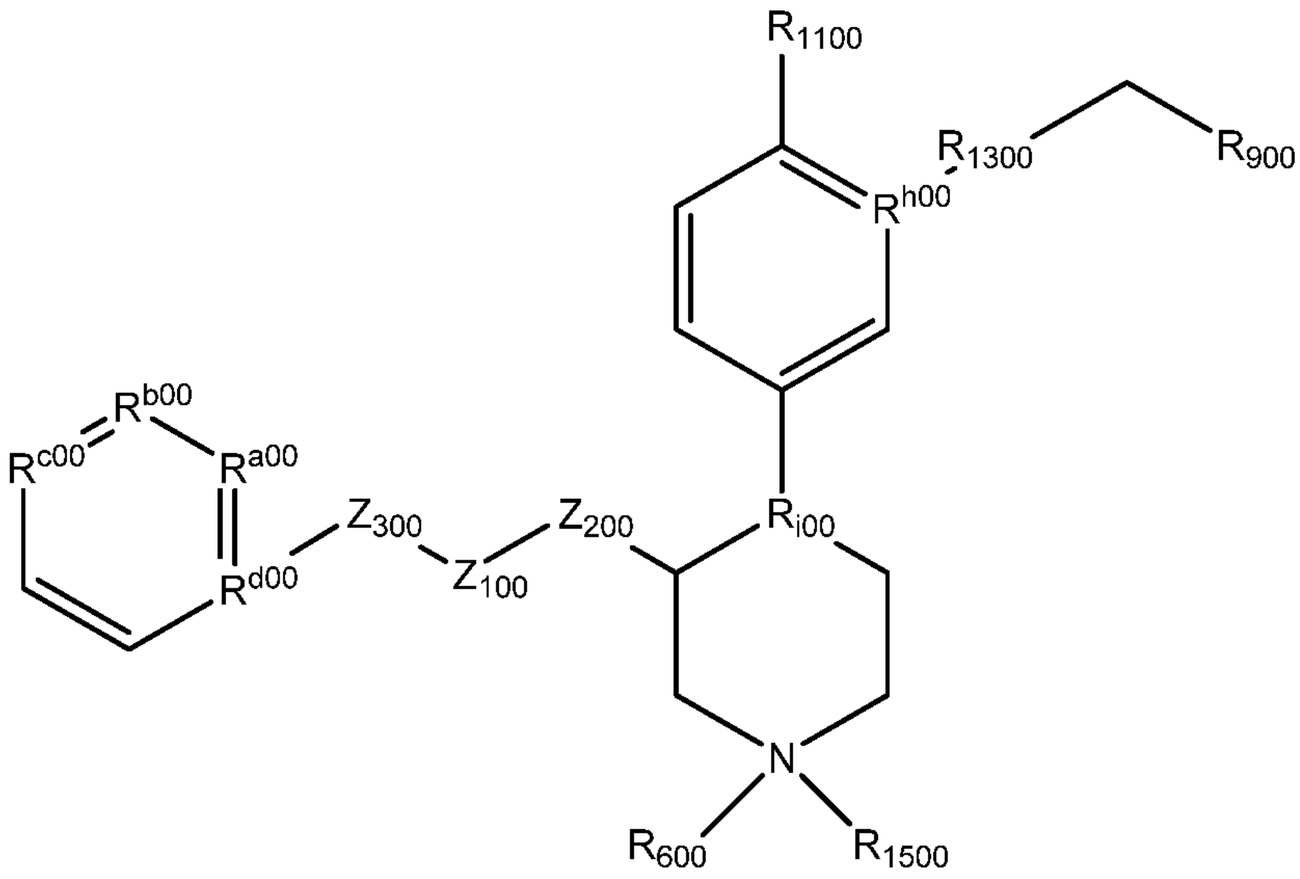
In some embodiments, a compound or salt thereof is provided, wherein y=1. In some embodiments, R_{900} is an optionally substituted C_1-C_6 alkyl or optionally substituted cycloalkyl.

In some embodiments, R^{a00}, R^{b00}, R^{c00}, R^{d00}, R^{h00}, and R^{i00} are C. In some embodiments, R_{1300} is O. In some embodiments, Z_{100} is O, Z_{200} is C, and Z_{300} is a bond. In some embodiments, R_{200} and R_{1100} are H. In some embodiments, R_{100} is $-C(=O)NR_{300}R_{400}$. In some embodiments, R_{600} is H or optionally substituted C_1-C_6 alkyl.

In some embodiments, a compound or salt thereof is provided wherein R^{h00} is N. In some embodiments, R^{a00}, R^{b00}, R^{c00}, R^{d00}, R^{i00} are C. In some embodiments, R_{200} is H. In some embodiments, R_{1300} is O. In some embodiments, Z_{100} is O, Z_{200} is C, and Z_{300} is a bond. In some embodiments, R_{1100} is H. In some embodiments, R_{600} is optionally

substituted C_2-C_6 alkenyl, optionally substituted C_1-C_6 alkyl, or H. In some embodiments, R_{100} is H or -C(=O)$NR_{300}R_{400}$.

In some embodiments, a compound or salt thereof is provided wherein R_{1100} is H or halo. In some embodiments, R^{a00}, R^{b00}, R^{c00}, R^{d00}, and R^{i00} are C. In some embodiments, Z_{100} is O, Z_{200} is C, Z_{300} is a bond. In some embodiments, R_{1300} is a bond or C. In some embodiments, y=1. In some embodiments, R_{900} is H. In some embodiments, R_{600} is H, optionally substituted C_1-C_6 alkyl, or optionally substituted C_2-C_6 alkenyl. In some embodiments, R_{200} is H. In some embodiments, R_{100} is H, -C(=O)$NR_{300}R_{400}$, or cyano. In some embodiments, y=0, R_{1300} is a bond and R_{900} is H. In some embodiments, the compound is of Formula 00X:



X, wherein R_{100}, R_{200}. R_{600}. and R_{900} are as defined in claim 1; Z_{100} is O, Z_{200} is C, Z_{300} is a bond; R^{a00}, R^{b00}, R^{c00}, R^{d00}, R^{h00}, and R^{i00} are C; R_{200} is H; R_{1100} is halo; R_{1300} is O; y=0-6; and R_{900} is C_1-C_6 alkyl.

In some embodiments, R_{600} is H, optionally substituted C_1-C_6 alkyl, or optionally substituted C_2-C_6 alkenyl. In some embodiments, R_{100} is H, cyano, or –C(=O)$NR_{300}R_{400}$.

In some embodiments, a compound or salt thereof is provided, wherein Z_{100} is O, Z_{200} and Z_{300} is C. In some embodiments, R^{i00} is C. In some embodiments, R_{200} and/or R_{1100} are

H. In some embodiments, R_{600} is H. In some embodiments, R_{100} is H, halo, cyano, -C(=O)OR_3, or -C(=O)$NR_{300}R_{400}$. In some embodiments, R_{1300} is O; R_{900} is H or –OR_3; and y is 0-6.

In some embodiments, a compound or salt thereof is provided, wherein Z_{100} is S or O; Z_{300} is absent; Z_{200} is C; R_{200} and/or R_{1100} are H; R^{i00} is C; R_{1300} is O; R_{900} is H or –OR_3; and y=0-6. In some embodiments, R^{a00}, R^{b00}, R^{c00}, R^{d00}, R^{h00}, and R^{i00} are C. In some embodiments, R_{600} is H or –C(=O)OR_3. In some embodiments, R_{100} is H or –C(=O)$NR_{300}R_{400}$.

In some embodiments, a compound or salt thereof is provided, wherein R^{i00} is N; R_{200} and/or R_{1100} are H; Z_{300} is a bond or C; Z_{100} is N or O; and Z_{200} is C or C(=O). In some embodiments, R^{a00}, R^{b00}, R^{c00}, R^{d00}, R^{h00} are C. In some embodiments, R_{1300} is O. In some embodiments, R_{900} is H and y=0-6. In some embodiments, wherein R_{100} is halo, H, cyano, -C(=O)$NR_{300}R_{400}$, or -OR_3. In some embodiments, R_{600} is H, optionally substituted C_1-C_6 alkyl, or -$(CH_2)_p$-aryl, wherein p is an integer from 0-6. In some embodiments, Z_{200} is C(=O), Z_{100} is N, and Z_{300} is C.

In some embodiments, a compound or salt thereof is provided, wherein Z_{200} is C(=O) or C; Z_{100} is N or O; and Z_{300} is C or absent. In some embodiments, R^{a00}, R^{b00}, R^{c00}, R^{d00}, and R^{h00} are C. In some embodiments, R_{200} is H. In some embodiments, R_{100} is H, halo, cyano, or –C(=O)$NR_{300}R_{400}$. In some embodiments, R_{1100} is H. In some embodiments, R_{1300} is O; and R_{900} is H or –OR_3. In some embodiments, R_{600} is H, C_1-C_6 alkyl, or -$(CH_2)_pR_{500}$. In some embodiments, Z_{100} is O; Z_{300} is absent; and Z_{200} is C. In some embodiments, the compoundor salt thereof has a structure of Formula I00B.

In some embodiments, a compound or salt thereof of Formula I00C is provided, wherein Z_{100} is C and R_{1400} is a pyridinone. In some embodiments, Z_{100} is O and R_{1400} is optionally substituted –CH2-pyridinone. In some embodiments, R_{600} is H. In some

embodiments, R^{i00} and R^{h00} are C. In some embodiments, R_{1300} is O. In some embodiments, y is an integer from 1-6.

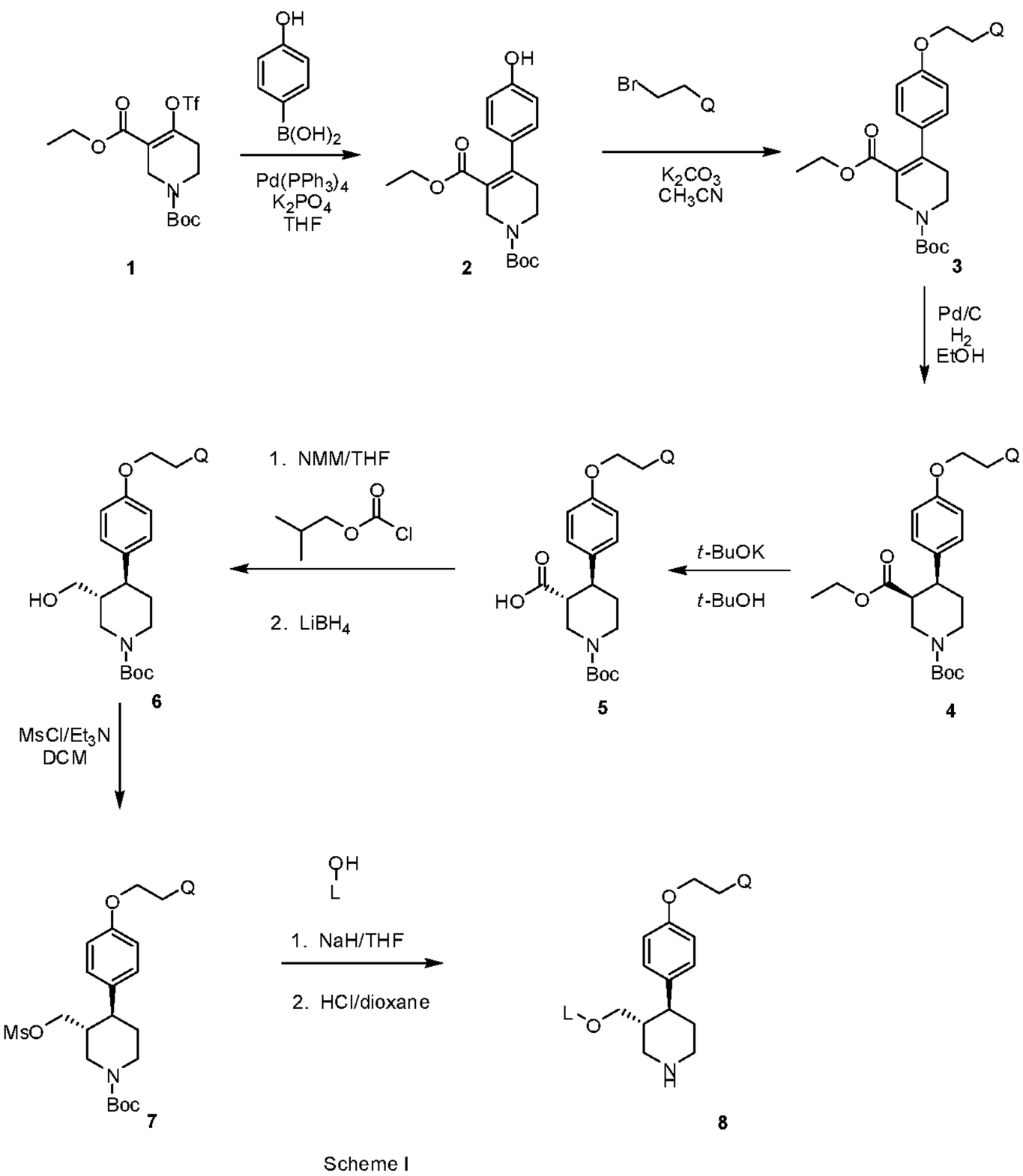
In some embodiments, a compound or salt thereof is chosen from a compound of as shown in Figure 1 and described herein, including in the Examples section of the present disclosure. The data for the compounds can be found in Figure 2 and the Examples. As described herein, the compounds can be prepared according to the schemes and methods described herein and below.

Although the compounds described herein may be shown with specific stereochemistries around certain atoms, such as *cis* or *trans*, the compounds can also be made in the opposite orientation or in a racemic mixture. Such isomers or racemic mixtures are encompassed by the present disclosure.

In some embodiments, the present invention provides pharmaceutical compositions comprising a compound or pharmaceutically salt thereof of any compound described herein.

The compounds described herein can be made by can be made according to the methods described herein and in the examples. The methods described herein can be adapted based upon the compounds desired and described herien. In some embodiments, the method is made according to the following schemes, wherein Q and L are the substituents as shown and described herein and would be apparent to one of skill in the art based upon the present disclosure. In some embodiments, this method can be used to make one or more compounds as described herein and will be apparent to one of skill in the art which compounds can be made according to the methods described herein.

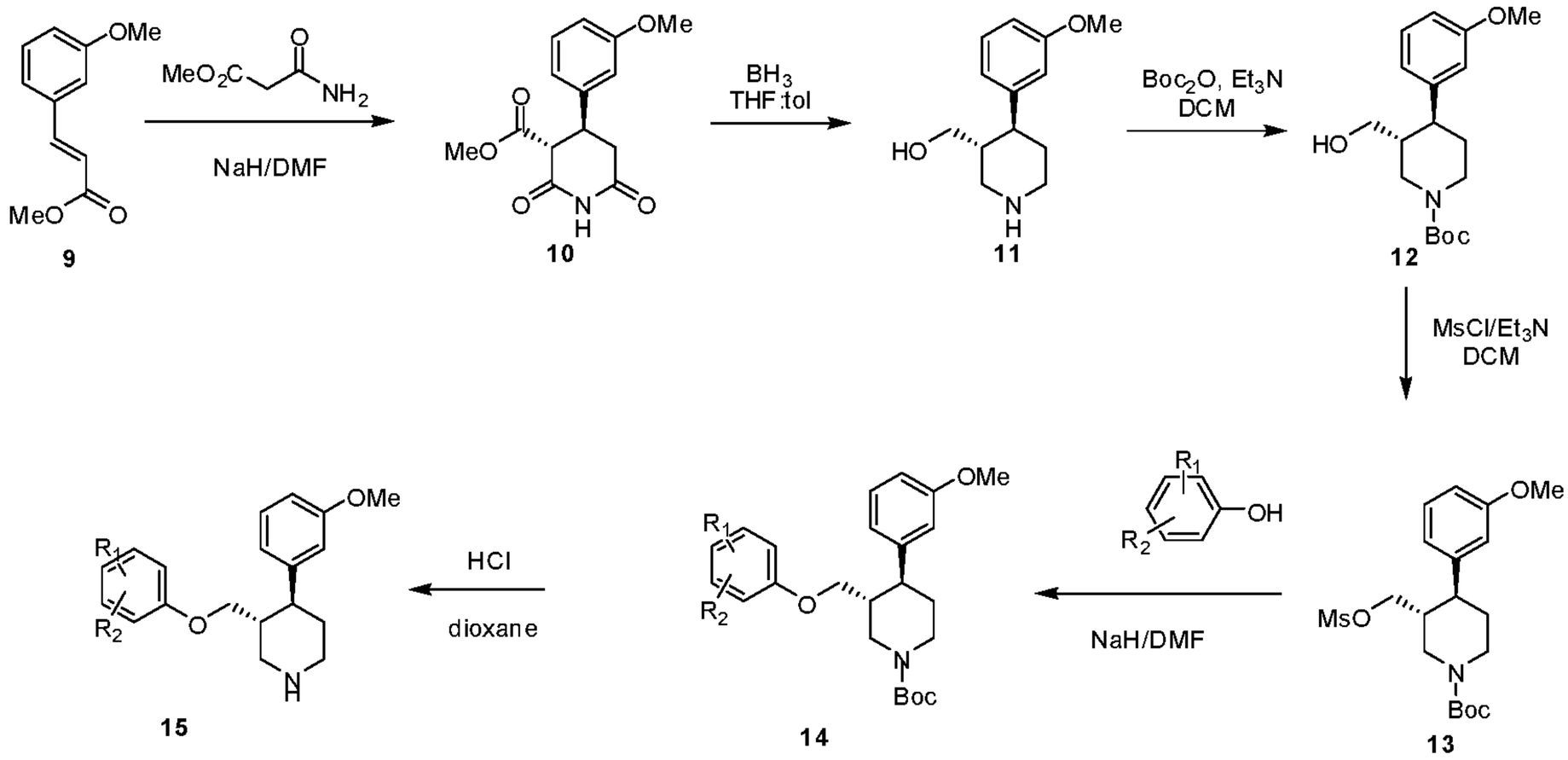
In some embodiments, the compounds made according to Scheme I.



Scheme I

The conditions and temperatures can be varied, or the synthesis can be performed according to the examples described herein.

In some embodiments, one or more compounds is made according to Scheme II.



Scheme II

The conditions and temperatures can be varied, such as shown in the examples described herein. These schemes are non-limiting synthetic schemes and the synthetic routes can be modified as would be apparent to one of skill in the art reading the present specification. The compounds can also be prepared according to the schemes described in the Examples.

The compounds can be used to modulate the δ-opioid receptor. Thus, in some embodiments, the compounds can be referred to as δ-opioid receptor modulating compounds

Although the compounds in the tables above or in the examples section are shown with specific stereochemistries around certain atoms, such as *cis* or *trans*, the compounds can also be made in the opposite orientation or in a racemic mixture.

In some embodiments, the present invention provides pharmaceutical compositions comprising a compound or pharmaceutically salt thereof any compound described herein.

The compounds described herein can be made by can be made according to the methods described herein and in the examples. The methods described herein can be adapted based upon the compounds desired and described herien. In some embodiments, the method is made according to the following schemes, wherein Q and L are the substituents as shown and described herein and would be apparent to one of skill in the art based upon the present disclosure. In some embodiments, this method can be used to make one or more compounds as described herein and will be apparent to one of skill in the art which compounds can be made according to the methods described herein.

In some embodiments, the compounds are made according to schemes described in the examples. The schemes can be used to prepare the compounds and compositions described herein. The conditions and temperatures can be varied, or the synthesis can be performed according to the examples described herein with modifications that are readily apparent based upon the compound being synthesized.

The conditions and temperatures can be varied, such as shown in the examples described herein. These schemes are non-limiting synthetic schemes and the synthetic routes can be modified as would be apparent to one of skill in the art reading the present specification.

The compounds described herein can be administered in any conventional manner by any route where they are active. Administration can be systemic, topical, or oral. For example, administration can be, but is not limited to, parenteral, subcutaneous, intravenous, intramuscular, intraperitoneal, transdermal, oral, buccal, sublingual, or ocular routes, or

intravaginally, by inhalation, by depot injections, or by implants. The mode of administration can depend on the conditions or disease to be targeted or treated. The selection of the specific route of administration can be selected or adjusted by the clinician according to methods known to the clinician to obtain the desired clinical response.

In some embodiments, it may be desirable to administer one or more compounds, or a pharmaceutically acceptable salt thereof, locally to an area in need of treatment. This may be achieved, for example, and not by way of limitation, by local infusion during surgery, topical application, e.g., in conjunction with a wound dressing after surgery, by injection, by means of a catheter, by means of a suppository, or by means of an implant, wherein the implant is of a porous, non-porous, or gelatinous material, including membranes, such as sialastic membranes, or fibers.

The compounds described herein can be administered either alone or in combination (concurrently or serially) with other pharmaceuticals. For example, the compounds can be administered in combination with other analgesics, antidepressants, anti-anxiety compounds, anti-overactive bladder compounds, compounds for the treatment of Parkinsons, and the like. In some embodiments, the compounds can be administered in combination with other PTSD therapeutics. Examples of other pharmaceuticals or medicaments are known to one of skill in the art and include, but are not limited to those described herein.

The means and methods for administration are known in the art and an artisan can refer to various pharmacologic references for guidance (see, for example, Modern Pharmaceutics, Banker & Rhodes, Marcel Dekker, Inc. (1979); and Goodman & Gilman's The Pharmaceutical Basis of Therapeutics, 6th Edition, MacMillan Publishing Co., New York (1980)).

The amount of compound to be administered is that amount which is therapeutically effective. The dosage to be administered will depend on the characteristics of the subject being treated, e.g., the particular animal treated, age, weight, health, types of concurrent treatment, if any, and frequency of treatments, and can be easily determined by one of skill in the art (e.g., by the clinician). The standard dosing for protamine can be used and adjusted (i.e., increased or decreased) depending upon the the factors described above. The selection of the specific dose regimen can be selected or adjusted or titrated by the clinician according to methods known to the clinician to obtain the desired clinical response.

The amount of a compound described herein that will be effective in the treatment and/or prevention of a particular disease, condition, or disorder will depend on the nature and

extent of the disease, condition, or disorder, and can be determined by standard clinical techniques. In addition, *in vitro* or *in vivo* assays may optionally be employed to help identify optimal dosage ranges. The precise dose to be employed in the compositions will also depend on the route of administration, and the seriousness of the disorder, and should be decided according to the judgment of the practitioner and each patient's circumstances. However, a suitable dosage range for oral administration is, generally, from about 0.001 milligram to about 200 milligrams per kilogram body weight, from about 0.01 milligram to about 100 milligrams per kilogram body weight, from about 0.01 milligram to about 70 milligrams per kilogram body weight, from about 0.1 milligram to about 50 milligrams per kilogram body weight, from 0.5 milligram to about 20 milligrams per kilogram body weight, or from about 1 milligram to about 10 milligrams per kilogram body weight. In some embodiments, the oral dose is about 5 milligrams per kilogram body weight.

In some embodiments, suitable dosage ranges for intravenous (i.v.) administration are from about 0.01 mg to about 500 mg per kg body weight, from about 0.1 mg to about 100 mg per kg body weight, from about 1 mg to about 50 mg per kg body weight, or from about 10 mg to about 35 mg per kg body weight. Suitable dosage ranges for other modes of administration can be calculated based on the forgoing dosages as known by those skilled in the art. For example, recommended dosages for intranasal, transmucosal, intradermal, intramuscular, intraperitoneal, subcutaneous, epidural, sublingual, intracerebral, intravaginal, transdermal administration or administration by inhalation are in the range of from about 0.001 mg to about 200 mg per kg of body weight, from about 0.01 mg to about 100 mg per kg of body weight, from about 0.1 mg to about 50 mg per kg of body weight, or from about 1 mg to about 20 mg per kg of body weight. Effective doses may be extrapolated from dose-response curves derived from *in vitro* or animal model test systems. Such animal models and systems are well known in the art.

The compounds described herein can be formulated for parenteral administration by injection, such as by bolus injection or continuous infusion. The compounds can be administered by continuous infusion subcutaneously over a period of about 15 minutes to about 24 hours. Formulations for injection can be presented in unit dosage form, such as in ampoules or in multi-dose containers, with an optinoally added preservative. The compositions can take such forms as suspensions, solutions or emulsions in oily or aqueous vehicles, and can contain formulatory agents such as suspending, stabilizing and/or dispersing agents. In some embodiments, the injectable is in the form of short-acting, depot,

or implant and pellet forms injected subcutaneously or intramuscularly. In some embodiments, the parenteral dosage form is the form of a solution, suspension, emulsion, or dry powder.

For oral administration, the compounds described herein can be formulated by combining the compounds with pharmaceutically acceptable carriers well known in the art. Such carriers enable the compounds to be formulated as tablets, pills, dragees, capsules, emulsions, liquids, gels, syrups, caches, pellets, powders, granules, slurries, lozenges, aqueous or oily suspensions, and the like, for oral ingestion by a patient to be treated. Pharmaceutical preparations for oral use can be obtained by, for example, adding a solid excipient, optionally grinding the resulting mixture, and processing the mixture of granules, after adding suitable auxiliaries, if desired, to obtain tablets or dragee cores. Suitable excipients include, but are not limited to, fillers such as sugars, including, but not limited to, lactose, sucrose, mannitol, and sorbitol; cellulose preparations such as, but not limited to, maize starch, wheat starch, rice starch, potato starch, gelatin, gum tragacanth, methyl cellulose, hydroxypropylmethyl-cellulose, sodium carboxymethylcellulose, and polyvinylpyrrolidone (PVP). If desired, disintegrating agents can be added, such as, but not limited to, the cross-linked polyvinyl pyrrolidone, agar, or alginic acid or a salt thereof such as sodium alginate.

Orally administered compositions can contain one or more optional agents, for example, sweetening agents such as fructose, aspartame or saccharin; flavoring agents such as peppermint, oil of wintergreen, or cherry; coloring agents; and preserving agents, to provide a pharmaceutically palatable preparation. Moreover, where in tablet or pill form, the compositions may be coated to delay disintegration and absorption in the gastrointestinal tract thereby providing a sustained action over an extended period of time. Selectively permeable membranes surrounding an osmotically active driving compound are also suitable for orally administered compounds. Oral compositions can include standard vehicles such as mannitol, lactose, starch, magnesium stearate, sodium saccharine, cellulose, magnesium carbonate, etc. Such vehicles are suitably of pharmaceutical grade.

Dragee cores can be provided with suitable coatings. For this purpose, concentrated sugar solutions can be used, which can optionally contain gum arabic, talc, polyvinyl pyrrolidone, carbopol gel, polyethylene glycol, and/or titanium dioxide, lacquer solutions, and suitable organic solvents or solvent mixtures. Dyestuffs or pigments can be added to the

tablets or dragee coatings for identification or to characterize different combinations of active compound doses.

Pharmaceutical preparations which can be used orally include, but are not limited to, push-fit capsules made of gelatin, as well as soft, sealed capsules made of gelatin and a plasticizer, such as glycerol or sorbitol. The push-fit capsules can contain the active ingredients in admixture with filler such as lactose, binders such as starches, and/or lubricants such as talc or magnesium stearate and, optionally, stabilizers. In soft capsules, the active compounds can be dissolved or suspended in suitable liquids, such as fatty oils, liquid paraffin, or liquid polyethylene glycols. In addition, stabilizers can be added.

For buccal administration, the compositions can take the form of, such as, tablets or lozenges formulated in a conventional manner.

For administration by inhalation, the compounds described herein can be delivered in the form of an aerosol spray presentation from pressurized packs or a nebulizer, with the use of a suitable propellant, such as dichlorodifluoromethane, trichlorofluoromethane, dichlorotetrafluoroethane, carbon dioxide or other suitable gas. In the case of a pressurized aerosol the dosage unit can be determined by providing a valve to deliver a metered amount. Capsules and cartridges of, such as gelatin for use in an inhaler or insufflator can be formulated containing a powder mix of the compound and a suitable powder base such as lactose or starch.

The compounds described herein can also be formulated in rectal compositions such as suppositories or retention enemas, such as containing conventional suppository bases such as cocoa butter or other glycerides. The compounds described herein can also be formulated in vaginal compositions such as vaginal creams, suppositories, pessaries, vaginal rings, and intrauterine devices.

In transdermal administration, the compounds can be applied to a plaster, or can be applied by transdermal, therapeutic systems that are consequently supplied to the organism. In some embodiments, the compounds are present in creams, solutions, powders, fluid emulsions, fluid suspensions, semi-solids, ointments, pastes, gels, jellies, and foams, or in patches containing any of the same.

The compounds described herein can also be formulated as a depot preparation. Such long acting formulations can be administered by implantation (for example subcutaneously or intramuscularly) or by intramuscular injection. Depot injections can be administered at about 1 to about 6 months or longer intervals. Thus, for example, the

compounds can be formulated with suitable polymeric or hydrophobic materials (for example as an emulsion in an acceptable oil) or ion exchange resins, or as sparingly soluble derivatives, for example, as a sparingly soluble salt.

In some embodiments, the compounds can be delivered in a controlled release system. In one embodiment, a pump may be used (see Langer, supra; Sefton, CRC Crit. Ref. Biomed. Eng., 1987, 14, 201; Buchwald et al., Surgery, 1980, 88, 507 Saudek et al., N. Engl. J. Med., 1989, 321, 574). In some embodiments, polymeric materials can be used (see Medical Applications of Controlled Release, Langer and Wise (eds.), CRC Pres., Boca Raton, Fla. (1974); Controlled Drug Bioavailability, Drug Product Design and Performance, Smolen and Ball (eds.), Wiley, New York (1984); Ranger et al., J. Macromol. Sci. Rev. Macromol. Chem., 1983, 23, 61; see, also Levy et al., Science, 1985, 228, 190; During et al., Ann. Neurol., 1989, 25, 351; Howard et al., J. Neurosurg., 1989, 71, 105). In yet another embodiment, a controlled-release system can be placed in proximity of the target of the compounds described herein, such as the liver, thus requiring only a fraction of the systemic dose (see, e.g., Goodson, in Medical Applications of Controlled Release, supra, vol. 2, pp. 115-138 (1984)). Other controlled-release systems discussed in the review by Langer, Science, 1990, 249, 1527-1533) may be used.

It is also known in the art that the compounds can be contained in such formulations with pharmaceutically acceptable diluents, fillers, disintegrants, binders, lubricants, surfactants, hydrophobic vehicles, water soluble vehicles, emulsifiers, buffers, humectants, moisturizers, solubilizers, preservatives and the like. The pharmaceutical compositions can also comprise suitable solid or gel phase carriers or excipients. Examples of such carriers or excipients include, but are not limited to, calcium carbonate, calcium phosphate, various sugars, starches, cellulose derivatives, gelatin, and polymers such as polyethylene glycols. In some embodiments, the compounds described herein can be used with agents including, but not limited to, topical analgesics (e.g., lidocaine), barrier devices (e.g., GelClair), or rinses (e.g., Caphosol).

In some embodiments, the compounds described herein can be delivered in a vesicle, in particular a liposome (see, Langer, Science, 1990, 249, 1527-1533; Treat et al., in Liposomes in the Therapy of Infectious Disease and Cancer, Lopez-Berestein and Fidler (eds.), Liss, New York, pp. 353-365 (1989); Lopez-Berestein, ibid., pp. 317-327; see generally ibid.).

Suitable compositions include, but are not limited to, oral non-absorbed compositions. Suitable compositions also include, but are not limited to saline, water, cyclodextrin solutions, and buffered solutions of pH 3-9.

The compounds described herein, or pharmaceutically acceptable salts thereof, can be formulated with numerous excipients including, but not limited to, purified water, propylene glycol, PEG 400, glycerin, DMA, ethanol, benzyl alcohol, citric acid/sodium citrate (pH3), citric acid/sodium citrate (pH5), tris(hydroxymethyl)amino methane HCl (pH7.0), 0.9% saline, and 1.2% saline, and any combination thereof. In some embodiments, excipient is chosen from propylene glycol, purified water, and glycerin.

In some embodiments, the formulation can be lyophilized to a solid and reconstituted with, for example, water prior to use.

When administered to a mammal (e.g., to an animal for veterinary use or to a human for clinical use) the compounds can be administered in isolated form.

When administered to a human, the compounds can be sterile. Water is a suitable carrier when the compound of Formula I is administered intravenously. Saline solutions and aqueous dextrose and glycerol solutions can also be employed as liquid carriers, particularly for injectable solutions. Suitable pharmaceutical carriers also include excipients such as starch, glucose, lactose, sucrose, gelatin, malt, rice, flour, chalk, silica gel, sodium stearate, glycerol monostearate, talc, sodium chloride, dried skim milk, glycerol, propylene, glycol, water, ethanol and the like. The present compositions, if desired, can also contain minor amounts of wetting or emulsifying agents, or pH buffering agents.

The compositions described herein can take the form of a solution, suspension, emulsion, tablet, pill, pellet, capsule, capsule containing a liquid, powder, sustained-release formulation, suppository, aerosol, spray, or any other form suitable for use. Examples of suitable pharmaceutical carriers are described in Remington's Pharmaceutical Sciences, A.R. Gennaro (Editor) Mack Publishing Co.

In some embodiments, the compounds are formulated in accordance with routine procedures as a pharmaceutical composition adapted for administration to humans. Typically, compounds are solutions in sterile isotonic aqueous buffer. Where necessary, the compositions can also include a solubilizing agent. Compositions for intravenous administration may optionally include a local anesthetic such as lidocaine to ease pain at the site of the injection. Generally, the ingredients are supplied either separately or mixed together in unit dosage form, for example, as a dry lyophilized powder or water free

concentrate in a hermetically sealed container such as an ampoule or sachette indicating the quantity of active agent. Where the compound is to be administered by infusion, it can be dispensed, for example, with an infusion bottle containing sterile pharmaceutical grade water or saline. Where the compound is administered by injection, an ampoule of sterile water for injection or saline can be provided so that the ingredients may be mixed prior to administration.

The pharmaceutical compositions can be in unit dosage form. In such form, the composition can be divided into unit doses containing appropriate quantities of the active component. The unit dosage form can be a packaged preparation, the package containing discrete quantities of the preparations, for example, packeted tablets, capsules, and powders in vials or ampules. The unit dosage form can also be a capsule, cachet, or tablet itself, or it can be the appropriate number of any of these packaged forms.

In some embodiments, a composition of the present invention is in the form of a liquid wherein the active agent (i.e., one of the facially amphiphilic polymers or oligomers disclosed herein) is present in solution, in suspension, as an emulsion, or as a solution/suspension. In some embodiments, the liquid composition is in the form of a gel. In other embodiments, the liquid composition is aqueous. In other embodiments, the composition is in the form of an ointment.

In some embodiments embodiments, the composition is in the form of a solid article. For example, in some embodiments, the ophthalmic composition is a solid article that can be inserted in a suitable location in the eye, such as between the eye and eyelid or in the conjunctival sac, where it releases the active agent as described, for example, U.S. Pat. No. 3,863,633; U.S. Pat. No. 3,867,519; U.S. Pat. No. 3,868,445; U.S. Pat. No. 3,960,150; U.S. Pat. No. 3,963,025; U.S. Pat. No. 4,186,184; U.S. Pat. No. 4,303,637; U.S. Pat. No. 5,443,505; and U.S. Pat. No. 5,869,079. Release from such an article is usually to the cornea, either via the lacrimal fluid that bathes the surface of the cornea, or directly to the cornea itself, with which the solid article is generally in intimate contact. Solid articles suitable for implantation in the eye in such fashion are generally composed primarily of polymers and can be bioerodible or non-bioerodible. Bioerodible polymers that can be used in the preparation of ocular implants carrying one or more of the anti-microbial, facially amphiphilic polymer or oligomer active agents in accordance with the present invention include, but are not limited to, aliphatic polyesters such as polymers and copolymers of poly(glycolide), poly(lactide), poly(epsilon-caprolactone), poly-(hydroxybutyrate) and

poly(hydroxyvalerate), polyamino acids, polyorthoesters, polyanhydrides, aliphatic polycarbonates and polyether lactones. Suitable non-bioerodible polymers include silicone elastomers.

The compositions described herein can contain preservatives. Suitable preservatives include, but are not limited to, mercury-containing substances such as phenylmercuric salts (e.g., phenylmercuric acetate, borate and nitrate) and thimerosal; stabilized chlorine dioxide; quaternary ammonium compounds such as benzalkonium chloride, cetyltrimethylammonium bromide and cetylpyridinium chloride; imidazolidinyl urea; parabens such as methylparaben, ethylparaben, propylparaben and butylparaben, and salts thereof; phenoxyethanol; chlorophenoxyethanol; phenoxypropanol; chlorobutanol; chlorocresol; phenylethyl alcohol; disodium EDTA; and sorbic acid and salts thereof.

Optionally one or more stabilizers can be included in the compositions to enhance chemical stability where required. Suitable stabilizers include, but are not limited to, chelating agents or complexing agents, such as, for example, the calcium complexing agent ethylene diamine tetraacetic acid (EDTA). For example, an appropriate amount of EDTA or a salt thereof, e.g., the disodium salt, can be included in the composition to complex excess calcium ions and prevent gel formation during storage. EDTA or a salt thereof can suitably be included in an amount of about 0.01% to about 0.5%. In those embodiments containing a preservative other than EDTA, the EDTA or a salt thereof, more particularly disodium EDTA, can be present in an amount of about 0.025% to about 0.1% by weight.

One or more antioxidants can also be included in the compositions. Suitable antioxidants include, but are not limited to, ascorbic acid, sodium metabisulfite, sodium bisulfite, acetylcysteine, polyquaternium-1, benzalkonium chloride, thimerosal, chlorobutanol, methyl paraben, propyl paraben, phenylethyl alcohol, edetate disodium, sorbic acid, or other agents know to those of skill in the art. Such preservatives are typically employed at a level of from about 0.001% to about 1.0% by weight.

In some embodiments, the compounds are solubilized at least in part by an acceptable solubilizing agent. Certain acceptable nonionic surfactants, for example polysorbate 80, can be useful as solubilizing agents, as can ophthalmically acceptable glycols, polyglycols, e.g., polyethylene glycol 400 (PEG-400), and glycol ethers.

Suitable solubilizing agents for solution and solution/suspension compositions are cyclodextrins. Suitable cyclodextrins can be chosen from α-cyclodextrin, β-cyclodextrin,

γ-cyclodextrin, alkylcyclodextrins (e.g., methyl-β-cyclodextrin, dimethyl-β-cyclodextrin, diethyl-β-cyclodextrin), hydroxyalkylcyclodextrins (e.g., hydroxyethyl-β-cyclodextrin, hydroxypropyl-β-cyclodextrin), carboxy-alkylcyclodextrins (e.g., carboxymethyl-β-cyclodextrin), sulfoalkylether cyclodextrins (e.g., sulfobutylether-β-cyclodextrin), and the like. Ophthalmic applications of cyclodextrins have been reviewed in Rajewski et al., Journal of Pharmaceutical Sciences, 1996, 85, 1155-1159.

In some embodiments, the composition optionally contains a suspending agent. For example, in those embodiments in which the composition is an aqueous suspension or solution/suspension, the composition can contain one or more polymers as suspending agents. Useful polymers include, but are not limited to, water-soluble polymers such as cellulosic polymers, for example, hydroxypropyl methylcellulose, and water-insoluble polymers such as cross-linked carboxyl-containing polymers.

One or more acceptable pH adjusting agents and/or buffering agents can be included in the compositions, including acids such as acetic, boric, citric, lactic, phosphoric and hydrochloric acids; bases such as sodium hydroxide, sodium phosphate, sodium borate, sodium citrate, sodium acetate, sodium lactate and tris-hydroxymethylaminomethane; and buffers such as citrate/dextrose, sodium bicarbonate and ammonium chloride. Such acids, bases and buffers are included in an amount required to maintain pH of the composition in an acceptable range.

One or more acceptable salts can be included in the compositions of the invention in an amount required to bring osmolality of the composition into an acceptable range. Such salts include, but are not limited to, those having sodium, potassium or ammonium cations and chloride, citrate, ascorbate, borate, phosphate, bicarbonate, sulfate, thiosulfate or bisulfite anions. In some embodiments, salts include sodium chloride, potassium chloride, sodium thiosulfate, sodium bisulfite and ammonium sulfate. In some embodiments, the salt is sodium chloride.

Optionally one or more acceptable surfactants, preferably nonionic surfactants, or co-solvents can be included in the compositions to enhance solubility of the components of the compositions or to impart physical stability, or for other purposes. Suitable nonionic surfactants include, but are not limited to, polyoxyethylene fatty acid glycerides and vegetable oils, e.g., polyoxyethylene (60) hydrogenated castor oil; and polyoxyethylene alkylethers and alkylphenyl ethers, e.g., octoxynol 10, octoxynol 40; polysorbate 20, 60 and

80; polyoxyethylene/polyoxypropylene surfactants (e.g., Pluronic® F-68, F84 and P-103); cyclodextrin; or other agents known to those of skill in the art. Typically, such co-solvents or surfactants are employed in the compositions at a level of from about 0.01% to about 2% by weight.

The present invention also provides pharmaceutical packs or kits comprising one or more containers filled with one or more compounds described herein. Optionally associated with such container(s) can be a notice in the form prescribed by a governmental agency regulating the manufacture, use or sale of pharmaceuticals or biological products, which notice reflects approval by the agency of manufacture, use or sale for human administration for treating a condition, disease, or disorder described herein. In some embodiments, the kit contains more than one compound described herein. In some embodiments, the kit comprises a compound described herein in a single injectable dosage form, such as a single dose within an injectable device such as a syringe with a needle.

Modulation of the δ-opioid receptor has been found to be a target for the treatment of brain disoders. (Trends Pharmacol Sci. 2011 Oct;32(10):581-90. Epub 2011 Sep 17). Specifically, preclinical data has confirmed that delta opioid receptor activation reduces persistent pain and improves negative emotional states. (*Id.*). δ-opioid receptor modulating compounds have also been found to have anxiolytic activities. (J Pharmacol Exp Ther. 2011 Jul;338(1):195-204. Epub 2011 Mar 28.) Therefore, the compounds described herien can be used to treat brain disorders, such as depression, Parkinsons, or anxiety. The compounds can be also used to treat pain. The compounds can also be used to treat overactive bladder.

The present invention also provides methods of treating pain, including, but not limited to neuropathic pain, migraines (chronic, episodic, or acute), headaches (e.g., episodic, chronic, acute, cluster, and the like), Parkinsons, depression, anxiety, overactive bladder, including, but not limited to, major depressive disorder, treatment resistant depression, anxiety, post traumatic stress disorder, neuropathic pain, including, diabetic peripheral neuropathy, post-herpetic neuralgia, chemotherapy induced neuropathic pain, prevention of chemotherapy-induced neuropathy, prevention of chemotherapy-induced neuropathic pain, trigeminal neuralgia, inflammatory pain, including, osteoarthritis, rheumatoid arthritis, Rett Syndrome, Autism spectrum disorders, migraine (chronic, episodic, or acute), cluster headaches, (e.g., episodic, chronic, acute, cluster, and the like), acute abortive treatment, prophylaxis of acute intermittent migraine, prophylaxis of chronic migraine, treatment of episodic and chronic cluster headache, prevention of episodic and chronic cluster headache,

Charcot-Marie Tooth disease, Traumatic brain injury, fibromyalgia, stroke, acute ischemic syndrome, ischemia/reperfusion injury, substance abuse intervention, and/or treatment of alcohol abuse in a subject comprising administering to the subject one or more compounds described herein or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of the same. In some embodiments, the subject is a subject in need of such treatment. As described herein, in some embodiments, the subject is a mammal, such as, but not limited to, a human.

The present invention also provides one or more compounds described above, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition comprising one or more compounds described above, for the treatment of methods of treating pain, including, but not limited to neuropathic pain, migraines (chronic or acute), headaches (e.g., chronic, acute, cluster, and the like) Parkinsons, depression, anxiety, overactive bladder, including, but not limited to, major depressive disorder, treatment resistant depression, anxiety, post traumatic stress disorder, neuropathic pain, including, diabetic peripheral neuropathy, post-herpetic neuralgia, chemotherapy induced neuropathic pain, prevention of chemotherapy-induced neuropathy, prevention of chemotherapy-induced neuropathic pain, trigeminal neuralgia, inflammatory pain, including, osteoarthritis, rheumatoid arthritis, Rett Syndrome, Autism spectrum disorders, migraine, cluster headaches, acute abortive treatment, prophylaxis of acute intermittent migraine, prophylaxis of chronic migraine, treatment of episodic and chronic cluster headache, prevention of episodic and chronic cluster headache, Charcot-Marie Tooth disease, Traumatic brain injury, fibromyalgia, stroke, acute ischemic syndrome, ischemia/reperfusion injury, substance abuse intervention, and/or treatment of alcohol abuse in a subject, such as a mammal or human. In some embodiments, the compounds are for the treatment of methods of treating pain, including, but not limited to neuropathic pain, migraines (chronic or acute), headaches (e.g., chronic, acute, cluster, and the like) Parkinsons, depression, anxiety, overactive bladder, including, but not limited to, major depressive disorder, treatment resistant depression, anxiety, post traumatic stress disorder, neuropathic pain, including, diabetic peripheral neuropathy, post-herpetic neuralgia, chemotherapy induced neuropathic pain, prevention of chemotherapy-induced neuropathy, prevention of chemotherapy-induced neuropathic pain, trigeminal neuralgia, inflammatory pain, including, osteoarthritis, rheumatoid arthritis, Rett Syndrome, Autism spectrum disorders, migraine, cluster headaches, acute abortive treatment, prophylaxis of acute intermittent migraine, prophylaxis of chronic migraine, treatment of episodic and chronic

cluster headache, prevention of episodic and chronic cluster headache, Charcot-Marie Tooth disease, Traumatic brain injury, fibromyalgia, stroke, acute ischemic syndrome, ischemia/reperfusion injury, substance abuse intervention, and/or treatment of alcohol abuse in a subject (*e.g.* mammal or human and others described herein) in need thereof.

The present invention also provides one or more compounds described above, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition comprising one or more compounds described above, for the treatment of hyperalgesia in a subject comprising administering to the subject one or more compounds, or a pharmaceutically acceptable salt thereof, of a compound described herein, or a pharmaceutical composition comprising one or more compounds, or apharmaceutically acceptable salt thereof, of a compound described herein. In some embodiments, the hyperalgesia is opioid induced hyperalgesia. In some embodiments, the opioid induced hyperalgesia is morphine, oxycodone, hydrocodone, hydromorphone, fentanyl, meperidine, alfentanil, remifentanil, sufentanil, etorphine, buprenorphine, methadone, and/or heroin induced hyperalgesia. In some embodiments, the subject has been administered an opioid prior to being administered the one or more compounds, or a pharmaceutically acceptable salt thereof, of the pharmaceutical composition comprising the one or more compounds, or a pharmaceutically acceptable salt thereof.

The present invention also provides one or more compounds described above, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition comprising one or more compounds described above, for decreasing nociceptive sensitization in a subject comprising administering to the subject one or more compounds, or a pharmaceutically acceptable salt thereof, of a compound described herein, or a pharmaceutical composition comprising one or more compounds, or apharmaceutically acceptable salt thereof, of a compound described herein. In some embodiments, the subject has opioid induced nociceptive sensitization. In some embodiments, the opioid induced nociceptive sensitization is morphine, oxycodone, hydrocodone, hydromorphone, fentanyl, meperidine, alfentanil, remifentanil, sufentanil, etorphine, buprenorphine, methadone, and/or heroin, or a pharmaceutically acceptable salt thereof, induced nociceptive sensitization.

The present invention also provides one or more compounds described above, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition comprising one or more compounds described above, for the treatment of pain in a subject comprising administering to the subject one or more compounds, or a pharmaceutically acceptable salt thereof, of a compound described herein, or a pharmaceutical composition comprising one or

more compounds, or a pharmaceutically acceptable salt thereof, of a compound described herein. In some embodiments, the method comprises administering an opioid agonist to the subject until the opioid increases nociceptive sensitization in the subject; and administering to the subject one or more compounds, or a pharmaceutically acceptable salt thereof, of a compound described herein, or a pharmaceutical composition comprising one or more compounds, or a pharmaceutically acceptable salt thereof, of a compound described herein. In some embodiments, the opioid agonist is morphine, oxycodone, hydrocodone, hydromorphone, fentanyl, meperidine, alfentanil, remifentanil, sufentanil, etorphine, buprenorphine, methadone, and/or heroin, or a pharmaceutically acceptable salt thereof.

The present invention also provides one or more compounds described above, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition comprising one or more compounds described above, for the treatment of pain in an opioid exposed subject comprising administering to the subject one or more compounds, or a pharmaceutically acceptable salt thereof, of a compound described herein, or a pharmaceutical composition comprising one or more compounds, or a pharmaceutically acceptable salt thereof, of a compound described herein. In some embodiments, the methods comprise: a)administering an opioid agonist to the subject; and b) administering to the subject of step a), in the absence of the opioid administered in step a), one or more compounds, or a pharmaceutically acceptable salt thereof, of a compound described herein, or a pharmaceutical composition comprising one or more compounds, or a pharmaceutically acceptable salt thereof, of a compound described herein. In some embodiments, the opioid that is administered in step a) is morphine, oxycodone, hydrocodone, hydromorphone, fentanyl, meperidine, alfentanil, remifentanil, sufentanil, etorphine, buprenorphine, methadone, and/or heroin, or a pharmaceutically acceptable salt thereof.

The present invention also provides one or more compounds described above, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition comprising one or more compounds described above, for the treatment of medication overuse headache in a subject comprising administering to the subject one or more compounds, or a pharmaceutically acceptable salt thereof, of a compound described herein, or a pharmaceutical composition comprising one or more compounds, or a pharmaceutically acceptable salt thereof, of a compound described herein. In some embodiments, the medication overuse headache is caused by acetaminophen, aspirin, a mu-opioid agonist, a non-steroidal anti-inflammatory drug (NSAID), or a triptan. In some embodiments, the

triptan is sumatriptan, rizatriptan, naratriptan, zolmitriptan, eletriptan, almotriptan, frovatriptan, avitriptan, or donitriptan, or a pharmaceutically acceptable salt thereof. In some embodiments, the mu-opioid agonist is morphine, oxycodone, hydrocodone, hydromorphone, fentanyl, meperidine, alfentanil, remifentanil, sufentanil, etorphine, buprenorphine, methadone, or heroin, or a pharmaceutically acceptable salt thereof.

The present invention also provides one or more compounds described above, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition comprising one or more compounds described above, for the treatment of migraines in a subject comprising administering a triptan to a subject; and administering to the subject one or more compounds, or a pharmaceutically acceptable salt thereof, of a compound described herein, or a pharmaceutical composition comprising one or more compounds, or a pharmaceutically acceptable salt thereof, of a compound described herein. In some embodiments, the one or more compounds, or a pharmaceutically acceptable salt thereof, of a compound described herein, or a pharmaceutical composition comprising one or more compounds, or a pharmaceutically acceptable salt thereof, of a compound described herein is administered in the absence of the triptan. In some embodiments, the triptan is sumatriptan, rizatriptan, naratriptan, zolmitriptan, eletriptan, almotriptan, frovatriptan, avitriptan, or donitriptan, or a pharmaceutically acceptable salt thereof. In some embodiments, the subject develops medication overuse headache prior to being administered the one or more compounds, or a pharmaceutically acceptable salt thereof, of a compound described herein, or a pharmaceutical composition comprising one or more compounds, or a pharmaceutically acceptable salt thereof, of a compound described herein.

The present invention also provides one or more compounds described above, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition comprising one or more compounds described above, for use in the manufacture of a medicament for the treatment of methods of treating pain, including, but not limited to neuropathic pain, medication overuse headache, hyperalgesia, decreasing nociceptive sensitization, pain in an opioid exposed subject, migraines (chronic or acute), headaches (e.g., chronic, acute, cluster, and the like) Parkinsons, depression, anxiety, overactive bladder, including, but not limited to, major depressive disorder, treatment resistant depression, anxiety, post traumatic stress disorder, neuropathic pain, including, diabetic peripheral neuropathy, post-herpetic neuralgia, chemotherapy induced neuropathic pain, prevention of chemotherapy-induced neuropathy, prevention of chemotherapy-induced neuropathic pain, trigeminal neuralgia, inflammatory

pain, including, osteoarthritis, rheumatoid arthritis, Rett Syndrome, Autism spectrum disorders, migraine, cluster headaches, acute abortive treatment, prophylaxis of acute intermittent migraine, prophylaxis of chronic migraine, treatment of episodic and chronic cluster headache, prevention of episodic and chronic cluster headache, Charcot-Marie Tooth disease, Traumatic brain injury, fibromyalgia, stroke, acute ischemic syndrome, ischemia/reperfusion injury, substance abuse intervention, and/or treatment of alcohol abuse in a subject, such as those described herein. In some embodiments, the mammal is a mammal in need thereof.

The present invention also provides the use of one or more compounds described above, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition comprising one or more compounds described above, in the modulation of a δ-opioid receptor. In some embodiments, the compounds, pharmaceutically acceptable salt thereof, or a pharmaceutical composition of the same modulate the Beta-arrestin modulated pathway of the δ-opioid receptor. In some embodiments, the compounds, pharmaceutically acceptable salt thereof, or a pharmaceutical composition of the same modulate the G-protein modulated pathway of the δ-opioid receptor.

As used herein, “modulation” can refer to either inhibition or enhancement of a specific activity. For example, the modulation of the δ-opioid receptor can refer to the inhibition and/or activation of the G-protein mediated pathway of the δ-opioid receptor. In some embodiments, the modulation refers to the inhibition or activation of the β-arrestin mediated pathway of the δ-opioid receptor. The activity of a δ-opioid receptor can be measured by any method including but not limited to the methods described herein.

The compounds described herien are agonists or antagonists of the delta opioid receptors (DORs). The ability of the compounds to stimulate or inhibit DOR mediated signaling may be measured using any assay known in the art used to detect DOR mediated signaling or DOR activity, or the absence of such signaling/activity. "DOR activity" refers to the ability of an DOR to transduce a signal. Such activity can be measured, e.g., in a heterologous cell, by coupling an DOR (or a chimeric DOR) to a downstream effector such as adenylate cyclase.

A “natural ligand-induced activity” as used herein, refers to activation of the DOR by a natural ligand of the DOR. Activity can be assessed using any number of endpoints to measure DOR activity.

Generally, assays for testing compounds that modulate DOR-mediated signal transduction include the determination of any parameter that is indirectly or directly under the influence of a DOR, e.g., a functional, physical, or chemical effect.

Samples or assays comprising DORs that are treated with a potential activator, inhibitor, or modulator are compared to control samples without the inhibitor, activator, or modulator to examine the extent of inhibition. Control samples (untreated with inhibitors) are assigned a relative DOR activity value of 100%. Inhibition of an DOR is achieved when the DOR activity value relative to the control is about 80%, 50%, or 25%. Activation of an DOR is achieved when the DOR activity value relative to the control (untreated with activators) is 110%, 150%, or 200-500% (i.e., two to five fold higher relative to the control), or 1000-3000% or higher.

The effects of the compounds upon the function of an DOR can be measured by examining any of the parameters described above. Any suitable physiological change that affects DOR activity can be used to assess the influence of a compound on the DORs and natural ligand-mediated DOR activity. When the functional consequences are determined using intact cells or animals, one can also measure a variety of effects such as changes in intracellular second messengers such as cAMP.

In some embodiments, The compound or a pharmaceutically acceptable salt thereof selectively inhibits the Beta-arrestin mediated pathway of the delta-opioid receptor. In some embodiments, The compound or a pharmaceutically acceptable salt thereof selectively inhibits the cAMP mediated pathway of the delta-opioid receptor. In some embodiments, The compound or a pharmaceutically acceptable salt thereof selectively activates the Beta-arrestin mediated pathway of the delta-opioid receptor. In some embodiments, The compound or a pharmaceutically acceptable salt thereof selectively activates the cAMP mediated pathway of the delta-opioid receptor.

Modulators of DOR activity can be tested using DOR polypeptides as described herein, either recombinant or naturally occurring. The protein can be isolated, expressed in a cell, expressed in a membrane derived from a cell, expressed in tissue or in an animal. For example, neuronal cells, cells of the immune system, transformed cells, or membranes can be used to test the GPCR polypeptides described above. Modulation is tested using one of the in vitro or in vivo assays described herein. Signal transduction can also be examined in vitro with soluble or solid state reactions, using a chimeric molecule such as an extracellular domain of a receptor covalently linked to a heterologous signal transduction domain, or a

heterologous extracellular domain covalently linked to the transmembrane and or cytoplasmic domain of a receptor. Furthermore, ligand-binding domains of the protein of interest can be used in vitro in soluble or solid state reactions to assay for ligand binding.

Ligand binding to an DOR, a domain, or chimeric protein can be tested in a number of formats. Binding can be performed in solution, in a bilayer membrane, attached to a solid phase, in a lipid monolayer, or in vesicles. For example, in an assay, the binding of the natural ligand to its receptor is measured in the presence of a candidate modulator, such as the compound described herein. Alternatively, the binding of the candidate modulator may be measured in the presence of the natural ligand. Often, competitive assays that measure the ability of a compound to compete with binding of the natural ligand to the receptor are used. Binding can be tested by measuring, e.g., changes in spectroscopic characteristics (e.g., fluorescence, absorbance, refractive index), hydrodynamic (e.g., shape) changes, or changes in chromatographic or solubility properties.

The activity of the compounds can also be measured using assays involving β-arrestin recruitment. β-arrestin serves as a regulatory protein that is distributed throughout the cytoplasm in unactivated cells. Ligand binding to an appropriate DOR is associated with redistribution of β-arrestin from the cytoplasm to the cell surface, where it associates with the DOR. Thus, receptor activation and the effect of candidate modulators on ligand-induced receptor activation, can be assessed by monitoring β-arrestin recruitment to the cell surface. This is frequently performed by transfecting a labeled β-arrestin fusion protein (*e.g.*, β-arrestin-green fluorescent protein (GFP)) into cells and monitoring its distribution using confocal microscopy (see, *e.g.*, Groarke *et al.*, J. Biol. Chem. 274(33):23263 69 (1999)).

Another technology that can be used to evaluate DOR-protein interactions in living cells involves bioluminescence resonance energy transfer (BRET). A detailed discussion regarding BRET can be found in Kroeger *et al.*, J. Biol. Chem., 276(16):12736 43 (2001).

Other assays can involve determining the activity of receptors which, when activated by ligand binding, result in a change in the level of intracellular cyclic nucleotides, *e.g.*, cAMP, by activating or inhibiting downstream effectors such as adenylate cyclase. In one embodiment, changes in intracellular cAMP can be measured using immunoassays. The method described in Offermanns & Simon, J. Biol. Chem. 270:15175 15180 (1995) may be used to determine the level of cAMP. Also, the method described in Felley-Bosco *et al.*, Am. J. Resp. Cell and Mol. Biol. 11:159 164 (1994) may be used to determine the level of cGMP.

Further, an assay kit for measuring cAMP a is described in U.S. Pat. No. 4,115,538, herein incorporated by reference.

In another embodiment, transcription levels can be measured to assess the effects of a test compound on ligand-induced signal transduction. A host cell containing the protein of interest is contacted with a test compound in the presence of the natural ligand for a sufficient time to effect any interactions, and then the level of gene expression is measured. The amount of time to effect such interactions may be empirically determined, such as by running a time course and measuring the level of transcription as a function of time. The amount of transcription may be measured by using any method known to those of skill in the art to be suitable. For example, mRNA expression of the protein of interest may be detected using northern blots or their polypeptide products may be identified using immunoassays. Alternatively, transcription based assays using reporter genes may be used as described in U.S. Pat. No. 5,436,128, herein incorporated by reference. The reporter genes can be, *e.g.*, chloramphenicol acetyltransferase, firefly luciferase, bacterial luciferase, β-galactosidase and alkaline phosphatase. Furthermore, the protein of interest can be used as an indirect reporter via attachment to a second reporter such as green fluorescent protein (see, *e.g.*, Mistili & Spector, Nature Biotechnology 15:961 964 (1997)).

The amount of transcription is then compared to the amount of transcription in either the same cell in the absence of the test compound, or it may be compared with the amount of transcription in a substantially identical cell that lacks the protein of interest. A substantially identical cell may be derived from the same cells from which the recombinant cell was prepared but which had not been modified by introduction of heterologous DNA. Any difference in the amount of transcription indicates that the test compound has in some manner altered the activity of the protein of interest.

Additional assays can also be used. For example, the activity of the compound can be measured in a cell based assay. For example a nucleic acid molecule encoding the delta-opioid receptor (Accession NP_000902) can be incoprorated into an expression vector and transfected or transformed into a cell. I some embodiments, the expression vector is a plasmid or virus. In some embodiments, the expression of the nucleic acid molecule is opoerably linked to a promoter. The promoter can be constitutive or respond to a drug or other response element so that the expression can be controlled. The type of expression vector is not critical and any expression vector can be used that is suitable for the cell type. In some embodiments, the plasmid is pCMV-Prolink. In some embodiments, the cell is a

mammalian cell. In some embodiments, the cell is a Chinese Hamster Ovary (CHO-1) cell. In some embodiments, the cell is an EA-arrestin parental line CHO-1 cell, which is available from from DiscoveRx Corporation (Fremont, CA). The expression of the receptor can be stable so that that stable cell lines can be selected. The selection of stably expressing receptor cell lines can be done to routien methods, such as selecting for expression under G418 (Geneticin). The expression of the receptor can also be transient.

After the receptor is expressed in a cell the cells can be grown in appropriate media in the appropraite cell plate. The cells can be plated, for example at 5000-10000 cells per well in a 384 well plate. In some embodiments, the cells are plated at about 1000, 2000, 3000, 4000, 5000, 6000, 7000, 8000, 9000, or 10000 cells/per well. The plates can have any nubmer of wells and the number of cells can be modified accordingly.

In some embodiments, to measure cAMP activity that is mediated by the receptor, responses can be determined by measuring changes in intracellular cAMP using. cAMP can be measured by any known method or kit. Examples of a kit that can be used, include but are not limited to, CisBio HTRF cAMP HiRange kit (cat # 62AM6PEJ) based on time-resolved fluorescence resonance energy transfer (TR-FRET). The compounds (*e.g.* test or control) can be contacted with the cells for a period of time and then cAMP can be measured.

In some embodiments, a compound's effect on beta-arrestin activity of the receptor is measured. The activity can be measured by any method or kit. For example, the beta-arrestin recruitment or activity was determined using the DiscoveRx beta-arrestin PathHunter Detection kit (cat # 93-0001). In this system, beta-Arrestin is fused to an N-terminal deletion mutant of beta-galactosidase (termed the enzyme acceptor of EA) and the GPCR of interest is fused to a smaller (42 amino acids), weakly complementing fragment termed ProLink™. In cells that stably express these fusion proteins, ligand stimulation results in the interaction of beta-arrestin and the Prolink-tagged GPCR, forcing the complementation of the two beta-galactosidase fragments and resulting in the formation of a functional enzyme that converts substrate to detectable signal. Compounds that enhance this activity will lead to an increase in functional enzyme and an increase in the detectable signal. Compounds that inhibit this activity will decrease the detectable signal. Compounds may also have no effect on the beta-arrestin recruitment.

The present invention also provides the use of one or more compounds described above, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition comprising one or more compounds described above, in the treatment of methods of treating

pain, including, but not limited to neuropathic pain, migraines (chronic or acute), headaches (e.g., chronic, acute, cluster, and the like) Parkinsons, depression, anxiety, overactive bladder, including, but not limited to, major depressive disorder, treatment resistant depression, anxiety, post traumatic stress disorder, neuropathic pain, including, diabetic peripheral neuropathy, post-herpetic neuralgia, chemotherapy induced neuropathic pain, prevention of chemotherapy-induced neuropathy, prevention of chemotherapy-induced neuropathic pain, trigeminal neuralgia, inflammatory pain, including, osteoarthritis, rheumatoid arthritis, Rett Syndrome, Autism spectrum disorders, migraine, cluster headaches, acute abortive treatment, prophylaxis of acute intermittent migraine, prophylaxis of chronic migraine, treatment of episodic and chronic cluster headache, prevention of episodic and chronic cluster headache, Charcot-Marie Tooth disease, Traumatic brain injury, fibromyalgia, stroke, acute ischemic syndrome, ischemia/reperfusion injury, substance abuse intervention, and/or treatment of alcohol abuse in a subject or a subject in need thereof, such as those described herein.

Any medicament having utility in an application described herein can be used in co-therapy, co-administration or co-formulation with a composition as described above. Such additional medicaments include, medicines for Parkinsons, such as but not limited to levodopa, carbidopa, Catechol-O-methyl Transferase Inhibitors (*e.g.* Entacapone or Tolcapone), dopamine agonists, ropinirole, bromocriptine, pramipexole, Monoamine Oxidase Inhibitors (MAOi) (*e.g.* rasagiline or selegiline), anti-cholinergics (*e.g.* Benztropine or Trihexyphenidyl), and amantadine. Examples of medicaments for overactive bladder include, but are not limited to, tolterodine (Detrol), oxybutynin (Ditropan), an oxybutynin skin patch (Oxytrol), trospium (Sanctura), solifenacin (Vesicare) and darifenacin (Enablex). Examples of medicaments for the treatment of depression and/or anxiety include, but are not limited to, selective serotonin reuptake inhibitors (SSRIs), such as fluoxetine (Prozac), paroxetine (Paxil), and sertraline (Zoloft); tricyclic and tetracyclic antidepressants, such as doxepin (Sinequan) and nortriptyline (Aventyl, Pamelor); other antidepressants, such as bupropion (Wellbutrin, Wellbutrin SR), mirtazapine (Remeron) and trazodone, and venlafaxine (Effexor, Effexor XR); monoamine oxidase inhibitors (MAOIs), such as isocarboxazid (Marplan), phenelzine sulfate (Nardil), and selegiline (Emsam), Ativan, Celexa, Cymbalta, Klonopin, Lexapro, Luvox CR, Norpramin, Paxil, Remeron, Tofranil, Valium, and Xanax.

Examples of pain medicaments include, but are not limited to non-steroidal anti-inflammaotry agents, opioids, non-narcotic analgesics, topical analgesics, topical anesthetics. Examples of suitable non-steroidal anti-inflammatory agents include, but are not limited to, prostaglandin H synthetase inhibitors (Cos I or Cox II), also referred to as cyclooxygenase type I and type II inhibitors, such as diclofenac, flurbiprofen, ketorolac, suprofen, nepafenac, amfenac, indomethacin, naproxen, ibuprofen, bromfenac, ketoprofen, meclofenamate, piroxicam, sulindac, mefanamic acid, diflusinal, oxaprozin, tolmetin, fenoprofen, benoxaprofen, nabumetome, etodolac, phenylbutazone, aspirin, oxyphenbutazone, tenoxicam and carprofen; cyclooxygenase type II selective inhibitors, such as vioxx, celecoxib, etodolac; PAF antagonists, such as apafant, bepafant, minopafant, nupafant and modipafant; PDE II inhibitors, such as ariflo, torbafylline, rolipram, filaminast, piclamilast, cipamfylline, and roflumilast; inhibitors of cytokine production, such as inhibitors of the NFkB transcription factor; or other anti-inflammatory agents know to those skilled in the art. Other examples of pain medicaments include, but are not limited to, acetaminophen, buprenorphine, butorphanol, codeine, hydrocodone, hydromorphone, levorphanol, meperidine, methadone, morphine, nalbuphine, oxycodone, oxymorphone, pentazocine, propoxyphene, tramadol, butalbital, capsaicin, benzocaine, dibucaine, prilocaine and lidocaine.

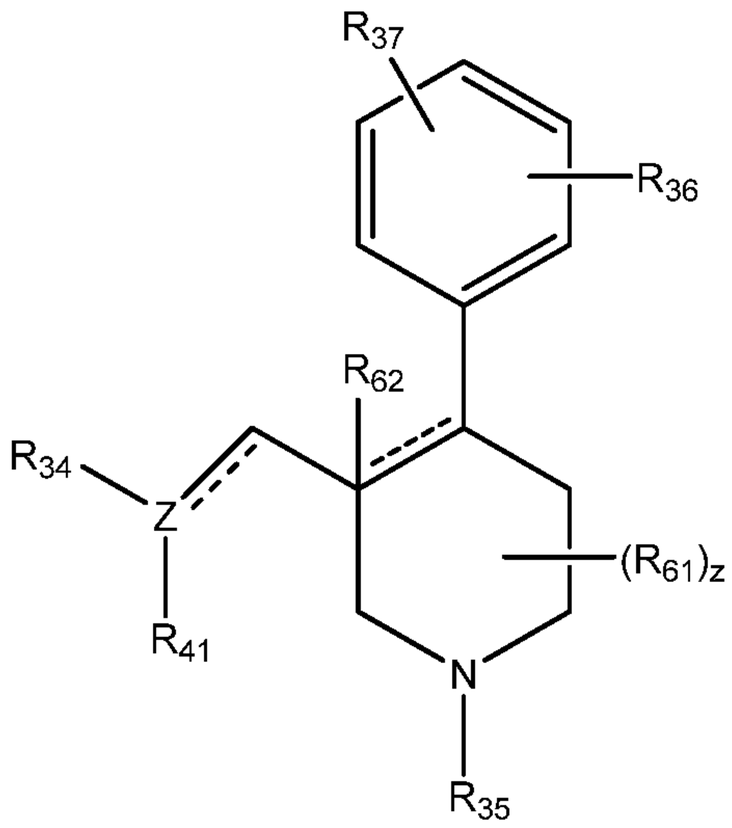
The additional medicament can be administered in co-therapy (including co-formulation) with the one or more of the compounds described herein.

In some embodiments, the response of the disease or disorder to the treatment is monitored and the treatment regimen is adjusted if necessary in light of such monitoring.

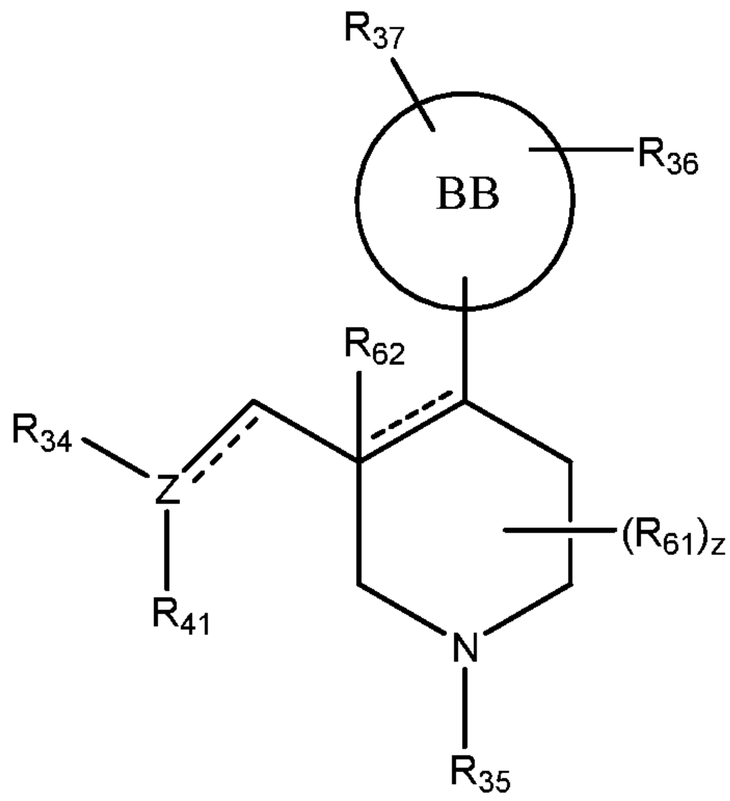
Frequency of administration is typically such that the dosing interval, for example, the period of time between one dose and the next, during waking hours is from about 2 to about 12 hours, from about 3 to about 8 hours, or from about 4 to about 6 hours. It will be understood by those of skill in the art that an appropriate dosing interval is dependent to some degree on the length of time for which the selected composition is capable of maintaining a concentration of the compound(s) in the subject and/or in the target tissue (e.g., above the EC_{50} (the minimum concentration of the compound which modulates the receptor's activity by 90%). Ideally the concentration remains above the EC_{50} for at least 100% of the dosing interval. Where this is not achievable it is desired that the concentration should remain above the EC_{50} for at least about 60% of the dosing interval, or should remain above the EC_{50} for at least about 40% of the dosing interval.

The present disclosure also provides the following non-limiting embodiments:

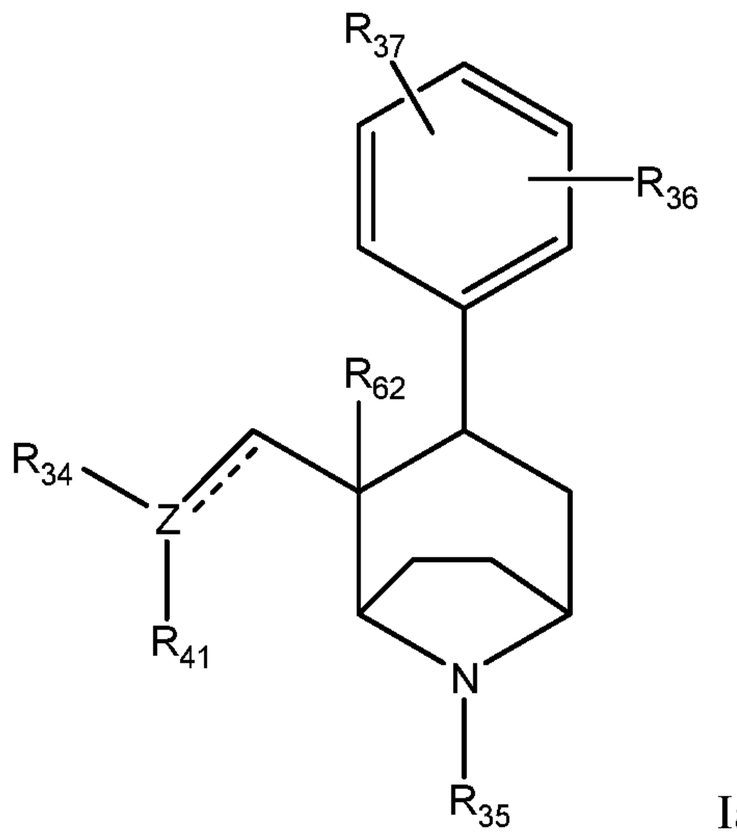
1. A compound having Formula I, I-1, I-a, I-a1 or I-b, Ib-1, or Ib-2



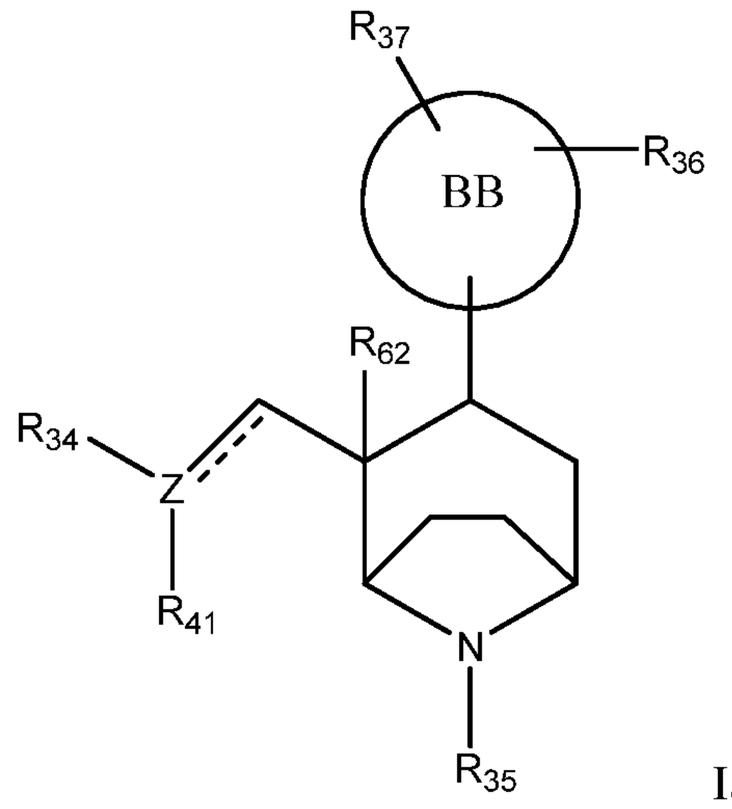
I



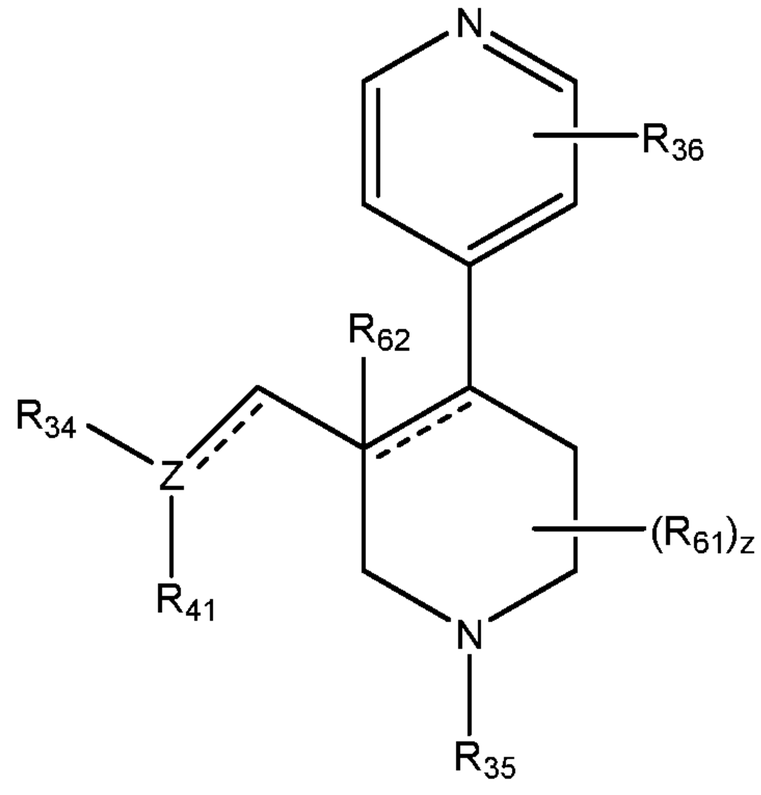
I-1



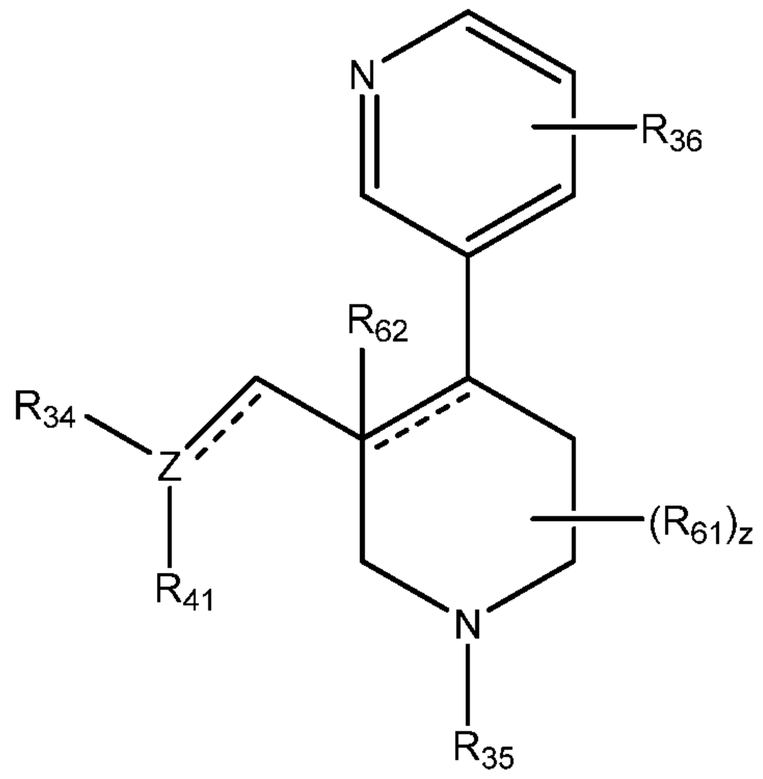
Ia, ,



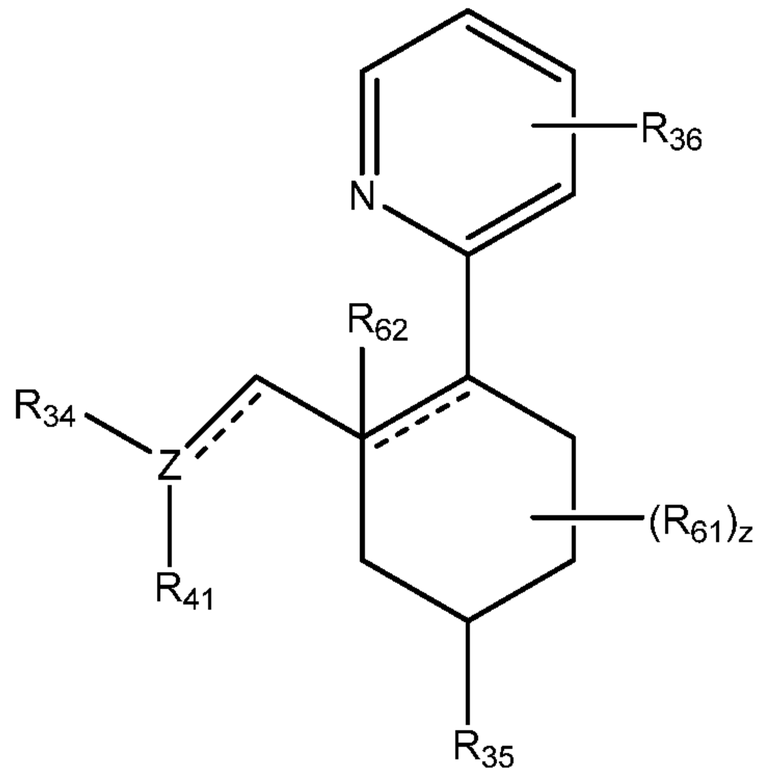
Ia-1



Ib,

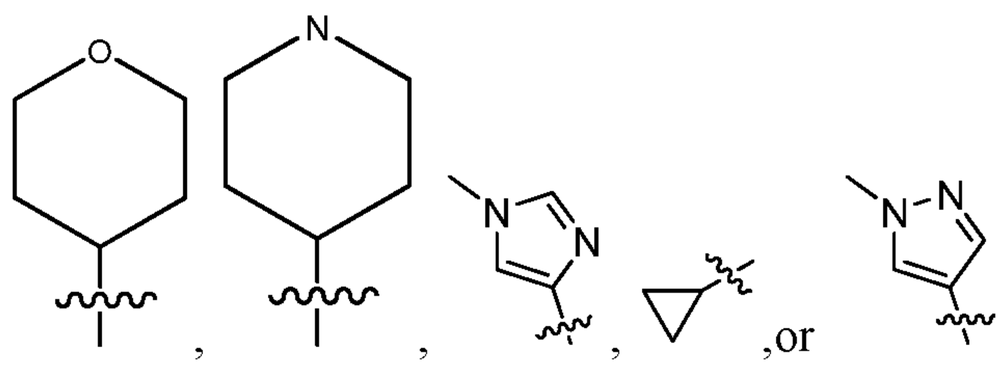


Ib-1, or



Ib-2

or pharmaceutically acceptable salt thereof, wherein:

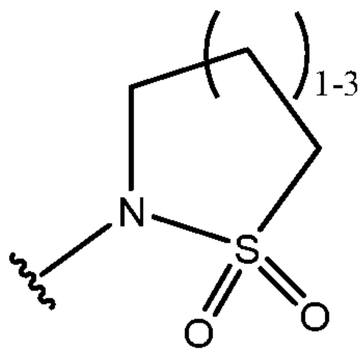
BB is  , or

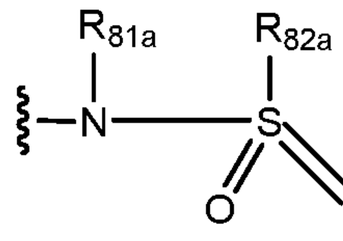
Z is C, S, N, $S(O)_2$ or O;

R_{35} is a protecting group, $C(=O)OR_{81b}$, H, optionally substituted aryl, optionally substituted C_1-C_6 haloalkyl, $-R_{63}R_{64}$, optionally substituted C_1-C_6 branched or unbranched alkyl, optionally substituted C_2-C_6 alkenyl, optionally substituted C_2-C_6 haloalkenyl – $(CH_2)_nR_{65}$, optionally substituted heterocycle, optionally substituted C_1-C_6 ester, optionally substituted cycloalkyl, optionally substituted C_1-C_6 alkoxy, optionally substituted pyrrolinyl,

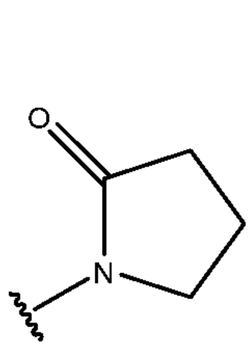
optionally substituted morpholinyl, , optionally substituted C_3-C_6 cyclic ether, or optionally substituted piperidyl;

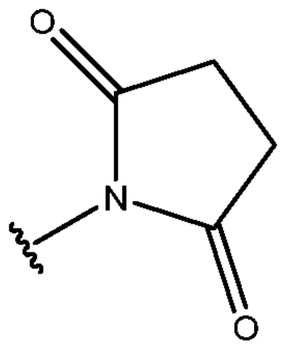
R_{36} is null, H, halo, optionally substituted C_1-C_6 haloalkyl, -SO_2C_1-C_6alkyl, -OCF_3, optionally substituted C_1-C_6 alkyl, or -OR_{75}; wherein R_{75} is H or optionally substituted C_1-C_6 alkyl;

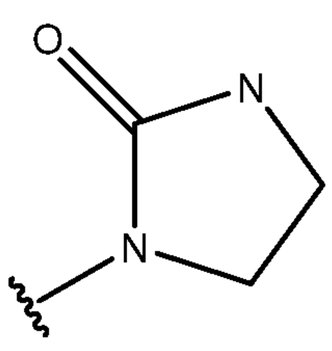
R_{37} is, null, H, halo, optionally substituted C_1-C_6 haloalkyl, -SO_2C_1-C_6alkyl, -OCF_3, optionally substituted sulfonamide, optionally substituted cyclic sulfonamide, or -$(CH_2)_q$-R_{38}, -NH-$(CH_2)_q$-R_{38}, -S-$(CH_2)_q$-R_{38}, -C(=O)R_{38}, or -O-$(CH_2)_q$-R_{38}, 

, 

;

R_{38} is H, C_1-C_6 alkyl, halo, C_1-C_6 haloalkyl, -C(=O)C_1-C_6 alkyl, –OR_{66}, $S(O)_2R_{67}$, 

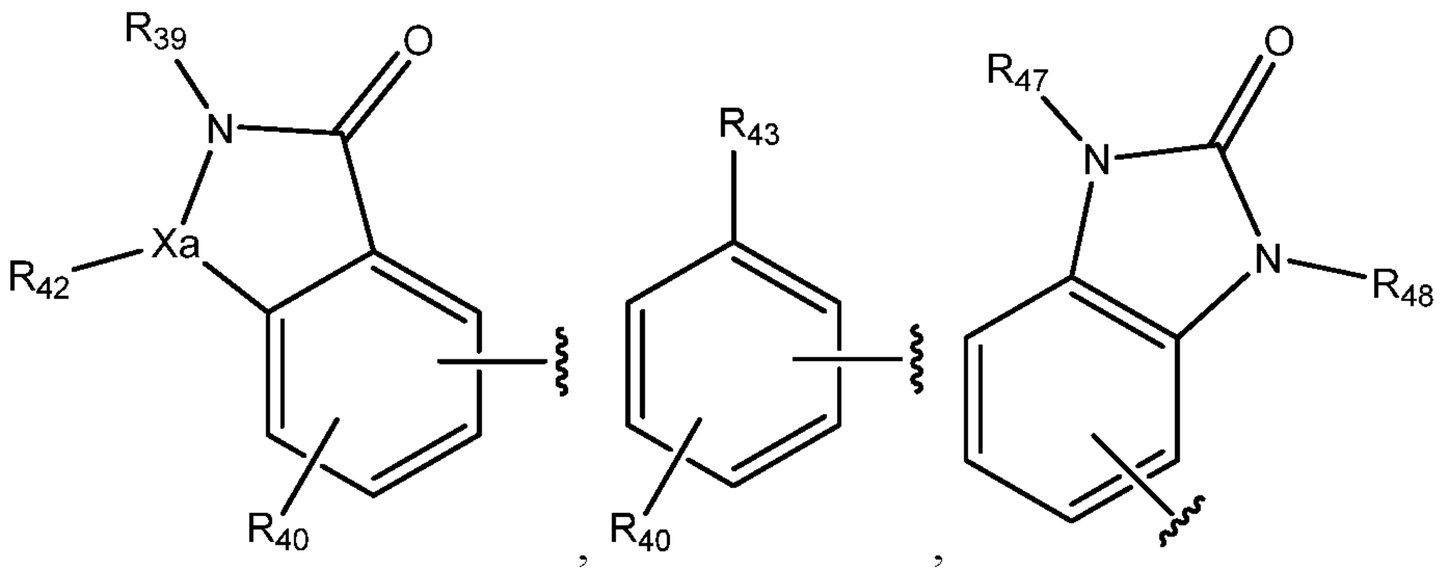
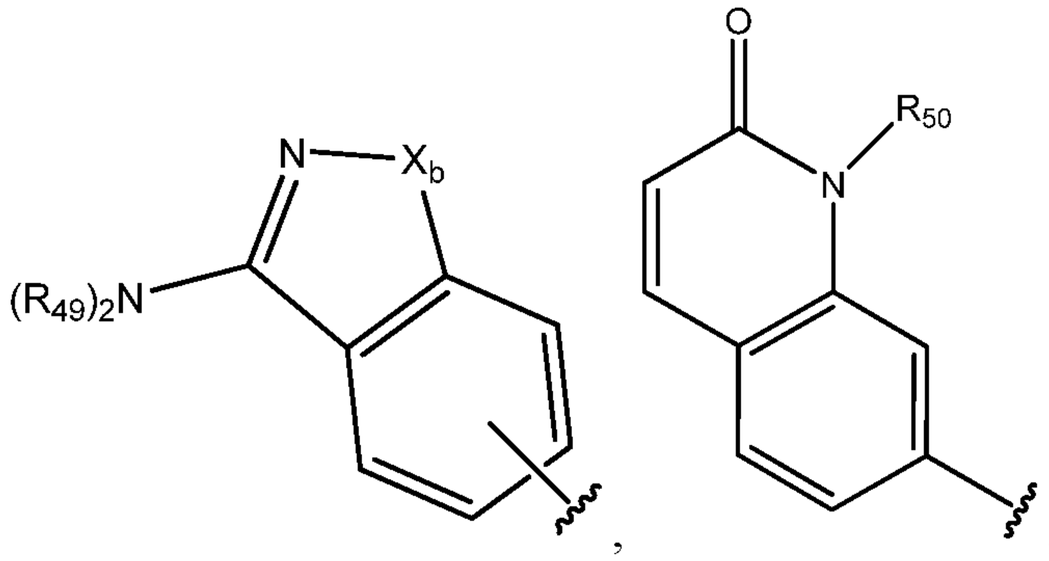
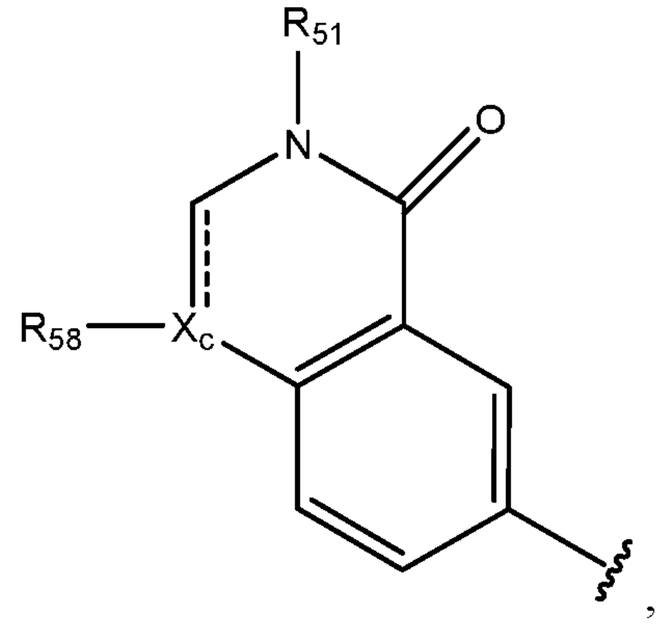
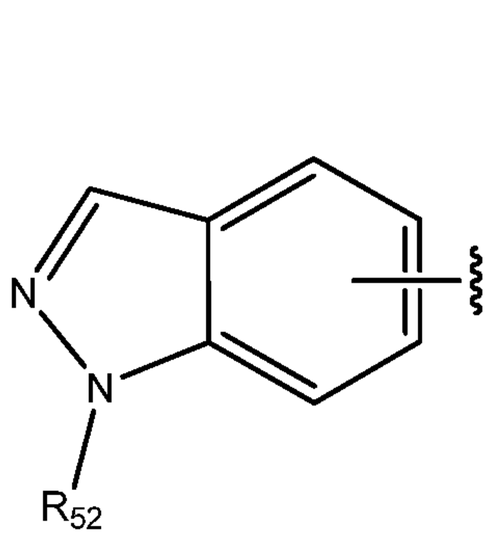
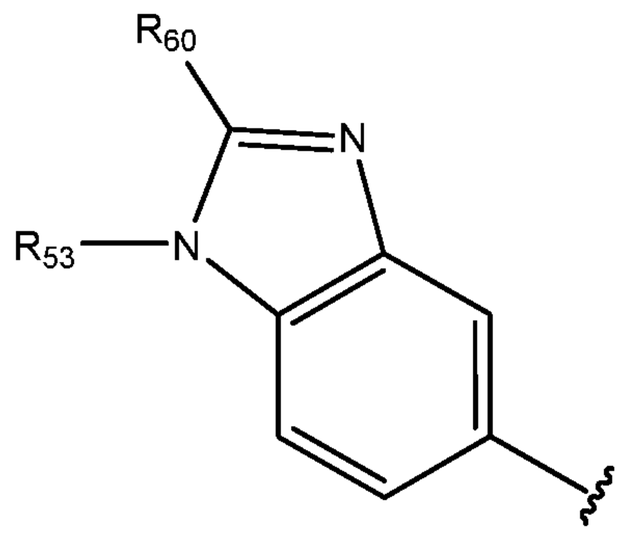
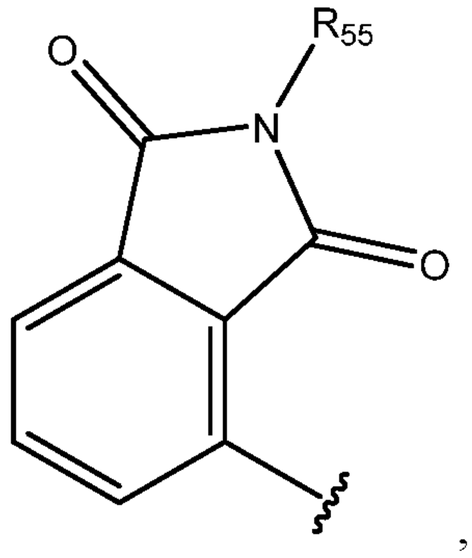
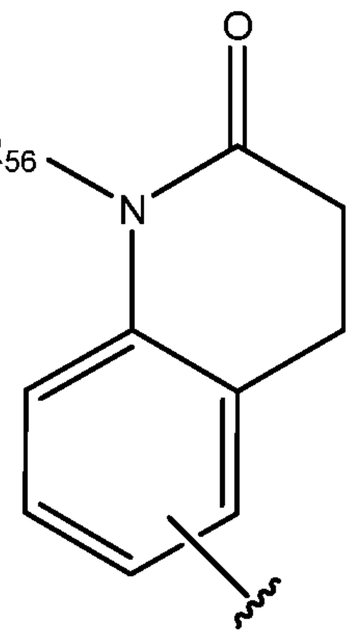
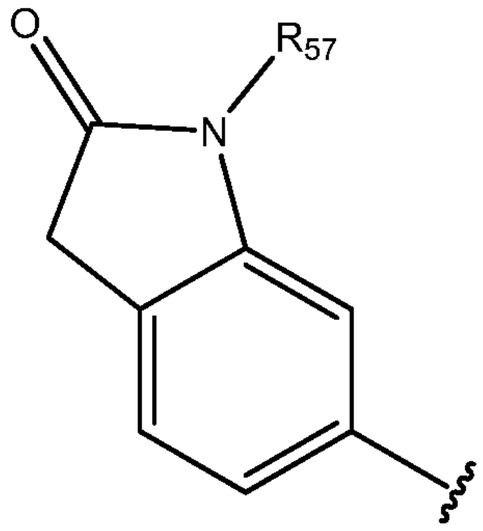
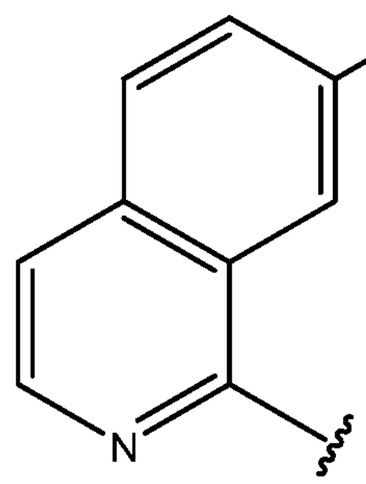
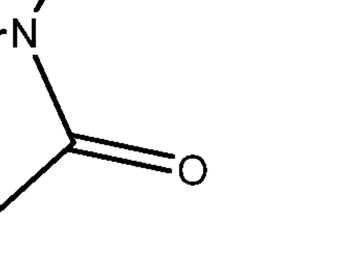
, 

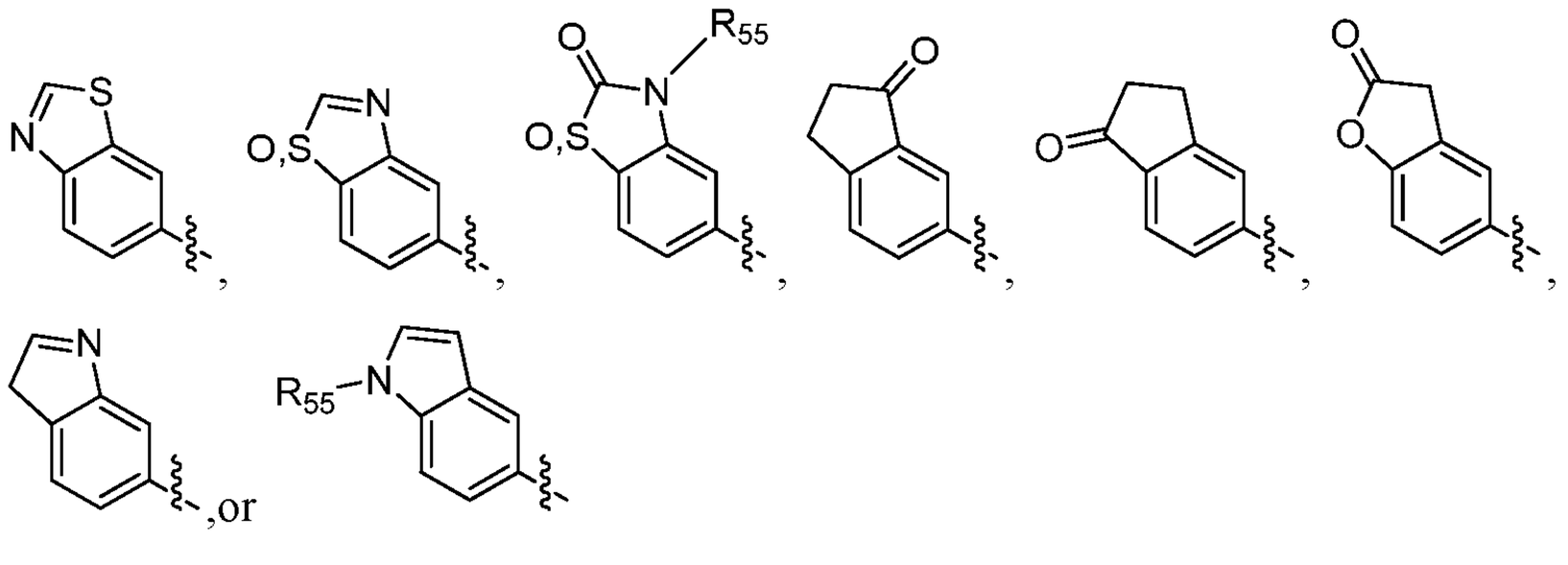
, 

, optionally substituted cycloalkyl, -$(CH_2)_pR_{65}$, or optionally substituted heterocycle;

or R_{37} is-$(CH_2)_q$-R_{38} or R_{36} and R_{37} form a heterocycle that is fused to the phenyl ring;

R_{41} is absent, H, or C_1-C_6 alkyl provided that when Z is S, O or $S(O)_2$, R_{41} is absent; or when Z is C, the bond connecting Z to the adjacent carbon is a double bond and R_{41} is H,

R_{34} is  ,  , ,  ,  ,  ,  ,  ,  ,  ,  ,



wherein,

R_{39} is H or C_1-C_6 alkyl;

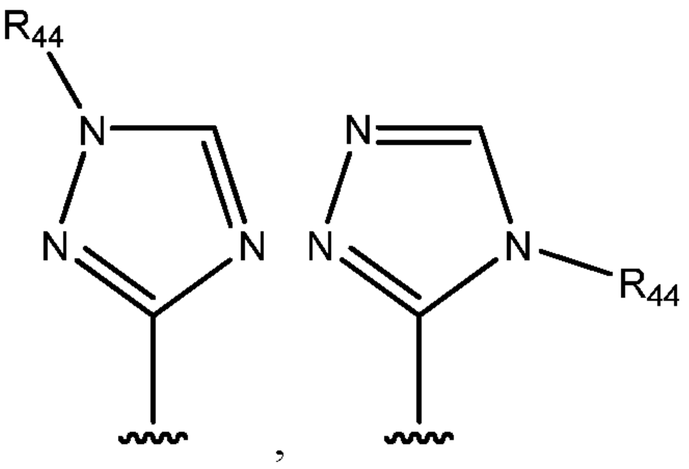
R_{40} is H, C_1-C_6 alkyl, halo, or alkoxy;

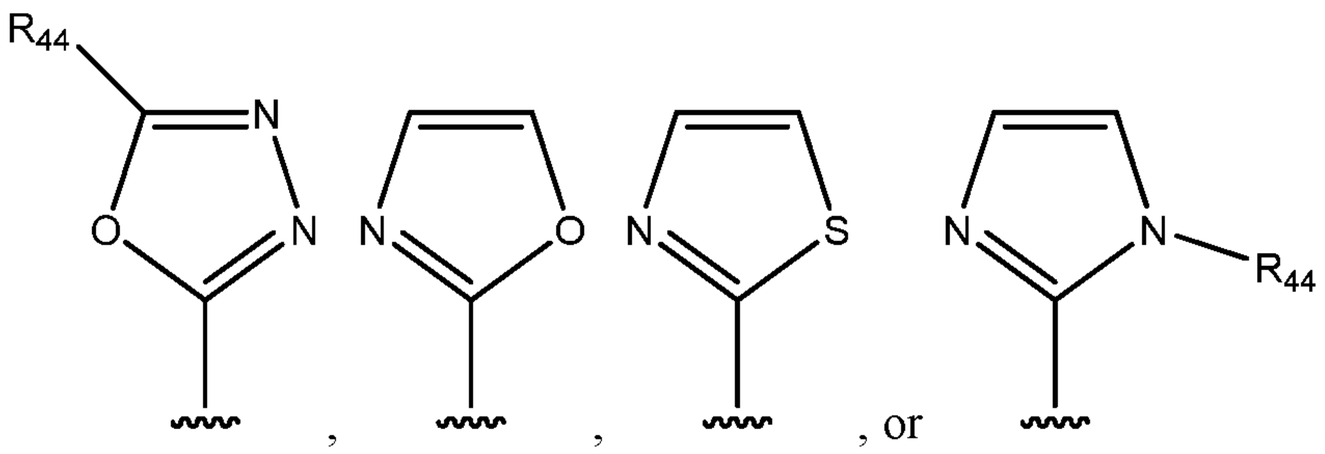
R_{42} is absent, H, C_1-C_6 alkyl, a member of a carbocyle that includes the atom to which it is attached, =O;

X_a is C or O, provided that when X_a is O, R_{42} is absent;

X_b is S or O;

X_c is C or N;

R_{43} is -OH, -CN, -C(=O)$NR_{45}R_{46}$, 



wherein: R_{44} is H or C_1-C_6 alkyl; R_{45} is H or C_1-C_6 alkyl; and R_{46} is H or C_1-C_6 alkyl;

R_{47} is H or C_1-C_6 alkyl;

R_{48} is H or C_1-C_6 alkyl;

each R_{49} is, independently, H or C_1-C_6 alkyl;

R_{50} is H or C_1-C_6 alkyl;

R_{51} is H or C_1-C_6 alkyl;

R_{52} is H or C_1-C_6 alkyl;

R_{53} is H or C_1-C_6 alkyl;

R_{55} is H or C_1-C_6 alkyl;

R_{56} is H or C_1-C_6 alkyl;

R_{57} is H or C_1-C_6 alkyl;

R_{58} is absent or H;

R_{59} is H or OH;

R_{60} is H or $N(R_{54})_2$;

each R_{54} is, independently, H or C_1-C_6 alkyl;

R_{61} is H, C_1-C_6 alkyl, optionally substituted C_1-C_6 haloalkyl, gem-dimethyl, cyclopropyl spirocycle, or CF_3;

R_{62} is absent, H, or C_1-C_6 alkyl;

each R_{63} and R_{64} are, independently, H, optionally substituted aryl, optionally substituted C_1-C_6 haloalkyl, optionally substituted C_1-C_6 branched or unbranched alkyl, optionally substituted C_2-C_6 alkenyl, $-(CH_2)_vR_{65}$, optionally substituted cycloalkyl, -OH, optionally substituted alkoxy, optionally substituted pyrrolinyl, optionally substituted morpholinyl, or optionally substituted piperidyl; or R_{63} and R_{64} together form a 5-10 membered optionally substituted heterocycle or a 5-10 membered optionally substituted heteroaryl with the atom to which R_{63} and R_{64} are bonded to;

each R_{65} is, independently, H, $-C(=O)R_{65A}$, optionally substituted C_1-C_6 haloalkyl, optionally substituted nitrogen, optionally substituted C_1-C_6 branched or unbranched alkyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted C_2-C_6 alkenyl, optionally substituted cycloalkyl, optionally substituted heterocycle, -OH, optionally substituted alkoxy, optionally substituted pyrrolinyl, optionally substituted phenyl, optionally substituted pyrrolidinyl, optionally substituted imidazolidinyl, optionally substituted morpholinyl, or optionally substituted piperidyl;

R_{65A} is phenyl or C_1-C_6 branched or unbranched alkyl;

R_{66} is H, optionally substituted aryl, optionally substituted C_1-C_6 haloalkyl, $-NR_{63}R_{64}$, optionally substituted C_1-C_6 branched or unbranched alkyl, optionally substituted C_2-C_6 alkenyl, $-(CH_2)_wR_{65}$, optionally substituted cycloalkyl, -OH, optionally substituted alkoxy, optionally substituted pyrrolinyl, optionally substituted morpholinyl, or optionally substituted piperidyl;

R_{67} is optionally substituted C_1-C_6 branched or unbranched alkyl, optionally substituted C_1-C_6 haloalkyl;

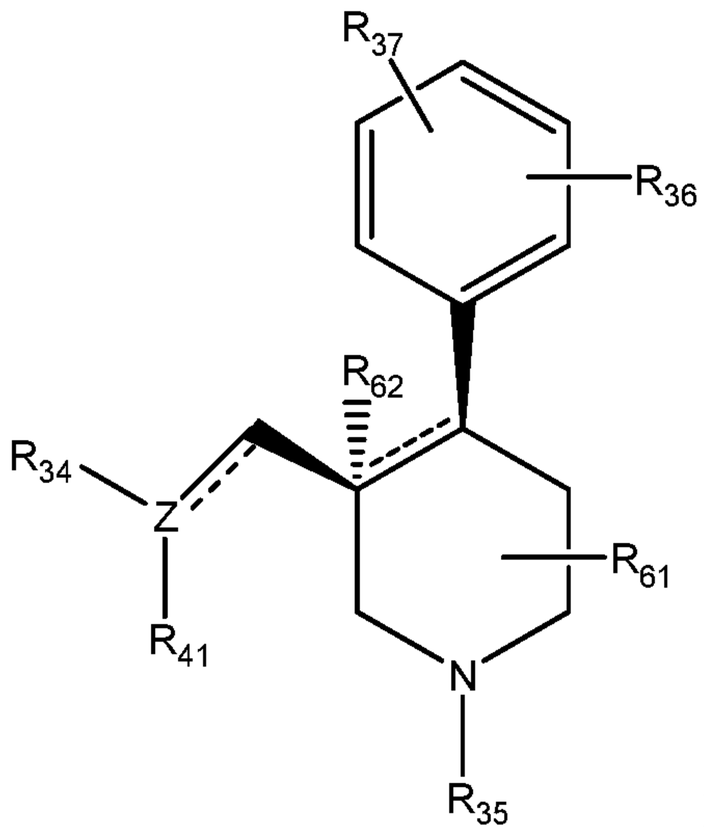
R_{81a} and R_{82a} are each independently H or optionally substituted C_1-C_6 alkyl;

R_{81b} is H or optionally substituted branched or unbranched C_1-C_6 alkyl;

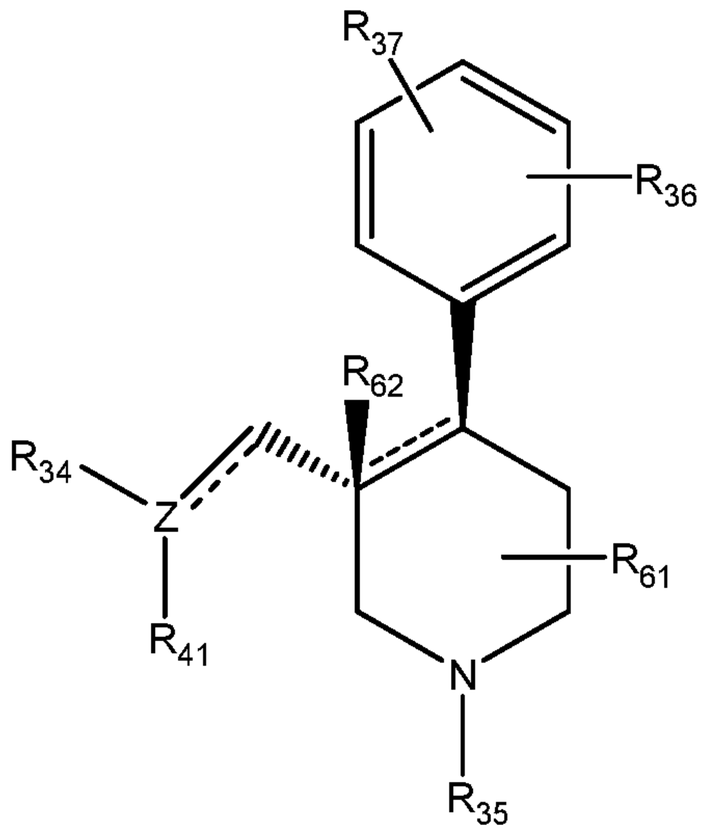
z is 1 or 2,

each n, p, v, w, and q is, independently, an integer from 0-6.

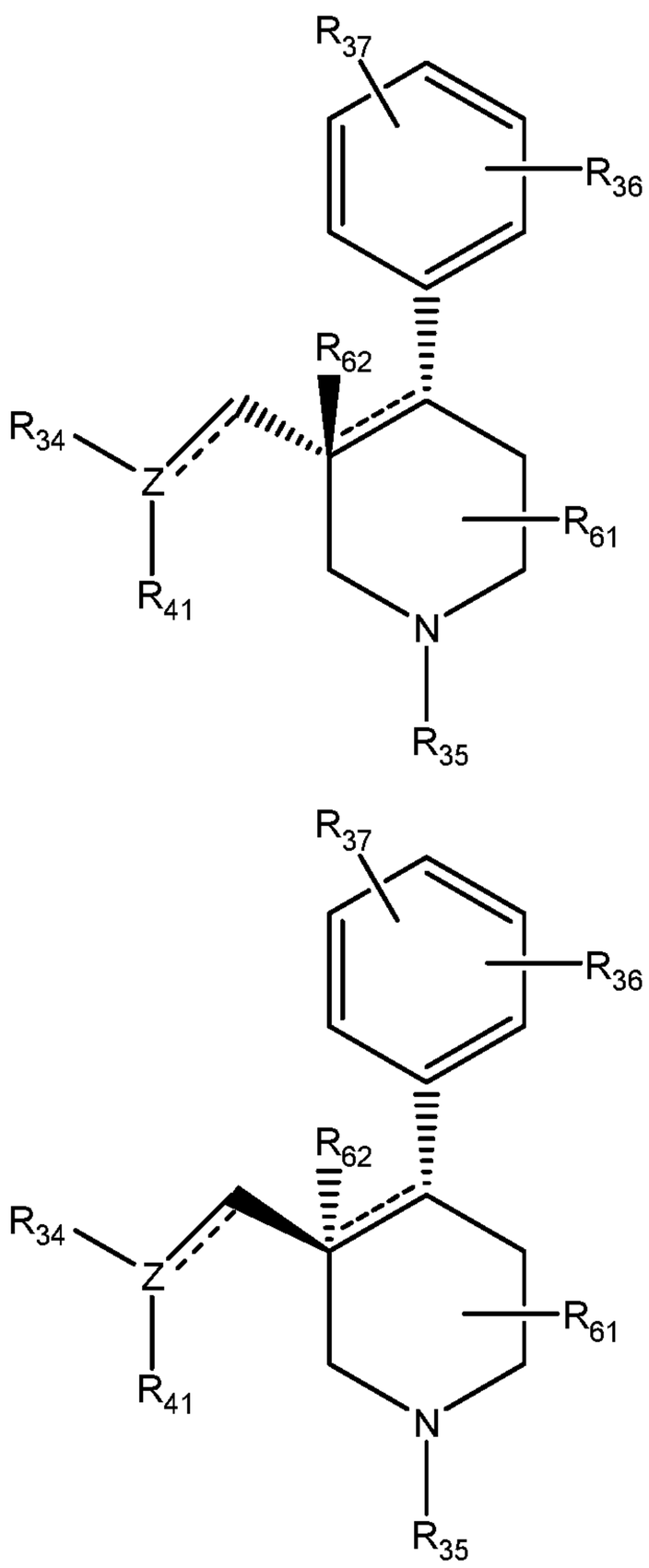
2. The compound of embodiment 1, or pharmaceutically acceptable salt thereof, having Formula II, III, IV, or V



II



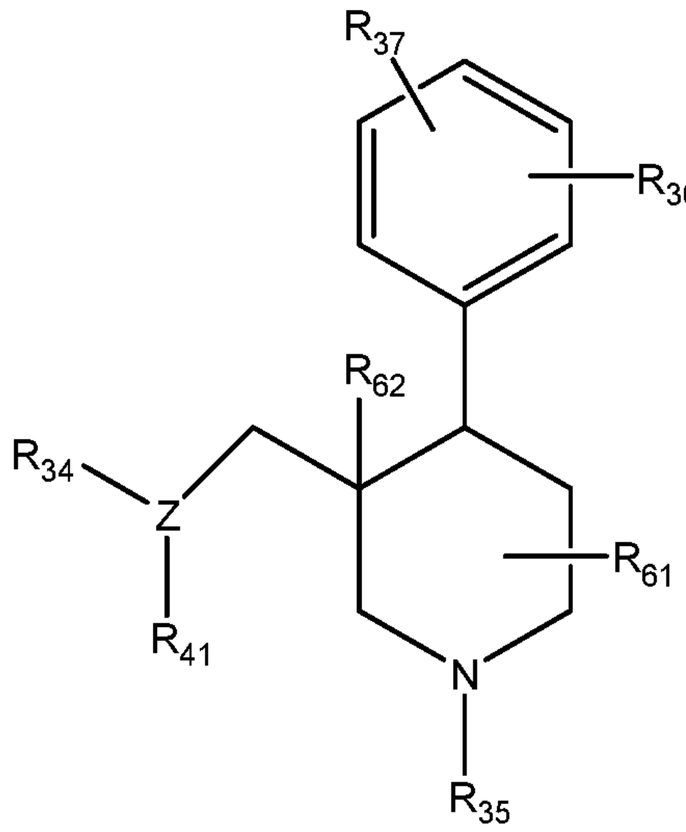
III



IV,

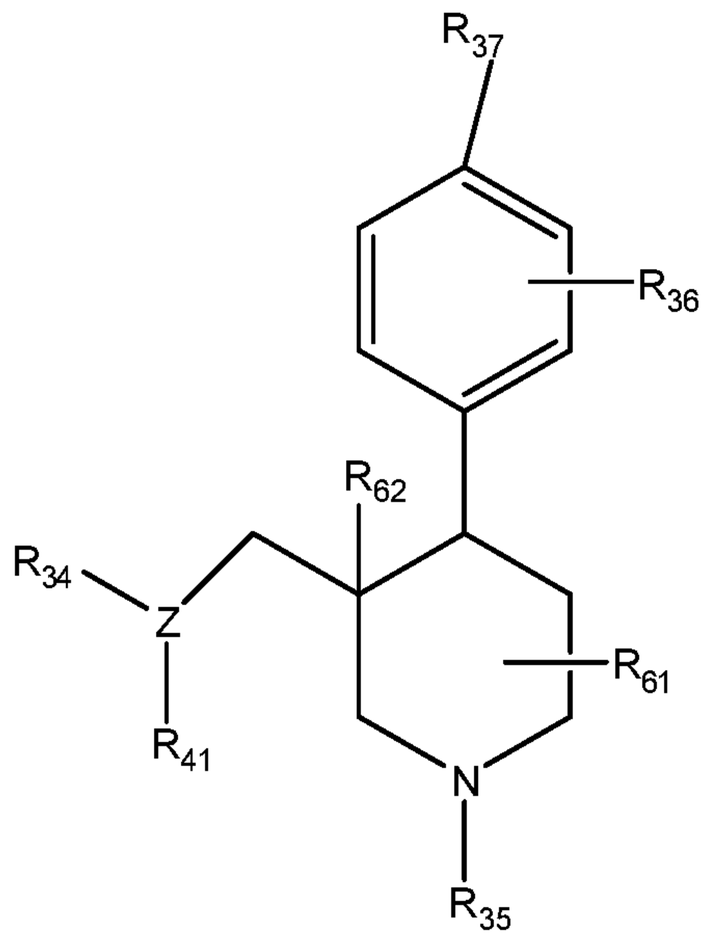
V.

3. The compound of embodiment 1, or pharmaceutically acceptable salt thereof, having Formula VI:

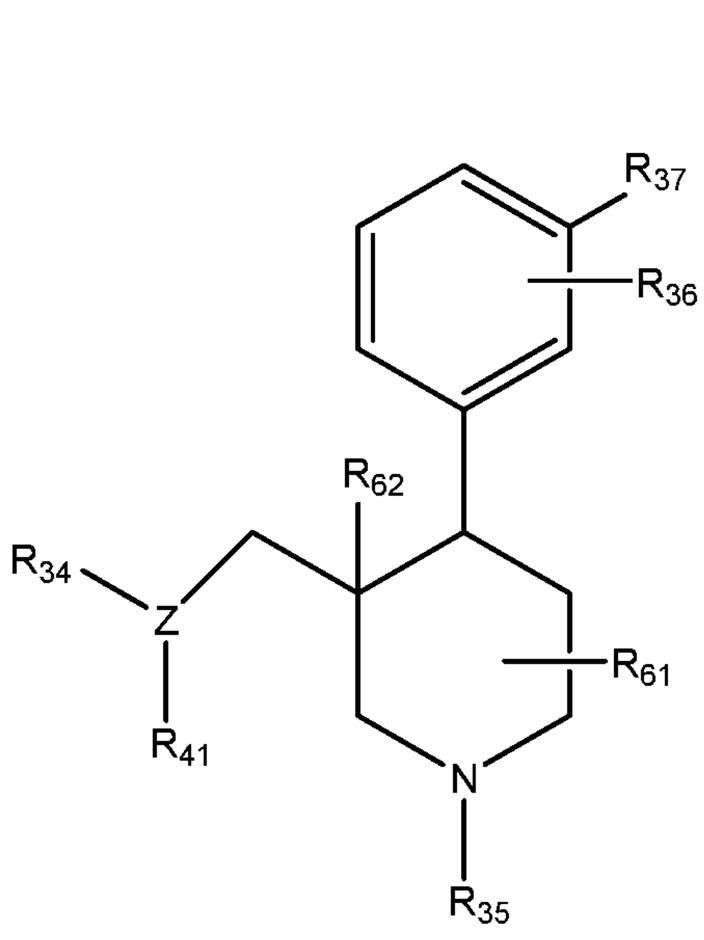


VI.

4. The compound of embodiment 1, or pharmaceutically acceptable salt thereof, having Formula VII or VIIa:



VII



VIIa.

5. The compound of embodiment any one of embodiments 1-4, or pharmaceutically acceptable salt thereof, wherein z is 1.

6. The compound of any one of embodiments embodiment 1-5, or pharmaceutically acceptable salt thereof, wherein each R_{61} is methyl.

7. The compound of embodiments 1-5, or pharmaceutically acceptable salt thereof, wherein each R_{61} is gem-dimethyl.

8. The compound of any one of embodiments 1-7, or a pharmaceutically acceptable salt thereof, wherien Z is O.

9. The compound of any one of embodiments 1-8, or pharmaceutically acceptable salt thereof, wherein Z is $S(O)_2$.

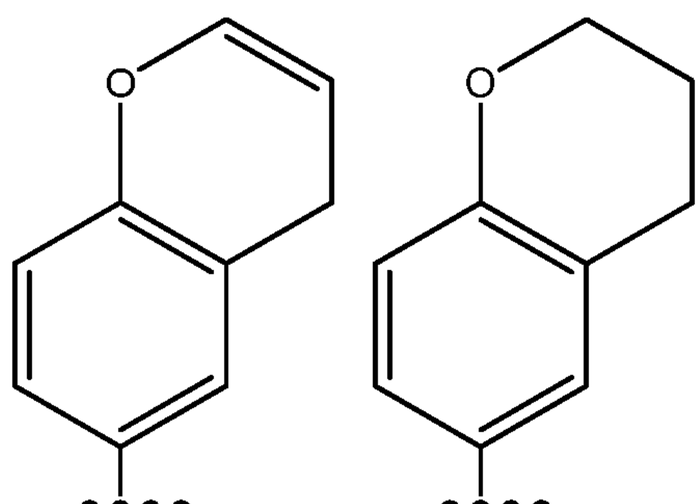
10. The compound of any one of embodiments 1-9, or pharmaceutically acceptable salt thereof, wherein R_{41} is absent.

11. The compound of any one of embodiments 1-10, or pharmaceutically acceptable salt thereof, wherein R_{37} is alkoxy, halo, optionally substituted sulfonamide, optionally substituted cyclic sulfonamide.

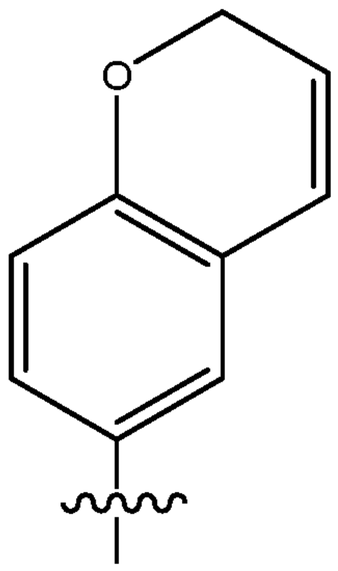
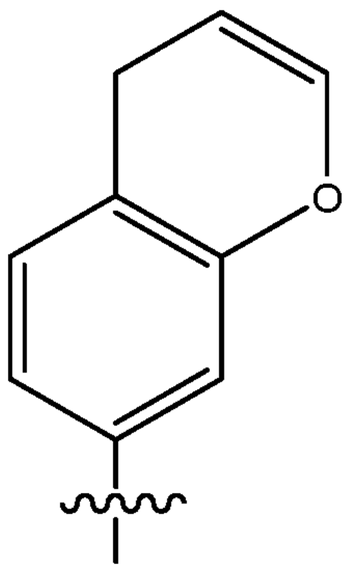
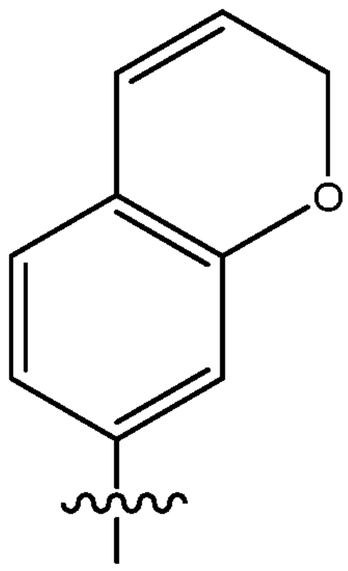
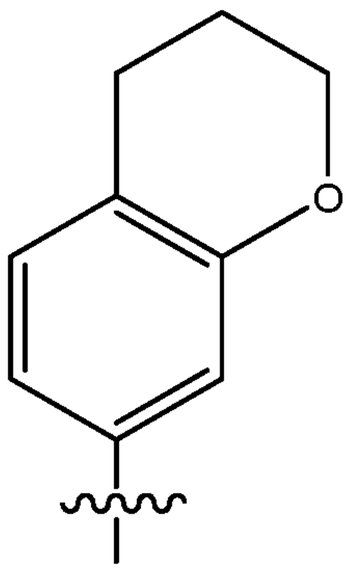
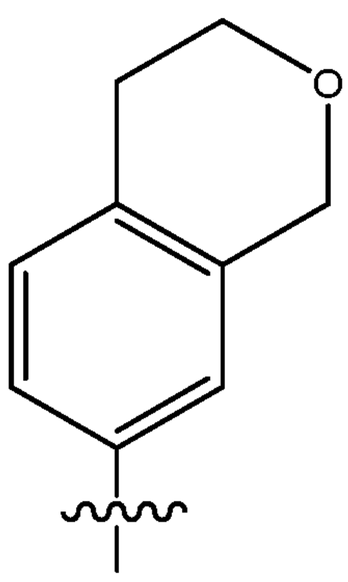
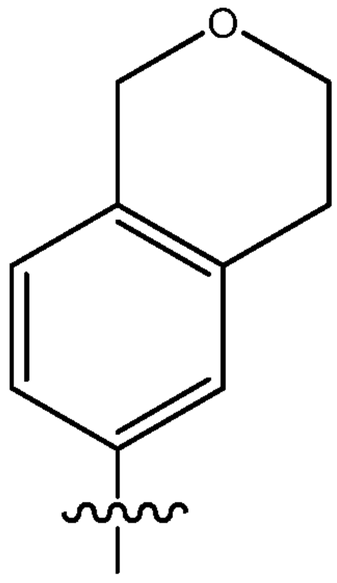
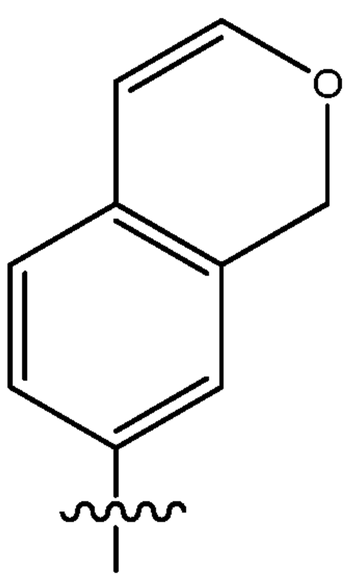
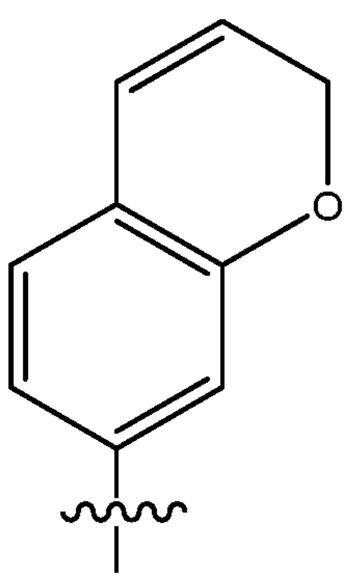
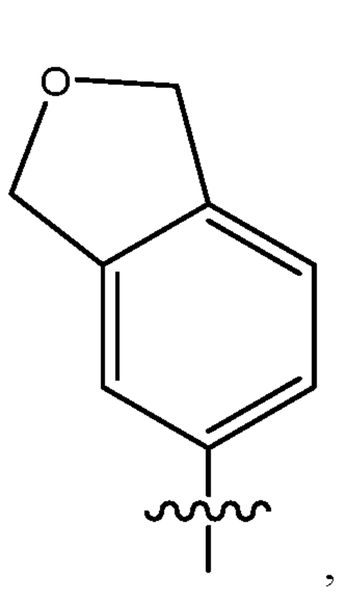
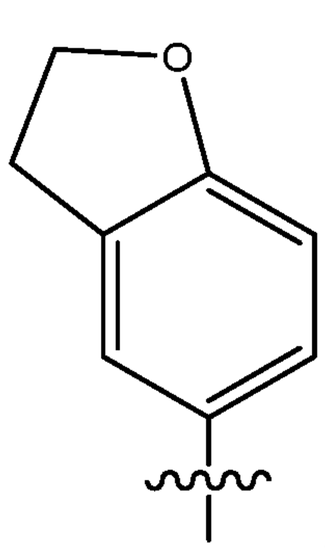
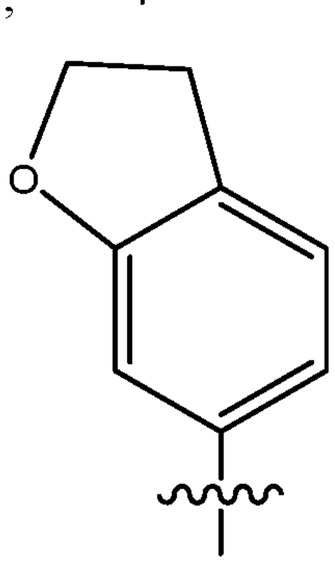
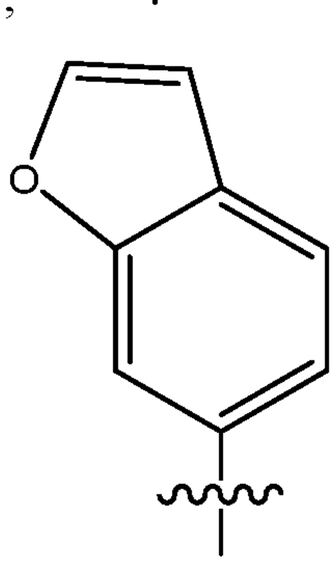
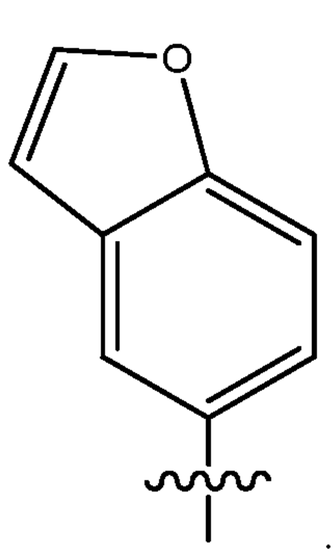
12. The compound of any one of embodiment 1-10, or pharmaceutically acceptable salt thereof, wherein R_{36} and R_{37} form a heterocycle that is fused to the phenyl ring.

13. The compound of embodiment 12, or pharmaceutically acceptable salt thereof, wherein the fused ring structure is an optionally substituted benzofuran or benzopyran.

14. The compound of embodiment 12, or pharmaceutically acceptable salt thereof,



wherein the fused ring has a formula of: , ,


,

,

,

,

,

,

,

,

,

,

,

, or

.

15. The compound of any one of embodiments 1-10, or pharmaceutically acceptable salt thereof, wherein R_{37} is absent.

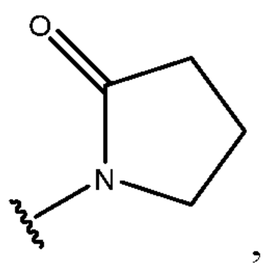
16. The compound of any one of embodiments 1-15, or pharmaceutically acceptable salt thereof, wherein q is 0.

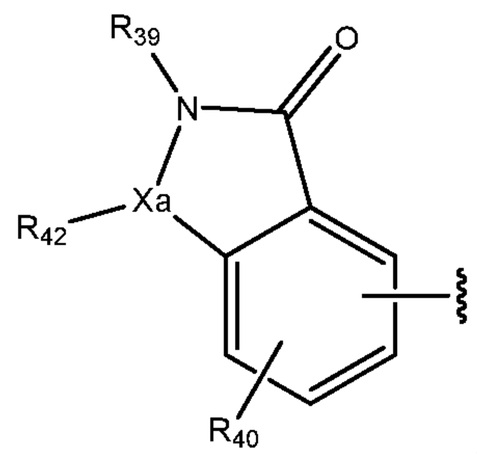
17. The compound, of any one of embodiments 1-15, or pharmaceutically acceptable salt thereof, wherein q is 1-4.

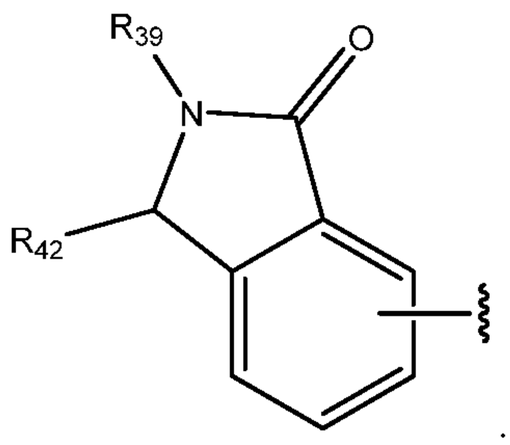
18. The compound of any one of embodiments 1-17, or pharmaceutically acceptable salt thereof, wherein R_{38} is absent or H.

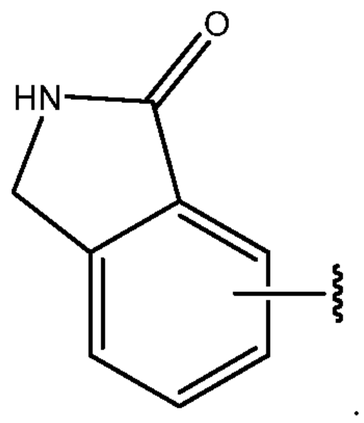
19. The compound of any one of embodiments 1-17, or pharmaceutically acceptable salt thereof, wherein R_{38} is C_1-C_6 haloalkyl.

20. The compound of any one of embodiments 1-17, or pharmaceutically acceptable salt thereof, wherein R_{38} is -C(=O)C_1-C_6 alkyl.

21. The compound of any one of embodiments 1-17, or pharmaceutically acceptable salt thereof, wherein R_{38} is $-OR_{66}$, $-S(O)_2R_{67}$,  , optionally substituted cycloalkyl, $-(CH_2)_pR_{65}$, or optionally substituted heterocycle.

22. The compound of any one of embodiments 1-21, or pharmaceutically acceptable salt thereof, wherein R_{34} is  .

23. The compound of any one of embodiments 1-21, or pharmaceutically acceptable salt thereof, wherein R_{34} is  .

24. The compound of any one of embodiments 1-23, or pharmaceutically acceptable salt thereof, wherein R_{34} is  .

25. The compound of any one of embodiments 1-24, or pharmaceutically acceptable salt thereof, wherein R_{61} is H, C_1-C_6 alkyl, optionally substituted C_1-C_6 haloalkyl, gem-dimethyl, cyclopropyl spirocycle, or CF_3.

26. The compound of any one of embodiments 1-25, or pharmaceutically acceptable salt thereof, wherein R_{35} is optionally substituted C_1-C_6 branched or unbranched alkyl, $–CH_2R_{76}$ or$–CH_2CH_2R_{76}$, wherein R_{76} is optionally substituted aryl, optionally substituted ketone, optionally substituted cycloalkyl, optionally substituted C_2-C_6 alkenyl, optionally substituted C_2-C_6 haloalkenyl, or optionally substituted heteroaryl.

27. The compound of embodiment 26, or pharmaceutically acceptable salt thereof, wherein R_{76} is cyclopropyl.

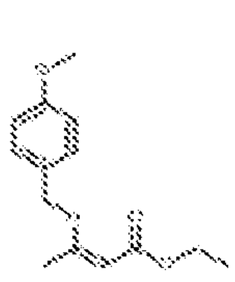
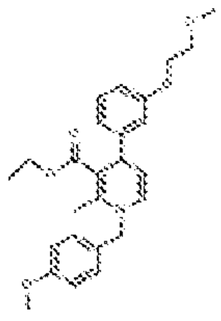
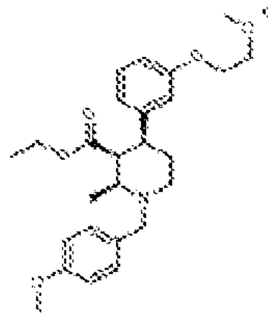
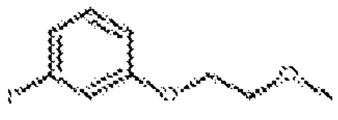
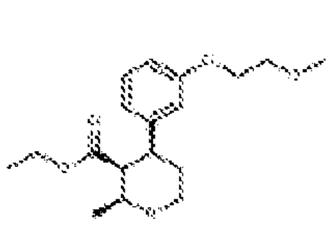
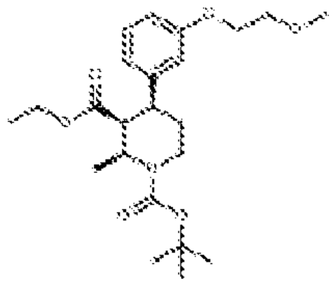
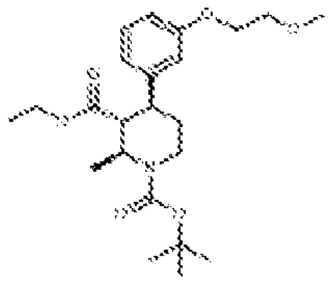
28. The compound of embodiment 26, or pharmaceutically acceptable salt thereof, wherein R_{76} is diflourocyclopropyl.

29. The compound of embodiment 26, or pharmaceutically acceptable salt thereof, wherein R_{76} is 2,2-diflourocyclopropyl.

30. The compound of embodiment 26, or pharmaceutically acceptable salt thereof, wherein R_{76} is $–CH=CF_2$.

31. The compound of any one of embodiments 1-30, or pharmaceutically acceptable salt thereof, wherein the compound is selected from the group consisting of a compound illustrated in Figure 1 and/or described herein.

32. A compound, or pharmaceutically acceptable salt thereof, wherein the compound is selected from the group consisting of a compound described herein, including, but not limited to those in Figure 1.

33. A compound, or a pharmaceutically acceptable salt thereof, selected from the group consisting of: B1049, B0704, B0707, B0720, B0876, B1079, B1145, B1194, B1205, B1211, B1365, B1401,  ,  ,  ,  ,  ,  ,  , and .

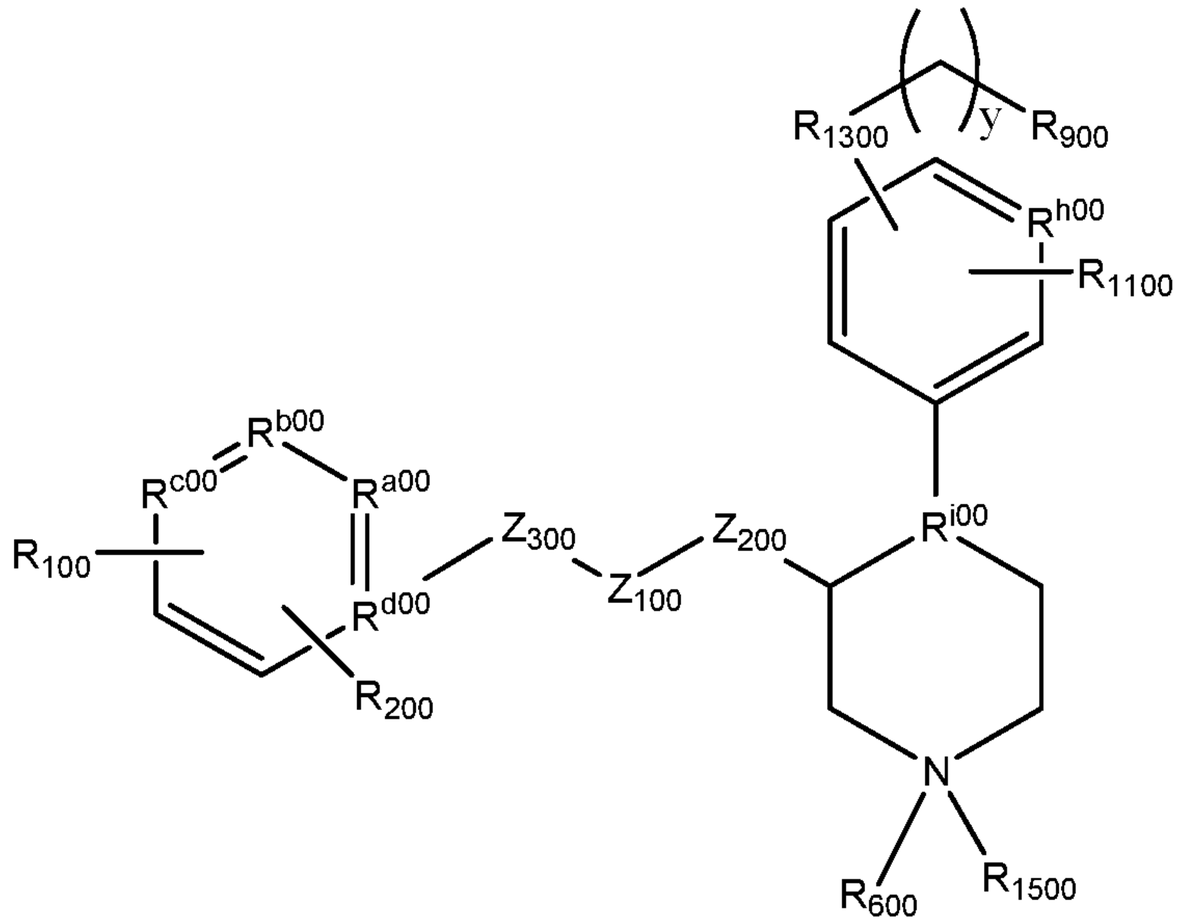
34. A pharmaceutical composition comprising a compound, or pharmaceutically acceptable salt thereof, of any one of embodiments 1-33.

35. A method of treating or preventing pain, neuropathic pain, migraine, headache, depression, Parkinson's disease, anxiety, overactive bladder, medication overuse headache, hyperalgesia, decreasing nociceptive sensitization, pain in an opioid exposed subject, PTSD, or other disorder or condition described herein in a subject comprising administering to the subject one or more compounds, or a pharmaceutically acceptable salt thereof, of any of embodiments 1-33 or a pharmaceutical composition comprising one or more compounds, or pharmaceutically acceptable salt thereof, of any one of embodiments 1-33.

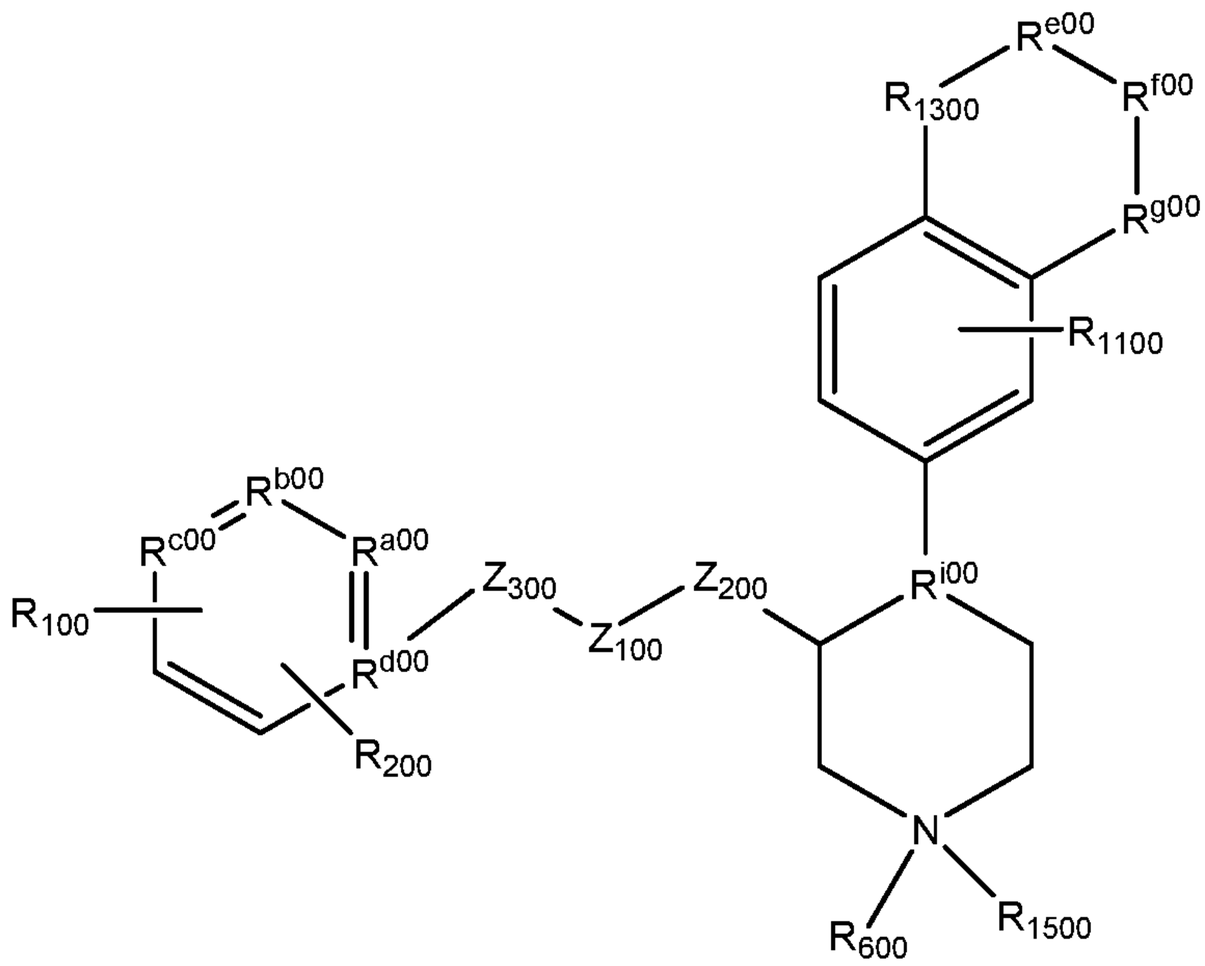
36. The method of embodiment 35, wherein the subject is a subject in need thereof.

37. A method of preparing a compound, or a pharmaceutically acceptable salt thereof, the method comprising preparing a compound according to one of the schemes described herein.

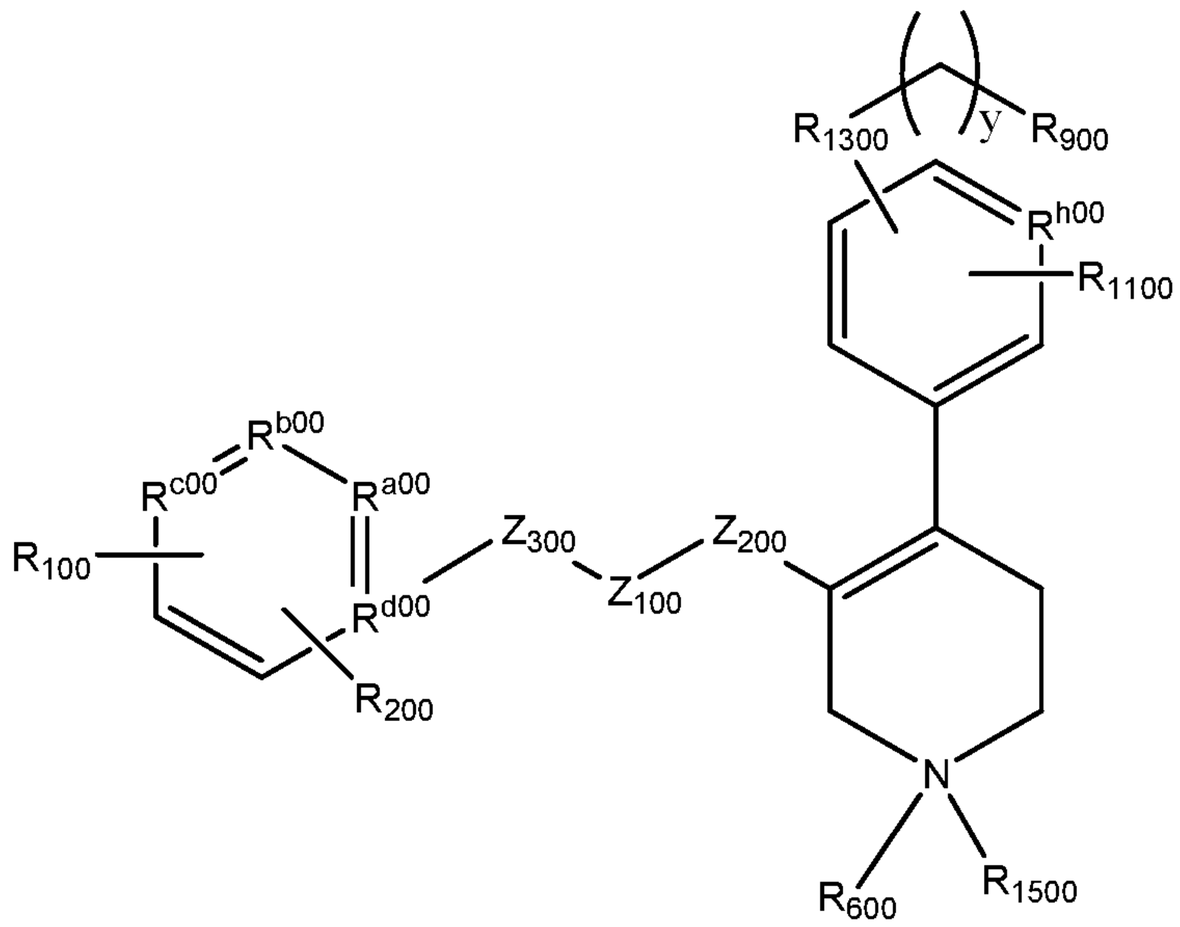
38. A compound having Formula I00, Formula I00A, Formula I00B, or Formula I00C, or pharmaceutically acceptable salt thereof:



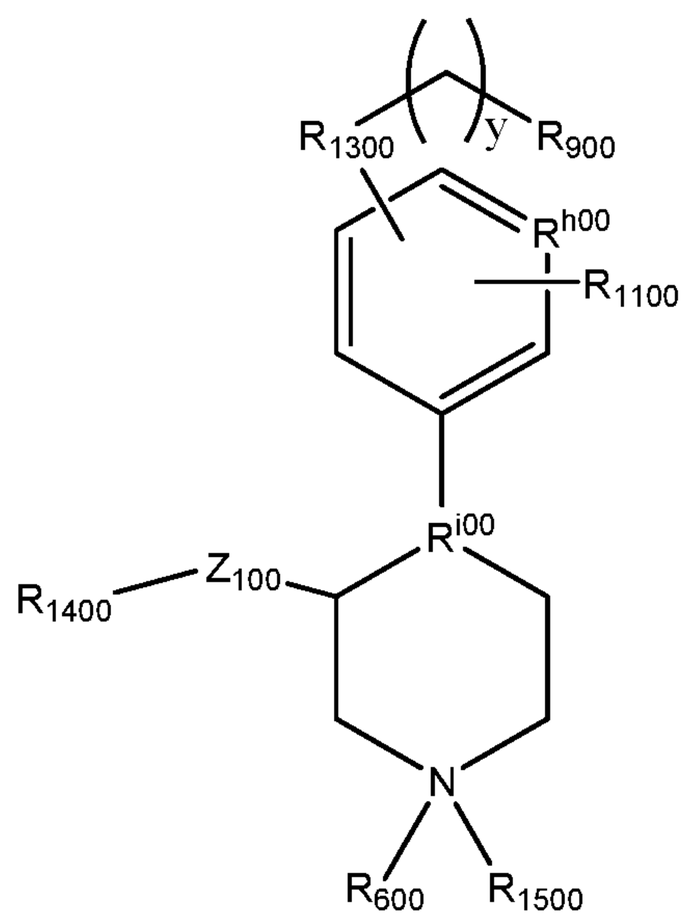
I00



I00A



I00B

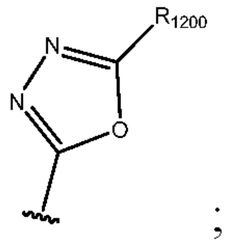


I00C

wherein:

R_{100}, R_{200}, and R_{1400} are each, independently, H, cyano, optionally substituted C_1-C_6 branched or unbranched alkyl, optionally substituted C_1-C_6 alkoxy, optionally substituted C_1-C_6 haloalkyl, optionally substituted C_2-C_6 alkenyl, optionally substituted pyrimidine, optionally substituted pyridyl, optionally substituted pyrazole, optionally substituted isoxazole, optionally substituted pyridinone, optionally substituted aryl, halo,-NC(=O)R_{300}, -

$C(=O)NR_{300}R_{400}$, $-C(=O)OR_3$, $S(=O)_2NR_{300}R_{400}$, $-C(=O)R_{300}$, $-OR_3$, $-(CH_2)_nR_{500}$, =O, or



;

R_{1500} is a protecting group, $C(=O)OR_{81b}$, absent, or C_2-C_6 alkenyl, wherein $R81_b$ is H or optionally substituted branched or unbranched C_1-C_6 alkyl;

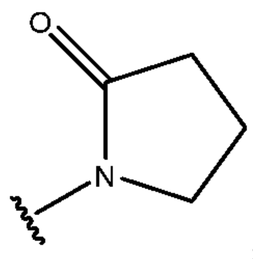
when R_{1500} is absent, R_{600} is H, optionally substituted aryl, optionally substituted C_1-C_6 haloalkyl, $-NR_{700}R_{800}$, optionally substituted C_1-C_6 branched or unbranched alkyl, optionally substituted C_2-C_6 alkenyl, $-(CH_2)_nR_{500}$, optionally substituted cycloalkyl, -OH, optionally substituted C_1-C_6 alkoxy, optionally substituted pyrrolinyl, optionally substituted morpholinyl, or optionally substituted piperldyl;

when R_{1500} is C_2-C_6 alkenyl, R_{600} is C_2-C_6 alkenyl;

R_{300}, R_{400}, and R_{1200} are each, independently, H, optionally substituted aryl, optionally substituted C_1-C_6 haloalkyl, $-NR_{700}R_{800}$, optionally substituted C_1-C_6 branched or unbranched alkyl, optionally substituted C_2-C_6 alkenyl, $-(CH_2)_nR_{500}$, optionally substituted cycloalkyl, -OH, optionally substituted alkoxy, optionally substituted pyrrolinyl, optionally substituted morpholinyl, or optionally substituted piperldyl; or R_{300} and R_{400} together form a 5-10 membered optionally substituted heterocycle or 5-10 membered optionally substituted heteroaryl with the atom to which R_{300} and R_{400} are bonded;

each R_{500} is, independently, H, optionally substituted C_1-C_6 haloalkyl, $-NR_{700}R_{800}$, optionally substituted C_1-C_6 branched or unbranched alkyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted C_2-C_6 alkenyl, optionally substituted cycloalkyl, optionally substituted heterocycle, -OH, optionally substituted alkoxy, optionally substituted pyrrolinyl, optionally substituted morpholinyl, or optionally substituted piperldyl;

R_{700} and R_{800} are, each, independently, H, optionally substituted aryl, optionally substituted C_1-C_6 haloalkyl, optionally substituted C_1-C_6 branched or unbranched alkyl, optionally substituted C_2-C_6 alkenyl, $-(CH_2)_nR_{500}$, optionally substituted cycloalkyl, -OH, optionally substituted alkoxy, optionally substituted pyrrolinyl, optionally substituted morpholinyl, or optionally substituted piperldyl; or R_{700} and R_{800} together form a 5-10 membered optionally substituted heterocycle or 5-10 membered optionally substituted heteroaryl with the atom to which R_{700} and R_{800} are bonded to,

R_{900} is absent, H, haloalkyl, $-OR_3$, or  , optionally substituted cycloalkyl, $-(CH_2)_pR_{500}$, or optionally substituted heterocycle;

R_{1100} is H, $-SO_2C_1$-C_6alkyl, $-OCF_3$, halo, or optionally substituted C_1-C_6 alkyl;

R_{1300} is a bond, C, N, S, or O;

R_{1400} is an optionally substituted pyridinone or optionally substituted –CH2-pyridinone;

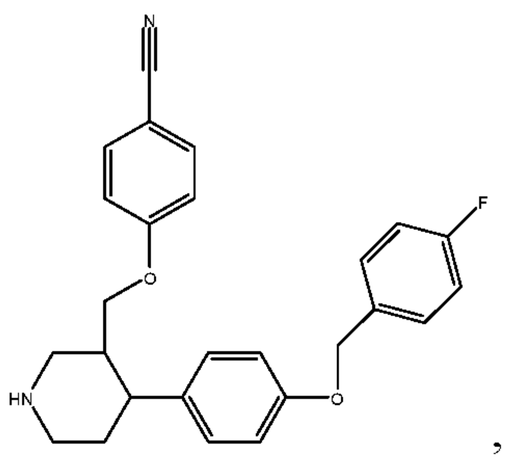
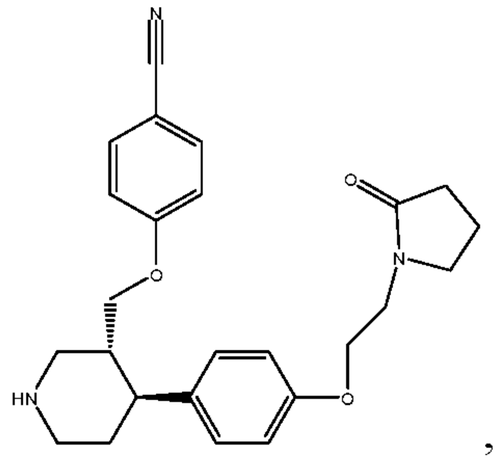
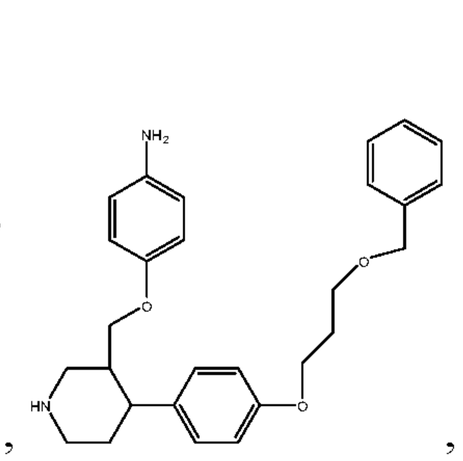
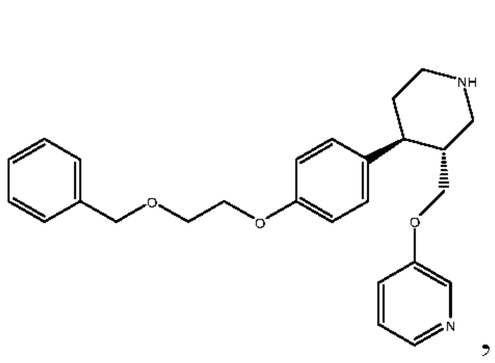
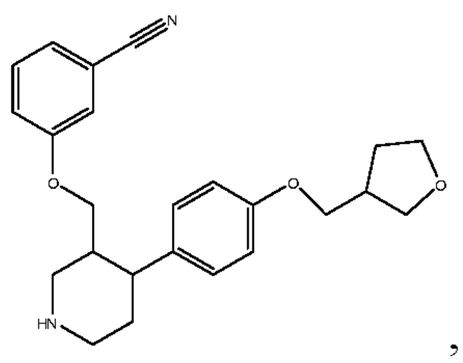
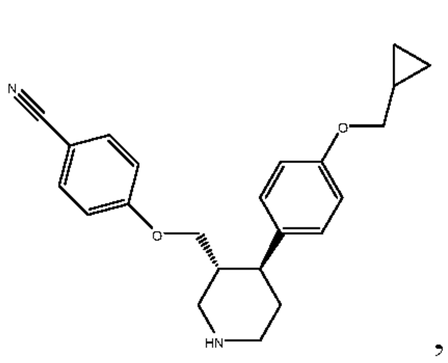
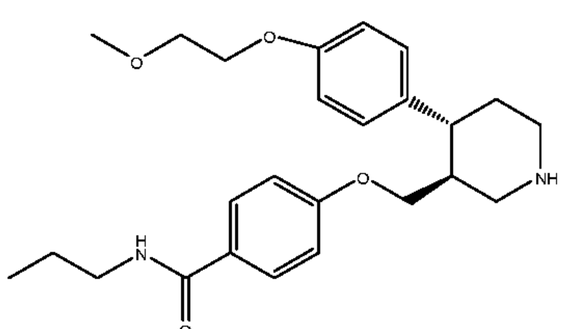
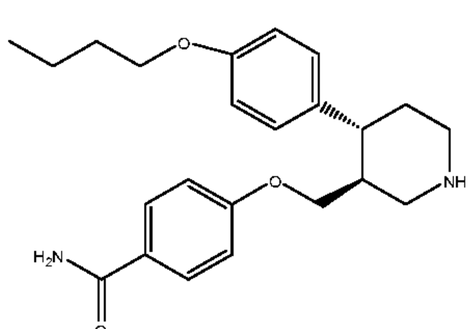
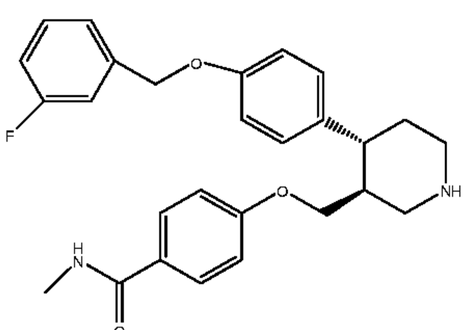
each n, p, and y is independently, an integer from 0-72;

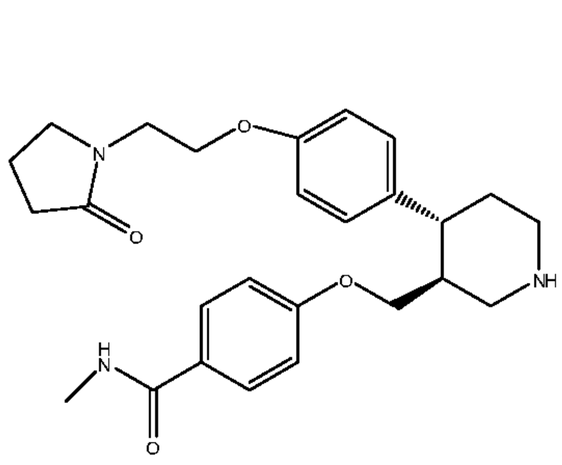
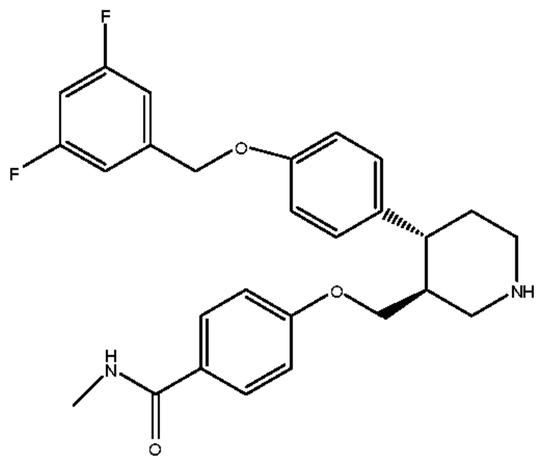
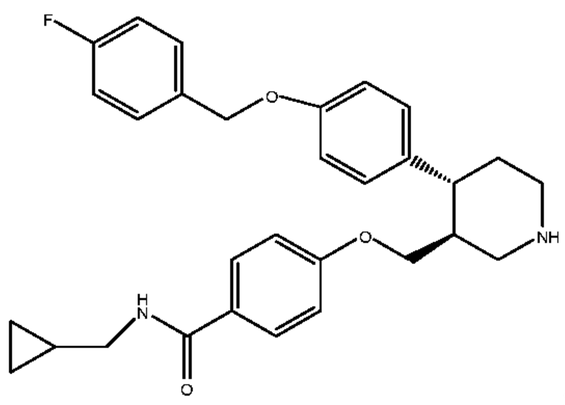
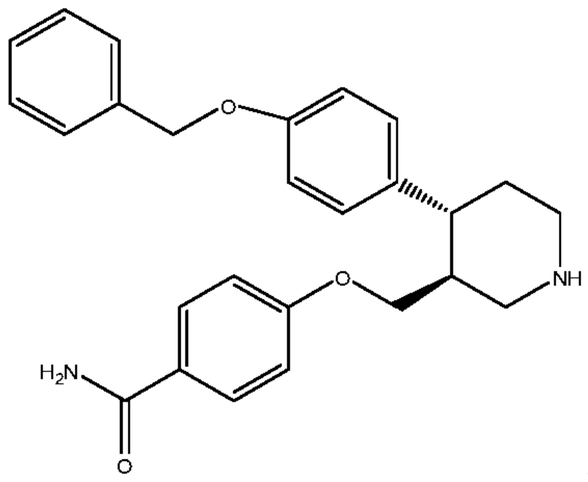
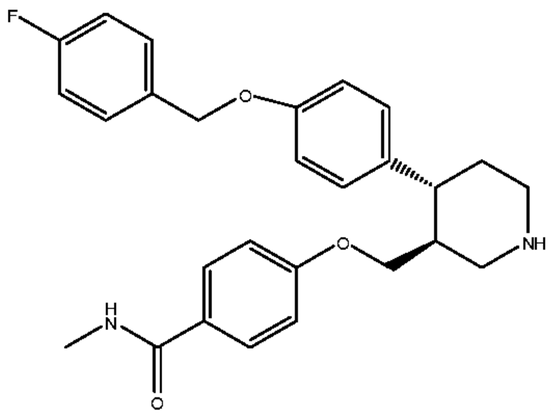
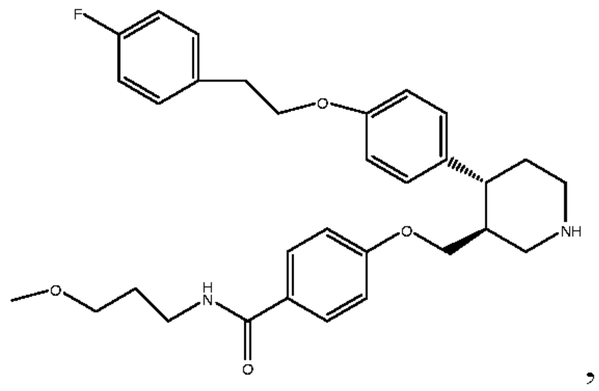
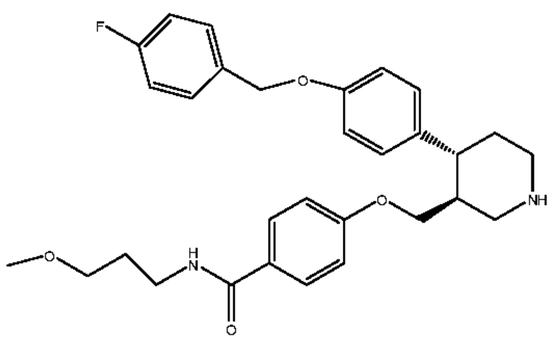
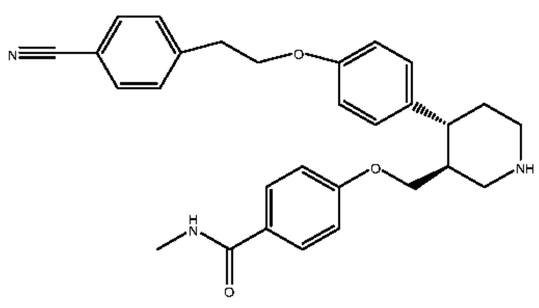
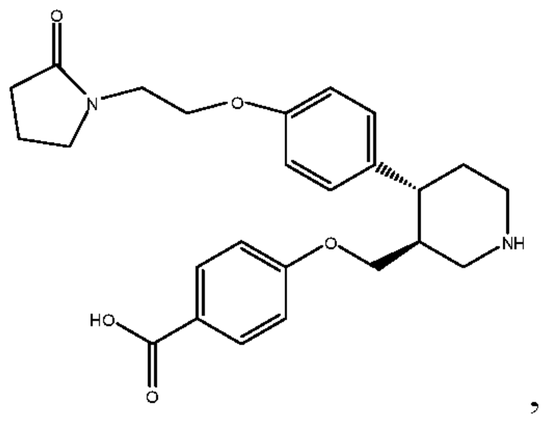
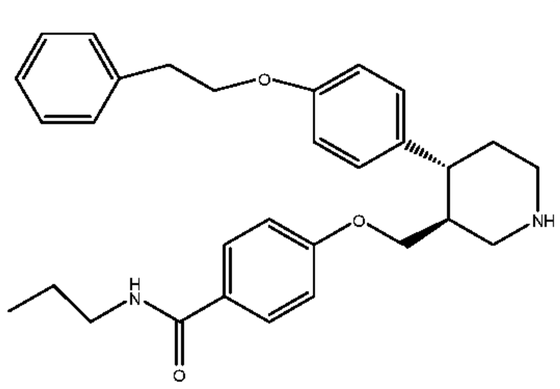
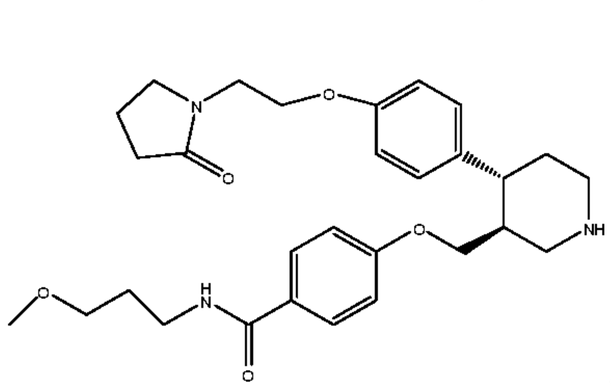
each R^{a00}, R^{b00}, R^{c00}, R^{d00}, R^{h00}, and R^{i00}, is, independently, C, N, or O,

each R^{e00}, R^{f00}, and R^{g00}, is, independently, C, N, S, O, or absent; and

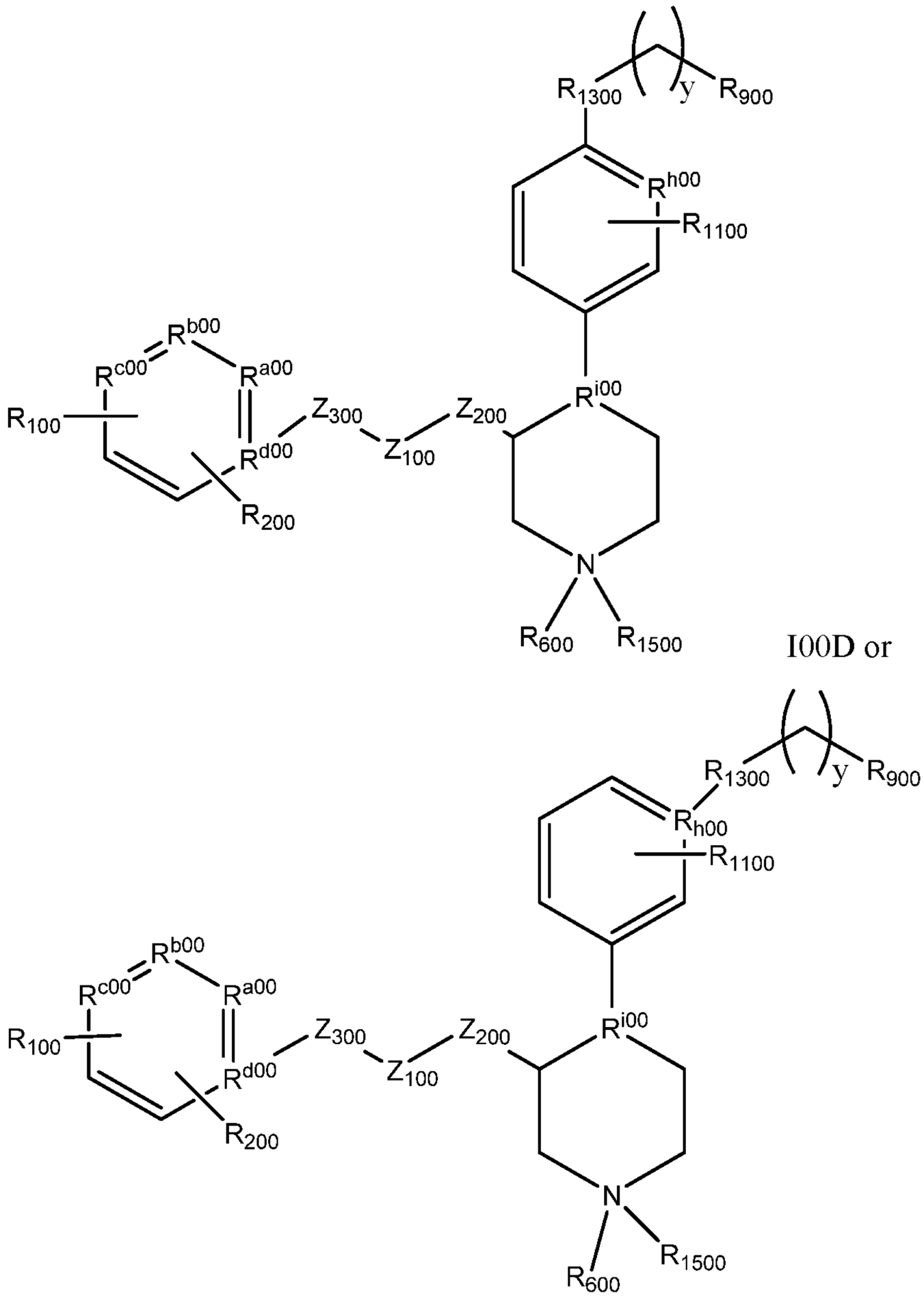
each Z_{100}, Z_{200}, and Z_{300}, is, independently, a bond, C(=O), C, N, S, or O,

provided that the compound or pharmaceutically acceptable thereof is not

 ,  ,  ,  ,  ,  ,  ,  ,  ,


,

,

,

,

,

,

,

,

,

, or

.

39. The compound of embodiment 38 or pharmaceutically acceptable salt thereof having Formula I00D or Formula I00E:



I00D or

I00E

wherein:

R_{100}, R_{200}, R_{600}, R_{900}, and R_{1500} are as defined in embodiment 67;

R^{a00}, R^{b00}, R^{c00}, R^{d00}, R^{h00}, and R^{i00} are C;

R_{1100} is H;

R_{1300} and Z_{100} is O;

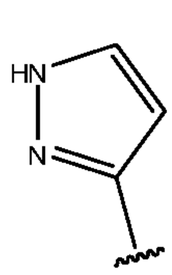
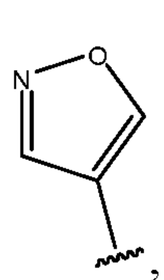
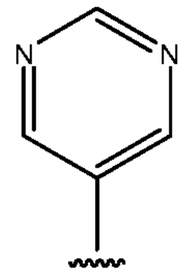
Z_{200} is C;

Z_{300} is a bond;

and y=2.

40. The compound or pharmaceutically acceptable salt thereof of embodiment 38 or 39, wherein R_{100} is $-C(=O)NR_{300}R_{400}$.

41. The compound or a pharmaceutically acceptable salt thereof of any one of embodiments 38-40, wherein each of R_{300} and R_{400} is, independently, H, halo, optionally substituted C_1-C_6 haloalkyl, or optionally substituted C_1-C_6 alkyl.

42. The compound or a pharmaceutically acceptable salt thereof of embodiments 38 or 39, wherein R_{100} is H, halo, -C(=O)NH_2, -C(=O)$NHCH_3$, -C(=O)$N(CH_3)_{68}$ -COOH, -C(=O)OCH_3, cyano, S(=O)$_2NH_2$, optionally substituted alkoxy, -OCF_3, CF_3, -NC(=O)CH_3, pyridyl,  ,  , or  .

43. The compound or a pharmaceutically acceptable salt thereof of any one of embodiments 38, 39, or 42, wherein R_{100} and R_{200} is each, independently, H, halo, or optionally substituted C_1-C_6 haloalkyl.

44. The compound or a pharmaceutically acceptable salt thereof of embodiment 43, wherein R_{100} and R_{200} are independently halo.

45. The compound or a pharmaceutically acceptable salt thereof of embodiment 43, wherein the optionally substituted C_1-C_6 haloalkyl is trifluoromethyl.

46. The compound or a pharmaceutically acceptable salt thereof of embodiment 43, wherein R_{100} is fluoro and R_{200} is trifluoromethyl.

47. The compound or a pharmaceutically acceptable salt thereof of any one of embodiments 38-46, wherein R_{100} and R_{200} are attached to different ring atoms.

48. The compound or a pharmaceutically acceptable salt thereof of embodiment 38 or 39, wherein R_{200} is H.

49. The compound or a pharmaceutically acceptable salt thereof of embodiment 38 or 39, wherein:

R_{600} is H, optionally substituted C_1-C_6 alkyl, or –C(=O)OR_3; and

R_{300} is an optionally substituted C_1-C_6 branched or unbranched alkyl.

50. The compound or a pharmaceutically acceptable salt thereof of embodiments 38 or 39, wherein:

R_{100} is -C(=O)NH_2 and R_{600} is H or optionally substituted C_1-C_6 alkyl; or

R_{100} is -C(=O)$NR_{300}R_{400}$, wherein R_{300} is H and R_{400} is optionally substituted branched or unbranched C_1-C_6 alkyl or optionally substituted branched or unbranched C_2-C_6 alkenyl and R_{600} is H or optionally substituted C_1-C_6 alkyl; or

R_{100} is -C(=O)$NR_{300}R_{400}$, wherein R_{300} and R_{400} are each, independently, optionally substituted branched or unbranched C_1-C_6 alkyl, and R_{600} is H, optionally substituted C_1-C_6 alkyl, or optionally substituted alkaryl.

51. The compound or a pharmaceutically acceptable salt thereof of embodiment 38 or 39, wherein R_{100} is -C(=O)$NR_{300}R_{400}$, wherein:

R_{300} and R_{400} are H;

R_{300} is H and R_{400} is optionally substituted C_1-C_6 unbranched or branched alkyl; or

R_{300} is H and R_{400} is optionally substituted C_2-C_6 unbranched or branched alkenyl; or

R_{300} is H and R_{400} is optionally substituted C_1-C_6 cycloalkyl; or

R_{300} is H and R_{400} is $–(CH_2)_nR_{500}$; wherein n is 1-6 and R_{500} is an optionally substituted cycloalkyl; or

R_{300} is H and R_{400} is $–(CH_2)_nR_{500}$, wherein n is 1-6 and R_{500} is an optionally substituted alkoxy; or

R_{300} and R_{400} are each, independently, optionally substituted C_1-C_6 alkyl.

52. The compound or a pharmaceutically acceptable salt thereof of embodiment 38 or 39, wherein R_{100} is $–C(=O)NR_{300}R_{400}$, wherein R_{300} and R_{400} together form a 5-10 membered optionally substituted heterocycle or 5-10 membered optionally substituted heteroaryl with the atom to which R_{300} and R_{400} are bonded.

53. The compound or a pharmaceutically acceptable salt thereof of embodiment 38, wherein R^{b00} is N.

54. The compound or a pharmaceutically acceptable salt thereof of embodiment 38, wherein R^{a00} is N.

55. The compound or a pharmaceutically acceptable salt thereof of embodiment 38, wherein R^{c00} is N.

56. The compound or a pharmaceutically acceptable salt thereof of embodiment 38, wherein R^{d00} is N.

57. The compound or a pharmaceutically acceptable salt thereof of any one of embodiments 53-55 wherein R_{1100} is H, R_{1300} is O, R^{i00} is C, Z_{100} is O, Z_{200} is C, Z_{300} is a bond, and y=2.

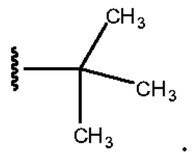
58. The compound or a pharmaceutically acceptable salt thereof of any one of embodiments 53-58, wherein R_{100}, R_{200}, and R_{600} are each H and Z is O.

59. The compound or a pharmaceutically acceptable salt thereof of any one of embodiments 53-58, wherein R_{100} is =O and R_{200} is H.

60. The compound or a pharmaceutically acceptable salt thereof of embodiment 38 or 39, wherein

R_{100} is $-C(=O)NR_{300}R_{400;}$ and

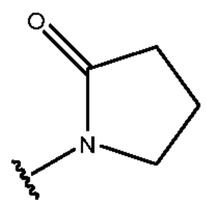
R_{600} is H, C_1-C_6 alkyl, or $-C(=O)OR_3$, wherein R_{300} is an optionally substituted C_1-C_6 branched or unbranched alkyl.

61. The compound or a pharmaceutically acceptable salt thereof of embodiment 60, wherein R_{300} is  .

62. The compound or a pharmaceutically acceptable salt thereof of any one of embodiments 38-61, wherein

R_{600} is H, optionally substituted C_1-C_6 alkyl, optionally substituted C_2-C_6 alkenyl, $-OR_3$, or $(CH_2)_n$-aryl,

n is an integer from 0-2;

R_{900} is  ;

R_{1100} is H or halo;

R_{1300} is O;

R^{i00} is C;

y=2; and

optionally R_{1500} is optionally substituted C_2-C_6 alkenyl when R_{600} is optionally substituted C_2-C_6 alkenyl.

63. The compound or a pharmaceutically acceptable salt thereof of any one of embodiments 38-62, wherein R_{1100} is fluoro.

64. The compound or a pharmaceutically acceptable salt thereof of any one of embodiments 38-42, 48, 49, 53-57, or 60-63, wherein R_{100} is $-C(=O)NH_2$.

65. The compound or a pharmaceutically acceptable salt thereof of any one of embodiments embodiment 38, 39, 42, or 53-57, wherein R_{100} is cyano.

66. The compound or a pharmaceutically acceptable salt thereof of embodiment 38 wherein:

R^{a00}, R^{b00}, R^{c00}, R^{d00}, R^{h00}, and R^{i00} are C;

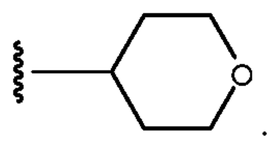
Z_{100} is O, Z_{200} is C, Z_{300} is a bond;

y=0;

R_{900} is branched or unbranched optionally substituted C_1-C_6 alkyl, optionally substituted haloalkyl, optionally substituted cycloalkyl, or optionally substituted heterocycle; and

R_{1300} is O.

67. The compound or a pharmaceutically acceptable salt thereof of embodiment 66, wherein R_{600} is H or optionally substituted branched or unbranched C_1-C_6 alkyl.

68. The compound or a pharmaceutically acceptable salt thereof of embodiment 66 or 67, wherein R_{900} is  .

69. The compound or a pharmaceutically acceptable salt thereof of any one of embodiments 66-68, wherein R_{100} is $-C(=O)NR_{300}R_{400}$ or cyano.

70. The compound or a pharmaceutically acceptable salt thereof of any one of embodiments 66-69, wherein R_{200} is H.

71. The compound or a pharmaceutically acceptable salt thereof of any one of embodiments 66-70, wherein R_{1100} is H.

72. The compound or a pharmaceutically acceptable salt thereof of embodiment 38, wherein:

one of R^{a00}, R^{b00}, R^{c00}, and R^{d00} is N;

Z_{100} is a bond or O;

Z_{200} is C, Z_{300} is a bond, and y=0;

R^{h00} and R^{i00} are C;

R_{100} is H, $-C(=O)NR_{300}R_{400}$ or =O;

R_{200} is H;

R_{600} is H, C_1-C_6 alkyl, or C_2-C_6 alkenyl;

R_{900} is C_1-C_6 alkyl, haloalkyl, or cycloalkyl;

R_{1100} is H; and

R_{1300} is O.

73. The compound or a pharmaceutically acceptable salt thereof of embodiment 72, wherein Z_{100} is a bond and R_{100} is =O.

74. The compound or a pharmaceutically acceptable salt thereof of embodiment 72, wherein R_{400} is H.

75. The compound or a pharmaceutically acceptable salt thereof of embodiment 72 or 74, wherein R^{d00} is N and R_{100} is =O.

76. The compound or a pharmaceutically acceptable salt thereof of embodiment 38, wherein:

R^{a00}, R^{b00}, R^{c00}, and R^{d00} are C;

R^{h00} and R^{i00} are C;

Z_{100} is O, Z_{200} is C, Z_{300} is a bond;

R_{1100} is halo or C_1-C_6 alkyl;

y=0;

R_{900} is H, haloalkyl or C_1-C_6 alkyl;

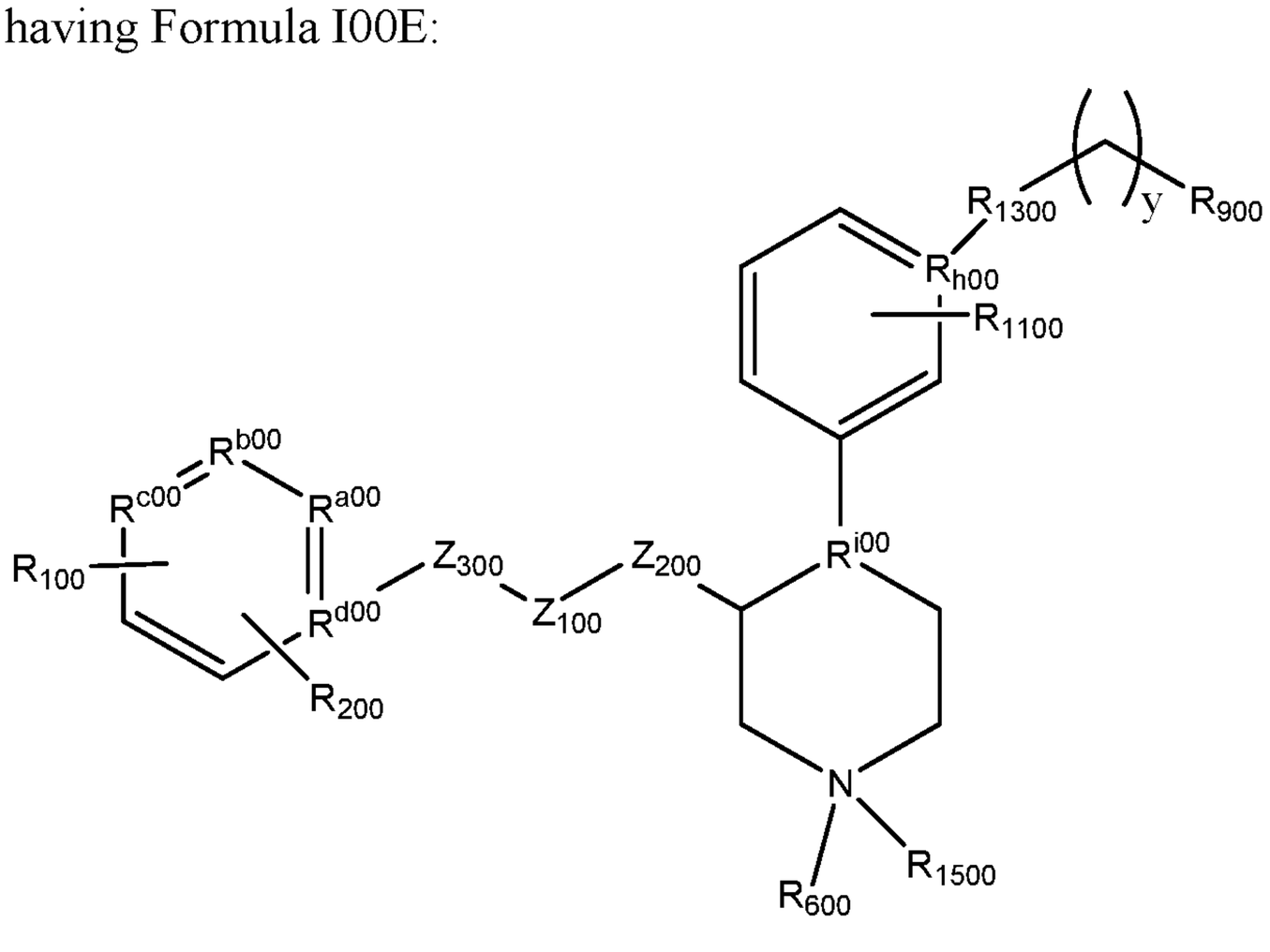
R_{1300} is O;

R_{600} is H, C_1-C_6 alkyl, or C_2-C_6 alkenyl;

R_{200} is H.

77. The compound or a pharmaceutically acceptable salt thereof of embodiment 76, wherein R_{100} is H, cyano or $-C(=O)NR_{300}R_{400}$.

78. The compound or a pharmaceutically acceptable salt thereof of embodiment 77 having Formula I00E:



I00E

wherein

R_{100}, R_{200}. R_{600}. and R_{900} are as defined in embodiment 77;

R^{a00}, R^{b00}, R^{c00}, R^{d00}, R^{h00} and R^{i00} are C;

R_{1300} is O;

Z_{100} is O, Z_{200} is C, Z_{300} is a bond; and

y=0.

79. The compound or a pharmaceutically acceptable salt thereof of embodiment 78, wherein R_{900} is H, haloalkyl, or C_1-C_6 alkyl.

80. The compound or a pharmaceutically acceptable salt thereof of embodiment 68 or 79, wherein R_{200} is H.

81. The compound or a pharmaceutically acceptable salt thereof of any one of embodiments 78-80, wherein R_{1100} is H.

82. The compound or a pharmaceutically acceptable salt thereof of any one of embodiments 78-81, wherein R_{600} is H, C_1-C_6 alkyl, or C_2-C_6 alkenyl.

84. The compound or a pharmaceutically acceptable salt thereof of any one of embodiments 78-82, wherein R_{100} is H, cyano, or $–C(=O)NR_{300}R_{400}$.

85. The compound or a pharmaceutically acceptable salt thereof of any one of embodiments 78-83, wherein R_{900} is H or C_1-C_6 alkyl.

86. The compound or a pharmaceutically acceptable salt thereof of Formula I00A of embodiment 38, wherein

R^{a00}, R^{b00}, R^{c00}, R^{d00}, R^{e00}, and R^{i00} are C,

R^{g00} is C or O;

R^{f00} is absent;

R_{1300} is O; and

Z_{100} is O, Z_{200} is C, and Z_{300} is a bond.

87. The compound or a pharmaceutically acceptable salt thereof of embodiment 86, wherein R_{200} is H.

88. The compound or a pharmaceutically acceptable salt thereof of embodiment 86 or 87, wherein R_{1100} is H.

89. The compound or a pharmaceutically acceptable salt thereof of any one of embodiments 86-88, wherein R_{600} is H, optionally substituted C_1-C_6 alkyl or optionally substituted C_2-C_6 alkenyl.

90. The compound or a pharmaceutically acceptable salt thereof of any one of embodiments 84-88, wherein R_{100} is H, cyano,
$–C(=O)NR_{300}R_{400}$, or C_1-C_6 alkyl.

91. The compound or a pharmaceutically acceptable salt thereof of any one of embodiments 84-89, wherein R^{g00} is O.

92. The compound or a pharmaceutically acceptable salt thereof of embodiment 38, wherein y=1.

93. The compound or a pharmaceutically acceptable salt thereof of embodiment 92, wherein R_{900} is an optionally substituted C_1-C_6 alkyl or optionally substituted cycloalkyl.

94. The compound or a pharmaceutically acceptable salt thereof of embodiment 92 or 93, wherein R^{a00}, R^{b00}, R^{c00}, R^{d00}, R^{h00}, and R^{i00} are C.

95. The compound or a pharmaceutically acceptable salt thereof of any of one of embodiments 91-94, wherein R_{1300} is O.

96. The compound or a pharmaceutically acceptable salt thereof of any of one of embodiments 91-95, wherein Z_{100} is O, Z_{200} is C, and Z_{300} is a bond.

97. The compound or a pharmaceutically acceptable salt thereof of any one of embodiments 91-96, wherein R_{200} and R_{1100} are H.

98. The compound or a pharmaceutically acceptable salt thereof of any one of embodiments 91-97, wherein R_{100} is $-C(=O)NR_{300}R_{400}$.

99. The compound or a pharmaceutically acceptable salt thereof of any one of embodiments 91-98, wherein R_{600} is H or optionally substituted C_1-C_6 alkyl.

100. The compound or a pharmaceutically acceptable salt thereof of embodiment 38, wherein R^{h00} is N.

101. The compound or a pharmaceutically acceptable salt thereof of embodiment 100, wherein R^{a00}, R^{b00}, R^{c00}, R^{d00}, R^{i00} are C.

102. The compound or a pharmaceutically acceptable salt thereof of embodiment 100 or 101, wherein R_{200} is H.

103. The compound or a pharmaceutically acceptable salt thereof of any one of embodiments 100-102, wherein R_{1300} is O.

104. The compound or a pharmaceutically acceptable salt thereof of any one of embodiments 100-103, wherein Z_{100} is O, Z_{200} is C, and Z_{300} is a bond.

105. The compound or a pharmaceutically acceptable salt thereof of any one of embodiments 100-104, wherein R_{1100} is H.

106. The compound or a pharmaceutically acceptable salt thereof of any one of embodiments 100-105, wherein R_{600} is optionally substituted C_2-C_6 alkenyl, optionally substituted C_1-C_6 alkyl, or H.

107. The compound or a pharmaceutically acceptable salt thereof of any one of embodiments 100-106, wherein R_{100} is H or $-C(=O)NR_{300}R_{400}$.

108. The compound or a pharmaceutically acceptable salt thereof of embodiment 38, wherein R_{1100} is H or halo.

109. The compound or a pharmaceutically acceptable salt thereof of embodiment 108, wherein R^{a00}, R^{b00}, R^{c00}, R^{d00}, and R^{i00} are C.

110. The compound or a pharmaceutically acceptable salt thereof of embodiment 108 or 109, wherein Z_{100} is O, Z_{200} is C, Z_{300} is a bond.

111. The compound or a pharmaceutically acceptable salt thereof of any one of embodiments 108-110, wherein R_{1300} is a bond or C.

112. The compound or a pharmaceutically acceptable salt thereof of any one of embodiments 108 -111, wherein y=1.

113. The compound or a pharmaceutically acceptable salt thereof of any one of embodiments

108 -112, wherein R_{900} is H.

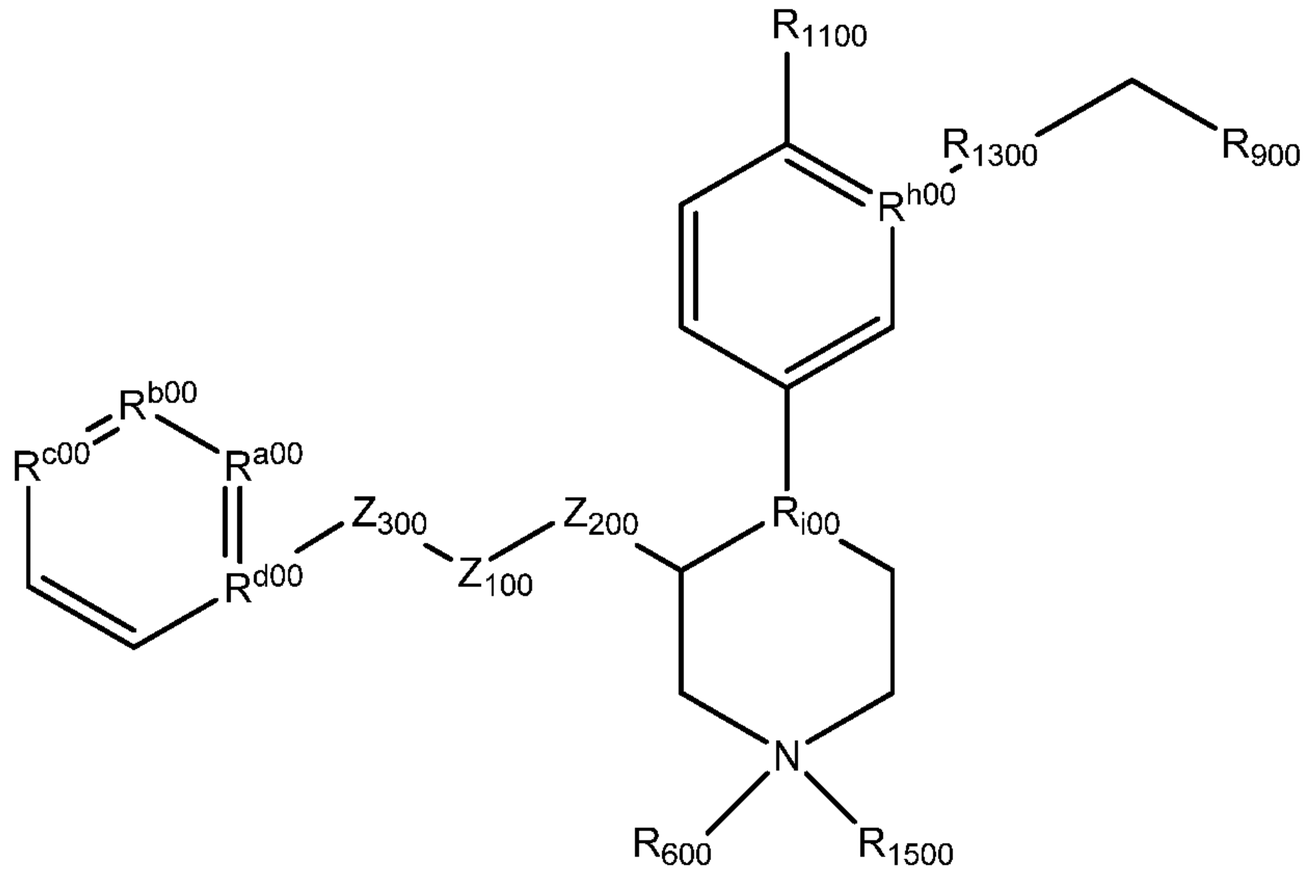
114. The compound or a pharmaceutically acceptable salt thereof of any one of embodiments 108-113, wherein R_{600} is H, optionally substituted C_1-C_6 alkyl, or optionally substituted C_2-C_6 alkenyl.

115. The compound or a pharmaceutically acceptable salt thereof of any one of embodiments 108-114, wherein R_{200} is H.

116. The compound or a pharmaceutically acceptable salt thereof of any one of embodiments 108-115, wherein R_{100} is H, -C(=O)$NR_{300}R_{400}$, or cyano.

117. The compound or a pharmaceutically acceptable salt thereof of embodiment 108, wherein y=0, R_{1300} is a bond and R_{900} is H.

118. The compound or a pharmaceutically acceptable salt thereof of embodiment 108, having Formula 00X:



00**X**,

wherein

R_{100}, R_{200}. R_{600}. and R_{900} are as defined above;

Z_{100} is O, Z_{200} is C, Z_{300} is a bond;

R^{a00}, R^{b00}, R^{c00}, R^{d00}, R^{h00}, and R^{i00} are C;

R_{200} is H;

R_{1100} is halo;

R_{1300} is O;

y=0-72; and

R_{900} is C_1-C_6 alkyl.

119. The compound or a pharmaceutically acceptable salt thereof of embodiment 118, wherein R_{600} is H, optionally substituted C_1-C_6 alkyl, or optionally substituted C_2-C_6 alkenyl.

120. The compound or a pharmaceutically acceptable salt thereof of embodiment 118 or 119, wherein R_{100} is H, cyano, or $-C(=O)NR_{300}R_{400}$.

121. The compound or a pharmaceutically acceptable salt thereof of embodiment 38, wherein Z_{100} is O, Z_{200} and Z_{300} is C.

122. The compound or a pharmaceutically acceptable salt thereof of embodiment 121, wherein R^{i00} is C.

123. The compound or a pharmaceutically acceptable salt thereof of any of embodiment 121 or 122, wherein R_{200} and/or R_{1100} are H.

124. The compound or a pharmaceutically acceptable salt thereof of any one of embodiments 121-123, wherein R_{600} is H.

125. The compound or a pharmaceutically acceptable salt thereof of any one of embodiments 121-124, wherein R_{100} is H, halo, cyano, -C(=O)OR_3, or -C(=O)$NR_{300}R_{400}$.

126. The compound or a pharmaceutically acceptable salt thereof of any one of embodiments 121-125, wherein:

R_{1300} is O;

R_{900} is H or –OR_3;

and y is 0-72.

127. The compound or a pharmaceutically acceptable salt thereof of embodiment 38, wherein:

Z_{100} is S or O;

Z_{300} is absent;

Z_{200} is C;

R_{200} and/or R_{1100} are H;

R^{i00} is C;

R_{1300} is O;

R_{900} is H or –OR_3;

and y=0-72.

128. The compound or a pharmaceutically acceptable salt thereof of embodiment 127, wherein R^{a00}, R^{b00}, R^{c00}, R^{d00}, R^{h00}, and R^{i00} are C.

129. The compound or a pharmaceutically acceptable salt thereof of embodiment 127 or 128, wherein R_{600} is H or –C(=O)OR_3.

130. The compound or a pharmaceutically acceptable salt thereof of any one of embodiments 127-129, wherein R_{100} is H or –C(=O)$NR_{300}R_{400}$.

131. The compound or a pharmaceutically acceptable salt thereof of embodiment 38, wherein:

R^{i00} is N;

R_{200} and/or R_{1100} are H;

Z_{300} is a bond or C;

Z_{100} is N or O; and

Z_{200} is C or C(=O).

132. The compound or a pharmaceutically acceptable salt thereof of embodiment 131, wherein R^{a00}, R^{b00}, R^{c00}, R^{d00}, R^{h00} are C.

133. The compound or a pharmaceutically acceptable salt thereof of embodiment 131 or 132, wherein R_{1300} is O.

134. The compound or a pharmaceutically acceptable salt thereof of any one of embodiments 131-133, wherein R_{900} is H and y=0-72.

135. The compound or a pharmaceutically acceptable salt thereof of any one of embodiments 131-134, wherein R_{100} is halo, H, cyano, $-C(=O)NR_{300}R_{400}$, or $-OR_3$.

136. The compound or a pharmaceutically acceptable salt thereof of any one of embodiments 131-135, wherein R_{600} is H, optionally substituted C_1-C_6 alkyl, or $-(CH_2)_p$-aryl, wherein p is an integer from 0-2.

137. The compound or a pharmaceutically acceptable salt thereof of any one of embodiments 131-136, wherein Z_{200} is C(=O), Z_{100} is N, and Z_{300} is C.

138. The compound or a pharmaceutically acceptable salt thereof of embodiment 38, wherein:

Z_{200} is C(=O) or C;

Z_{100} is N or O; and

Z_{300} is C or absent.

139. The compound or a pharmaceutically acceptable salt thereof of embodiment 138, wherein R^{a00}, R^{b00}, R^{c00}, R^{d00}, and R^{h00} are C.

140. The compound or a pharmaceutically acceptable salt thereof of any one of embodiments 138-139, wherein R_{200} is H.

141. The compound or a pharmaceutically acceptable salt thereof of any one of embodiments 138-140, wherein R_{100} is H, halo, cyano, or $-C(=O)NR_{300}R_{400}$.

142. The compound or a pharmaceutically acceptable salt thereof of any one of embodiments 138-141, wherein R_{1100} is H.

143. The compound or a pharmaceutically acceptable salt thereof of any one of embodiments 138-142, wherein

R_{1300} is O; and

R_{900} is H or $-OR_3$.

144. The compound or a pharmaceutically acceptable salt thereof of any one of embodiments 138-143, wherein R_{600} is H, C_1-C_6 alkyl, or $-(CH_2)_pR_{500}$.

145. The compound or a pharmaceutically acceptable salt thereof of any one of embodiments 138-144, wherein:

Z_{100} is O;

Z_{300} is absent; and

Z_{200} is C.

146. The compound or salt there of any one of embodiments 138-145, having Formula I00B.

147. The compound or a pharmaceutically acceptable salt thereof of Formula I00C of embodiment 38, wherein Z_{100} is C or O and R_{1400} is a pyridinone or optionally substituted -CH2-pyridinone.

148. The compound or a pharmaceutically acceptable salt thereof of embodiment 147, wherein R_{600} is H.

149. The compound or a pharmaceutically acceptable salt thereof of embodiment 147 or 148, wherein R^{i00} and R^{h00} are C.

150. The compound or a pharmaceutically acceptable salt thereof of any one of embodiments 147-149, wherein R_{1300} is O.

151. The compound or a pharmaceutically acceptable salt thereof of any one of embodiments 147-150, wherein y is an integer from 1-4.

152. The compound of embodiment 38, wherein the compound is chosen from a compound of Figure 1.

153. A pharmaceutical composition comprising a compound or pharmaceutically acceptable salt thereof of any one of embodiments 38-152.

154. A method of treating pain, neuropathic pain, migraine, headache, depression, Parkinson's disease, anxiety, overactive bladder, medication overuse headache, hyperalgesia, decreasing nociceptive sensitization, pain in an opioid exposed subject, PTSD, or other disorder or condition described herein in a mammal comprising administering to the mammal one or more compounds, or a salt thereof, of any of embodiments 38-152 or a pharmaceutical composition comprising one or more compounds, or salt thereof, of any one of embodiments 38-152.

155. The method of embodiment 154, wherein the mammal is a mammal in need thereof.

156. A method of treating hyperalgesia in a subject comprising administering to the subject comprising administering to the mammal one or more compounds, or a salt thereof, of any of embodiments 38-152 or a pharmaceutical composition comprising one or more compounds, or salt thereof, of any one of embodiments 38-152.

157. The method of embodiment 156, wherein the hyperalgesia is opioid induced hyperalgesia.

158. The method of embodiment 157, wherein the opioid induced hyperalgesia is morphine, oxycodone, hydrocodone, hydromorphone, fentanyl, meperidine, alfentanil, remifentanil, sufentanil, etorphine, buprenorphine, methadone, and/or heroin induced hyperalgesia.

159. The method of embodiment 156, wherein the subject has been administered an opioid prior to being administered the one or more compounds, or a salt thereof, of the pharmaceutical composition comprising the one or more compounds, or salt thereof.

160. A method of decreasing nociceptive sensitization in a subject comprising administering to the subject one or more compounds, or a salt thereof, of any of embodiments 38-152 or a pharmaceutical composition comprising one or more compounds, or salt thereof, of any one of embodiments 38-152.

161. The method of embodiment 160, wherein the subject has opioid induced nociceptive sensitization.

162. The method of embodiment 161, wherein the opioid induced nociceptive sensitization is morphine, oxycodone, hydrocodone, hydromorphone, fentanyl, meperidine, alfentanil, remifentanil, sufentanil, etorphine, buprenorphine, methadone, and/or heroin, or a pharmaceutically acceptable salt thereof, induced nociceptive sensitization.

163. A method of treating pain in a subject comprising:

administering an opioid agonist to the subject until the opioid increases nociceptive sensitization in the subject; and

administering to the subject one or more compounds, or a salt thereof, of any of embodiments 38-152 or a pharmaceutical composition comprising one or more compounds, or salt thereof, of any one of embodiments 38-152.

164. The method of embodiment 163, wherein the opioid agonist is morphine, oxycodone, hydrocodone, hydromorphone, fentanyl, meperidine, alfentanil, remifentanil, sufentanil, etorphine, buprenorphine, methadone, and/or heroin, or a pharmaceutically acceptable salt thereof.

165. A method of treating pain in an opioid exposed subject comprising:

a) administering an opioid agonist to the subject;

b) administering to the subject of step a), in the absence of the opioid administered in step a), one or more compounds, or a salt thereof, of any of embodiments 38-152 or a pharmaceutical composition comprising one or more compounds, or salt thereof, of any one of embodiments 38-152.

166. The method of embodiment 165, wherein the opioid is morphine, oxycodone, hydrocodone, hydromorphone, fentanyl, meperidine, alfentanil, remifentanil, sufentanil, etorphine, buprenorphine, methadone, and/or heroin, or a pharmaceutically acceptable salt thereof.

167. A method of treating medication overuse headache in a subject comprising administering to the subject one or more compounds, or a salt thereof, of any of embodiments 38-152 or a pharmaceutical composition comprising one or more compounds, or salt thereof, of any one of embodiments 38-152.

168. The method of embodiment 167, wherein the medication overuse headache is caused by acetaminophen, aspirin, a mu-opioid agonist, a non-steroidal anti-inflammatory drug (NSAID), or a triptan.

169. The method of embodiment 168, wherein the triptan is sumatriptan, rizatriptan, naratriptan, zolmitriptan, eletriptan, almotriptan, frovatriptan, avitriptan, or donitriptan, or a pharmaceutically acceptable salt thereof.

170. The method of embodiment 168, wherein the mu-opioid agonist is morphine, oxycodone, hydrocodone, hydromorphone, fentanyl, meperidine, alfentanil, remifentanil, sufentanil, etorphine, buprenorphine, methadone, or heroin, or a pharmaceutically acceptable salt thereof.

171. A method of treating a migraine in a subject, the method comprising:

administering a triptan to a subject; and

administering to the subject one or more compounds, or a salt thereof, of any of embodiments 38-152 or a pharmaceutical composition comprising one or more compounds, or salt thereof, of any one of embodiments 38-152.

172. The method of embodiment 171, wherein the one or more compounds, or a salt thereof, of any of embodiments 38-152 or the pharmaceutical composition comprising one or more compounds, or salt thereof, of any one of embodiments 38-152 is administered in the absence of the triptan.

173. The method of embodiment 171, wherein the triptan is sumatriptan, rizatriptan, naratriptan, zolmitriptan, eletriptan, almotriptan, frovatriptan, avitriptan, or donitriptan, or a pharmaceutically acceptable salt thereof.

174. The method of embodiment 171, wheren the subject develops mediation overuse headache prior to being administered the one or more compounds, or a salt thereof, of any of embodiments 38-152 or the pharmaceutical composition comprising one or more compounds, or salt thereof, of any one of embodiments 38-152.

175. The method of any one of embodiments 154-174, wherein the compound, or a pharmaceutically acceptable salt thereof, is selected from the group consisting of: B1049, B0704, B0707, B0720, B0876, B1079, B1145, B1194, B1205, B1211, B1365, B1401, or the pharmaceutical composition comprises a compound, or a pharmaceutically acceptable salt thereof, is selected from the group consisting of: B1049, B0704, B0707, B0720, B0876, B1079, B1145, B1194, B1205, B1211, B1365, B1401.

In order that the embodiments disclosed herein may be more efficiently understood, examples are provided below. It should be understood that these examples are for illustrative purposes only and are not to be construed as limiting the embodiments in any manner. Throughout these examples, there may be molecular cloning reactions, and other standard recombinant DNA techniques described and these were carried out according to methods described in Maniatis et al., Molecular Cloning - A Laboratory Manual, 2nd ed., Cold Spring Harbor Press (1989), using commercially available reagents, except where otherwise noted.

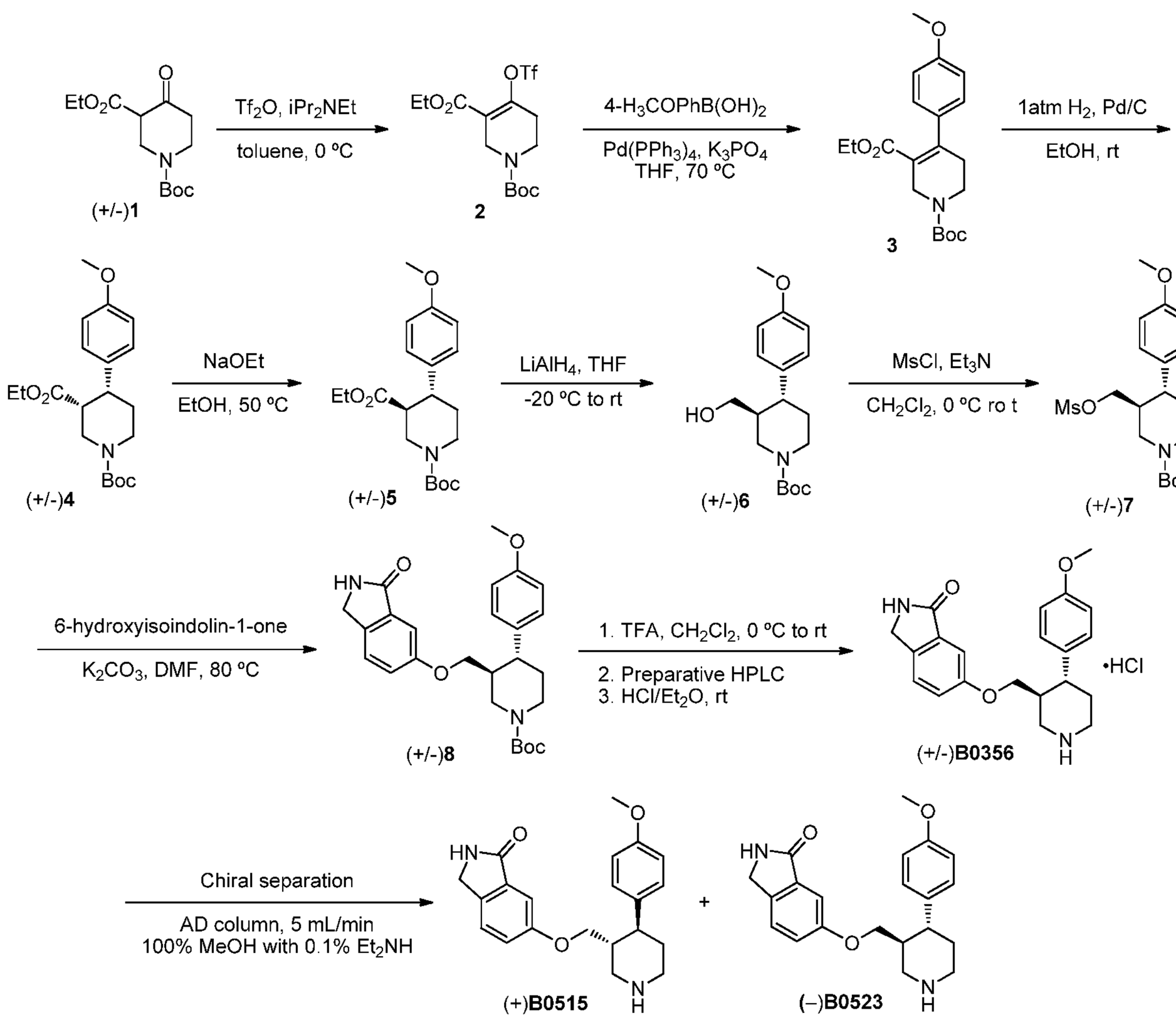
Examples

Example 1

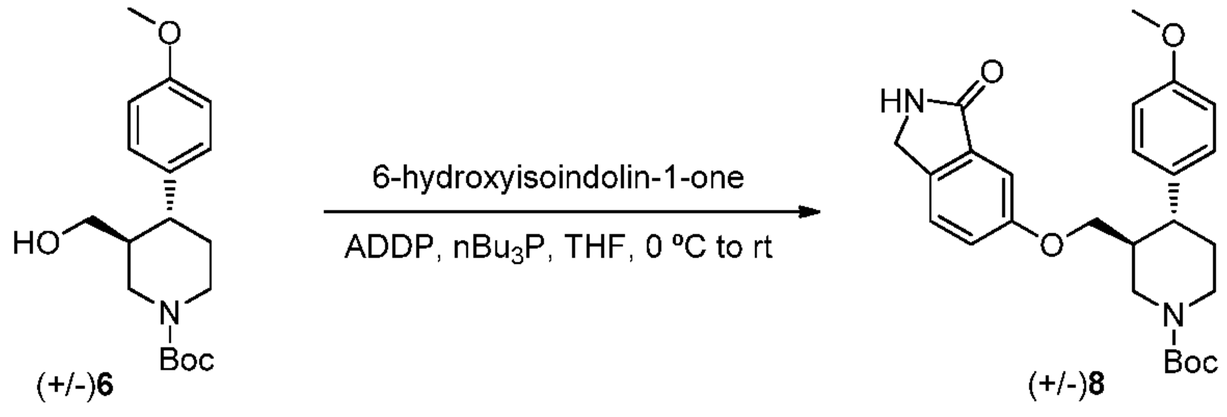
Example 1:

General Procedures A1: Preparation of 3,4-Piperidine N-H Analogs

Scheme 1



Scheme 2



5

Preparation of (+)-6-{[*trans*-4-(4-Methoxyphenyl)piperidin-3-yl]methoxy}isoindolin-1-one [(+)B0515] and (–)-6-{[*trans*-4-(4-Methoxyphenyl)piperidin-3-yl]methoxy}isoindolin-1-one [(-)B0523] (Scheme 1)

10 **1-*tert*-Butyl 3-Ethyl 4-(Trifluoromethylsulfonyloxy)-5,6-dihydropyridine-1,3(2*H*)-dicarboxylate (2)**

Trifluoromethanesulfonic anyhydride (33.3 mL, 203 mmol) was added portion-wise to a mixture of commercially available (+/-)-1-*tert*-butyl 3-ethyl 4-oxopiperidine-1,3-dicarboxylate [(+/-)**1**, 50.0 g, 184 mmol] and *N*,*N*-diisopropylethylamine (48.3 mL, 277 mmol) in anhydrous toluene (922 mL) at 0 °C under nitrogen, at a rate which kept the internal reaction temperature below 40 °C. The mixture was stirred at 0 °C for 2 h after which it was warmed to room temperature and the solids were removed by filtration. The filtrate solvents were removed under reduced pressure to provide crude **2** as a brown oil that was used in the next step without purification (74 g, 99%). The ^{1}H NMR spectral data were consistent with the literature (III. I. Elitzin, *et al. Org. Process Res. Dev.* **2010**, *14*, 912–917).

1-*tert*-Butyl 3-Ethyl 4-Phenyl-5,6-dihydropyridine-1,3(2*H*)-dicarboxylate (3)

Tetrakis(triphenylphosphine)palladium (4.2 g, 3.7 mmol) was added to a degassed mixture of crude 1-*tert*-butyl 3-ethyl 4-(trifluoromethylsulfonyloxy)-5,6-dihydropyridine-1,3(2*H*)-dicarboxylate (**2**, 74 g, 184 mmol), 4-methoxyphenylboronic acid (36.0 g, 239 mmol) and potassium phosphate (48 g, 276 mmol) in anhydrous THF (915 mL) at room temperature under nitrogen, after which the mixture was heated to 70 °C and stirred for 12 h. The cooled mixture was diluted with ethyl acetate (200 mL) and the solids were removed by filtration through a pad of Celite. The filtrate solvents were removed under reduced pressure to half-volume (about 600 mL) and then washed with water (200 mL) and brine (200 mL). The solvents were removed under reduced pressure and the crude product was purified by flash column chromatography on silica gel, eluting with hexanes/ethyl acetate (9:1), to afford **3** as a yellow solid that was suitable for use without further purification (63 g, 95%): LCMS (M+H) 362.

(+/-)-*cis*-1-*tert*-Butyl 3-Ethyl 4-(4-Methoxyphenyl)piperidine-1,3-dicarboxylate [(+/-)4]

A mixture of 1-*tert*-butyl 3-ethyl 4-phenyl-5,6-dihydropyridine-1,3(2*H*)-dicarboxylate (**3**, 60.0 g, 166 mmol) and 10% palladium on carbon (50% wet, 6.0 g) in anhydrous ethanol (60 mL) at room temperature under nitrogen was exchanged for a hydrogen atmosphere (balloon) after which the mixture stirred for 48 h. The atmosphere was exchanged for nitrogen, the mixture was diluted with methylene chloride (150 mL) and the solids were removed by filtration under reduced pressure through a plug of Celite, eluting with methylene chloride (150 mL). The organic extract solvents were removed under reduced pressure to provide (+/-)**4** as an off-white solid (56.6 g, 94%): LCMS (M+H) 364.

(+/-)-*trans*-1-*tert*-Butyl 3-Ethyl 4-(4-Methoxyphenyl)piperidine-1,3-dicarboxylate [(+/-)5]

Sodium ethoxide (36 mL, 21 weight % solution in ethanol) was added to a solution of (+/-)-*cis*-1-*tert*-butyl 3-ethyl 4-(4-methoxyphenyl)piperidine-1,3-dicarboxylate [(+/-)**4**, 10.0 g, 27.5 mmol] in anhydrous ethanol (150 mL) at room temperature under nitrogen, after which the mixture was heated to 50 °C and stirred for 12 h. The cooled mixture was treated with saturated ammonium chloride solution (100 mL) and extracted with ethyl acetate (3 x 100 mL). The combined organic extracts were washed with brine solution (100 mL), dried over sodium sulfate and filtered. The solvents were removed under reduced pressure to afford (+/-)**5** as a yellow oil that was suitable for use without further purification (9.8 g, 98%): LCMS (M+H) 364.

(+/-)-*trans-tert*-Butyl 3-(Hydroxymethyl)-4-(4-methoxyphenyl)-piperidine-1-carboxylate [(+/-)6]

Lithium aluminum hydride (41.2 mL, 41.2 mmol, 1 M in tetrahydrofuran) was added dropwise to a solution of (+/-)-*trans*-1-*tert*-butyl 3-ethyl 4-(4-methoxyphenyl)piperidine-1,3-dicarboxylate [(+/-)**5**, 11.2 g, 27.5 mmol] in anhydrous tetrahydrofuran (225 mL) at -20 °C under nitrogen, after which the mixture was warmed to 0 °C. The mixture was stirred for 4 h and then slowly warmed to room temperature, stirring for a total of 12 h. The mixture was cooled to 0 °C and slowly treated with water (2 mL) and then 1N sodium hydroxide solution (2 mL) and stirred for an additional 1 h. The solids were removed by filtration under reduced pressure and the filtrate solvents were removed under reduced pressure. The residue was purified by flash column chromatography on silica gel, eluting with hexanes/ethyl acetate (2:3), to afford (+/-)**6** as a colorless oil (3.8 g, 58%): LCMS (M+H) 322.

(+/-)-*trans-tert*-Butyl 4-(4-Methoxyphenyl)-3-{[(methylsulfonyl)oxy]-methyl}piperidine-1-carboxylate [(+/-)7]

Methanesulfonyl chloride (1.4 mL, 18.1 mmol) was added dropwise to a solution of (+/-)-*trans-tert*-butyl 3-(hydroxymethyl)-4-(4-methoxyphenyl)piperidine-1-carboxylate [(+/-)**6**, 4.40 g, 13.7 mmol] and triethylamine (2.3 mL, 16.5 mmol) in anhydrous methylene chloride (150 mL) at 0 °C under nitrogen, after which the mixture was slowly warmed to room temperature, stirring for a total of 5 h. The mixture was treated with brine solution (100 mL)

and extracted with ethyl acetate (2 x 150 mL). The combined organic extracts were washed with brine solution (100 mL), dried over sodium sulfate and filtered. The solvents were removed under reduced pressure to afford (+/-)**7** as a yellow oil that was suitable for use without further purification (5.08 g, 88%).

(+/-)-*trans*-*tert*-Butyl 4-(4-Methoxyphenyl)-3-{[(3-oxoisoindolin-5-yl)oxy]methyl}piperidine-1-carboxylate [(+/-)8]

Potassium carbonate (727 mg, 5.3 mmol) [Note: An equivalent amount of sodium hydride can also be used interchangeably] was added to a solution of 6-hydroxyisoindolin-1-one (523 mg, 3.5 mmol) and (+/-)-*trans*-*tert*-butyl 4-(4-methoxyphenyl)-3-{[(methylsulfonyl)oxy]methyl}piperidine-1-carboxylate [(+/-)**7**, 600 mg, 1.8 mmol] in anhydrous *N,N*-dimethylformamide (30 mL) at room temperature under nitrogen, after which the mixture was heated to 80 °C and stirred for 18 h. The cooled mixture was diluted with ethyl acetate (200 mL) and the solids were removed by filtration under reduced pressure. The filtrate solvents were removed under reduced pressure and the residue was purified by flash column chromatography on silica gel, eluting with methylene chloride/methanol (9:1), to afford (+/-)**8** as a white solid (240 mg, 35%): LCMS (M+H) 453.

(+/-)-6-{[*trans*-4-(4-Methoxyphenyl)piperidin-3-yl]methoxy}isoindolin-1-one Hydrochloride [(+/-)B0356]

Trifluoroacetic acid (0.70 mL, 10 mmol) was added dropwise to a solution of (+/-)-*trans*-*tert*-butyl 4-(4-methoxyphenyl)-3-{[(3-oxoisoindolin-5-yl)oxy]methyl}piperidine-1-carboxylate [(+/-)**8**, 432 mg, 1.0 mmol] in anhydrous methylene chloride (30 mL) at 0 °C under nitrogen, after which the mixture was slowly warmed to room temperature, stirring for a total of 5 h. The solvents were removed under reduced pressure and the residue was dissolved in methanol for purification by reversed-phase preparative HPLC, eluting with 0.05% TFA in acetonitrile/water (gradient from 2% to 60%, Phenomenex Luna column). The isolated residue was acidified with HCl (2 mL, 2M in diethyl ether), diluted with acetonitrile/water and lyophilized to afford (+/-)**B0356** as a white solid (91 mg, 24%): LCMS (M+H) 353; ^{1}H NMR (500 MHz, CD_3OD) δ 7.43 (dd, J = 8.5, 0.5 Hz, 1H), 7.18 (d, J = 11.5 Hz, 2H), 7.12–7.09 (m, 2H), 6.88 (d, J = 8.5 Hz, 2H), 4.36 (s, 2H), 3.82 (dd, J = 10.0, 3.0 Hz, 1H), 3.75 (s, 3H), 3.72–3.69 (m, 2H), 3.56–3.49 (m, 1H), 3.21–3.15 (m, 2H), 2.96–2.90 (m, 1H), 2.46–2.40 (m, 1H), 2.08–2.00 (m, 2H).

Separation of [(+/-)B0356] into (+)-6-{[*trans*-4-(4-Methoxyphenyl)piperidin-3-yl]methoxy}isoindolin-1-one [(+)B0515] and (–)-6-{[*trans*-4-(4-Methoxyphenyl)piperidin-3-yl]methoxy}isoindolin-1-one [(-)B0523]

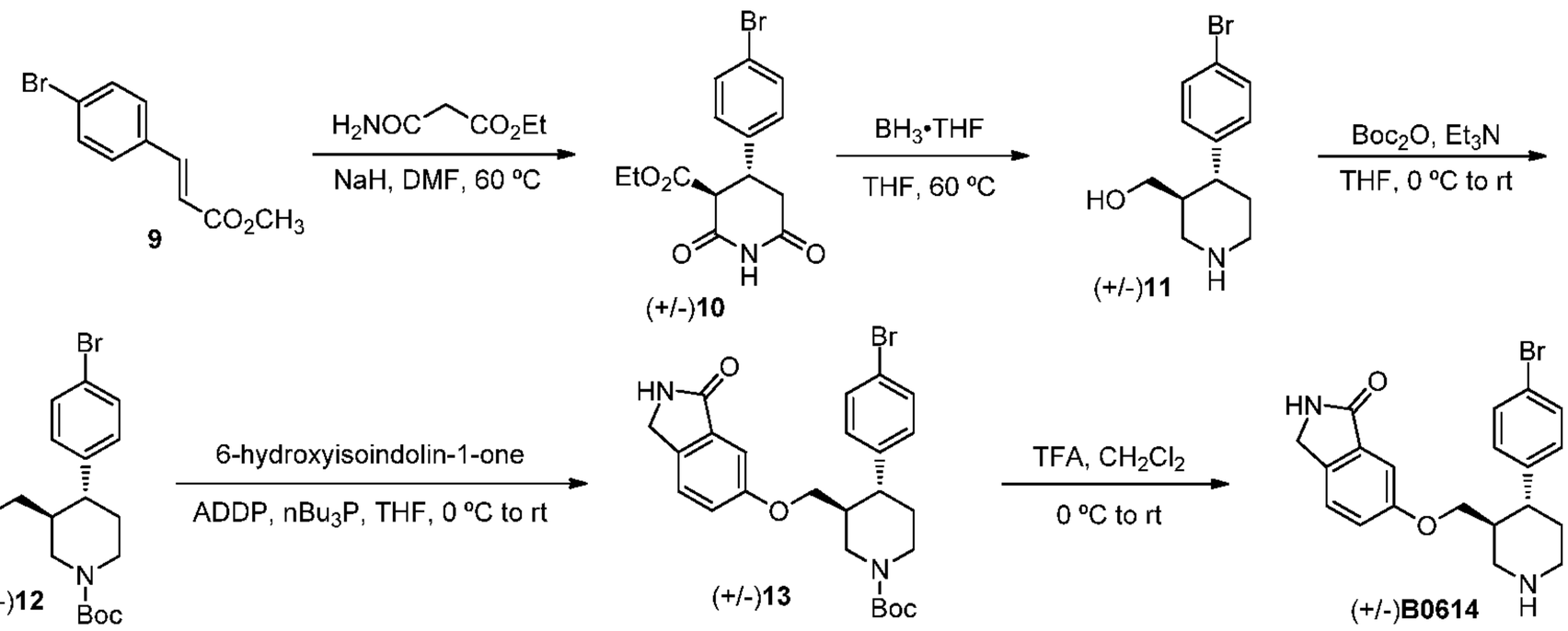
A solution of (+/-)-6-{[*trans*-4-(4-Methoxyphenyl)piperidin-3-yl]methoxy}isoindolin-1-one [(+/-)**B0356**, 48 mg] in methanol was separated by chiral preparative HPLC (10 μM CHIRALPAK AD, 2 cm x 25 cm, 5 mL/min flow rate, 3 mg/injection), eluting with 0.1% diethylamine in methanol, to provide (+)**B0515** as a white solid (12 mg, 25%), followed by (-)**B0523**, (11 mg, 23%) as a white solid.

Alternative Preparation of (+/-)-*trans*-*tert*-Butyl 4-(4-Methoxyphenyl)-3-{[(3-oxoisoindolin-5-yl)oxy]methyl}piperidine-1-carboxylate [(+/-)8] (Scheme 2)

1,1'-(Azodicarbonyl)dipiperidine (5.9 g, 23.4 mmol) was added to a solution of (+/-)-*trans*-*tert*-butyl 3-(hydroxymethyl)-4-(4-methoxyphenyl)piperidine-1-carboxylate [(+/-)**6**, 3.75 g, 11.7 mmol], 6-hydroxyisoindolin-1-one (1.74 g, 11.7 mmol) and tributylphosphine (4.73 g, 23.4 mmol) in anhydrous tetrahydrofuran (100 mL) at 0 °C under nitrogen, after which the mixture was slowly warmed to room temperature, stirring for a total of 12 h. The mixture was cooled to 0 °C and the solids were removed by filtration under reduced pressure. The filtrate solvents were removed under reduced pressure and the residue was purified by flash column chromatography on silica gel, eluting with methylene chloride/methanol (9:1), to afford [(+/-)**8**] as a white solid (3.01 g, 57%).

General Procedure A2: Alternative Preparation of 3,4-Piperidine N-H Analogs

Scheme 3



Preparation of (+/-)-6-{[*trans*-4-(4-Bromophenyl)piperidin-3-yl]methoxy}-2,3-dihydro-1*H*-isoindol-1-one [(+/-)B0614]

(+/-)-*trans*-Ethyl 4-(4-Bromophenyl)-2,6-dioxopiperidine-3-carboxylate [(+/-)10]

A solution of ethyl 3-amino-3-oxopropanoate (13.1 g, 100 mmol) in anhydrous DMF (100 mL) was added to a suspension of sodium hydride (6.0 g, 150 mmol, 60% in mineral oil) in anhydrous DMF (200 mL) at 0 °C under nitrogen. The mixture was stirred at 0 °C for 30 min, after which commercially available (*E*)-methyl 3-(4-bromophenyl)acrylate (**9**, 24.0 g, 100 mmol) was added portionwise, and the mixture was slowly warmed to room temperature, stirring for a total of 2 h. The mixture was further heated to 60 °C and stirred for 5 h, after which the mixture was cooled to room temperature and treated with saturated aqueous ammonium chloride solution (50 mL) and then 2 N HCl (200 mL). The mixture was extracted with ethyl acetate (3 x 200 mL) and the combined organic extracts were dried over sodium sulfate and filtered. The solvents were removed under reduced pressure to provide (+/-)**10** as an off-white semi-solid that was used in the next step without purification (26.2 g): LCMS (M-H) 338.

(+/-)-[*trans*-4-(4-Bromophenyl)piperidin-3-yl]methanol [(+/-)11]

Borane (269 mL, 269 mmol, 1.0 M solution in THF) was added slowly to a solution of crude (+/-)-(3*S*,4*R*)-ethyl 4-(4-bromophenyl)-2,6-dioxopiperidine-3-carboxylate [(+/-)**10**, 26.2 g, 67.2 mmol] in anhydrous THF (400 mL) at room temperature under nitrogen, after which the mixture was heated to 60 °C and stirred for 16 h. The cooled mixture was treated with anhydrous methanol (30 mL) followed by 2 N HCl (250 mL), after which the organic layer was collected. The solvent was removed under reduced pressure to (+/-)**11** as a white solid that was used in the next step without purification (25.6 g): LCMS (M+H) 270.

(+/-)-*trans-tert*-Butyl 4-(4-Bromophenyl)-3-(hydroxymethyl)-piperidine-1-carboxylate [(+/-)12]

Triethylamine (47 mL, 335 mmol) was added to a solution of crude (+/-)-[*trans*-4-(4-bromophenyl)piperidin-3-yl]methanol [(+/-)**11**, 25.6 g, 83.8 mmol] in anhydrous THF (200 mL) at room temperature under nitrogen, after which the mixture was cooled to 0 °C. A solution of di-*tert*-butyl dicarbonate (18.3 g, 83.8 mmol) in anhydrous THF (100 mL) was slowly added, after which the mixture was stirred at 0 °C for 4 h. The mixture was warmed

to room temperature, washed with water (300 mL) and the organic layer was collected. The solvent was removed under reduced pressure and the residue was purified by flash column chromatography on silica gel, eluting with hexanes/ethyl acetate (2:3), to afford (+/-)**12** as a white solid (15.8 g, 50% over three steps): LCMS (M+H) 370.

(+/-)-*trans-tert*-Butyl 4-(4-Bromophenyl)-3-{[(3-oxoisoindolin-5-yl)oxy]methyl}piperidine-1-carboxylate [(+/-)13]

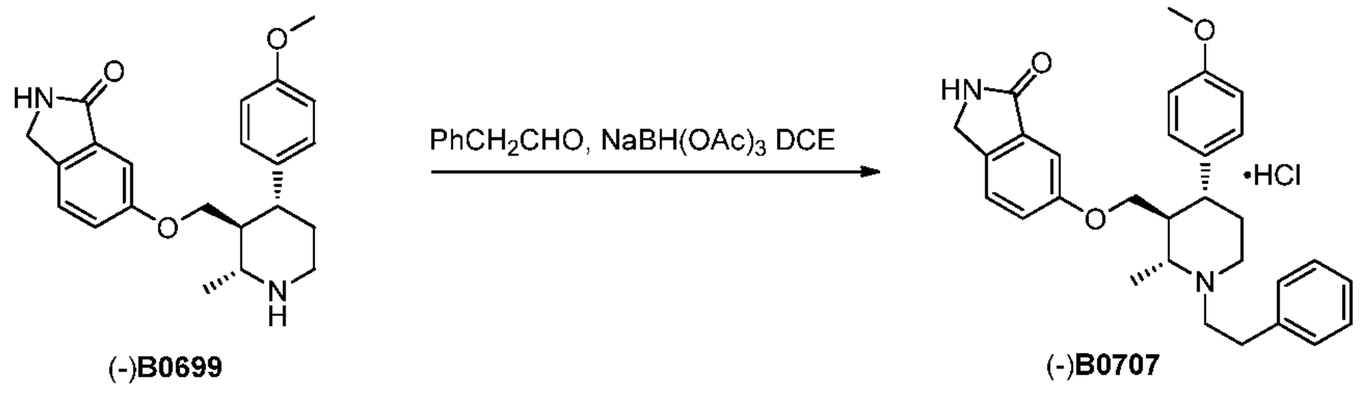
Prepared according to General Procedure A1 to afford (+/-)**13** as an off-white semi-solid that was used in the next step without further purification (700 mg): LCMS (M+H) 501.

(+/-)-6-{[*trans*-4-(4-Bromophenyl)piperidin-3-yl]methoxy}-2,3-dihydro-1*H*-isoindol-1-one [(+/-)B0614]

Prepared according to General Procedure A1 to yield (+/-)**B0614** as a white solid (87 mg, 54% over two steps): LCMS (M+H) 401; ^{1}H NMR (500 MHz, CD_3OD) δ 7.49 (d, J = 8.5 Hz, 2H), 7.45 (d, J = 8.5 Hz, 1H), 7.21 (d, J = 8.5 Hz, 2H), 7.14 (d, J = 2.5 Hz, 1H), 7.11 (dd, J = 8.5, 2.5 Hz, 1H), 4.37 (s, 2H), 3.83 (dd, J = 9.5, 3.0 Hz, 1H), 3.74–3.70 (m, 2H), 3.54 (m, 1H), 3.23–3.16 (m, 2H), 3.02 (dt, J = 12.0, 4.0 Hz, 1H), 2.46 (m, 1H), 2.11–2.00 (m, 2H).

General Procedure A3: Preparation of N-Alkyl Analogs

Scheme 4

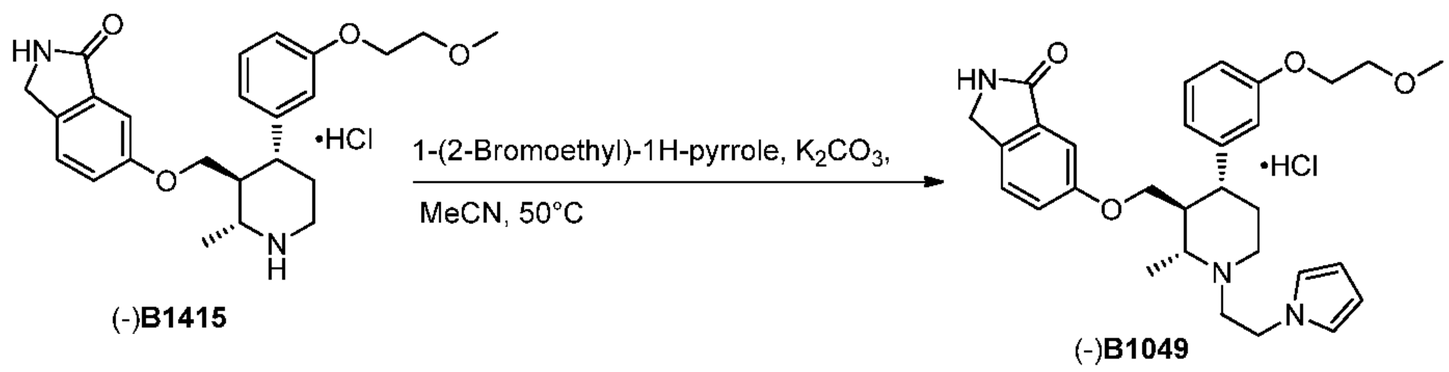


(-)**B0699** (-)**B0707**

Preparation of (-)-6-{[(trans, trans)-4-(4-methoxyphenyl)-2-methyl-1-(2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one [(-)B0707]

A solution of (-)-6-{[(trans, trans)-4-(4-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one [**(-)B0699**, 2.6 g, 7.09 mmol] and sodium triacetoxyborohydride (4.5 g, 21.3 mmol) in DCE (80 mL) was allowed to stir at rt for 30 min. To this was added phenylacetaldehyde (1.3 mL, 10.6 mmol). After stirring for three days, LCMS indicated no starting material remaining. The reaction was quenched with addition of methanol (~10 mL) and concentrated. The crude product was purified by reverse phase chromatography (Phenomenex Luna 5µ C18 column, 10% - 50% MeCN/water/0.1% TFA. Fractions containing product were combined and concentrated. The concentrate was treated with sat $NaHCO_3$ solution until basic and extracted with DCM (X3). The combined extracts were passed through a hydrophobic frit and concentrated to yield 2.6 g (71%) of **[(-)B0707].** The hydrochloride salt may be formed by dissolving the free base in MeCN/water, adding 1.05 eq of 1N HCl and lyophilizing to yield a white powder. LCMS (M+H) 471.2; HCl salt ^{1}H NMR (400 MHz, MeOD) δ 7.52 – 7.37 (m, 5H), 7.37 – 7.25 (m, 1H), 7.23 – 7.10 (m, 4H), 6.86 (dd, 2H), 4.39 (s, 2H), 4.10 (d, 1H), 3.99 – 3.42 (m, 9H), 3.29 – 3.02 (m, 3H), 2.45 – 1.97 (m, 3H), 1.68 – 1.44 (m, 3H).

Scheme 5a

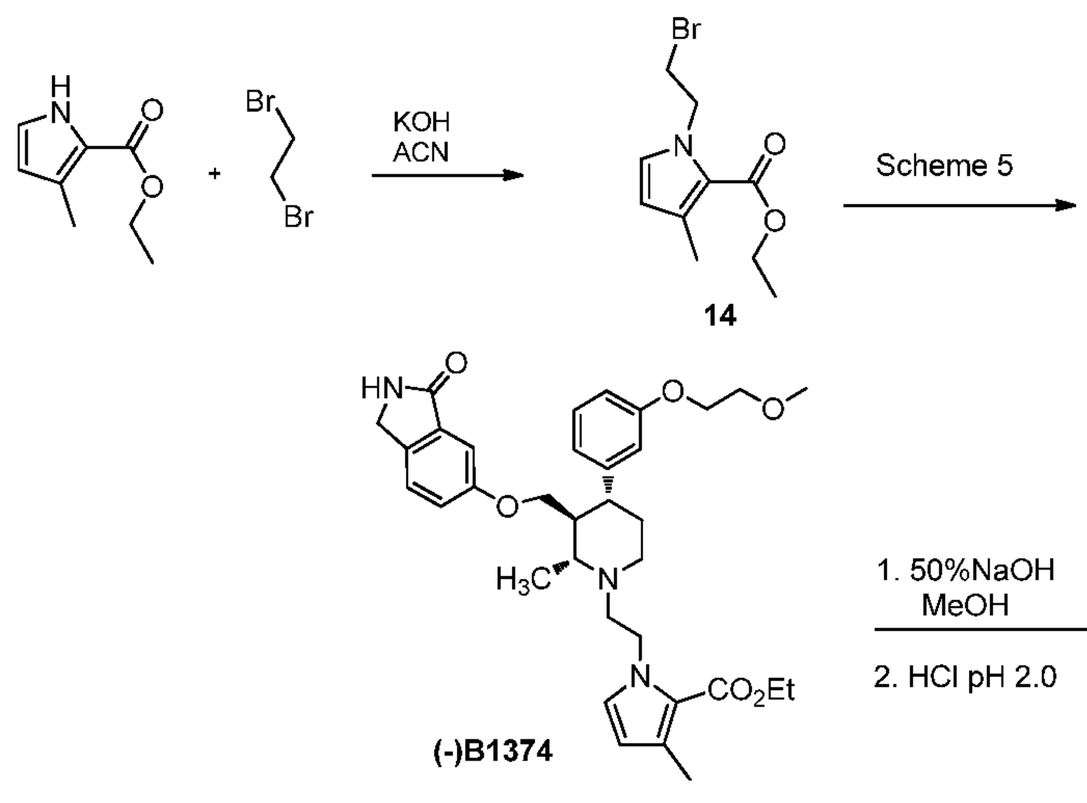


Preparation of (-)-6-{[(trans, trans)-4-[3-(2-methoxyethoxy)phenyl]-2-methyl-1-[2-(1H-pyrrol-1-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one [(-)B1049]

To a solution of (-)-6-{[(trans, trans)-4-[3-(2-methoxyethoxy)phenyl]-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one [**(-)B1415**, 5.10 g, 12.42 mmol] in anhydrous acetonitrile (25 mL) was added potassium carbonate (3.43 g, 24.85 mmol, 2.0 eq) and 1-pyrroleethylbromide (4.32 g, 24.85 mmol, 2.0 eq) and the reaction heated at 50°C for 168 hr. The reaction was cooled to rt, filtered of inorganics, and concentrated. The crude product was purified by reverse phase chromatography (Phenomenex Luna 5µ C18 column, 30% - 50

% MeCN/water/0.1% TFA. The product fractions were concentrated, and the residue dissolved in 25 mL DCM and washed with 1N NaOH (ensuring aqueous basic by pH paper). The layers were separated, and the aqueous extracted 3X 10 mL DCM. The combined organics were washed with brine, filtered through cotton and concentrated to yield 6.4 g (84%) of **[(-)B1049]** as a white solid. The hydrochloride salt may be formed by dissolving the free base in MeCN/water, adding 1.05 eq. 1N HCl, and lyophilizing to yield a white powder. LCMS (M+H) 504.3; HCl salt ^{1}H NMR (400 MHz, DMSO) δ 11.15 – 10.65 (m, 1H), 8.55 (s, 1H), 7.48 – 7.42 (m, 1H), 7.25 – 7.08 (m, 2H), 7.07 – 6.96 (m, 3H), 6.95 – 6.67 (m, 3H), 6.10 – 6.05 (m, 2H), 4.55 – 4.31 (m, 2H), 4.27 (s, 2H), 4.09 (d, J = 8.7, 1H), 4.03 – 3.82 (m, 3H), 3.76 – 3.62 (m, 1H), 3.61 – 3.48 (m, 5H), 3.27 – 3.23 (m, 3H), 3.22 – 2.96 (m, 2H), 2.46 – 2.12 (m, 2H), 1.95 – 1.71 (m, 1H), 1.48 – 1.37 (m, 3H).

Scheme 5b



Preparation of (-)-6-{[(trans, trans)-4-[3-(2-methoxyethoxy)phenyl]-2-methyl-1-[2-(3-methyl-1H-pyrrol-1-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one [(-)14]

Ethyl 1-(2-bromoethyl)-3-methyl-1H-pyrrole-2-carboxylate (14)

To a mixture of potassium hydroxide (431 mg, 7.84 mmol) and 1,2-dibromoethane (2453 mg, 13.06 mmol) in 5 mL of acetonitrile, a solution of ethyl 3-methyl-1-H-pyrrole carboxylate (727 mg, 5.22 mmol) in 20 mL of acetonitrile was slowly added over 2 h. After 1h, the reaction mixture was quench with water and extracted with hexanes (3X10 mL). The

organics were combined, concentrated and subjected to the Biotage purification under flash chromatography (45 g silica gel column, eluted with EtOAc in hexane: 2% - 20%, 10CV; 100% EtOAc, 10CV) to give 316 mg of **14** in 23% yield. LCMS (M+H = 262.0).

Ethyl 1-(2-bromoethyl)-5-methyl-1H-pyrrole-2-carboxylate was also made by the above procedure in 7% yield. LCMS (M+H = 262.2).

(-)-Ethyl 1-{2-[(trans, trans)-4-[3-(2-methoxyethoxy)phenyl]-2-methyl-3-{[(3-oxo-2,3-dihydro-1H-isoindol-5-yl) oxy]methyl}piperidin-1-yl]ethyl}-3-methyl-1H-pyrrole-2-carboxylate [(-)B1374]

The title compound was prepared from ethyl 1-(2-bromoethyl)-3-methyl-1H-pyrrole-2-carboxylate (**14**) according to Scheme 5. LCMS (M+H = 590.2).

(-)-6-{[(trans, trans)-4-[3-(2-methoxyethoxy)phenyl]-2-methyl-1-[2-(3-methyl-1H-pyrrol-1-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one [(-)B1396]

To a suspension of (-)-ethyl 1-{2-[(trans, trans)-4-[3-(2-methoxyethoxy)phenyl]-2-methyl-3-{[(3-oxo-2,3-dihydro-1H-isoindol-5-yl)oxy]methyl}piperidin-1-yl]ethyl}-3-methyl-1H-pyrrole-2-carboxylate [**(-)B1374**, 94 mg, 0.13 mmol) in MeOH (6.69 mL) was added 50% NaOH(aq) (1.5 mL) and the reaction heated at 50 °C for 30 minutes. The reaction was cooled to room temperature, acidified to pH 2 then heated at 50 °C for 4 hours. The reaction mixture was filtered and subjected to HPLC purification. HPLC purification method: Luna acid medium column, 5% - 55% acetonitrile in H_2O over 15 min, followed by 100% acetonitrile, 0.1% TFA modifier was employed. Lyophilizing of the combined fractions gave 26.93 mg of **(-)B1396** as a light pink solid. LCMS (M+H = 518.2); ^{1}H NMR (400 MHz, CD_3CN) δ 7.43 (d, J = 8.3, 1H), 7.20 (t, J = 7.8, 1H), 7.11 (dd, J = 8.3, 2.4, 1H), 7.06 (s, 1H), 6.77 (dd, J = 16.2, 8.1, 5H), 6.62 (s, 1H), 5.99 – 5.93 (m, 1H), 4.43 – 4.33 (m, 2H), 4.30 (s, 2H), 4.06 (d, J = 9.9, 1H), 4.02 – 3.80 (m, 3H), 3.70 – 3.39 (m, 7H), 3.31 (s, 3H), 3.10 (dd, J = 20.2, 10.9, 2H), 2.37 (d, J = 11.2, 2H), 2.06 (s, 3H), 1.45 (dd, J = 28.0, 6.1, 3H).

The following compounds were prepared by General Procedure A1 and A3:

(-)-6-{[trans, trans-4-(1-benzofuran-6-yl)-2-methyl-1-[2-(1H-pyrrol-1-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one [(-)B1400] LCMS (MH+ = 471.2); ^{1}H NMR (400 MHz, DMSO) δ 9.88 – 9.68 (m, 1H), 8.56 (s, 1H), 7.57 – 7.32 (m, 1H), 7.27 – 7.46 (m, 1H), 7.14 – 7.08 (m, 1H), 7.05 – 7.01 (m, 1H), 7.00 – 6.95 (m, 2H), 6.94 – 6.46 (m, 3H), 6.12 – 6.06 (m, 2H), 5.16 – 5.01 (m, 1H), 4.88 – 4.80 (m, 1H), 4.80 – 4.69 (m, 1H), 4.66 – 4.31 (m, 5H), 4.28 (s, 2H), 4.13 – 3.14 (m, 8H), 3.10 – 2.97 (m, 1H), 2.28 – 1.70 (m, 4H), 1.45 – 1.30 (m, 3H).

(+/-)-6-{[(trans, trans)-4-(1-acetylpiperidin-4-yl)-2-methyl-1-(2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one [(+/-)B1413] LCMS (MH+ = 490.2); ^{1}H NMR (400MHz ,CD_3OD): 7.53 (d, *J*=8.4Hz, 1H), 7.27-7.38 (m, 7H), 4.61 (t, *J*=13.2Hz, 1H), 4.42 (s, 2H), 4.27-4.38 (m, 2H), 3.97 (t, *J*=12.4Hz, 1H), 3.80 (m, 1H), 3.61 (m, 1H), 3.58 (m, 1H), 3.30 (m, 1H), 3.20 (m, 1H), 3.10 (m, 2H), 2.56 (m, 1H), 1.90-2.20 (m, 7H), 1.70 (m, 2H), 1.56 (d, *J*=6.0Hz, 3H), 1.40-1.50 (m, 2H), 1.20-1.40 (m, 1H).

(+/-)-6-{[(trans, trans)-4-(1-acetylpiperidin-4-yl)-2-methyl-1-[2-(1H-pyrrol-1-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one [(+/-)B1413] LCMS (MH+ = 490.2); ^{1}H NMR (400MHz ,CD_3OD): 7.53 (d, *J*=8.0Hz, 1H), 7.37(s, 1H), 7.27 (d, *J*=7.6Hz, 1H), 6.88 (s, 2H), 6.17 (s, 2H), 4.60 (t, *J*=12.0Hz, 1H), 4.30-4.50 (m, 5H), 4.10-4.30 (m, 1H), 3.96 (t, *J*=14.0Hz, 1H), 3.77 (m, 1H), 3.65 (m, 1H), 3.51 (m, 2H), 3.07 (m, 2H), 2.54 (m, 1H), 1.88-2.15 (m, 7H), 1.60-1.85 (m, 2H), 1.35-1.55 (m, 5H), 1.10-1.35 (m, 1H).

(-)-6-{[trans, trans-4-(3-hydroxyphenyl)-2-methyl-1-[2-(1H-pyrrol-1-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one [(-)B1416] LCMS (MH+ = 446.2); ^{1}H NMR (400 MHz, DMSO) δ 9.53 (s, 1H), 9.35 – 9.20 (m, 1H), 8.46 (s, 1H), 7.46 – 7.28 (m, 1H), 7.05 – 6.86 (m, 5H), 6.68 – 6.45 (m, 3H), 6.01 (s, 2H), 4.40 – 4.23 (m, 2H), 4.20 (s, 2H), 3.98 (d, *J* = 10.0, 1H), 3.89 – 3.12 (m, 15H), 2.95 – 2.81 (m, 1H), 2.15 – 1.65 (m, 4H), 1.34 – 1.24 (m, 3H).

(-)-6-{[trans, trans-4-[3-(2-hydroxyethoxy)phenyl]-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one [(-)B1417] LCMS (MH+ = 397.1); ^{1}H NMR (400 MHz, DMSO) δ 8.80 (d, *J* = 10.0, 1H), 8.65 – 8.46 (m, 2H), 7.44 (d, *J* = 8.3, 1H), 7.21 (t, *J* = 7.9,

1H), 7.09 (dd, *J* = 8.3, 2.3, 1H), 7.02 (d, *J* = 2.2, 1H), 6.79 (dd, *J* = 8.1, 2.0, 1H), 6.73 (d, *J* = 7.6, 1H), 6.69 (s, 1H), 4.27 (s, 2H), 4.02 (d, *J* = 8.7, 1H), 3.93 – 3.86 (m, 1H), 3.82 – 3.74 (m, 1H), 3.64 (t, *J* = 4.9, 2H), 3.51 (dd, *J* = 10.2, 2.3, 1H), 3.48 – 3.35 (m, 2H), 3.14 (d, *J* = 9.1, 1H), 3.07 – 2.98 (m, 1H), 2.11 (t, *J* = 11.1, 1H), 2.04 – 1.86 (m, 2H), 1.35 (d, *J* = 6.4, 3H).

(-)-6-{[trans, trans-4-(3,4-dihydro-2H-1-benzopyran-7-yl)-2-methyl-1-[2-(1H-pyrrol-1-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one [(-)-B1365] LCMS (MH+ = 486.2); ^{1}H NMR (400 MHz, DMSO) δ 10.93 – 10.45 (m, 1H), 8.56 (s, 1H), 7.50 – 7.40 (m, 1H), 7.17 – 7.07 (m, 1H), 7.05 – 7.01 (m, 1H), 7.00 – 6.88 (m, 3H), 6.78 – 6.49 (m, 2H), 6.15 - 6.00 (m, 2H), 4.54 – 4.31 (m, 2H), 4.28 (s, 2H), 4.19 – 3.80 (m, 8H), 3.77 – 3.61 (m, 1H), 3.60 – 3.43 (m, 4H), 3.39 – 2.85 (m, 3H), 2.67 (t, *J* = 6.0, 2H), 2.41 – 2.04 (m, 3H), 1.96 – 1.66 (m, 4H), 1.46 – 1.33 (m, 3H).

(-)-6-{[trans, trans-4-(4-methoxyphenyl)-2-methyl-1-[2-(1H-pyrrol-1-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one [(-)B0876] LCMS (MH+ = 460.3); ^{1}H NMR (400 MHz, MeOD) δ 7.36 (d, *J* = 9.1, 1H), 7.17 – 6.92 (m, 4H), 6.81 (t, *J* = 2.1, 2H), 6.74 (d, *J* = 8.8, 2H), 6.08 (t, *J* = 2.1, 2H), 4.47 – 4.13 (m, 4H), 4.02 – 3.32 (m, 9H), 3.06 – 2.86 (m, 1H), 2.32 – 1.69 (m, 4H), 1.53 – 1.05 (m, 4H).

(-)-6-{[trans, trans-4-[3-fluoro-4-(2-methoxyethoxy)phenyl]-2-methyl-1-[2-(1H-pyrrol-1-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one [(-)B1205] LCMS (MH+ = 522.2); ^{1}H NMR (400 MHz, MeOD) δ 7.49 (d, *J* = 9.1, 1H), 7.25 – 6.80 (m, 7H), 6.20 (s, 2H), 4.63 – 4.31 (m, 4H), 4.19 – 3.36 (m, 13H), 3.30 – 3.04 (m, 2H), 2.40 – 1.85 (m, 3H), 1.67 – 1.31 (m, 3H).

(-)-6-{[trans, trans-4-[3-fluoro-4-(2-methoxyethoxy)phenyl]-2-methyl-1-(2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one [(-)B1194] LCMS (MH+ = 533.2); ^{1}H NMR (400 MHz, MeOD) δ 7.41 – 7.15 (m, 6H), 7.06 (d, *J* = 7.9, 2H), 7.03 – 6.79 (m, 3H), 4.28 (s, 2H), 4.02 (dd, *J* = 5.4, 3.7, 3H), 3.95 – 3.32 (m, 8H), 3.29 (s, 3H), 3.19 – 2.89 (m, 3H), 2.39 – 1.81 (m, 3H), 1.62 – 1.25 (m, 3H).

[(+/-)-6-{[(trans, trans)-4-(3-fluoro-5-methoxyphenyl)-2-methyl-1-[2-(1H-pyrrol-1-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one [(+/-)B1274] LCMS

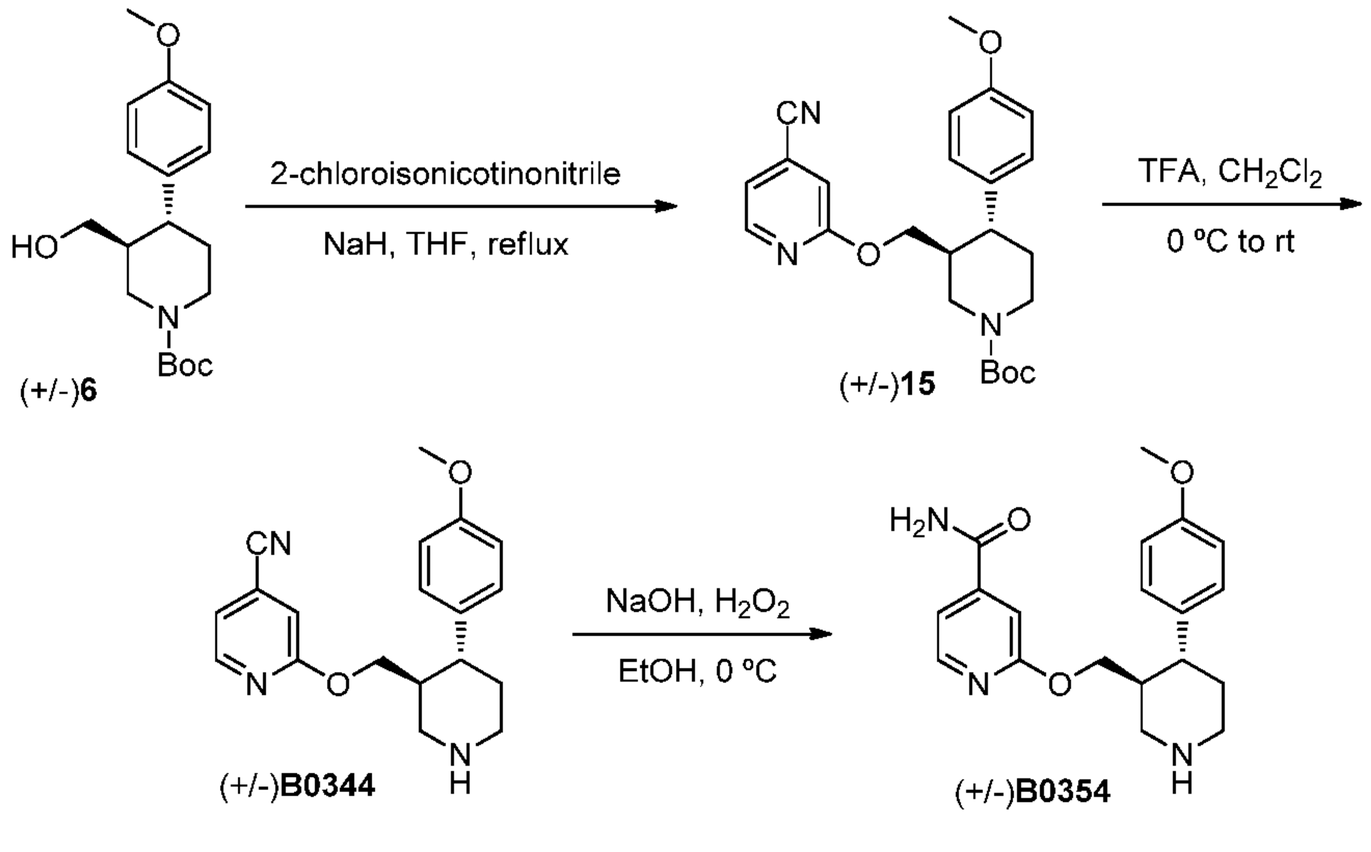
(MH+ = 478.3); ^{1}H NMR (300MHz ,CD_3OD): 7.48 (m, 1H), 7.18 (m, 2H), 6.91 (t, *J*=2.1Hz, 2H), 6.58 (m, 3H), 6.19 (t, *J*=2.1Hz, 2H), 4.49 (m, 2H), 4.39 (s, 2H), 4.10 (m, 1H), 3.90 (m, 1H), 3.65-3.80 (m, 2H), 3.61 (s, 3H), 3.55 (m, 1H), 3.40 (m, 1H), 3.20 (m, 2H), 2.00-2.40 (m, 3H), 1.20-1.28 (m, 3H).

(-)-6-{[trans, trans-1-(4,4-difluorobut-3-en-1-yl)-4-(4-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one [(-)B1145] LCMS (MH+ = 457.2); ^{1}H NMR (400 MHz, DMSO) δ 10.75 – 10.40 (m, 1H), 8.53 (s, 1H), 7.45 (d, *J* = 8.3, 1H), 7.27 – 7.06 (m, 3H), 7.04 – 7.00 (m, 1H), 6.91 – 6.80 (m, 2H), 4.68 (dt, *J* = 26.6, 7.6, 1H), 4.27 (s, 2H), 4.11 – 3.88 (m, 1H), 3.72 – 3.68 (m, 3H), 3.64 – 3.45 (m, 3H), 3.42 – 3.12 (m, 3H), 3.06 – 2.96 (m, 1H), 2.40 – 2.08 (m, 2H), 1.97 – 1.75 (m, 1H), 1.50 – 1.35 (m, 3H).

General Procedure A4: Preparation of 3,4-Piperidine N-H Analogs:

Reversed Coupling and Hydrolysis Example

Scheme 6



Preparation of (+/-)-2-{[*trans*-4-(4-methoxyphenyl)piperidin-3-yl]methoxy}-isonicotinamide [(+/-)B0354]

(+/-)-*trans*-*tert*-Butyl 3-{[(4-Cyanopyridin-2-yl)oxy]methyl}-4-(4-methoxyphenyl)piperidine-1-carboxylate [(+/-)15]

A solution of (+/-)-*trans*-*tert*-butyl 3-(hydroxymethyl)-4-(4-methoxyphenyl)piperidine-1-carboxylate [(+/-)**6**, 500 mg, 1.6 mmol, prepared as described in General Procedure A1, Scheme 1] in anhydrous tetrahydrofuran (2 mL) was added dropwise to a solution of sodium hydride (73 mg, 1.8 mmol, 60% dispersion in mineral oil) in anhydrous tetrahydrofuran (8 mL) at 0 °C under nitrogen, after which the mixture was stirred for 15 min. A solution of 2-chloroisonicotinonitrile (251 mg, 1.8 mmol) in anhydrous tetrahydrofuran (2 mL) was added, after which the mixture was heated to reflux and stirred for 3 h. The cooled mixture was treated with water (0.5 mL), diluted with ethyl acetate (60 mL), dried over sodium sulfate and filtered. The filtrate solvents were removed under reduced pressure and the residue was purified by flash column chromatography on silica gel, eluting with hexanes/ethyl acetate (1:1), to afford (+/-)**15** as a white solid (132 mg, 52%): LCMS (M+H) 424.

(+/-)-2-{[*trans*-4-(4-Methoxyphenyl)piperidin-3-yl]methoxy}-isonicotinonitrile [(+/-)B0344]

Prepared according General Procedure A2, to provide (+/-)**B0344** as an off-white solid (95 mg, 92%): LCMS (M+H) 324; ^{1}H NMR (500 MHz, CD_3OD) δ 8.23 (d, J = 5.0 Hz, 1H), 7.20 (dd, J = 5.0, 1.0 Hz, 1H), 7.16 (d, J = 9.0 Hz, 2H), 7.11 (d, J = 1.0 Hz, 1H), 6.88 (d, J = 9.0 Hz, 2H), 4.17 (dd, J = 11.0, 3.0 Hz, 1H), 3.99 (dd, J = 11.0, 7.0 Hz, 1H), 3.76 (s, 3H), 3.66 (dd, J = 12.5, 3.0 Hz, 1H), 3.54–3.48 (m, 1H), 3.17–3.07 (m, 2H), 2.84 (dt, J = 12.0, 4.5 Hz, 1H), 2.47–2.43 (m, 1H), 2.06–1.96 (m, 2H).

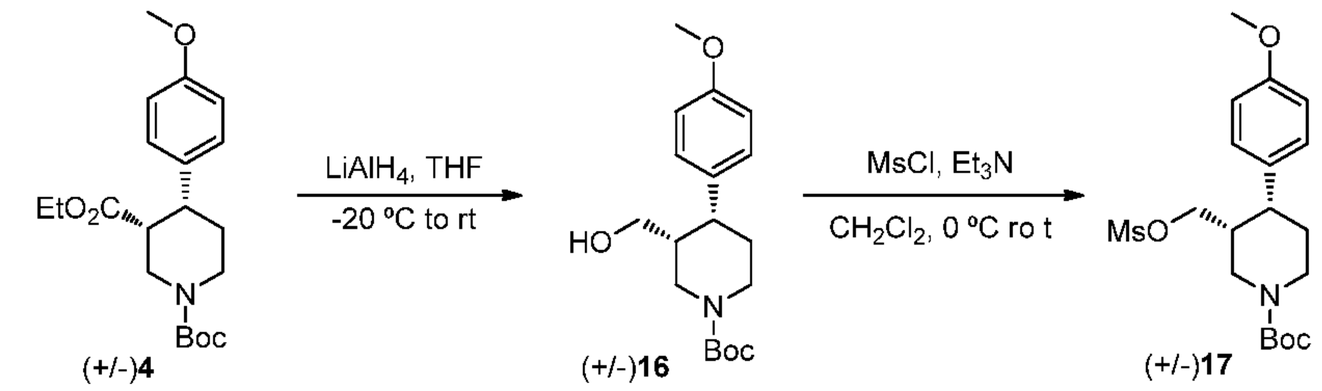
(+/-)-2-{[*trans*-4-(4-Methoxyphenyl)piperidin-3-yl]methoxy}-isonicotinamide [(+/-)B0354]

A solution of (+/-)-2-{[*trans*-4-(4-methoxyphenyl)piperidin-3-yl]methoxy}-isonicotinonitrile [(+/-)**B0344**, 100 mg, 0.31 mmol] in ethanol (1 mL) was added to a mixture of hydrogen peroxide (0.2 mL, 30% solution in water) and 2N sodium hydroxide solution (0.2 mL) at 0 °C, after which the mixture was stirred for 1 h. A solution of 1M potassium phosphate monobasic was added (1 mL), after which the solvents were removed under reduced pressure. The residue was purified by flash column chromatography on silica gel, eluting with methylene chloride/methanol/concentrated ammonium chloride (6:3:1), to afford (+/-)**B0354** as a white solid (31 mg, 29%). LCMS (M-H) 340; ^{1}H NMR (500 MHz, CD_3OD) δ 8.15 (d, J = 5.0 Hz, 1H), 7.29 (dd, J = 5.0, 1.0 Hz, 1H), 7.19 (d, J = 9.0 Hz, 2H), 7.14 (d, J = 1.0 Hz, 1H), 6.87 (d, J = 9.0 Hz, 2H), 4.08 (dd, J = 11.0, 3.0 Hz, 1H), 3.90 (dd, J = 11.0, 2.5

Hz, 1H), 3.78 (s, 3H), 3.41 (dd, *J* = 12.5, 3.5 Hz, 1H), 3.18 (m, 1H), 2.81–2.62 (m, 3H), 2.25–2.21 (m, 1H), 1.83–1.78 (m, 2H).

General Procedure A5: Preparation of *syn*-3,4-Piperidine Analogs

Scheme 7



Preparation of (+/-)-3-{[*cis*-4-(4-Methoxyphenyl)piperidin-3-yl]methoxy}-benzonitrile [(+/-)B0550]

(+/-)-*cis*-*tert*-Butyl 3-(Hydroxymethyl)-4-(4-methoxyphenyl)-piperidine-1-carboxylate [(+/-)16]

Prepared according General Procedure A1 to provide (+/-)**16** as a light yellow oil (3.56 g, 80%): LCMS (M+H) 322.

(+/-)-*cis*-*tert*-Butyl 4-(4-Methoxyphenyl)-3-{[(methylsulfonyl)oxy]-methyl}piperidine-1-carboxylate [(+/-)17]

Prepared according General Procedure A1 to provide (+/-)**17** as a yellow oil (1.2 g, 99%).

(+/-)-*cis*-*tert*-Butyl 3-[(3-Cyanophenoxy)methyl]-4-(4-methoxyphenyl)piperidine-1-carboxylate [(+/-)18]

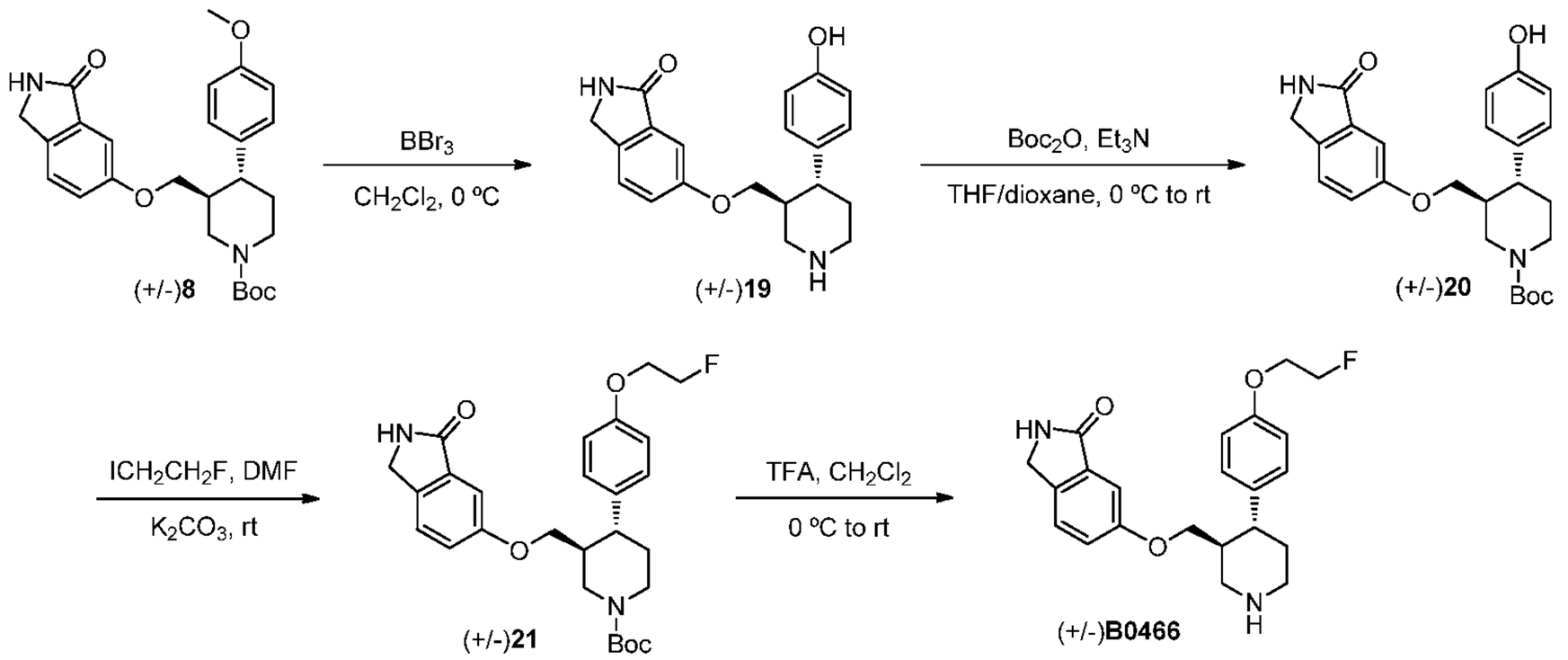
A solution of 3-hydroxybenzonitrile (268 mg, 2.2 mmol) in anhydrous *N,N*-dimethylformamide (4 mL) was added dropwise to a solution of sodium hydride (90 mg, 2.2 mmol, 60% dispersion in mineral oil) in anhydrous *N,N*-dimethylformamide (4 mL) at 0 ºC

under nitrogen, after which the mixture was stirred for 15 min. A solution of (+/-)-*cis*-*tert*-butyl 4-(4-methoxyphenyl)-3-{[(methylsulfonyl)oxy]-methyl}piperidine-1-carboxylate [(+/-)**17**, 300 mg, 0.75 mmol] in anhydrous *N,N*-dimethylformamide (4 mL) was added, after which the mixture was heated to 80 °C and stirred for 3 h. The cooled mixture was treated with water (0.5 mL), diluted with ethyl acetate (60 mL), dried over sodium sulfate and filtered. The filtrate solvents were removed under reduced pressure and the residue was purified by flash column chromatography on silica gel, eluting with methylene chloride/methanol (9:1), to afford (+/-)**18** as a light yellow oil (116 mg, 29%): LCMS (M+H) 423.

(+/-)-3-{[*cis*-4-(4-Methoxyphenyl)piperidin-3-yl]methoxy}-benzonitrile [(+/-)B0550]. Prepared according General Procedure A2 to provide (+/-)**B0550** as an off-white solid (40 mg, 87%): LCMS (M+H) 323; ^{1}H NMR (500 MHz, CD_3OD) δ 7.42–7.40 (m, 1H), 7.29 (d, *J* = 7.5 Hz, 1H), 7.21 (d, *J* = 8.5 Hz, 2H), 7.14–7.13 (m, 2H), 6.92 (d, *J* = 8.5 Hz, 2H), 4.06 (dd, *J* = 9.5, 3.0 Hz, 1H), 3.81–3.78 (m, 4H), 3.71–3.67 (m, 1H), 3.57–3.53 (m, 1H), 3.37–3.32 (m, 2H), 3.16 (dt, *J* = 13.0, 3.5 Hz, 1H), 2.58–2.54 (m, 1H), 2.35 (ddd, *J* = 27.0, 13.0, 4.0 Hz, 1H), 2.02–1.98 (m, 1H).

General Procedure A6: Preparation of O-Substituted 3,4-Piperidine N-H Analogs

Scheme 8



Preparation of (+/-)-6-{[*trans*-4-[4-(2-Fluoroethoxy)phenyl]piperidin-3-yl]methoxy}isoindolin-1-one [(+/-)B0466]

(+/-)-6-{[*trans*-4-(4-Hydroxyphenyl)piperidin-3-yl]methoxy}isoindolin-1-one [(+/-)19]

Boron tribromide (1.3 mL, 13.3 mmol) was added dropwise to a solution of (+/-)-*trans*-*tert*-butyl 4-(4-methoxyphenyl)-3-{[(3-oxoisoindolin-5-yl)oxy]methyl}-piperidine-1-carboxylate [(+/-)**8**, 2.0 g, 4.4 mmol] in anhydrous methylene chloride (80 mL) at 0 °C under nitrogen, after which the mixture was stirred for 2 h. The mixture was slowly diluted with 10% aqueous potassium carbonate solution (50 mL) and warmed to room temperature. The organic layer was collected and the solvent was removed under reduced pressure. The residue was purified by flash column chromatography on silica gel, eluting with methylene chloride/methanol (1:1), to afford (+/-)**19** as a white solid (748 mg, 50%): LCMS (M+H) 339; ^{1}H NMR (500 MHz, CD_3OD) δ 7.44 (d, J = 8.5 Hz, 1H), 7.14 (d, J = 2.5 Hz, 1H), 7.10 (dd, J = 8.5, 2.5 Hz, 1H), 7.07 (d, J = 8.5 Hz, 2H), 6.74 (d, J = 8.5 Hz, 2H), 4.36 (s, 2H), 3.82 (dd, J = 9.5, 3.0 Hz, 1H), 3.75–3.69 (m, 2H), 3.54–3.50 (m, 1H), 3.20–3.13 (m, 2H), 2.88 (dt, J = 11.5, 4.5 Hz, 1H), 2.41–2.37 (m, 1H), 2.07–1.99 (m, 2H).

(+/-)-*trans*-*tert*-Butyl 4-(4-Hydroxyphenyl)-3-{[(3-oxoisoindolin-5-yl)oxy]methyl}piperidine-1-carboxylate [(+/-)20]

Triethylamine (1.4 mL, 10.0 mmol) was added to a solution of 6-{[*trans*-4-(4-hydroxyphenyl)piperidin-3-yl]methoxy}isoindolin-1-one [(+/-)**19**, 672 mg, 2.0 mmol] in anhydrous THF (10 mL) and dioxane (10 mL) at room temperature under nitrogen, after which the mixture was cooled to 0 °C. Di-*tert*-butyl dicarbonate (434 mg, 2.0 mmol) was added, after which the mixture was stirred at 0 °C for 3 h. The mixture was warmed to room temperature, diluted with 10% aqueous citric acid solution (30 mL) and extracted with ethyl acetate (2 x 70 mL). The combined organic extracts were dried over sodium sulfate, filtered and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography on silica gel, eluting with methylene chloride/methanol (4:1), to afford (+/-)**20** as a white solid (643 mg, 74%): LCMS (M+H) 439.

(+/-)-*trans*-*tert*-Butyl 4-[4-(2-Fluoroethoxy)phenyl]-3-{[(3-oxoisoindolin-5-yl)oxy]methyl}piperidine-1-carboxylate [(+/-)21].

1-Fluoro-2-iodoethane (16 mg, 0.091 mmol) was added to a mixture of potassium carbonate (38 mg, 0.27 mmol) and (+/-)-*trans*-*tert*-butyl 4-(4-hydroxyphenyl)-3-{[(3-oxoisoindolin-5-yl)oxy]methyl}piperidine-1-carboxylate [(+/-)**20**, 40 mg, 0.091 mmol] in anhydrous *N,N*-

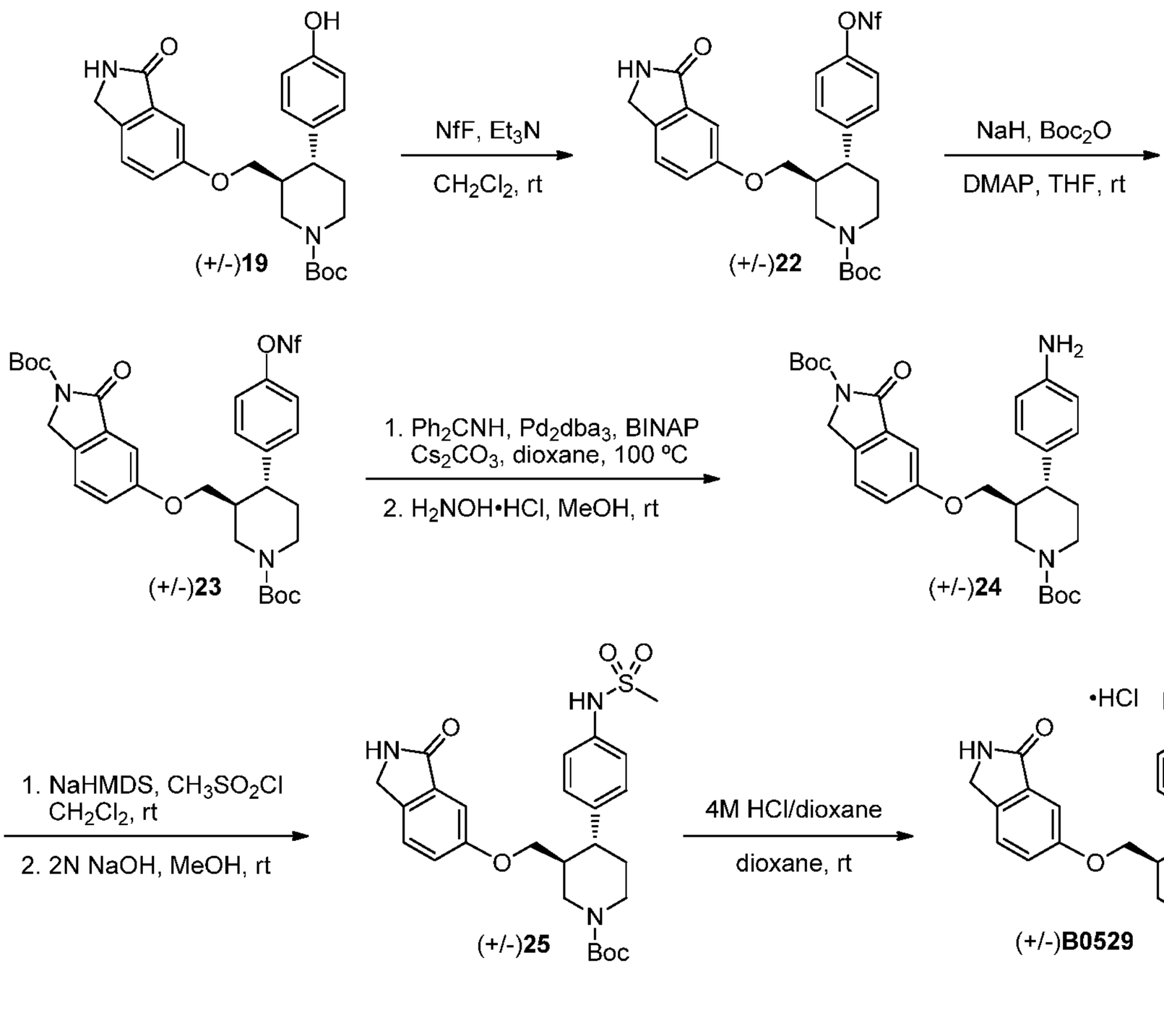
dimethylformamide (2 mL) at room temperature under nitrogen, after which the mixture was stirred for 24 h. The mixture was diluted with water (30 mL) and extracted with ethyl acetate (3 x 40 mL). The combined organic extracts were washed with 10% aqueous lithium chloride solution (30 mL), dried over sodium sulfate and filtered. The filtrate solvents were removed under reduced pressure and the residue was purified by flash column chromatography on silica gel, eluting with methylene chloride/methanol (4:1), to afford (+/-)**21** as a colorless semi-solid (36 mg, 87%): LCMS (M+H) 485.

(+/-)-6-{[*trans*-4-[4-(2-Fluoroethoxy)phenyl]piperidin-3-yl]methoxy}-isoindolin-1-one [(+/-)B0466]

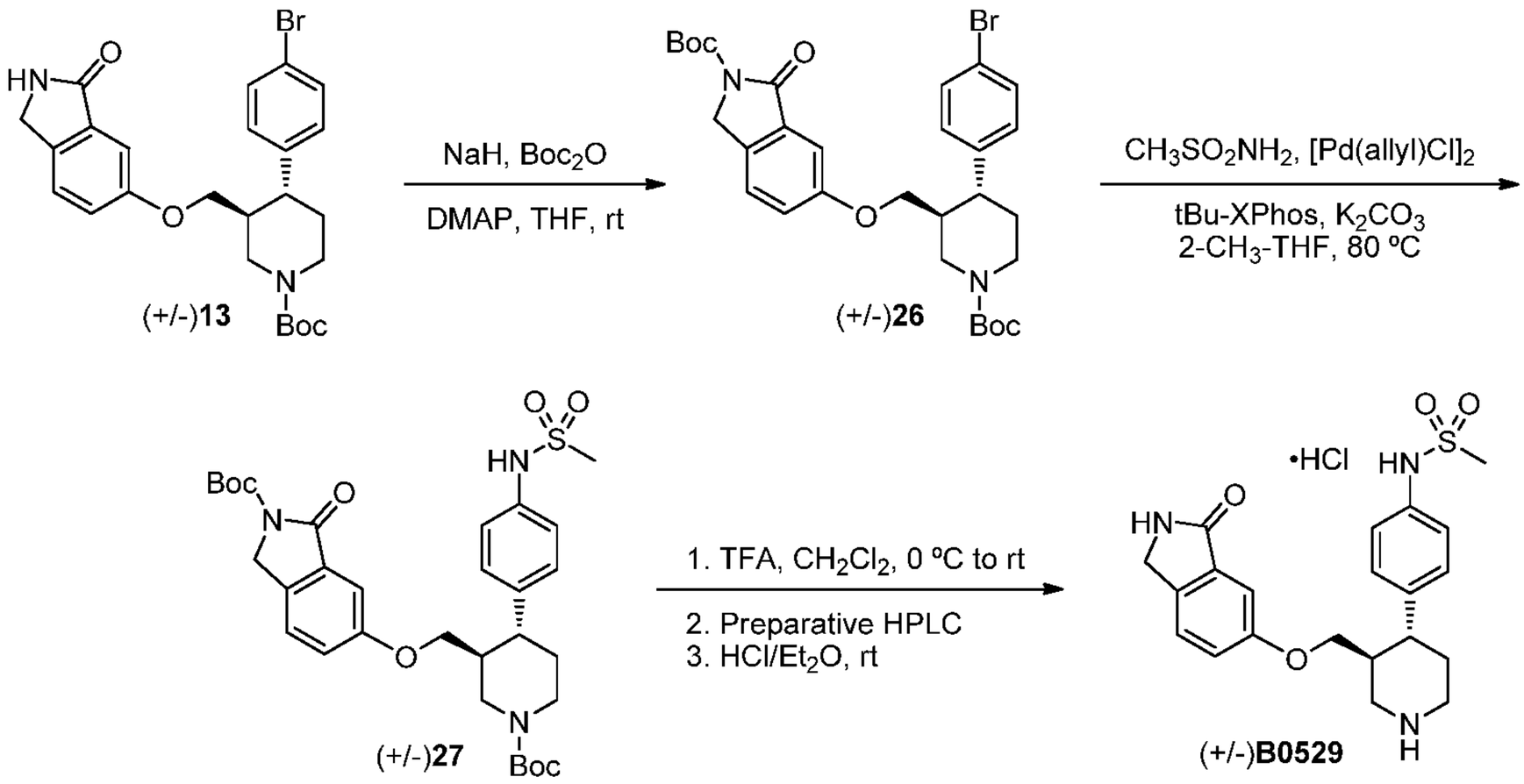
Prepared according General Procedure A2 to provide (+/-)**B0466** as a white solid (10 mg, 35%): LCMS (M+H) 385; ^{1}H NMR (500 MHz, CD_3OD) δ 7.34 (d, J = 8.5 Hz, 1H), 7.10 (d, J = 9.0 Hz, 2H), 7.03 (d, J = 2.0 Hz, 1H), 7.00 (dd, J = 8.5, 2.0 Hz, 1H), 6.83 (d, J = 9.0 Hz, 2H), 4.63 (t, J = 4.0 Hz, 1H), 4.54 (t, J = 4.0 Hz, 1H), 4.26 (s, 2H), 4.11 (t, J = 4.0 Hz, 1H), 4.05 (t, J = 4.0 Hz, 1H), 3.73 (dd, J = 9.5, 4.0 Hz, 1H), 3.65–3.59 (m, 2H), 3.45–4.41 (m, 1H), 3.10–3.05 (m, 2H), 2.83 (dt, J = 11.5, 4.0 Hz, 1H), 2.33–2.29 (m, 1H), 1.96–1.90 (m, 2H).

General Procedure A7: Preparation of N-Substituted 3,4-Piperidine N-H Analogs

Scheme 9



Scheme 10



Preparation of (+/-)-*N*-[4-(*trans*-3-{[(3-Oxoisoindolin-5-yl)oxy]methyl}piperidin-4-yl)phenyl]methanesulfonamide Hydrochloride [(+/-)B0529] (Scheme 9)

(+/-)-*trans-tert*-Butyl 3-{[(3-Oxoisoindolin-5-yl)oxy]methyl}-4-(4-{[(perfluorobutyl)sulfonyl]oxy}phenyl)piperidine-1-carboxylate [(+/-)22]

Perfluorobutanesulfonyl fluoride (nonafluorobutanesulfonyl fluoride, 0.42 mL, 2.4 mmol) was added to a solution of (+/-)-*trans-tert*-butyl 4-(4-hydroxyphenyl)-3-{[(3-oxoisoindolin-5-yl)oxy]methyl}piperidine-1-carboxylate [(+/-)**19**, 870 mg, 2.0 mmol] and triethylamine (0.33 mL, 2.4 mmol) in anhydrous methylene chloride (20 mL) at room temperature under nitrogen, after which the mixture was stirred for 24 h. The mixture was washed with 2N NaOH (30 mL) and water (20 mL) and dried over sodium sulfate and filtered. The solvents were removed under reduced pressure and the residue was purified by flash column chromatography on silica gel, eluting with hexanes/ethyl acetate (gradient from 1:1 to 0:100), to afford (+/-)**22** as a white solid (1.24 g, 87%): LCMS (M+H) 721.

(+/-)-*tert*-Butyl 6-{[*trans*-1-(*tert*-Butoxycarbonyl)-4-(4-{[(perfluorobutyl)sulfonyl]oxy}phenyl)piperidin-3-yl]methoxy}-1-oxoisoindoline-2-carboxylate [(+/-)23]

A solution of (+/-)-*trans-tert*-butyl 3-{[(3-oxoisoindolin-5-yl)oxy]methyl}-4-(4-{[(perfluorobutyl)sulfonyl]-oxy}phenyl)piperidine-1-carboxylate [(+/-)**22**, 1.24 g, 1.72 mmol] in anhydrous THF (10 mL) was added to a suspension of sodium hydride (83 mg, 2.1 mmol, 60% dispersion in mineral oil) in anhydrous THF (30 mL) at room temperature under nitrogen, after which the mixture was stirred for 5 min. Di-*tert*-butyl dicarbonate (752 mg, 3.4 mmol) was added followed by 4-dimethylaminopyridine (201 mg, 1.7 mmol), after which the mixture was stirred for 12 h. Water (0.5 mL) was added and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography on silica gel, eluting with hexanes/ethyl acetate (gradient from 1:1 to 0:100), to afford (+/-)**23** as a light yellow solid (1.28 g, 91%): LCMS (M+H) 821.

(+/-)-*trans-tert*-Butyl 6-{[4-(4-Aminophenyl)-1-(*tert*-butoxycarbonyl)piperidin-3-yl]methoxy}-1-oxoisoindoline-2-carboxylate [(+/-)24]

A mixture of (+/-)-*tert*-butyl 6-{[*trans*-1-(*tert*-butoxycarbonyl)-4-(4-{[(perfluorobutyl)sulfonyl]oxy}phenyl)piperidin-3-yl]methoxy}-1-oxoisoindoline-2-carboxylate [(+/-)**23**, 400 mg, 0.49 mmol], benzophenone imine (132 mg, 0.75 mmol), tris(dibenzylideneacetone)dipalladium(0) (45 mg, 10 mol%), 2,2'-bis(diphenylphosphino)-1,1'-binaphthyl (BINAP, 60 mg, 20 mol%) and cesium carbonate (318 mg, 2.0 mmol) in

anhydrous dioxane (20 mL) was heated at 100 °C under nitrogen for 3 h. The cooled mixture was diluted with ethyl acetate (120 mL), dried over sodium sulfate and filtered. The solvents were removed under reduced pressure and the residue was dissolved in methanol (5 mL) and stirred at room temperature under nitrogen. Hydroxylamine hydrochloride (170 mg, 2.4 mmol) was added and the mixture was stirred for 3 h. The solvent was removed under reduced pressure and the residue was purified by flash column chromatography on silica gel, eluting with hexanes/ethyl acetate (gradient from 1:1 to 0:100), to afford (+/-)**24** as a yellow oil (121 mg, 41% over two steps): LCMS (M+H) 538.

(+/-)-*trans-tert*-Butyl 4-[4-(Methylsulfonamido)phenyl]-3-{[(3-oxoisoindolin-5-yl)oxy]methyl}piperidine-1-carboxylate [(+/-)25]

Sodium bis(trimethylsilyl)amide (0.45 mL, 0.45 mmol, 1.0 M in THF) was added to a solution of (+/-)-*trans-tert*-butyl 6-{[4-(4-aminophenyl)-1-(*tert*-butoxycarbonyl)piperidin-3-yl]methoxy}-1-oxoisoindoline-2-carboxylate [(+/-)**24**, 120 mg, 0.23 mmol] in anhydrous methylene chloride (5 mL) and the mixture was stirred for 15 min. Methanesulfonyl chloride (93 mg, 0.81 mmol) was added after which the mixture was stirred for an additional 3 h. The mixture was treated with water (0.5 mL), diluted with methylene chloride (50 mL), dried over sodium sulfate and filtered. The solvents were removed under reduced pressure and the residue was dissolved in methanol (5 mL) at room temperature. 2N NaOH solution (2 mL) was added and the mixture was stirred for 2 h. The solvents were removed under reduced pressure and the residue was diluted with methylene chloride (50 mL), washed with 10% citric acid solution (20 mL), dried over sodium sulfate and filtered. The solvent was removed under reduced pressure and the residue was purified by flash column chromatography on neutral alumina, eluting with methylene chloride/methanol (gradient from 19:1 to 4:1), to afford (+/-)**25** as a yellow solid (59 mg, 51% over two steps): LCMS (M+H) 516.

(+/-)-*N*-[4-(*trans*-3-{[(3-Oxoisoindolin-5-yl)oxy]methyl}piperidin-4-yl)phenyl]methanesulfonamide Hydrochloride [(+/-)B0529]

Hydrochloric acid (0.30 mL, 4M in dioxane) was added to a solution of (+/-)-*trans-tert*-butyl 4-[4-(methylsulfonamido)phenyl]-3-{[(3-oxoisoindolin-5-yl)oxy]methyl}-piperidine-1-carboxylate [(+/-)**25**, 39 mg, 0.076 mmol] in in anhydrous dioxane (2 mL) at room temperature under nitrogen, after which the mixture was stirred for 2 h. The solvents were removed under reduced pressure and the residue was dissolved in methanol for purification

by reversed-phase preparative HPLC, eluting with 0.05% TFA in acetonitrile/water (gradient from 2% to 60%, Phenomenex Luna column). The isolated residue was acidified with HCl (2 mL, 2M in diethyl ether), diluted with acetonitrile/water and lyophilized to afford (+/-)**B0529** as a yellow solid (28 mg, 82%): LCMS (M+H) 416; ^{1}H NMR (500 MHz, CD_3OD) δ 7.43 (d, *J* = 8.5 Hz, 1H), 7.27–7.21 (m, 4H), 7.12–7.01 (m, 2H), 4.36 (s, 2H), 3.84 (dd, *J* = 9.5, 3.0 Hz, 1H), 3.76–3.65 (m, 3H), 3.60–3.53 (m, 2H), 3.22–3.18 (m, 1H), 2.99 (dt, *J* = 11.5, 4.0 Hz, 1H), 2.93 (s, 3H), 2.47–2.43 (m, 1H), 2.11–2.03 (m, 2H).

Alternative Preparation of (+/-)-*N*-[4-(*trans*-3-{[(3-Oxoisoindolin-5-yl)oxy]methyl}piperidin-4-yl)phenyl]methanesulfonamide Hydrochloride [(+/-)B0529] (Scheme 10)

(+/-)-*tert*-Butyl 6-{[*trans*-4-(4-Bromophenyl)-1-(*tert*-butoxycarbonyl)-piperidin-3-yl]methoxy}-1-oxoisoindoline-2-carboxylate [(+/-)26]

Prepared according General Procedure A7, Scheme 9 to provide (+/-)**26** as a white solid (645 mg, 53%): LCMS (M+H) 601.

(+/-)-*tert*-Butyl 6-{[*trans*-1-(*tert*-Butoxycarbonyl)-4-(4-[methylsulfonamido]phenyl)piperidin-3-yl]methoxy}-1-oxoisoindoline-2-carboxylate [(+/-)27]

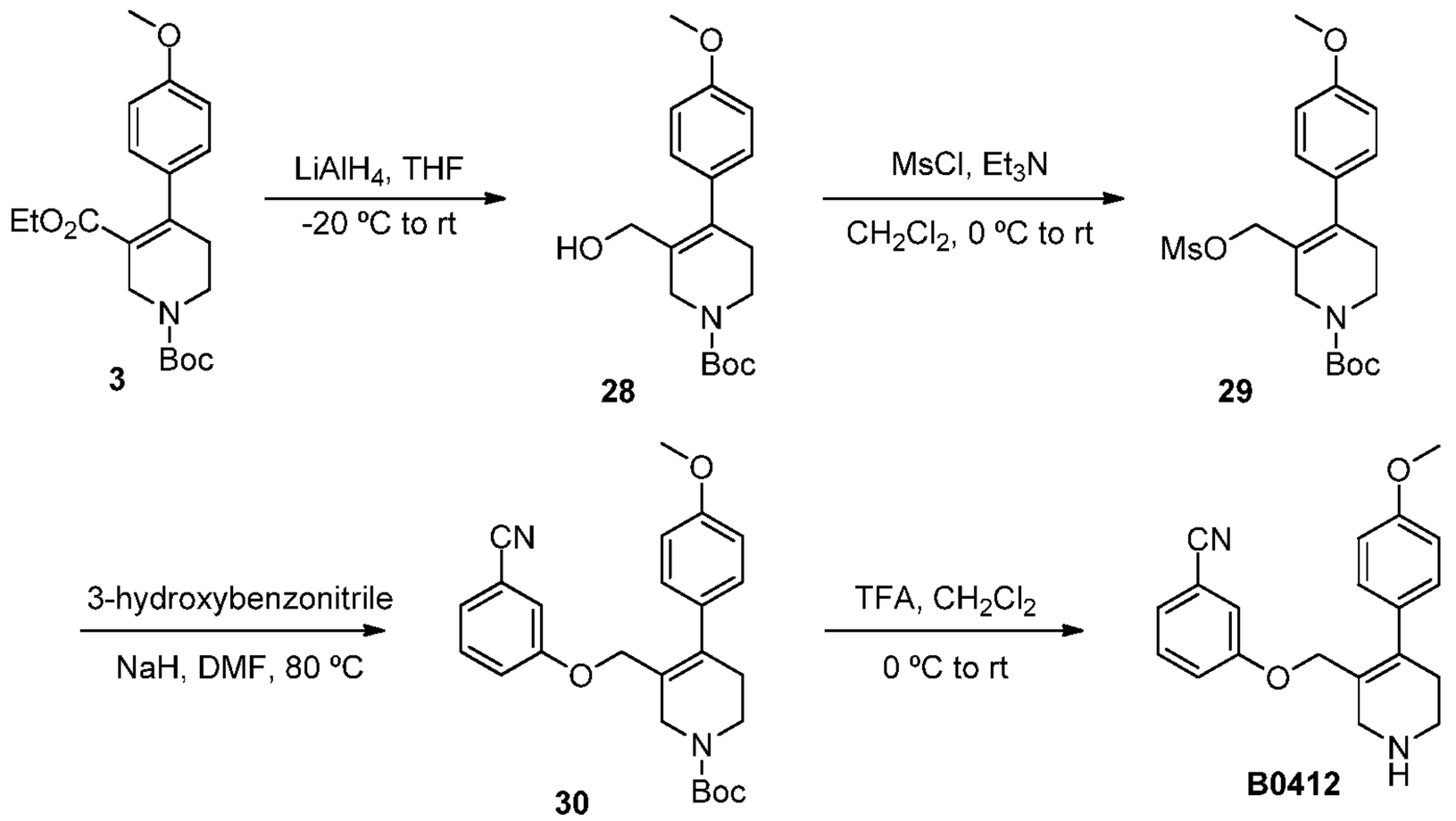
A mixture of (+/-)-*tert*-butyl 6-{[*trans*-4-(4-bromophenyl)-1-(*tert*-butoxycarbonyl)-piperidin-3-yl]methoxy}-1-oxoisoindoline-2-carboxylate [(+/-)**26**, 150 mg, 0.25 mmol], methanesulfonamide (29 mg, 0.30 mmol), allylpalladium(II) chloride dimer (2.3 mg, 5 mol%), 2-di-*tert*-butylphosphino-2′,4′,6′-triisopropylbiphenyl (tBu-XPhos, 21 mg, 20 mol%) and potassium carbonate (69 mg, 0.50 mmol) in anhydrous 2-methyltetrahydrofuran (5 mL) was heated at 80 °C under nitrogen for 12 h. The cooled mixture was diluted with ethyl acetate (120 mL), dried over sodium sulfate and filtered. The solvent was removed under reduced pressure and the residue was purified by flash column chromatography on silica gel, eluting with hexanes/ethyl acetate (gradient from 1:1 to 0:100), to afford (+/-)**27** as a yellow oil (91 mg, 59%): LCMS (M+H) 616.

(+/-)-*N*-[4-(*trans*-3-{[(3-Oxoisoindolin-5-yl)oxy]methyl}piperidin-4-yl)phenyl]methanesulfonamide Hydrochloride [(+/-)B0529]

Prepared according General Procedure A1 to afford (+/-)**B0529** as a yellow solid (54 mg, 61%): LCMS (M+H) 416; ^{1}H NMR (500 MHz, CD_3OD) δ 7.43 (d, *J* = 8.5 Hz, 1H), 7.27–7.21 (m, 4H), 7.12–7.01 (m, 2H), 4.36 (s, 2H), 3.84 (dd, *J* = 9.5, 3.0 Hz, 1H), 3.76–3.65 (m, 3H), 3.60–3.53 (m, 2H), 3.22–3.18 (m, 1H), 2.99 (dt, *J* = 11.5, 4.0 Hz, 1H), 2.93 (s, 3H), 2.47–2.43 (m, 1H), 2.11–2.03 (m, 2H).

General Procedure A8: Preparation of 3,4-Tetrahydropyridine N-H Analogs

Scheme 11



Preparation of 3-{[4-(4-Methoxyphenyl)-1,2,5,6-tetrahydropyridin-3-yl]methoxy}benzonitrile [B0412]

***tert*-Butyl 3-(Hydroxymethyl)-4-(4-methoxyphenyl)-5,6-dihydropyridine-1(2*H*)-carboxylate [28]**

Prepared according General Procedure A1 to afford **28** as a colorless oil (1.9 g, 71%): LCMS (M+H) 320.

***tert*-Butyl 4-(4-Methoxyphenyl)-3-{[(methylsulfonyl)oxy]methyl}-5,6-dihydropyridine-1(2*H*)-carboxylate [29]**

Prepared according General Procedure A1 to afford **29** as a light yellow oil that was suitable for use without further purification (2.4 g, 99%): LCMS (M+H) 398.

***tert*-Butyl 3-[(3-Cyanophenoxy)methyl]-4-(4-methoxyphenyl)-5,6-dihydropyridine-1(2*H*)-carboxylate [30]**

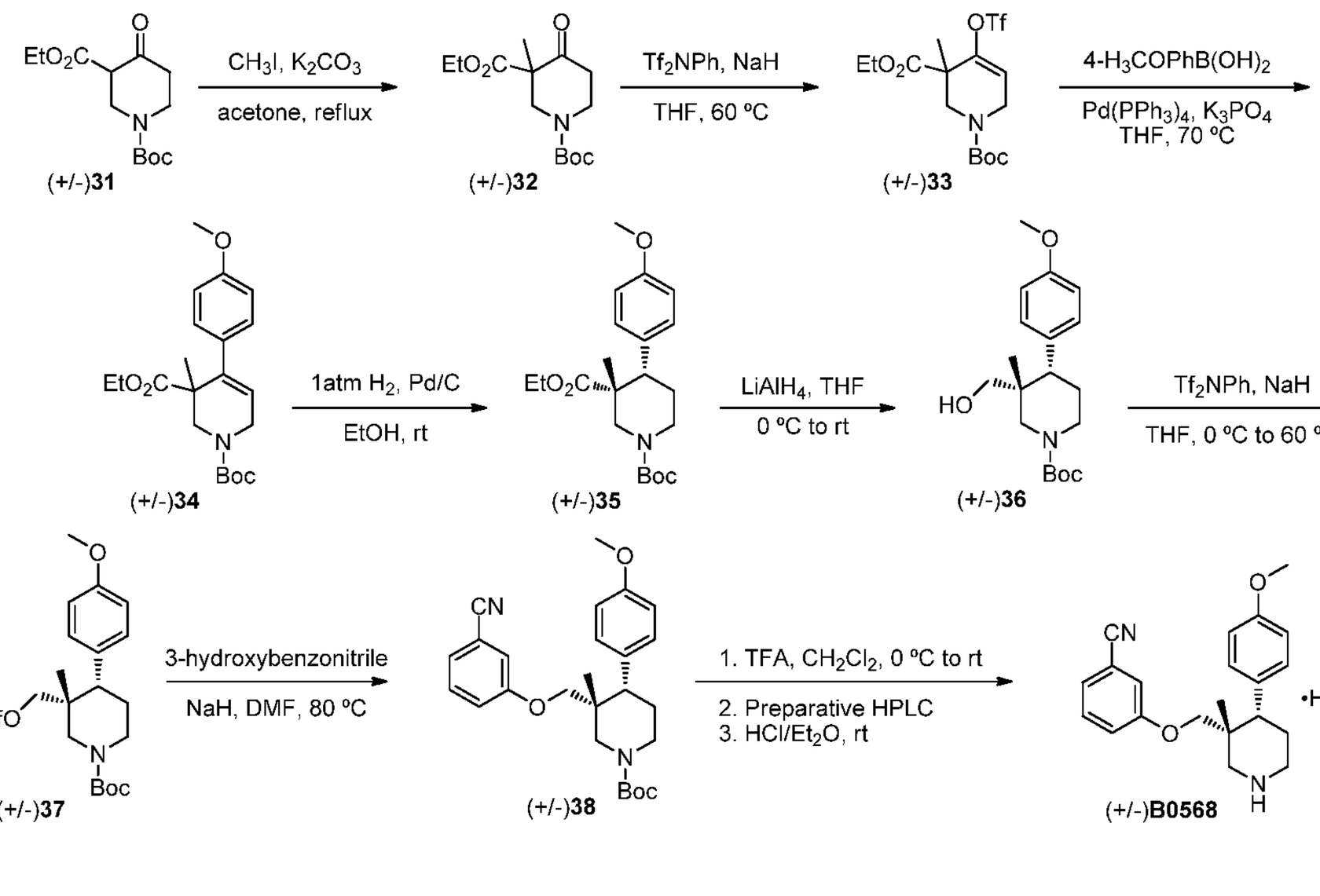
Prepared according General Procedure A5 afford **30** as a yellow oil (506 mg, 97%): LCMS (M+H) 421.

3-{[4-(4-Methoxyphenyl)-1,2,5,6-tetrahydropyridin-3-yl]methoxy}-benzonitrile [B0412]

Prepared according General Procedure A2 to afford **B0412** as a white solid (51 mg, 61%): LCMS (M+H) 321; ^{1}H NMR (500 MHz, CD_3OD) δ 7.41 (t, J = 7.5 Hz, 1H), 7.28 (d, J = 7.5 Hz, 1H), 7.20 (d, J = 8.5 Hz, 2H), 7.12 (dd, J = 7.5, 2.5 Hz, 1H), 7.09–7.05 (m, 1H), 6.95 (d, J = 8.5 Hz, 2H), 4.54 (s, 2H), 3.84 (s, 2H), 3.80 (s, 3H), 3.36 (t, J = 6.0 Hz, 2H), 2.68 (t, J = 6.0 Hz, 2H).

General Procedure A9: Preparation of 3-Methyl-3,4-Piperidine N-H Analogs

Scheme 12



Preparation of 3-{[(+/-)-*cis*-4-(4-Methoxyphenyl)-3-methylpiperidin-3-yl]methoxy}benzonitrile Hydrochloride [(+/-)B0568].

(+/-)-1-*tert*-Butyl 3-Ethyl 3-Methyl-4-oxopiperidine-1,3-dicarboxylate [(+/-)32]

A mixture of iodomethane (4.6 mL, 73.7 mmol), potassium carbonate (10.2 g, 73.7 mmol) and commercially available (+/-)-1-*tert*-butyl 3-ethyl 4-oxopiperidine-1,3-dicarboxylate [(+/-)**31**, 10.0 g, 36.9 mmol] in anhydrous acetone (150 mL) was heated at reflux under nitrogen for 12 h. The cooled mixture was filtered and the filtrate solvent was removed under reduced pressure to provide (+/-)**32** as a light yellow oil (8.6 g, 82%): LCMS (M+H) 286.

(+/-)-1-*tert*-Butyl 3-Ethyl 3-Methyl-4-{[(trifluoromethyl)sulfonyl]oxy}-2,3-dihydropyridine-1,3(6*H*)-dicarboxylate [(+/-)33]

Sodium hydride (2.3 g, 60.3 mmol, 60% in mineral oil) was added portionwise to a solution of (+/-)-1-*tert*-butyl 3-ethyl 3-methyl-4-oxopiperidine-1,3-dicarboxylate [(+/-)**32**, 8.6 g, 30.1 mmol] in anhydrous THF (100 mL) at 0 °C under nitrogen. The mixture was stirred at 0 °C for 5 min, after which *N*-phenylbis(trifluoromethanesulfonamide) (16.2 g, 45.2 mmol) was added portionwise. The mixture was warmed to room temperature and then further heated to 60 °C and stirred for 1 h. The cooled mixture was treated with saturated aqueous sodium chloride solution (150 mL) and extracted with ethyl acetate (3 x 100 mL). The combined organic extracts were dried over sodium sulfate and filtered, and the solvents were removed under reduced pressure to provide (+/-)**33** as a dark amber oil (7.2 g, 57%): LCMS (M+H) 418.

(+/-)-1-*tert*-Butyl 3-Ethyl 4-(4-Methoxyphenyl)-3-methyl-2,3-dihydropyridine-1,3(6*H*)-dicarboxylate [(+/-)34]

Prepared according General Procedure A1 to provide (+/-)**34** as a dark amber solid (5.8 g, 89%): LCMS (M+H) 376.

(+/-)-1-*tert*-Butyl 3-Ethyl *cis*-4-(4-Methoxyphenyl)-3-methylpiperidine-1,3-dicarboxylate [(+/-)35]

Prepared according General Procedure A1 to provide (+/-)**35** as a crude amber oil (4.6 g) that was suitable for use in the next step without purification: LCMS (M+H) 377.

(+/-)-1-*tert*-Butyl *cis*-3-(Hydroxymethyl)-4-(4-methoxyphenyl)-3-methylpiperidine-1-carboxylate [(+/-)36]

Prepared according General Procedure A1 to provide (+/-)**36** as a light yellow oil (2.5 g, 62% over two steps): LCMS (M+H) 336.

(+/-)-1-*tert*-Butyl *cis*-4-(4-Methoxyphenyl)-3-methyl-3-({[(trifluoromethyl)sulfonyl]oxy}methyl)piperidine-1-carboxylate [(+/-)37]

Prepared according General Procedure A9 to provide (+/-)**37** as a dark amber solid (1.4 g, 43%): LCMS (M+H) 468.

(+/-)-*tert*-Butyl 3-[(3-Cyanophenoxy)methyl]-4-(4-methoxyphenyl)-3-methylpiperidine-1-carboxylate [(+/-)38]

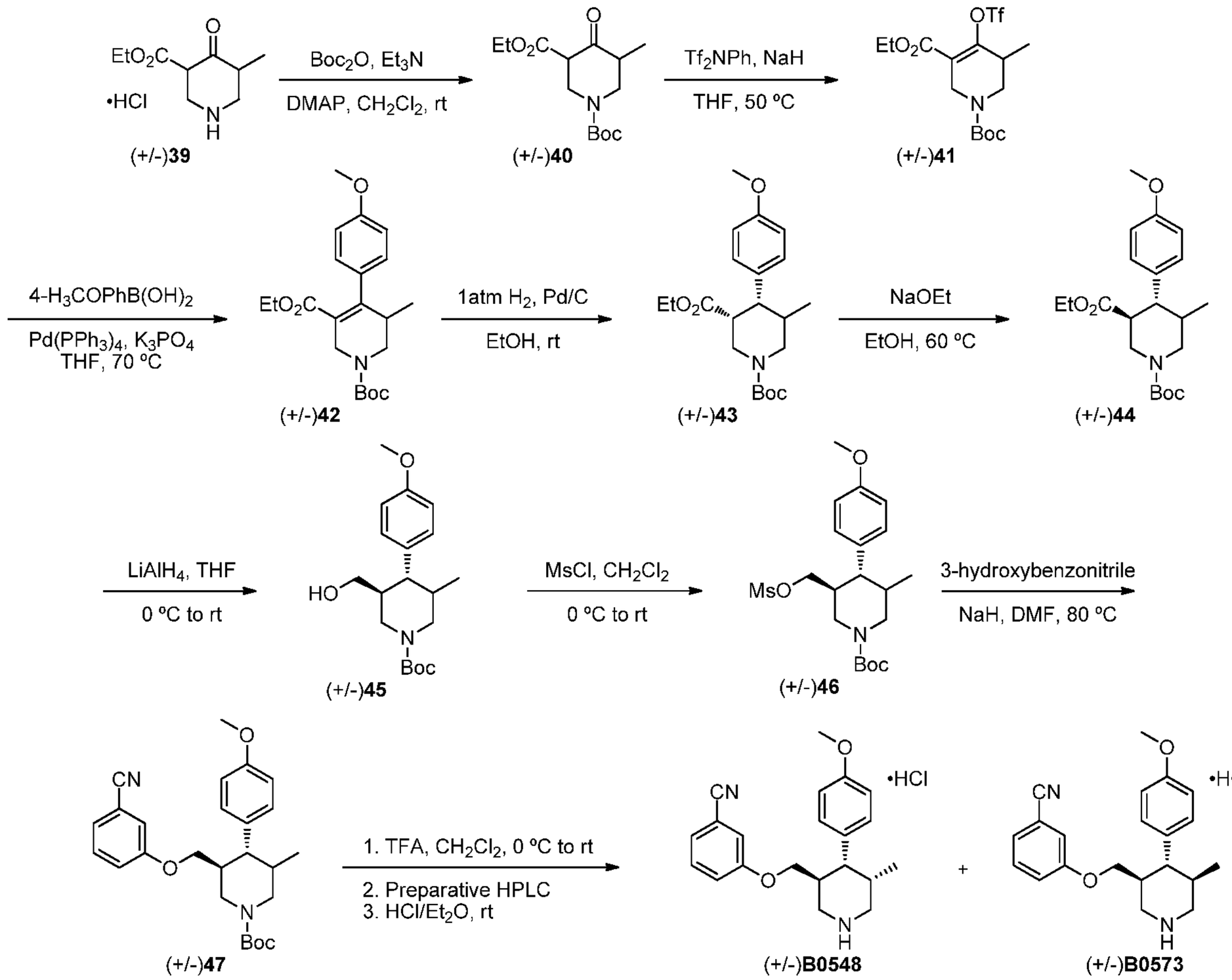
Prepared according General Procedure A5 to provide (+/-)**38** as a crude amber oil (120 mg) that was suitable for use in the next step without purification: LCMS (M+H) 437.

3-{[(+/-)-*cis*-4-(4-Methoxyphenyl)-3-methylpiperidin-3-yl]methoxy}benzonitrile Hydrochloride [(+/-)B0568]

Prepared according General Procedure A1 to provide (+/-)**B0568** as a white solid (84 mg, 40% over two steps): LCMS (M+H) 337; ^{1}H NMR (500 MHz, CD_3OD) δ 7.51–7.48 (m, 1H), 7.41–7.40 (m, 1H), 7.38–7.33 (m, 2H), 7.16 (d, *J* = 9.5 Hz, 2H), 6.88 (d, *J* = 9.5 Hz, 2H), 4.17 (d, *J* = 9.5 Hz, 1H), 3.79 (s, 3H), 3.74–3.70 (m, 2H), 3.62–3.59 (m, 1H), 2.34–3.16 (m, 1H), 3.07 (d, *J* = 13.0 Hz, 1H), 2.96 (dd, *J* = 13.5, 3.5 Hz, 1H), 1.94–1.90 (m, 1H), 1.00 (m, 3H).

General Procedure A10: Preparation of 5-Methyl-3,4-Piperidine N-H Analogs

Scheme 13



Preparation of 3-{[(+/-)-*trans,cis*-4-(4-Methoxyphenyl)-5-methylpiperidin-3-yl]methoxy}benzonitrile Hydrochloride [(+/-)B0548] and 3-{[(+/-)-*trans,trans*-4-(4-Methoxyphenyl)-5-methylpiperidin-3-yl]methoxy}benzonitrile Hydrochloride [(+/-)B0573].

(+/-)-1-*tert*-Butyl 3-Ethyl 5-Methyl-4-oxopiperidine-1,3-dicarboxylate [(+/-)40]

Triethylamine (2.2 mL, 13.8 mmol) was added to a solution of commercially available (+/-)-ethyl 5-methyl-4-oxopiperidine-3-carboxylate hydrochloride [(+/-)**39**, 2.5 g, 9.2 mmol] and 4-dimethylaminopyridine (DMAP, 20 mg) in anhydrous methylene chloride (10 mL) at room temperature under nitrogen, after which a solution of di-*tert*-butyl dicarbonate (3.0 g, 13.8 mmol) in anhydrous methylene chloride (10 mL) was slowly added. The mixture was stirred for 4 h, after which it was diluted with water (30 mL) and the organic layer was collected. The solvent was removed under reduced pressure and the residue was purified by flash

column chromatography on silica gel, eluting with hexanes/ethyl acetate (2:3), to (+/-)**40** as a white solid (3.0 g, 87%): LCMS (M+H) 286.

(+/-)-1-*tert*-Butyl 3-Ethyl 5-Methyl-4-{[(trifluoromethyl)sulfonyl]oxy}-5,6-dihydropyridine-1,3(2*H*)-dicarboxylate [(+/-)41]

Prepared according General Procedure A9 to provide (+/-)**41** as a dark amber oil (3.8 g, 86%): LCMS (M+H) 418.

(+/-)-1-*tert*-Butyl 3-Ethyl 4-(4-Methoxyphenyl)-5-methyl-5,6-dihydropyridine-1,3(2*H*)-dicarboxylate [(+/-)42]

Prepared according General Procedure A1 to provide (+/-)**42** as a crude amber oil (2.9 g) that was used without further purification in the next step: LCMS (M+H) 376.

(+/-)-1-*tert*-Butyl 3-Ethyl *cis,cis/trans*-4-(4-Methoxyphenyl)-5-methylpiperidine-1,3-dicarboxylate [(+/-)43]

Prepared according General Procedure A1 to provide (+/-)**43** as an amber oil (1.6 g, 53% over two steps): LCMS (M+H) 378.

(+/-)-1-*tert*-Butyl 3-Ethyl *trans,cis/trans*-4-(4-Methoxyphenyl)-5-methylpiperidine-1,3-dicarboxylate [(+/-)44]

Prepared according General Procedure A1 to provide (+/-)**44** as a crude amber oil (1.6 g) that was used without further purification in the next step: LCMS (M+H) 378.

(+/-)-1-*tert*-Butyl *trans,cis/trans*-3-(Hydroxymethyl)-4-(4-methoxyphenyl)-5-methylpiperidine-1-carboxylate [(+/-)45]

Prepared according General Procedure A1 to provide (+/-)**45** as a crude amber oil (900 mg) that was used without further purification in the next step: LCMS (M+H) 336.

(+/-)-1-*tert*-Butyl *trans,cis/trans*-4-(4-Methoxyphenyl)-3-methyl-5-{[(methylsulfonyl)oxy]methyl}piperidine-1-carboxylate [(+/-)46]

Prepared according General Procedure A1 to provide (+/-)**46** as a light yellow oil (600 mg, 56% over three steps): LCMS (M+H) 414.

(+/-)-*tert*-Butyl *trans,cis/trans*-3-[(3-Cyanophenoxy)methyl]-4-(4-methoxyphenyl)-5-methylpiperidine-1-carboxylate [(+/-)47]

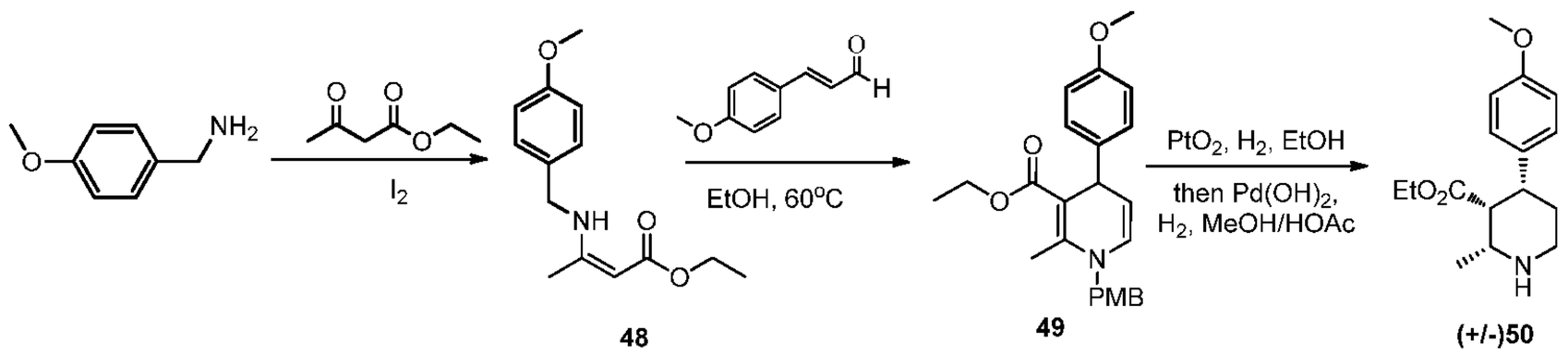
Prepared according General Procedure A5 to provide (+/-)**47** as a crude amber oil (155 mg) that was suitable for use in the next step without purification: LCMS (M+H) 437.

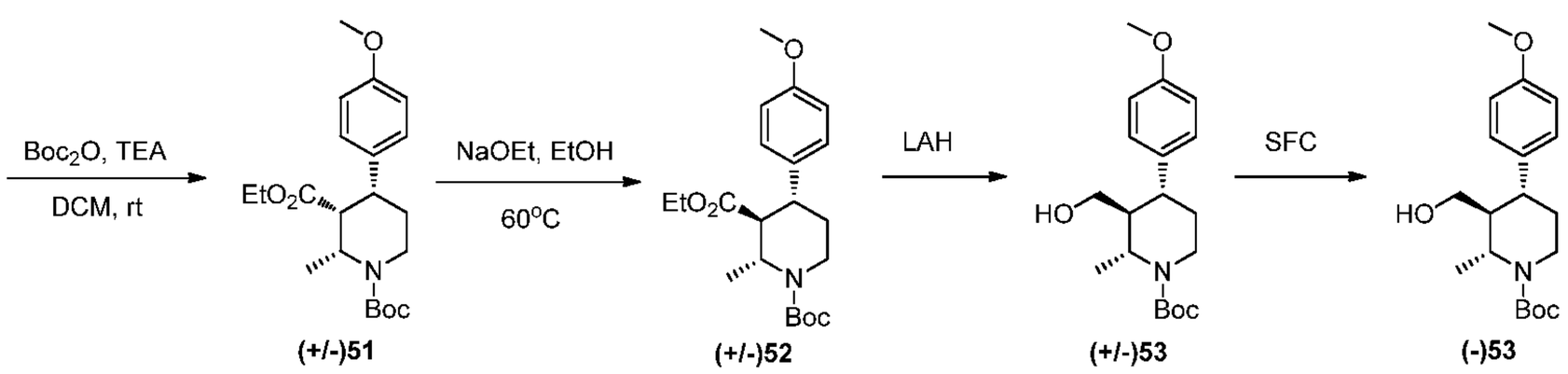
3-{[(+/-)-*trans,cis*-4-(4-Methoxyphenyl)-5-methylpiperidin-3-yl]methoxy}benzonitrile Hydrochloride [(+/-)B0548] and 3-{[(+/-)-*trans,trans*-4-(4-Methoxyphenyl)-5-methylpiperidin-3-yl]methoxy}benzonitrile Hydrochloride [(+/-)B0573].

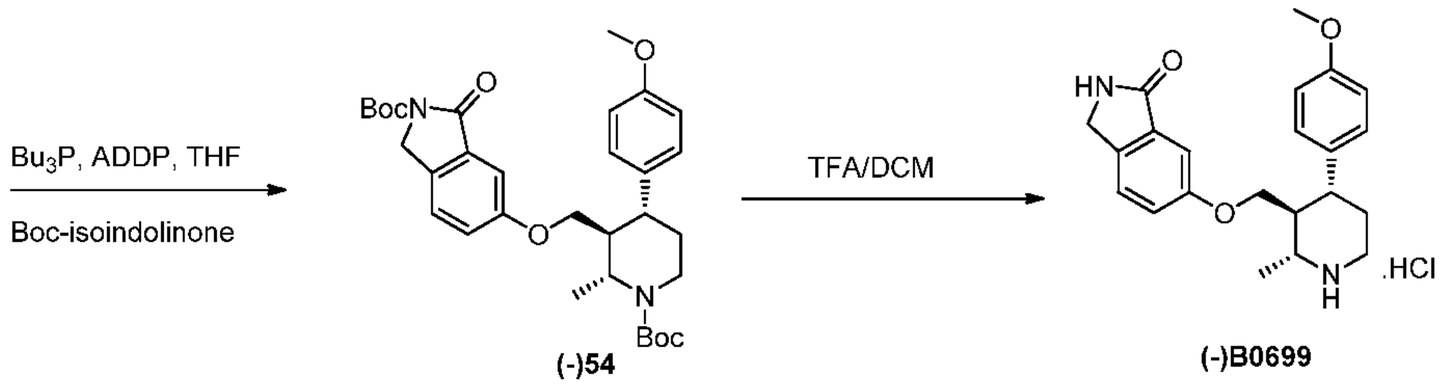
Prepared according General Procedure A1 (+/-)**B0548** was isolated as a white solid (15 mg, 16% over two steps): LCMS (M+H) 337; ^{1}H NMR (500 MHz, CD_3OD) δ 7.40–7.37 (m, 1H), 7.27–7.25 (m, 1H), 7.18–7.14 (m, 2H), 7.11–7.09 (m, 2H), 6.91 (d, *J* = 10.5 Hz, 2H), 3.96 (dd, *J* = 10.0, 3.0 Hz, 1H), 3.84–3.79 (m, 1H), 3.77 (s, 3H), 3.67 (dd, *J* = 12.5, 4.0 Hz, 1H), 3.38 (d, *J* = 2.9 Hz, 2H), 3.19–3.12 (m, 2H), 2.91–2.84 (m, 1H), 2.27–2.22 (m, 1H), 0.99 (d, *J* = 7.5 Hz, 3H). Also, (+/-)**B0573** was isolated as a white solid (17 mg, 18% over two steps): LCMS (M+H) 337; ^{1}H NMR (500 MHz, CD_3OD) δ 7.40 (t, *J* = 8.0 Hz, 1H), 7.27 (d, *J* = 8.0 Hz, 1H), 7.16–7.08 (m, 4H), 6.92–6.90 (m, 1H), 3.77–3.73 (m, 4H), 3.67–3.62 (m, 2H), 3.49–3.44 (m, 1H), 3.38–3.33 (m, 1H), 3.18–3.12 (m, 1H), 2.85 (t, *J* = 12.5 Hz, 1H), 2.51 (t, *J* = 11.5 Hz, 1H), 2.48–2.34 (m, 1H), 2.10–2.07 (m, 1H), 0.76 (d, *J* = 6.5 Hz, 3H).

General Procedure A11: Preparation of 2-Substituted-3,4-Piperidine N-H Analogs

Scheme 14a







Preparation of (-)-6-{[(trans,trans)-4-(4-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one [(-)B0699]

Ethyl (2Z)-3-[[(4-methoxyphenyl)methyl]amino]but-2-enoate (48)

Into a 100-mL round-bottom flask, was placed a mixture of ethyl 3-oxobutanoate (1 g, 7.68 mmol, 1.00 equiv), (4-methoxyphenyl)methanamine (1.05 g, 7.65 mmol, 1.00 equiv), iodine (195 mg, 0.77 mmol, 0.10 equiv). The resulting mixture was stirred for 1 h at room temperature. The mixture was diluted with 20 mL of DCM. The resulting solution was washed with 2x30 mL of H_2O. The organic solution was dried over sodium sulfate and concentrated under vacuum. This resulted in 2 g (crude) of **48** as a yellow oil.

Ethyl 4-(4-methoxyphenyl)-1-[(4-methoxyphenyl)methyl]-2-methyl-1,4-dihydropyridine-3-carboxylate (49)

Into a 100-mL round-bottom flask, was placed a solution of ethyl (2Z)-3-[(4-methoxyphenyl)amino]but-2-enoate (**48**, 1 g, 4.25 mmol, 1.00 equiv) and (3E)-4-(4-methoxyphenyl)but-3-en-2-one (1.54 g, 8.74 mmol, 2.06 equiv) in ethanol (20 mL). The resulting solution was stirred overnight at 60°C. The resulting solution was concentrated under vacuum. This resulted in 2.4 g (crude) of **49** as a yellow oil.

(+/-)-ethyl (cis, cis)-4-(4-methoxyphenyl)-2-methylpiperidine-3-carboxylate [(+/-)50]

Into a 2000-mL pressure tank reactor, was placed a solution of ethyl 4-(4-methoxyphenyl)-1-[(4-methoxyphenyl)methyl]-2-methyl-1,4-dihydropyridine-3-carboxylate (**49**, 77 g, 195.69 mmol, 1.00 equiv) and PtO_2 (7 g) in ethanol (1000 mL). The resulting solution was hydrogenated at 1.5 MPa and stirred overnight at room temperature. The solids were filtered out. The filtrate was concentrated under vacuum. The residue was dissolved in MeOH (700 mL), then $Pd(OH)_2$ (77 g) and AcOH (70 mL) was added to the solution. The resulting mixture was hydrogenated at 50 psi and stirred at rt for 3h. The solids were filtered out. The filtrate was concentrated under vacuum. This resulted in 60 g (77%) of **(+/-)50** as a light yellow oil.

(+/-)-3-Ethyl (cis,cis)-4-(4-methoxyphenyl)-2-methylpiperidine-1,3-dicarboxylate [(+/-)51]

Into a 100-mL round-bottom flask, was placed a solution of ethyl (2S,3S,4S)-4-(4-methoxyphenyl)-2-methylpiperidine-3-carboxylate [**(+/-)50**, 200 mg, 0.72 mmol, 1.00 equiv], Boc_2O (318.4 mg, 1.46 mmol, 2.02 equiv) and TEA (145.8 mg, 1.44 mmol, 2.00 equiv) in DCM (10 mL). The resulting solution was stirred for 2 h at room temperature. The resulting mixture was concentrated under vacuum. The residue was purified by Flash-Prep-HPLC with the following conditions (IntelFlash-1): Column, silica gel; mobile phase, EA:PE=05 increasing to EA:PE=60% within 30 min; Detector, UV 254 nm. 100 mg product was obtained. This resulted in 100 mg (37%) of **(+/-)51** as a yellow oil.

(+/-)-1-tert-butyl 3-ethyl (trans, trans)-4-(4-methoxyphenyl)-2-methylpiperidine-1,3-dicarboxylate [(+/-)52]

Into a 500-mL round-bottom flask, was placed a solution of (+/-)-1-tert-butyl 3-ethyl (cis, cis)-4-(4-methoxyphenyl)-2-methylpiperidine-1,3-dicarboxylate [**(+/-)51**, 10 g, 26.49 mmol, 1.00 equiv) and sodium ethoxide (3.6 g, 52.90 mmol, 2.00 equiv) in ethanol (200 mL). The

resulting solution was stirred for 2 h at 60°C. The resulting solution was extracted with 2x200 mL of DCM and the organic layers combined. The organic solution was washed with 2x200 mL of H_2O and concentrated under vacuum. This resulted in 10 g (100%) of **(+/-)52** as a yellow oil.

(+/-)-tert-butyl (trans, trans)-3-(hydroxymethyl)-4-(4-methoxyphenyl)-2-methylpiperidine-1-carboxylate [(+/-)53]

Into a 100-mL 3-necked round-bottom flask, was placed a mixture of (+/-)-1-tert-butyl 3-ethyl (trans, trans)-4-(4-methoxyphenyl)-2-methylpiperidine-1,3-dicarboxylate [**(+/-)52**, 5 g, 13.25 mmol, 1.00 equiv) and $LiAlH_4$ (680 mg, 17.89 mmol, 1.51 equiv) in THF (50 mL). The resulting mixture was stirred for 2 h at 0°C. The reaction was then quenched by the addition of 100 mL of water. The resulting solution was extracted with 2x100 mL of dichloromethane and the organic layers combined, then concentrated under vacuum. The residue was purified by Flash-Prep-HPLC with the following conditions (IntelFlash-1): Column, silica gel; mobile phase, EA:PE=0% increasing to EA:PE=100% within 50 min; Detector, UV 254 nm. 2.8675 g product was obtained. This resulted in 2.86 g (64%) of **(+/-)53** as a white solid. LC-MS (ES, *m/z*): 280[M-55]; ^{1}H-NMR (400MHz, CD_3OD,*ppm*): 7.17 (d, *J*=8.8Hz, 2H),7.85 (m, *J*=8.4Hz, 2H), 4.39 (t, *J*=4.4Hz, 1H), 4.14 (t, *J*=6.4Hz, 1H), 3.73(s, 3H), 3.62~3.57(m, 1H), 3.34~3.21(m, 2H), 3.07~3.01(m, 1H), 2.52~2.45(m, 1H), 1.89~1.74(m, 2H), 1.73~1.60(m, 1H), 1.55~1.53(m, 9H), 1.15(d, *J*=6.4Hz, 3H)

(-)-tert-butyl (trans, trans)-3-(hydroxymethyl)-4-(4-methoxyphenyl)-2-methylpiperidine-1-carboxylate [(-)53]

11.04 g of (+/-)-tert-butyl (trans, trans)-3-(hydroxymethyl)-4-(4-methoxyphenyl)-2-methylpiperidine-1-carboxylate [(+/-)53] was purified by supercritical fluid chromatography (Thar 350 preparative SFC, ChiralPak AD-10μ 300x50mm, 25% isopropanol/0.05% DEA/CO_2) to yield 4.42 g of **(-)53** as a white solid. LC-MS (ES, *m/z*): 280[M-55]; ^{1}H NMR (400 MHz, DMSO) δ 7.25 – 7.03 (m, *J* = 8.6, 2H), 6.86 (d, *J* = 8.6, 2H), 4.37 (s, 1H), 4.13 (p, *J* = 6.6, 1H), 3.73 (s, 3H), 3.64 – 3.52 (m, 1H), 3.33 (s, 4H), 3.22 (dt, *J* = 13.4, 6.8, 2H), 3.04 (d, *J* = 4.7, 1H), 2.48 – 2.41 (m, 1H), 1.91 – 1.67 (m, 2H), 1.61 (tt, *J* = 10.0, 5.0, 1H), 1.42 (s, 9H), 1.17 (d, *J* = 6.7, 3H); OR = -40.3° (5.4 mg/mL in MeOH).

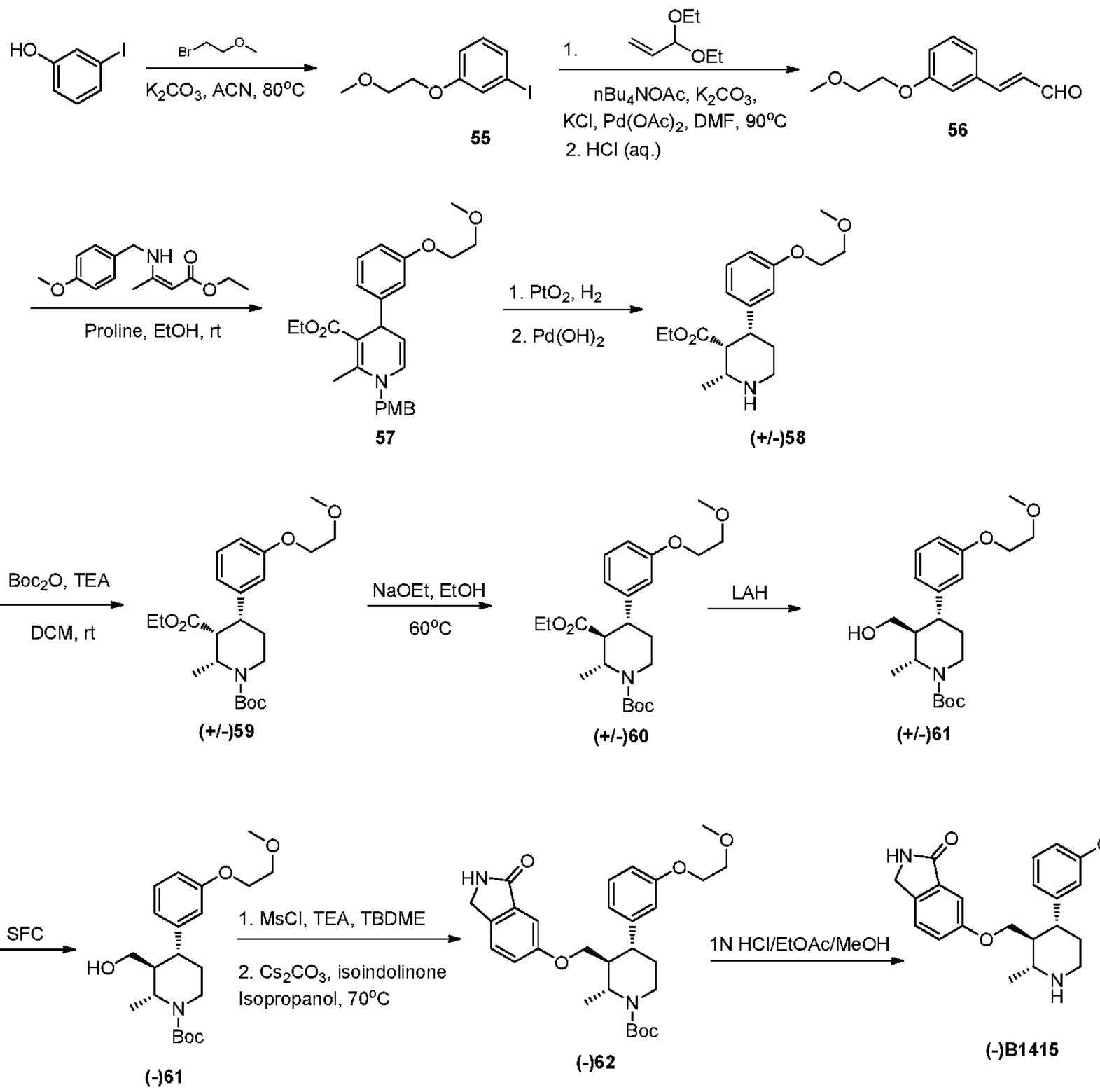
(-)-tert-butyl 6-{[(trans, trans)-1-[(tert-butoxy)carbonyl]-4-(4-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}-1-oxo-2,3-dihydro-1H-isoindole-2-carboxylate [(-)54]

An oven-dried flask was brought to room temperature under vacuum, then purged with nitrogen. (-)-tert-butyl (trans, trans)-3-(hydroxymethyl)-4-(4-methoxyphenyl)-2-methylpiperidine-1-carboxylate [**(-)53**, previously dried in a 50°C vacuum oven overnight, 4.5 g, 13.4 mmol) was dissolved in dry THF (100 mL) and chilled on an ice bath. Tri-*n*-butyl phosphine (5.0 mL, 20.1 mmol, 1.5 eq was added, followed by 1,1'-(azodicarbonyl)dipiperidine (5.1 g, 20.1 mmol, 1.5 eq) and the resulting mixture stirred cold for two hr. tert-Butyl 6-hydroxy-1-oxo-2,3-dihydro-1H-isoindole-2-carboxylate (4.0 g, 16.1 mmol, 1.2 eq) was added, the ice bath was removed, and the reaction was stirred at rt overnight. The mixture was filtered and concentrated. The residue was taken up in a minimal amount of EtOAc, and purified by flash column chromatography (5% - 40% EtOAc/hexanes) to yield 7.4 g of **(-)54** as a white solid (97%). LCMS (M-Boc-tBu) 411.

(-)-6-{[(trans, trans)-4-(4-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one [(-)B0699)]

To a solution of (-)-tert-butyl 6-{[(trans, trans)-1-[(tert-butoxy)carbonyl]-4-(4-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}-1-oxo-2,3-dihydro-1H-isoindole-2-carboxylate [**(-)54**, 1.7 g, 3.0 mmol] in DCM (20 mL) was added TFA (10 mL). After 90 minutes, the reaction was concentrated and the residue was dissolved in DCM (20 mL) and shaken with 1 N NaOH (10 mL). The layers were separated, and the aqueous extracted twice more with DCM. The combined organics were washed with brine, filtered through cotton, and concentrated to yield 0.86 g (78%) of **(-)B0699** as a white solid. LCMS (MH+) 367. ^{1}H NMR (400 MHz, DMSO) δ 8.88 – 8.71 (m, J = 9.5, 1H), 8.70 – 8.45 (m, 2H), 7.44 (d, J = 8.3, 1H), 7.08 (d, J = 8.5, 3H), 7.00 (d, J = 2.2, 1H), 6.87 (d, J = 8.6, 2H), 4.27 (s, 2H), 3.99 (d, J = 8.5, 1H), 3.70 (s, 3H), 3.52 (d, J = 7.7, 1H), 3.48 – 3.34 (m, 2H), 3.20 – 3.05 (m, 1H), 3.00 (dt, J = 16.5, 8.4, 1H), 2.06 (t, J = 11.0, 1H), 2.0 – 1.85 (m, 2H), 1.34 (d, J = 6.4, 3H).

Scheme 14b



Preparation of (-)-6-{[(trans)-4-[3-(2-methoxyethoxy)phenyl]-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one [(-)B1415]

1-Iodo-3-(2-methoxyethoxy)benzene (55)

Into a 2000-mL round-bottom flask, was placed a solution of 3-iodophenol (50 g, 227.26 mmol, 1.00 equiv), potassium carbonate (94.1 g, 680.85 mmol, 3.00 equiv) and 1-bromo-2-methoxyethane (94.1 g, 677.02 mmol, 3.00 equiv) in ACN (1000 mL). The resulting solution was stirred overnight at 80°C. The resulting solution was diluted with 500 mL of water. The resulting solution was extracted with 3x200 mL of ethyl acetate and the organic layers combined, then dried over anhydrous magnesium sulfate and concentrated under vacuum. This resulted in 50 g (79%) of **55** as a light-yellow oil.

(2E)-3-[3-(2-methoxyethoxy)phenyl]prop-2-enal (56)

Into a 2000-mL round-bottom flask, which was purged and maintained with an inert atmosphere of nitrogen, was placed a solution of 1-iodo-3-(2-methoxyethoxy)benzene (**55**, 63 g, 226.55 mmol, 1.00 equiv), n-BuNOAc (136.5 g, 451.99 mmol, 2.00 equiv), potassium carbonate (46.8 g, 338.62 mmol, 1.50 equiv), KCl (16.84 g, 226.04 mmol, 1.00 equiv), Pd(OAc)2 (1.52 g, 6.77 mmol, 0.03 equiv) and 3,3-diethoxyprop-1-ene (88.4 g, 679.03 mmol, 3.00 equiv) in DMF (500 mL). The resulting solution was stirred overnight at 90°C. The reaction mixture was cooled to room temperature with a water/ice bath. The pH value of the solution was adjusted to 4 with 1N hydrogen chloride. The mixture was stirred at rt for 20 min. The resulting solution was extracted with 3x200 mL of ethyl acetate and the organic layers combined, then dried over anhydrous magnesium sulfate and concentrated under vacuum. The residue was applied onto a silica gel column with ethyl acetate/petroleum ether (1:2) as eluent. This resulted in 30 g (64%) of **56** as a yellow semi-solid.

Ethyl 4-[4-(2-methoxyethoxy)phenyl]-1-[(4-methoxyphenyl)methyl]-2-methyl-1,4-dihydropyridine-3-carboxylate (57)

Into a 1000-mL round-bottom flask, was placed a solution of (2E)-3-[4-(2-methoxyethoxy)phenyl]prop-2-enal (**56**, 35 g, 169.71 mmol, 1.00 equiv), proline (3.4 g, 29.53 mmol, 0.17 equiv) and ethyl (2E)-3-[[(4-methoxyphenyl)methyl]amino]but-2-enoate (50.8 g, 203.77 mmol, 1.20 equiv) in ethanol (500 mL). The resulting solution was stirred for 3 h at room temperature. The reaction was then quenched by the addition of 200 mL of water. The resulting solution was extracted with 3x100 mL of ethyl acetate and the organic layers combined, then dried over anhydrous magnesium sulfate and concentrated. The residue was applied onto a silica gel column with ethyl acetate/petroleum ether (1:2). This resulted in 44 g (59%) of **57** as a yellow oil.

(+/-)-Ethyl (cis, cis)-4-[3-(2-methoxyethoxy)phenyl]-2-methylpiperidine-3-carboxylate [(+/-)58]

Into a 2-L pressure tank reactor, was placed a mixture of ethyl 4-[3-(2-methoxyethoxy)phenyl]-1-[(4-methoxyphenyl)methyl]-2-methyl-1,4-dihydropyridine-3-carboxylate (**57**, 50 g, 114.28 mmol, 1.00 equiv) and PtO_2 (4 g) in ethanol (1000 mL). The resulting solution was hydrogenated at 1.5 MPa and stirred overnight at room temperature. The solids were filtered out. The filtrate was concentrated and the residue was dissolved in

MeOH (500 mL), then $Pd(OH)_2$ (50 g) and AcOH(50 mL) was added. The resulting mixture was hydrogenated at 50 psi and stirred for 3h at room temperature. The solids were filtered out. The filtrate was concentrated under vacuum. This resulted in 23 g (63%) of **(+/-)58** as a yellow oil.

(+/-)-1-tert-Butyl 3-ethyl (cis, cis)-1-tert-butyl 3-ethyl 4-(3-(2-methoxyethoxy)phenyl)-2-methylpiperidine-1,3-dicarboxylate [(+/-)59]

Into a 1000-mL round-bottom flask, was placed a solution of (+/-)-ethyl (cis, cis)-4-[3-(2-methoxyethoxy)phenyl]-2-methylpiperidine-3-carboxylate [**(+/-)58**, 23 g, 71.56 mmol, 1.00 equiv], $(Boc)_2O$ (31.24 g, 143.30 mmol, 2.00 equiv) and TEA (21.3 g, 210.47 mmol, 3.00 equiv) in DCM (300 mL). The resulting solution was stirred for 3 h at room temperature, then concentrated under vacuum. The residue was applied onto a silica gel column with ethyl acetate/petroleum ether (1:2) as eluent. This resulted in 26 g (86%) of **(+/-)59** as a yellow oil.

(+/-)-1-tert-Butyl 3-ethyl (trans, trans)-4-[3-(2-methoxyethoxy)phenyl]-2-methylpiperidine-1,3-dicarboxylate [(+/-)60]

Into a 500-mL round-bottom flask, was placed a solution of (+/-)-1-tert-butyl 3-ethyl (cis, cis)-1-tert-butyl 3-ethyl 4-(3-(2-methoxyethoxy)phenyl)-2-methylpiperidine-1,3-dicarboxylate [**(+/-)59**, 22 g, 52.19 mmol, 1.00 equiv] in freshly distilled ethanol (100 mL). EtONa (104 mL, 1 mol/L, 2.00 equiv) was added at 60°C . The resulting solution was stirred for 2 h at 60°C, then cooled to rt with a water/ice bath. The reaction was then quenched by the addition of 300 mL of saturated NH_4Cl. The resulting solution was extracted with 3x100 mL of ethyl acetate and the organic layers combined. The organic solution was washed with brine (3x200 mL) and dried over anhydrous magnesium sulfate, then concentrated under vacuum. This resulted in 19.8 g (90%) of **(+/-)60** as a light-yellow oil.

(+/-)-tert-Butyl (trans, trans)-3-(hydroxymethyl)-4-[3-(2-methoxyethoxy)phenyl]-2-methylpiperidine-1-carboxylate [(+/-)61]

Into a 1000-mL 3-necked round-bottom flask purged and maintained with an inert atmosphere of nitrogen, was placed a suspension of LAH (5.59 g, 147 mmol, 2.00 equiv) in THF (200 mL). This was followed by the addition of a solution of (+/-)-1-tert-butyl 3-ethyl (trans, trans)-4-[3-(2-methoxyethoxy)phenyl]-2-methylpiperidine-1,3-dicarboxylate [**(+/-)60**,

31 g, 73.54 mmol, 1.00 equiv) in THF (300 mL) dropwise with stirring at 0°C. The resulting solution was stirred for 30 min at room temperature. The reaction mixture was cooled to 0°C with a water/ice bath. The reaction was then quenched by the addition of 5.9 mL of water.(0.04 mL water permmol LAH) and stirred at rt for 15min. Then 5.9 mL of 15% NaOH(0.04 mL 15% NaOH per/mmol LAH) was added and stirred at rt for 15min. To this was added 14.7 mL of water (0.1 mL water permmol LAH) and the mixture stirred at rt for 15min. The solids were filtered out through celite. The filtrate was extracted with 3x100 mL of ethyl acetate and the organic layers combined. The organic solution was washed with brine (3x200 mL) and dried over anhydrous magnesium sulfate, then concentrated under vacuum. The residue was applied onto a silica gel column with ethyl acetate/petroleum ether (1:1). This resulted in 23 g (82%) of **(+/-)61** as a pink semi-solid. LCMS (ES, *m/z*): 380 $[M+H]^+$; ^1H NMR400MHz ,CD3OD, *ppm*): 7.2(t, *J*=8.0Hz, 1H), 6.8(d, *J*=6.4Hz, 2H), 6.7(d, *J*=8.0Hz, 1H),4.4(t, *J*=4.4Hz, 1H), 4.1(m, 3H), 3.6(m, 3H), 3.3(s, 3H), 3.2(m, 2H), 3.0(m, 1H),2.5 (s, 1H), 1.8(m, 2H), 1.7(m, 1H), 1.68(m, 1H), 1.6(s, 9H), 1.1(d, *J*=6.0Hz, 3H).

(-)-tert-Butyl (trans, trans)-3-(hydroxymethyl)-4-[3-(2-methoxyethoxy)phenyl]-2-methylpiperidine-1-carboxylate [(-)61]

14.7 g of tert-butyl (trans, trans)-3-(hydroxymethyl)-4-[3-(2-methoxyethoxy)phenyl]-2-methylpiperidine-1-carboxylate **[(+/-)61]** was purified by supercritical fluid chromatography (Thar 200 preparative SFC, ChiralPak AD-10μ 300x50mm, 25% isopropanol/0.05% DEA/CO_2) to yield 6.3 g **(-)61** as a white solid. LC-MS (ES, *m/z*, M-tBu): 324.1; ^1H NMR (400 MHz, $CDCl_3$) δ 7.24 (t, *J* = 8.1, 1H), 6.88 – 6.82 (m, 2H), 6.80 (dd, *J* = 7.9, 2.0, 1H), 4.24 – 4.16 (m, 1H), 4.16 – 4.10 (m, 2H), 3.91 – 3.80 (m, 1H), 3.78 (dd, *J* = 5.4, 3.9, 2H), 3.51 (dd, *J* = 11.3, 3.6, 1H), 3.48 (s, 3H), 3.39 (dd, *J* = 11.4, 4.7, 1H), 3.34 – 3.23 (m, 1H), 2.69 – 2.59 (m, 1H), 2.14 – 1.99 (m, 1H), 1.92 – 1.80 (m, 1H), 1.78 – 1.69 (m, 1H), 1.51 (s, 9H), 1.29 (d, *J* = 6.8, 3H); OR = -33.1 (4.1 mg/mL in MeOH)

(-)-tert-Butyl (trans, trans)-4-[3-(2-methoxyethoxy)phenyl]-2-methyl-3-{[(3-oxo-2,3-dihydro-1H-isoindol-5-yl)oxy]methyl}piperidine-1-carboxylate [(-)62]

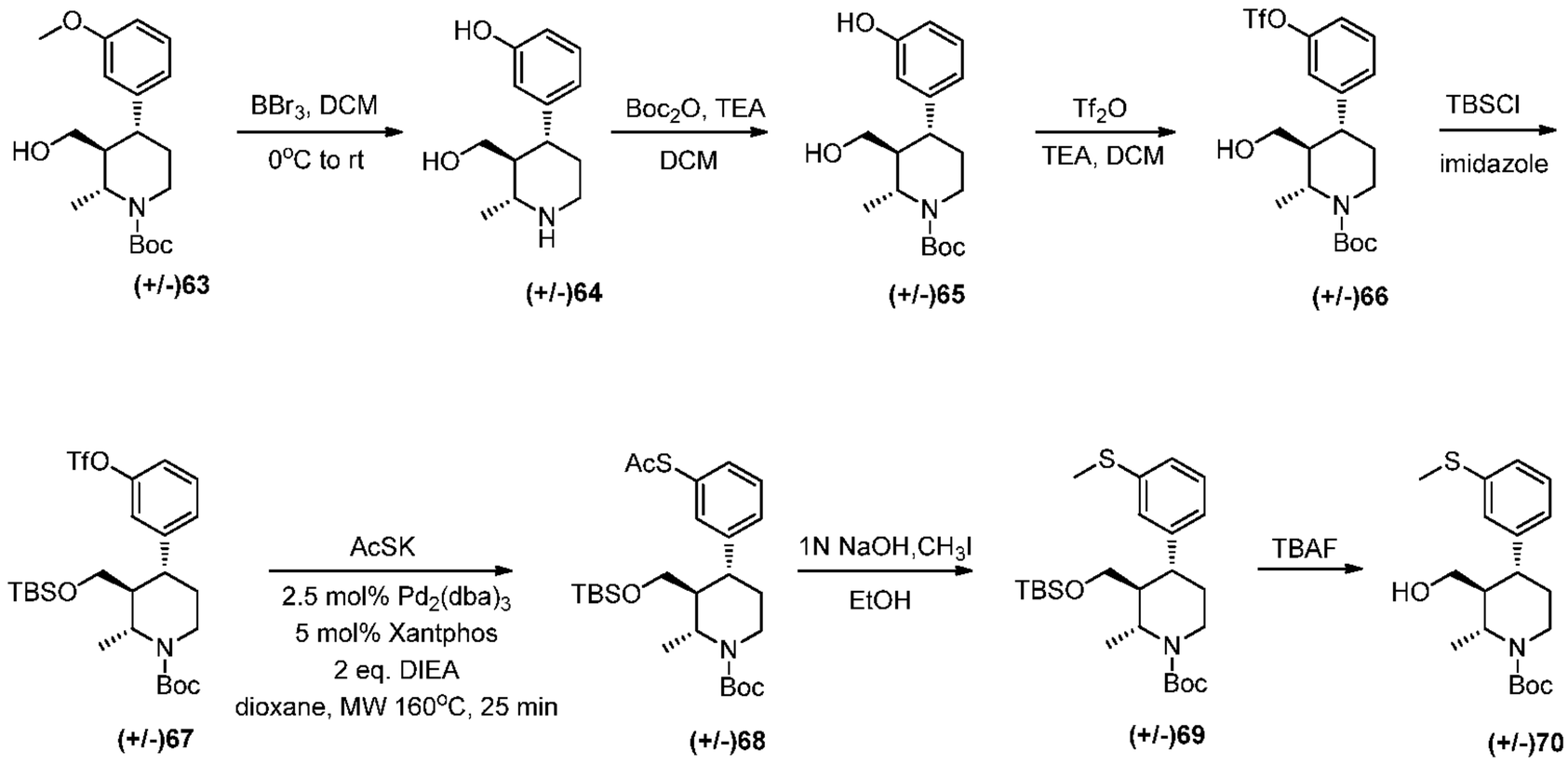
To an ice-cold solution of (-)-tert-butyl (trans, trans)-3-(hydroxymethyl)-4-[3-(2-methoxyethoxy)phenyl]-2-methylpiperidine-1-carboxylate

[**(-)61**, 5.3 g, 14.0 mmol] in *tert*-butylmethylether (25 mL) was added trimethylamine (2.5 mL, 18.2 mmol, 1.3 eq) followed by mesylchloride dropwise (1.4 mL, 18.2 mmol, 1.3 eq) to yield a thick white suspension. The ice bath was removed, and the reaction was stirred at rt for 2 hr. To the reaction was added 25 mL ice water, and the mixture stirred vigorously for 45 minutes, and then for an additional 15 minutes in an ice bath. The mixture was filtered and washed 3X 20 mL water and dried under vacuum in the filter funnel, then in a rt vacuum oven for 24 hours to yield 5.5 g of the mesylate as a white solid. A 250 mL 2-neck flask was oven-dried, brought to rt under vacuum, and purged with nitrogen. Cesium carbonate (7.8 g, 24.0 mmol, 2.0 eq) and 6-hydroxy-2,3-dihydro-1H-isoindol-1-one (2.2 g, 15.0 mmol, 1.25 eq) were added, followed by isopropyl alcohol (previously dried over 3 angstrom molecular sieves, 75 mL). The resulting mixture was stirred with an overhead mechanical stirrer under nitrogen for 2.5 hr, and then the mesylate was added (5.5 g, 12.0 mmol). The mixture was heated at 70°C overnight. The reaction was cooled to rt, filtered of inorganics, and concentrated. The crude product was purified by normal phase chromatography (120 g Biotage Zip Sphere column; 8% - 70% acetone/hexanes) to yield 3.7 g (60%) of **(-)62** as a white solid. LC-MS (ES, *m/z*, M-tBu): 455.3.

(-)-6-{[(trans, trans)-4-[3-(2-methoxyethoxy)phenyl]-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one [(-)B1415]

To a solution of (-)-tert-butyl (trans, trans)-4-[3-(2-methoxyethoxy)phenyl]-2-methyl-3-{[(3-oxo-2,3-dihydro-1H-isoindol-5-yl)oxy]methyl}piperidine-1-carboxylate [**(-)62**, 6.2 g, 12.1 mmol] in methanol (20 mL) was added 1N HCl/EtOAc (61 mL, 61 mmol, 5 eq) and the resulting solution was stirred at rt overnight. The reaction was concentrated to a white foam, which was triturated with diethyl ether, then dried under high vacuum overnight to yield 5.8 g (quant.) **(-)B1415** as a white solid. LCMS (ES, *m/z*, MH+): 411.2. ^{1}H NMR (400 MHz, DMSO) δ 8.93 (d, *J* = 20.5, 2H), 8.54 (s, 1H), 7.44 (d, *J* = 8.3, 1H), 7.21 (t, *J* = 7.9, 1H), 7.10 (dd, *J* = 8.3, 2.3, 1H), 7.02 (d, *J* = 2.2, 1H), 6.79 (dd, *J* = 8.2, 2.1, 1H), 6.75 (d, *J* = 7.6, 1H), 6.69 (s, 1H), 4.26 (s, 2H), 4.07 – 3.92 (m, 2H), 3.91 – 3.79 (m, 1H), 3.56 (t, *J* = 4.5, 2H), 3.50 (d, *J* = 7.8, 1H), 3.25 (s, 3H), 3.18 – 2.93 (m, 2H), 2.18 (t, *J* = 10.9, 1H), 2.06 (ddd, *J* = 16.0, 13.3, 3.4, 1H), 1.92 (d, *J* = 12.3, 1H), 1.37 (d, *J* = 6.4, 3H).

Scheme 14c



(+/-)63 (+/-)64 (+/-)65 (+/-)66

(+/-)67 (+/-)68 (+/-)69 (+/-)70

(+/-)71

Preparation of (+/-)-6-{[(trans, trans)-2-methyl-4-[3-(methylsulfanyl)phenyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one [(+/-)71]

(+/-)-3-[(trans, trans)-3-(hydroxymethyl)-2-methylpiperidin-4-yl]phenol [(+/-)64]

Into a 500-mL 3-necked round-bottom flask purged and maintained with an inert atmosphere of nitrogen, was placed a solution of (+/-)-tert-butyl (trans, trans)-3-(hydroxymethyl)-4-(3-methoxyphenyl)-2-methylpiperidine-1-carboxylate [**(+/-)63**, prepared according to Scheme 14a, 10.5 g, 31.30 mmol, 1.00 equiv] in DCM (100 mL). This was followed by the addition of BBr_3 (19.59 g, 78.36 mmol, 2.50 equiv) dropwise with stirring at 0°C. The resulting solution was stirred for 1h at room temperature. The reaction was then quenched by the addition of water. The pH value of the mixture was adjusted to 8 with 1N sodium hydroxide. The resulting mixture was extracted with 100 mL of DCM. The organic solution was concentrated under vacuum. This resulted in 6 g (87%) of **(+/-)64** as an off-white solid.

(+/-)-tert-Butyl (trans, trans)-3-(hydroxymethyl)-4-(3-hydroxyphenyl)-2-methylpiperidine-1-carboxylate [(+/-)65]

Into a 500-mL round-bottom flask, was placed a solution of (+/-)-3-[(trans, trans)-3-(hydroxymethyl)-2-methylpiperidin-4-yl]phenol [**(+/-)64**, 6.85 g, 30.95 mmol, 1.00 equiv] and TEA (9.58 g, 94.67 mmol, 3.00 equiv) in DCM (200 mL). This was followed by the addition of tert-butyl dicarbonate (8.78 g, 40.23 mmol, 1.30 equiv) at 0°C. The resulting solution was stirred for 2 h at room temperature and diluted with 100 mL of water. The resulting mixture was extracted with 3x60 mL of DCM and the organic layers combined, then concentrated under vacuum. This resulted in 9 g (90%) of **(+/-)65** as an off-white solid.

(+/-)-tert-butyl (trans, trans)-3-(hydroxymethyl)-2-methyl-4-[3-[(trifluoromethane)sulfonyloxy]phenyl]piperidine-1-carboxylate [(+/-)66]

Into a 200-mL round-bottom flask, was placed a solution of **(+/-)**-tert-butyl (trans, trans)-3-(hydroxymethyl)-4-(3-hydroxyphenyl)-2-methylpiperidine-1-carboxylate [**(+/-)65**, 9 g, 28.00 mmol, 1.00 equiv)] and TEA (8.57 g, 84.69 mmol, 3.00 equiv) in DCM (200 mL). This was followed by the addition of (trifluoromethane)sulfonyl trifluoromethanesulfonate (15.82 g, 56.07 mmol, 2.00 equiv) dropwise with stirring at 0°C. The resulting solution was stirred for 2 h at room temperature. The reaction was then quenched by the addition of 100 mL of water. The resulting solution was extracted with 3x100 mL of dichloromethane and the organic layers combined, then dried over anhydrous magnesium sulfate and concentrated under vacuum. The residue was applied onto a silica gel column with ethyl acetate/petroleum ether (1:5). This resulted in 6 g (47%) of **(+/-)66** as a yellow oil.

(+/-)-tert-Butyl (trans, trans)-3-[[(tert-butyldimethylsilyl)oxy]methyl]-2-methyl-4-[3-[(trifluoromethane)sulfonyloxy]phenyl]piperidine-1-carboxylate [(+/-)67]

Into a 250-mL round-bottom flask, was placed a solution of (+/-)-tert-butyl (trans, trans)-3-(hydroxymethyl)-2-methyl-4-[3-[(trifluoromethane)sulfonyloxy]phenyl]piperidine-1-carboxylate [**(+/-)66**, 3 g, 6.62 mmol, 1.00 equiv], imidazole (1.35 g, 19.85 mmol, 3.00 equiv) and tert-butyl(chloro)dimethylsilane (2.99 g, 19.84 mmol, 3.00 equiv) in DCM (80 mL). The resulting solution was stirred for 3 h at room temperature. The reaction was then quenched by the addition of 100 mL of water. The resulting solution was extracted with 3x100 mL of dichloromethane and the organic layers combined, then dried over anhydrous

magnesium sulfate and concentrated under vacuum. The residue was applied onto a silica gel column with ethyl acetate/petroleum ether (1:5). This resulted in 3 g (80%) of **(+/-)67** as a yellow oil.

(+/-)-tert-Butyl (trans, trans)-4-[3-(acetylsulfanyl)phenyl]-3-[[(tert-butyldimethylsilyl)oxy]methyl]-2-methylpiperidine-1-carboxylate [(+/-)68]

Into a 5-mL vial purged and maintained with an inert atmosphere of argon, was placed a solution of (+/-)-tert-butyl (trans, trans)-3-[[(tert-butyldimethylsilyl)oxy]methyl]-2-methyl-4-[3-[(trifluoromethane)sulfonyloxy]phenyl]piperidine-1-carboxylate **[(+/-)67**, 1 g, 1.76 mmol, 1.00 equiv], $Pd_2(dba)_3.CHCl_3$ (45.54 mg, 0.04 mmol, 0.03 equiv), 1-(potassiomsulfanyl)ethan-1-one (300.96 mg, 2.64 mmol, 1.50 equiv), Xantphos (59.92 mg, 0.10 mmol, 0.05 equiv) and DIEA (454.93 mg, 3.52 mmol, 2.00 equiv) in dioxane (3 mL). The final reaction mixture was irradiated with microwave radiation for 30 min at 160°C. The reaction was then quenched by water. The resulting solution was extracted with 3x30 mL of ethyl acetate and the organic layers combined. The organic solution was washed with 2x100 mL of brine and dried over anhydrous magnesium sulfate, then concentrated under vacuum. The residue was applied onto a silica gel column with ethyl acetate/petroleum ether (1:10). This resulted in 260 mg (30%) of **(+/-)68** as a yellow oil.

(+/-)-tert-Butyl (trans, trans)-3-[[(tert-butyldimethylsilyl)oxy]methyl]-2-methyl-4-[3-(methylsulfanyl)phenyl]piperidine-1-carboxylate [(+/-)69]

Into a 50-mL round-bottom flask purged and maintained with an inert atmosphere of nitrogen, was placed a solution of (+/-)-tert-butyl (trans, trans)-4-[3-(acetylsulfanyl)phenyl]-3-[[(tert-butyldimethylsilyl)oxy]methyl]-2-methylpiperidine-1-carboxylate **[(+/-)68**, 600 mg, 1.22 mmol, 1.00 equiv] and CH_3I (205.9 mg, 1.45 mmol, 1.20 equiv) in ethanol (6 mL), then 1N sodium hydroxide (1.46 mL, 1.20 equiv) was added to the solution. The resulting solution was stirred for 1 h at 0°C. The reaction was then quenched by water. The resulting solution was extracted with 3x30 mL of ethyl acetate and the organic layers combined. The organic solution was washed with 3x60 mL of brine and dried over anhydrous magnesium sulfate, then concentrated under vacuum. This resulted in 450 mg (80%) of **(+/-)69** as a yellow oil.

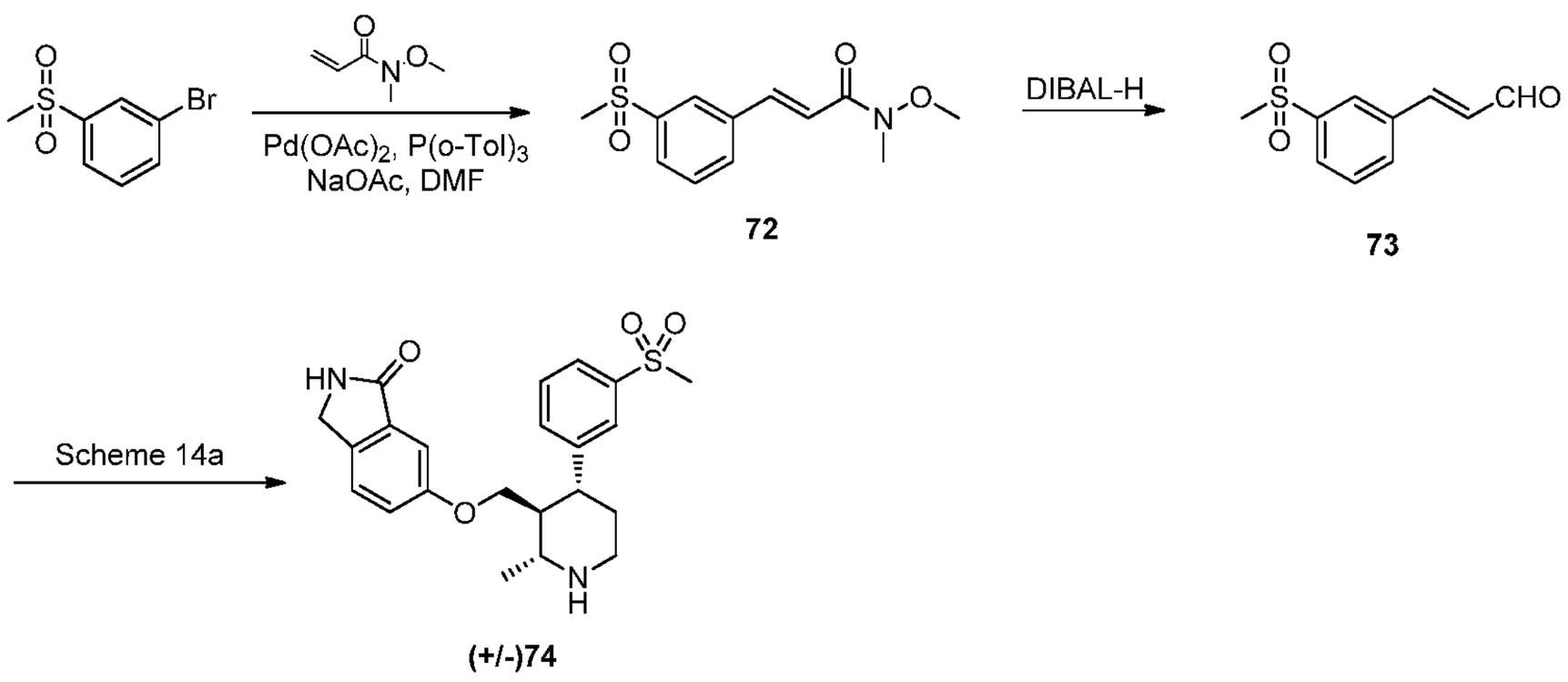
(+/-)-tert-butyl (trans, trans)-3-(hydroxymethyl)-2-methyl-4-[3-(methylsulfanyl)phenyl]piperidine-1-carboxylate [(+/-)70]

Into a 50-mL round-bottom flask purged and maintained with an inert atmosphere of nitrogen, was placed a solution of tert-butyl (+/-)-tert-butyl (trans, trans)-3-[[(tert-butyldimethylsilyl)oxy]methyl]-2-methyl-4-[3-(methylsulfanyl)phenyl]piperidine-1-carboxylate [**(+/-)69**, 465 mg, 1.00 mmol, 1.00 equiv] in THF (5 mL). This was followed by the addition of TBAF (1mol/L in tetrahydrofuran) (2 mL, 2.00 equiv) dropwise with stirring at 0°C. The resulting solution was stirred overnight at room temperature. The reaction was then quenched by water/ice. The resulting solution was extracted with 3x30 mL of ethyl acetate and the organic layers combined. The organic solution was washed with 3x50 mL of brine and dried over anhydrous magnesium sulfate, then concentrated under vacuum. The residue was applied onto a silica gel column with ethyl acetate/petroleum ether (1:3). This resulted in 320 mg (91%) of **(+/-)70** as a yellow oil.

(+/-)-6-{[(trans, trans)-2-methyl-4-[3-(methylsulfanyl)phenyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one [(+/-)71]

(+/-)71 may be prepared from (+/-)-tert-butyl (trans, trans)-3-(hydroxymethyl)-2-methyl-4-[3-(methylsulfanyl)phenyl]piperidine-1-carboxylate **[(+/-)70]** according to Scheme 14a. LCMS (M+H) 383.1.

Scheme 14d



(+/-)74

Preparation of (+/-)-6-{[(trans, trans)-4-(3-methanesulfonylphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one (74)

(2E)-3-(3-methanesulfonylphenyl)-N-methoxy-N-methylprop-2-enamide (72)

Into a 1000-mL round-bottom flask purged and maintained with an inert atmosphere of nitrogen, was placed a solution of 1-bromo-3-methanesulfonylbenzene (40 g, 170.14 mmol, 1.00 equiv), N-methoxy-N-methylprop-2-enamide (29.52 g, 256.40 mmol, 1.50 equiv) and sodium acetate (27.88 g, 339.86 mmol, 2.00 equiv) in DMF (500 mL). The resulting solution was stirred for 30 min. Then $P(o\text{-}Tol)_3$ (5.175 g, 17.00 mmol, 0.10 equiv) and $Pd(OAc)_2$ (1.9 g, 8.46 mmol, 0.05 equiv) was added to the solution. The resulting solution was stirred overnight at 120°C. The reaction was then quenched by the addition of 500 mL of water. The resulting mixture was extracted with 3x200 mL of ethyl acetate and the organic layers combined. The organic solution was washed with 3x500 mL of brine and dried over anhydrous magnesium sulfate. The solids were filtered out. The filtrate was concentrated under vacuum. The residue was re-crystallized from ethyl acetate:hexane in the ratio of 1:20. This resulted in 36.6 g (80%) of **72** as a yellow solid.

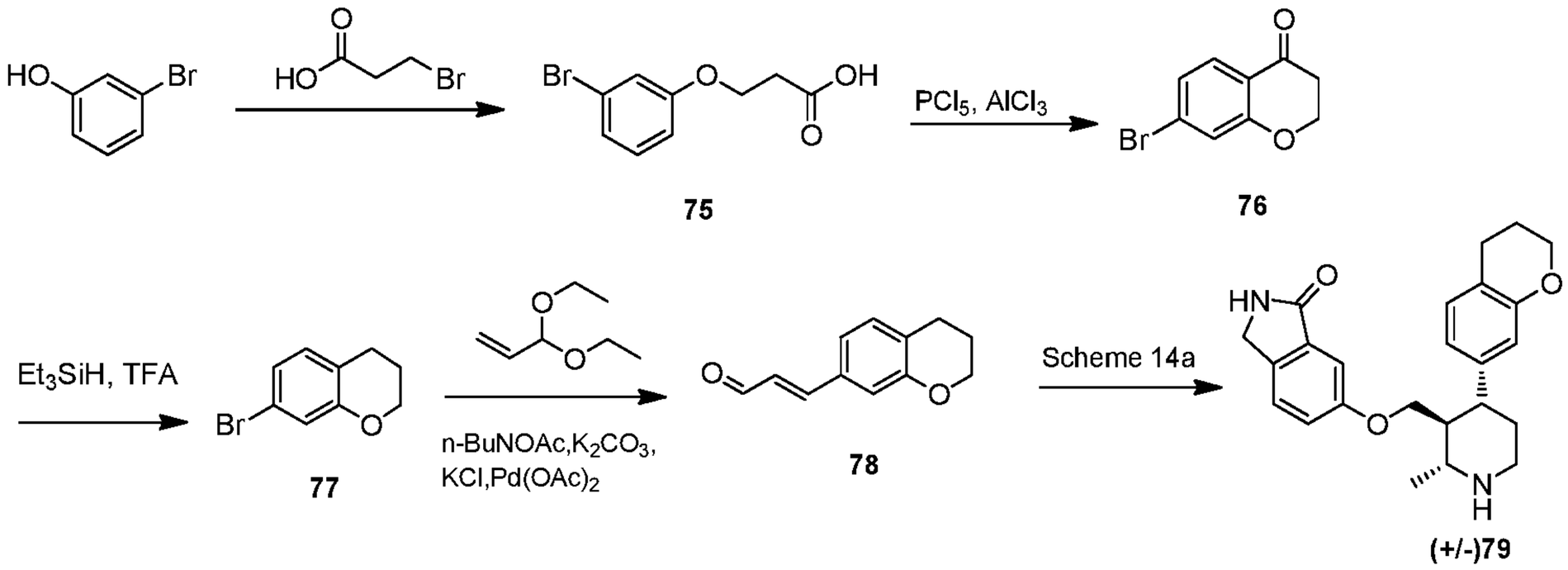
(2E)-3-(3-methanesulfonylphenyl)prop-2-enal (73)

Into a 100-mL round-bottom flask purged and maintained with an inert atmosphere of nitrogen, was placed a solution of (2E)-3-(3-methanesulfonylphenyl)-N-methoxy-N-methylprop-2-enamide (**72**, 2.69 g, 9.99 mmol, 1.00 equiv) and DIBAL-H (1N in hexane, 20 mL, 2.00 equiv) in THF (30 mL, distilled). The resulting solution was stirred for 2h at -78°C. The reaction was then quenched by the addition of 50 mL of 1N hydrogen chloride at -78°C. The resulting mixture was extracted with 3x20 mL of ethyl acetate and the organic layers combined, then dried over anhydrous magnesium sulfate and concentrated under vacuum. The residue was applied onto a silica gel column with ethyl acetate/petroleum ether (1:1). This resulted in 1.6 g (76%) of **73** as a yellow solid.

(+/-)-6-{[(trans, trans)-4-(3-methanesulfonylphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one [(+/-)74]

(+/-)74 may be prepared from (2E)-3-(3-methanesulfonylphenyl)prop-2-enal (**73**) according to Scheme 14a. LCMS (M+H) 415.1.

Scheme 14e



Preparation of (+/-)-6-{[(2R,3S)-4-(3,4-dihydro-2H-1-benzopyran-7-yl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one [(+/-)79]

3-(3-Bromophenoxy)propanoic acid (75)

Into a 2-L 3-necked round-bottom flask, was placed a solution of NaOH (120 g) in water (2000 mL), 3-bromophenol (519 g, 3.00 mol, 1.00 equiv). This was followed by the addition of a solution of 3-bromopropanoic acid (459 g, 3.00 mol, 1.00 equiv) and NaOH (120 g) in water (3000 mL) dropwise with stirring at 100°C. The resulting solution was stirred for 48 h at 100°C. The reaction mixture was cooled to 0°C with a water/ice bath. The pH value of the solution was adjusted to 1 with hydrogen chloride (12 mol/L). The solids were collected by filtration. The crude product was washed with water and n-pentane. This resulted in 110 g (15%) of **75** as an off-white solid.

7-Bromo-3,4-dihydro-2H-1-benzopyran-4-one (76)

Into a 250-mL 3-necked round-bottom flask purged and maintained with an inert atmosphere of nitrogen, was placed 3-(3-bromophenoxy)propanoic acid (**75**, 20 g, 81.61 mmol, 1.00 equiv), PCl_5 (25.57 g, 122.79 mmol, 1.50 equiv). The mixture was stirred for 30 min at room temperature. This was followed by the addition of trichloroaluminum, (21.89 g, 164.17 mmol, 2.00 equiv). The resulting solution was stirred for 1 h at 130°C. The reaction mixture was cooled to room temperature. The reaction was then quenched by the addition of ice. The resulting solution was extracted with 3x60 mL of ethyl acetate and the organic layers

combined. The residue was applied onto a silica gel column with ethyl acetate/petroleum ether (1:5). This resulted in 9.3 g (50%) of **76** as a yellow solid.

7-Bromo-3,4-dihydro-2H-1-benzopyran (77)

Into a 1000-mL round-bottom flask, was placed a solution of 7-bromo-3,4-dihydro-2H-1-benzopyran-4-one (**76**, 60 g, 264.25 mmol, 1.00 equiv) in trifluoroacetic acid (600 mL), triethylsilane (154.2 g, 1.33 mol, 5.00 equiv). The resulting solution was stirred overnight at 65°C. The resulting mixture was concentrated under vacuum. The pH value of the solution was adjusted to 8 with sodium bicarbonate. The resulting solution was extracted with 3x100 mL of dichloromethane and the organic layers combined. The residue was applied onto a silica gel column with ethyl acetate/petroleum ether (1:15). This resulted in 35 g (62%) of **77** as colorless oil.

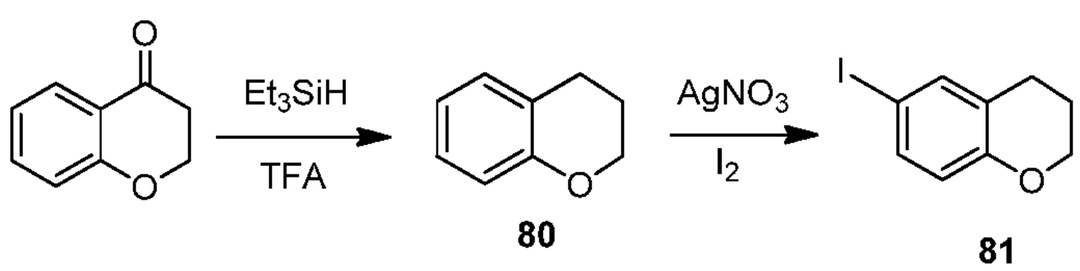
(2E)-3-(3,4-Dihydro-2H-1-benzopyran-7-yl)prop-2-enal (78)

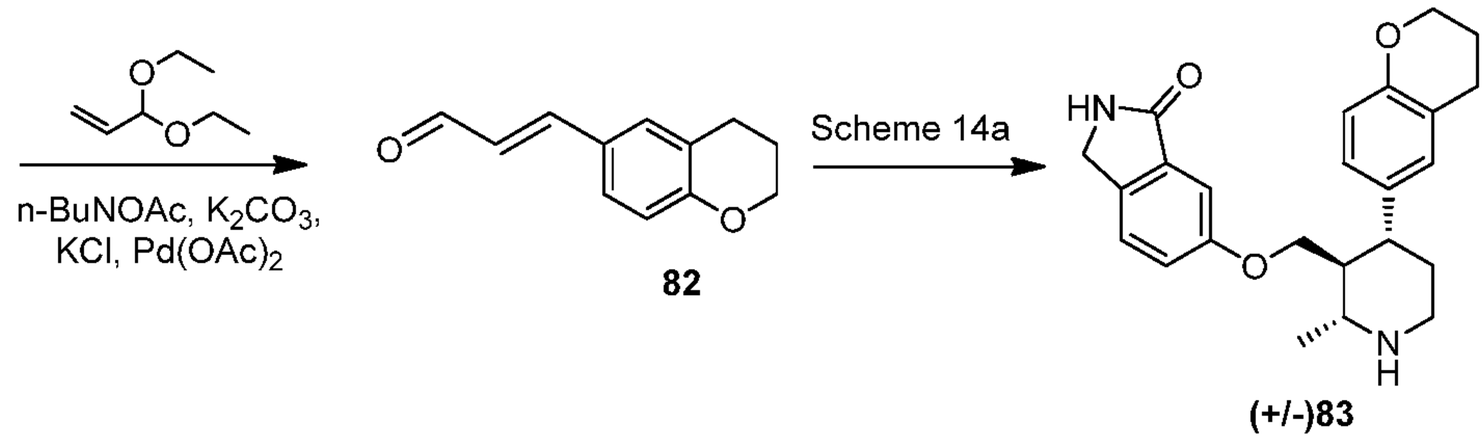
Into a 1000-mL round-bottom flask purged and maintained with an inert atmosphere of nitrogen, was placed a solution of 7-bromo-3,4-dihydro-2H-1-benzopyran (**77**, 35 g, 164.26 mmol, 1.00 equiv) in N,N-dimethylformamide (500 mL), n-Bu_4NOAc (99.7 g, 330.13 mmol, 2.00 equiv), potassium carbonate (34.15 g, 247.09 mmol, 1.50 equiv), KCl (12.3 g, 165.10 mmol, 1.00 equiv), $Pd(OAc)_2$ (1.1 g, 4.90 mmol, 0.03 equiv), 3,3-diethoxyprop-1-ene (64.38 g, 494.53 mmol, 3.00 equiv). The resulting solution was stirred overnight at 90°C. The reaction mixture was cooled to room temperature with a water/ice bath. The pH value of the solution was adjusted to 4 with hydrogen chloride (2 mol/L). The mixture was stirred for 30 mins at room temperature. The resulting solution was extracted with 3x100 mL of ethyl acetate and the organic layers combined. The resulting mixture was washed with 3x500 mL of brine. The mixture was dried over anhydrous magnesium sulfate. The residue was applied onto a silica gel column with ethyl acetate/petroleum ether (1:5). This resulted in 9.3 g (30%) of **78** as a yellow oil.

(-)-
6-{[(2R,3S)-4-(3,4-dihydro-2H-1-benzopyran-7-yl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one [(+/-)79]

(+/-)79 may be prepared from (2E)-3-(3,4-dihydro-2H-1-benzopyran-7-yl)prop-2-enal (**78**) according to Scheme 14a. LCMS (M+H) 393.1.

Scheme 14f





Preparation of (+/-)-6-{[(trans, trans)-4-(3,4-dihydro-2H-1-benzopyran-6-yl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one [(+/-)83]

3,4-Dihydro-2H-1-benzopyran (80)

Into a 1000-mL round-bottom flask, was placed a solution of 3,4-dihydro-2H-1-benzopyran-4-one (45 g, 303.73 mmol, 1.00 equiv) and Et_3SiH (176.63 g, 1.52 mol, 5.00 equiv) in trifluoroacetic acid (450 mL). The resulting solution was stirred overnight at 65°C. The reaction was then quenched by the addition of water (500 mL). The resulting solution was extracted with 2X300 mL of DCM and the organic layers combined, then concentrated under vacuum. The residue was applied onto a silica gel column with ethyl acetate/petroleum ether (1:10). This resulted in 28.77 g (71%) of **80** as a colorless oil.

6-Iodo-3,4-dihydro-2H-1-benzopyran (81)

Into a 1000-mL round-bottom flask, was placed a mixture of 3,4-dihydro-2H-1-benzopyran (**80**, 40.7 g, 303.33 mmol, 1.00 equiv) and $AgNO_3$ (51.6 g, 303.89 mmol, 1.12 equiv), I_2 (85.3 g, 335.83 mmol, 1.00 equiv) in methanol (400 mL). The resulting mixture was stirred for 1 h at room temperature. The reaction was then quenched by the addition of saturated sodium thiosulfate (400 mL). The resulting solution was extracted with 3X200 mL of dichloromethane and the organic layers combined, then dried and concentrated under vacuum. The residue was applied onto a silica gel column with dichloromethane/petroleum ether (1:1). This resulted in 39 g (49%) of **81** as a yellow oil.

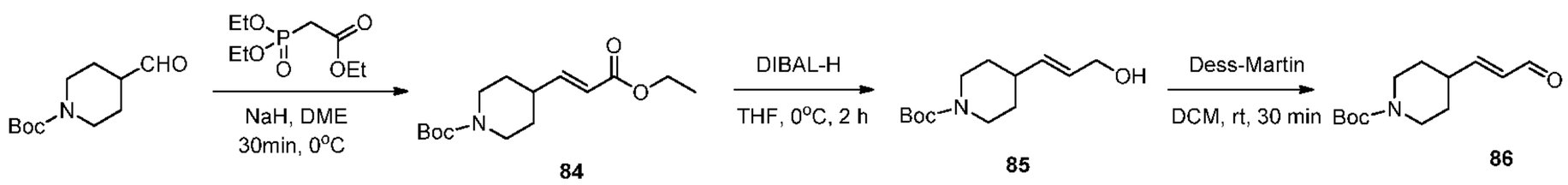
(2E)-3-(3,4-Dihydro-2H-1-benzopyran-6-yl)prop-2-enal (82)

Into a 2-L round-bottom flask purged and maintained with an inert atmosphere of nitrogen, was placed a solution of 6-iodo-3,4-dihydro-2H-1-benzopyran (**81**, 52 g, 199.94 mmol, 1.00 equiv), n-BuNOAc (120.8 g, 400.00 mmol, 2.00 equiv), potassium carbonate (41.4 g, 299.54 mmol, 1.50 equiv), KCl (14.9 g, 200.00 mmol, 1.00 equiv), $Pd(OAc)_2$ (1.35 g, 6.01 mmol, 0.03 equiv) and 3,3-diethoxyprop-1-ene (78 g, 599.15 mmol, 3.00 equiv) in DMF (500 mL). The resulting solution was stirred overnight at 90°C. The reaction solution was cooled to room temperature with a water/ice bath. The pH value of the solution was adjusted to 4 with 2N hydrogen chloride. The resulting solution was extracted with 3x200 mL of ethyl acetate and the organic layers combined. The resulting mixture was washed with 3x500 mL of water. The mixture was dried over anhydrous magnesium sulfate and concentrated under vacuum. The residue was applied onto a silica gel column with ethyl acetate/petroleum ether (1:5). This resulted in 24 g (64%) of **82** as a yellow solid.

(+/-)-6-{[(trans, trans)-4-(3,4-dihydro-2H-1-benzopyran-6-yl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one [(+/-)83]

(+/-)83 may be prepared from (2E)-3-(3,4-dihydro-2H-1-benzopyran-6-yl)prop-2-enal (**82**) according to Scheme 14a. LCMS (M+H) 393.3.

Scheme 14g



Preparation of (+/-)-6-{[(trans, trans)-4-(1-acetylpiperidin-4-yl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one [(+/-)90]

tert-Butyl 4-[(1E)-3-ethoxy-3-oxoprop-1-en-1-yl]piperidine-1-carboxylate (84)

Into a 1000-mL 3-necked round-bottom flask purged and maintained with an inert atmosphere of nitrogen, was placed a solution of sodium hydride (18.24 g, 760.00 mmol, 1.80 equiv) in ethylene glycol dimethyl ether (300 mL). This was followed by the addition of ethyl 2-(diethoxyphosphoryl)acetate (102.22 g, 455.95 mmol, 1.80 equiv) dropwise with stirring at 0°C. The resulting solution was stirred for 15 min at 0°C.To this was added a solution of tert-butyl 4-formylpiperidine-1-carboxylate (54 g, 253.20 mmol, 1.00 equiv) in ethylene glycol dimethyl ether (200 mL) dropwise with stirring at 0°C. The resulting solution was stirred for 10 min at 0°C. The reaction was then quenched by the addition of water/ice. The resulting solution was extracted with 3x300 mL of ethyl acetate and the organic layers combined. The resulting mixture was washed with 1x300 mL of brine. The mixture was dried over anhydrous magnesium sulfate. This resulted in 71 g (99%) of **84** as a yellow oil.

tert-Butyl 4-[(1E)-3-hydroxyprop-1-en-1-yl]piperidine-1-carboxylate (85)

Into a 2000-mL 3-necked round-bottom flask purged and maintained with an inert atmosphere of nitrogen, was placed a solution of tert-butyl 4-[(1E)-3-ethoxy-3-oxoprop-1-en-1-yl]piperidine-1-carboxylate (**84**, 65.1 g, 229.74 mmol, 1.00 equiv) in tetrahydrofuran(distilled) (600 mL). This was followed by the addition of DIBAL-H (1M in hexane, 460 mL, 2.00 equiv) dropwise with stirring at 0°C. The resulting solution was stirred for 1h at 0°C. The reaction was poured in water/ice and filtered through celite. The product was extracted with 3x100 mL of ethyl acetate and the organic layers combined, then washed with 2x300 mL of brine. The organic solution was dried over anhydrous magnesium sulfate and concentrated under vacuum. The residue was applied onto a silica gel column with ethyl acetate/petroleum ether (1:1). This resulted in 32 g (58%) of **85** as a light yellow oil.

tert-Butyl 4-[(1E)-3-oxoprop-1-en-1-yl]piperidine-1-carboxylate (86)

Into a 1000-mL round-bottom flask purged and maintained with an inert atmosphere of nitrogen, was placed a solution of tert-butyl 4-[(1E)-3-hydroxyprop-1-en-1-yl]piperidine-1-carboxylate (**85**, 18 g, 74.59 mmol, 1.00 equiv) in DCM (500 mL). This was followed by the addition of Dess-Martin (38 g, 89.62 mmol, 1.20 equiv), in portions at 0°C. The resulting solution was stirred for 30 min at room temperature.The reaction was then quenched by the addition of saturated sodium bicarbonate. The resulting solution was extracted with 3x100

mL of ethyl acetate and the organic layers combined. The resulting mixture was washed with 3x100 mL of brine. The organic solution was dried over anhydrous magnesium sulfate and concentrated under vacuum. The residue was applied onto a silica gel column with ethyl acetate/petroleum ether (1:2). The resulting mixture was concentrated under vacuum. This resulted in 14.3 g (80%) of **86** as a colorless oil.

(+/-)-Ethyl 4-[1-[(tert-butoxy)carbonyl]piperidin-4-yl]-1-[(4-methoxyphenyl)methyl]-2-methylpiperidine-3-carboxylate [(+/-)87]

(+/-)87 may be prepared from tert-butyl 4-[(1E)-3-oxoprop-1-en-1-yl]piperidine-1-carboxylate (**86**) according to Scheme 14a.

(+/-)-Ethyl 1-[(4-methoxyphenyl)methyl]-2-methyl-4-(piperidin-4-yl)piperidine-3-carboxylate [(+/-)88]

Into a 50-mL round-bottom flask, was placed a solution of (+/-)-ethyl 4-[1-[(tert-butoxy)carbonyl]piperidin-4-yl]-1-[(4-methoxyphenyl)methyl]-2-methylpiperidine-3-carboxylate [**(+/-)87**, 474 mg, 1.00 mmol, 1.00 equiv] in ethyl acetate (10 mL). HCl (gas) was introducted to the resulting solution and stirred for 2 h at room temperature. The resulting mixture was concentrated under vacuum. This resulted in 340 mg (91%) of **(+/-)88** as an off-white solid.

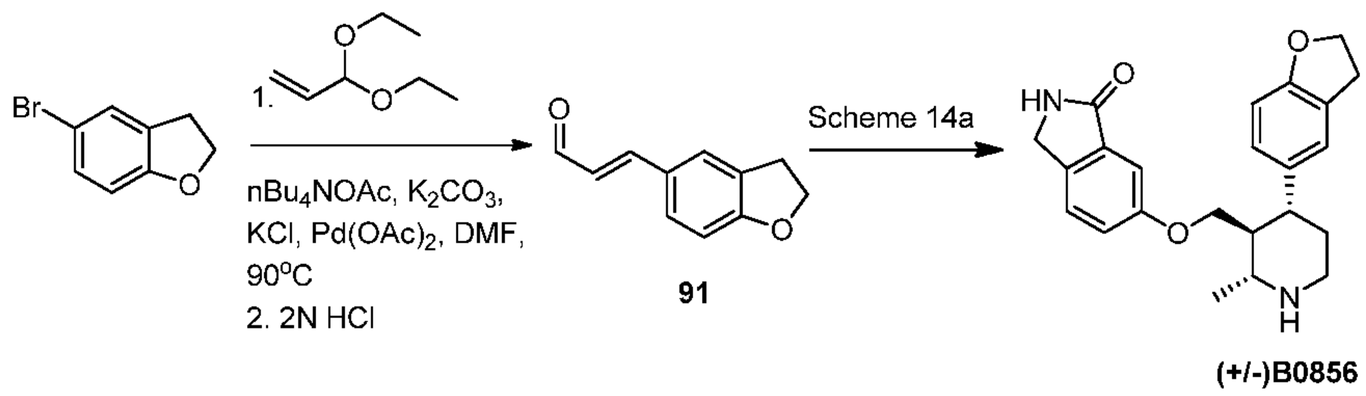
(+/-)-Ethyl 4-(1-acetylpiperidin-4-yl)-1-[(4-methoxyphenyl)methyl]-2-methylpiperidine-3-carboxylate [(+/-)89]

Into a 250-mL 3-necked round-bottom flask purged and maintained with an inert atmosphere of nitrogen, was placed a solution of (+/-)-ethyl 1-[(4-methoxyphenyl)methyl]-2-methyl-4-(piperidin-4-yl)piperidine-3-carboxylate [**(+/-)88**, 5 g, 13.35 mmol, 1.00 equiv] and pyridine (2.11 g, 26.68 mmol, 2.00 equiv) in DCM (100 mL). This was followed by the addition of acetic anhydride (2.7 g, 26.47 mmol, 1.98 equiv) dropwise with stirring at 0°C. The resulting solution was stirred for 2 h at room temperature. The resulting mixture was concentrated under vacuum to remove pyridine. This resulted in 3.8 g (68%) of **(+/-)89** as a yellow oil.

(+/-)-6-{[(trans, trans)-4-(1-Acetylpiperidin-4-yl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one [(+/-)90]

(+/-)90 may be prepared from (+/-)-ethyl 4-(1-acetylpiperidin-4-yl)-1-[(4-methoxyphenyl)methyl]-2-methylpiperidine-3-carboxylate **[(+/-)89]** by Scheme 14a. LCMS (M+H) 386.1.

Scheme 14h



Synthesis of (+/-)-6-{[(trans, trans)-4-(2,3-dihydro-1-benzofuran-5-yl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one [(+/-)B0856]

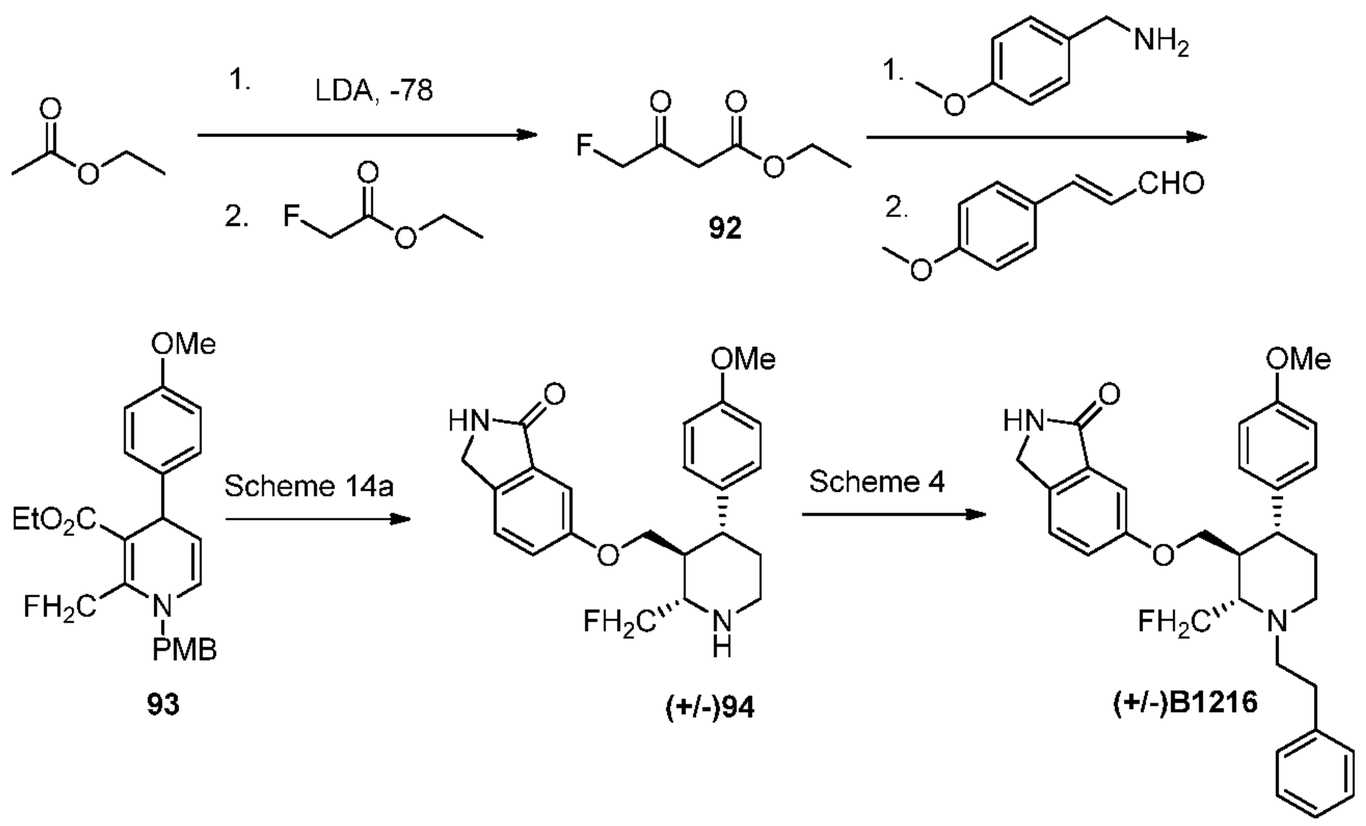
(2E)-3-(2,3-dihydro-1-benzofuran-5-yl)prop-2-enal (91)

Into a 1000-mL round-bottom flask, was placed a solution of 5-bromo-2,3-dihydro-1-benzofuran (70 g, 351.68 mmole, 1.00 equiv) in N,N-dimethylformamide (500 mL), nBu_4NOAc (213.5 g, 706.95 mmol, 2.01 equiv), K_2CO_3 (73.2 g, 529.63 mmol, 1.51 equiv), KCl (26.3 g, 353.02 mmol, 1.00 equiv), $Pd(OAc)_2$ (2.35 g, 10.47 mmol, 0.03 equiv), 1,1-diethoxypropane (137.8 g, 1.04 mol, 2.96 equiv). The resulting solution was stirred overnight at 90°C. The pH value of the solution was adjusted to 4 with hydrogen chloride (2 M). The resulting solution was extracted with 3x200 mL of ethyl acetate and the organic layers combined and concentrated under vacuum. The crude product (25 g) was purified by Flash-Prep-HPLC with the following conditions (IntelFlash-1): Column, silica gel; mobile phase, EA/PE(0~50%) within 50 min; Detector, UV 254 nm. 18 g product was obtained. This resulted in 18 g (29%) of (2E)-3-(2,3-dihydro-1-benzofuran-5-yl)prop-2-enal (**91**) as a yellow oil.

(+/-)-6-{[(trans, trans)-4-(2,3-dihydro-1-benzofuran-5-yl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one [(+/-)B0856]

(+/-)B0856 may be prepared from (2E)-3-(3,4-dihydro-2H-1-benzopyran-6-yl)prop-2-enal (**91**) according to Scheme 14a. LCMS (M+H) 379.2.

Scheme 14i



Synthesis of (+/-)-6-{[(trans, trans)-2-(fluoromethyl)-4-(4-methoxyphenyl)-1-(2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one [(+/-)B1216]

Ethyl 4-fluoro-3-oxobutanoate (92)

Into a 500-mL 3-necked round-bottom flask purged and maintained with an inert atmosphere of nitrogen, was placed a solution of ethyl acetate (16 g, 181.60 mmol, 1.10 equiv) in tetrahydrofuran (100 mL). This was followed by the addition of LDA (freshly prepared) (120 mL, 1.20 equiv) dropwise with stirring at -78°C. The resulting solution was stirred for 0.5 at -78°C. To this was added ethyl 2-fluoroacetate (18 g, 169.66 mmol, 1.00 equiv) dropwise with stirring at -78°C. The resulting solution was stirred overnight at r.t. The reaction was then quenched by the addition of 200 mL of 10% hydrogen chloride. The resulting solution was extracted with 3x500 mL of ethyl acetate and the organic layers combined and dried over

anhydrous sodium sulfate and concentrated under vacuum. The residue was applied onto a silica gel column with ethyl acetate/petroleum ether (1:10). This resulted in 17.6 g (70%) of (**92**) as a brown liquid.

Ethyl (2E)-4-fluoro-3-[[(4-methoxyphenyl)methyl]amino]but-2-enoate

Into a 250-mL round-bottom flask purged and maintained with an inert atmosphere of nitrogen, was placed (4-methoxyphenyl)methanamine (16.3 g, 118.82 mmol, 1.00 equiv), dichloromethane (100 mL), **92** (17.6 g, 118.81 mmol, 1.00 equiv), I_2 (3.1 g, 0.10 equiv). The resulting solution was stirred overnight at room temperature. The resulting mixture was washed with 2x300 mL of H_2O. The mixture was dried over anhydrous sodium sulfate and concentrated under vacuum. The residue was applied onto a silica gel column with ethyl acetate/petroleum ether (1:20). This resulted in 17.5 g (55%) of ethyl (2E)-4-fluoro-3-[[(4-methoxyphenyl)methyl]amino]but-2-enoate as light yellow oil.

Ethyl 2-(fluoromethyl)-4-(4-methoxyphenyl)-1-[(4-methoxyphenyl)methyl]-1,4-dihydropyridine-3-carboxylate (93)

Into a 500-mL round-bottom flask, was placed (2E)-3-(4-methoxyphenyl)prop-2-enal (17.5 g, 107.90 mmol, 1.00 equiv), ethyl (2E)-4-fluoro-3-[(4-methoxyphenyl)methyl]aminobut-2-enoate (10.6 g, 39.66 mmol, 1.00 equiv), ethanol (200 mL). The resulting solution was stirred for 3 days at 60°C. The resulting mixture was concentrated under vacuum. The residue was applied onto a silica gel column with ethyl acetate/petroleum ether (1:15). This resulted in 12 g (27%) of **93** as a brown oil.

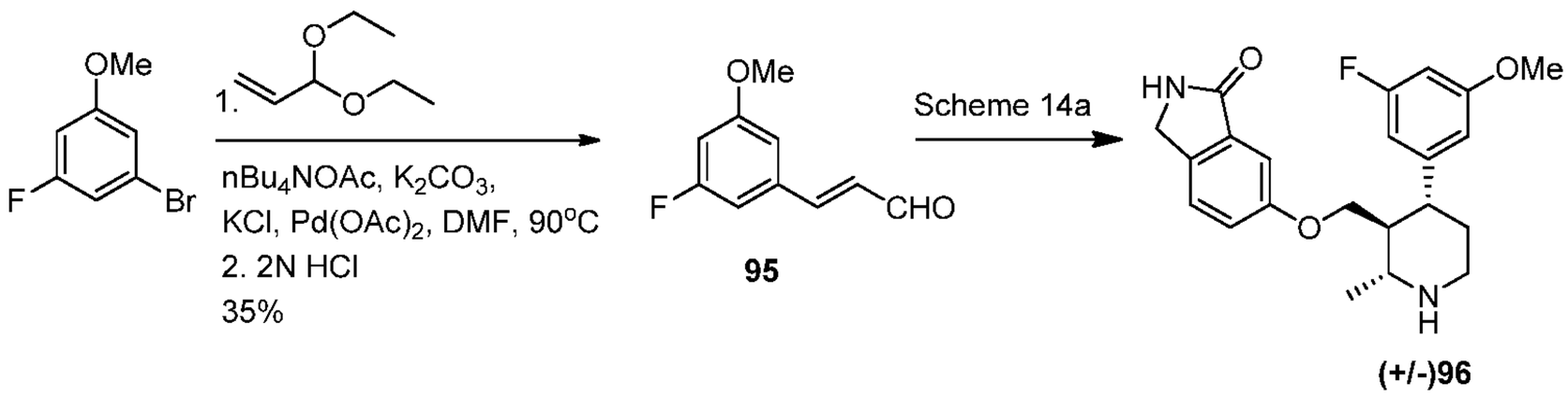
(+/-)-6-{[(trans, trans)-2-(fluoromethyl)-4-(4-methoxyphenyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one [(+/-)94]

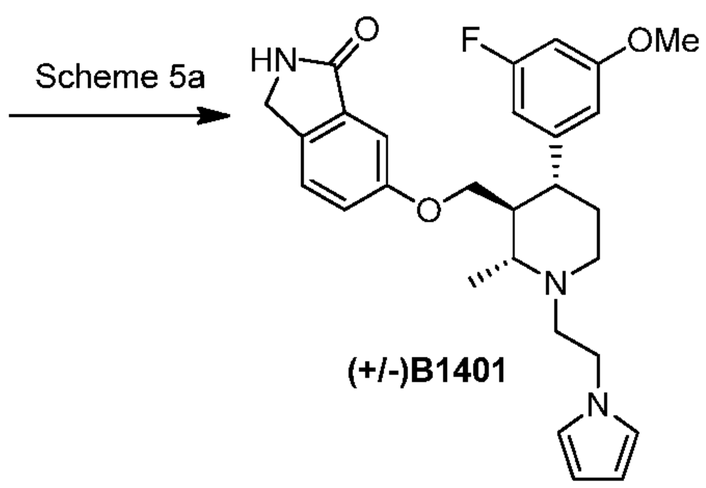
(+/-)94 may be prepared from ethyl 2-(fluoromethyl)-4-(4-methoxyphenyl)-1-[(4-methoxyphenyl)methyl]-1,4-dihydropyridine-3-carboxylate (**93**) according to Scheme 14a.

(+/-)-6-{[(trans, trans)-2-(fluoromethyl)-4-(4-methoxyphenyl)-1-(2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one [(+/-)B1216]

(+/-)B1216 may be prepared from (+/-)**94** according to Scheme 4. LCMS (M+H) 489.1.

Scheme 14j





Synthesis of (-)-6-{[trans, trans-4-(3-fluoro-5-methoxyphenyl)-2-methyl-1-[2-(1H-pyrrol-1-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one [(+/-)B1401]

(2E)-3-(3-fluoro-5-methoxyphenyl)prop-2-enal (95)

Into a 2-L round-bottom flask purged and maintained with an inert atmosphere of nitrogen, was placed 1-bromo-3-fluoro-5-methoxybenzene (45 g, 219.49 mmol, 1.00 equiv), nBu_4NOAc (132.9 g, 2.00 equiv), potassium carbonate (45.5 g, 329.21 mmol, 1.50 equiv), KCl (16.4 g, 1.00 equiv), $Pd(OAc)_2$ (1.32 g, 5.88 mmol, 0.03 equiv), N,N-dimethylformamide (1 L), 3,3-diethoxyprop-1-ene (85.8 g, 659.06 mmol, 3.00 equiv). The resulting solution was stirred overnight at 90°C. The reaction was then quenched by the addition of 500 mL of 2N hydrogen chloride. The resulting solution was extracted with 3x1 L of ethyl acetate and the organic layers combined. The resulting mixture was washed with 3x1 L of H_2O. The mixture was dried over anhydrous sodium sulfate and concentrated under vacuum. The crude product was re-crystallized from hexane. This resulted in 13 g (33%) of **95** as a yellow solid.

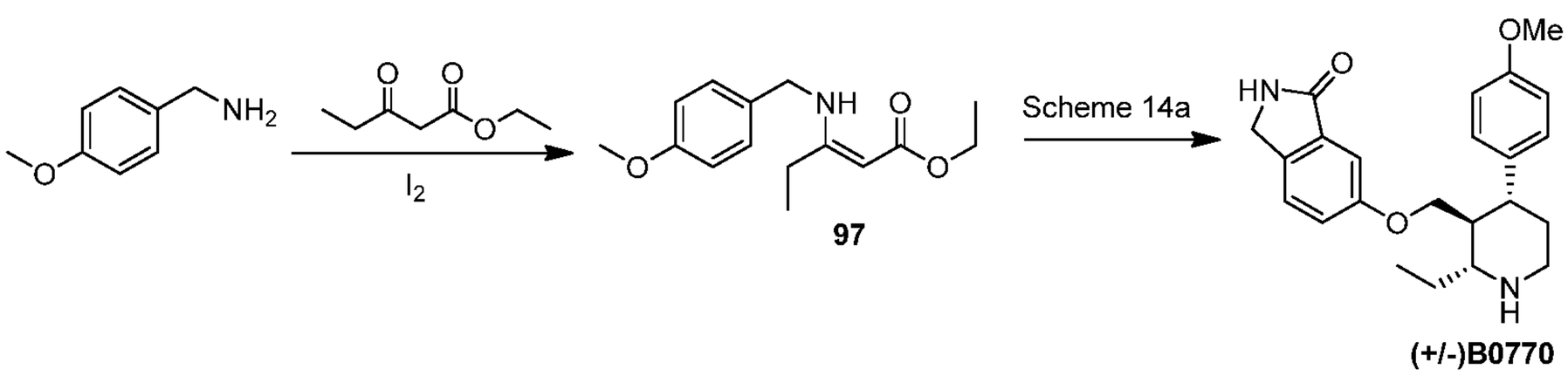
(+/-)-6-{[(trans, trans)-4-(3-fluoro-5-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one [(+/-)96]

(+/-)96 may be prepared from (2E)-3-(3-fluoro-5-methoxyphenyl)prop-2-enal (**95**) according to Scheme 14a.

(-)-6-{[trans, trans-4-(3-fluoro-5-methoxyphenyl)-2-methyl-1-[2-(1H-pyrrol-1-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one [(+/-)B1401]

(-)B1401 may be prepared from **(+/-)96** according to Scheme 5a. LCMS (M+H) 478.2

Scheme 14k



(+/-)B0770

Synthesis of (+/-)-6-{[(trans, trans)-2-ethyl-4-(4-methoxyphenyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one [(+/-)B0770]

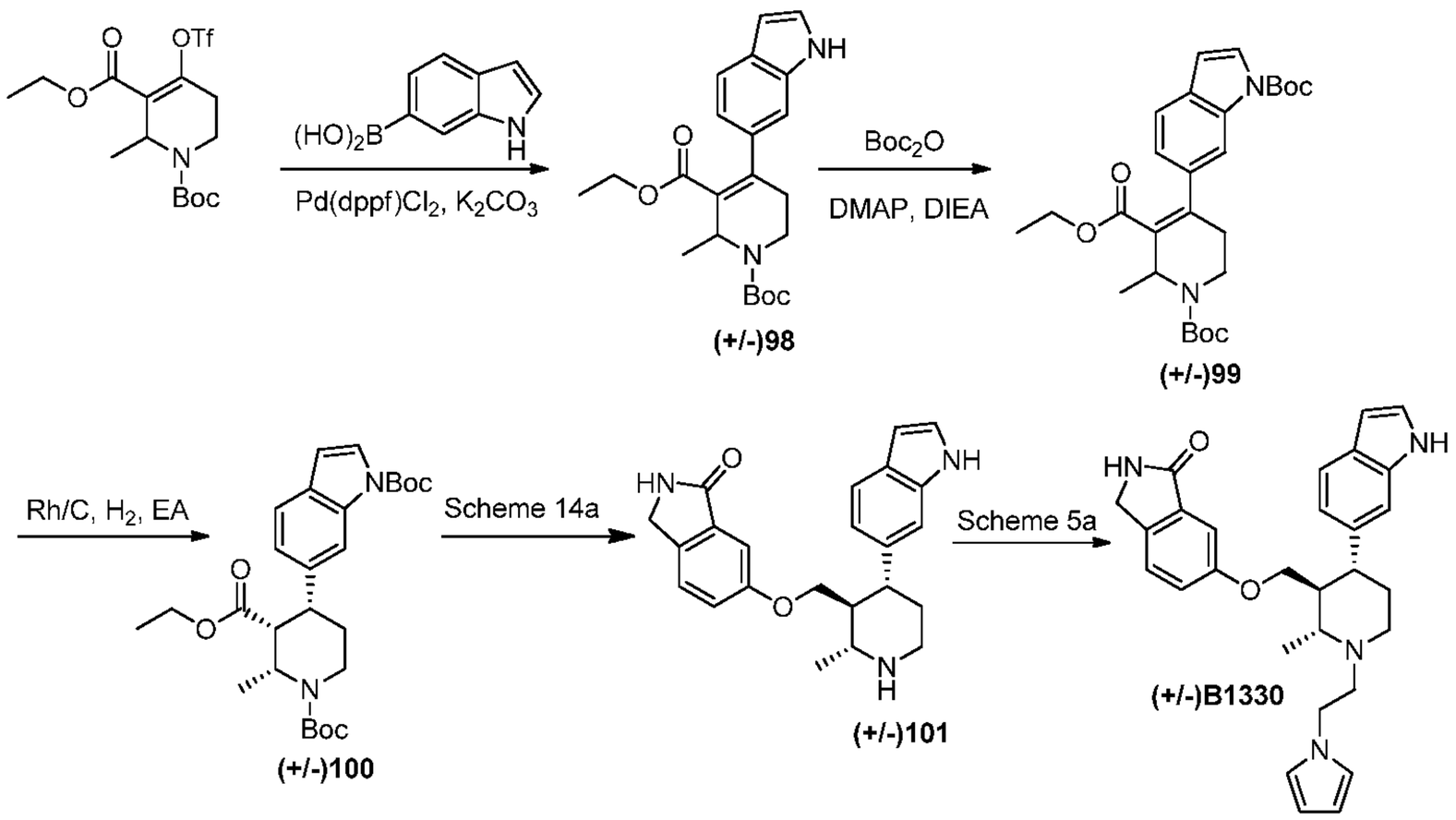
Ethyl (2Z)-3-{[(4-methoxyphenyl)methyl]amino}pent-2-enoate (97)

Into a 100-mL round-bottom flask, was placed (4-methoxyphenyl)methanamine (10 g, 72.90 mmol, 1.00 equiv), ethyl 3-oxopentanoate (10.5 g, 72.83 mmol, 1.00 equiv), iodide (1.9 g, 7.49 mmol, 0.20 equiv). The resulting solution was stirred for 20 min at 25°C. The resulting solution was diluted with 50 mL of brine. The resulting solution was extracted with 3x50 mL of dichloromethane and the organic layers combined and concentrated under vacuum. This resulted in 20 g (crude) of **97** as a red oil.

(+/-)-6-{[(trans, trans)-2-ethyl-4-(4-methoxyphenyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one [(+/-)B0770]

(+/-)B0770 may be prepared from ethyl (2Z)-3-{[(4-methoxyphenyl)methyl]amino}pent-2-enoate (**97**) according to Scheme 14a. LCMS (M+H) 381.2

Scheme 14l



Synthesis of (+/-)-6-{[(2R,3S,4R)-4-(1H-indol-6-yl)-2-methyl-1-[2-(1H-pyrrol-1-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one [(+/-)B1330

(+/-)-1-tert-Butyl 3-ethyl 4-(1H-indol-6-yl)-2-methyl-1,2,5,6-tetrahydropyridine-1,3-dicarboxylate [(+/-)98]

Into a 250-mL round-bottom flask, was placed 1-tert-butyl 3-ethyl 2-methyl-4-[(trifluoromethane)sulfonyloxy]-1,2,5,6-tetrahydropyridine-1,3-dicarboxylate (7.5 g, 17.97 mmol, 1.00 equiv), CH3COOK (5.25 g, 53.50 mmol, 3.00 equiv), a solution of dioxane (75 mL) in water (75 mL), $Pd(dppf)Cl_2$ (680 mg, 0.93 mmol, 0.05 equiv), (1H-indol-5-yl)boronic acid (2.88 g, 17.89 mmol, 1.00 equiv). The resulting solution was stirred for 1 h at 100°C in an oil bath. Then it was extracted with 3x50 mL of DCM and the organic layers combined. The resulting mixture was washed with 2x50 mL of sodium chloride. The solution was dried and concentrated under vacuum. This resulted in 5.5 g (80%) of **(+/-)98** as a white solid.

(+/-)-1-tert-Butyl 3-ethyl 4-[1-[(tert-butoxy)carbonyl]-1H-indol-6-yl]-2-methyl-1,2,5,6-tetrahydropyridine-1,3-dicarboxylate [(+/-)99]

Into a 500-mL round-bottom flask, was placed a solution of **(+/-)98** (5.4 g, 14.05 mmol, 1.00 equiv) in dichloromethane (200 mL), di-tert-butyl dicarbonate (3.37 g, 15.44 mmol, 1.10 equiv), 4-dimethylaminopyridine (514 mg, 4.21 mmol, 0.30 equiv), DIEA (3.63 g, 28.09 mmol, 2.00 equiv). The resulting solution was stirred overnight at room temperature. Then it was washed with 2x100 mL of hydrogen chloride (1M). The resulting solution was extracted with 3x200 mL of dichloromethane and the organic layers combined and dried and concentrated under vacuum. This resulted in 6 g (88%) of **(+/-)99** as a white solid.

(+/-)-1-tert-Butyl 3-ethyl (trans, trans)-4-[1-[(tert-butoxy)carbonyl]-1H-indol-6-yl]-2-methylpiperidine-1,3-dicarboxylate [(+/-)100]

Into a 25-mL round-bottom flask, was placed a solution of **(+/-)99** (80 mg, 0.17 mmol, 1.00 equiv) in EA (5 mL), Rh/C (60 mg), H_2 (3atm). The resulting solution was stirred overnight at room temperature. The solids were filtered out. The resulting mixture was concentrated under vacuum. This resulted in 70 mg (87%) of **(+/-)100** as a yellow oil.

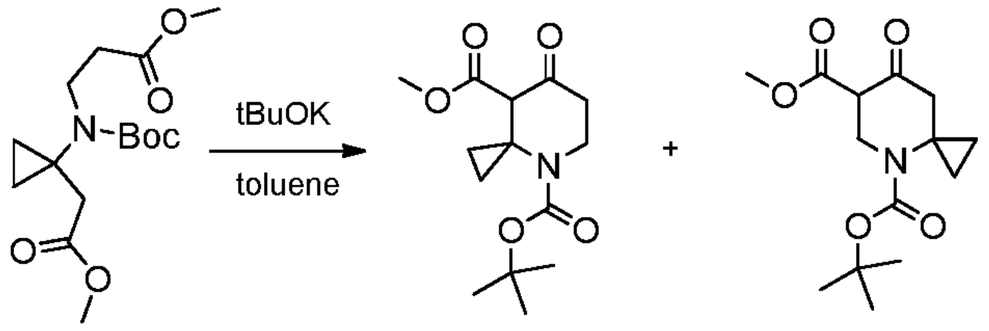
(+/-)-6-[[(trans, trans)-4-(1H-indol-6-yl)-2-methylpiperidin-3-yl]methoxy]-2,3-dihydro-1H-isoindol-1-one [(+/-)101]

[(+/-)101] may be prepared from (+/-)-1-tert-Butyl 3-ethyl (trans, trans)-4-[1-[(tert-butoxy)carbonyl]-1H-indol-6-yl]-2-methylpiperidine-1,3-dicarboxylate according to Scheme 14a.

(+/-)-6-{[(2R,3S,4R)-4-(1H-indol-6-yl)-2-methyl-1-[2-(1H-pyrrol-1-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one [(+/-)B1330]

(+/-)B1330 may be prepared from (+/-)-6-[[(trans, trans)-4-(1H-indol-6-yl)-2-methylpiperidin-3-yl]methoxy]-2,3-dihydro-1H-isoindol-1-one according to Scheme 5a. LCMS (M+H) 469.4.

Scheme14m


tBuOK
toluene
N-Boc
O
O
O
O
O
O
O
O
O
O
N
N
O
O
O
O
O
O
O
O
O
O

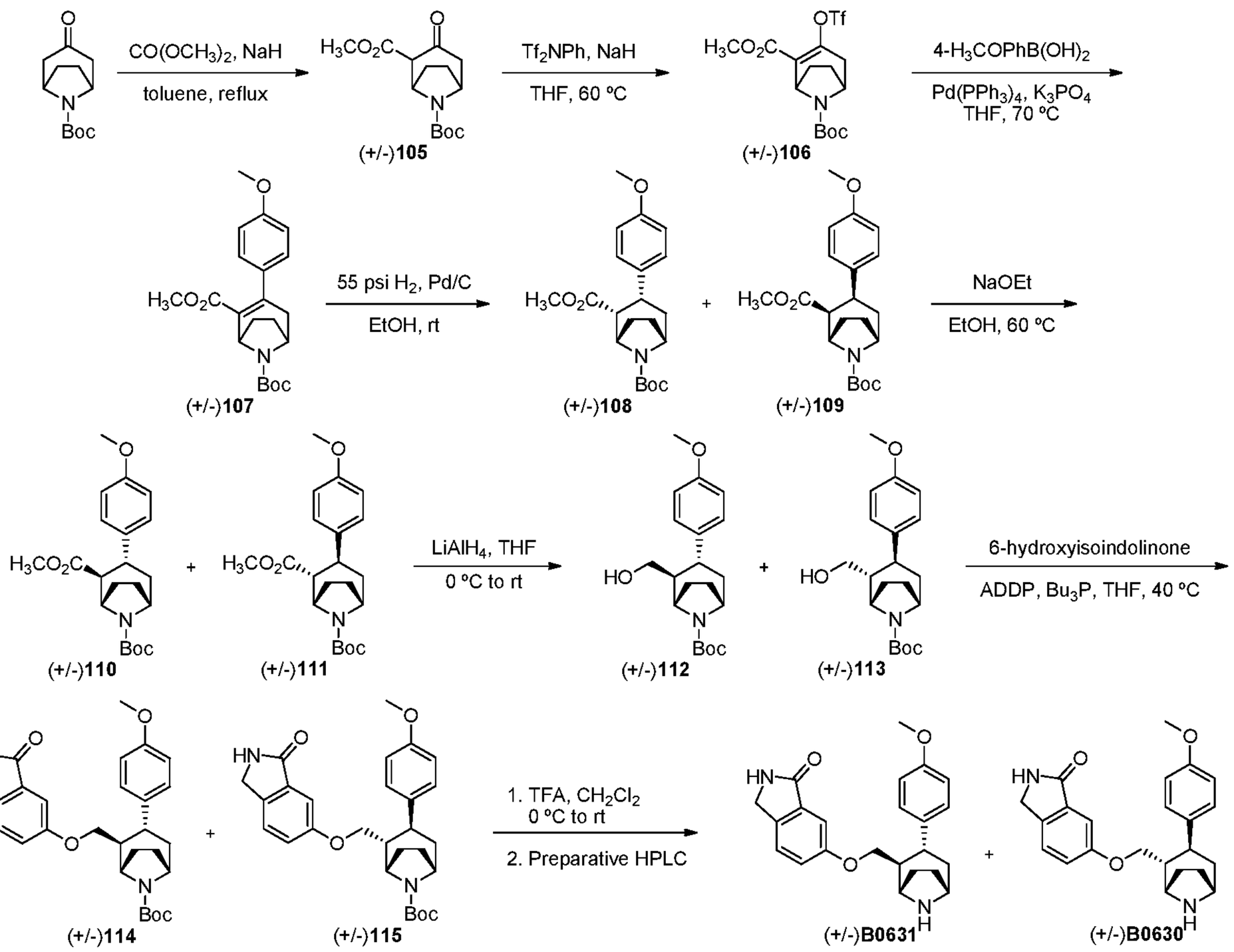
[(+/-)104] may be prepared from 4-tert-butyl 8-methyl 7-oxo-4-azaspiro[2.5]octane-4,8-dicarboxylate according to Schemes 1 and 14a.

(+/-)-6-{[(trans)-7-(4-methoxyphenyl)-4-(2-phenylethyl)-4-azaspiro[2.5]octan-8-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one [(+/-)B1126]

(+/-)B1126 may be prepared from **(+/-)**-6-{[(trans)-7-(4-methoxyphenyl)-4-azaspiro[2.5]octan-8-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one according to Scheme 4. LCMS (M+H) 483.2.

General Procedure A12: Preparation of Bridged Bicyclic 3,4-Piperidine N-H Analogs

Scheme 15



Preparation of (+/-)-*exo-trans*-6-{[3-(4-Methoxyphenyl)-8-azabicyclo[3.2.1]octan-2-yl]methoxy}isoindolin-1-one [(+/-)B0631] and (+/-)-*endo-trans*-6-{[3-(4-Methoxyphenyl)-8-azabicyclo[3.2.1]octan-2-yl]methoxy}isoindolin-1-one [(+/-)B0630]

(+/-)- 8-*tert*-Butyl 2-Methyl 3-Oxo-8-azabicyclo[3.2.1]octane-2,8-dicarboxylate [(+/-)105]

A solution of dimethyl carbonate (4.0 g, 44.4 mmol) in anhydrous toluene (20 mL) was added dropwise over 30 min to a suspension of sodium hydride (3.2 g, 82.1 mmol, 60% dispersion in mineral oil) in anhydrous toluene (60 mL) at room temperature under nitrogen, after which the mixture was heated to 80 °C. Anhydrous methanol (0.5 mL) was added, followed by the dropwise addition of a solution of commercially available (+/-)-*tert*-butyl 3-oxo-8-azabicyclo[3.2.1]octane-8-carboxylate [5.0 g, 22.2 mmol] in anhydrous toluene (20 mL) over 30 min. Stirring at 80 °C was continued for 12 h, after which the mixture was cooled to room temperature, slowly diluted with water (5 mL) and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography on silica gel, eluting with hexanes/ethyl acetate (1:1), to afford (+/-)**105** as a light yellow oil (5.4 g, 82%): LCMS (M+H) 284.

(+/-)-8-*tert*-Butyl 2-Methyl 3-{[(Trifluoromethyl)sulfonyl]oxy}-8-azabicyclo[3.2.1]oct-2-ene-2,8-dicarboxylate [(+/-)106]

Prepared according General Procedure A9 to provide (+/-)**106** as a crude amber oil (8.4 g) that was suitable for use in the next step without purification: LCMS (M+H) 416.

(+/-)-8-*tert*-Butyl 2-Methyl 3-(4-Methoxyphenyl)-8-azabicyclo[3.2.1]oct-2-ene-2,8-dicarboxylate [(+/-)107]

Prepared according General Procedure A1 to provide (+/-)**107** as a light yellow oil (5.4 g, 71% over two steps): LCMS (M+H) 374.

(+/-)-*exo-cis*-8-*tert*-Butyl 2-Methyl 3-(4-Methoxyphenyl)-8-azabicyclo[3.2.1]octane-2,8-dicarboxylate [(+/-)108] and (+/-)-*endo-cis*-8-*tert*-Butyl 2-Methyl 3-(4-Methoxyphenyl)-8-azabicyclo[3.2.1]octane-2,8-dicarboxylate [(+/-)109]

Prepared according General Procedure A1 to provide (+/-)**108** and (+/-)**109** as an inseparable mixture in an indeterminate ratio as a colorless oil (840 mg) that was suitable for use in the next step without purification: LCMS (M+H) 376.

(+/-)-*exo-trans*-8-*tert*-Butyl 2-Methyl 3-(4-Methoxyphenyl)-8-azabicyclo[3.2.1]octane-2,8-dicarboxylate [(+/-)110] and (+/-)-*endo-trans*-8-*tert*-Butyl 2-Methyl 3-(4-Methoxyphenyl)-8-azabicyclo[3.2.1]octane-2,8-dicarboxylate [(+/-)111]

Prepared according General Procedure A1 to provide (+/-)**110** and (+/-)**111** as an inseparable mixture in an indeterminate ratio as a colorless oil (730 mg, 97% over two steps): LCMS (M+H) 376.

(+/-)-*exo-trans-tert*-Butyl 2-(Hydroxymethyl)-3-(4-methoxyphenyl)-8-azabicyclo[3.2.1]octane-8-carboxylate [(+/-)112] and (+/-)-*endo-trans-tert*-Butyl 2-(Hydroxymethyl)-3-(4-methoxyphenyl)-8-azabicyclo[3.2.1]octane-8-carboxylate [(+/-)113]

Prepared according General Procedure A1 to provide (+/-)**112** and (+/-)**113** as an inseparable mixture in an indeterminate ratio as a colorless oil (510 mg, 78%): LCMS (M+H) 348.

(+/-)-*exo-trans-tert*-Butyl 3-(4-Methoxyphenyl)-2-{[(3-oxoisoindolin-5-yl)oxy]methyl}-8-azabicyclo[3.2.1]octane-8-carboxylate [(+/-)114] and (+/-)-*endo-trans-tert*-Butyl 3-(4-Methoxyphenyl)-2-{[(3-oxoisoindolin-5-yl)oxy]methyl}-8-azabicyclo[3.2.1]octane-8-carboxylate [(+/-)115]

Prepared according General Procedure A1 to provide (+/-)**114** and (+/-)**115** as an inseparable mixture in an indeterminate ratio as a colorless oil (162 mg) that was suitable for use in the next step without purification: LCMS (M+H) 479.

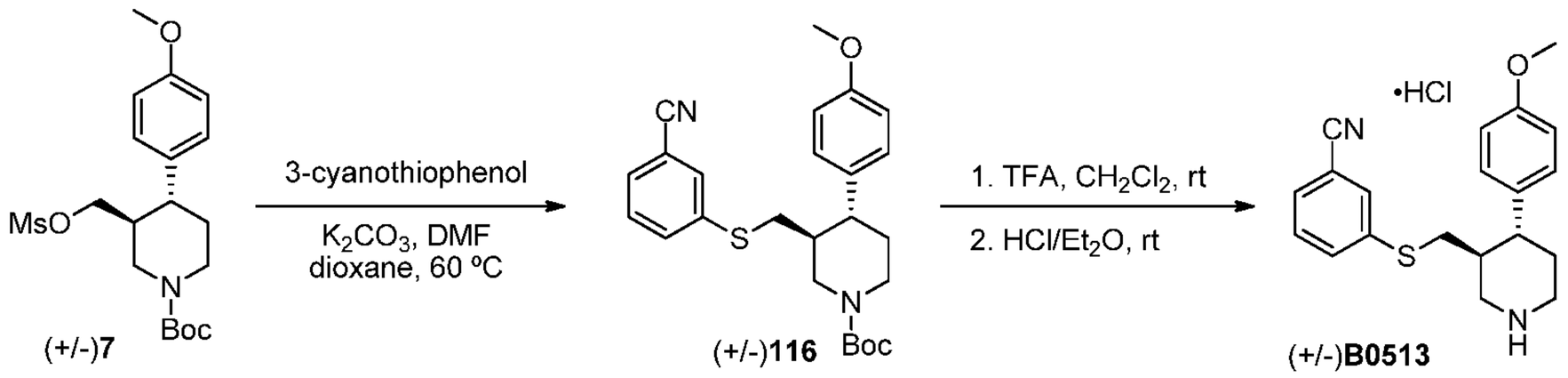
(+/-)-*exo-trans*-6-{[3-(4-Methoxyphenyl)-8-azabicyclo[3.2.1]octan-2-yl]methoxy}isoindolin-1-one [(+/-)B0631] and (+/-)-*endo-trans*-6-{[3-(4-Methoxyphenyl)-8-azabicyclo[3.2.1]octan-2-yl]methoxy}isoindolin-1-one [(+/-)B0630].

Prepared according General Procedure A1, (+/-)**B0631** was isolated as a white solid (22 mg, 8% over two steps): LCMS (M+H) 379; ^{1}H NMR (500 MHz, CD_3OD) δ 7.47 (d, J = 9.0 Hz, 1H), 7.23–7.19 (m, 4H), 6.84 (d, J = 7.0 Hz, 2H), 4.41–4.38 (m, 3H), 4.28–4.25 (m, 1H), 3.91 (dd, J = 10.0, 3.5 Hz, 1H), 3.82 (dd, J = 10.0, 6.5 Hz, 1H), 3.73 (s, 3H), 3.59–3.54 (m, 1H), 2.62 (dt, J = 14.0, 2.5 Hz, 1H), 2.45–2.44 (m, 1H), 2.36–2.33 (m, 2H), 2.25–2.20 (m, 2H), 1.97–1.92 (m, 1H). Also, (+/-)**B0630** was isolated as a white solid (18 mg, 7% over two steps): LCMS (M+H) 379; ^{1}H NMR (500 MHz, CD_3OD) δ 7.47 (d, J = 9.0 Hz, 1H), 7.25–

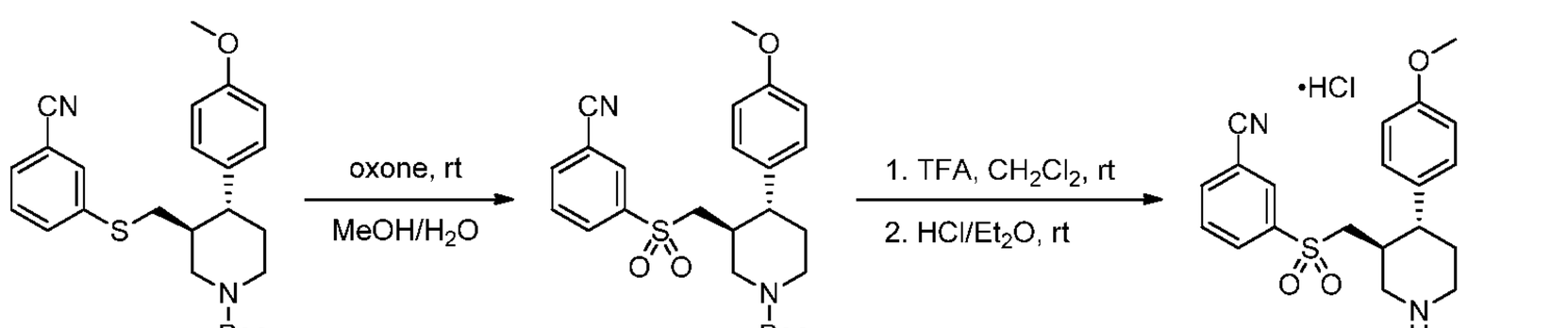
7.19 (m, 4H), 6.89 (d, J = 7.0 Hz, 2H), 4.38 (s, 2H), 4.17–4.11 (m, 2H), 3.95–3.90 (m, 1H), 3.84–3.81 (m, 1H), 3.76 (s, 3H), 2.96–2.89 (m, 1H), 2.61–2.55 (m, 1H), 2.36–2.29 (m, 2H), 2.27–2.16 (m, 2H), 2.10–2.04 (m, 1H), 1.80–1.75 (m, 1H).

General Procedures A13: Preparation of Linker-Modified 3,4-Piperidine N-H Analogs

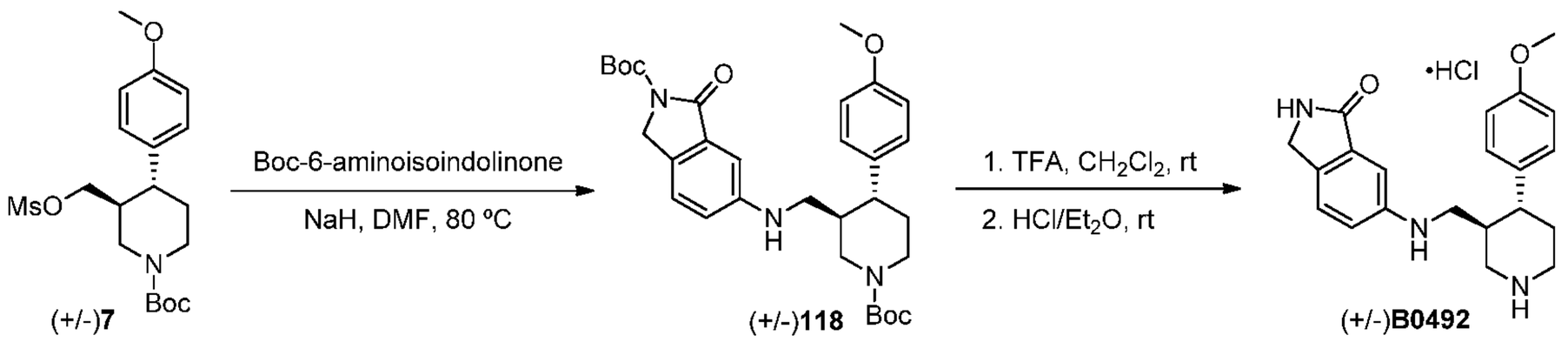
Scheme 16



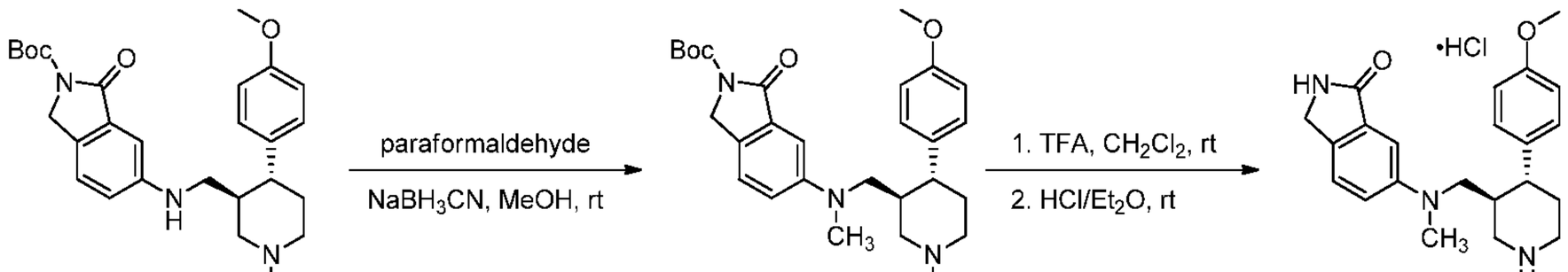
Scheme 17



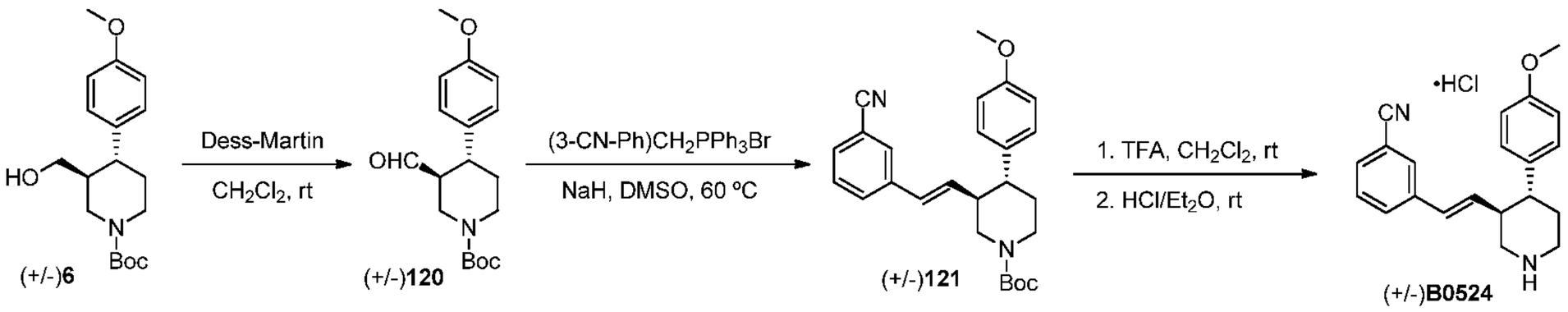
Scheme 18



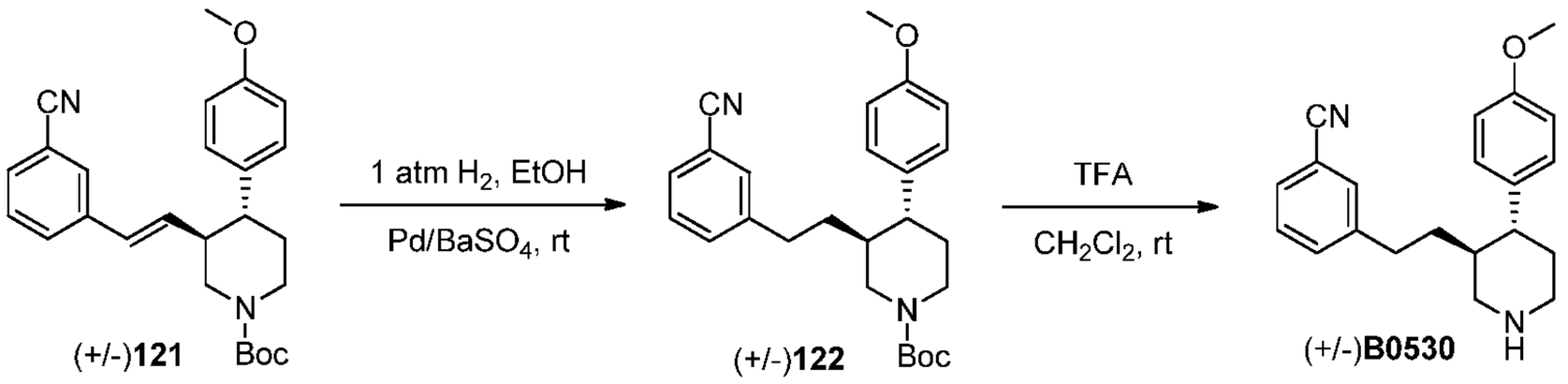
Scheme 19



Scheme 20



Scheme 21



Preparation of (+/-)-3-({[*trans*-4-(4-Methoxyphenyl)piperidin-3-yl]methyl}thio)benzonitrile Hydrochloride [(+/-)B0513], Scheme 16

(+/-)-*trans*-*tert*-Butyl 3-{[(3-Cyanophenyl)thio]methyl}-4-(4-methoxyphenyl)piperidine-1-carboxylate [(+/-)116]

Prepared according General Procedure A1 to provide (+/-)**116** as a yellow oil (170 mg, 77%): LCMS (M+H) 439.

(+/-)-3-({[*trans*-4-(4-Methoxyphenyl)piperidin-3-yl]methyl}thio)benzonitrile Hydrochloride [(+/-)B0513]

Prepared according General Procedure A1 to provide (+/-)**B0513** as a hygroscopic white solid (94 mg, 64%): LCMS (M+H) 339; ^{1}H NMR (300 MHz, CD_3OD) δ 7.58–7.53 (m, 1H), 7.43–7.39 (m, 2H), 7.32–7.29 (m, 1H), 7.09 (d, *J* = 8.8 Hz, 2H), 6.96 (d, *J* = 8.8 Hz, 2H), 3.81 (s, 3H), 3.77 (d, *J* = 2.3 Hz, 1H), 3.44 (d, *J* = 12.6 Hz, 1H), 3.16–2.86 (m, 3H), 2.73–2.55 (m, 2H), 2.19–1.81 (m, 3H).

Preparation of (+/-)-3-({[*trans*-4-(4-Methoxyphenyl)piperidin-3-yl]methyl}sulfonyl)-benzonitrile Hydrochloride [(+/-)B0538], Scheme 17

(+/-)-*trans-tert*-Butyl 3-{[(3-Cyanophenyl)sulfonyl]methyl}-4-(4-methoxyphenyl)piperidine-1-carboxylate [(+/-)117].

A solution of (+/-)-*trans-tert*-butyl 3-{[(3-cyanophenyl)thio]methyl}-4-(4-methoxyphenyl)piperidine-1-carboxylate [(+/-)**116**, 210 mg, 0.48 mmol] in methanol (3 mL) was added dropwise to a solution of Oxone (590 mg, 0.96 mmol) in water (3 mL) at 0 ºC, after which the mixture was slowly warmed to room temperature, stirring for a total of 12 h. The methanol was removed under reduced pressure and the aqueous mixture was diluted with saturated aquous sodium bicarbonate (50 mL) and extracted with methylene chloride (3 x 25 mL). The combined organic extracts were washed with brine (20 mL), the solvents were removed under reduced pressure and the residue was purified by flash column chromatography on silica gel, eluting with hexanes/ethyl acetate (1:1), to (+/-)**117** as a white solid (148 mg, 59%): LCMS (M+H) 471.

(+/-)-3-({[*trans*-4-(4-Methoxyphenyl)piperidin-3-yl]methyl}sulfonyl)-benzonitrile Hydrochloride [(+/-)B0538]

Prepared according General Procedure A1 to provide (+/-)**B0538** as a white solid (101 mg, 83%): LCMS (M+H) 371; ^{1}H NMR (500 MHz, CD_3OD) δ 8.12 (d, *J* = 7.8 Hz, 1H), 8.03 (s, 1H), 8.01 (d, *J* = 8.6 Hz, 1H), 7.79 (t, *J* = 7.9 Hz, 1H), 6.82 (d, *J* = 8.4 Hz, 2H), 6.76 (d, *J* = 8.8 Hz, 2H), 4.04 (dd, *J* = 12.8, 4.0 Hz, 1H), 3.80 (s, 3H), 3.49 (d, *J* = 12.8 Hz, 1H), 3.23 (dd, *J* = 4.8, 3.2 Hz, 1H), 3.14–2.98 (m, 3H), 2.62 (dt, *J* = 11.8, 4.0 Hz, 1H), 2.39 (dq, *J* = 10.2, 1.2 Hz, 1H), 2.03–1.84 (m, 2H).

Preparation of (+/-)-6-{[*trans*-4-(4-Methoxyphenyl)piperidin-3-yl)methyl]amino}isoindolin-1-one Hydrochloride [(+/-)B0492], Scheme 18

(+/-)-*trans-tert*-Butyl 6-({[1-(*tert*-Butoxycarbonyl)-4-(4-methoxyphenyl)-piperidin-3-yl]methyl}amino)-1-oxoisoindoline-2-carboxylate [(+/-)118]

Prepared according General Procedure A5 to provide (+/-)**118** as a crude orange oil (85 mg) that was suitable for use in the next step without purification: LCMS (M+H) 552.

(+/-)-6-{[*trans*-4-(4-Methoxyphenyl)piperidin-3-yl)methyl]amino}isoindolin-1-one Hydrochloride [(+/-)B0492]

Prepared according General Procedure A1 to provide (+/-)**B0492** as a yellow solid (8 mg, 4% over two steps): LCMS (M+H) 352; ^{1}H NMR (500 MHz, CD_3OD) δ 7.67 (d, *J* = 8.6 Hz, 2H), 7.57 (d, *J* = 7.2 Hz, 1H), 7.26 (d, *J* = 8.2 Hz, 2H), 6.85 (d, *J* = 8.0 Hz, 2H), 4.44 (d, *J* = 17.4 Hz, 1H), 4.29 (d, *J* = 17.4 Hz, 1H), 3.72 (s, 3H), 3.62–3.53 (m, 1H), 3.47 (d, *J* = 11.9 Hz, 2H), 3.18–3.09 (m, 1H), 2.96 (t, *J* = 11.6 Hz, 1H), 2.79–2.62 (m, 2H), 1.98 (s, 2H).

Preparation of (+/-)-6-{[(*trans*-4-(4-Methoxyphenyl)piperidin-3-yl)methyl](methyl)-amino}isoindolin-1-one Dihydrochloride [(+/-)B0504], Scheme 19

(+/-)-*trans*-*tert*-Butyl 6-({[-1-(*tert*-Butoxycarbonyl)-4-(4-methoxyphenyl)-piperidin-3-yl]methyl}[methyl]amino)-1-oxoisoindoline-2-carboxylate [(+/-)119]

Paraformaldehyde (13 mg, 0.45 mmol) was added to a solution of (+/-)-*trans*-*tert*-butyl 6-({[1-(*tert*-butoxycarbonyl)-4-(4-methoxyphenyl)piperidin-3-yl]methyl}amino)-1-oxoisoindoline-2-carboxylate [(+/-)**118**, 83 mg, 0.15 mmol] in methanol (5 mL) at room temperature under nitrogen and the mixture was stirred for 10 min. Sodium cyanoborohydride (28 mg, 0.45 mmol) was then added, after which the mixture was stirred at room temperature for 12 h. The mixture was diluted with water (60 mL) and extracted with methylene chloride (3 x 30 mL). The combined organic extracts were washed with brine (20 mL) and the solvents were removed under reduced pressure. The residue was purified twice by flash column chromatography on silica gel, the first time eluting with hexanes/ethyl acetate (1:9) and the second time eluting with methylene chloride/methanol (4:2), to afford (+/-)**119** as an orange oil (18 mg) that was suitable for use in the next step without purification: LCMS (M+H) 566.

(+/-)-6-{[(*trans*-4-(4-Methoxyphenyl)piperidin-3-yl)methyl](methyl)-amino}isoindolin-1-one Dihydrochloride [(+/-)B0504]

Prepared according General Procedure A1 to provide (+/-)**B0504** as a yellow solid (10 mg, 15% over two steps): LCMS (M+H) 366; ^{1}H NMR (500 MHz, CD_3OD) δ 7.72 (s, 1H), 7.67 (s, 2H), 7.24 (d, *J* = 8.2 Hz, 2H), 6.87 (d, *J* = 8.2 Hz, 2H), 4.44 (d, *J* = 17.6 Hz, 1H), 4.28 (d, *J* = 17.6 Hz, 1H), 3.70 (s, 3H), 3.59–3.54 (m, 1H), 3.46 (d, *J* = 11.7 Hz, 2H), 3.38–3.34 (m, 1H), 3.18–3.09 (m, 1H), 2.96 (t, *J* = 11.8 Hz, 1H), 2.78–2.62 (m, 2H), 2.02–1.93 (m, 2H).

Preparation of (+/-)-3-{(*E*)-2-[*trans*-4-(4-Methoxyphenyl)piperidin-3-yl]vinyl}benzonitrile Hydrochloride [(+/-)B0524], Scheme 20

(+/-)-*trans-tert*-Butyl 3-Formyl-4-(4-methoxyphenyl)piperidine-1-carboxylate [(+/-)120]

Dess-Martin periodinane (1.74 g, 4.1 mmol) was added to a solution of (+/-)-*trans-tert*-butyl 3-(hydroxymethyl)-4-(4-methoxyphenyl)piperidine-1-carboxylate [(+/-)**6**, 880 mg, 2.7 mmol, prepared as described in General Procedure A] in methylene chloride (30 mL) at room temperature under nitrogen, and the mixture was stirred for 12 h. The mixture was washed with saturated sodium bicarbonate and sodium bisulfite solutions (20 mL each) and the solvent was removed under reduced pressure. The residue was purified by flash column chromatography on silica gel, eluting with hexanes/ethyl acetate (2:1), to afford (+/-)**120** as a yellow oil (470 mg, 53%): LCMS (M+H) 320.

(+/-)-*trans-tert*-Butyl 3-[(*E*)-3-Cyanostyryl]-4-(4-methoxyphenyl)piperidine-1-carboxylate [(+/-)121]

Sodium hydride (50 mg, 1.2 mmol, 60% in mineral oil) was added to a solution of [(3-cyanophenyl)methyl]triphenylphosphonium bromide (574 mg, 1.2 mmol) in anhydrous DMSO (5 mL) at room temperature under nitrogen, and the mixture was heated to 60 °C and stirred for 2 h. The mixture was cooled to room temperature for the addition of a solution of (+/-)-*trans-tert*-butyl 3-formyl-4-(4-methoxyphenyl)piperidine-1-carboxylate [(+/-)**120**, 200 mg, 0.63 mmol] in anhydrous DMSO (5 mL), after which the mixture was heated back to 60 °C and stirred for 12 h. The cooled mixture was treated with water (0.5 mL), further diluted with saturated sodium bicarbonate solution (40 mL) and extracted with ethyl acetate (3 x 20 mL). The organic extracts were combined and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography on silica gel, eluting with hexanes/ethyl acetate (1:1), to afford (+/-)**121** as an amber oil (179 mg, 68%): LCMS (M+H) 419.

(+/-)-3-{(*E*)-2-[*trans*-4-(4-Methoxyphenyl)piperidin-3-yl]vinyl}benzonitrile Hydrochloride [(+/-)B0524]

Prepared according General Procedure A1 to provide (+/-)**B0524** as a white solid (20 mg, 90%): LCMS (M+H) 319; ^{1}H NMR (300 MHz, CD_3OD) δ 7.57–7.38 (m, 4H), 7.16 (d, *J* =

8.7 Hz, 2H), 6.84 (d, *J* = 8.8 Hz, 2H), 6.31 (d, *J* = 16.1 Hz, 1H), 6.02 (dd, *J* = 16.0, 7.7 Hz, 1H), 3.72 (s, 3H), 3.49 (t, *J* = 10.9 Hz, 2H), 3.22–3.03 (m, 2H), 2.89–2.78 (m, 2H), 2.10–1.93 (m, 2H).

Preparation of (+/-)-3-{2-[*trans*-4-(4-Methoxyphenyl)piperidin-3-yl]ethyl}benzonitrile [(+/-)B0530], Scheme 21

(+/-)-*trans*-*tert*-Butyl 3-(3-Cyanophenethyl)-4-(4-methoxyphenyl)piperidine-1-carboxylate [(+/-)122]

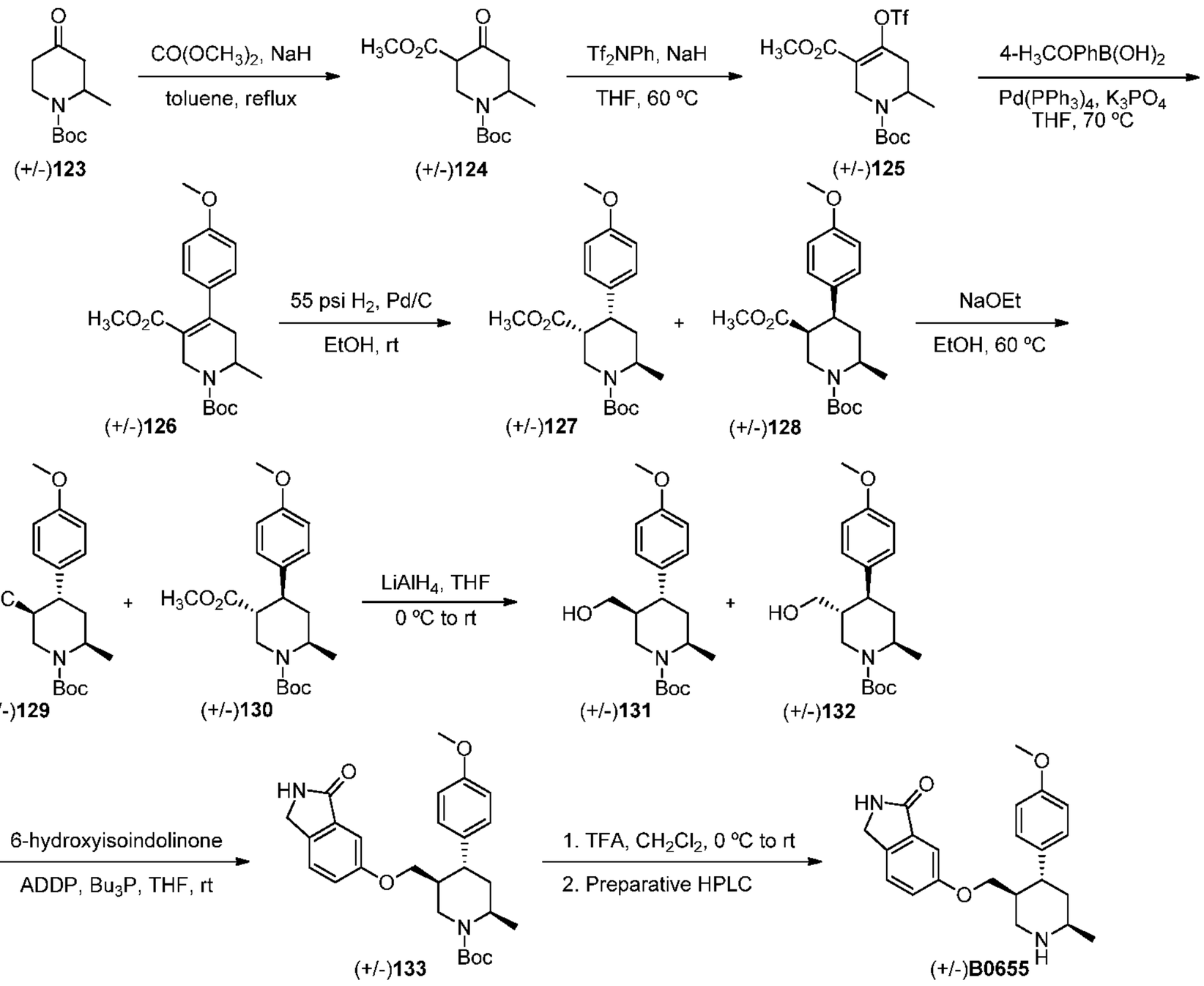
A mixture of (+/-)-*trans*-*tert*-butyl 3-[(*E*)-3-cyanostyryl]-4-(4-methoxyphenyl)piperidine-1-carboxylate [(+/-)**121**, 150 mg, 0.35 mmol] and 10% palladium on barium sulfate (100 mg) in anhydrous ethanol (10 mL) at room temperature under nitrogen was exchanged for a hydrogen atmosphere (balloon) after which the mixture stirred for 12 h. The atmosphere was exchanged for nitrogen, the mixture was diluted with methylene chloride (50 mL) and the solids were removed by filtration under reduced pressure through a plug of Celite, eluting with methylene chloride (50 mL). The organic extract solvents were removed under reduced pressure and the residue was purified by flash column chromatography on silica gel, eluting with hexanes/ethyl acetate (1:1), to afford (+/-)**122** as an amber oil (52 mg, 35%): LCMS (M+H) 421.

(+/-)-3-{2-[*trans*-4-(4-Methoxyphenyl)piperidin-3-yl]ethyl}benzonitrile [(+/-)B0530]

Prepared according General Procedure A1 to provide (+/-)**B0530** as a white solid (27 mg, 70%): LCMS (M+H) 321; ^{1}H NMR (300 MHz, CD_3OD) δ 7.51 (d, *J* = 7.6 Hz, 1H), 7.38 (t, *J* = 7.6 Hz, 1H), 7.32–7.26 (m, 2H), 7.04 (d, *J* = 8.7 Hz, 2H), 6.85 (d, *J* = 8.8 Hz, 2H), 3.78 (s, 3H), 3.48 (dd, *J* = 12.5, 3.1 Hz, 1H), 3.28–3.22 (m, 1H), 3.92 (dt, *J* = 12.5, 3.5 Hz, 1H), 2.71–2.56 (m, 2H), 2.50–2.33 (m, 2H), 1.92–1.66 (m, 3H), 1.58–1.47 (m, 1H), 1.38–1.23 (m, 1H).

<u>General Procedure A14: Preparation of 6-Methyl-3,4-Piperidine N-H Analogs</u>

Scheme 22



Preparation of (+/-)-6-{[*trans,trans*-4-(4-Methoxyphenyl)-6-methylpiperidin-3-yl]methoxy}isoindolin-1-one [(+/-)B0655], Scheme 22

(+/-)-*tert*-Butyl 3-Methyl 6-Methyl-4-oxopiperidine-1,3-dicarboxylate [(+/-)124]

Prepared according General Procedure A12 to provide (+/-)**124** as an amber oil (3.7 g, 58%): LCMS (M+H) 272.

(+/-)-1-*tert*-Butyl 3-Methyl 6-Methyl-4-{[(trifluoromethyl)sulfonyl]oxy}-5,6-dihydropyridine-1,3(2*H*)-dicarboxylate [(+/-)125]

Prepared according General Procedure A9 to provide crude (+/-)**125** as an amber oil (5.2 g) that was used in the next step without purification: LCMS (M+H) 404.

(+/-)-1-*tert*-Butyl 3-Methyl 4-(4-Methoxyphenyl)-6-methyl-5,6-dihydropyridine-1,3(2*H*)-dicarboxylate [(+/-)126]

Prepared according General Procedure A1 to afford (+/-)**126** as a light brown oil (3.7 g, 81% over two steps): LCMS (M+H) 362.

(+/-)-1-*tert*-Butyl *cis,trans*-3-Methyl 4-(4-Methoxyphenyl)-6-methylpiperidine-1,3-dicarboxylate [(+/-)-*cis,trans*-127] and (+/-)-1-*tert*-Butyl *cis,cis*-3-Methyl 4-(4-Methoxyphenyl)-6-methylpiperidine-1,3-dicarboxylate [(+/-)-*cis,cis*-128]

Prepared according General Procedure A1 to provide (+/-)-*cis,trans*-**127** and (+/-)-*cis,cis*-**128** as an inseparable mixture of an indeterminate ratio as a colorless oil (3.2 g, 85%): LCMS (M+H) 364.

(+/-)-1-*tert*-Butyl *trans,trans*-3-Methyl 4-(4-Methoxyphenyl)-6-methylpiperidine-1,3-dicarboxylate [(+/-)-*trans,trans*-129] and (+/-)-1-*tert*-Butyl *trans,cis*-3-Methyl 4-(4-Methoxyphenyl)-6-methylpiperidine-1,3-dicarboxylate [(+/-)-*trans,cis*-130]

Prepared according General Procedure A1 to provide (+/-)-*trans,trans*-**129** and (+/-)-*trans,cis*-**130** as an inseparable mixture of an indeterminate ratio as an amber oil (2.3 g, 73%): LCMS (M+H) 364.

(+/-)-1-*tert*-Butyl *trans,trans*-5-(Hydroxymethyl)-4-(4-methoxyphenyl)-2-methylpiperidine-1-carboxylate [(+/-)-*trans,trans*-131] and (+/-)-1-*tert*-Butyl *trans,cis*-5-(Hydroxymethyl)-4-(4-methoxyphenyl)-2-methylpiperidine-1-carboxylate [(+/-)-*trans,cis*-132]

Prepared according General Procedure A1 to provide (+/-)-*trans,trans*-**131** and (+/-)-*trans,cis*-**132** as an inseparable mixture of an indeterminate ratio as an amber oil (900 mg, 74%): LCMS (M+H) 336.

(+/-)-1-*tert*-Butyl *trans,trans*-4-(4-Methoxyphenyl)-2-methyl-5-{[(3-oxoisoindolin-5-yl)oxy]methyl}piperidine-1-carboxylate [(+/-)133]

Prepared according General Procedure A1 to provide crude (+/-)**133** as an amber oil (224 mg) that was used without purification in the next step: LCMS (M+H) 467.

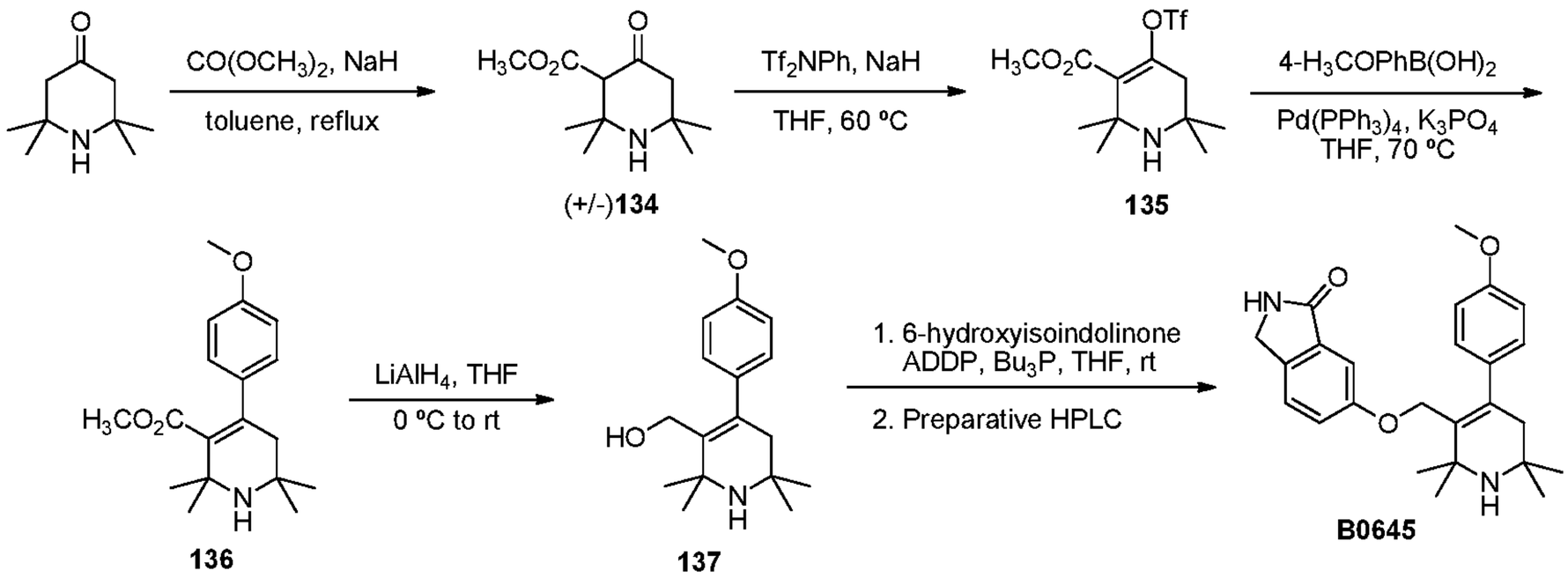
(+/-)-6-{[*trans,trans*-4-(4-Methoxyphenyl)-6-methylpiperidin-3-yl]methoxy}isoindolin-1-one [(+/-)B0655]

Prepared according General Procedure A1 to provide (+/-)**B0655** as a white solid (12 mg, 6% over two steps): LCMS (M+H) 367; ^{1}H NMR (300 MHz, CD_3OD) δ 7.45 (d, J = 9.3 Hz, 1H),

7.16–7.08 (m, 4H), 6.83 (d, *J* = 8.7 Hz, 2H), 4.37 (s, 2H), 4.04–4.00 (m, 1H), 3.73 (s, 3H), 3.67–3.48 (m, 3H), 3.27–3.04 (m, 2H), 2.10–1.96 (m, 3H), 1.46 (d, *J* = 6.6 Hz, 3H).

General Procedure A15: Preparation of Tetramethyl-3,4-Tetrahydropyridine N-H Analogs

Scheme 23



Preparation of 6-{[4-(4-Methoxyphenyl)-2,2,6,6-tetramethyl-1,2,5,6-tetrahydropyridin-3-yl]methoxy}isoindolin-1-one [B0645], Scheme 23

(+/-)-Methyl 2,2,6,6-Tetramethyl-4-oxopiperidine-3-carboxylate [(+/-)134]

Prepared according General Procedure A12 to afford (+/-)**134** as a brown oil (5.6 g, 77%): LCMS (M+H) 214.

Methyl 2,2,6,6-Tetramethyl-4-{[(trifluoromethyl)sulfonyl]oxy}-1,2,5,6-tetrahydropyridine-3-carboxylate (135)

Prepared according General Procedure A9 to provide crude **135** as a colorless oil (7.5 g) that was used in the next step without purification: LCMS (M+H) 346.

Methyl 4-(4-Methoxyphenyl)-2,2,6,6-tetramethyl-1,2,5,6-tetrahydropyridine-3-carboxylate (136)

Prepared according General Procedure A1 to provide **136** as a brown oil (3.5 g, 53% over two steps): LCMS (M+H) 304.

[4-(4-Methoxyphenyl)-2,2,6,6-tetramethyl-1,2,5,6-tetrahydropyridin-3-yl]methanol (137)

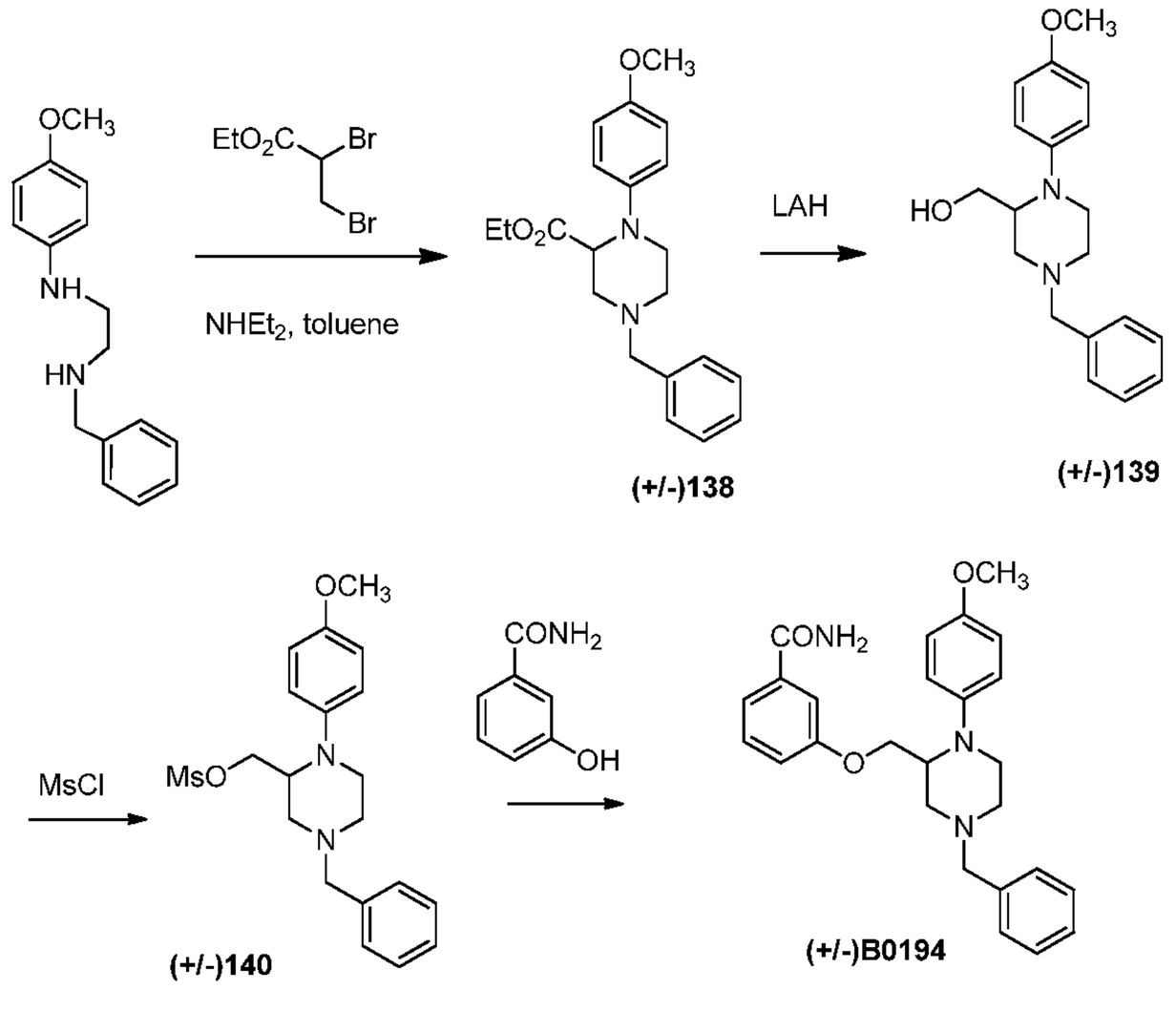
Prepared according General Procedure A1 to provide **137** as an off-white solid (2.3 g, 76%): LCMS (M+H) 276.

6-{[4-(4-Methoxyphenyl)-2,2,6,6-tetramethyl-1,2,5,6-tetrahydropyridin-3-yl]methoxy}isoindolin-1-one (B0645)

Prepared according General Procedure A1 to provide **B0645** as a white solid (92 mg, 31%): LCMS (M+H) 407; ^{1}H NMR (300 MHz, CD_3OD) δ 7.45 (d, J = 8.1 Hz, 1H), 7.23 (d, J = 8.7 Hz, 2H), 7.15–7.11 (m, 2H), 6.85 (d, J = 8.7 Hz, 2H), 4.76–4.72 (m, 2H), 4.39–4.35 (m, 2H), 3.73 (s, 3H), 2.69–2.65 (m, 2H), 1.74 (s, 6H), 1.57 (s, 6H).

General Procedure A16: Preparation of Piperazine Analogs

Scheme 24



Preparation of (+/-)-3-{[4-benzyl-1-(4-methoxyphenyl)piperazin-2-yl]methoxy}benzamide [(+/-)B0194]

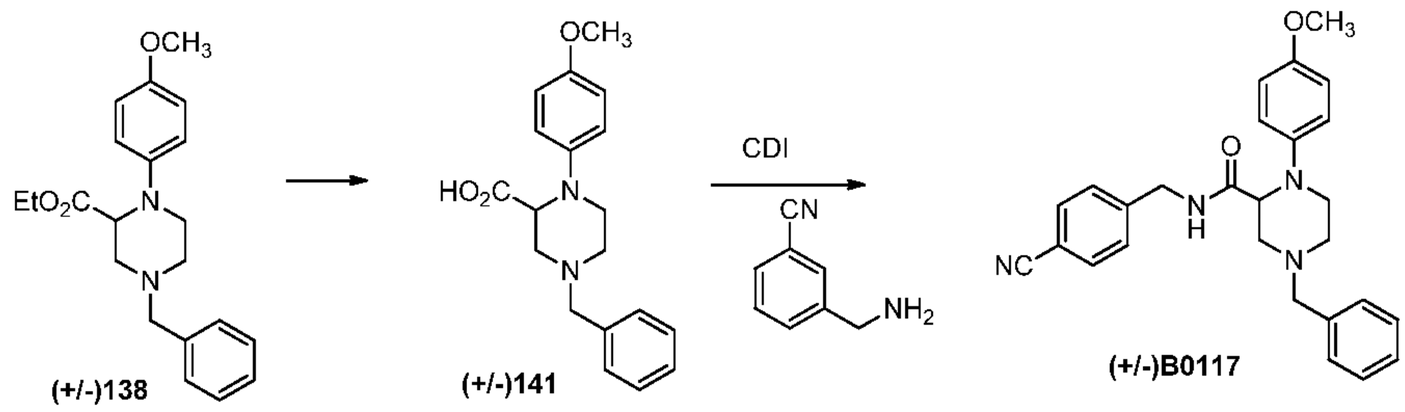
Ethyl 4-benzyl-1-(4-methoxyphenyl)piperazine-2-carboxylate [(+/-)138]

A solution of benzyl ({2-[(4-methoxyphenyl)amino]ethyl})amine (**137**, 8.15 g) and diethylamine (18 mL) in toluene was added dropwise to a solution of the ethyl 2,3-dibromopropanoate (9 mL) in toluene at 50^0C. The reaction was heated to 100^0C for 6h then cooled to room temperature. The reaction was partitioned between EtOAc (250 mL) and water 9100 mL). The organics were separated off, washed with brine and dried over Na_2SO_4. Evaporation of the solvent gave an oil which was purified on silica gel to give 2.5 g of **(+/-)138**.

3-{[4-Benzyl-1-(4-Methoxyphenyl)piperazin-2-yl]methoxy}benzamide [(+/-)B0194]

The title compound was prepared by General procedure A1 to yield **(+/-)B0194**. LCMS (M+H) 432.

Scheme 25



Preparation of (+/-)-4-benzyl-N-[(4-cyanophenyl)methyl]-1-(4-methoxyphenyl)piperazine-2-carboxamide

4-Benzyl-1-(4-methoxyphenyl)piperazine-2-carboxylic acid [(+/-)141]

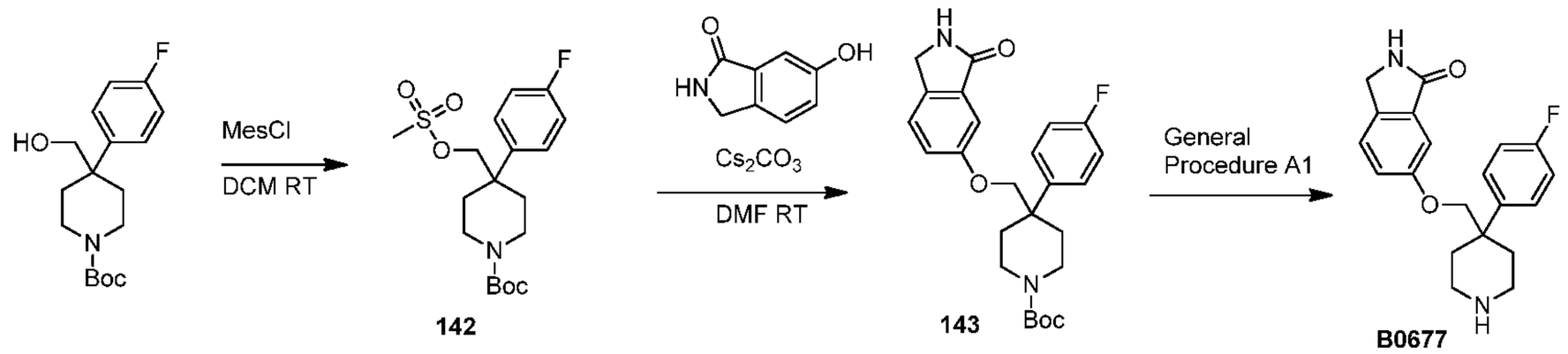
A solution of (+/-)-ethyl 4-benzyl-1-(4-methoxyphenyl)piperazine-2-carboxylate [**(+/-)138**, 0.32 g, 0.9 mmol] in THF was added to a solution of LiOH (60 mg, 3 mmol) in EtOH-water and stirred for 18h at room temperature. The reaction mixture was treated to pH 5 with 10% HCl and then extracted with three 20 mL portions of EtOAc. The organics were combined and washed with brine and dried over Na_2SO_4. The solvent was evaporated to give **(+/-)141** as an oil.

(+/-)-4-Benzyl-N-[(4-cyanophenyl)methyl]-1-(4-methoxyphenyl)piperazine-2-carboxamide [(+/-)B0117]

(+/-)-4-Benzyl-1-(4-methoxyphenyl)piperazine-2-carboxylic acid [**(+/-)141,** 87.5 mg, 0.23 mmol] and CDI were stirred together in 2 mL ACN for 2 h. 4-cyanobenzylamine (37.8 uL, 0.35 mmol) added and the reaction stirred overnight. The solvent was then evaporated in vacuo and the residue passed through a silica gel column 1:1 DCM:EtOAc to give 99.6 mg (98%) of **(+/-)B0117** as an oil. LCMS (M+H) 441.

General Procedure A17: Preparation of 1,1-Disubstituted Piperidine Analogs

Scheme 26



Preparation of 6-{[4-(4-Fluorophenyl)piperidin-4-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one (B0677)

tert-Butyl 4-(4-fluorophenyl)-4-[(methanesulfonyloxy)methyl]piperidine-1-carboxylate (142)

To a solution of the commercially available tert-butyl 4-(4-fluorophenyl)-4-(hydroxymethyl)piperidine-1-carboxylate (68 mg, 0.22 mmol) and triethylamine (92 mL, 0.66 mmol) in dichloromethane at 0°C was added methanesulfonyl chloride (26 mL, 0.33 mmol) dropwise. After 30 min, the mixture was warmed to rt. After 1h, the mixture was quenched with 1 mL of NH_4Cl statured solution and the aqueous was extracted with dichloromethane (3X5 mL). The organics were pass through phase separator and concentrated to give **142** in quantitative yield. LCMS (M+Na = 410.1)

tert-Butyl 4-(4-fluorophenyl)-4-{[(3-oxo-2,3-dihydro-1H-isoindol-5-yl)oxy]methyl}piperidine-1-carboxylate (143)

A solution of 4-(4-fluorophenyl)-4-[(methanesulfonyloxy)methyl]piperidine-1-carboxylate (**142,** 85 mg, 0.22 mmol), isoindolinone (45 mg, 0.22 mmol) and Cs_2CO_3 (358 mg, 1.1 mmol) in 2.2 mL of *N,N*-dimethylformamide was stirred at RT. After 30 min, the mixture was heated to gradually 120°C over 10 h with 2 h interval at every 20°C from 20°C. Then,

the mixture was quenched with 1 mL of NH_4Cl statured solution and the aqueous was extracted with dichloromethane (3X5 mL). The organics were passed through a phase separator and concentrated to give **143** in 40% yield. LCMS (M+Na = 463.1).

6-{[4-(4-Fluorophenyl)piperidin-4-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one (B0677)

The title compound was prepared by General Procedure A1 from tert-butyl 4-(4-fluorophenyl)-4-{[(3-oxo-2,3-dihydro-1H-isoindol-5-yl)oxy]methyl}piperidine-1-carboxylate **(B0677)** at the scale of 5 mg in 12% yield. LCMS of product peak (M+H = 341.1); ^1H NMR (400 MHz, CD_3CN) δ 7.53 (dd, *J* = 8.7, 5.3, 2H), 7.40 (d, *J* = 8.3, 1H), 7.17 (t, *J* = 8.8, 3H), 7.07 (d, *J* = 8.2, 1H), 6.77 (s, 1H), 4.29 (s, 2H), 4.05 (s, 2H), 3.33 (s, 2H), 2.98 (s, 2H), 2.49 (d, *J* = 13.9, 2H), 2.33 (d, *J* = 12.1, 2H).

The compounds depicted in Figure 1 were prepared according to the methods described herein or the schemes were modified by routine modifications to prepare the compounds depicted in Figure 1.

Example 2: Compounds are Effective as Modulators of delta (δ)-opioid receptor

The compounds described herein were tested as modulators of δ-opioid receptor. The compounds were found to be modulators of the receptors activity. Some of the compounds inhbited the β-arrestin pathway and the G-protein mediated pathway, whereas others would agonize or enhance either the β-arrestin mediated pathway or the G-protein mediated pathway. The activity was measured according to the methods described herein. The compounds described herein were also tested as modulators of μ and κ-opioid receptor.

In vitro assay

Plasmids encoding delta-opioid receptor (Accession NP_000902), mu-opioid receptor (Accession NP_000905) and kappa-opioid receptor (Accession Assession NP_000903) were generated in the pCMV-Prolink backbone and transfected into an EA-arrestin parental human embryonic kidney (HEK-293) cell line from DiscoveRx Corporation. Clonal stable lines were subsequently selected under G418.

Cell Culture and plating

Cell lines were grown adherently in Minimum Essential Media (Cellgro cat # 10-010-CM) containing 10% fetal bovine serum (Hyclone cat # SH30071.03), 4 mM glutamine (Cellgro cat # 25-005-CI), 150 ug/ml hygromycin B (Cellgro cat # 30-240-CR), 150 ug/ml G418

(Cellgro cat # 30-234-CR), and 50 u/ 50ug penicillin/streptomycin (Lonza cat # 17-603E). Prior to the assay cells were removed from the flasks with CellStripper (Cellgro cat # 25-056-CI), repeatedly pipetted to disperse cells, and spun at low speed for 5 min at room temperature. Cells were then resuspended at 250,000 cells/ml in growth media and plated at 5,000 cells/well in 384 well plates (Greiner part # 784080). Plates were incubated overnight at 37°C, 5% CO2 in a humidified incubator.

cAMP Assay

Receptor G-protein mediated responses were determined by measuring changes in intracellular cAMP using CisBio HTRF cAMP HiRange kit (cat # 62AM6PEJ) based on time-resolved fluorescence resonance energy transfer (TR-FRET). Growth media was removed and replaced with Ham's F12 containing IBMX (500 uM), NKH-477 (1 uM, a water soluble forskolin derivative) and test or control compounds at the desired concentrations. Following a 30 minute incubation at 37°C the components of the cAMP HiRange kit were added as directed and the plates were read after 1 hour on a BMG PheraStar plate reader. Responses were measured as the ratio of fluorescence at 665 nm / 620nm per manufacturer's instructions.

β-arrestin Assay

Receptor mediated beta-arrestin recruitment was determined using the DiscoveRx β-arrestin PathHunter Detection kit (cat # 93-0001). In this system, β-Arrestin is fused to an N-terminal deletion mutant of β-galactosidase (termed the enzyme acceptor of EA) and the GPCR of interest is fused to a smaller (42 amino acids), weakly complementing fragment termed ProLink™. In cells that stably express these fusion proteins, ligand stimulation results in the interaction of β-arrestin and the Prolink-tagged GPCR, forcing the complementation of the two β-galactosidase fragments and resulting in the formation of a functional enzyme that converts substrate to detectable signal. Growth media was removed and replaced with Ham's F12 containing HEPES (10 mM), IBMX (500 uM), NKH-477 (1 uM) and test or control compounds at the desired concentrations. Following a 60 minute incubation at 37°C the components of the DiscoveRx β-arrestin PathHunter Detection kit were added as directed and the plates were read after 1 hour on a BMG PheraStar plate reader.

The data for the compounds described herein is shown in Figure 2.

In vitro experiments for paroxetine a non-selective agonist was also collected. Representative data is shown here:

	hDOR G pEC50	hDOR G Span	hDOR G N	hDOR B pEC50	hDOR B Span	hDOR B N
Paroxetine	<6	<100	8	<6	<100	9

Many of the compounds were found to be selective against the delta-opioid receptor as indicated by the data, which is in contrast to the non-selectivity of paroxetine.

Example 3

Compounds Are Effective for Treating Depression and Anxiety

Assessment of activity in the tail suspension test (TST):

The compounds indicated below were determined to be efficacious and were evaluated for side effects in an *in vivo* model.

The experiments were performed using adult male C57 mice (6-10 weeks of age, 20-30 g, Hilltop Lab, PA). The mice were housed in standard rodent cages with stainless steel mesh wire bar lids in groups of 4 with controlled temperature and light cycle (6:00 a.m. – 6:00 p.m.). Animals were given free access to food (Harlan Teklad Global 18% protein (Madison, WI)) and water during a minimum 2-day habituation period to the laboratory. Animals that were used in the study were handled, housed, and sacrificed (using compressed CO_2) in accord with the current NIH guidelines regarding the use and care of laboratory animals, and all applicable local, state, and federal regulations and guidelines. Animals are identified by cage number, and by markings applied to the proximal tip of the tail using a permanent marker. Group sizes (n=8, and therefore 30-50 animals per study) provide reliable estimates of treatment effects, and this species and strain of mouse has been recognized as appropriate for pharmacology studies.

To measure efficacy of the compounds the compounds were tested using a tail suspension test. The tail suspension test is a behavioral test used to evaluate the efficacy of antidepressant drugs in rodents. In the TST, mice (n=8/group) were suspended by the tail

with tape approximately 30-50 cm above the lab bench. Mice are positioned such that the base of their tail is perpendicular to the lab bench. Each mouse is given 1 trial that last 6 minutes. The total duration of immobility is calculated as the percentage of time that the mouse is immobile. The duration of immobility is the main parameter measured. This is calculated from the cumulated time during which the animals is absent of initiated movements including passive swaying. When antidepressant drugs are administered, immobility is decreased by a variety of classes of antidepressant drugs. One or more of the compounds show antidepressant activity.

The compounds were also tested for side effects. The side effect tested is Acute Seizure Liability. Animals will acclimate to the vivarium for at least 48 hr prior to behavioral testing. Mice were placed into a glass jar (8 cm wide x 17 cm tall for mice, 17 cm wide x 31 cm tall for rats). Animals are administered various doses of test compounds at specified times prior to testing. Test drugs are administered by any of the following routes: s.c., p.o., i.v., or i.p. using a 1-2 ml/100g injection volume (mice) or 1-5 ml/kg injection volume (rat). II volumes will not exceed 2 ml and the tail vein is utilized for injection. Immediately after the injection, the animal is placed in the observational glass jar. Animals are observed for a minimum of 30 minutes for the presence of seizure-like behaviors. The behavior will be rated absent, mild, or severe. One or more of the compounds showed no significant side effects at relevant doses.

The compounds below were found to be effective in the TST model at the doses indicated, although other doses may also be active. Other compounds described herein were not necessarily tested, but are expected to be able have some level of efficacy. The data for TST activity are shown in the following table.

Compound	**TST Route**	**Active* TST Dose (mg/kg)**	**Compound**	**TST Route**	**Active* TST Dose (mg/kg)**	**Compound**	**TST Route**	**Active* TST Dose (mg/kg)**
B0060	sc	≤ 10	B0874	sc, po	≤ 30	B1097	sc	≤ 10
B0080	sc	≤ 60	B0875	po	≤ 30	B1112	sc, po	≤ 60
B0136	sc	≤ 30	B0876	sc, po	≤ 30	B1113	sc	≤ 10
B0292	sc	≤ 30	B0878	sc, po	≤ 60	B1114	sc, po	≤ 10
B0374	sc	≤ 60	B0880	sc	≤ 30	B1117	sc, po	≤ 30
B0595	sc	≤ 10	B0887	po	≤ 30	B1121	sc	≤ 10
B0635	sc, po	≤ 10	B0888	sc, po	≤ 30	B1122	sc	≤ 10
B0637	sc	≤ 10	B0889	sc	≤ 10	B1128	sc	≤ 10
B0660	sc	≤ 10	B0896	po	≤ 60	B1129	sc	≤ 10
B0673	sc	≤ 10	B0902	sc, po	≤ 10	B1130	sc, po	≤ 30
B0674	sc	≤ 10	B0905	sc, po	≤ 60	B1134	sc	≤ 10

B0681	sc, po	≤ 10	B0906	sc, po	≤ 30	B1135	sc	≤ 10
B0683	sc, po	≤ 10	B0911	sc	≤ 10	B1137	sc	≤ 10
B0685	sc	≤ 10	B0915	po	≤ 60	B1142	sc, po	≤ 60
B0697	po	≤ 30	B0917	sc, po	≤ 30	B1145	sc, po	≤ 10
B0701	sc, po	≤ 10	B0918	sc, po	≤ 60	B1147	po	≤ 60
B0702	po	≤ 30	B0931	sc	≤ 10	B1148	sc, po	≤ 60
B0704	sc, po	≤ 30	B0935	sc	≤ 10	B1156	sc	≤ 10
B0705	sc, po	≤ 10	B0937	sc, po	≤ 30	B1161	sc	≤ 10
B0707	sc, po	≤ 30	B0942	sc	≤ 30	B1162	sc, po	≤ 60
B0708	sc, po	≤ 10	B0945	sc, po	≤ 60	B1165	sc, po	≤ 60
B0720	sc, po	≤ 10	B0947	po	≤ 60	B1166	po	≤ 60
B0721	po	≤ 10	B0948	po	≤ 60	B1168	po	≤ 60
B0722	po	≤ 10	B0949	sc	≤ 10	B1171	sc	≤ 10
B0724	po	≤ 30	B0950	sc, po	≤ 60	B1187	sc	≤ 10
B0727	po	≤ 60	B0966	sc, po	≤ 60	B1194	sc	≤ 10
B0743	sc	≤ 10	B0981	sc	≤ 10	B1205	sc, po	≤ 30
B0746	sc, po	≤ 10	B0995	sc, po	≤ 60	B1209	sc	≤ 10
B0754	sc, po	≤ 30	B0997	sc	≤ 10	B1210	sc	≤ 10
B0757	sc, po	≤ 60	B1008	sc	≤ 10	B1211	sc	≤ 10
B0760	sc	≤ 10	B1009	sc	≤ 10	B1212	sc	≤ 10
B0763	sc	≤ 10	B1023	sc, po	≤ 30	B1213	sc	≤ 10
B0764	po	≤ 60	B1031	sc	≤ 10	B1221	sc	≤ 10
B0766	po	≤ 10	B1033	sc	≤ 10	B1223	sc	≤ 10
B0774	sc, po	≤ 60	B1038	sc	≤ 10	B1227	sc	≤ 10
B0775	po	≤ 30	B1039	sc	≤ 10	B1229	sc	≤ 10
B0779	sc, po	≤ 10	B1043	sc	≤ 10	B1231	sc	≤ 10
B0787	po	≤ 10	B1047	sc	≤ 10	B1243	sc	≤ 10
B0795	sc	≤ 10	B1049	sc, po	≤ 30	B1256	sc	≤ 30
B0801	sc, po	≤ 30	B1050	sc, po	≤ 30	B1260	sc	≤ 10
B0837	po	≤ 10	B1051	sc	≤ 10	B1274	sc	≤ 10
B0838	sc, po	≤ 10	B1052	sc	≤ 10	B1300	sc	≤ 10
B0839	sc, po	≤ 10	B1056	sc	≤ 10	B1317	sc	≤ 10
B0840	sc, po	≤ 30	B1058	sc	≤ 10	B1332	sc	≤ 10
B0841	po	≤ 60	B1064	sc	≤ 10	B1350	sc	≤ 10
B0858	sc	≤ 10	B1066	sc	≤ 10	B1352	sc	≤ 10
B0861	sc	≤ 10	B1078	sc, po	≤ 30	B1356	sc	≤ 10
B0863	sc	≤ 10	B1079	sc, po	≤ 30	B1365	sc	≤ 10
B0864	sc, po	≤ 30	B1087	sc	≤ 10	B1401	sc	≤ 10
B0867	sc	≤ 10	B1089	sc	≤ 10			
B0868	sc, po	≤ 10	B1094	sc	≤ 10			
* $p < 0.05$ compared to vehicle-treated mice								

5

Example 4: Compounds are Effective for Treating Inflammation and Pain

Assessment of Tactile Allodynia Produced by Intraplantar Freund's Complete Adjuvant in mice and rats:

Animals were acclimated to the vivarium for at least 48 hr prior to behavioral testing. Inflammation was induced for both rodent species with the administration of an intraplantar (subcutaneous injection into the plantar surface of the hind paw, i.pl.) injection of 0.10 ml Freund's Complete Adjuvant (FCA).

For mouse studies, the experiments were conducted 48 hours after FCA administration. Tactile allodynia was measured using a series of von Frey monofilaments. These filaments are bendable, plastic and intended to poke, not penetrate, the skin. Animals were placed in a Plexiglas chamber (approximately 10 cm x 20 cm x 25 cm) and allowed to habituate for 5 - 10 minutes. The chamber was positioned on top of a mesh screen so that von Frey monofilaments can be presented to the plantar surface of the hind paw that is inflamed. The measurement of tactile sensitivity for the injected hind paw is obtained using the up/down method (LaBuda and Little, 2005, J Neurosci. Methods, 144, 175) with seven von Frey monofilaments (0.07, 0.16, 0.4, 0.6, 1, and 2 grams). Each trial will start with a von Frey force of 0.6 grams delivered to the hind paw for approximately 1 – 2 seconds. If there was no withdrawal response, the next higher force was be delivered. If there was a response, the next lower force was delivered. This procedure was performed until no response was made at the highest force (2 grams) or until four stimuli are administered following the initial response. The 50% paw withdrawal threshold for the hind paw was be calculated using the following formula: $[Xth]log = [vFr]log + ky$ where [vFr] is the force of the last von Frey used, k is the average interval (in log units) between the von Frey monofilaments, and y is a value that depends upon the pattern of withdrawal responses (Dixon, Annual Review Pharmacol Toxicol, 1980, 20, 441).

For rat studies, the experiments were conducted 24 hours after CFA administration. Rats are tested for mechanical allodynia in a Randall-Selitto apparatus. The inflamed paw is put on a pedestal and a pointed force of increasing intensity (0 to 250 grams) is applied to the paw. When the animal struggles to withdraw from the force the test is stopped and the force to induce that struggle is recorded. Data may be presented as mean grams of force to withdrawal or a percentage of the maximum possible effect.

The compounds below were found to be effective in the CFA model at the doses indicated, although other doses may also be active. Other compounds described herein were not necessarily tested, but are expected to be able have some level of efficacy.

Compound	**Species**	**CFA Route**	**Active* CFA Dose (mg/kg)**
B0136	mouse	sc	≤ 60
B0292	mouse	sc	≤ 60
B0707	mouse	po	≤ 30
	rat	sc	≤ 10
B0720	rat	sc	≤ 30
B1049	mouse	sc	≤ 10
	rat	sc	≤ 10
B1145	mouse	sc	≤ 10
* $p < 0.05$ compared to vehicle-treated mice			

Exampmle 5: Compounds are Effective for Treating Migraines

Assessment of tactile allodynia produced by nitroglycerin:

Compounds were tested for efficacy in rodent models of nitroglycerine induced migraine. In this model both rats and mice can be induced to have a behavioral response consistent with the progression of a migraine attack by the intraperitoneal injection of nitroglycerin. In this test mice or rats (n=8/group) are given an intraperitoneal injection of nitroglycerin at 10 mg/kg. After 90 minutes the animals are subcutaneously dosed with test compound. A measurement of mechanical allodynia will be obtained using the up/down method with seven von Frey monofilaments. There is a specific series used for rat and mouse. Each monofilament is delivered to the hind paw for approximately 1-2 seconds. If there is a response, the next lower force will be delivered. This procedure will be performed until no response was made at the highest force or until four stimuli are administered following the initial response. The 50% paw withdrawal threshold for the hind paw will be calculated using the following formula: [Xth]log = [vFr]log + ky where [vFr] is the force of the last von Frey used, k is the average interval (in log units) between the von Frey monofilaments, and y is a value that depends upon the pattern of withdrawal responses.

Testing for tactile sensitivity will be performed and a withdrawal value will be assigned as the tactile sensitivity (expressed in grams of force required to elicit a response) for the injected paw for each animal. Data is presented as the mean grams required to produce a hind paw withdrawal from the von Frey stimulus. The compounds below were found to have anti-allodynic activity. Data for some of the compounds is included below. Compounds found to be effective in this model of migraine at the doses indicated, although other doses may also be active. Other compounds described herein were not necessarily tested, but are expected to be able have some level of efficacy.

Compound	Species	Migraine Route	Active* Migraine Doses (mg/kg)
B0707	rat	sc	≤ 10
	mouse	sc	≤ 10
B0720	mouse	sc	≤ 10
B0876	rat	sc	≤ 10
	mouse	sc	≤ 10
B1049	rat	sc, po	≤ 30
	mouse	sc	≤ 10
B1145	mouse	sc	≤ 10
B1165	rat	sc	≤ 10
B1194	mouse	sc	≤ 10
B1205	rat	sc	≤ 10
	mouse	sc	≤ 10
B1211	mouse	sc	≤ 10
B1243	mouse	sc	≤ 10
B1365	rat	sc	≤ 10
	mouse	sc	≤ 10
B1401	rat	sc	≤ 10
	mouse	sc	≤ 10
* $p < 0.05$ compared to vehicle-treated mice			

Example 6: Compounds Are Effective in Parkinson's disease

Compounds were tested for efficacy in reversing akinesia and bradykinesia in two well accepted rodent Parkinson's disease (PD) models; the haloperidol-induced rat catalepsy [1] and 6-OHDA rat hemiparkinson lesion models [3].

In the haloperidol induced catalepsy model, compounds were dosed subcutaneously and motor impairments (akinesia/bradykinesia) were measured in the "bar test" [1] which measures the ability of the rat to respond to an externally imposed static posture as well as the "drag test" a modification of the "wheelbarrow" test [2] which measures the ability of the rat to balance its body posture using forelimbs in response to an externally imposed dynamic (dragging) stimulus. Compounds were administered subcutaneously and efficacy was evaluated between 60 min post dose.

The compounds below were found to be effective in the haloperidol induced catalepsy model at the doses indicated, although other doses may also be active. Other compounds described herein were not necessarily tested, but are expected to be able have some level of efficacy.

Compound	**Species**	**Route**	**Active* Dose (mg/kg)**
B0136	rat	sc	≤ 100
B0292	rat	sc	≤ 100
* $p < 0.05$ compared to vehicle-treated mice			

In the hemilesioned rat 6-OHDA model, the effect of compound on the akinetic response to lesioning of the contralateral forepaw in the bar test and stepping activity as measured by the drag test were determined. L-DOPA has been shown to be efficacious at relevant doses in this model. This assay examines efficacy for reversing PD motor symptoms (i.e. akinesia/bradykinesia and gait abilities). The behavioral readouts will include immobility time in the bar test (akinesia), number of steps in the drag test (akinesia/bradykinesia) and time spent on rod in the rotarod test (overall gait ability, gross motor behavior). Compounds were administered subcutaneously and efficacy was evaluated between 30 and 90 min post dose.

The referenced referred to in the paragraphs above are: [1] Marti M, Mela F, Guerrini R, Calo G, Bianchi C, Morari M (2004). Blockade of nociceptin/orphanin FQ transmission in rat substantia nigra reverses haloperidol-induced akinesia and normalizes nigral glutamate release. J Neurochem 91(6): 1501-1504. [2] Mabrouk, O.S., et al., Stimulation of delta opioid receptors located in substantia nigra reticulata but not globus pallidus or striatum restores motor activity in 6-hydroxydopamine lesioned rats: new insights into the role of delta receptors in parkinsonism. Journal of Neurochemistry, 2008. 107(6): p. 1647-1659. [3] Sanberg, P.R., et al., The catalepsy test: its ups and downs. Behav Neurosci, 1988. 102(5): p. 748-59.

The compounds below were found to be effective in the hemilesioned rat 6-OHDA model at the doses indicated, although other doses may also be active. Other compounds described herein were not necessarily tested, but are expected to be able have some level of efficacy. Thus, the compounds can used to treat Parkinson's Disease.

Compound	Species	Route	Active* Dose (mg/kg)
B0136	rat	sc	≤ 100
B0292	rat	sc	≤ 100
B0707	rat	sc	≤ 30
B1049	rat	sc	≤ 30
* $p < 0.05$ compared to vehicle-treated mice			

Example 7: Compounds are Effective in Treating Medication Overuse Headache and Opioid-Induced Hyperalgesia

Compounds were evaluated for their ability to treat Medication Overuse Headache ("MOH"). Assessment of reversal of tactile allodynia produced by repeat dosing of sumatriptan in mice: Mice (44 male c57bl6J mice, n=8-9/group) were habituated for 2 days on testing rack prior to injections. Mice were treated with vehicle (VEH-VEH (saline) VEH-B1049 (10%BCD-saline)) or sumatriptan (SUMA) (0.6 mg/kg, i.p.) daily for 11 days. Mechanical sensitivity was measured as the 50% withdrawal threshold to manual von Frey hair stimulation on day 12. Baseline measurement were taken 24 hours after final SUMA/VEH injection and 3 h later, post-drug measurements were taken after dosing with B1049 (10 mg/kg, s.c., 30 min prior to testing) or SNC80 (10 mg/kg, i.p., 45 min prior to

testing). (***p<0.001 compared to post-drug SUMA-VEH). The results are illustrated in Figure 3. B1049, a compound of the preseent disclosure, was found to be able to reverse tactile allodynia produced by repeat dosing of sumatriptan, which means that it can be used to reverse medication overuse headache.

Next it was determined that B1049 could reverse opioid-induced hyperalgesia. Mice (44 male c57bl6J mice, n=8-9/group) were habituated for 2 days on testing rack prior to injections. Mice were treated with vehicle (VEH-VEH (saline), VEH-B1049 (10%BCD-saline)) or morphine (MORPH) (20 mg/kg, s.c. days 1-3, 40 mg/kg s.c. day 4) twice daily (9 a.m. and 5 p.m.) for 4 days. Mechanical sensitivity was measured as the 50% withdrawal threshold to manual von Frey hair stimulation on day 5. Baseline measurement were taken 16 hours after final MORPH/VEH injection and 3 h later, post-drug measurements were taken after dosing with B1049 (10 mg/kg, s.c., 30 min prior to testing) or SNC80 (10 mg/kg, i.p., 45 min prior to testing). (***p<0.001 compared to post-drug SUMA-VEH). The results are illustrated in Figure 4. B1049, a compound of the preseent disclosure, was found to be able to reverse opioid induced hyperalgesia.

Example 8: Compounds do not induce Medication Overuse Headache

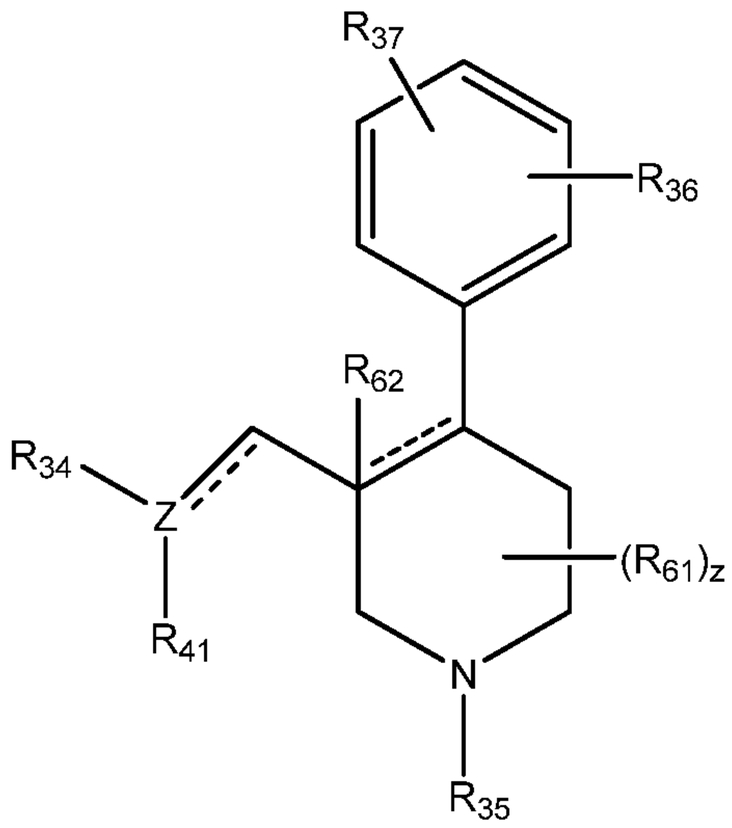
Assessment of tactile allodynia produced by repeat dosing of B1049 in mice demonsrated that it does not induce medication overuse headache. Mice (25 male c57bl6J mice, n=4-5/group) were habituated for 2 days on testing rack prior to injections. Mice were treated with vehicle (VEH-VEH (saline), VEH-B1049 (10%BCD-saline)), sumatriptan (SUMA) (0.6 mg/kg, i.p.), SNC80 (10 mg/kg, i.p.), or B1049 (10 mg/kg, s.c.) daily for 11 days. Mechanical sensitivity was measured as the 50% withdrawal threshold to manual von Frey hair stimulation on days 1 and 11. On these days, mice were habituated to the rack for 15-20 min, following which baseline mechanical thresholds were determined prior to administration of drug or control. On day 1 following assessment of baseline mechanical threshold, mice were weighed and injected with drug or control and returned to home cage. The results are illustrated in Figure 5. Figure 5 illustrates that sumatriptan causes medication overuse headace, whereas B1049 does not and is the same as the vehicle control (negative control). Accordingly, it has been surprisingly been found that not only is B1049 effective to treat migraines, but it also does not have the side effects that other migraine medications that are used today do have.

The compounds described herein have been found to be active and effective against various conditions, such as those described herein. The experiments described herein are

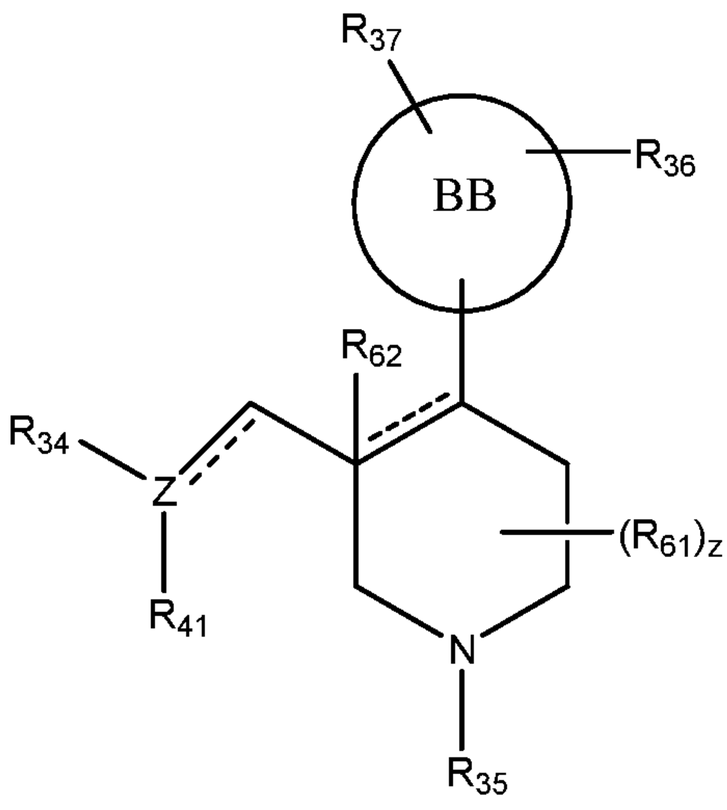
exemplary in manner and are not intended, nor should they be used, to limit the scope of the embodiments. Each and every reference, publication, accession number, patent, document, etc, is hereby incorporated by reference in its entirety for its intended purpose.

What Is Claimed Is:

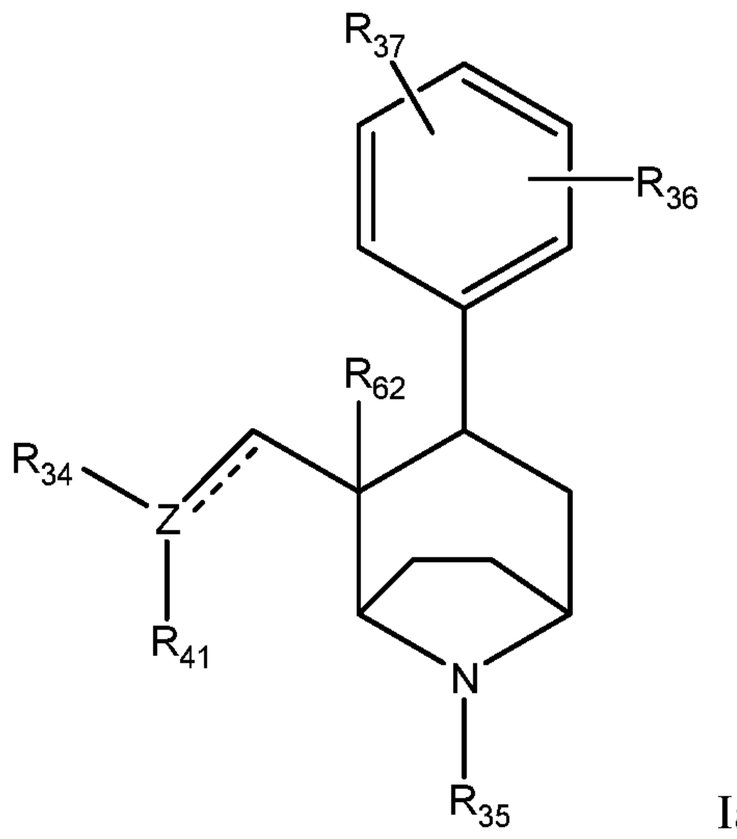
1. A compound having Formula I, I-1, I-a, I-a1 or I-b, Ib-1, or Ib-2



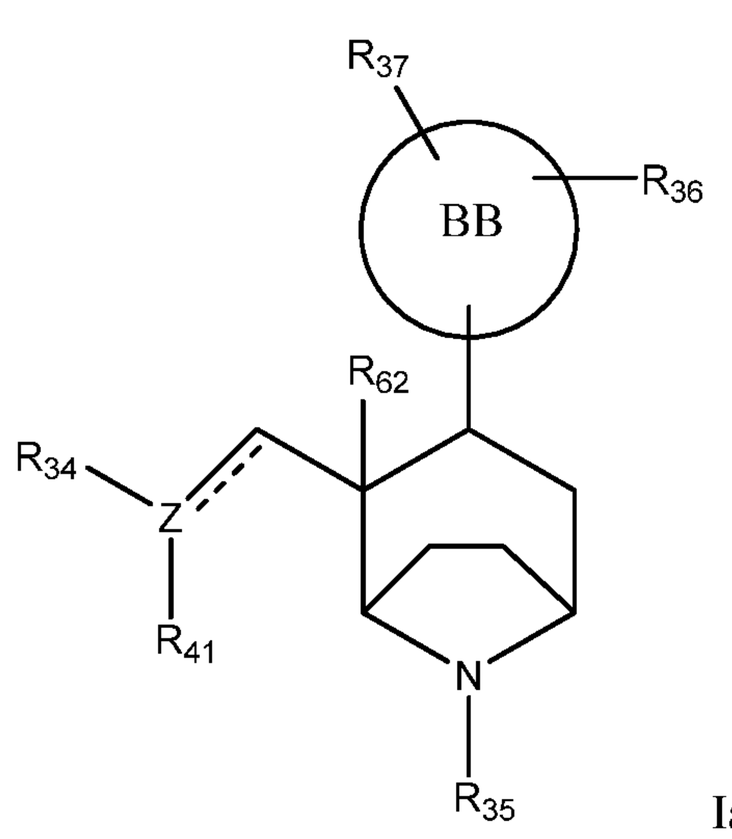
I



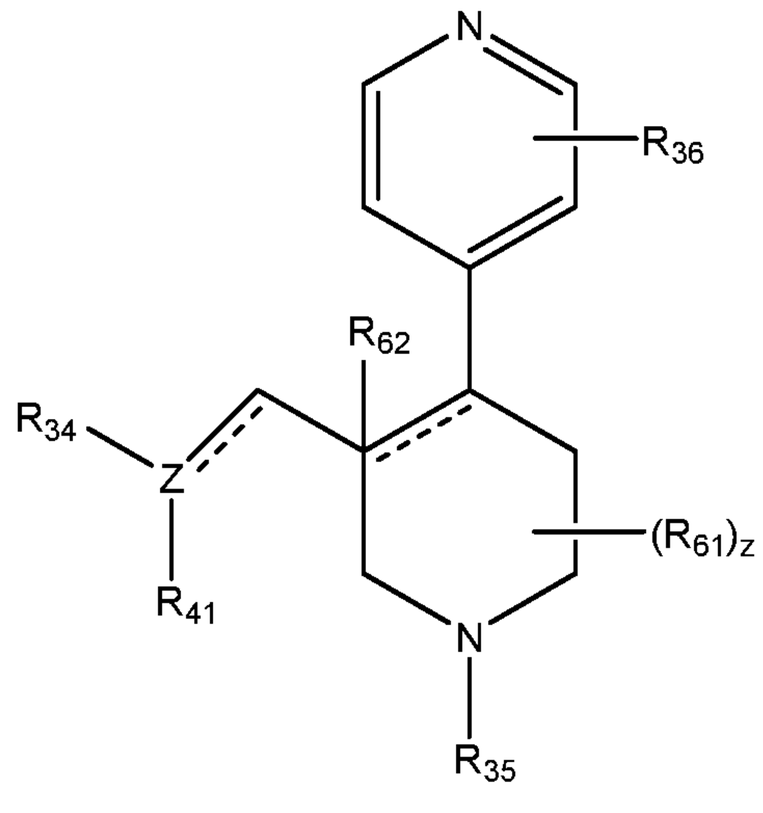
I-1



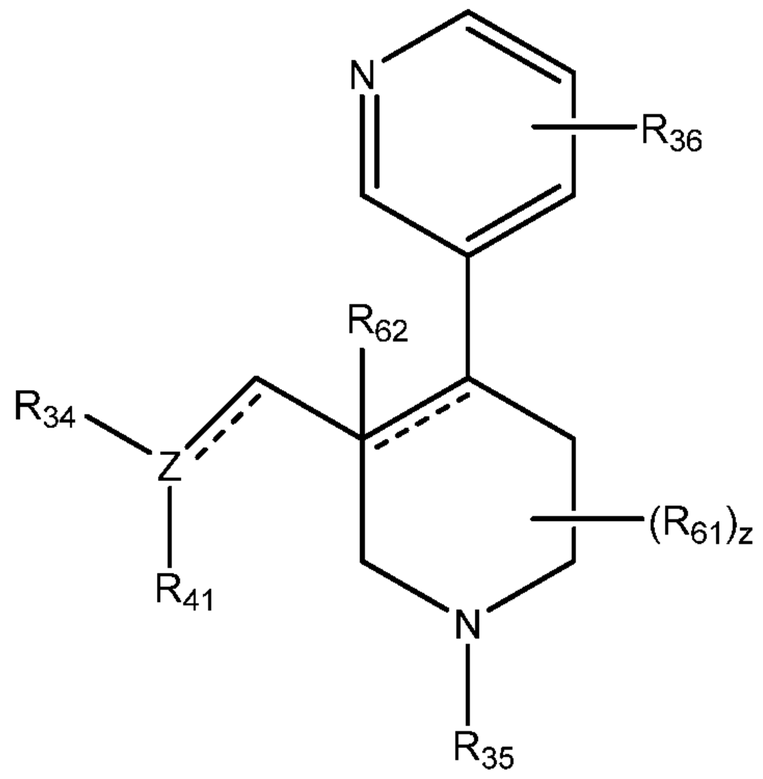
Ia,



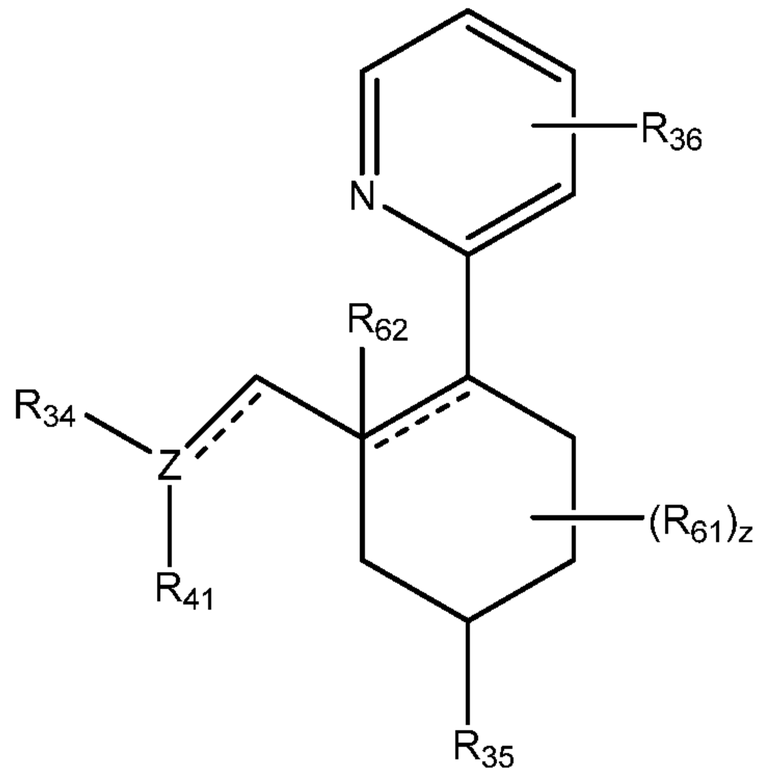
Ia-1



Ib,

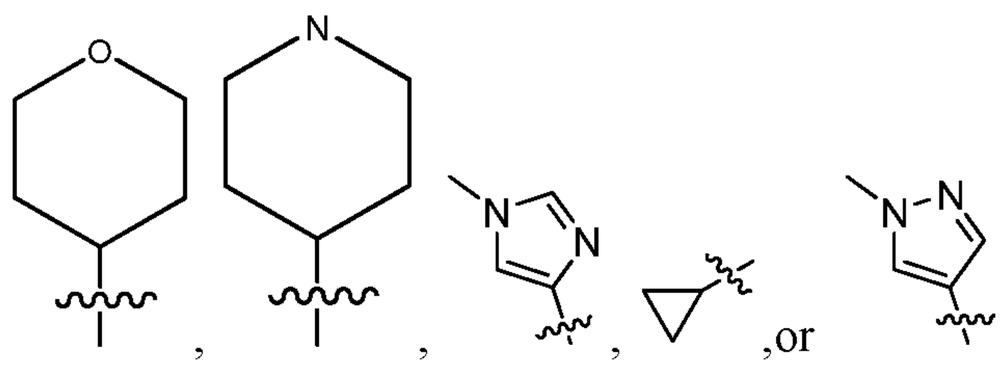


Ib-1, or



Ib-2

or pharmaceutically acceptable salt thereof, wherein:

BB is  , , , , ,or

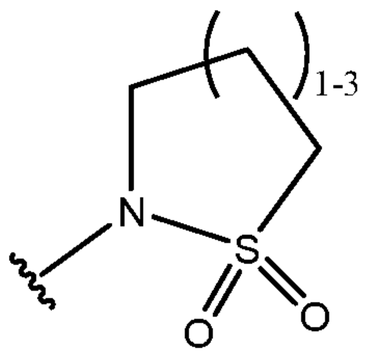
Z is C, S, N, $S(O)_2$ or O;

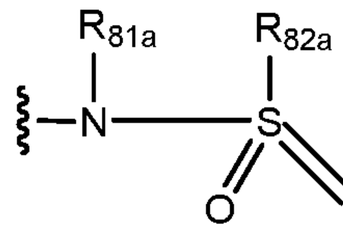
R_{35} is a protecting group, $C(=O)OR_{81b}$, H, optionally substituted aryl, optionally substituted C_1-C_6 haloalkyl, $-R_{63}R_{64}$, $-NR_{63}R_{64}$, optionally substituted C_1-C_6 branched or unbranched alkyl, optionally substituted C_2-C_6 alkenyl, optionally substituted C_2-C_6 haloalkenyl $-(CH_2)_nR_{65}$, optionally substituted heterocycle, optionally substituted C_1-C_6 ester, optionally substituted cycloalkyl, optionally substituted C_1-C_6 alkoxy, optionally

substituted pyrrolinyl, optionally substituted morpholinyl, , optionally substituted C_3-C_6 cyclic ether, or optionally substituted piperidyl;

R_{36} is null, H, halo, optionally substituted C_1-C_6 haloalkyl, -SO_2C_1-C_6alkyl, -OCF_3, optionally substituted C_1-C_6 alkyl, or -OR_{75}; wherein R_{75} is H or optionally substituted C_1-C_6 alkyl;

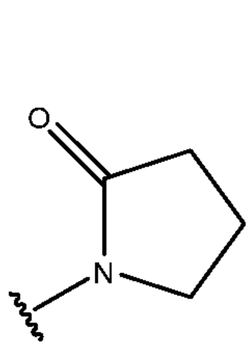
R_{37} is, null, H, halo, optionally substituted C_1-C_6 haloalkyl, -SO_2C_1-C_6alkyl, -OCF_3, optionally substituted sulfonamide, optionally substituted cyclic sulfonamide, or -$(CH_2)_q$-R_{38}, -NH-$(CH_2)_q$-R_{38}, -S-$(CH_2)_q$-R_{38}, -C(=O)R_{38}, or

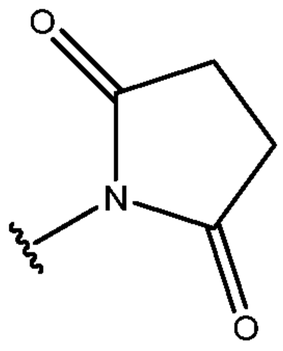
-O-$(CH_2)_q$-R_{38}, 

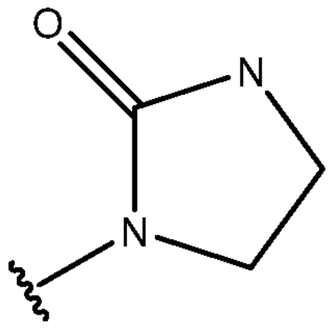
, 

;

R_{38} is H, C_1-C_6 alkyl, halo, C_1-C_6 haloalkyl, -C(=O)C_1-C_6 alkyl, –OR_{66}, $S(O)_2R_{67}$,



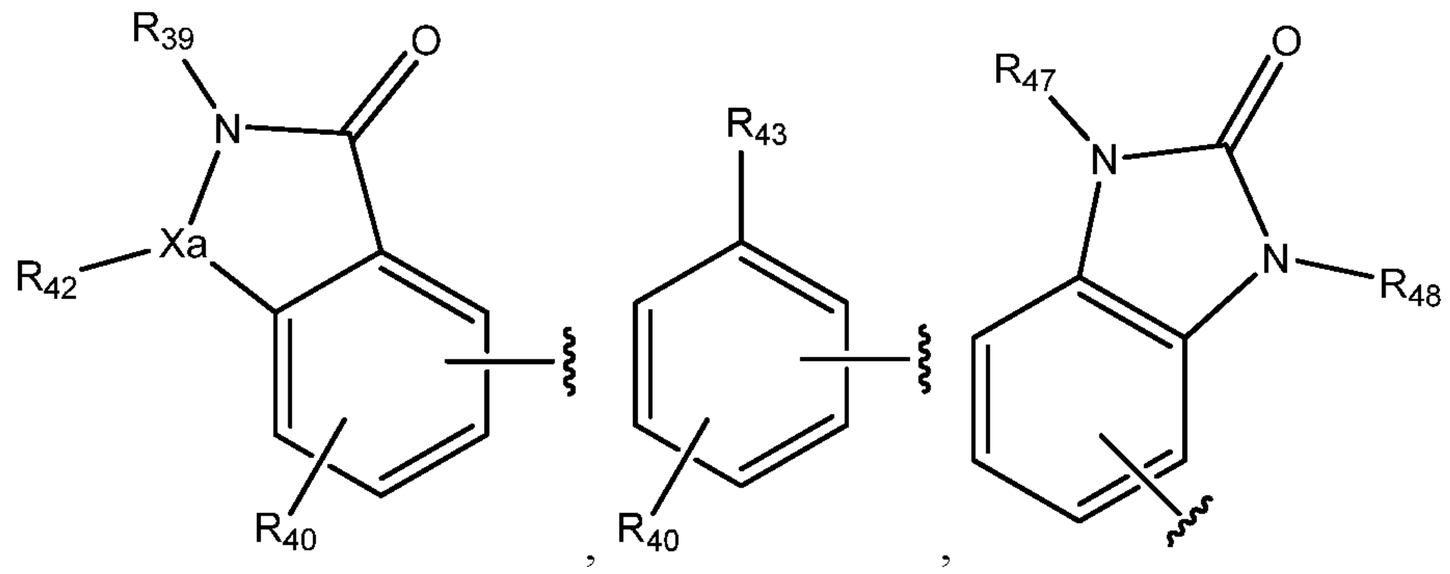
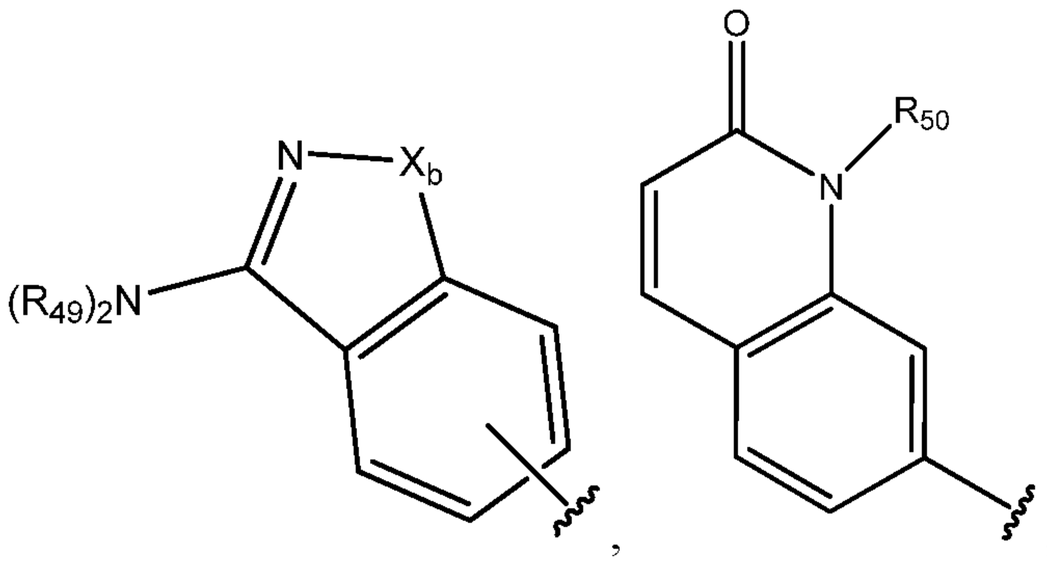
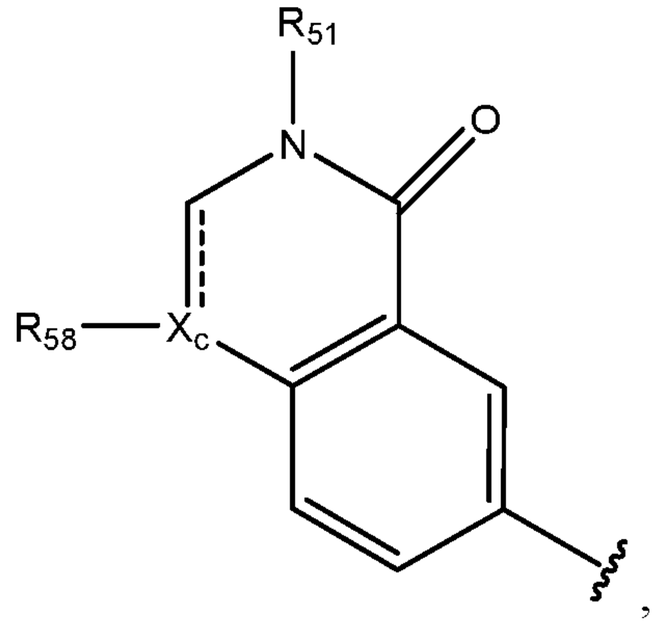
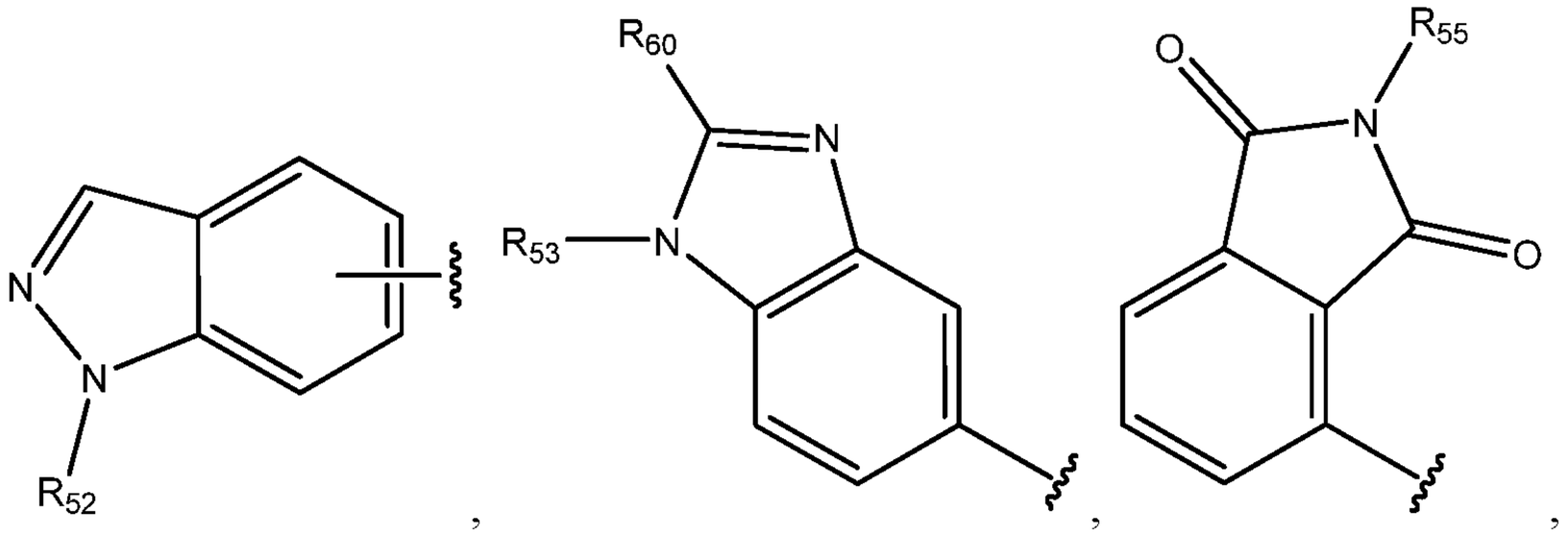
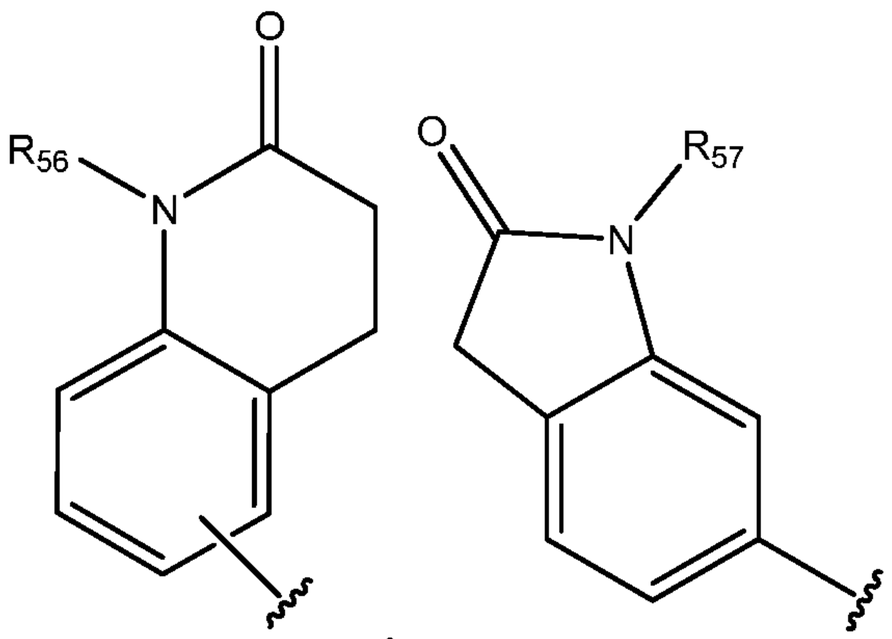
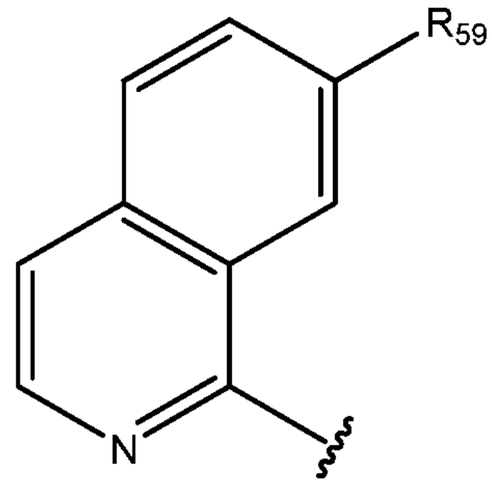
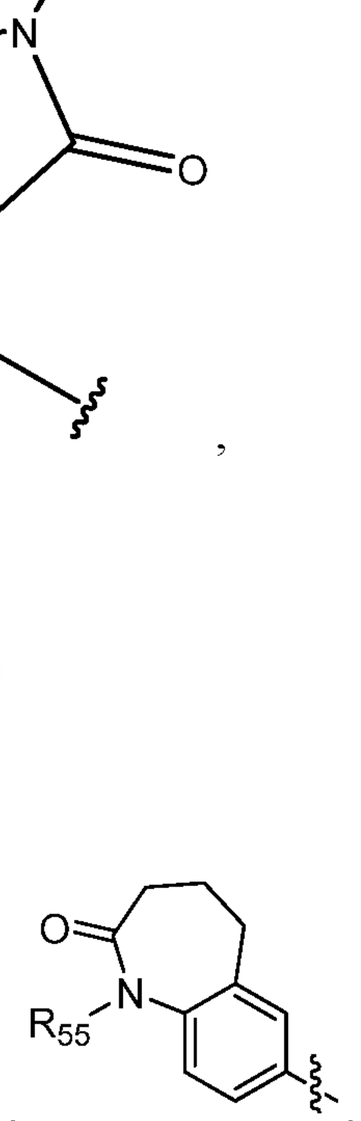
, 

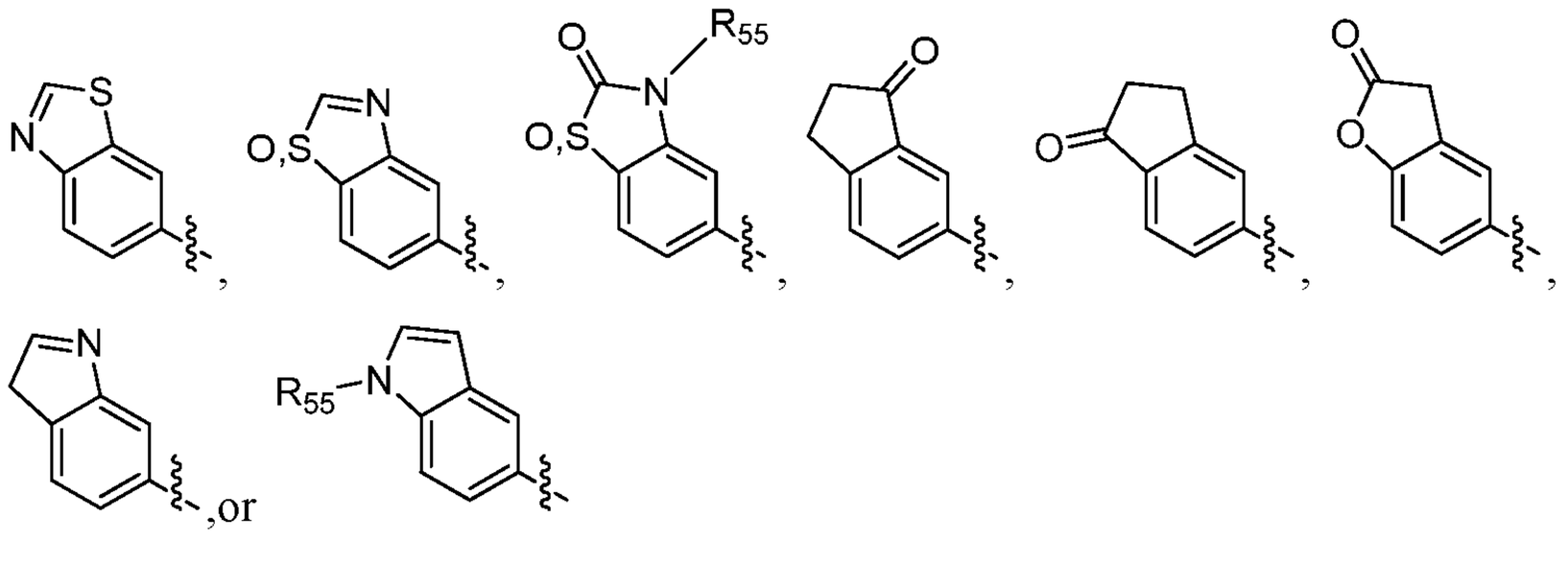
, 

, optionally substituted cycloalkyl, -$(CH_2)_pR_{65}$, or optionally substituted heterocycle;

or R_{37} is-$(CH_2)_q$-R_{38} or R_{36} and R_{37} form a heterocycle that is fused to the phenyl ring;

R_{41} is absent, H, or C_1-C_6 alkyl provided that when Z is S, O or $S(O)_2$, R_{41} is absent; or when Z is C, the bond connecting Z to the adjacent carbon is a double bond and R_{41} is H,

R_{34} is  ,  ,  ,  , ,  , ,  ,  ,



,or

wherein,

R_{39} is H or C_1-C_6 alkyl;

R_{40} is H, C_1-C_6 alkyl, halo, or alkoxy;

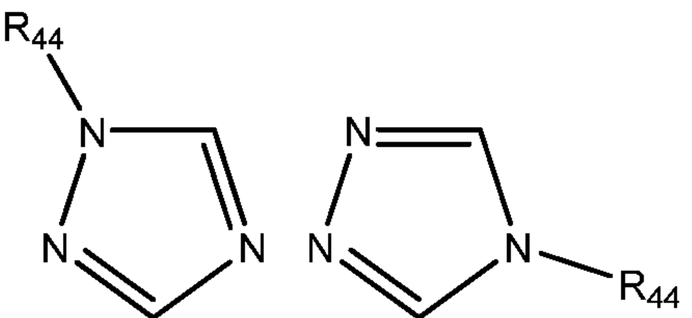
R_{42} is absent, H, C_1-C_6 alkyl, a member of a carbocyle that includes the atom to which it is attached, =O;

X_a is C or O, provided that when X_a is O, R_{42} is absent;

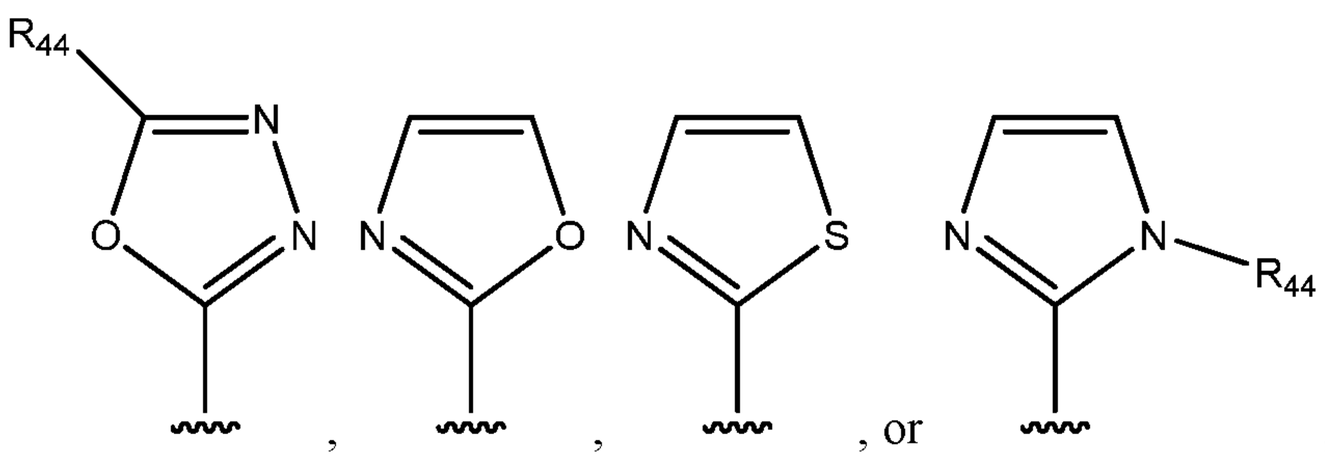
X_b is S or O;

X_c is C or N;

R_{43} is -OH, -CN, -C(=O)$NR_{45}R_{46}$,



,



, or

,

wherein: R_{44} is H or C_1-C_6 alkyl; R_{45} is H or C_1-C_6 alkyl; and R_{46} is H or C_1-C_6 alkyl;

R_{47} is H or C_1-C_6 alkyl;

R_{48} is H or C_1-C_6 alkyl;

each R_{49} is, independently, H or C_1-C_6 alkyl;

R_{50} is H or C_1-C_6 alkyl;

R_{51} is H or C_1-C_6 alkyl;

R_{52} is H or C_1-C_6 alkyl;

R_{53} is H or C_1-C_6 alkyl;

R_{55} is H or C_1-C_6 alkyl;

R_{56} is H or C_1-C_6 alkyl;

R_{57} is H or C_1-C_6 alkyl;

R_{58} is absent or H;

R_{59} is H or OH;

R_{60} is H or $N(R_{54})_2$;

each R_{54} is, independently, H or C_1-C_6 alkyl;

R_{61} is H, C_1-C_6 alkyl, optionally substituted C_1-C_6 haloalkyl, gem-dimethyl, cyclopropyl spirocycle, or CF_3;

R_{62} is absent, H, or C_1-C_6 alkyl;

each R_{63} and R_{64} are, independently, H, optionally substituted aryl, optionally substituted C_1-C_6 haloalkyl, optionally substituted C_1-C_6 branched or unbranched alkyl, optionally substituted C_2-C_6 alkenyl, $-(CH_2)_vR_{65}$, optionally substituted cycloalkyl, -OH, optionally substituted alkoxy, optionally substituted pyrrolinyl, optionally substituted morpholinyl, or optionally substituted piperidyl; or R_{63} and R_{64} together form a 5-10 membered optionally substituted heterocycle or a 5-10 membered optionally substituted heteroaryl with the atom to which R_{63} and R_{64} are bonded to;

each R_{65} is, independently, H, $-C(=O)R_{65A}$, optionally substituted C_1-C_6 haloalkyl, optionally substituted nitrogen, optionally substituted C_1-C_6 branched or unbranched alkyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted C_2-C_6 alkenyl, optionally substituted cycloalkyl, optionally substituted heterocycle, -OH, optionally substituted alkoxy, optionally substituted pyrrolinyl, optionally substituted phenyl, optionally substituted pyrrolidinyl, optionally substituted imidazolidinyl, optionally substituted morpholinyl, or optionally substituted piperidyl;

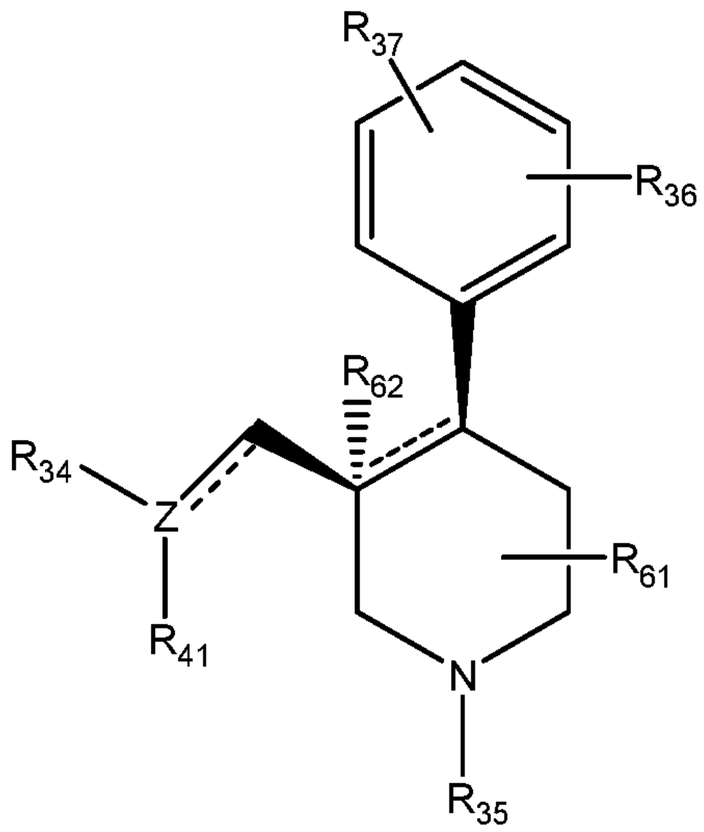
R_{65A} is phenyl or C_1-C_6 branched or unbranched alkyl;

R_{66} is H, optionally substituted aryl, optionally substituted C_1-C_6 haloalkyl, $-R_{63}R_{64}$, $-NR_{63}R_{64}$, optionally substituted C_1-C_6 branched or unbranched alkyl, optionally substituted C_2-C_6 alkenyl, $-(CH_2)_wR_{65}$, optionally substituted cycloalkyl, -OH, optionally substituted alkoxy, optionally substituted pyrrolinyl, optionally substituted morpholinyl, or optionally substituted piperidyl;

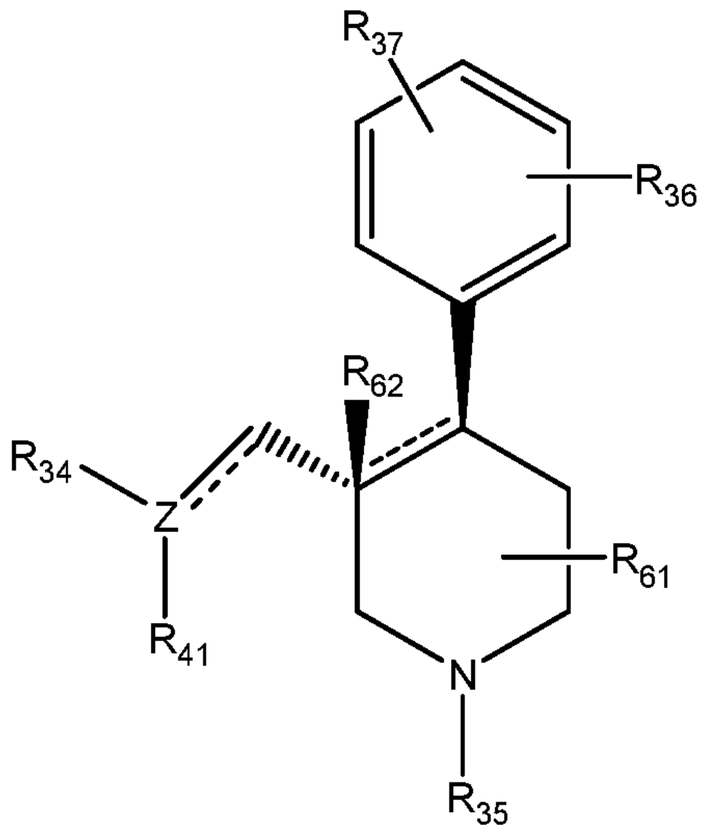
R_{67} is optionally substituted C_1-C_6 branched or unbranched alkyl, optionally substituted C_1-C_6 haloalkyl;

R_{81a} and R_{82a} are each independently H or optionally substituted C_1-C_6 alkyl;
R_{81b} is H or optionally substituted branched or unbranched C_1-C_6 alkyl;
z is 1 or 2,
each n, p, v, w, and q is, independently, an integer from 0-6.

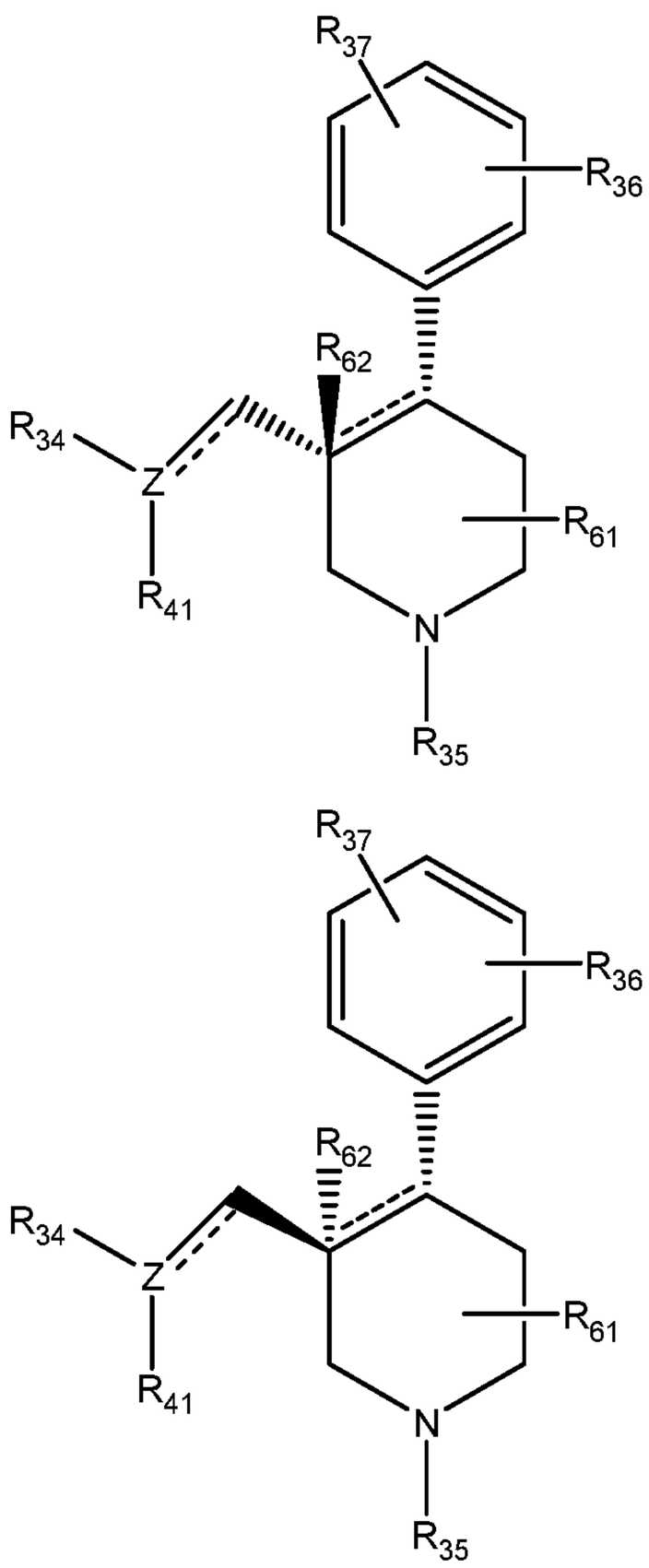
2. The compound of claim 1, or pharmaceutically acceptable salt thereof, having Formula II, III, IV, or V



II



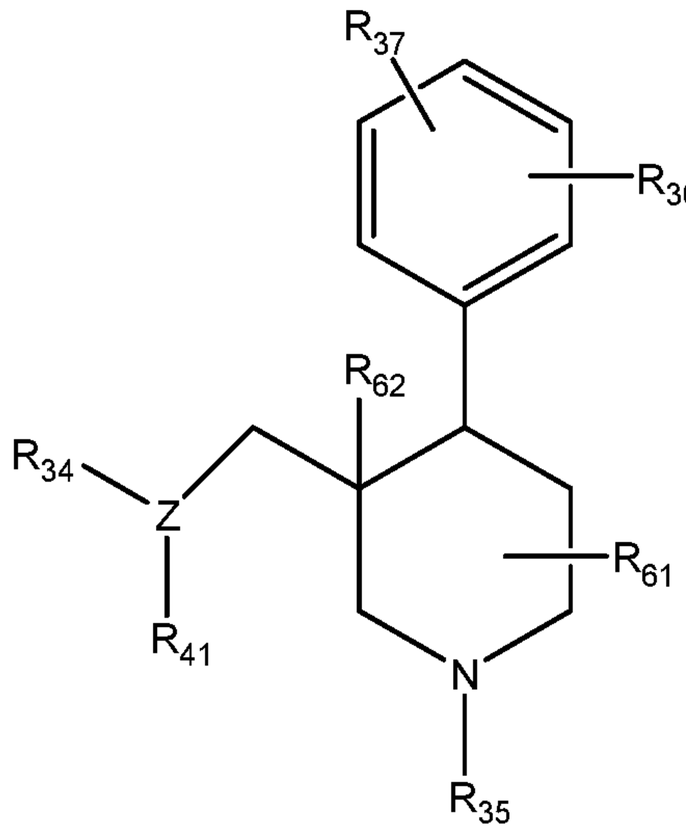
III



IV,

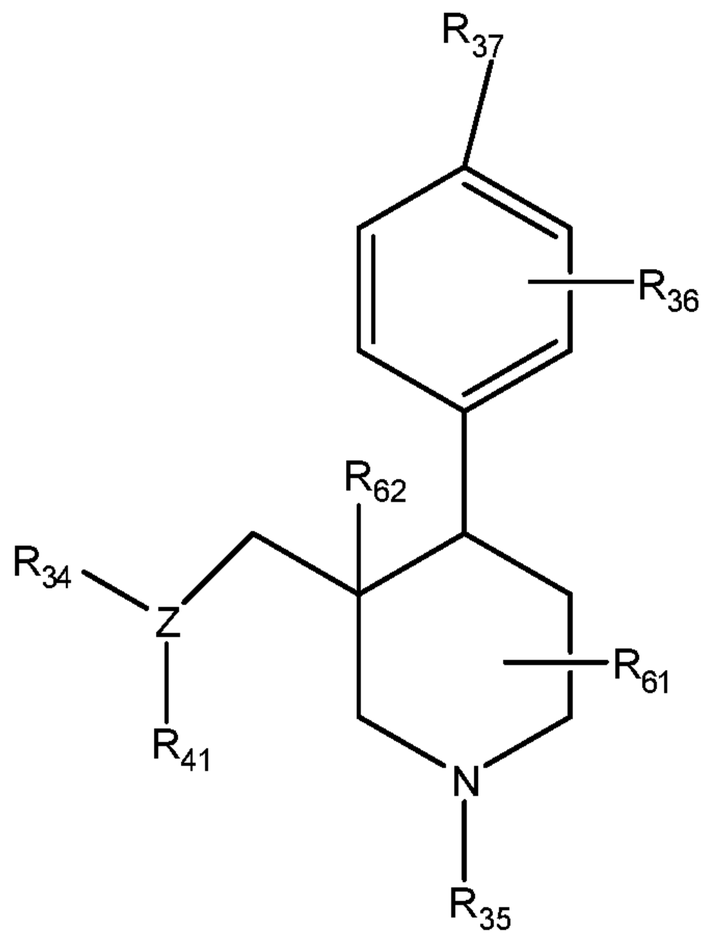
V.

3. The compound of claim 1, or pharmaceutically acceptable salt thereof, having Formula VI:

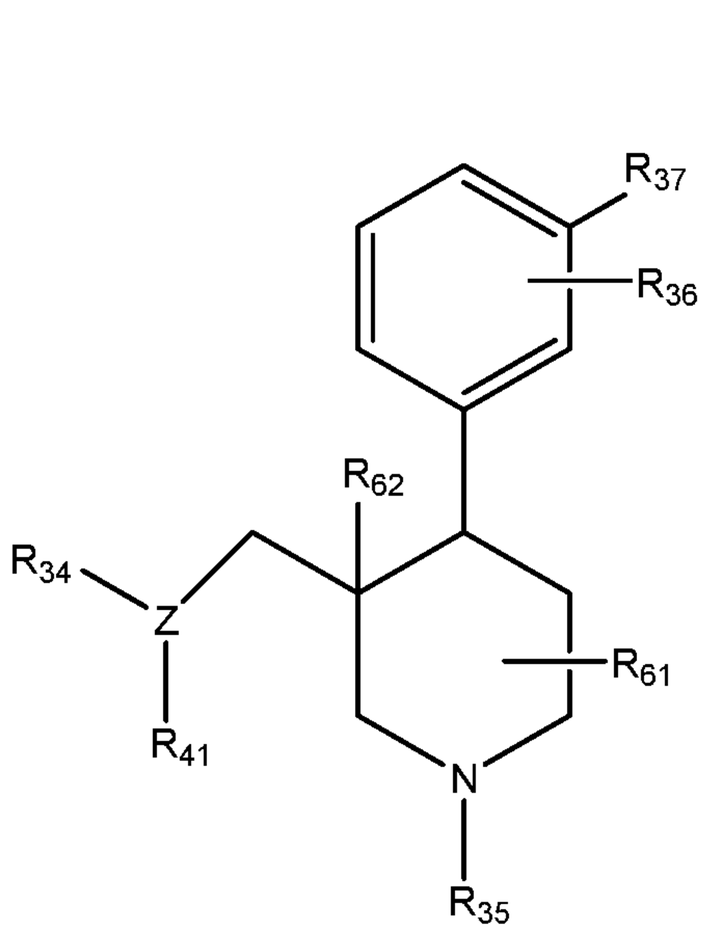


VI.

4. The compound of claim 1, or pharmaceutically acceptable salt thereof, having Formula VII or VIIa:



VII



VIIa.

5. The compound of claim any one of claims 1-4, or pharmaceutically acceptable salt thereof, wherein z is 1.

6. The compound of any one of claims claim 1-5, or pharmaceutically acceptable salt thereof, wherein each R_{61} is methyl.

7. The compound of claims 1-5, or pharmaceutically acceptable salt thereof, wherein each R_{61} is gem-dimethyl.

8. The compound of any one of claims 1-7, or a pharmaceutically acceptable salt thereof, wherien Z is O.

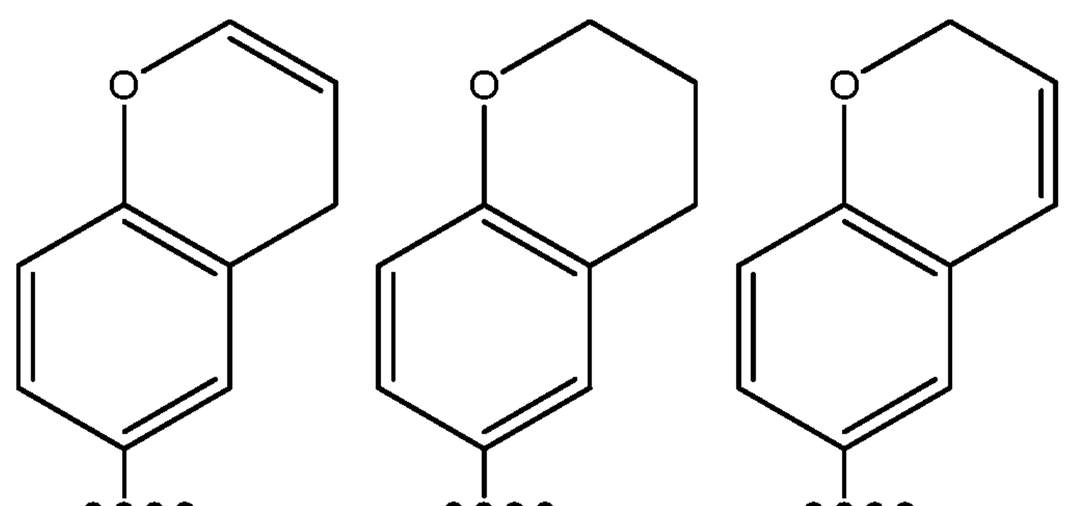
9. The compound of any one of claims 1-7, or pharmaceutically acceptable salt thereof, wherein Z is $S(O)_2$.

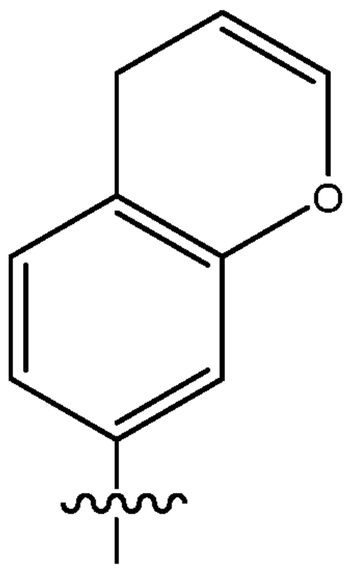
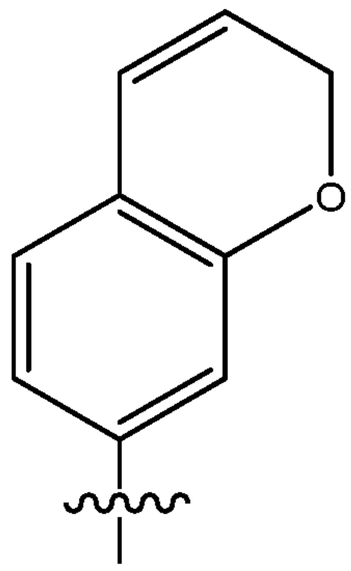
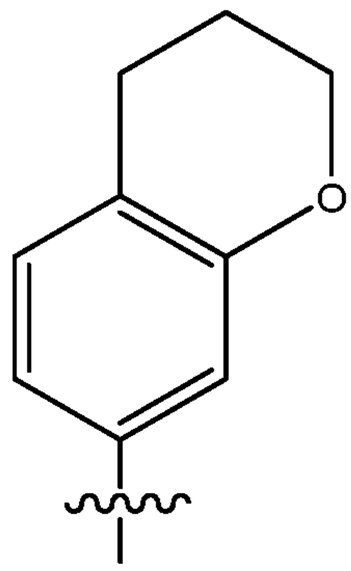
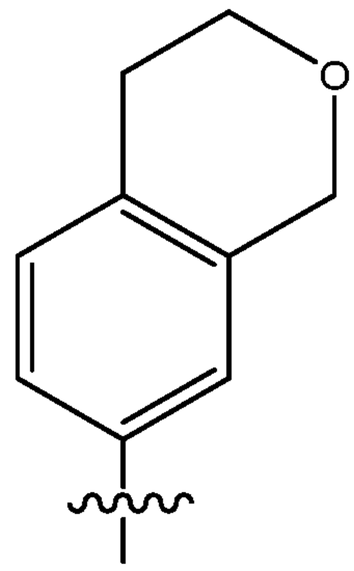
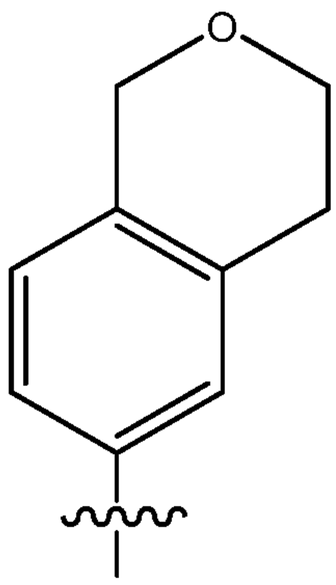
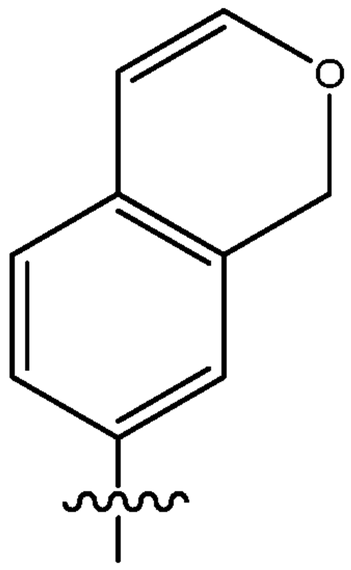
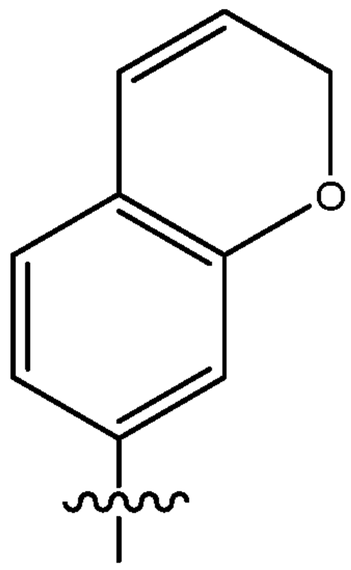
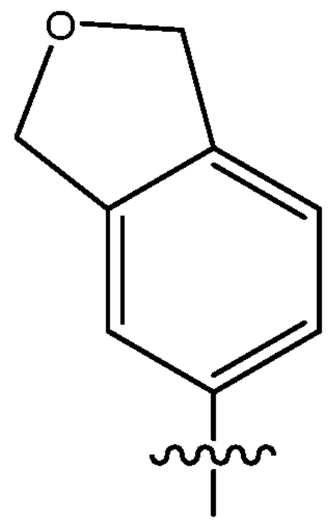
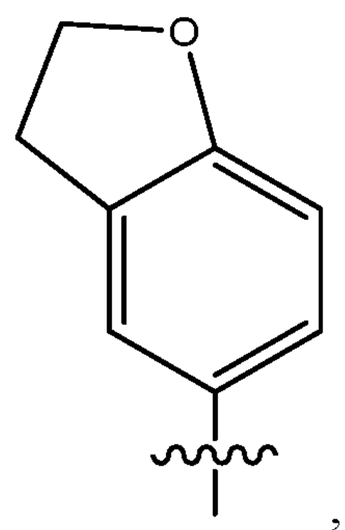
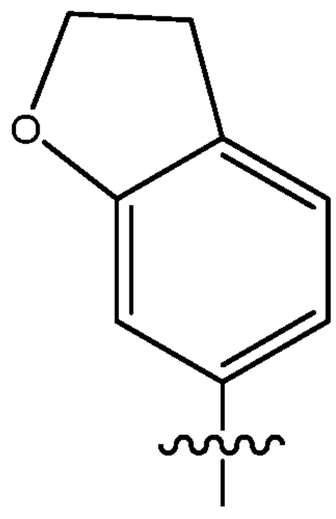
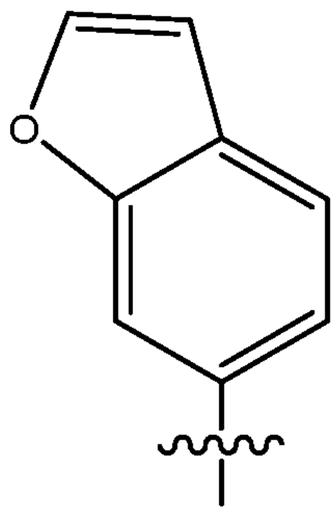
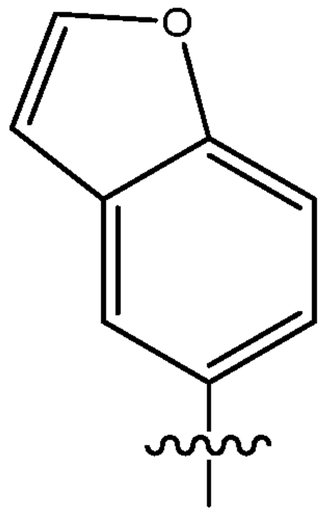
10. The compound of any one of claims 1-7, or pharmaceutically acceptable salt thereof, wherein R_{41} is absent.

11. The compound of any one of claims 1-10, or pharmaceutically acceptable salt thereof, wherein R_{37} is alkoxy, halo, optionally substituted sulfonamide, optionally substituted cyclic sulfonamide.

12. The compound of any one of claim 1-10, or pharmaceutically acceptable salt thereof, wherein R_{36} and R_{37} form a heterocycle that is fused to the phenyl ring.

13. The compound of claim 12, or pharmaceutically acceptable salt thereof, wherein the fused ring structure is an optionally substituted benzofuran or benzopyran.

14. The compound of claim 12, or pharmaceutically acceptable salt thereof, wherein the fused ring has a formula of:  , , ,


,

,

,

,

,

,

,

,

,

,

, or

.

15. The compound of any one of claims 1-10, or pharmaceutically acceptable salt thereof, wherein R_{37} is absent.

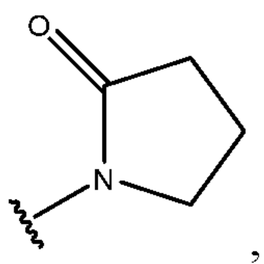
16. The compound of any one of claims 1-15, or pharmaceutically acceptable salt thereof, wherein q is 0.

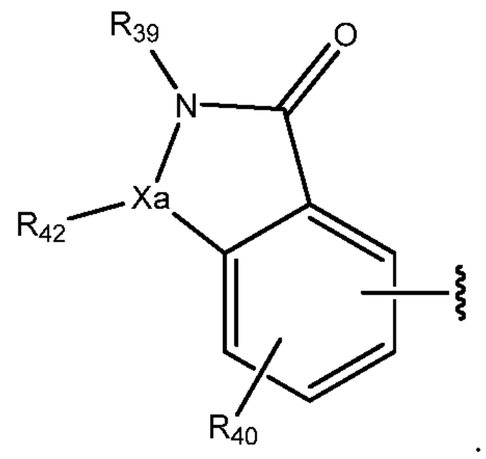
17. The compound, of any one of claims 1-15, or pharmaceutically acceptable salt thereof, wherein q is 1-4.

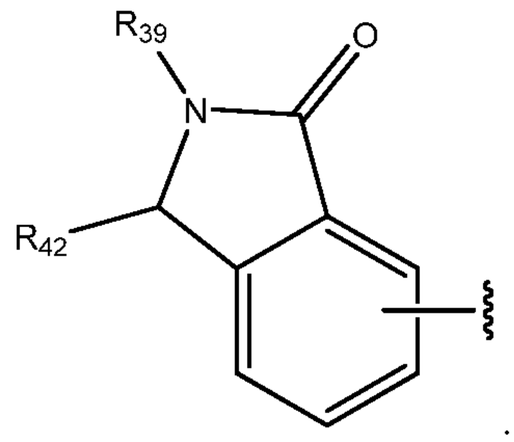
18. The compound of any one of claims 1-17, or pharmaceutically acceptable salt thereof, wherein R_{38} is absent or H.

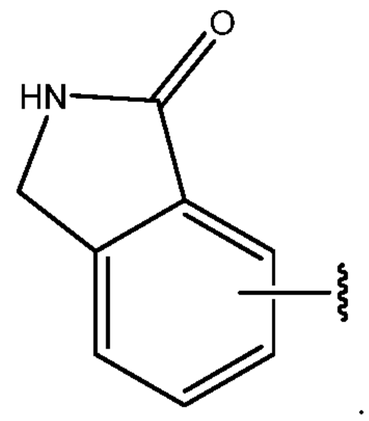
19. The compound of any one of claims 1-17, or pharmaceutically acceptable salt thereof, wherein R_{38} is C_1-C_6 haloalkyl.

20. The compound of any one of claims 1-17, or pharmaceutically acceptable salt thereof, wherein R_{38} is -C(=O)C_1-C_6 alkyl.

21. The compound of any one of claims 1-17, or pharmaceutically acceptable salt thereof, wherein R_{38} is $-OR_{66}$, $-S(O)_2R_{67}$,  , optionally substituted cycloalkyl, $-(CH_2)_pR_{65}$, or optionally substituted heterocycle.

22. The compound of any one of claims 1-21, or pharmaceutically acceptable salt thereof, wherein R_{34} is  .

23. The compound of any one of claims 1-21, or pharmaceutically acceptable salt thereof, wherein R_{34} is  .

24. The compound of any one of claims 1-23, or pharmaceutically acceptable salt thereof, wherein R_{34} is  .

25. The compound of any one of claims 1-24, or pharmaceutically acceptable salt thereof, wherein R_{61} is H, C_1-C_6 alkyl, optionally substituted C_1-C_6 haloalkyl, gem-dimethyl, cyclopropyl spirocycle, or CF_3.

26. The compound of any one of claims 1-25, or pharmaceutically acceptable salt thereof, wherein R_{35} is optionally substituted C_1-C_6 branched or unbranched alkyl, $–CH_2R_{76}$ or– $CH_2CH_2R_{76}$, wherein R_{76} is optionally substituted aryl, optionally substituted ketone, optionally substituted cycloalkyl, optionally substituted C_2-C_6 alkenyl, optionally substituted C_2-C_6 haloalkenyl, or optionally substituted heteroaryl.

27. The compound of claim 26, or pharmaceutically acceptable salt thereof, wherein R_{76} is cyclopropyl.

28. The compound of claim 26, or pharmaceutically acceptable salt thereof, wherein R_{76} is diflourocyclopropyl.

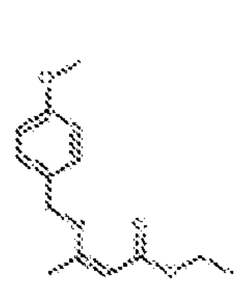
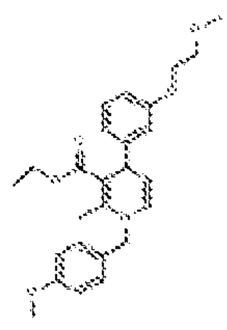
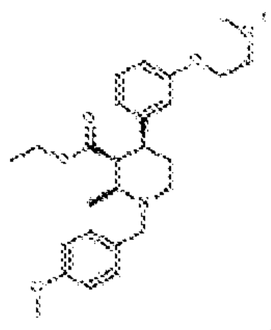
29. The compound of claim 26, or pharmaceutically acceptable salt thereof, wherein R_{76} is 2,2-diflourocyclopropyl.

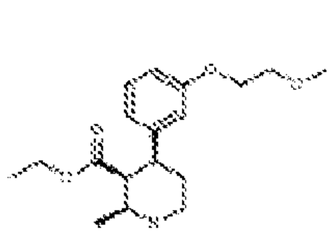
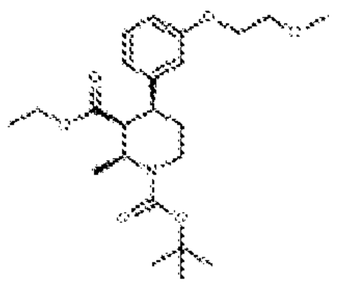
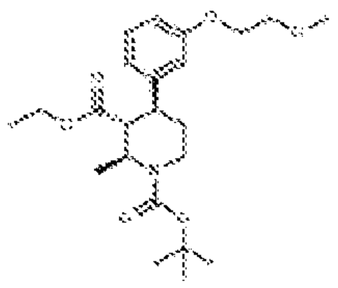
30. The compound of claim 26, or pharmaceutically acceptable salt thereof, wherein R_{76} is $–CH=CF_2$.

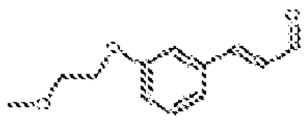
31. The compound of any one of claims 1-30, or pharmaceutically acceptable salt thereof, wherein the compound is selected from the group consisting of a compound illustrated in Figure 1 and/or described herein.

32. A compound, or pharmaceutically acceptable salt thereof, wherein the compound is selected from the group consisting of a compound described herein, including, but not limited to those in Figure 1.

33. A compound, or a pharmaceutically acceptable salt thereof, selected from the group consisting of: B1049, B0704, B0707, B0720, B0876, B1079, B1145, B1194, B1205, B1211,

B1365, B1401,  ,  ,  ,

,  ,  ,  , and



.

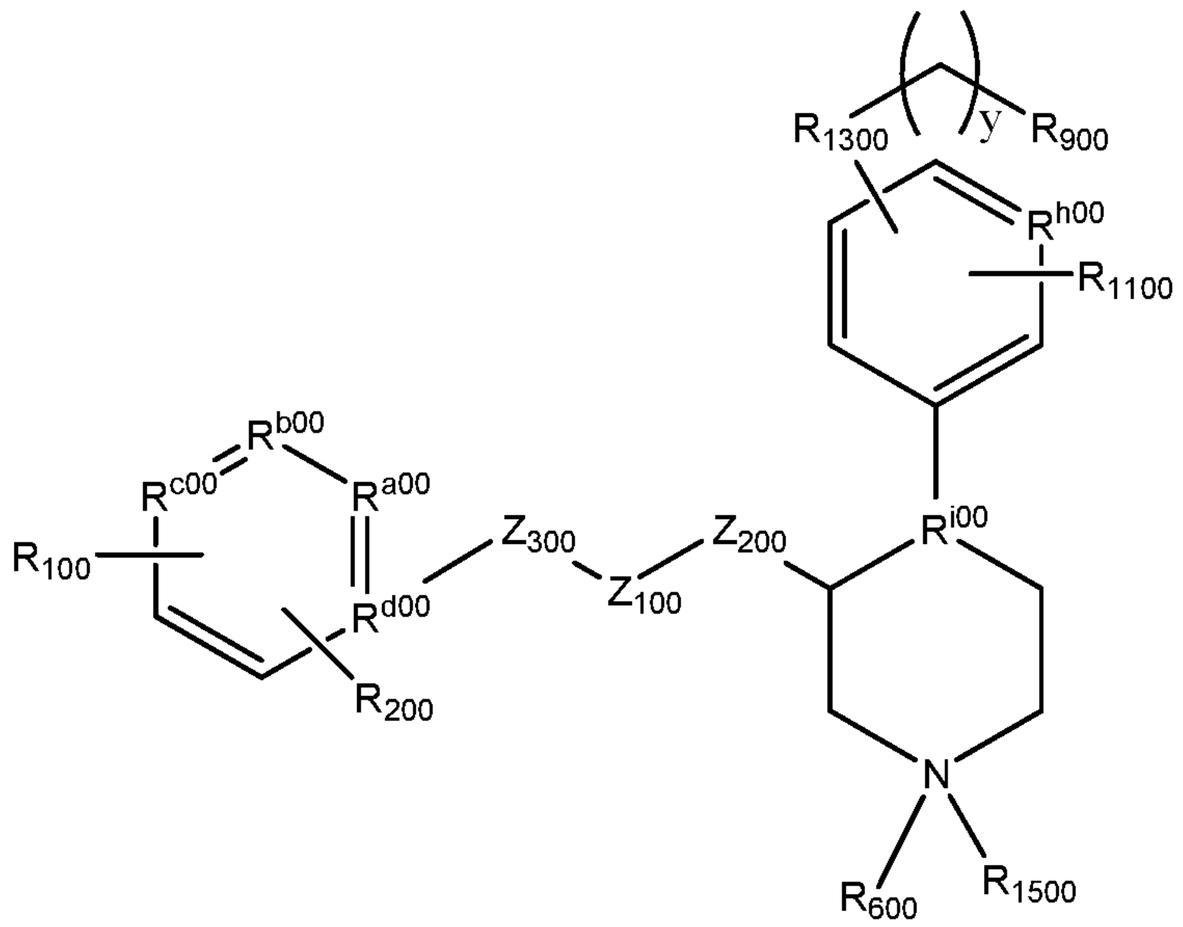
34. A pharmaceutical composition comprising a compound, or pharmaceutically acceptable salt thereof, of any one of claims 1-33.

35. A method of treating or preventing pain, neuropathic pain, migraine, headache, depression, Parkinson's disease, anxiety, overactive bladder, medication overuse headache, hyperalgesia, decreasing nociceptive sensitization, pain in an opioid exposed subject, PTSD, or other disorder or condition described herein in a subject comprising administering to the subject one or more compounds, or a pharmaceutically acceptable salt thereof, of any of claims 1-33 or a pharmaceutical composition comprising one or more compounds, or pharmaceutically acceptable salt thereof, of any one of claims 1-33.

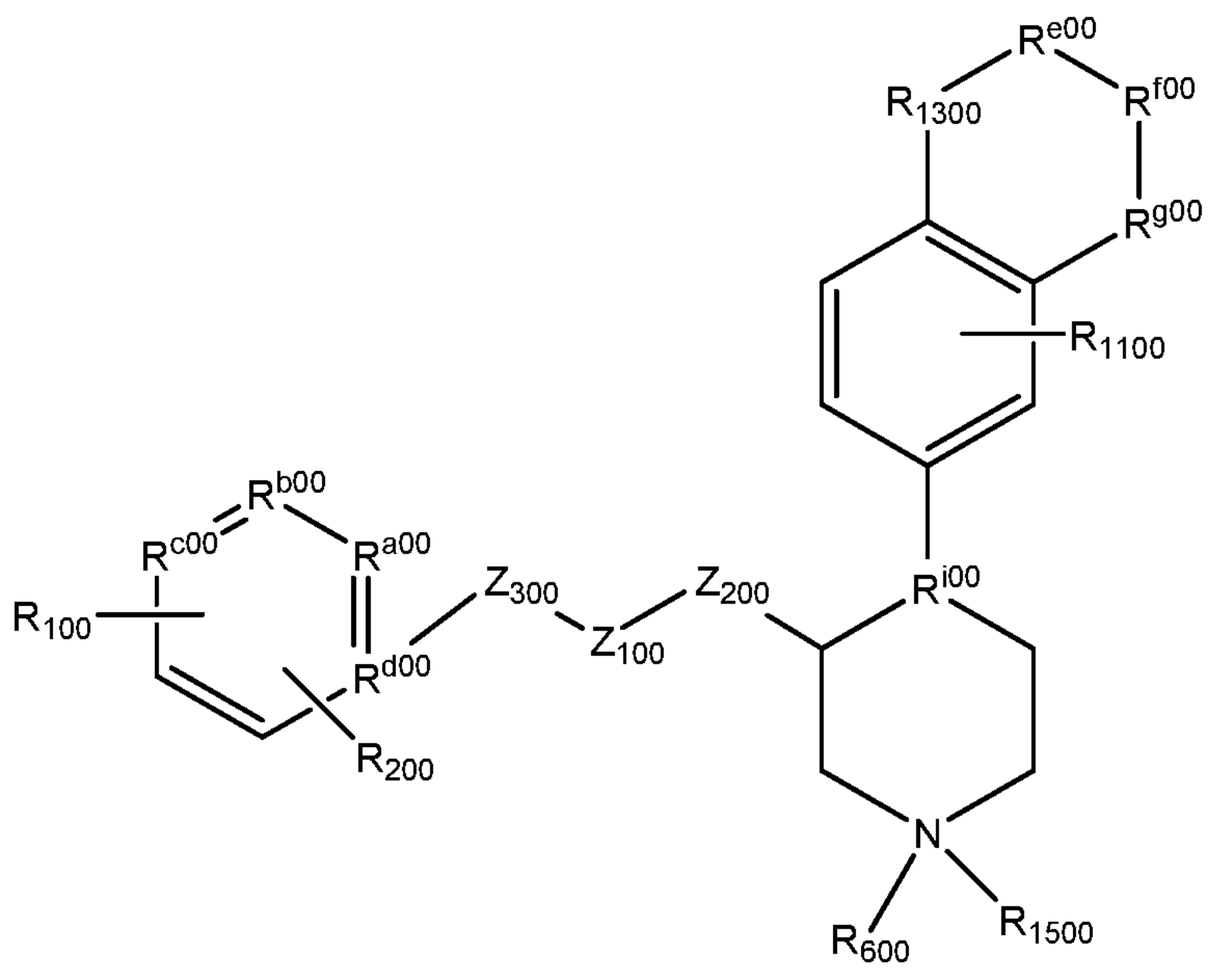
36. The method of claim 35, wherein the subject is a subject in need thereof.

37. A method of preparing a compound, or a pharmaceutically acceptable salt thereof, the method comprising preparing a compound according to one of the schemes described herein.

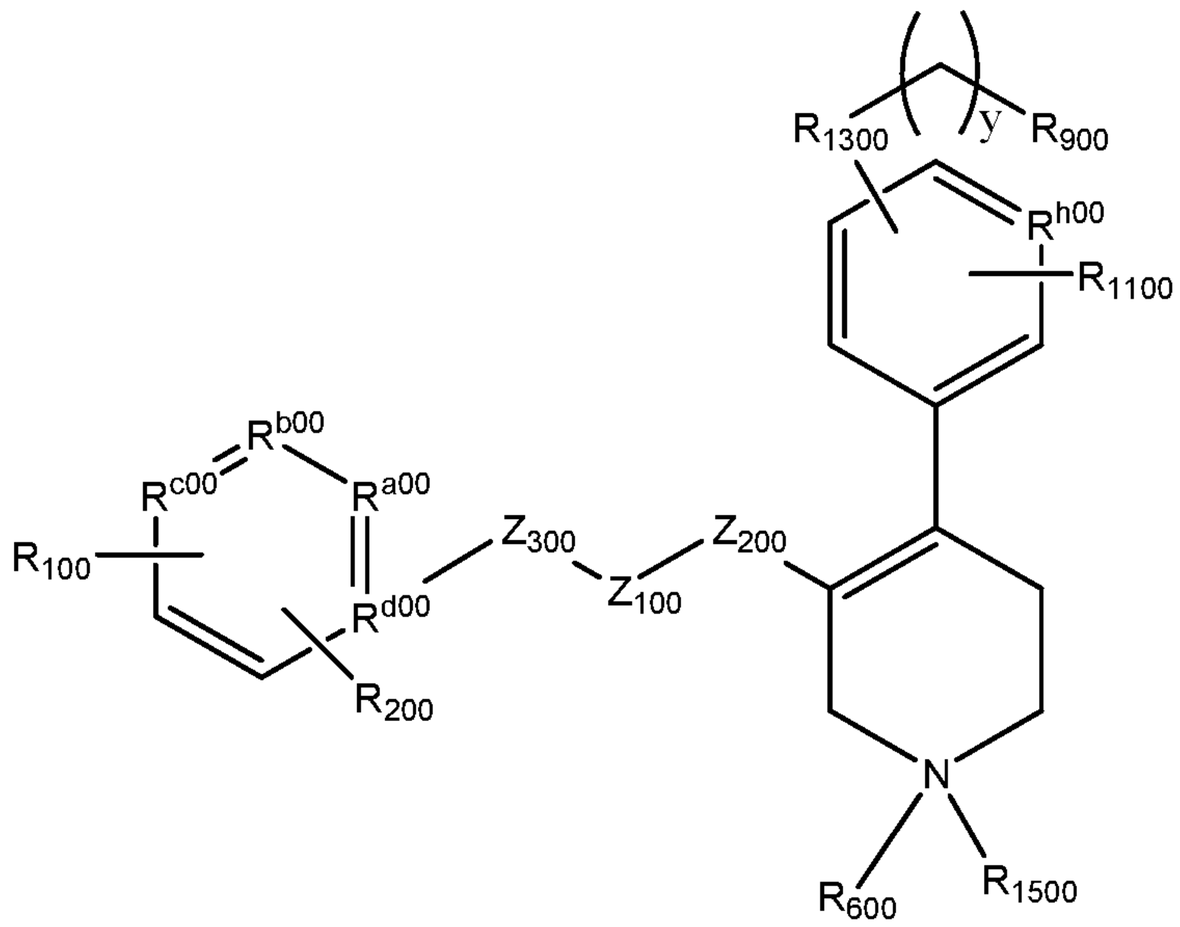
38. A compound having Formula I00, Formula I00A, Formula I00B, or Formula I00C, or pharmaceutically acceptable salt thereof:


R1300
y
R900
Rh00
R1100
Rb00
Rc00
Ra00
R100
Z300
Z200
Ri00
Z100
Rd00
R200
N
R600
R1500

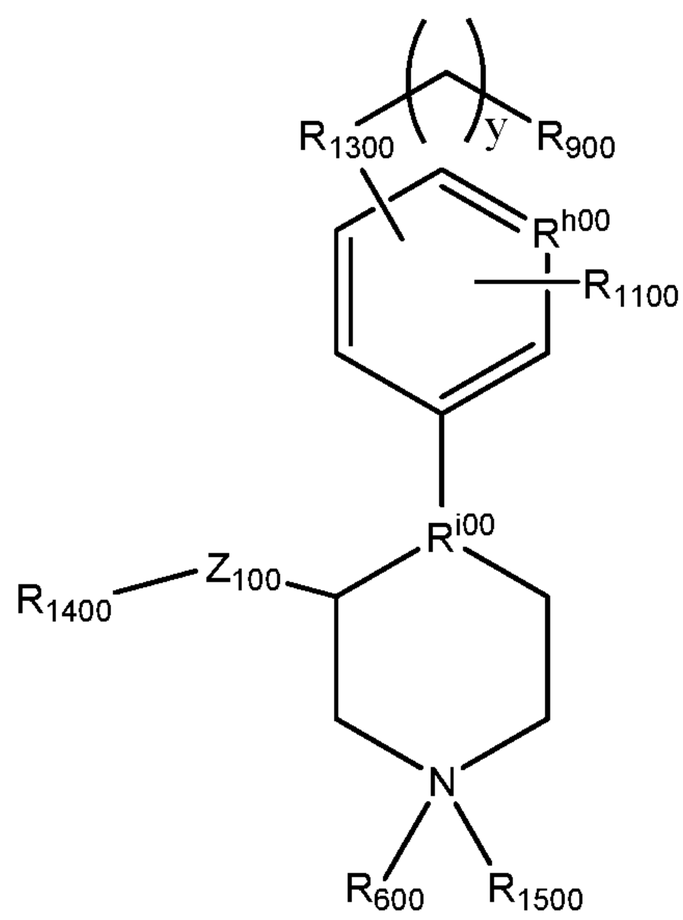
I00


Re00
R1300
Rf00
Rg00
R1100
Rb00
Rc00
Ra00
R100
Z300
Z200
Ri00
Z100
Rd00
R200
N
R600
R1500

I00A



I00B

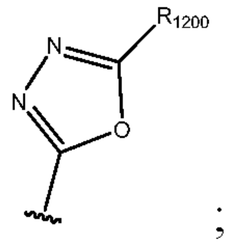


I00C

wherein:

R_{100}, $R_{200,}$ and R_{1400} are each, independently, H, cyano, optionally substituted C_1-C_6 branched or unbranched alkyl, optionally substituted C_1-C_6 alkoxy, optionally substituted C_1-C_6 haloalkyl, optionally substituted C_2-C_6 alkenyl, optionally substituted pyrimidine, optionally substituted pyridyl, optionally substituted pyrazole, optionally substituted isoxazole, optionally substituted pyridinone, optionally substituted aryl, halo,-NC(=O)R_{300}, -

$C(=O)NR_{300}R_{400}$, $-C(=O)OR_3$, $S(=O)_2NR_{300}R_{400}$, $-C(=O)R_{300}$, $-OR_3$, $-(CH_2)_nR_{500}$, =O, or



;

R_{1500} is a protecting group, $C(=O)OR_{81b}$, absent, or C_2-C_6 alkenyl, wherein $R81_b$ is H or optionally substituted branched or unbranched C_1-C_6 alkyl;

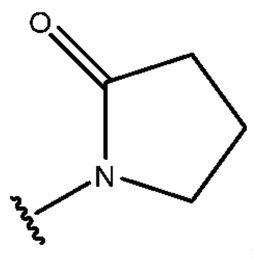
when R_{1500} is absent, R_{600} is H, optionally substituted aryl, optionally substituted C_1-C_6 haloalkyl, $-NR_{700}R_{800}$, optionally substituted C_1-C_6 branched or unbranched alkyl, optionally substituted C_2-C_6 alkenyl, $-(CH_2)_nR_{500}$, optionally substituted cycloalkyl, -OH, optionally substituted C_1-C_6 alkoxy, optionally substituted pyrrolinyl, optionally substituted morpholinyl, or optionally substituted piperldyl;

when R_{1500} is C_2-C_6 alkenyl, R_{600} is C_2-C_6 alkenyl;

R_{300}, R_{400}, and R_{1200} are each, independently, H, optionally substituted aryl, optionally substituted C_1-C_6 haloalkyl, $-NR_{700}R_{800}$, optionally substituted C_1-C_6 branched or unbranched alkyl, optionally substituted C_2-C_6 alkenyl, $-(CH_2)_nR_{500}$, optionally substituted cycloalkyl, -OH, optionally substituted alkoxy, optionally substituted pyrrolinyl, optionally substituted morpholinyl, or optionally substituted piperldyl; or R_{300} and R_{400} together form a 5-10 membered optionally substituted heterocycle or 5-10 membered optionally substituted heteroaryl with the atom to which R_{300} and R_{400} are bonded;

each R_{500} is, independently, H, optionally substituted C_1-C_6 haloalkyl, $-NR_{700}R_{800}$, optionally substituted C_1-C_6 branched or unbranched alkyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted C_2-C_6 alkenyl, optionally substituted cycloalkyl, optionally substituted heterocycle, -OH, optionally substituted alkoxy, optionally substituted pyrrolinyl, optionally substituted morpholinyl, or optionally substituted piperldyl;

R_{700} and R_{800} are, each, independently, H, optionally substituted aryl, optionally substituted C_1-C_6 haloalkyl, optionally substituted C_1-C_6 branched or unbranched alkyl, optionally substituted C_2-C_6 alkenyl, $-(CH_2)_nR_{500}$, optionally substituted cycloalkyl, -OH, optionally substituted alkoxy, optionally substituted pyrrolinyl, optionally substituted morpholinyl, or optionally substituted piperldyl; or R_{700} and R_{800} together form a 5-10 membered optionally substituted heterocycle or 5-10 membered optionally substituted heteroaryl with the atom to which R_{700} and R_{800} are bonded to,

R_{900} is absent, H, haloalkyl, $-OR_3$, or  , optionally substituted cycloalkyl, $-(CH_2)_pR_{500}$, or optionally substituted heterocycle;

R_{1100} is H, $-SO_2C_1$-C_6alkyl, $-OCF_3$, halo, or optionally substituted C_1-C_6 alkyl;

R_{1300} is a bond, C, N, S, or O;

R_{1400} is an optionally substituted pyridinone or optionally substituted –CH2-pyridinone;

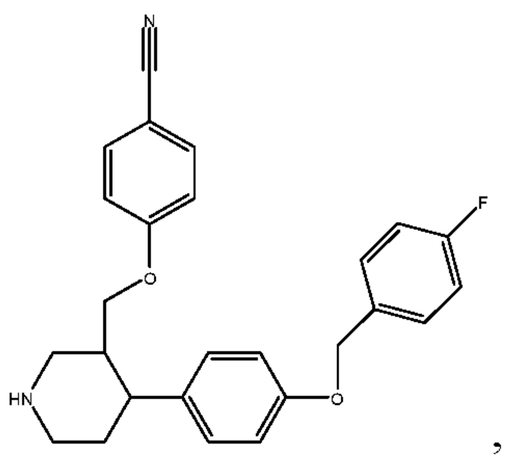
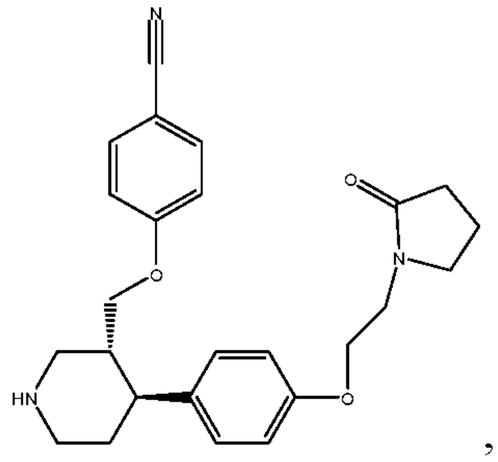
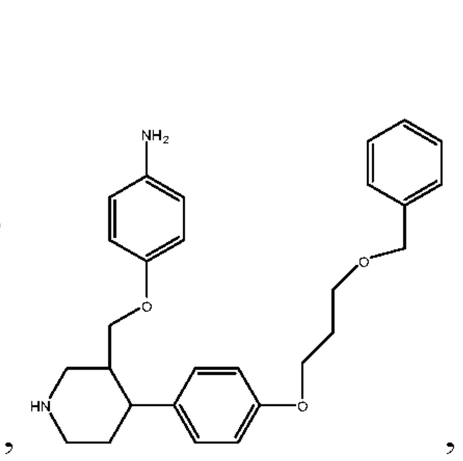
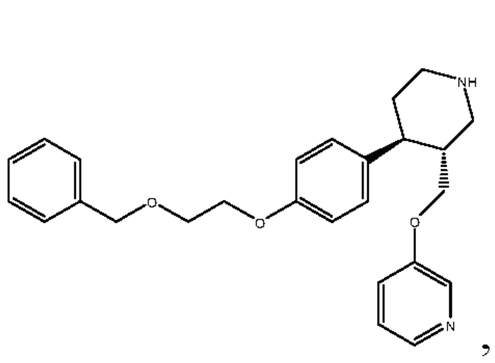
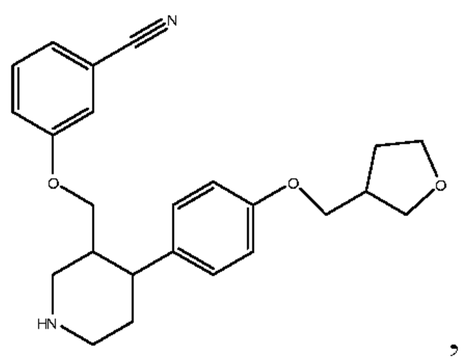
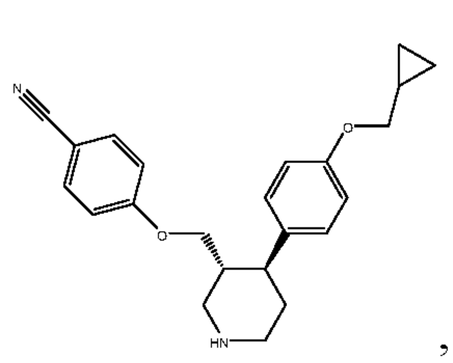
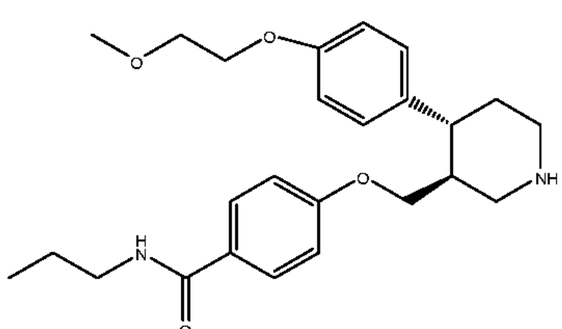
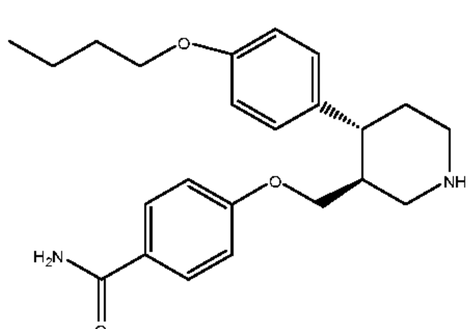
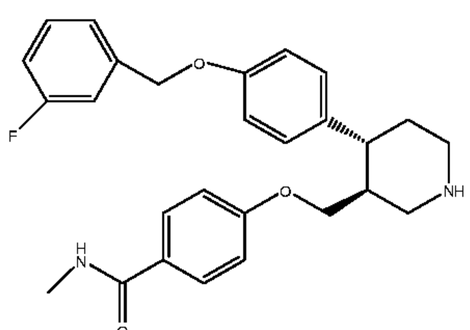
each n, p, and y is independently, an integer from 0-72;

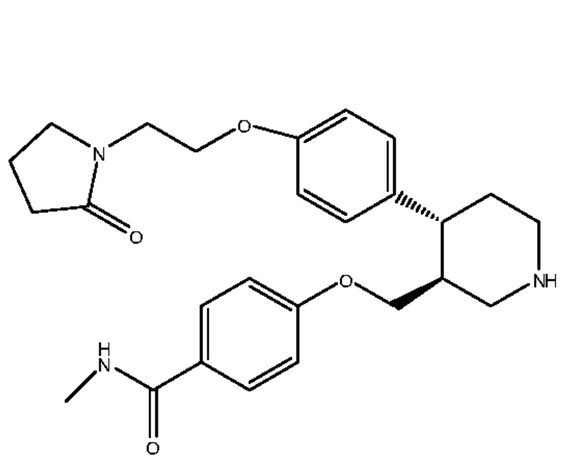
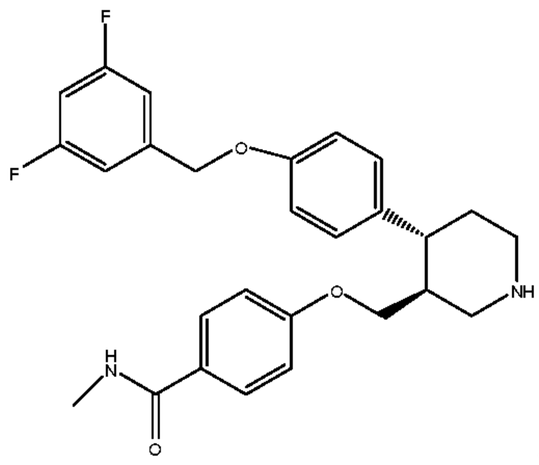
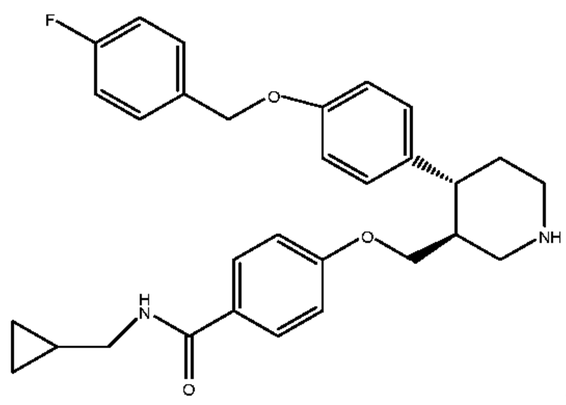
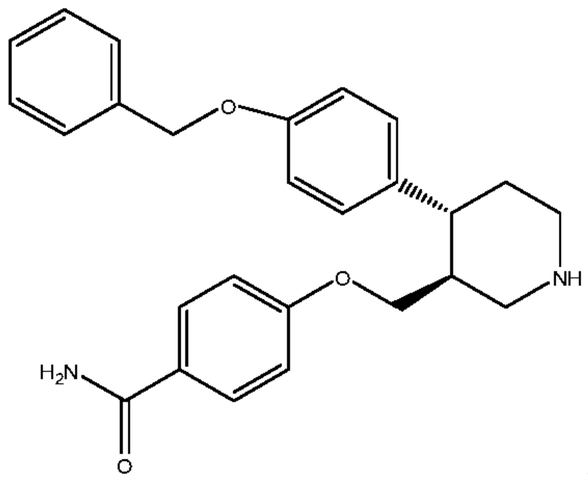
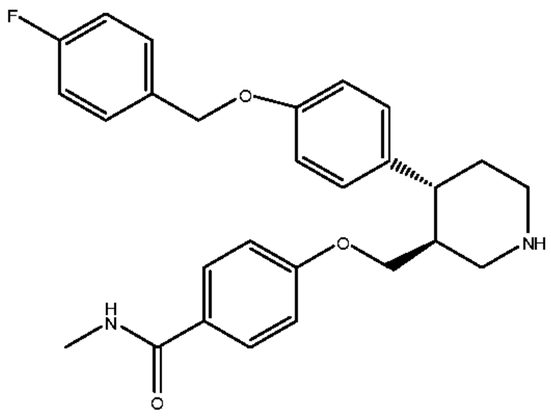
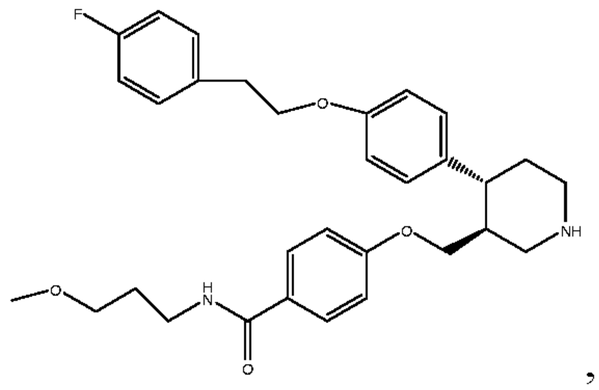
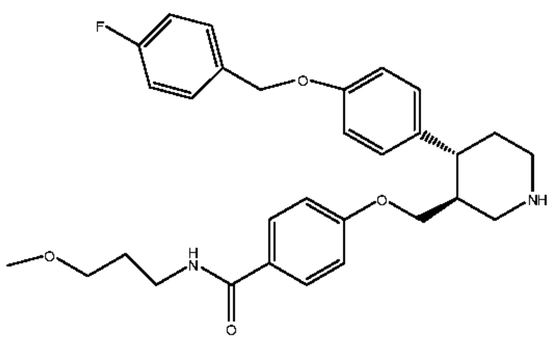
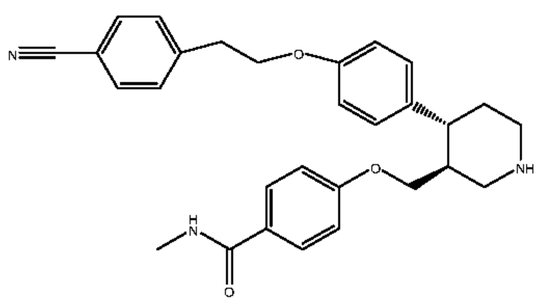
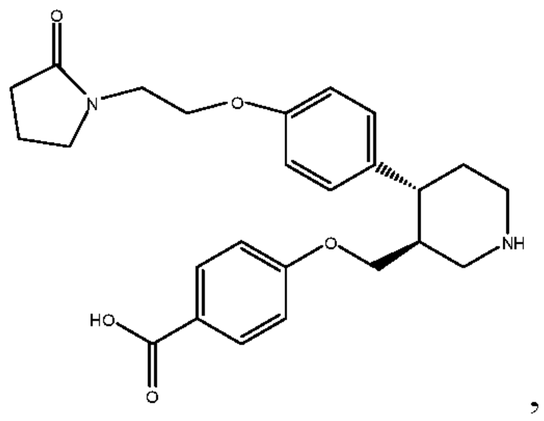
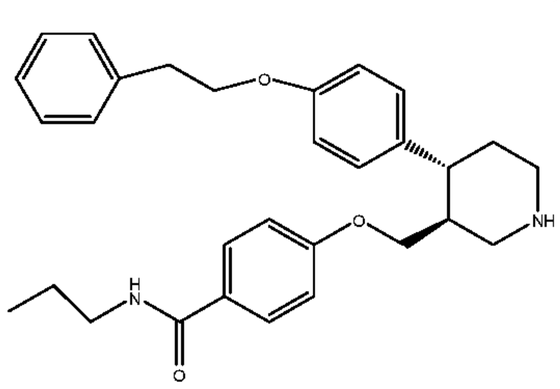
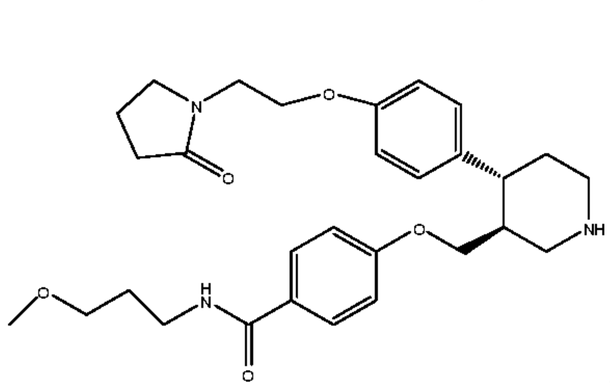
each R^{a00}, R^{b00}, R^{c00}, R^{d00}, R^{h00}, and R^{i00}, is, independently, C, N, or O,

each R^{e00}, R^{f00}, and R^{g00}, is, independently, C, N, S, O, or absent; and

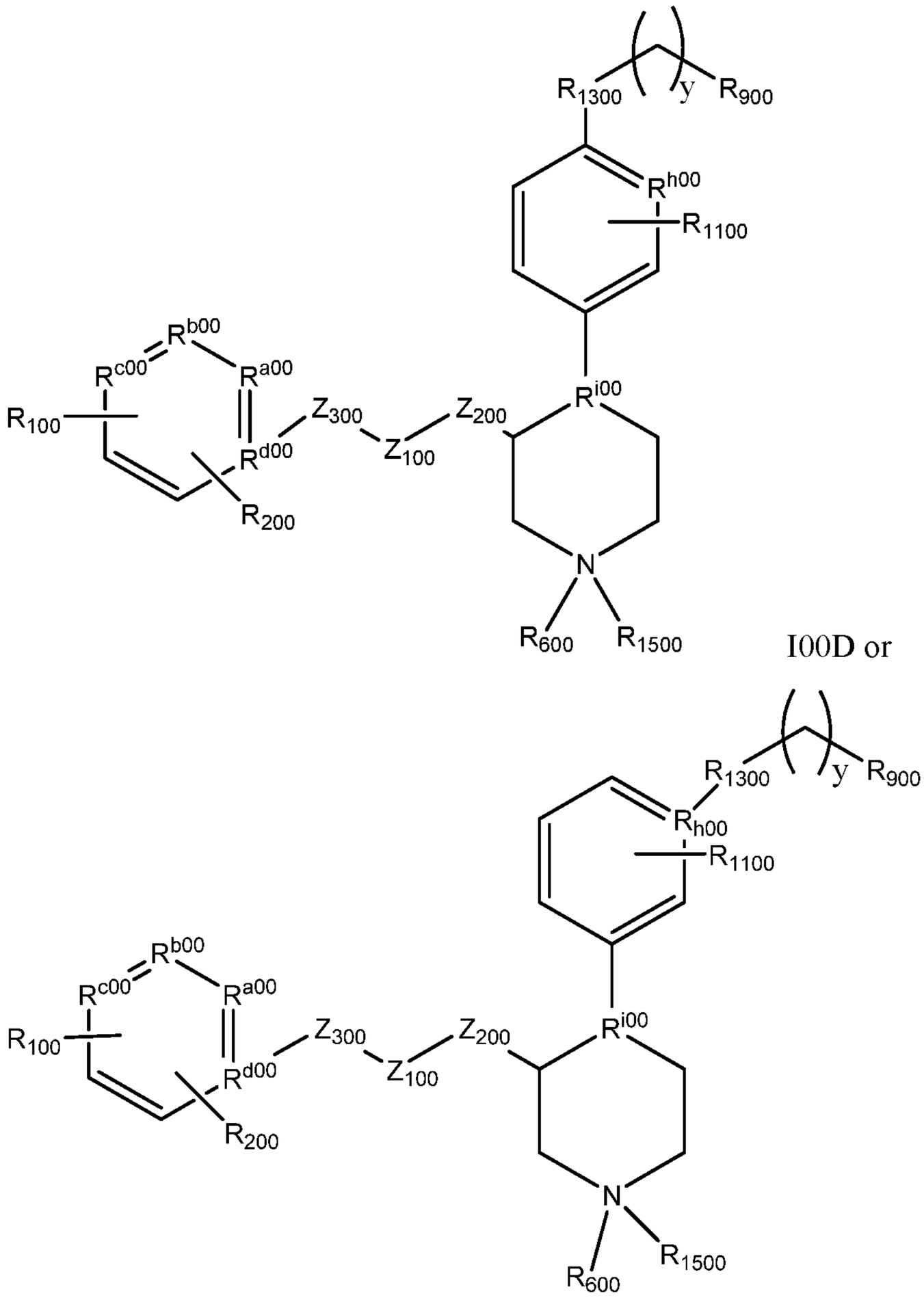
each Z_{100}, Z_{200}, and Z_{300}, is, independently, a bond, C(=O), C, N, S, or O,

provided that the compound or pharmaceutically acceptable thereof is not

 ,  ,  ,  ,  ,  ,  ,  ,  , , , ,


,

,

,

,

,

,

,

,

,

, or

.

39. The compound of claim 38 or pharmaceutically acceptable salt thereof having Formula I00D or Formula I00E:



I00D or

I00E

wherein:

R_{100}, R_{200}, R_{600}, R_{900}, and R_{1500} are as defined in claim 67;

R^{a00}, R^{b00}, R^{c00}, R^{d00}, R^{h00}, and R^{i00} are C;

R_{1100} is H;

R_{1300} and Z_{100} is O;

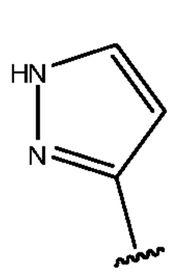
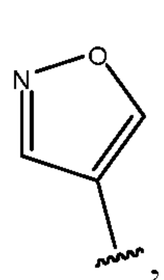
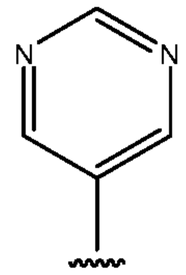
Z_{200} is C;

Z_{300} is a bond;

and y=2.

40. The compound or pharmaceutically acceptable salt thereof of claim 38 or 39, wherein R_{100} is $-C(=O)NR_{300}R_{400}$.

41. The compound or a pharmaceutically acceptable salt thereof of any one of claims 38-40, wherein each of R_{300} and R_{400} is, independently, H, halo, optionally substituted C_1-C_6 haloalkyl, or optionally substituted C_1-C_6 alkyl.

42. The compound or a pharmaceutically acceptable salt thereof of claims 38 or 39, wherein R_{100} is H, halo, -C(=O)NH_2, -C(=O)$NHCH_3$, -C(=O)$N(CH_3)_{68}$ -COOH, -C(=O)OCH_3, cyano, S(=O)$_2NH_2$, optionally substituted alkoxy, -OCF_3, CF_3, -NC(=O)CH_3, pyridyl,  ,  , or  .

43. The compound or a pharmaceutically acceptable salt thereof of any one of claims 38, 39, or 42, wherein R_{100} and R_{200} is each, independently, H, halo, or optionally substituted C_1-C_6 haloalkyl.

44. The compound or a pharmaceutically acceptable salt thereof of claim 43, wherein R_{100} and R_{200} are independently halo.

45. The compound or a pharmaceutically acceptable salt thereof of claim 43, wherein the optionally substituted C_1-C_6 haloalkyl is trifluoromethyl.

46. The compound or a pharmaceutically acceptable salt thereof of claim 43, wherein R_{100} is fluoro and R_{200} is trifluoromethyl.

47. The compound or a pharmaceutically acceptable salt thereof of any one of claims 38-46, wherein R_{100} and R_{200} are attached to different ring atoms.

48. The compound or a pharmaceutically acceptable salt thereof of claim 38 or 39, wherein R_{200} is H.

49. The compound or a pharmaceutically acceptable salt thereof of claim 38 or 39, wherein:

R_{600} is H, optionally substituted C_1-C_6 alkyl, or –C(=O)OR_3; and

R_{300} is an optionally substituted C_1-C_6 branched or unbranched alkyl.

50. The compound or a pharmaceutically acceptable salt thereof of claims 38 or 39, wherein:

R_{100} is -C(=O)NH_2 and R_{600} is H or optionally substituted C_1-C_6 alkyl; or

R_{100} is -C(=O)$NR_{300}R_{400}$, wherein R_{300} is H and R_{400} is optionally substituted branched or unbranched C_1-C_6 alkyl or optionally substituted branched or unbranched C_2-C_6 alkenyl and R_{600} is H or optionally substituted C_1-C_6 alkyl; or

R_{100} is -C(=O)$NR_{300}R_{400}$, wherein R_{300} and R_{400} are each, independently, optionally substituted branched or unbranched C_1-C_6 alkyl, and R_{600} is H, optionally substituted C_1-C_6 alkyl, or optionally substituted alkaryl.

51. The compound or a pharmaceutically acceptable salt thereof of claim 38 or 39, wherein R_{100} is -C(=O)$NR_{300}R_{400}$, wherein:

R_{300} and R_{400} are H;

R_{300} is H and R_{400} is optionally substituted C_1-C_6 unbranched or branched alkyl; or

R_{300} is H and R_{400} is optionally substituted C_2-C_6 unbranched or branched alkenyl; or

R_{300} is H and R_{400} is optionally substituted C_1-C_6 cycloalkyl; or

R_{300} is H and R_{400} is $–(CH_2)_nR_{500}$; wherein n is 1-6 and R_{500} is an optionally substituted cycloalkyl; or

R_{300} is H and R_{400} is $–(CH_2)_nR_{500}$, wherein n is 1-6 and R_{500} is an optionally substituted alkoxy; or

R_{300} and R_{400} are each, independently, optionally substituted C_1-C_6 alkyl.

52. The compound or a pharmaceutically acceptable salt thereof of claim 38 or 39, wherein R_{100} is $–C(=O)NR_{300}R_{400}$, wherein R_{300} and R_{400} together form a 5-10 membered optionally substituted heterocycle or 5-10 membered optionally substituted heteroaryl with the atom to which R_{300} and R_{400} are bonded.

53. The compound or a pharmaceutically acceptable salt thereof of claim 38, wherein R^{b00} is N.

54. The compound or a pharmaceutically acceptable salt thereof of claim 38, wherein R^{a00} is N.

55. The compound or a pharmaceutically acceptable salt thereof of claim 38, wherein R^{c00} is N.

56. The compound or a pharmaceutically acceptable salt thereof of claim 38, wherein R^{d00} is N.

57. The compound or a pharmaceutically acceptable salt thereof of any one of claims 53-55 wherein R_{1100} is H, R_{1300} is O, R^{i00} is C, Z_{100} is O, Z_{200} is C, Z_{300} is a bond, and y=2.

58. The compound or a pharmaceutically acceptable salt thereof of any one of claims 53-58, wherein R_{100}, R_{200}, and R_{600} are each H and Z is O.

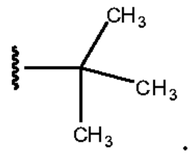
59. The compound or a pharmaceutically acceptable salt thereof of any one of claims 53-58, wherein R_{100} is =O and R_{200} is H.

60. The compound or a pharmaceutically acceptable salt thereof of claim 38 or 39, wherein

R_{100} is $-C(=O)NR_{300}R_{400;}$ and

R_{600} is H, C_1-C_6 alkyl, or $-C(=O)OR_3$, wherein R_{300} is an optionally substituted C_1-C_6 branched or unbranched alkyl.

61. The compound or a pharmaceutically acceptable salt thereof of claim 60, wherein

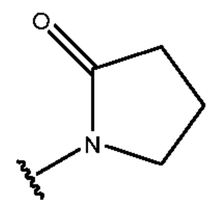
R_{300} is 

.

62. The compound or a pharmaceutically acceptable salt thereof of any one of claims 38-61, wherein

R_{600} is H, optionally substituted C_1-C_6 alkyl, optionally substituted C_2-C_6 alkenyl, $-OR_3$, or $(CH_2)_n$-aryl,

n is an integer from 0-2;

R_{900} is 

;

R_{1100} is H or halo;

R_{1300} is O;

R^{i00} is C;

y=2; and

optionally R_{1500} is optionally substituted C_2-C_6 alkenyl when R_{600} is optionally substituted C_2-C_6 alkenyl.

63. The compound or a pharmaceutically acceptable salt thereof of any one of claims 38-62, wherein R_{1100} is fluoro.

64. The compound or a pharmaceutically acceptable salt thereof of any one of claims 38-42, 48, 49, 53-57, or 60-63, wherein R_{100} is $-C(=O)NH_2$.

65. The compound or a pharmaceutically acceptable salt thereof of any one of claims claim 38, 39, 42, or 53-57, wherein R_{100} is cyano.

66. The compound or a pharmaceutically acceptable salt thereof of claim 38 wherein:

R^{a00}, R^{b00}, R^{c00}, R^{d00}, R^{h00}, and R^{i00} are C;

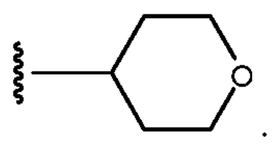
Z_{100} is O, Z_{200} is C, Z_{300} is a bond;

y=0;

R_{900} is branched or unbranched optionally substituted C_1-C_6 alkyl, optionally substituted haloalkyl, optionally substituted cycloalkyl, or optionally substituted heterocycle; and

R_{1300} is O.

67. The compound or a pharmaceutically acceptable salt thereof of claim 66, wherein R_{600} is H or optionally substituted branched or unbranched C_1-C_6 alkyl.

68. The compound or a pharmaceutically acceptable salt thereof of claim 66 or 67, wherein R_{900} is  .

69. The compound or a pharmaceutically acceptable salt thereof of any one of claims 66-68, wherein R_{100} is $-C(=O)NR_{300}R_{400}$ or cyano.

70. The compound or a pharmaceutically acceptable salt thereof of any one of claims 66-69, wherein R_{200} is H.

71. The compound or a pharmaceutically acceptable salt thereof of any one of claims 66-70, wherein R_{1100} is H.

72. The compound or a pharmaceutically acceptable salt thereof of claim 38, wherein:

one of R^{a00}, R^{b00}, R^{c00}, and R^{d00} is N;

Z_{100} is a bond or O;

Z_{200} is C, Z_{300} is a bond, and y=0;

R^{h00} and R^{i00} are C;

R_{100} is H, $-C(=O)NR_{300}R_{400}$ or =O;

R_{200} is H;

R_{600} is H, C_1-C_6 alkyl, or C_2-C_6 alkenyl;

R_{900} is C_1-C_6 alkyl, haloalkyl, or cycloalkyl;

R_{1100} is H; and

R_{1300} is O.

73. The compound or a pharmaceutically acceptable salt thereof of claim 72, wherein Z_{100} is a bond and R_{100} is =O.

74. The compound or a pharmaceutically acceptable salt thereof of claim 72, wherein R_{400} is H.

75. The compound or a pharmaceutically acceptable salt thereof of claim 72 or 74, wherein R^{d00} is N and R_{100} is =O.

76. The compound or a pharmaceutically acceptable salt thereof of claim 38, wherein:

R^{a00}, R^{b00}, R^{c00}, and R^{d00} are C;

R^{h00} and R^{i00} are C;

Z_{100} is O, Z_{200} is C, Z_{300} is a bond;

R_{1100} is halo or C_1-C_6 alkyl;

y=0;

R_{900} is H, haloalkyl or C_1-C_6 alkyl;

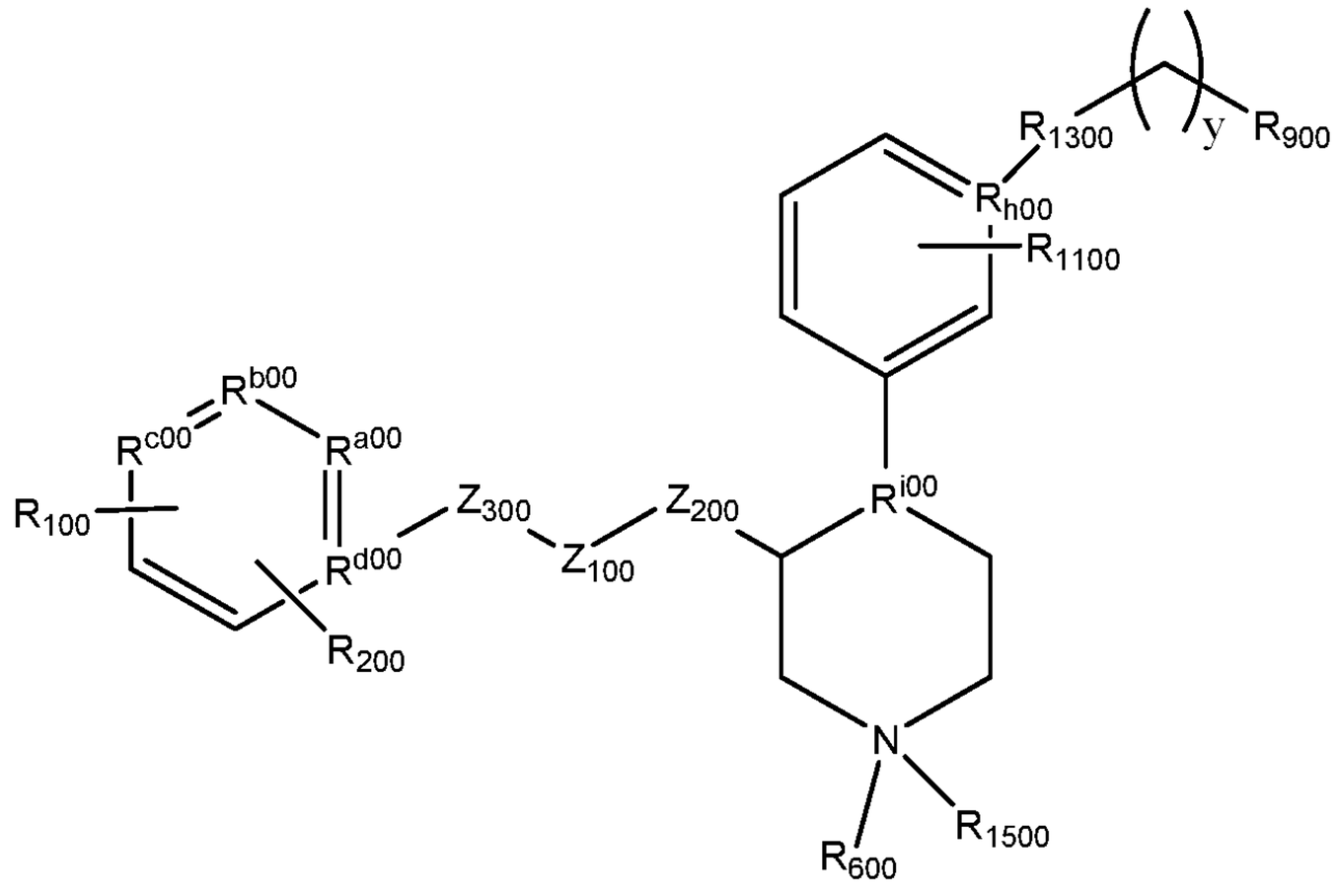
R_{1300} is O;

R_{600} is H, C_1-C_6 alkyl, or C_2-C_6 alkenyl;

R_{200} is H.

77. The compound or a pharmaceutically acceptable salt thereof of claim 76, wherein R_{100} is H, cyano or $-C(=O)NR_{300}R_{400}$.

78. The compound or a pharmaceutically acceptable salt thereof of claim 77 having Formula I00E:



I00E

wherein

R_{100}, R_{200}. R_{600}. and R_{900} are as defined in claim 77;

R^{a00}, R^{b00}, R^{c00}, R^{d00}, R^{h00} and R^{i00} are C;

R_{1300} is O;

Z_{100} is O, Z_{200} is C, Z_{300} is a bond; and

y=0.

79. The compound or a pharmaceutically acceptable salt thereof of claim 78, wherein R_{900} is H, haloalkyl, or C_1-C_6 alkyl.

80. The compound or a pharmaceutically acceptable salt thereof of claim 68 or 79, wherein R_{200} is H.

81. The compound or a pharmaceutically acceptable salt thereof of any one of claims 78-80, wherein R_{1100} is H.

82. The compound or a pharmaceutically acceptable salt thereof of any one of claims 78-81, wherein R_{600} is H, C_1-C_6 alkyl, or C_2-C_6 alkenyl.

84. The compound or a pharmaceutically acceptable salt thereof of any one of claims 78-82, wherein R_{100} is H, cyano, or $–C(=O)NR_{300}R_{400}$.

85. The compound or a pharmaceutically acceptable salt thereof of any one of claims 78-83, wherein R_{900} is H or C_1-C_6 alkyl.

86. The compound or a pharmaceutically acceptable salt thereof of Formula I00A of claim 38, wherein

R^{a00}, R^{b00}, R^{c00}, R^{d00}, R^{e00}, and R^{i00} are C,

R^{g00} is C or O;

R^{f00} is absent;

R_{1300} is O; and

Z_{100} is O, Z_{200} is C, and Z_{300} is a bond.

87. The compound or a pharmaceutically acceptable salt thereof of claim 86, wherein R_{200} is H.

88. The compound or a pharmaceutically acceptable salt thereof of claim 86 or 87, wherein R_{1100} is H.

89. The compound or a pharmaceutically acceptable salt thereof of any one of claims 86-88, wherein R_{600} is H, optionally substituted C_1-C_6 alkyl or optionally substituted C_2-C_6 alkenyl.

90. The compound or a pharmaceutically acceptable salt thereof of any one of claims 84-88, wherein R_{100} is H, cyano,

$–C(=O)NR_{300}R_{400}$, or C_1-C_6 alkyl.

91. The compound or a pharmaceutically acceptable salt thereof of any one of claims 84-89, wherein R^{g00} is O.

92. The compound or a pharmaceutically acceptable salt thereof of claim 38, wherein y=1.

93. The compound or a pharmaceutically acceptable salt thereof of claim 92, wherein R_{900} is an optionally substituted C_1-C_6 alkyl or optionally substituted cycloalkyl.

94. The compound or a pharmaceutically acceptable salt thereof of claim 92 or 93, wherein R^{a00}, R^{b00}, R^{c00}, R^{d00}, R^{h00}, and R^{i00} are C.

95. The compound or a pharmaceutically acceptable salt thereof of any of one of claims 91-94, wherein R_{1300} is O.

96. The compound or a pharmaceutically acceptable salt thereof of any of one of claims 91-95, wherein Z_{100} is O, Z_{200} is C, and Z_{300} is a bond.

97. The compound or a pharmaceutically acceptable salt thereof of any one of claims 91-96, wherein R_{200} and R_{1100} are H.

98. The compound or a pharmaceutically acceptable salt thereof of any one of claims 91-97, wherein R_{100} is $-C(=O)NR_{300}R_{400}$.

99. The compound or a pharmaceutically acceptable salt thereof of any one of claims 91-98, wherein R_{600} is H or optionally substituted C_1-C_6 alkyl.

100. The compound or a pharmaceutically acceptable salt thereof of claim 38, wherein R^{h00} is N.

101. The compound or a pharmaceutically acceptable salt thereof of claim 100, wherein R^{a00}, R^{b00}, R^{c00}, R^{d00}, R^{i00} are C.

102. The compound or a pharmaceutically acceptable salt thereof of claim 100 or 101, wherein R_{200} is H.

103. The compound or a pharmaceutically acceptable salt thereof of any one of claims 100-102, wherein R_{1300} is O.

104. The compound or a pharmaceutically acceptable salt thereof of any one of claims 100-103, wherein Z_{100} is O, Z_{200} is C, and Z_{300} is a bond.

105. The compound or a pharmaceutically acceptable salt thereof of any one of claims 100-104, wherein R_{1100} is H.

106. The compound or a pharmaceutically acceptable salt thereof of any one of claims 100-105, wherein R_{600} is optionally substituted C_2-C_6 alkenyl, optionally substituted C_1-C_6 alkyl, or H.

107. The compound or a pharmaceutically acceptable salt thereof of any one of claims 100-106, wherein R_{100} is H or $-C(=O)NR_{300}R_{400}$.

108. The compound or a pharmaceutically acceptable salt thereof of claim 38, wherein R_{1100} is H or halo.

109. The compound or a pharmaceutically acceptable salt thereof of claim 108, wherein R^{a00}, R^{b00}, R^{c00}, R^{d00}, and R^{i00} are C.

110. The compound or a pharmaceutically acceptable salt thereof of claim 108 or 109, wherein Z_{100} is O, Z_{200} is C, Z_{300} is a bond.

111. The compound or a pharmaceutically acceptable salt thereof of any one of claims 108-110, wherein R_{1300} is a bond or C.

112. The compound or a pharmaceutically acceptable salt thereof of any one of claims 108 -111, wherein y=1.

113. The compound or a pharmaceutically acceptable salt thereof of any one of claims 108 -112, wherein R_{900} is H.

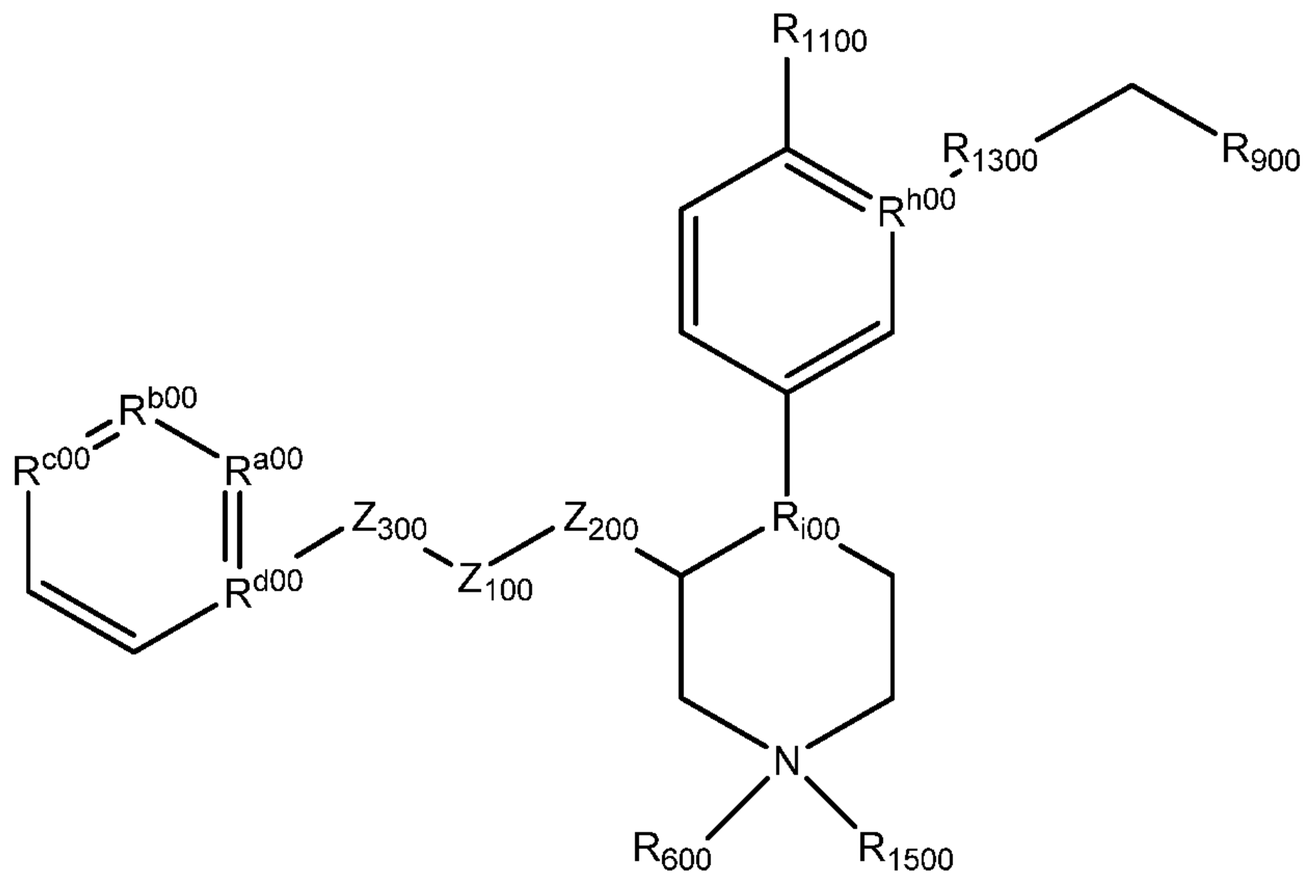
114. The compound or a pharmaceutically acceptable salt thereof of any one of claims 108-113, wherein R_{600} is H, optionally substituted C_1-C_6 alkyl, or optionally substituted C_2-C_6 alkenyl.

115. The compound or a pharmaceutically acceptable salt thereof of any one of claims 108-114, wherein R_{200} is H.

116. The compound or a pharmaceutically acceptable salt thereof of any one of claims 108-115, wherein R_{100} is H, -C(=O)$NR_{300}R_{400}$, or cyano.

117. The compound or a pharmaceutically acceptable salt thereof of claim 108, wherein y=0, R_{1300} is a bond and R_{900} is H.

118. The compound or a pharmaceutically acceptable salt thereof of claim 108, having Formula 00X:



00**X**,

wherein

R_{100}, R_{200}. R_{600}. and R_{900} are as defined above;

Z_{100} is O, Z_{200} is C, Z_{300} is a bond;

R^{a00}, R^{b00}, R^{c00}, R^{d00}, R^{h00}, and R^{i00} are C;

R_{200} is H;

R_{1100} is halo;

R_{1300} is O;

y=0-72; and

R_{900} is C_1-C_6 alkyl.

119. The compound or a pharmaceutically acceptable salt thereof of claim 118, wherein R_{600} is H, optionally substituted C_1-C_6 alkyl, or optionally substituted C_2-C_6 alkenyl.

120. The compound or a pharmaceutically acceptable salt thereof of claim 118 or 119, wherein R_{100} is H, cyano, or $-C(=O)NR_{300}R_{400}$.

121. The compound or a pharmaceutically acceptable salt thereof of claim 38, wherein Z_{100} is O, Z_{200} and Z_{300} is C.

122. The compound or a pharmaceutically acceptable salt thereof of claim 121, wherein R^{i00} is C.

123. The compound or a pharmaceutically acceptable salt thereof of any of claim 121 or 122, wherein R_{200} and/or R_{1100} are H.

124. The compound or a pharmaceutically acceptable salt thereof of any one of claims 121-123, wherein R_{600} is H.

125. The compound or a pharmaceutically acceptable salt thereof of any one of claims 121-124, wherein R_{100} is H, halo, cyano, $-C(=O)OR_3$, or $-C(=O)NR_{300}R_{400}$.

126. The compound or a pharmaceutically acceptable salt thereof of any one of claims 121-125, wherein:

R_{1300} is O;

R_{900} is H or $-OR_3$;

and y is 0-72.

127. The compound or a pharmaceutically acceptable salt thereof of claim 38, wherein:

Z_{100} is S or O;

Z_{300} is absent;

Z_{200} is C;

R_{200} and/or R_{1100} are H;

R^{i00} is C;

R_{1300} is O;

R_{900} is H or $-OR_3$;

and y=0-72.

128. The compound or a pharmaceutically acceptable salt thereof of claim 127, wherein R^{a00}, R^{b00}, R^{c00}, R^{d00}, R^{h00}, and R^{i00} are C.

129. The compound or a pharmaceutically acceptable salt thereof of claim 127 or 128, wherein R_{600} is H or $-C(=O)OR_3$.

130. The compound or a pharmaceutically acceptable salt thereof of any one of claims 127-129, wherein R_{100} is H or $-C(=O)NR_{300}R_{400}$.

131. The compound or a pharmaceutically acceptable salt thereof of claim 38, wherein:

R^{i00} is N;

R_{200} and/or R_{1100} are H;

Z_{300} is a bond or C;

Z_{100} is N or O; and

Z_{200} is C or C(=O).

132. The compound or a pharmaceutically acceptable salt thereof of claim 131, wherein R^{a00}, R^{b00}, R^{c00}, R^{d00}, R^{h00} are C.

133. The compound or a pharmaceutically acceptable salt thereof of claim 131 or 132, wherein R_{1300} is O.

134. The compound or a pharmaceutically acceptable salt thereof of any one of claims 131-133, wherein R_{900} is H and y=0-72.

135. The compound or a pharmaceutically acceptable salt thereof of any one of claims 131-134, wherein R_{100} is halo, H, cyano, $-C(=O)NR_{300}R_{400}$, or $-OR_3$.

136. The compound or a pharmaceutically acceptable salt thereof of any one of claims 131-135, wherein R_{600} is H, optionally substituted C_1-C_6 alkyl, or $-(CH_2)_p$-aryl, wherein p is an integer from 0-2.

137. The compound or a pharmaceutically acceptable salt thereof of any one of claims 131-136, wherein Z_{200} is C(=O), Z_{100} is N, and Z_{300} is C.

138. The compound or a pharmaceutically acceptable salt thereof of claim 38, wherein:

Z_{200} is C(=O) or C;

Z_{100} is N or O; and

Z_{300} is C or absent.

139. The compound or a pharmaceutically acceptable salt thereof of claim 138, wherein R^{a00}, R^{b00}, R^{c00}, R^{d00}, and R^{h00} are C.

140. The compound or a pharmaceutically acceptable salt thereof of any one of claims 138-139, wherein R_{200} is H.

141. The compound or a pharmaceutically acceptable salt thereof of any one of claims 138-140, wherein R_{100} is H, halo, cyano, or $–C(=O)NR_{300}R_{400}$.

142. The compound or a pharmaceutically acceptable salt thereof of any one of claims 138-141, wherein R_{1100} is H.

143. The compound or a pharmaceutically acceptable salt thereof of any one of claims 138-142, wherein

R_{1300} is O; and

R_{900} is H or $–OR_3$.

144. The compound or a pharmaceutically acceptable salt thereof of any one of claims 138-143, wherein R_{600} is H, C_1-C_6 alkyl, or $-(CH_2)_pR_{500}$.

145. The compound or a pharmaceutically acceptable salt thereof of any one of claims 138-144, wherein:

Z_{100} is O;

Z_{300} is absent; and

Z_{200} is C.

146. The compound or salt there of any one of claims 138-145, having Formula I00B.

147. The compound or a pharmaceutically acceptable salt thereof of Formula I00C of claim 38, wherein Z_{100} is C or O and R_{1400} is a pyridinone or optionally substituted -CH2-pyridinone.

148. The compound or a pharmaceutically acceptable salt thereof of claim 147, wherein R_{600} is H.

149. The compound or a pharmaceutically acceptable salt thereof of claim 147 or 148, wherein R^{i00} and R^{h00} are C.

150. The compound or a pharmaceutically acceptable salt thereof of any one of claims 147-149, wherein R_{1300} is O.

151. The compound or a pharmaceutically acceptable salt thereof of any one of claims 147-150, wherein y is an integer from 1-4.

152. The compound of claim 38, wherein the compound is chosen from a compound of Figure 1.

153. A pharmaceutical composition comprising a compound or pharmaceutically acceptable salt thereof of any one of claims 38-152.

154. A method of treating pain, neuropathic pain, migraine, headache, depression, Parkinson's disease, anxiety, overactive bladder, medication overuse headache, hyperalgesia, decreasing nociceptive sensitization, pain in an opioid exposed subject, PTSD, or other disorder or condition described herein in a mammal comprising administering to the mammal one or more compounds, or a salt thereof, of any of claims 38-152 or a pharmaceutical composition comprising one or more compounds, or salt thereof, of any one of claims 38-152.

155. The method of claim 154, wherein the mammal is a mammal in need thereof.

156. A method of treating hyperalgesia in a subject comprising administering to the subject comprising administering to the mammal one or more compounds, or a salt thereof, of any of claims 38-152 or a pharmaceutical composition comprising one or more compounds, or salt thereof, of any one of claims 38-152.

157. The method of claim 156, wherein the hyperalgesia is opioid induced hyperalgesia.

158. The method of claim 157, wherein the opioid induced hyperalgesia is morphine, oxycodone, hydrocodone, hydromorphone, fentanyl, meperidine, alfentanil, remifentanil, sufentanil, etorphine, buprenorphine, methadone, and/or heroin induced hyperalgesia.

159. The method of claim 156, wherein the subject has been administered an opioid prior to being administered the one or more compounds, or a salt thereof, of the pharmaceutical composition comprising the one or more compounds, or salt thereof.

160. A method of decreasing nociceptive sensitization in a subject comprising administering to the subject one or more compounds, or a salt thereof, of any of claims 38-152 or a pharmaceutical composition comprising one or more compounds, or salt thereof, of any one of claims 38-152.

161. The method of claim 160, wherein the subject has opioid induced nociceptive sensitization.

162. The method of claim 161, wherein the opioid induced nociceptive sensitization is morphine, oxycodone, hydrocodone, hydromorphone, fentanyl, meperidine, alfentanil, remifentanil, sufentanil, etorphine, buprenorphine, methadone, and/or heroin, or a pharmaceutically acceptable salt thereof, induced nociceptive sensitization.

163. A method of treating pain in a subject comprising:

administering an opioid agonist to the subject until the opioid increases nociceptive sensitization in the subject; and

administering to the subject one or more compounds, or a salt thereof, of any of claims 38-152 or a pharmaceutical composition comprising one or more compounds, or salt thereof, of any one of claims 38-152.

164. The method of claim 163, wherein the opioid agonist is morphine, oxycodone, hydrocodone, hydromorphone, fentanyl, meperidine, alfentanil, remifentanil, sufentanil, etorphine, buprenorphine, methadone, and/or heroin, or a pharmaceutically acceptable salt thereof.

165. A method of treating pain in an opioid exposed subject comprising:

a) administering an opioid agonist to the subject;

b) administering to the subject of step a), in the absence of the opioid administered in step a), one or more compounds, or a salt thereof, of any of claims 38-152 or a pharmaceutical composition comprising one or more compounds, or salt thereof, of any one of claims 38-152.

166. The method of claim 165, wherein the opioid is morphine, oxycodone, hydrocodone, hydromorphone, fentanyl, meperidine, alfentanil, remifentanil, sufentanil, etorphine, buprenorphine, methadone, and/or heroin, or a pharmaceutically acceptable salt thereof.

167. A method of treating medication overuse headache in a subject comprising administering to the subject one or more compounds, or a salt thereof, of any of claims 38-152 or a pharmaceutical composition comprising one or more compounds, or salt thereof, of any one of claims 38-152.

168. The method of claim 167, wherein the medication overuse headache is caused by acetaminophen, aspirin, a mu-opioid agonist, a non-steroidal anti-inflammatory drug (NSAID), or a triptan.

169. The method of claim 168, wherein the triptan is sumatriptan, rizatriptan, naratriptan, zolmitriptan, eletriptan, almotriptan, frovatriptan, avitriptan, or donitriptan, or a pharmaceutically acceptable salt thereof.

170. The method of claim 168, wherein the mu-opioid agonist is morphine, oxycodone, hydrocodone, hydromorphone, fentanyl, meperidine, alfentanil, remifentanil, sufentanil,

etorphine, buprenorphine, methadone, or heroin, or a pharmaceutically acceptable salt thereof.

171. A method of treating a migraine in a subject, the method comprising:
administering a triptan to a subject; and
administering to the subject one or more compounds, or a salt thereof, of any of claims 38-152 or a pharmaceutical composition comprising one or more compounds, or salt thereof, of any one of claims 38-152.

172. The method of claim 171, wherein the one or more compounds, or a salt thereof, of any of claims 38-152 or the pharmaceutical composition comprising one or more compounds, or salt thereof, of any one of claims 38-152 is administered in the absence of the triptan.

173. The method of claim 171, wherein the triptan is sumatriptan, rizatriptan, naratriptan, zolmitriptan, eletriptan, almotriptan, frovatriptan, avitriptan, or donitriptan, or a pharmaceutically acceptable salt thereof.

174. The method of claim 171, wheren the subject develops mediation overuse headache prior to being administered the one or more compounds, or a salt thereof, of any of claims 38-152 or the pharmaceutical composition comprising one or more compounds, or salt thereof, of any one of claims 38-152.

175. The method of any one of claims 154-174, wherein the compound, or a pharmaceutically acceptable salt thereof, is selected from the group consisting of: B1049, B0704, B0707, B0720, B0876, B1079, B1145, B1194, B1205, B1211, B1365, B1401, or the pharmaceutical composition comprises a compound, or a pharmaceutically acceptable salt thereof, is selected from the group consisting of: B1049, B0704, B0707, B0720, B0876, B1079, B1145, B1194, B1205, B1211, B1365, B1401.

Figure 1

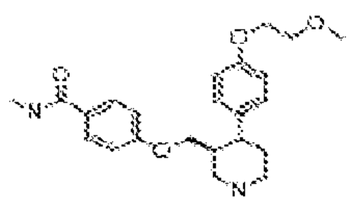
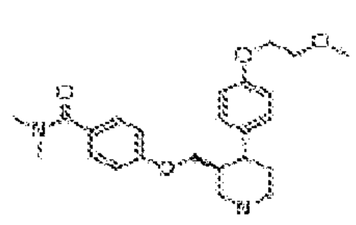
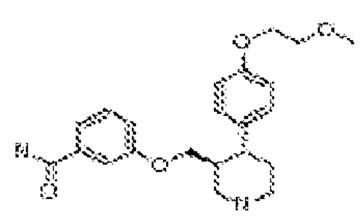
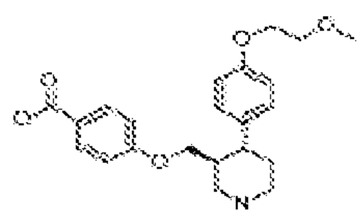
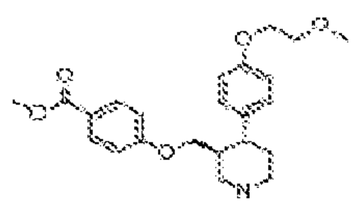
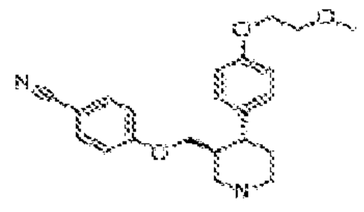
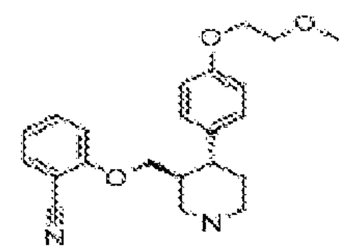
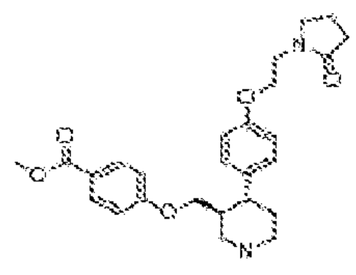
Structure	Compound	Name	calc. MW	LCMS
	B0001	4-{[(trans)-4-[4-(2-methoxyethoxy)phenyl]piperidin-3-yl]methoxy}-N-methylbenzamide	398.5	399
	B0002	4-{[(trans)-4-[4-(2-methoxyethoxy)phenyl]piperidin-3-yl]methoxy}-N,N-dimethylbenzamide	412.52	413
	B0003	3-{[(trans)-4-[4-(2-methoxyethoxy)phenyl]piperidin-3-yl]methoxy}benzamide	384.47	385
	B0004	4-{[(trans)-4-[4-(2-methoxyethoxy)phenyl]piperidin-3-yl]methoxy}benzoic acid	385.45	386
	B0005	methyl 4-{[(trans)-4-[4-(2-methoxyethoxy)phenyl]piperidin-3-l]methoxy}benzoate	399.48	400
	B0006	4-{[(trans)-4-[4-(2-methoxyethoxy)phenyl]piperidin-3-yl]methoxy}benzonitrile	366.45	367
	B0007	2-{[(trans)-4-[4-(2-methoxyethoxy)phenyl]piperidin-3-yl]methoxy}benzonitrile	366.45	367
	B0008	methyl 4-{[(trans)-4-{4-[2-(2-oxopyrrolidin-1-yl)ethoxy]phenyl}piperidin-3-yl]methoxy}benzoate	452.54	453

Figure 1-Continued

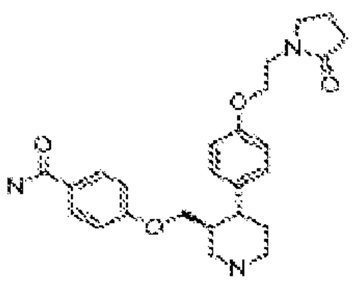
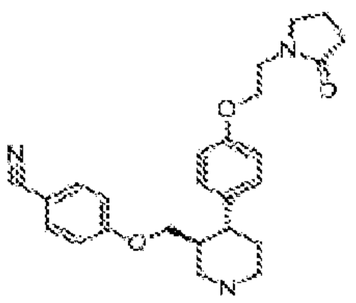
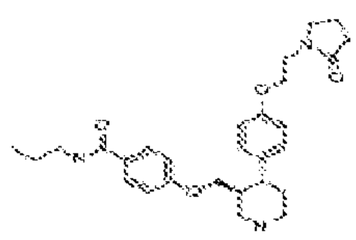
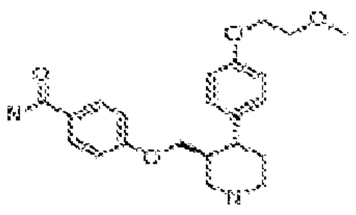
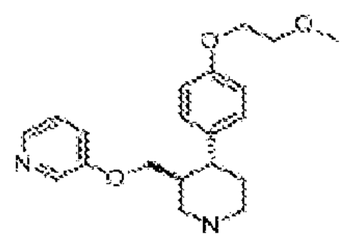
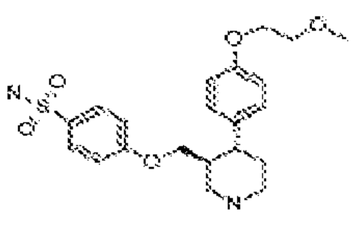
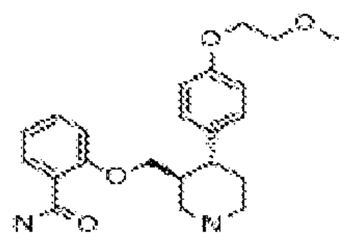
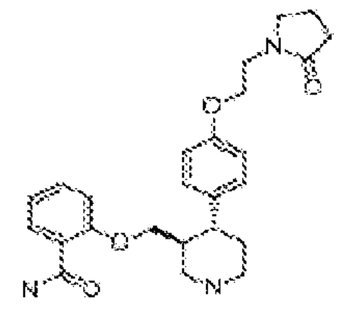
	B0009	4-{[(trans)-4-{4-[2-(2-oxopyrrolidin-1-yl)ethoxy]phenyl}piperidin-3-yl]methoxy}benzamide	437.53	438
	B0010	4-{[(trans)-4-{4-[2-(2-oxopyrrolidin-1-yl)ethoxy]phenyl}piperidin-3-yl]methoxy}benzonitrile	419.52	420
	B0011	4-{[(trans)-4-{4-[2-(2-oxopyrrolidin-1-yl)ethoxy]phenyl}piperidin-3-yl]methoxy}-N-propylbenzamide	479.61	480
	B0012	4-{[(trans)-4-[4-(2-methoxyethoxy)phenyl]piperidin-3-yl]methoxy}benzamide	384.47	385
	B0013	3-{[(trans)-4-[4-(2-methoxyethoxy)phenyl]piperidin-3-yl]methoxy}pyridine	342.43	343
	B0014	4-{[(trans)-4-[4-(2-methoxyethoxy)phenyl]piperidin-3-yl]methoxy}benzene-1-sulfonamide	420.52	421
	B0015	2-{[(trans)-4-[4-(2-methoxyethoxy)phenyl]piperidin-3-yl]methoxy}benzamide	384.47	385
	B0016	2-{[(trans)-4-{4-[2-(2-oxopyrrolidin-1-yl)ethoxy]phenyl}piperidin-3-yl]methoxy}benzamide	437.53	438

Figure 1-Continued

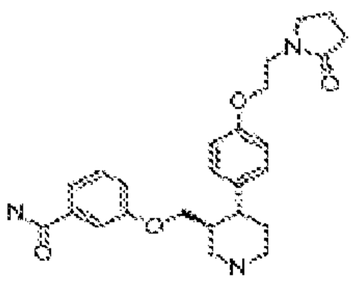
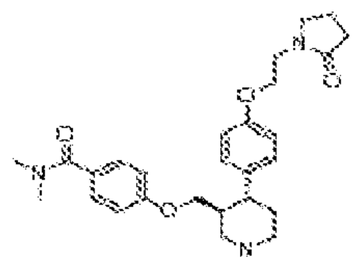
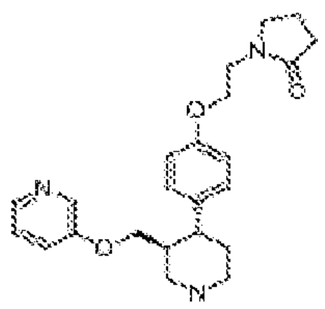
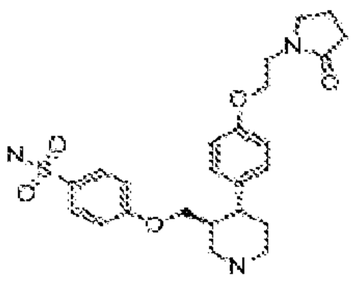
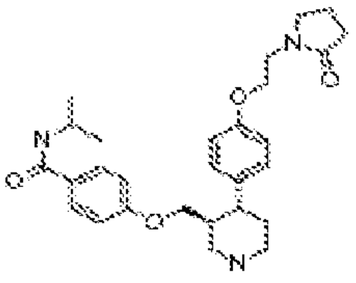
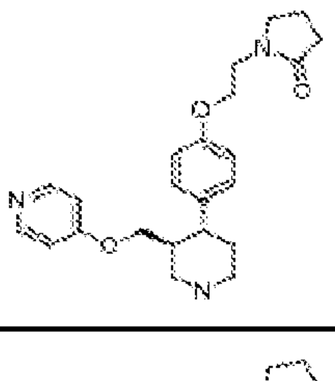
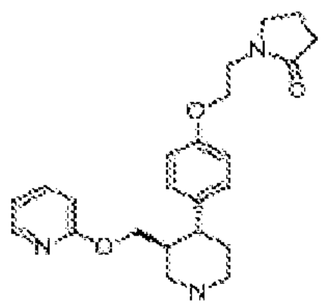
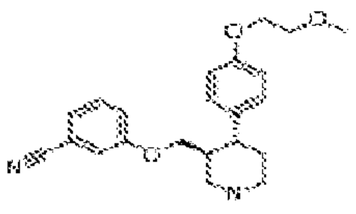
	B0017	3-{[(trans)-4-{4-[2-(2-oxopyrrolidin-1-yl)ethoxy]phenyl}piperidin-3-yl]methoxy}benzamide	437.53	438
	B0018	N,N-dimethyl-4-{[(trans)-4-{4-[2-(2-oxopyrrolidin-1-yl)ethoxy]phenyl}piperidin-3-yl]methoxy}benzamide	465.58	466
	B0019	1-(2-{4-[(trans)-3-[(pyridin-3-yloxy)methyl]piperidin-4-yl]phenoxy}ethyl)pyrrolidin-2-one	395.49	396
	B0020	4-{[(trans)-4-{4-[2-(2-oxopyrrolidin-1-yl)ethoxy]phenyl}piperidin-3-yl]methoxy}benzene-1-sulfonamide	473.59	474
	B0021	4-{[(trans)-4-{4-[2-(2-oxopyrrolidin-1-yl)ethoxy]phenyl}piperidin-3-yl]methoxy}-N-(propan-2-yl)benzamide	479.61	480
	B0022	1-(2-{4-[(trans)-3-[(pyridin-4-yloxy)methyl]piperidin-4-yl]phenoxy}ethyl)pyrrolidin-2-one	395.49	396
	B0023	1-(2-{4-[(trans)-3-[(pyridin-2-yloxy)methyl]piperidin-4-yl]phenoxy}ethyl)pyrrolidin-2-one	395.49	396
	B0024	3-{[(trans)-4-[4-(2-methoxyethoxy)phenyl]piperidin-3-yl]methoxy}benzonitrile	366.45	367

Figure 1-Continued

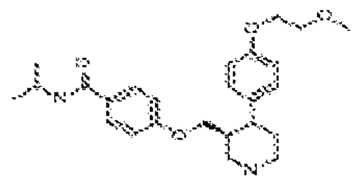
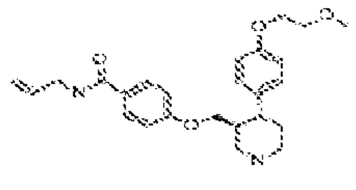
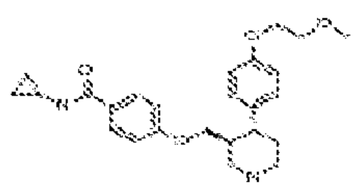
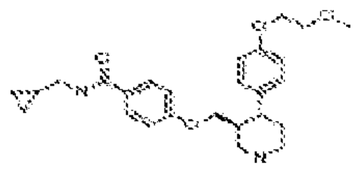
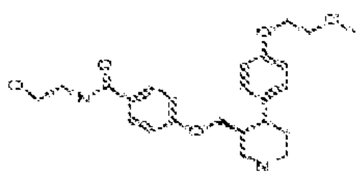
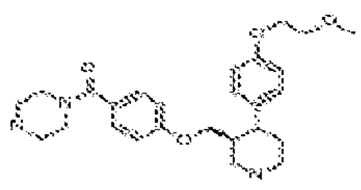
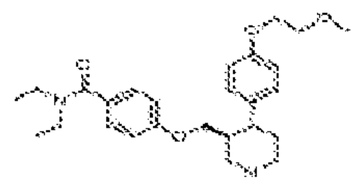
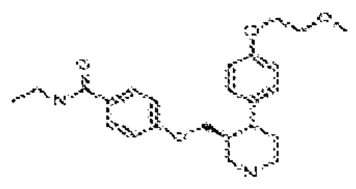
	B0025	4-{[(trans)-4-[4-(2-methoxyethoxy)phenyl]piperidin-3-yl]methoxy}-N-(propan-2-yl)benzamide	426.55	427
	B0026	4-{[(trans)-4-[4-(2-methoxyethoxy)phenyl]piperidin-3-yl]methoxy}-N-(prop-2-en-1-yl)benzamide	424.53	425
	B0027	N-cyclopropyl-4-{[(trans)-4-[4-(2-methoxyethoxy)phenyl]piperidin-3-yl]methoxy}benzamide	424.53	425
	B0028	N-(cyclopropylmethyl)-4-{[(trans)-4-[4-(2-methoxyethoxy)phenyl]piperidin-3-yl]methoxy}benzamide	438.56	439
	B0029	N-(2-hydroxyethyl)-4-{[(trans)-4-[4-(2-methoxyethoxy)phenyl]piperidin-3-yl]methoxy}benzamide	428.52	429
	B0030	1-(4-{[(trans)-4-[4-(2-methoxyethoxy)phenyl]piperidin-3-yl]methoxy}benzoyl)piperazine	453.57	454
	B0031	N,N-diethyl-4-{[(trans)-4-[4-(2-methoxyethoxy)phenyl]piperidin-3-yl]methoxy}benzamide	440.58	441
	B0032	N-ethyl-4-{[(trans)-4-[4-(2-methoxyethoxy)phenyl]piperidin-3-yl]methoxy}benzamide	412.52	413

Figure 1-Continued

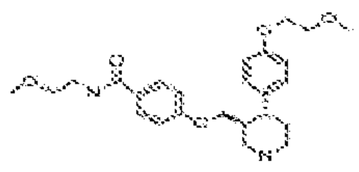
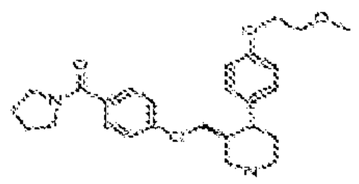
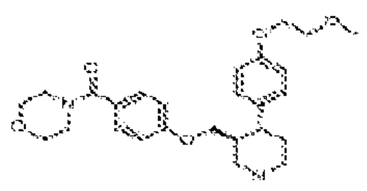
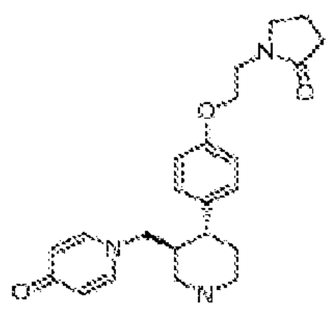
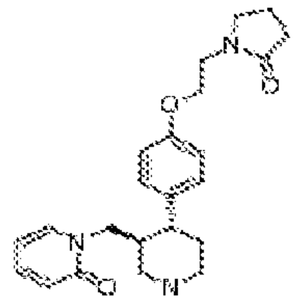
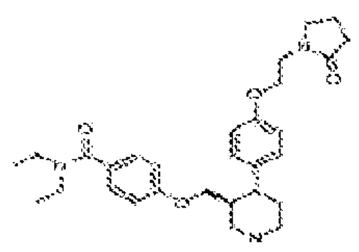
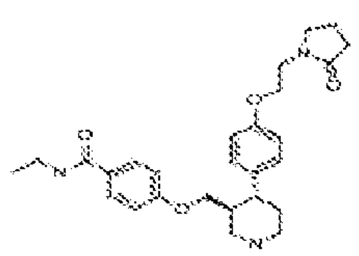
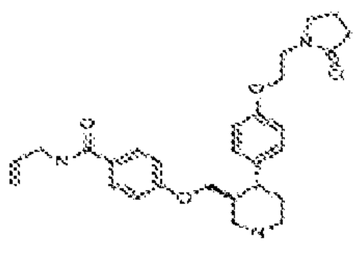
	B0033	4-{[(trans)-4-[4-(2-methoxyethoxy)phenyl]piperidin-3-yl]methoxy}-N-(2-methoxyethyl)benzamide	442.55	443
	B0034	(trans)-4-[4-(2-methoxyethoxy)phenyl]-3-[4-(pyrrolidine-1-carbonyl)phenoxymethyl]piperidine	438.56	439
	B0035	4-(4-{[(trans)-4-[4-(2-methoxyethoxy)phenyl]piperidin-3-yl]methoxy}benzoyl)morpholine	454.56	455
	B0036	1-{[(trans)-4-{4-[2-(2-oxopyrrolidin-1-yl)ethoxy]phenyl}piperidin-3-yl]methyl}-1,4-dihydropyridin-4-one	395.49	396
	B0037	1-{[(trans)-4-{4-[2-(2-oxopyrrolidin-1-yl)ethoxy]phenyl}piperidin-3-yl]methyl}-1,2-dihydropyridin-2-one	395.49	396
	B0038	N,N-diethyl-4-{[(trans)-4-{4-[2-(2-oxopyrrolidin-1-yl)ethoxy]phenyl}piperidin-3-yl]methoxy}benzamide	493.64	494
	B0039	N-ethyl-4-{[(trans)-4-{4-[2-(2-oxopyrrolidin-1-yl)ethoxy]phenyl}piperidin-3-yl]methoxy}benzamide	465.58	466
	B0040	4-{[(trans)-4-{4-[2-(2-oxopyrrolidin-1-yl)ethoxy]phenyl}piperidin-3-yl]methoxy}-N-(prop-2-en-1-yl)benzamide	477.6	478

Figure 1-Continued

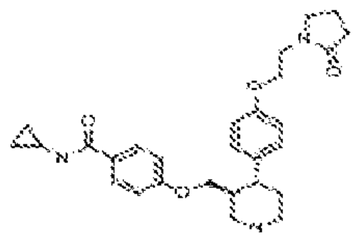
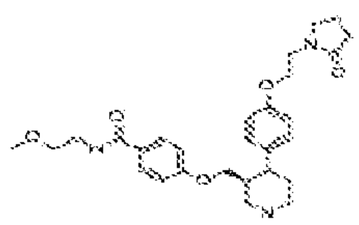
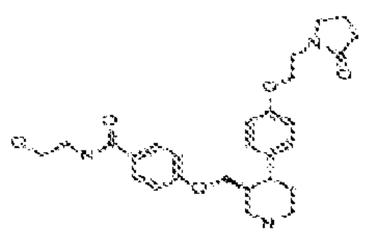
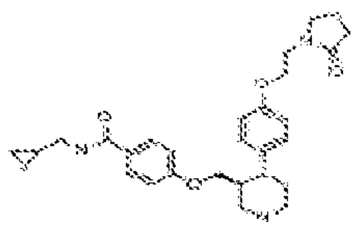
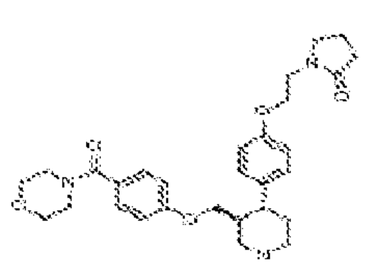
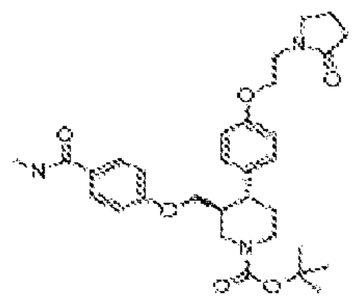
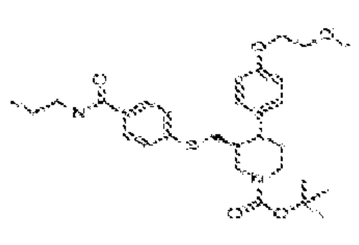
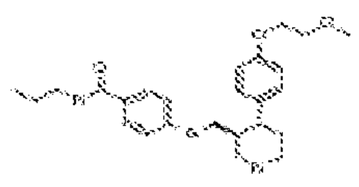
	B0041	N-cyclopropyl-4-{[(trans)-4-{4-[2-(2-oxopyrrolidin-1-yl)ethoxy]phenyl}piperidin-3-yl]methoxy}benzamide	477.6	478
	B0042	N-(2-methoxyethyl)-4-{[(trans)-4-{4-[2-(2-oxopyrrolidin-1-yl)ethoxy]phenyl}piperidin-3-yl]methoxy}benzamide	495.61	496
	B0043	N-(2-hydroxyethyl)-4-{[(trans)-4-{4-[2-(2-oxopyrrolidin-1-yl)ethoxy]phenyl}piperidin-3-yl]methoxy}benzamide	481.58	482
	B0044	N-(cyclopropylmethyl)-4-{[(trans)-4-{4-[2-(2-oxopyrrolidin-1-yl)ethoxy]phenyl}piperidin-3-yl]methoxy}benzamide	491.62	492
	B0045	1-(2-{4-[(trans)-3-[4-(morpholine-4-carbonyl)phenoxymethyl]piperidin-4-yl]phenoxy}ethyl)pyrrolidin-2-one	507.62	508
	B0046	tert-butyl (trans)-3-[4-(methylcarbamoyl)phenoxymethyl]-4-{4-[2-(2-oxopyrrolidin-1-yl)ethoxy]phenyl}piperidine-1-carboxylate	551.67	552
	B0047	tert-butyl (trans)-4-[4-(2-methoxyethoxy)phenyl]-3-({[4-(propylcarbamoyl)phenyl]sulfanyl}methyl)piperidine-1-carboxylate	``-	487
	B0048	4-({[(trans)-4-[4-(2-methoxyethoxy)phenyl]piperidin-3-yl]methyl}sulfanyl)-N-propylbenzamide	442.61	443

Figure 1-Continued

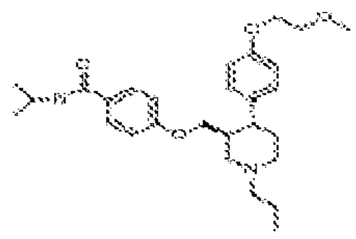
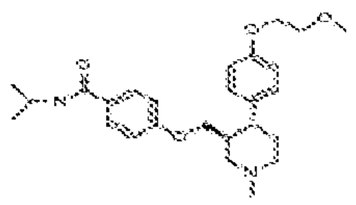
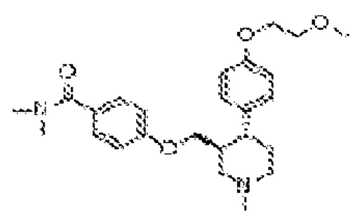
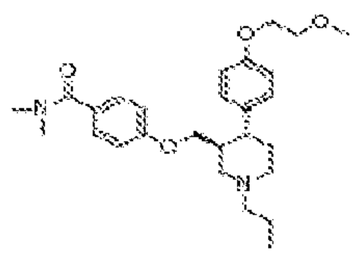
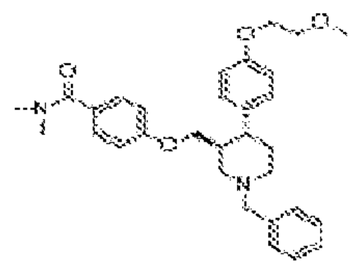
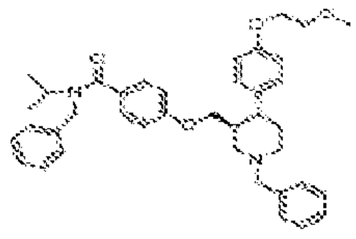
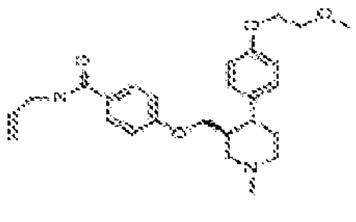
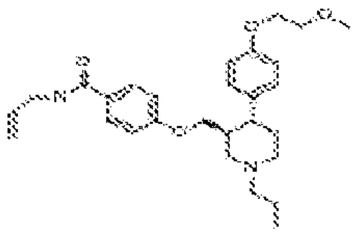
	B0049	4-{[(trans)-4-[4-(2-methoxyethoxy)phenyl]-1-propylpiperidin-3-yl]methoxy}-N-(propan-2-yl)benzamide	468.63	469
	B0050	4-{[(trans)-4-[4-(2-methoxyethoxy)phenyl]-1-methylpiperidin-3-yl]methoxy}-N-(propan-2-yl)benzamide	440.58	441
	B0051	4-{[(trans)-4-[4-(2-methoxyethoxy)phenyl]-1-methylpiperidin-3-yl]methoxy}-N,N-dimethylbenzamide	426.55	427
	B0052	4-{[(trans)-4-[4-(2-methoxyethoxy)phenyl]-1-propylpiperidin-3-yl]methoxy}-N,N-dimethylbenzamide	454.6	455
	B0053	4-{[(trans)-1-benzyl-4-[4-(2-methoxyethoxy)phenyl]piperidin-3-yl]methoxy}-N,N-dimethylbenzamide	502.64	503
	B0054	N-benzyl-4-{[(trans)-1-benzyl-4-[4-(2-methoxyethoxy)phenyl]piperidin-3-yl]methoxy}-N-(propan-2-yl)benzamide	606.79	N.D.
	B0055	4-{[(trans)-4-[4-(2-methoxyethoxy)phenyl]-1-methylpiperidin-3-yl]methoxy}-N-(prop-2-en-1-yl)benzamide	438.56	439
	B0056	4-{[(trans)-4-[4-(2-methoxyethoxy)phenyl]-1-propylpiperidin-3-yl]methoxy}-N-(prop-2-en-1-yl)benzamide	466.61	467

Figure 1-Continued

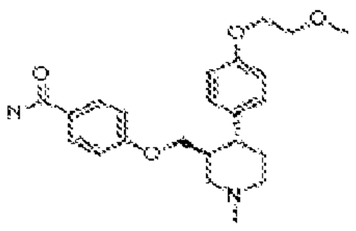
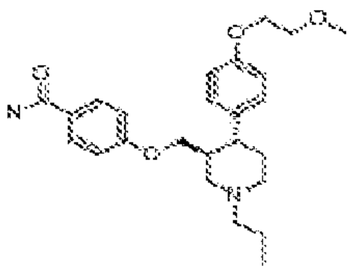
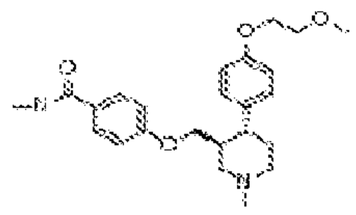
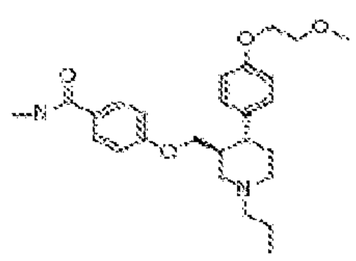
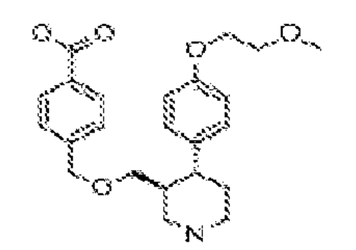
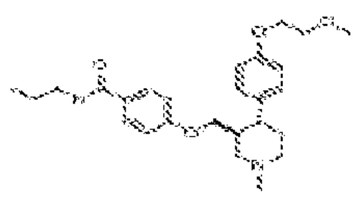
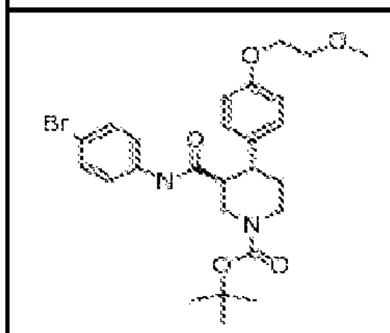
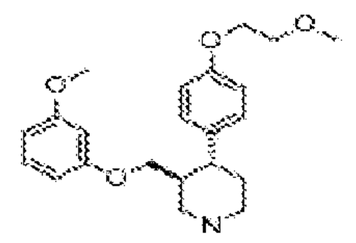
	B0057	4-{[(trans)-4-[4-(2-methoxyethoxy)phenyl]-1-methylpiperidin-3-yl]methoxy}benzamide	398.5	399
	B0058	4-{[(trans)-4-[4-(2-methoxyethoxy)phenyl]-1-propylpiperidin-3-yl]methoxy}benzamide	426.55	427
	B0059	4-{[(trans)-4-[4-(2-methoxyethoxy)phenyl]-1-methylpiperidin-3-yl]methoxy}-N-methylbenzamide	412.52	413
	B0060	4-{[(trans)-4-[4-(2-methoxyethoxy)phenyl]-1-propylpiperidin-3-yl]methoxy}-N-methylbenzamide	440.58	441
	B0061	4-({[(trans)-4-[4-(2-methoxyethoxy)phenyl]piperidin-3-yl]methoxy}methyl)benzoic acid	399.48	400
	B0062	4-{[(trans)-4-[4-(2-methoxyethoxy)phenyl]-1-methylpiperidin-3-yl]methoxy}-N-propylbenzamide	440.58	441
	B0063	tert-butyl (trans)-3-[(4-bromophenyl)carbamoyl]-4-[4-(2-methoxyethoxy)phenyl]piperidine-1-carboxylate	533.45	479
	B0064	(trans)-4-[4-(2-methoxyethoxy)phenyl]-3-(3-methoxyphenoxymethyl)piperidine	371.47	372

Figure 1-Continued

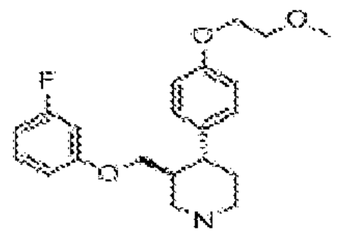
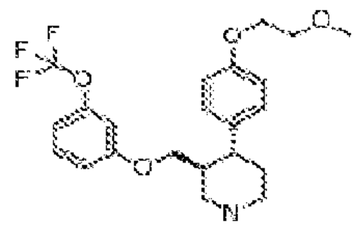
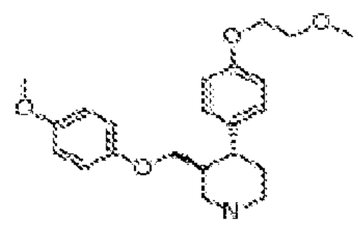
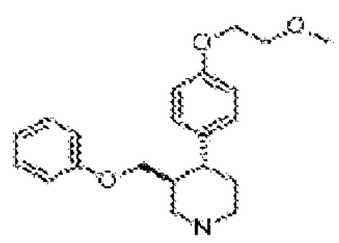
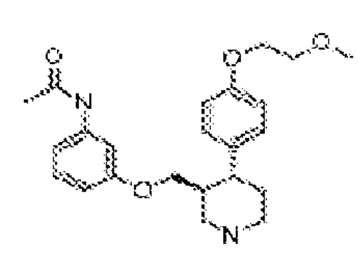
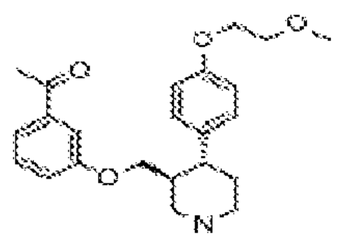
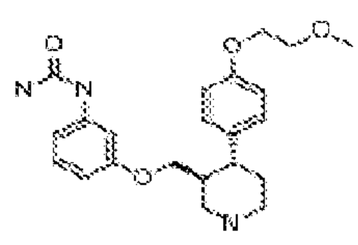
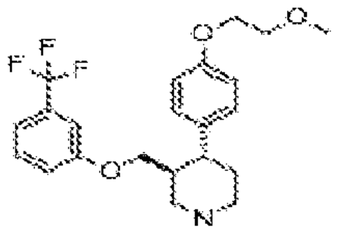
	B0065	(trans)-3-(3-fluorophenoxymethyl)-4-[4-(2-methoxyethoxy)phenyl]piperidine	359.43	360
	B0066	(trans)-4-[4-(2-methoxyethoxy)phenyl]-3-[3-(trifluoromethoxy)phenoxymethyl]piperidine	425.44	426
	B0067	(trans)-4-[4-(2-methoxyethoxy)phenyl]-3-(4-methoxyphenoxymethyl)piperidine	371.47	372
	B0068	(trans)-4-[4-(2-methoxyethoxy)phenyl]-3-(phenoxymethyl)piperidine	341.44	342
	B0069	N-(3-{[(trans)-4-[4-(2-methoxyethoxy)phenyl]piperidin-3-yl]methoxy}phenyl)acetamide	398.5	399
	B0070	1-(3-{[(trans)-4-[4-(2-methoxyethoxy)phenyl]piperidin-3-yl]methoxy}phenyl)ethan-1-one	383.48	384
	B0071	(3-{[(trans)-4-[4-(2-methoxyethoxy)phenyl]piperidin-3-yl]methoxy}phenyl)urea	399.48	400
	B0072	(trans)-4-[4-(2-methoxyethoxy)phenyl]-3-[3-(trifluoromethyl)phenoxymethyl]piperidine	409.44	410

Figure 1-Continued

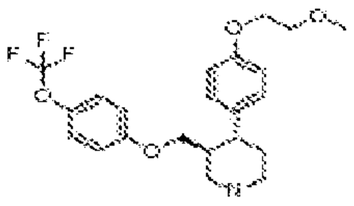
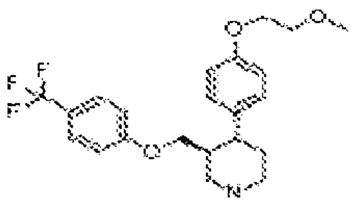
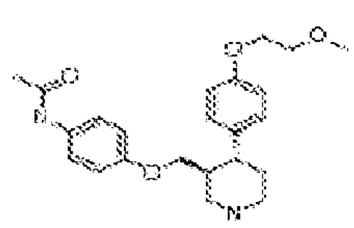
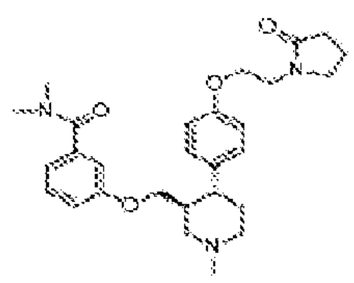
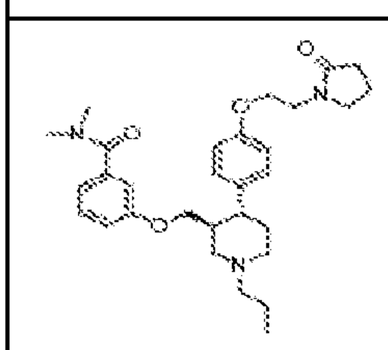
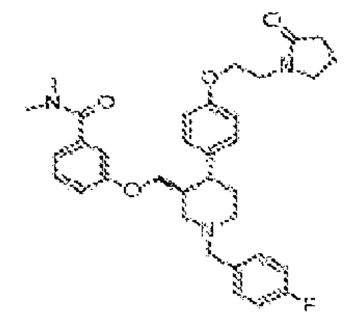
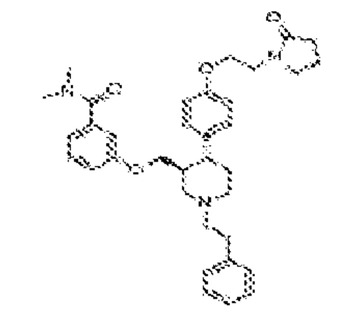
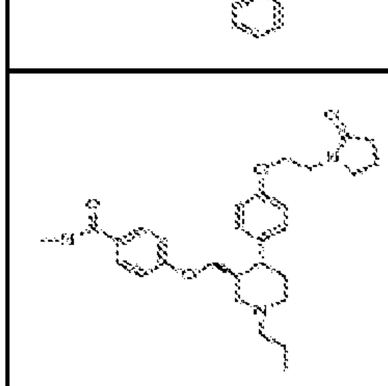
	B0073	(trans)-4-[4-(2-methoxyethoxy)phenyl]-3-[4-(trifluoromethoxy)phenoxymethyl]piperidine	425.44	427
	B0074	(trans)-4-[4-(2-methoxyethoxy)phenyl]-3-[4-(trifluoromethyl)phenoxymethyl]piperidine	409.44	410
	B0075	N-(4-{[(trans)-4-[4-(2-methoxyethoxy)phenyl]piperidin-3-yl]methoxy}phenyl)acetamide	398.5	399
	B0076	N,N-dimethyl-3-{[(trans)-1-methyl-4-{4-[2-(2-oxopyrrolidin-1-yl)ethoxy]phenyl}piperidin-3-yl]methoxy}benzamide	479.61	480
	B0077	N,N-dimethyl-3-{[(trans)-4-{4-[2-(2-oxopyrrolidin-1-yl)ethoxy]phenyl}-1-propylpiperidin-3-yl]methoxy}benzamide	507.66	508
	B0078	3-{[(trans)-1-[(4-fluorophenyl)methyl]-4-{4-[2-(2-oxopyrrolidin-1-yl)ethoxy]phenyl}piperidin-3-yl]methoxy}-N,N-dimethylbenzamide	573.7	574
	B0079	N,N-dimethyl-3-{[(trans)-4-{4-[2-(2-oxopyrrolidin-1-yl)ethoxy]phenyl}-1-(2-phenylethyl)piperidin-3-yl]methoxy}benzamide	569.73	570
	B0080	N-methyl-4-{[(trans)-4-{4-[2-(2-oxopyrrolidin-1-yl)ethoxy]phenyl}-1-propylpiperidin-3-yl]methoxy}benzamide	493.64	494

Figure 1-Continued

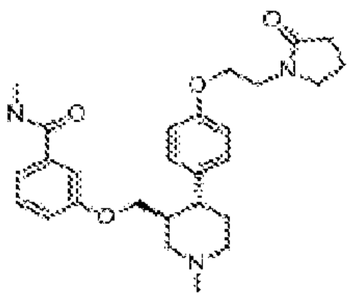
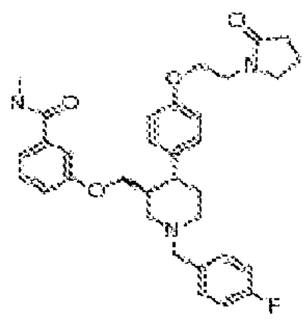
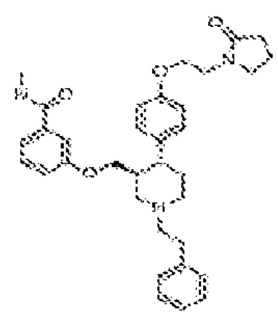
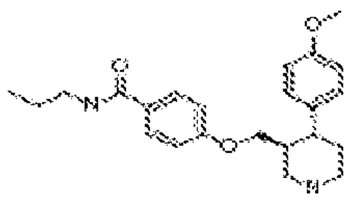
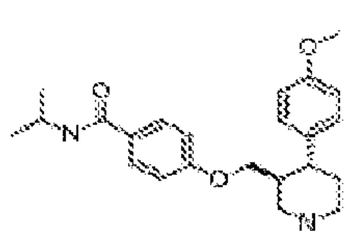
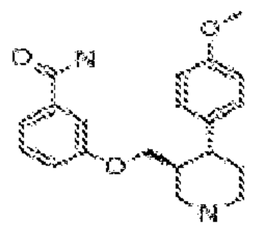
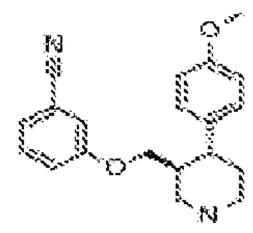
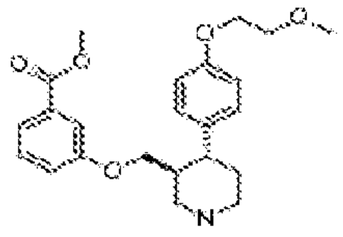
	B0081	N-methyl-3-{[(trans)-1-methyl-4-{4-[2-(2-oxopyrrolidin-1-yl)ethoxy]phenyl}piperidin-3-yl]methoxy}benzamide	465.58	466
	B0082	3-{[(trans)-1-[(4-fluorophenyl)methyl]-4-{4-[2-(2-oxopyrrolidin-1-yl)ethoxy]phenyl}piperidin-3-yl]methoxy}-N-methylbenzamide	559.67	560
	B0083	N-methyl-3-{[(trans)-4-{4-[2-(2-oxopyrrolidin-1-yl)ethoxy]phenyl}-1-(2-phenylethyl)piperidin-3-yl]methoxy}benzamide	555.71	556
	B0084	4-{[(trans)-4-(4-methoxyphenyl)piperidin-3-yl]methoxy}-N-propylbenzamide	382.5	383
	B0085	4-{[(trans)-4-(4-methoxyphenyl)piperidin-3-yl]methoxy}-N-(propan-2-yl)benzamide	382.5	383
	B0086	3-{[(trans)-4-(4-methoxyphenyl)piperidin-3-yl]methoxy}benzamide	340.42	341
	B0087	3-{[(trans)-4-(4-methoxyphenyl)piperidin-3-yl]methoxy}benzonitrile	322.4	323
	B0088	methyl 3-{[(trans)-4-[4-(2-methoxyethoxy)phenyl]piperidin-3-yl]methoxy}benzoate	399.48	400

Figure 1-Continued

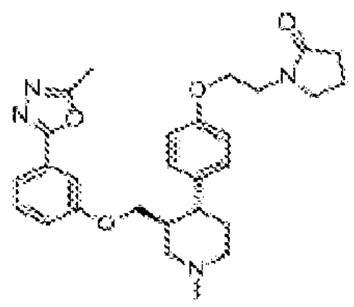
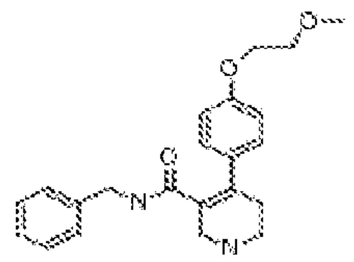
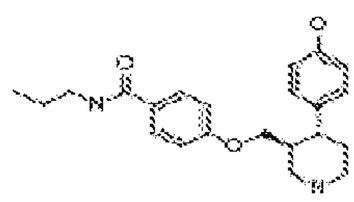
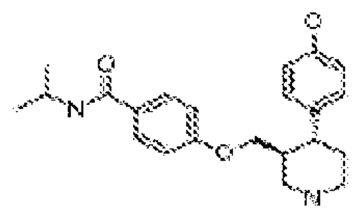
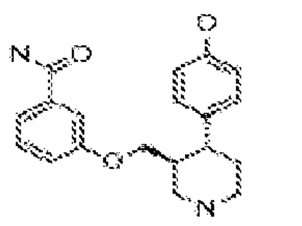
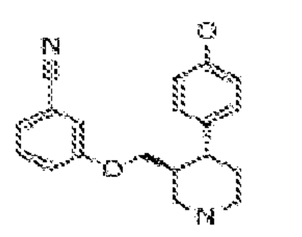
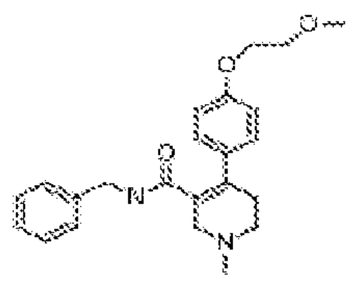
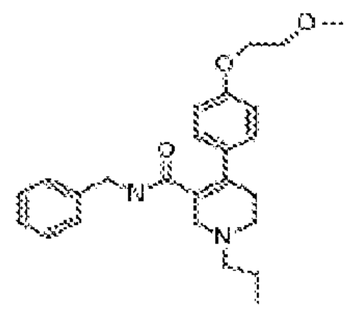
	B0089	1-(2-{4-[(trans)-1-methyl-3-[3-(5-methyl-1,3,4-oxadiazol-2-yl)phenoxymethyl]piperidin-4-yl]phenoxy}ethyl)pyrrolidin-2-one	490.59	491
	B0090	N-benzyl-4-[4-(2-methoxyethoxy)phenyl]-1,2,5,6-tetrahydropyridine-3-carboxamide	366.45	367
	B0091	4-{[(trans)-4-(4-hydroxyphenyl)piperidin-3-yl]methoxy}-N-propylbenzamide	368.47	369
	B0092	4-{[(trans)-4-(4-hydroxyphenyl)piperidin-3-yl]methoxy}-N-(propan-2-yl)benzamide	368.47	369
	B0093	3-{[(trans)-4-(4-hydroxyphenyl)piperidin-3-yl]methoxy}benzamide	326.39	327
Chiral 	B0094	3-{[(trans)-4-(4-hydroxyphenyl)piperidin-3-yl]methoxy}benzonitrile	308.37	309
	B0095	N-benzyl-4-[4-(2-methoxyethoxy)phenyl]-1-methyl-1,2,5,6-tetrahydropyridine-3-carboxamide	380.48	381
	B0096	N-benzyl-4-[4-(2-methoxyethoxy)phenyl]-1-propyl-1,2,5,6-tetrahydropyridine-3-carboxamide	408.53	409

Figure 1-Continued

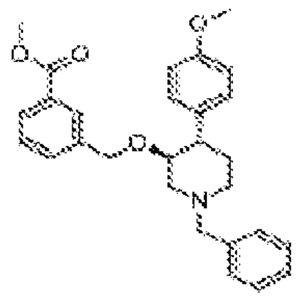
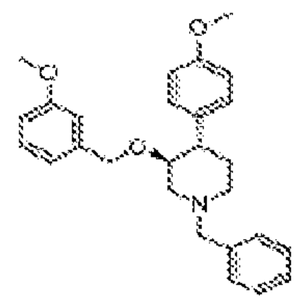
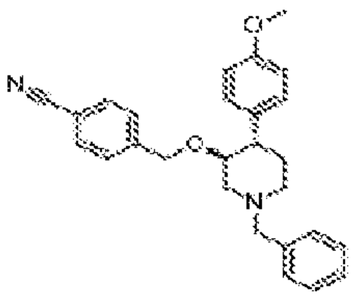
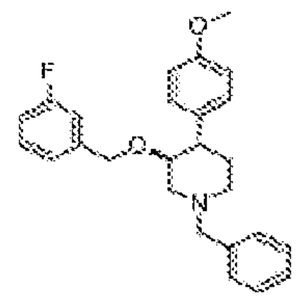
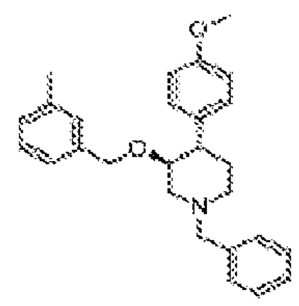
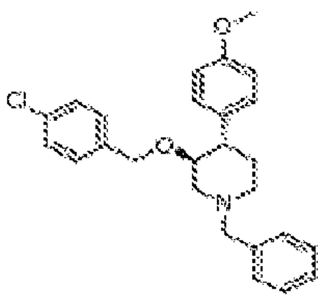
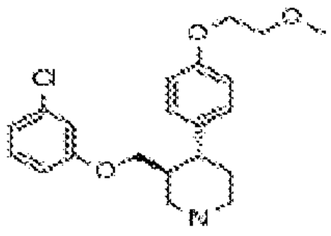
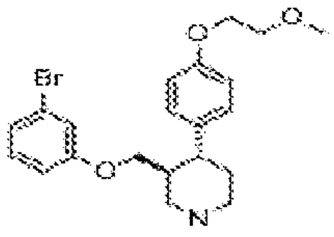
	B0097	methyl 3-({[(trans)-1-benzyl-4-(4-methoxyphenyl)piperidin-3-yl]oxy}methyl)benzoate	445.55	446
	B0098	(trans)-1-benzyl-4-(4-methoxyphenyl)-3-[(3-methoxyphenyl)methoxy]piperidine	417.54	418
	B0099	4-({[(trans)-1-benzyl-4-(4-methoxyphenyl)piperidin-3-yl]oxy}methyl)benzonitrile	412.52	413
	B0100	(trans)-1-benzyl-3-[(3-fluorophenyl)methoxy]-4-(4-methoxyphenyl)piperidine	405.5	406
	B0101	(trans)-1-benzyl-4-(4-methoxyphenyl)-3-[(3-methylphenyl)methoxy]piperidine	401.54	402
	B0102	(trans)-1-benzyl-3-[(4-chlorophenyl)methoxy]-4-(4-methoxyphenyl)piperidine	421.96	422
	B0103	(trans)-3-(3-chlorophenoxymethyl)-4-[4-(2-methoxyethoxy)phenyl]piperidine	375.89	376
	B0104	(trans)-3-(3-bromophenoxymethyl)-4-[4-(2-methoxyethoxy)phenyl]piperidine	420.34	422

Figure 1-Continued

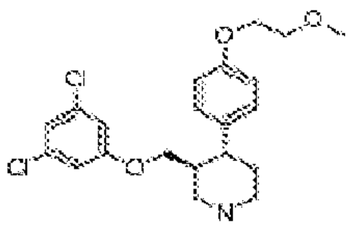
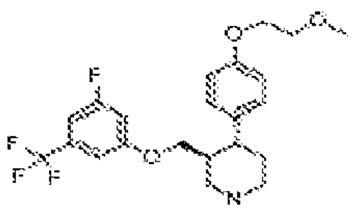
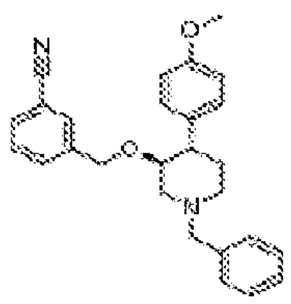
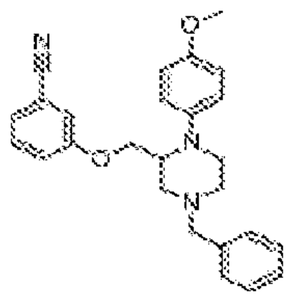
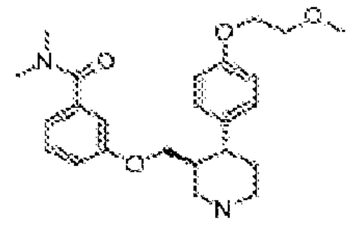
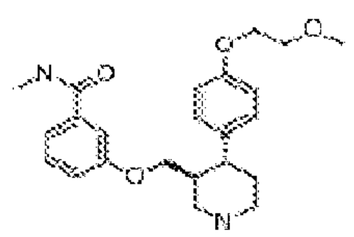
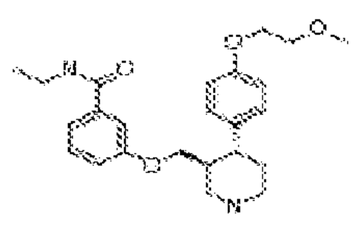
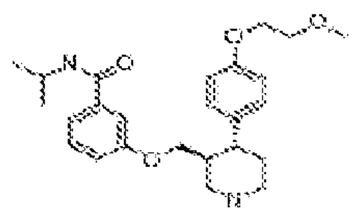
	B0105	(trans)-3-(3,5-dichlorophenoxymethyl)-4-[4-(2-methoxyethoxy)phenyl]piperidine	410.33	410
	B0106	(trans)-3-[3-fluoro-5-(trifluoromethyl)phenoxymethyl]-4-[4-(2-methoxyethoxy)phenyl]piperidine	427.43	428
	B0107	3-({[(trans)-1-benzyl-4-(4-methoxyphenyl)piperidin-3-yl]oxy}methyl)benzonitrile	412.52	413
	B0108	3-{[4-benzyl-1-(4-methoxyphenyl)piperazin-2-yl]methoxy}benzonitrile	413.51	414
	B0109	3-{[(trans)-4-[4-(2-methoxyethoxy)phenyl]piperidin-3-yl]methoxy}-N,N-dimethylbenzamide	412.52	413
	B0110	3-{[(trans)-4-[4-(2-methoxyethoxy)phenyl]piperidin-3-yl]methoxy}-N-methylbenzamide	398.5	399
	B0111	N-ethyl-3-{[(trans)-4-[4-(2-methoxyethoxy)phenyl]piperidin-3-yl]methoxy}benzamide	412.52	413
	B0112	3-{[(trans)-4-[4-(2-methoxyethoxy)phenyl]piperidin-3-yl]methoxy}-N-(propan-2-yl)benzamide	426.55	427

Figure 1-Continued

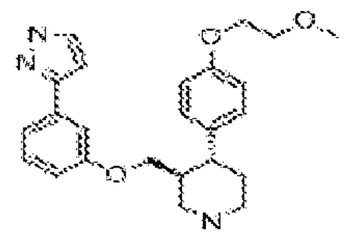
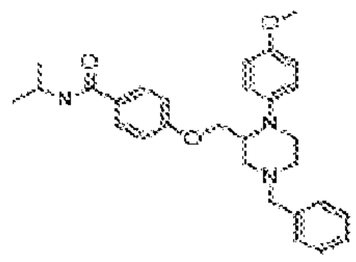
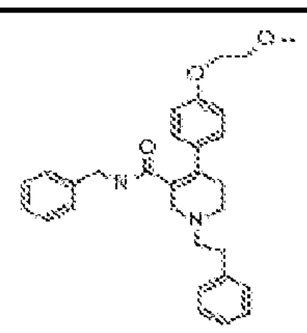
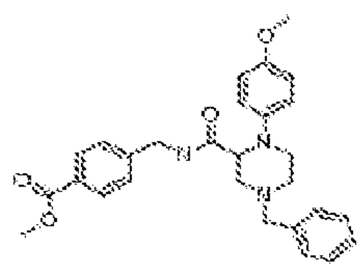
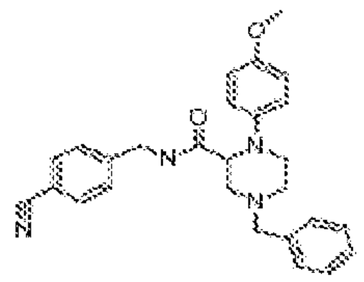
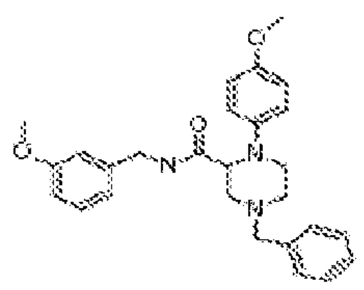
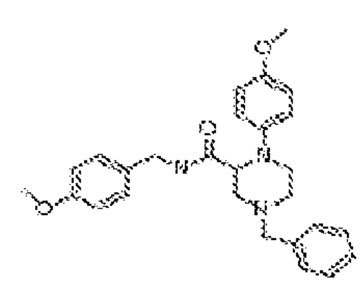
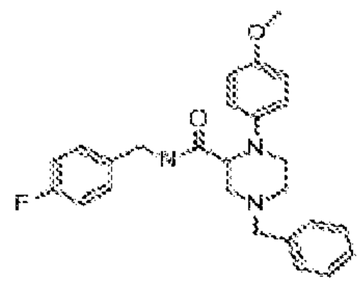
	B0113	(trans)-4-[4-(2-methoxyethoxy)phenyl]-3-[3-(1H-pyrazol-3-yl)phenoxymethyl]piperidine	407.51	408
	B0114	4-{[4-benzyl-1-(4-methoxyphenyl)piperazin-2-yl]methoxy}-N-(propan-2-yl)benzamide	473.61	474
	B0115	N-benzyl-4-[4-(2-methoxyethoxy)phenyl]-1-(2-phenylethyl)-1,2,5,6-tetrahydropyridine-3-carboxamide	470.6	N.D.
	B0116	methyl-4-({[4-benzyl-1-(4-methoxyphenyl)piperazin-2-yl]formamido}methyl)benzoate	473.56	N.D.
	B0117	4-benzyl-N-[(4-cyanophenyl)methyl]-1-(4-methoxyphenyl)piperazine-2-carboxamide	440.54	441
	B0118	4-benzyl-1-(4-methoxyphenyl)-N-[(3-methoxyphenyl)methyl]piperazine-2-carboxamide	445.55	446
	B0119	4-benzyl-1-(4-methoxyphenyl)-N-[(4-methoxyphenyl)methyl]piperazine-2-carboxamide	445.55	446
	B0120	4-benzyl-N-[(4-fluorophenyl)methyl]-1-(4-methoxyphenyl)piperazine-2-carboxamide	433.52	434

Figure 1-Continued

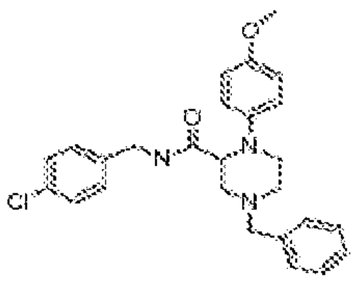
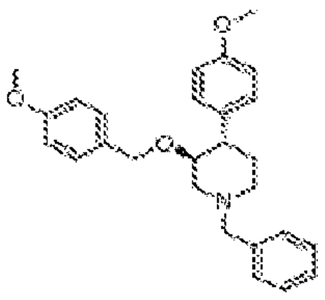
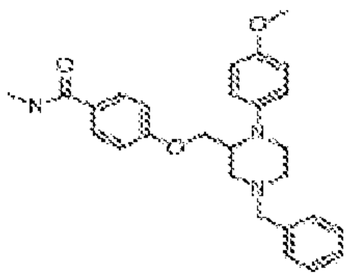
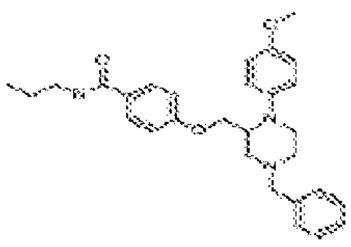
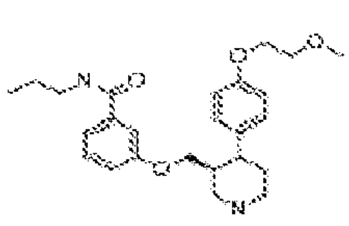
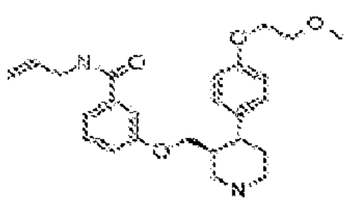
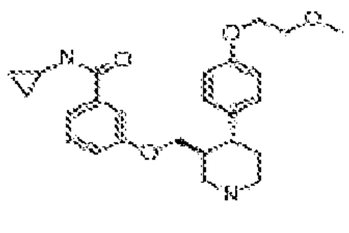
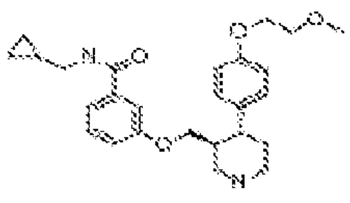
	B0121	4-benzyl-N-[(4-chlorophenyl)methyl]-1-(4-methoxyphenyl)piperazine-2-carboxamide	449.97	450
	B0122	(trans)-1-benzyl-4-(4-methoxyphenyl)-3-[(4-methoxyphenyl)methoxy]piperidine	417.54	418
	B0123	4-{[4-benzyl-1-(4-methoxyphenyl)piperazin-2-yl]methoxy}-N-methylbenzamide	445.55	446
	B0124	4-{[4-benzyl-1-(4-methoxyphenyl)piperazin-2-yl]methoxy}-N-propylbenzamide	473.61	474
	B0125	3-{[(trans)-4-[4-(2-methoxyethoxy)phenyl]piperidin-3-yl]methoxy}-N-propylbenzamide	426.55	427
	B0126	3-{[(trans)-4-[4-(2-methoxyethoxy)phenyl]piperidin-3-yl]methoxy}-N-(prop-2-en-1-yl)benzamide	424.53	425
	B0127	N-cyclopropyl-3-{[(trans)-4-[4-(2-methoxyethoxy)phenyl]piperidin-3-yl]methoxy}benzamide	424.53	425
	B0128	N-(cyclopropylmethyl)-3-{[(trans)-4-[4-(2-methoxyethoxy)phenyl]piperidin-3-yl]methoxy}benzamide	438.56	439

Figure 1-Continued

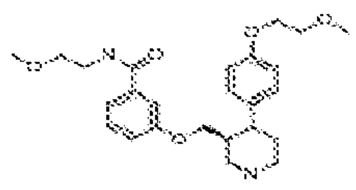
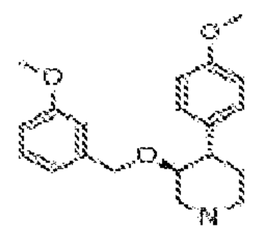
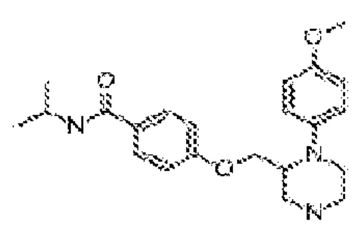
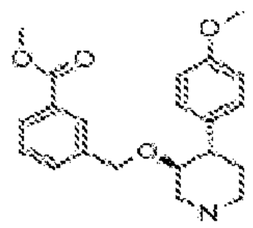
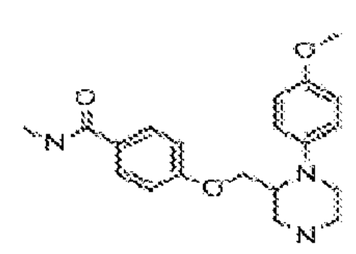
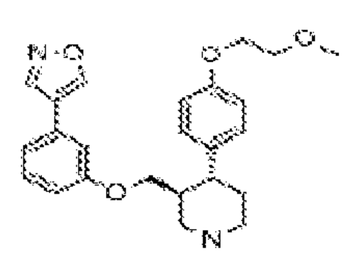
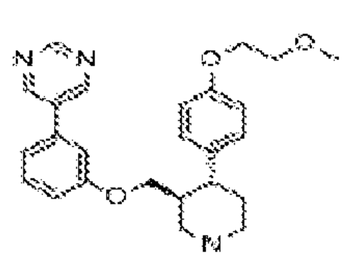
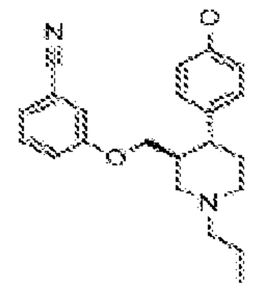
	B0129	3-{[(trans)-4-[4-(2-methoxyethoxy)phenyl]piperidin-3-yl]methoxy}-N-(2-methoxyethyl)benzamide	442.55	443
	B0130	(trans)-4-(4-methoxyphenyl)-3-[(3-methoxyphenyl)methoxy]piperidine	327.42	328
	B0131	4-{[1-(4-methoxyphenyl)piperazin-2-yl]methoxy}-N-(propan-2-yl)benzamide	383.48	384
	B0132	methyl 3-({[(trans)-4-(4-methoxyphenyl)piperidin-3-yl]oxy}methyl)benzoate	355.43	356
	B0133	4-{[1-(4-methoxyphenyl)piperazin-2-yl]methoxy}-N-methylbenzamide	355.43	356
	B0134	(trans)-4-[4-(2-methoxyethoxy)phenyl]-3-[3-(1,2-oxazol-4-yl)phenoxymethyl]piperidine	408.49	409
	B0135	5-(3-{[(trans)-4-[4-(2-methoxyethoxy)phenyl]piperidin-3-yl]methoxy}phenyl)pyrimidine	419.52	420
	B0136	3-{[(trans)-4-(4-hydroxyphenyl)-1-propylpiperidin-3-yl]methoxy}benzonitrile	350.45	351

Figure 1-Continued

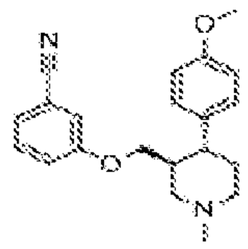
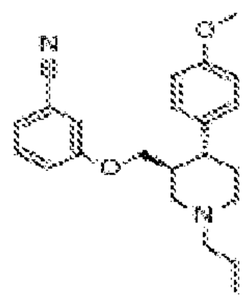
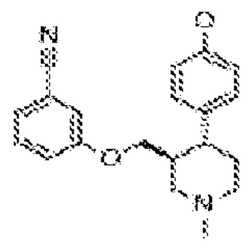
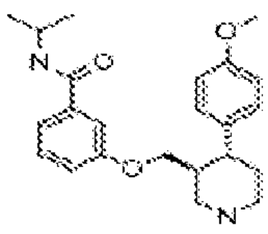
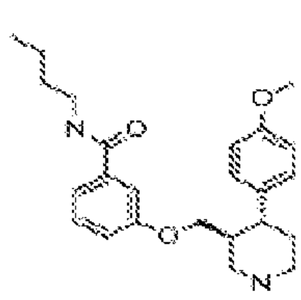
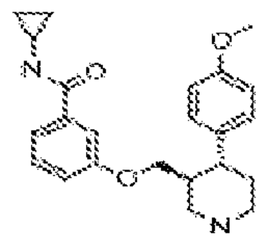
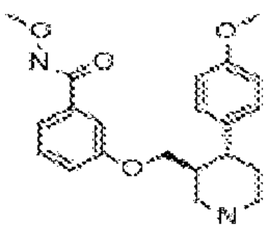
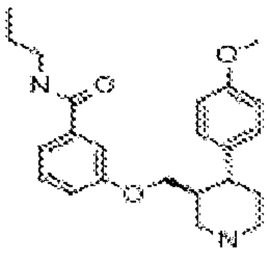
	B0137	3-{[(trans)-4-(4-methoxyphenyl)-1-methylpiperidin-3-yl]methoxy}benzonitrile	336.43	337
	B0138	3-{[4-(4-methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}benzonitrile	364.48	365
	B0139	3-{[(trans)-4-(4-hydroxyphenyl)-1-methylpiperidin-3-yl]methoxy}benzonitrile	322.4	323
	B0140	3-{[(trans)-4-(4-methoxyphenyl)piperidin-3-yl]methoxy}-N-(propan-2-yl)benzamide	382.5	383
	B0141	N-butyl-3-{[(trans)-4-(4-methoxyphenyl)piperidin-3-yl]methoxy}benzamide	396.52	397
	B0142	N-cyclopropyl-3-{[(trans)-4-(4-methoxyphenyl)piperidin-3-yl]methoxy}benzamide	380.48	381
	B0143	N-methoxy-3-{[(trans)-4-(4-methoxyphenyl)piperidin-3-yl]methoxy}benzamide	370.44	371
	B0144	3-{[(trans)-4-(4-methoxyphenyl)piperidin-3-yl]methoxy}-N-propylbenzamide	382.5	383

Figure 1-Continued

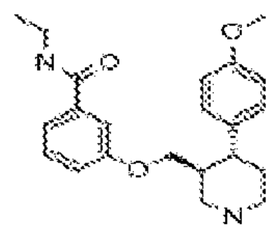
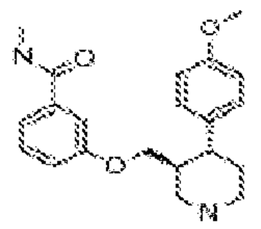
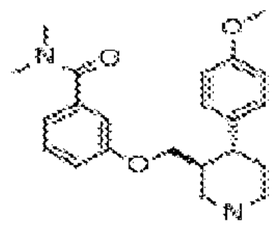
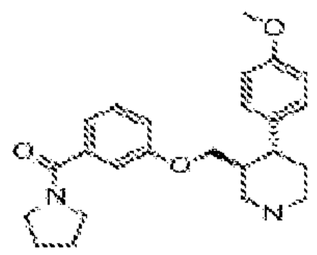
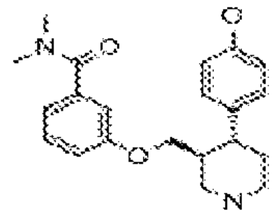
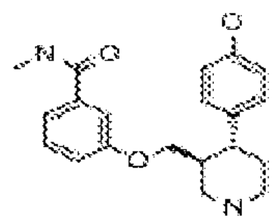
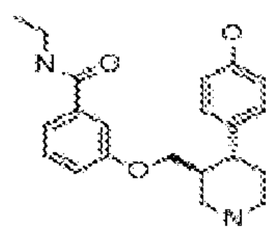
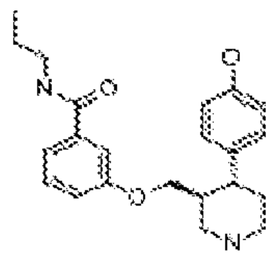
	B0145	N-ethyl-3-{[(trans)-4-(4-methoxyphenyl)piperidin-3-yl]methoxy}benzamide	368.47	369
	B0146	3-{[(trans)-4-(4-methoxyphenyl)piperidin-3-yl]methoxy}-N-methylbenzamide	354.44	355
	B0147	3-{[(trans)-4-(4-methoxyphenyl)piperidin-3-yl]methoxy}-N,N-dimethylbenzamide	368.47	369
	B0148	(trans)-4-(4-methoxyphenyl)-3-[3-(pyrrolidine-1-carbonyl)phenoxymethyl]piperidine	394.51	395
	B0149	3-{[(trans)-4-(4-hydroxyphenyl)piperidin-3-yl]methoxy}-N,N-dimethylbenzamide	354.44	355
	B0150	3-{[(trans)-4-(4-hydroxyphenyl)piperidin-3-yl]methoxy}-N-methylbenzamide	340.42	341
	B0151	N-ethyl-3-{[(trans)-4-(4-hydroxyphenyl)piperidin-3-yl]methoxy}benzamide	354.44	355
	B0152	3-{[(trans)-4-(4-hydroxyphenyl)piperidin-3-yl]methoxy}-N-propylbenzamide	368.47	369

Figure 1-Continued

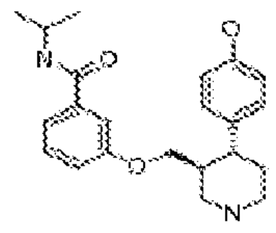
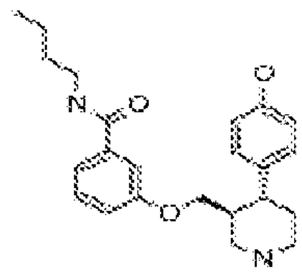
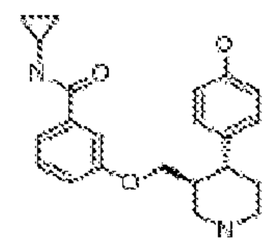
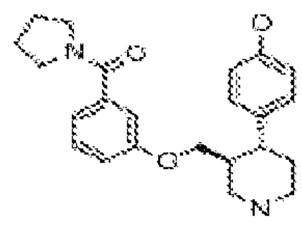
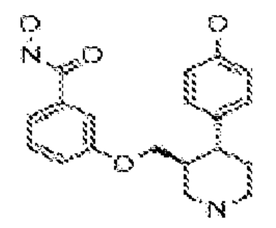
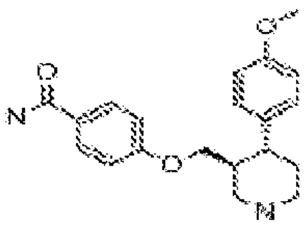
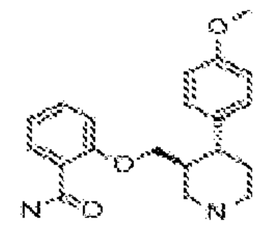
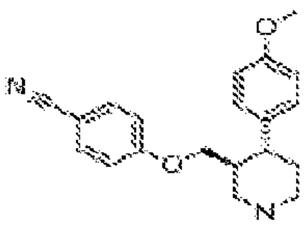
	B0153	3-{[(trans-4-(4-hydroxyphenyl)piperidin-3-yl]methoxy}-N-(propan-2-yl)benzamide	368.47	369
	B0154	N-butyl-3-{[(trans)-4-(4-hydroxyphenyl)piperidin-3-yl]methoxy}benzamide	382.5	383
	B0155	N-cyclopropyl-3-{[(trans)-4-(4-hydroxyphenyl)piperidin-3-yl]methoxy}benzamide	366.45	367
	B0156	4-[(trans)-3-[3-(pyrrolidine-1-carbonyl)phenoxymethyl]piperidin-4-yl]phenol	380.48	381
	B0157	N-hydroxy-3-{[(trans)-4-(4-hydroxyphenyl)piperidin-3-yl]methoxy}benzamide	342.39	343
	B0158	4-{[(trans)-4-(4-methoxyphenyl)piperidin-3-yl]methoxy}benzamide	340.42	341
	B0159	2-{[(trans)-4-(4-methoxyphenyl)piperidin-3-yl]methoxy}benzamide	340.42	341
	B0160	4-{[(trans)-4-(4-methoxyphenyl)piperidin-3-yl]methoxy}benzonitrile	322.4	323

Figure 1-Continued

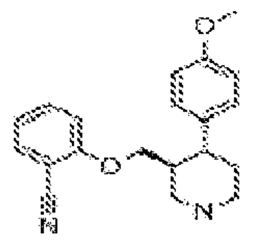
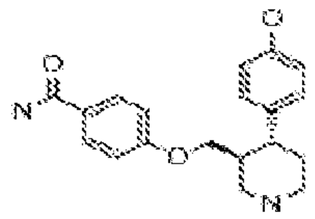
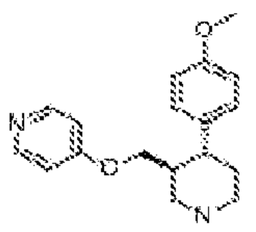
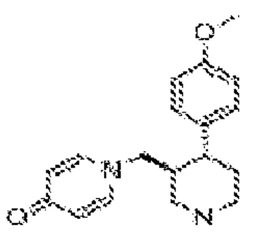
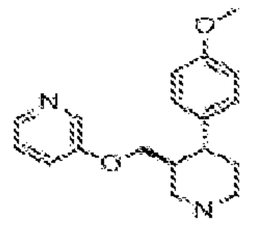
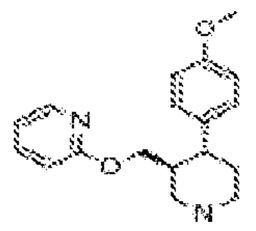
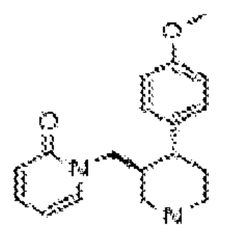
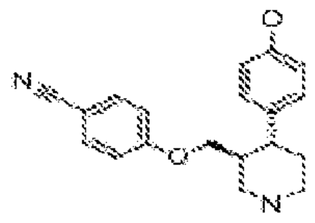
	B0161	2-{[(trans)-4-(4-methoxyphenyl)piperidin-3-yl]methoxy}benzonitrile	322.4	323
	B0162	4-{[(trans)-4-(4-hydroxyphenyl)piperidin-3-yl]methoxy}benzamide	326.39	327
	B0163	4-{[(trans-4-(4-methoxyphenyl)piperidin-3-yl]methoxy}pyridine	298.38	299
	B0164	1-{[(trans)-4-(4-methoxyphenyl)piperidin-3-yl]methyl}-1,4-dihydropyridin-4-one	298.38	299
	B0165	3-{[(trans)-4-(4-methoxyphenyl)piperidin-3-yl]methoxy}pyridine	298.38	299
	B0166	2-{[(trans)-4-(4-methoxyphenyl)piperidin-3-yl]methoxy}pyridine	298.38	299
	B0167	1-{[(trans-4-(4-methoxyphenyl)piperidin-3-yl]methyl}-1,2-dihydropyridin-2-one	298.38	299
	B0168	4-{[(trans)-4-(4-hydroxyphenyl)piperidin-3-yl]methoxy}benzonitrile	308.37	309

Figure 1-Continued

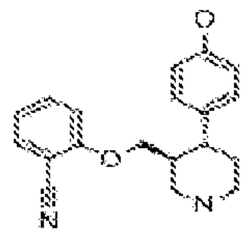
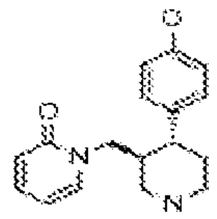
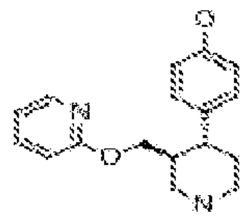
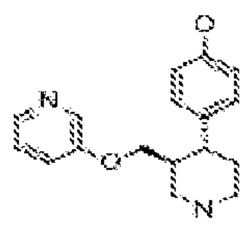
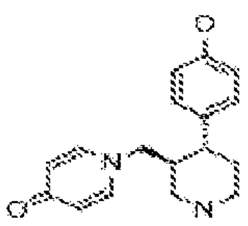
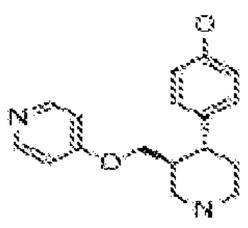
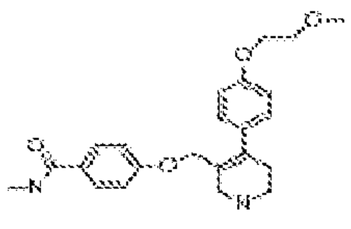
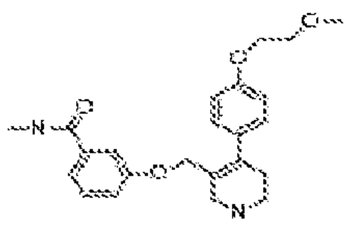
	B0169	2-{[(trans)-4-(4-hydroxyphenyl)piperidin-3-yl]methoxy}benzonitrile	308.37	309
	B0170	1-{[(trans)-4-(4-hydroxyphenyl)piperidin-3-yl]methyl}-1,2-dihydropyridin-2-one	284.35	285
	B0171	4-[(trans)-3-[(pyridin-2-yloxy)methyl]piperidin-4-yl]phenol	284.35	285
	B0172	4-[(trans-3-[(pyridin-3-yloxy)methyl]piperidin-4-yl]phenol	284.35	285
	B0173	1-{[(trans)-4-(4-hydroxyphenyl)piperidin-3-yl]methyl}-1,4-dihydropyridin-4-one	284.35	285
	B0174	4-[(trans)-3-[(pyridin-4-yloxy)methyl]piperidin-4-yl]phenol	284.35	285
	B0175	4-({4-[4-(2-methoxyethoxy)phenyl]-1,2,5,6-tetrahydropyridin-3-yl}methoxy)-N-ethylbenzamide	396.48	397
	B0176	3-({4-[4-(2-methoxyethoxy)phenyl]-1,2,5,6-tetrahydropyridin-3-yl}methoxy)-N-methylbenzamide	396.48	397

Figure 1-Continued

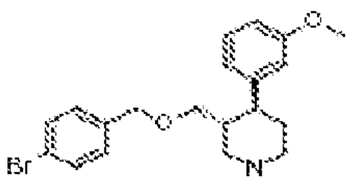
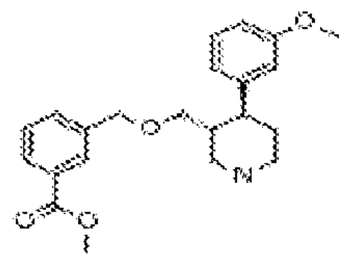
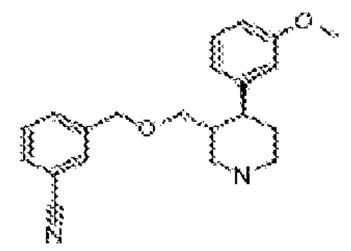
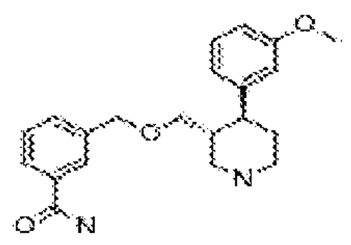
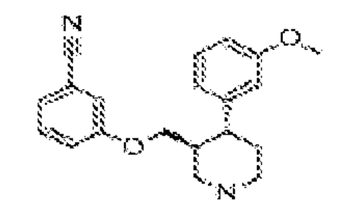
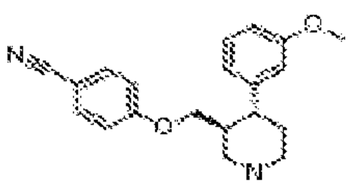
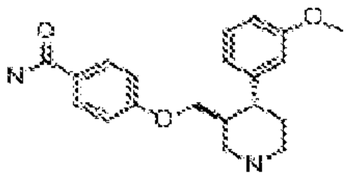
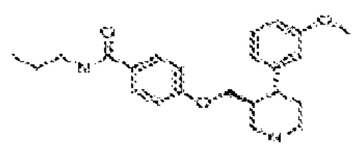
	B0177	(trans-3-{[(4-bromophenyl)methoxy]methyl}-4-(3-methoxyphenyl)piperidine	390.31	390
	B0178	3-({[(trans)-4-(3-methoxyphenyl)piperidin-3-yl]methoxy}methyl)benzoate	369.45	370
	B0179	3-({[(trans)-4-(3-methoxyphenyl)piperidin-3-yl]methoxy}methyl)benzonitrile	336.43	337
	B0180	3-({[(trans-4-(3-methoxyphenyl)piperidin-3-yl]methoxy}methyl)benzamide	354.44	355
	B0181	3-{[(trans)-4-(3-methoxyphenyl)piperidin-3-yl]methoxy}benzonitrile	322.4	323
	B0182	4-{[(trans-4-(3-methoxyphenyl)piperidin-3-yl]methoxy}benzonitrile	322.4	323
	B0183	4-{[(trans)-4-(3-methoxyphenyl)piperidin-3-yl]methoxy}benzamide	340.42	341
	B0184	4-{[(trans)-4-(3-methoxyphenyl)piperidin-3-yl]methoxy}-N-propylbenzamide	382.5	383

Figure 1-Continued

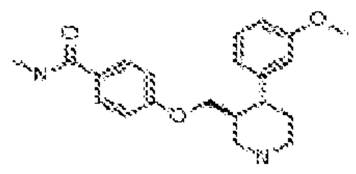
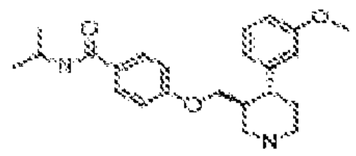
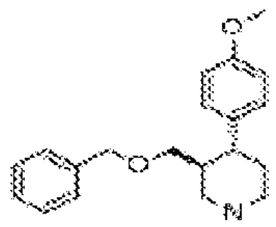
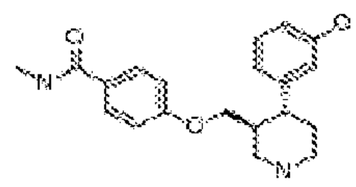
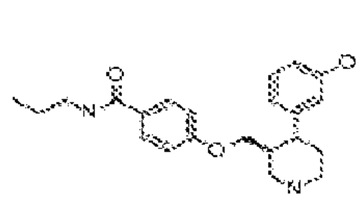
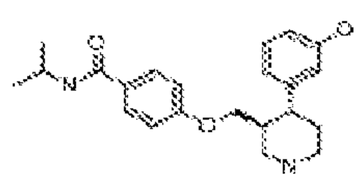
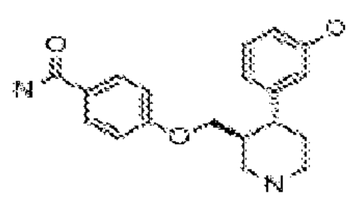
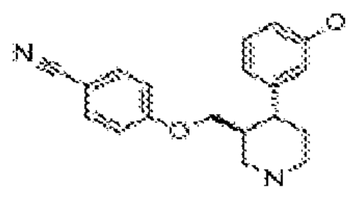
	B0185	4-{[(trans)-4-(3-methoxyphenyl)piperidin-3-yl]methoxy}-N-methylbenzamide	354.44	355
	B0186	4-{[(trans)-4-(3-methoxyphenyl)piperidin-3-yl]methoxy}-N-(propan-2-yl)benzamide	382.5	383
	B0187	(trans)-3-[(benzyloxy)methyl]-4-(4-methoxyphenyl)piperidine	311.42	312
	B0188	4-{[(trans)-4-(3-hydroxyphenyl)piperidin-3-yl]methoxy}-N-methylbenzamide	340.42	341
	B0189	4-{[(trans)-4-(3-hydroxyphenyl)piperidin-3-yl]methoxy}-N-propylbenzamide	368.47	369
	B0190	4-{[(trans)-4-(3-hydroxyphenyl)piperidin-3-yl]methoxy}-N-(propan-2-yl)benzamide	368.47	369
	B0191	4-{[(trans)-4-(3-hydroxyphenyl)piperidin-3-yl]methoxy}benzamide	326.39	327
	B0192	4-{[(trans)-4-(3-hydroxyphenyl)piperidin-3-yl]methoxy}benzonitrile	308.37	309

Figure 1-Continued

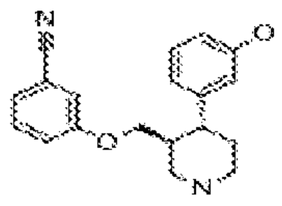
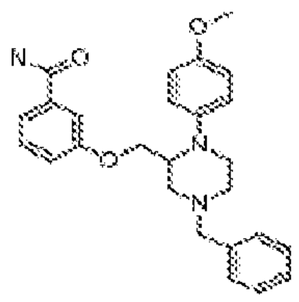
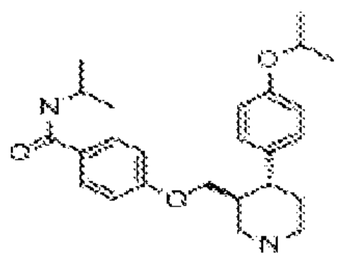
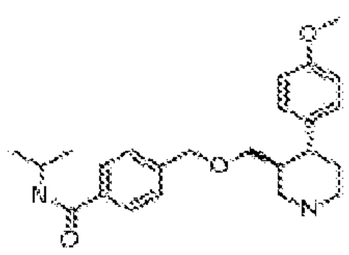
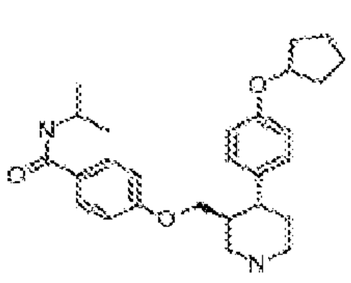
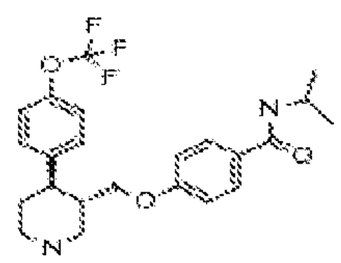
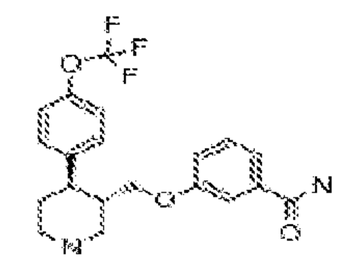
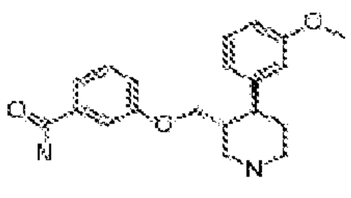
	B0193	3-{[(trans)-4-(3-hydroxyphenyl)piperidin-3-yl]methoxy}benzonitrile	308.37	309
	B0194	3-{[4-benzyl-1-(4-methoxyphenyl)piperazin-2-yl]methoxy}benzamide	431.53	432
	B0195	N-(propan-2-yl)-4-{[(trans)-4-[4-(propan-2-yloxy)phenyl]piperidin-3-yl]methoxy}benzamide	410.55	411
	B0196	4-({[(trans)-4-(4-methoxyphenyl)piperidin-3-yl]methoxy}methyl)-N-(propan-2-yl)benzamide	396.52	397
	B0197	4-{[(trans4-[4-(cyclopentyloxy)phenyl]piperidin-3-yl]methoxy}-N-(propan-2-yl)benzamide	436.59	437
	B0198	N-(propan-2-yl)-4-{[(trans)-4-[4-(trifluoromethoxy)phenyl]piperidin-3-yl]methoxy}benzamide	436.47	437
	B0199	3-{[(trans-4-[4-(trifluoromethoxy)phenyl]piperidin-3-yl]methoxy}benzamide	394.39	395
	B0200	3-{[(trans)-4-(3-methoxyphenyl)piperidin-3-yl]methoxy}benzamide	340.42	341

Figure 1-Continued

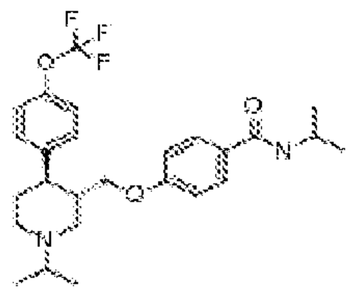
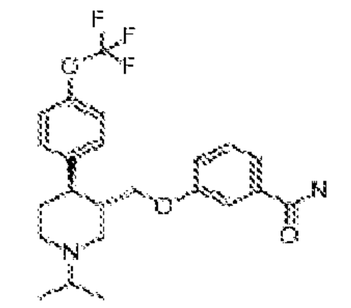
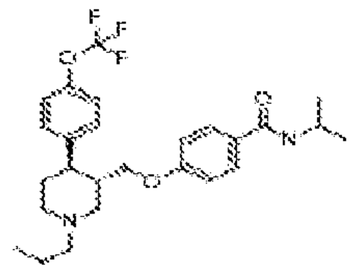
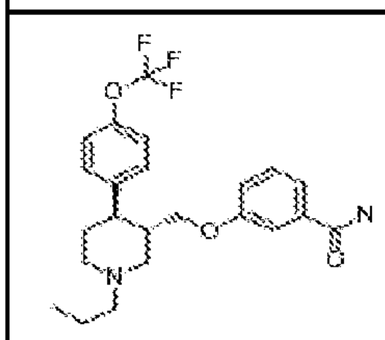
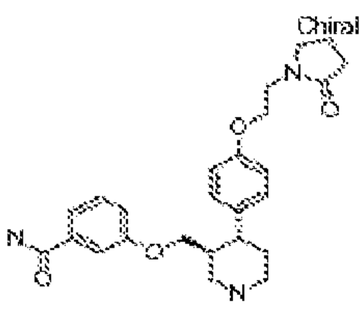
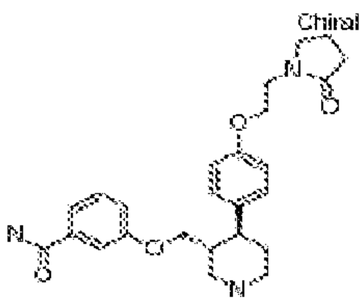
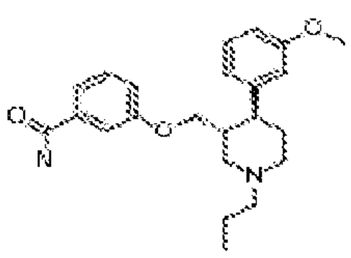
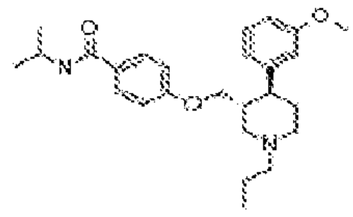
	B0201	N-(propan-2-yl)-4-{[(trans)-1-(propan-2-yl)-4-[4-(trifluoromethoxy)phenyl]piperidin-3-yl]methoxy}benzamide	478.55	479
	B0202	3-{[(trans)-1-(propan-2-yl)-4-[4-(trifluoromethoxy)phenyl]piperidin-3-yl]methoxy}benzamide	436.47	437
	B0203	N-(propan-2-yl)-4-{[(trans)-1-propyl-4-[4-(trifluoromethoxy)phenyl]piperidin-3-yl]methoxy}benzamide	478.55	479
	B0204	3-{[(trans)-1-propyl-4-[4-(trifluoromethoxy)phenyl]piperidin-3-yl]methoxy}benzamide	436.47	437
	B0205	(-)-3-{[(trans)-4-{4-[2-(2-oxopyrrolidin-1-yl)ethoxy]phenyl}piperidin-3-yl]methoxy}benzamide	437.53	438.3
	B0206	(+)-3-{[(trans)-4-{4-[2-(2-oxopyrrolidin-1-yl)ethoxy]phenyl}piperidin-3-yl]methoxy}benzamide	437.53	438.3
	B0207	3-{[(trans)-4-(3-methoxyphenyl)-1-propyl piperidin-3-yl]methoxy}benzamide	382.5	383
	B0208	4-{[(trans)-4-(3-methoxyphenyl)-1-propyl piperidin-3-yl]methoxy}-N-(propan-2-yl)benzamide	424.58	425

Figure 1-Continued

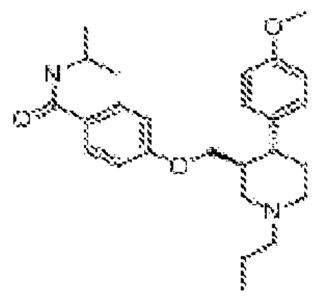
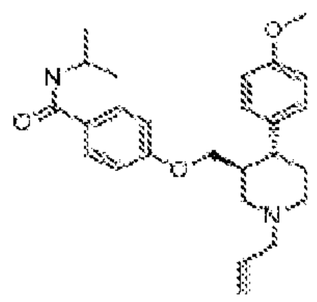
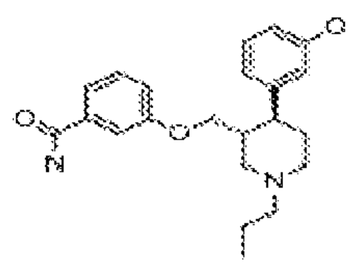
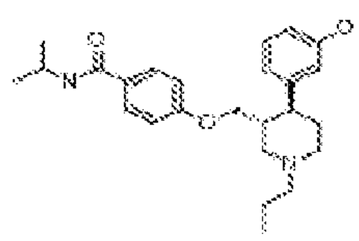
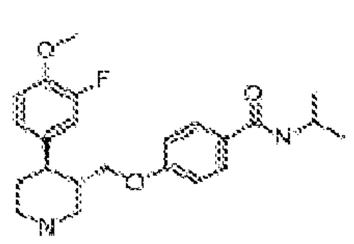
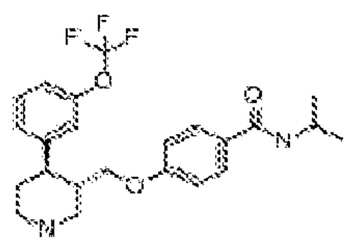
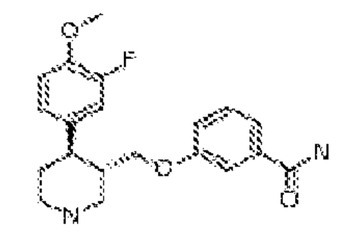
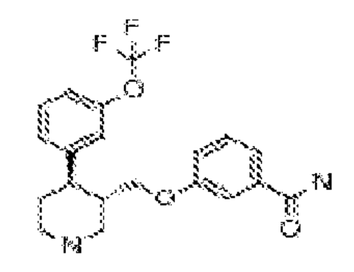
	B0209	4-{[(trans)-4-(4-methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}-N-(propan-2-yl)benzamide	424.58	425
	B0210	4-{[(trans)-4-(4-methoxyphenyl)-1-(prop-2-en-1-yl)piperidin-3-yl]methoxy}-N-(propan-2-yl)benzamide	422.56	423
	B0211	3-{[(trans)-4-(3-hydroxyphenyl)-1-propylpiperidin-3-yl]methoxy}benzamide	368.47	369
	B0212	4-{[(trans)-4-(3-hydroxyphenyl)-1-propylpiperidin-3-yl]methoxy}-N-(propan-2-yl)benzamide	410.55	411
	B0213	4-{[(trans)-4-(3-fluoro-4-methoxyphenyl)piperidin-3-yl]methoxy}-N-(propan-2-yl)benzamide	400.49	401
	B0214	N-(propan-2-yl)-4-{[(trans)-4-[3-(trifluoromethoxy)phenyl]piperidin-3-yl]methoxy}benzamide	436.47	437
	B0215	3-{[(trans)-4-(3-fluoro-4-methoxyphenyl)piperidin-3-yl]methoxy}benzamide	358.41	358
	B0216	3-{[(trans)-4-[3-(trifluoromethoxy)phenyl]piperidin-3-yl]methoxy}benzamide	394.39	395

Figure 1-Continued

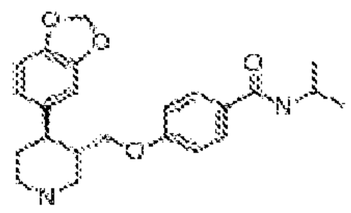
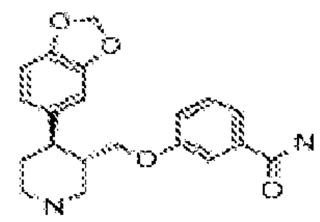
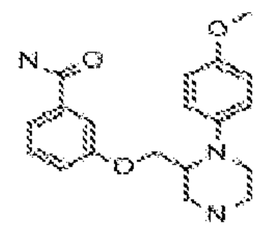
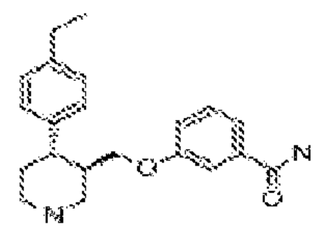
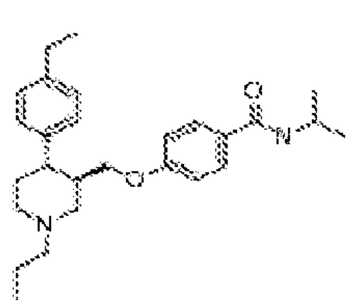
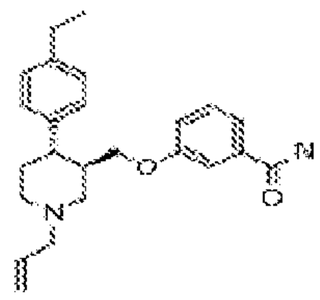
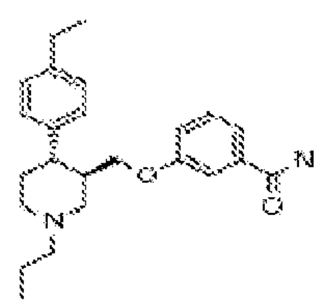
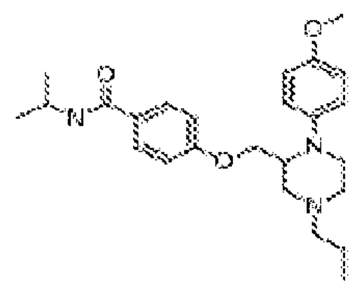
	B0217	4-{[(trans)-4-(2H-1,3-benzodioxol-5-yl)piperidin-3-yl]methoxy}-N-(propan-2-yl)benzamide	396.48	397
	B0218	3-{[(trans)-4-(2H-1,3-benzodioxol-5-yl)piperidin-3-yl]methoxy}benzamide	354.4	355
	B0219	3-{[1-(4-methoxyphenyl)piperazin-2-yl]methoxy}benzamide	341.4	342
	B0220	3-{[(trans)-4-(4-ethylphenyl)piperidin-3-yl]methoxy}benzamide	338.44	339
	B0221	4-{[(trans)-4-(4-ethylphenyl)-1-propylpiperidin-3-yl]methoxy}-N-(propan-2-yl)benzamide	422.6	423
	B0222	3-{[(trans)-4-(4-ethylphenyl)-1-(prop-2-en-1-yl)piperidin-3-yl]methoxy}benzamide	378.51	379
	B0223	3-{[(trans)-4-(4-ethylphenyl)-1-propylpiperidin-3-yl]methoxy}benzamide	380.56	381
	B0224	4-{[1-(4-methoxyphenyl)-4-propylpiperazin-2-yl]methoxy}-N-(propan-2-yl)benzamide	425.56	426

Figure 1-Continued

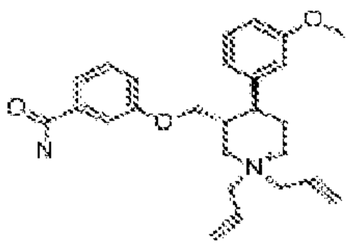
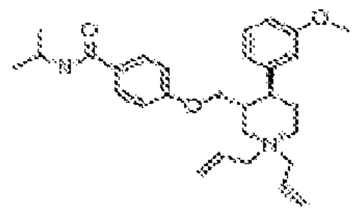
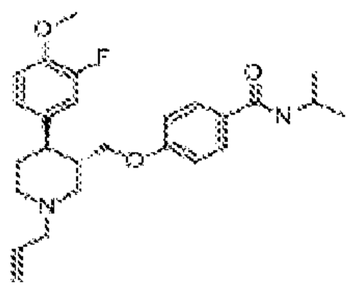
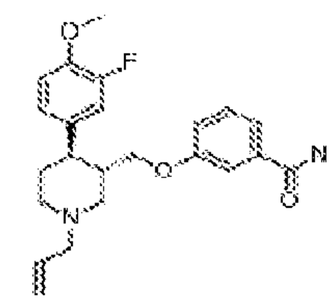
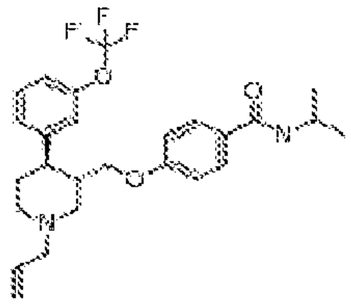
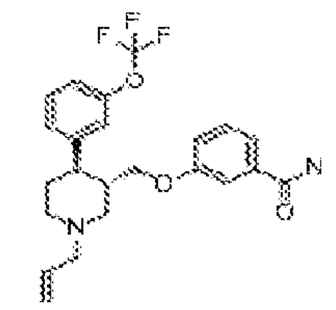
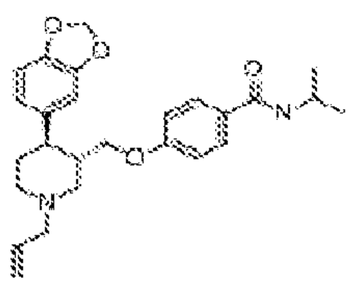
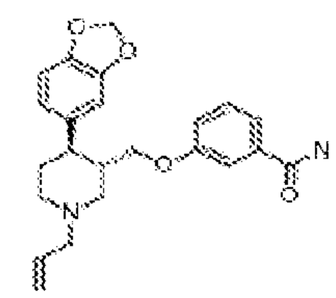
	B0225	(trans)-3-(3-carbamoylphenoxymethyl)-4-(3-methoxyphenyl)-1,1-bis(prop-2-en-1-yl)piperidin-1-ium	421.55	421
	B0226	(trans)-4-(3-methoxyphenyl)-1,1-bis(prop-2-en-1-yl)-3-{4-[(propan-2-yl)carbamoyl]phenoxymethyl}piperidin-1-ium	463.63	463
	B0227	4-{[(trans)-4-(3-fluoro-4-methoxyphenyl)-1-(prop-2-en-1-yl)piperidin-3-yl]methoxy}-N-(propan-2-yl)benzamide	440.55	441
	B0228	3-{[(trans)-4-(3-fluoro-4-methoxyphenyl)-1-(prop-2-en-1-yl)piperidin-3-yl]methoxy}benzamide	398.47	399
	B0229	4-{[(trans)-1-(prop-2-en-1-yl)-4-[3-(trifluoromethoxy)phenyl]piperidin-3-yl]methoxy}-N-(propan-2-yl)benzamide	476.53	477
	B0230	3-{[(trans)-1-(prop-2-en-1-yl)-4-[3-(trifluoromethoxy)phenyl]piperidin-3-yl]methoxy}benzamide	434.45	435
	B0231	4-{[(trans)-4-(2H-1,3-benzodioxol-5-yl)-1-(prop-2-en-1-yl)piperidin-3-yl]methoxy}-N-(propan-2-yl)benzamide	436.54	437
	B0232	3-{[(trans)-4-(2H-1,3-benzodioxol-5-yl)-1-(prop-2-en-1-yl)piperidin-3-yl]methoxy}benzamide	394.46	395

Figure 1-Continued

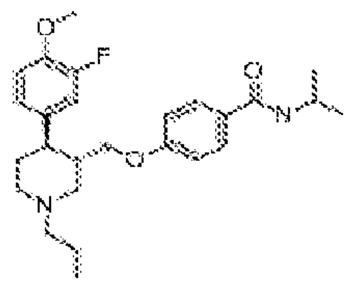
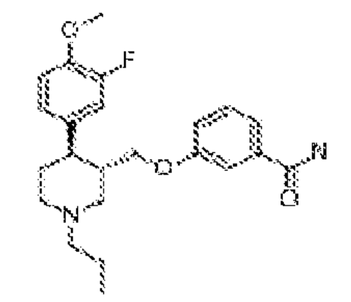
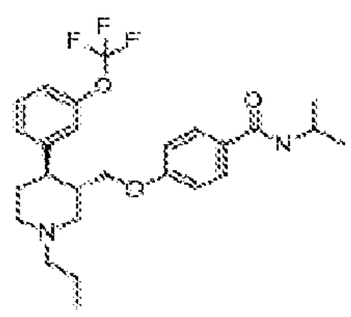
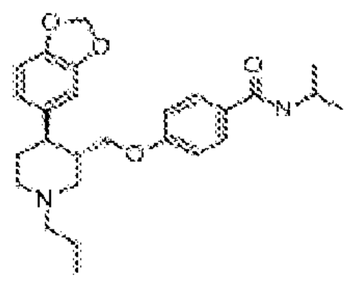
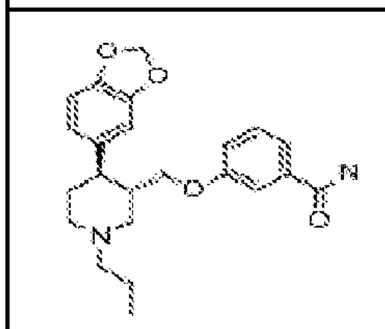
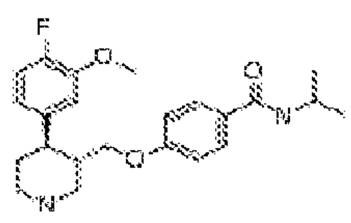
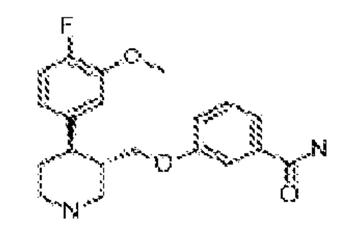
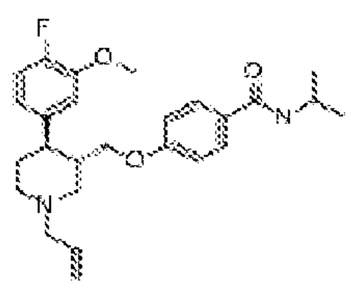
	B0233	4-{[(trans)-4-(3-fluoro-4-methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}-N-(propan-2-yl)benzamide	442.57	443
	B0234	3-{[(trans)-4-(3-fluoro-4-methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}benzamide	400.49	401
	B0235	N-(propan-2-yl)-4-{[(trans)-1-propyl-4-[3-(trifluoromethoxy)phenyl]piperidin-3-yl]methoxy}benzamide	478.55	479
	B0236	4-{[(trans)-4-(2H-1,3-benzodioxol-5-yl)-1-propylpiperidin-3-yl]methoxy}-N-(propan-2-yl)benzamide	438.56	439
	B0237	3-{[(trans)-4-(2H-1,3-benzodioxol-5-yl)-1-propylpiperidin-3-yl]methoxy}benzamide	396.48	397
	B0238	4-{[(trans)-4-(4-fluoro-3-methoxyphenyl)piperidin-3-yl]methoxy}-N-(propan-2-yl)benzamide	400.49	401
	B0239	3-{[(trans)-4-(4-fluoro-3-methoxyphenyl)piperidin-3-yl]methoxy}benzamide	358.41	359
	B0240	4-{[(trans)-4-(4-fluoro-3-methoxyphenyl)-1-(prop-2-en-1-yl)piperidin-3-yl]methoxy}-N-(propan-2-yl)benzamide	440.55	441

Figure 1-Continued

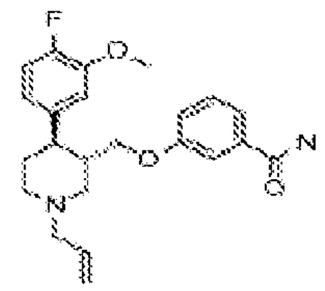
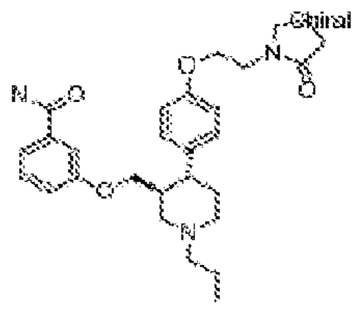
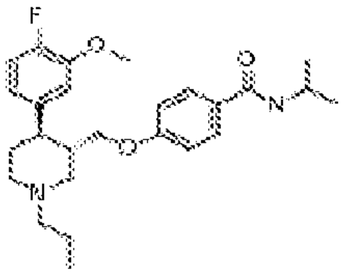
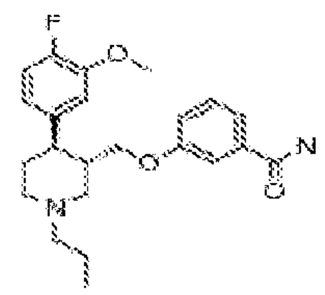
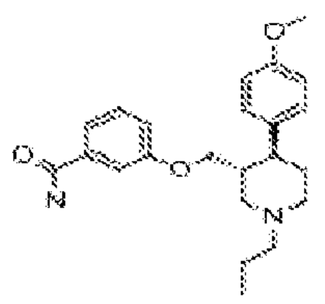
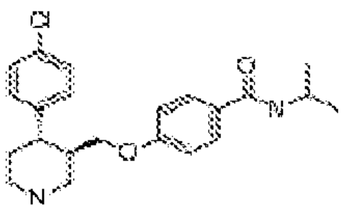
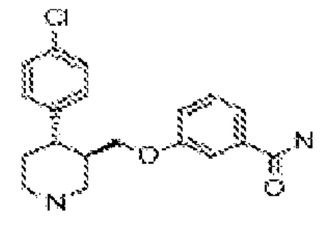
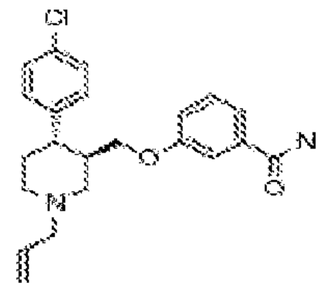
	B0241	3-{[(trans)-4-(4-fluoro-3-methoxyphenyl)-1-(prop-2-en-1-yl)piperidin-3-yl]methoxy}benzamide	398.47	399
	B0242	3-{[(trans)-4-{4-[2-(2-oxopyrrolidin-1-yl)ethoxy]phenyl}-1-propylpiperidin-3-yl]methoxy}benzamide	479.61	480
	B0243	4-{[(trans)-4-(4-fluoro-3-methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}-N-(propan-2-yl)benzamide	442.57	443
	B0244	3-{[(trans)-4-(4-fluoro-3-methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}benzamide	400.49	401
	B0245	3-{[(trans)-4-(4-methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}benzamide	382.5	383
	B0246	4-{[(trans)-4-(4-chlorophenyl)piperidin-3-yl]methoxy}-N-(propan-2-yl)benzamide	386.92	387
	B0247	3-{[(trans)-4-(4-chlorophenyl)piperidin-3-yl]methoxy}benzamide	344.84	345
	B0248	3-{[(trans)-4-(4-chlorophenyl)-1-(prop-2-en-1-yl)piperidin-3-yl]methoxy}benzamide	384.9	385

Figure 1-Continued

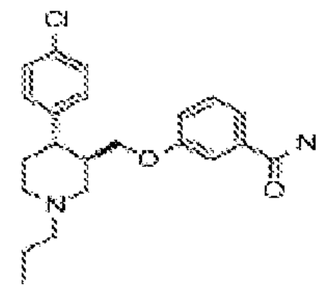
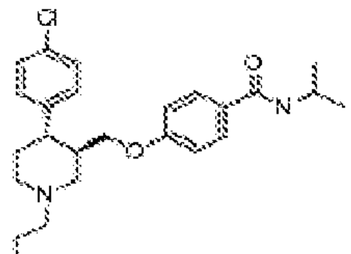
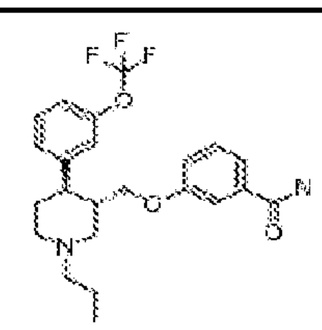
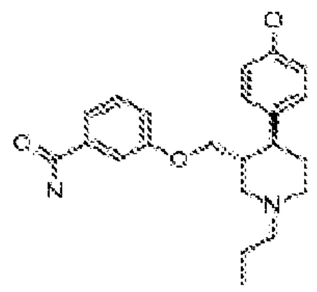
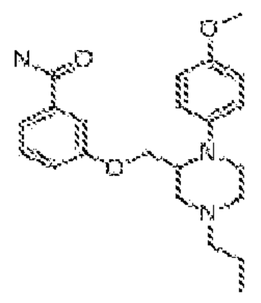
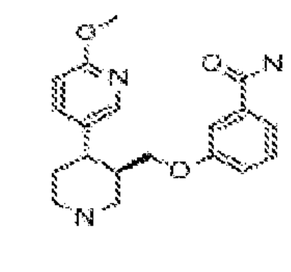
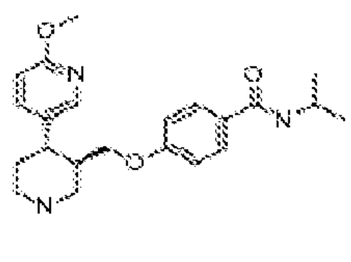
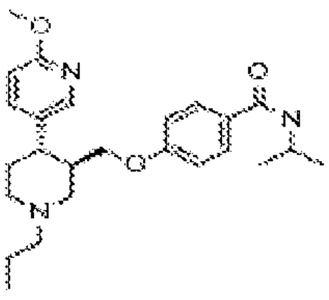
	B0249	3-{[(trans)-4-(4-chlorophenyl)-1-propylpiperidin-3-yl]methoxy}benzamide	386.92	387
	B0250	4-{[(trans)-4-(4-chlorophenyl)-1-propylpiperidin-3-yl]methoxy}-N-(propan-2-yl)benzamide	428.99	429
	B0251	3-{[(trans)-1-propyl-4-[3-(trifluoromethoxy)phenyl]piperidin-3-yl]methoxy}benzamide	436.47	437
	B0252	3-{[(trans)-4-(4-hydroxyphenyl)-1-propylpiperidin-3-yl]methoxy}benzamide	368.47	369
	B0253	3-{[1-(4-methoxyphenyl)-4-propylpiperazin-2-yl]methoxy}benzamide	383.48	384
	B0254	3-{[(trans)-4-(6-methoxypyridin-3-yl)piperidin-3-yl]methoxy}benzamide	341.4	342
	B0255	4-{[(trans)-4-(6-methoxypyridin-3-yl)piperidin-3-yl]methoxy}-N-(propan-2-yl)benzamide	383.48	384
	B0256	4-{[(trans)-4-(6-methoxypyridin-3-yl)-1-propylpiperidin-3-yl]methoxy}-N-(propan-2-yl)benzamide	425.56	426

Figure 1-Continued

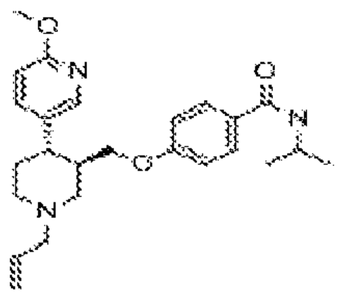
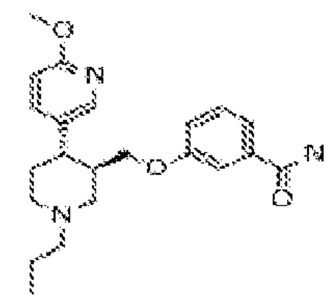
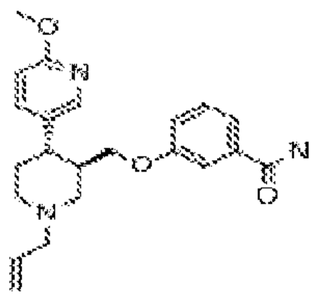
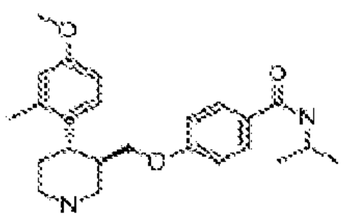
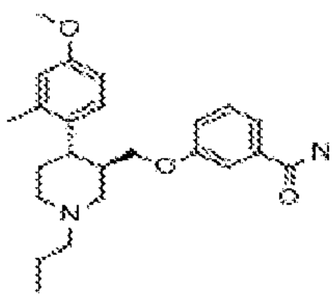
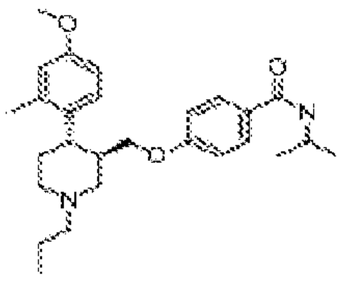
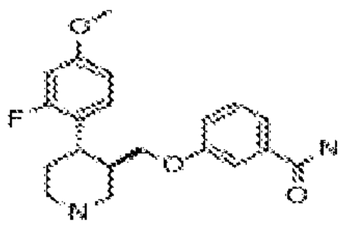
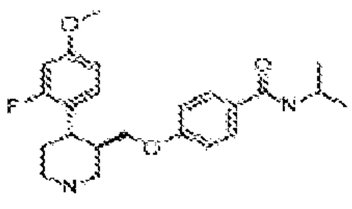
	B0257	4-{[(trans)-4-(6-methoxypyridin-3-yl)-1-(prop-2-en-1-yl)piperidin-3-yl]methoxy}-N-(propan-2-yl)benzamide	423.55	424
	B0258	3-{[(trans)-4-(6-methoxypyridin-3-yl)-1-propylpiperidin-3-yl]methoxy}benzamide	383.48	384
	B0259	3-{[(trans)-4-(6-methoxypyridin-3-yl)-1-propylpiperidin-3-yl]methoxy}benzamide	381.47	382
	B0260	4-{[(trans)-4-(4-methoxy-2-methylphenyl)piperidin-3-yl]methoxy}-N-(propan-2-yl)benzamide	396.52	397
	B0261	3-{[(trans)-4-(4-methoxy-2-methylphenyl)-1-propylpiperidin-3-yl]methoxy}benzamide	396.52	397
	B0262	4-{[(trans)-4-(4-methoxy-2-methylphenyl)-1-propylpiperidin-3-yl]methoxy}-N-(propan-2-yl)benzamide	438.6	439
	B0263	3-{[(trans)-4-(2-fluoro-4-methoxyphenyl)piperidin-3-yl]methoxy}benzamide	358.41	359
	B0264	4-{[(trans)-4-(2-fluoro-4-methoxyphenyl)piperidin-3-yl]methoxy}-N-(propan-2-yl)benzamide	400.49	401

Figure 1-Continued

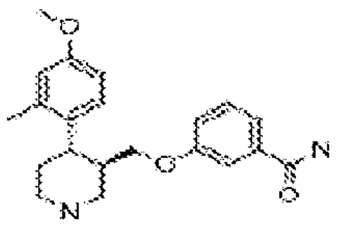
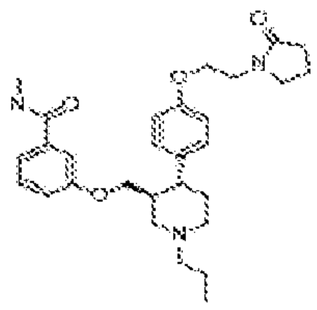
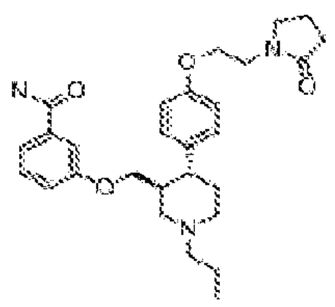
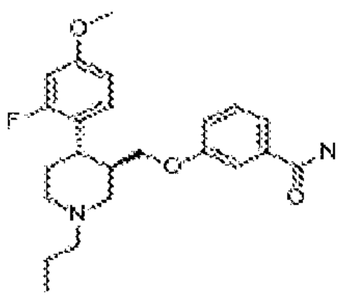
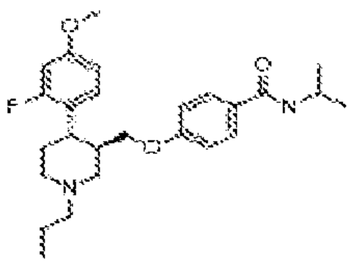
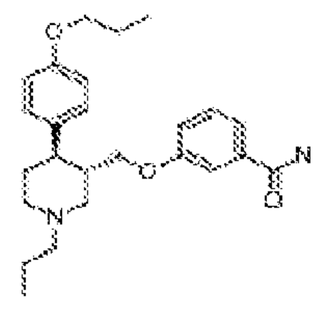
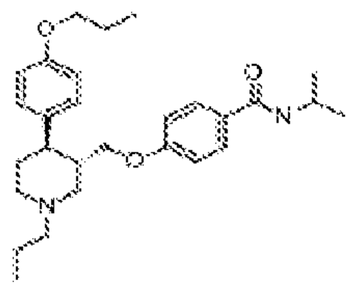
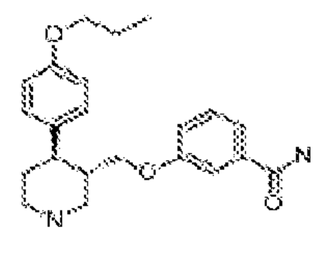
	B0265	3-{[(trans)-4-(4-methoxy-2-methylphenyl) piperidin-3-yl]methoxy}benzamide	354.44	355
	B0266	N-methyl-3-{[(trans)-4-{4-[2-(2-oxopyrroli din-1-yl)ethoxy]phenyl}-1-propylpiperidin -3-yl]methoxy}benzamide	493.64	494
	B0267	3-{[(trans)-4-{4-[2-(2-oxopyrrolidin-1-yl)et hoxy]phenyl}-1-propylpiperidin-3-yl]meth oxy}benzamide	479.61	480
	B0268	3-{[(trans)-4-(2-fluoro-4-methoxyphenyl)- 1-propylpiperidin-3-yl]methoxy}benzami de	400.49	401
	B0269	4-{[(trans)-4-(2-fluoro-4-methoxyphenyl)- 1-propylpiperidin-3-yl]methoxy}-N-(propa n-2-yl)benzamide	442.57	443
	B0270	3-{[(trans)-4-(4-propoxyphenyl)-1-propylp iperidin-3-yl]methoxy}benzamide	410.55	411
	B0271	N-(propan-2-yl)-4-{[(trans)-4-(4-propoxyp henyl)-1 -propylpiperidin-3-yl]methoxy}benzamid e	452.63	453
	B0272	3-{[(trans)-4-(4-propoxyphenyl)piperidin- 3-yl]methoxy}benzamide	368.47	369

Figure 1-Continued

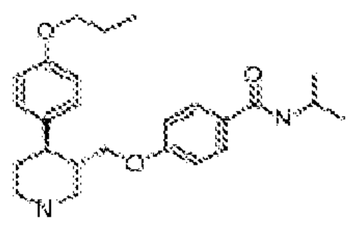
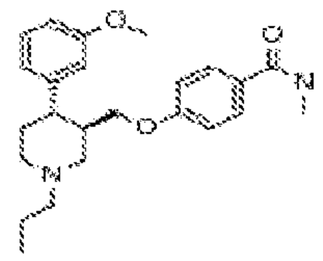
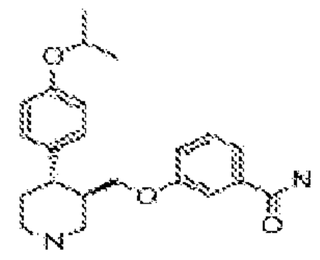
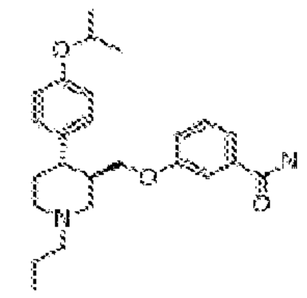
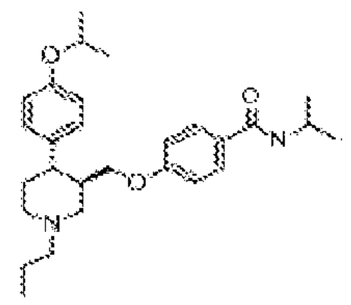
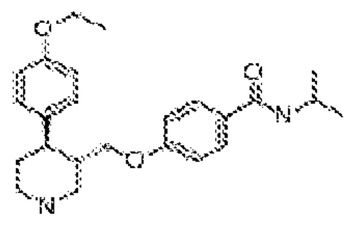
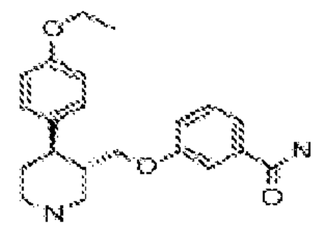
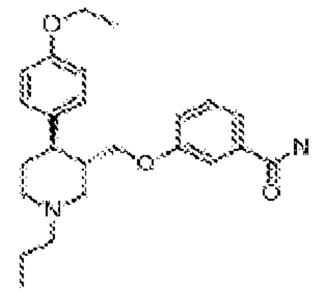
	B0273	N-(propan-2-yl)-4-{[(trans)-4-(4-propoxyphenyl)piperidin-3-yl]methoxy}benzamide	410.55	411
	B0274	4-{[(trans)-4-(3-methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}-N-methylbenzamide	396.52	397
	B0275	3-{[(trans)-4-[4-(propan-2-yloxy)phenyl]piperidin-3-yl]methoxy}benzamide	368.47	369
	B0276	3-{[(trans)-4-[4-(propan-2-yloxy)phenyl]-1-propylpiperidin-3-yl]methoxy}benzamide	410.55	411
	B0277	N-(propan-2-yl)-4-{[(trans)-4-[4-(propan-2-yloxy)phenyl]-1-propylpiperidin-3-yl]methoxy}benzamide	452.63	453
	B0278	4-{[(trans)-4-(4-ethoxyphenyl)piperidin-3-yl]methoxy}-N-(propan-2-yl)benzamide	396.52	397
	B0279	3-{[(trans)-4-(4-ethoxyphenyl)piperidin-3-yl]methoxy}benzamide	354.44	355
	B0280	3-{[(trans)-4-(4-ethoxyphenyl)-1-propylpiperidin-3-yl]methoxy}benzamide	396.52	397

Figure 1-Continued

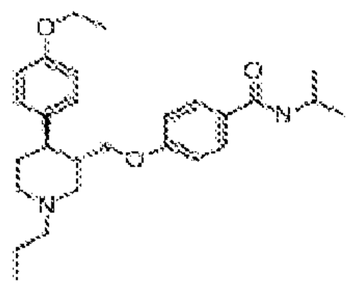
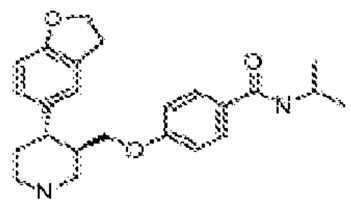
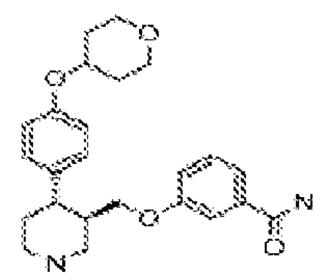
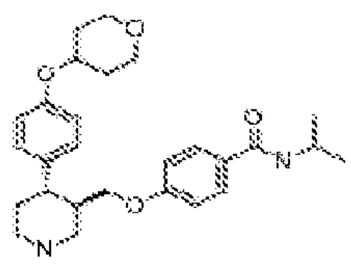
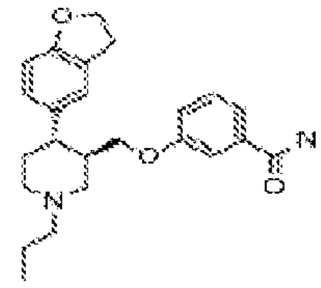
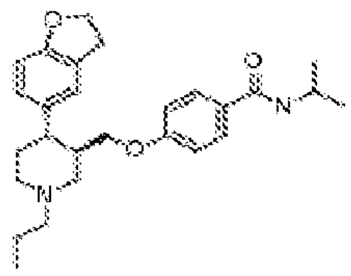
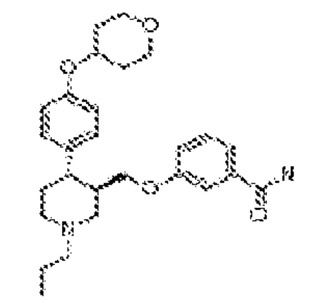
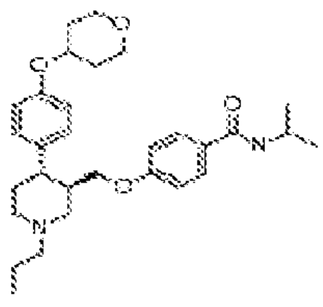
	B0281	4-{[(trans)-4-(4-ethoxyphenyl)-1-propylpiperidin-3-yl]methoxy}-N-(propan-2-yl)benzamide	438.6	439
	B0282	4-{[(trans)-4-(2,3-dihydro-1-benzofuran-5-yl)piperidin-3-yl]methoxy}-N-(propan-2-yl)benzamide	394.51	395
	B0283	3-{[(trans)-4-[4-(oxan-4-yloxy)phenyl]piperidin-3-yl]methoxy}benzamide	410.51	411
	B0284	4-{[(trans)-4-[4-(oxan-4-yloxy)phenyl]piperidin-3-yl]methoxy}-N-(propan-2-yl)benzamide	452.59	453
	B0285	3-{[(trans)-4-(2,3-dihydro-1-benzofuran-5-yl)-1-propylpiperidin-3-yl]methoxy}benzamide	394.51	395
	B0286	4-{[(trans)-4-(2,3-dihydro-1-benzofuran-5-yl)-1-propylpiperidin-3-yl]methoxy}-N-(propan-2-yl)benzamide	436.59	437
	B0287	3-{[(trans)-4-[4-(oxan-4-yloxy)phenyl]-1-propylpiperidin-3-yl]methoxy}benzamide	452.59	453
	B0288	4-{[(trans)-4-[4-(oxan-4-yloxy)phenyl]-1-propylpiperidin-3-yl]methoxy}-N-(propan-2-yl)benzamide	494.67	495

Figure 1-Continued

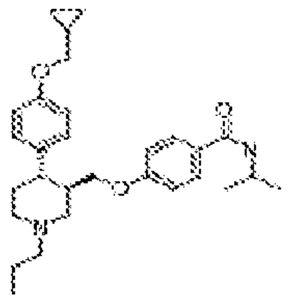
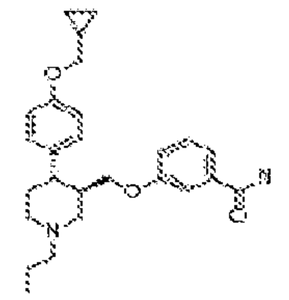
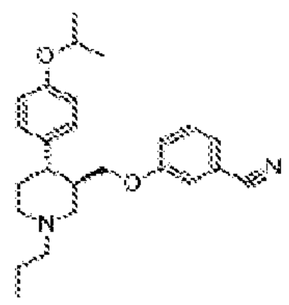
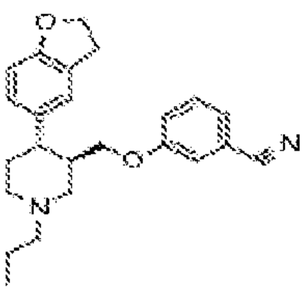
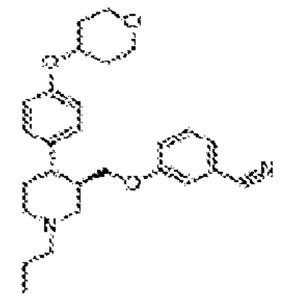
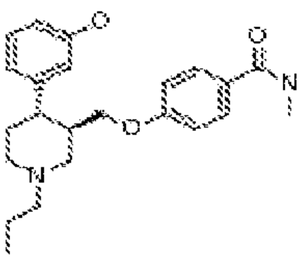
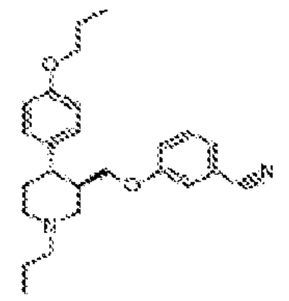
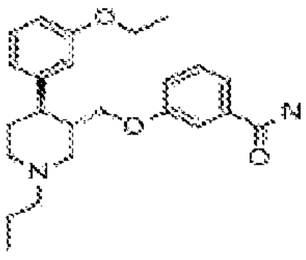
	B0289	4-{[(trans)-4-[4-(cyclopropylmethoxy)phenyl]-1-propylpiperidin-3-yl]methoxy}-N-(propan-2-yl)benzamide	464.64	465
	B0290	3-{[(trans)-4-[4-(cyclopropylmethoxy)phenyl]-1-propylpiperidin-3-yl]methoxy}benzamide	422.56	423
	B0291	3-{[(trans)-4-[4-(propan-2-yloxy)phenyl]-1-propylpiperidin-3-yl]methoxy}benzonitrile	392.53	393
	B0292	3-{[(trans)-4-(2,3-dihydro-1-benzofuran-5-yl)-1-propylpiperidin-3-yl]methoxy}benzonitrile	376.49	377
	B0293	3-{[(trans)-4-[4-(oxan-4-yloxy)phenyl]-1-propylpiperidin-3-yl]methoxy}benzonitrile	434.57	435
	B0294	4-{[(trans)-4-(3-hydroxyphenyl)-1-propylpiperidin-3-yl]methoxy}-N-methylbenzamide	382.5	383
	B0295	3-{[(trans)-4-(4-propoxyphenyl)-1-propylpiperidin-3-yl]methoxy}benzonitrile	392.53	393
	B0296	3-{[(trans)-4-(3-ethoxyphenyl)-1-propylpiperidin-3-yl]methoxy}benzamide	396.52	397

Figure 1-Continued

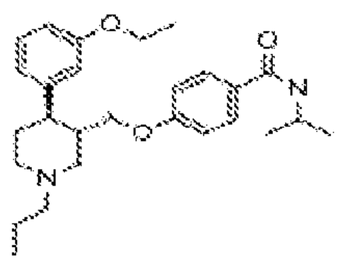
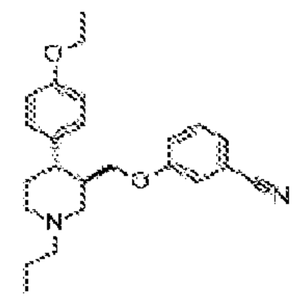
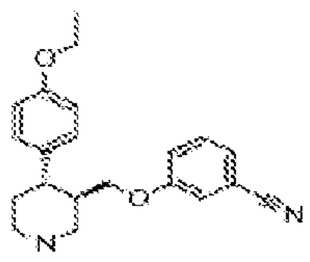
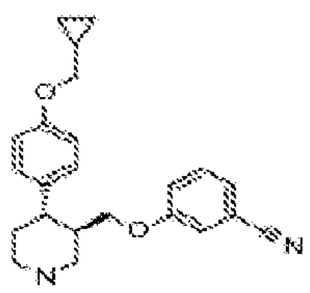
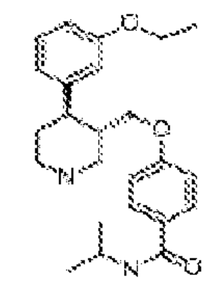
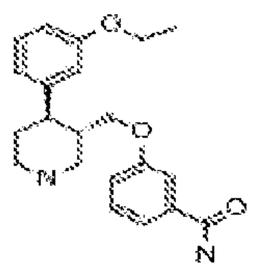
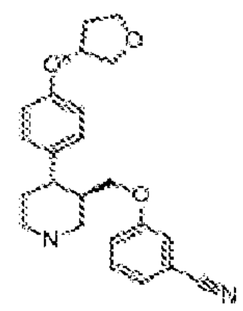
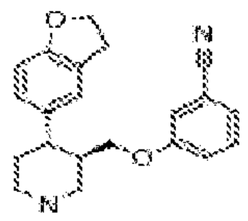
	B0297	4-{[(trans)-4-(3-ethoxyphenyl)-1-propylpiperidin-3-yl]methoxy}-N-(propan-2-yl)benzamide	438.6	438
	B0298	3-{[(trans)-4-(4-ethoxyphenyl)-1-propylpiperidin-3-yl]methoxy}benzonitrile	378.51	379
	B0299	3-{[(trans)-4-(4-ethoxyphenyl)piperidin-3-yl]methoxy}benzonitrile	336.43	337
	B0300	3-{[(trans)-4-[4-(cyclopropylmethoxy)phenyl]piperidin-3-yl]methoxy}benzonitrile	362.46	363
	B0301	4-{[(trans)-4-(3-ethoxyphenyl)piperidin-3-yl]methoxy}-N-(propan-2-yl)benzamide	396.52	397
	B0302	3-{[(trans)-4-(3-ethoxyphenyl)piperidin-3-yl]methoxy}benzamide	354.44	355
	B0303	3-{[(trans)-4-{4-[(3R)-oxolan-3-yloxy]phenyl}piperidin-3-yl]methoxy}benzonitrile	378.46	379
	B0304	3-{[(trans)-4-(2,3-dihydro-1-benzofuran-5-yl)piperidin-3-yl]methoxy}benzonitrile	334.41	335

Figure 1-Continued

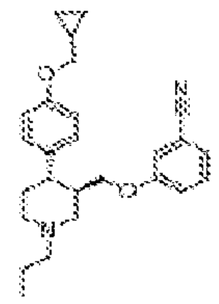
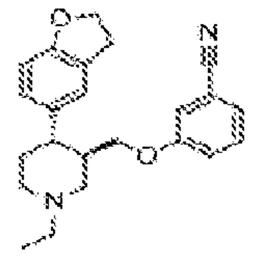
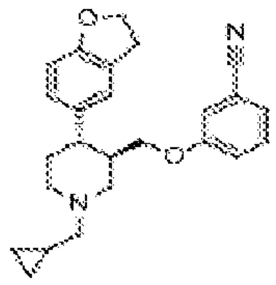
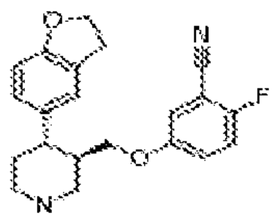
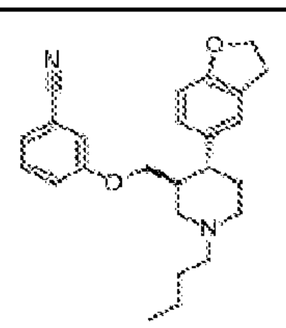
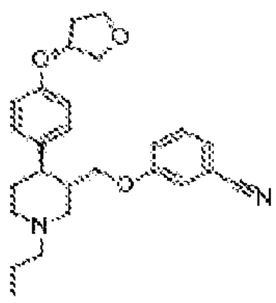
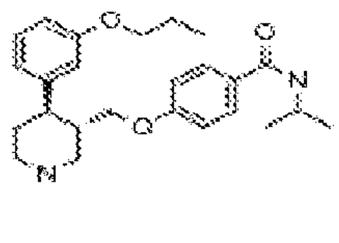
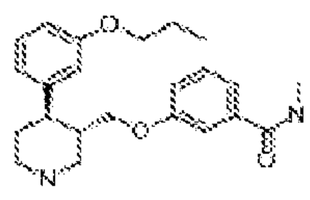
	B0305	3-{[(trans)-4-[4-(cyclopropylmethoxy)phenyl]-1-propylpiperidin-3-yl]methoxy}benzonitrile	404.54	405
	B0306	3-{[(trans)-4-(2,3-dihydro-1-benzofuran-5-yl)-1-ethylpiperidin-3-yl]methoxy}benzonitrile	362.46	363
	B0307	3-{[(trans)-1-(cyclopropylmethyl)-4-(2,3-dihydro-1-benzofuran-5-yl)piperidin-3-yl]methoxy}benzonitrile	388.5	389
	B0308	5-{[(trans)-4-(2,3-dihydro-1-benzofuran-5-yl)piperidin-3-yl]methoxy}-2-fluorobenzonitrile	352.4	353
	B0309	3-{[(trans)-1-butyl-4-(2,3-dihydro-1-benzofuran-5-yl)piperidin-3-yl]methoxy}benzonitrile	390.52	391
	B0310	3-{[(trans)-4-{4-[(3R)-oxolan-3-yloxy]phenyl}-1-propylpiperidin-3-yl]methoxy}benzonitrile	420.54	421
	B0311	N-(propan-2-yl)-4-{[(trans)-4-(3-propoxyphenyl)piperidin-3-yl]methoxy}benzamide	410.55	411
	B0312	N-methyl-3-{[(trans)-4-(3-propoxyphenyl)piperidin-3-yl]methoxy}benzamide	382.5	383

Figure 1-Continued

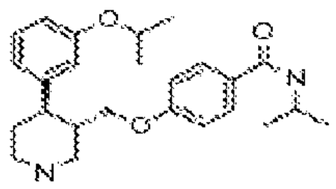
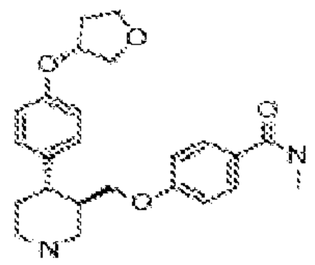
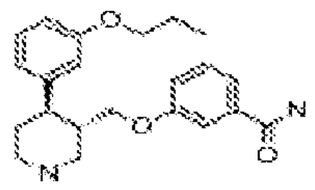
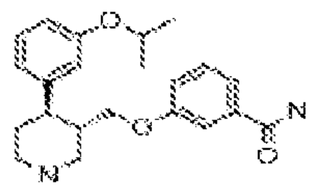
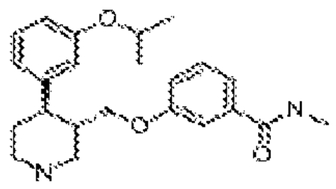
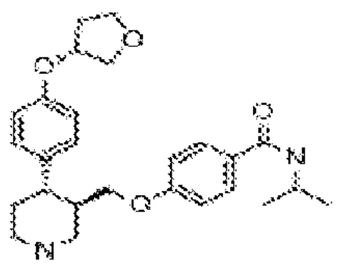
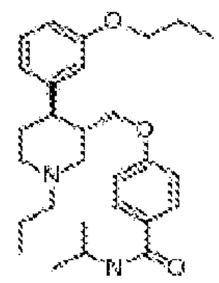
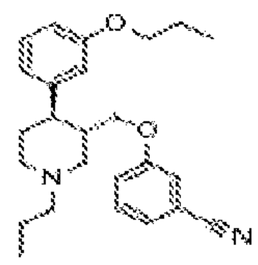
	B0313	N-(propan-2-yl)-4-{[(trans)-4-[3-(propan-2-yloxy)phenyl]piperidin-3-yl]methoxy}benzamide	410.55	411
	B0314	N-methyl-4-{[(trans)-4-{4-[(3R)-oxolan-3-yloxy]phenyl}piperidin-3-yl]methoxy}benzamide	410.51	411
	B0315	3-{[(trans)-4-(3-propoxyphenyl)piperidin-3-yl]methoxy}benzamide	368.47	369
	B0316	3-{[(trans)-4-[3-(propan-2-yloxy)phenyl]piperidin-3-yl]methoxy}benzamide	368.47	369
	B0317	N-methyl-3-{[(trans)-4-[3-(propan-2-yloxy)phenyl]piperidin-3-yl]methoxy}benzamide	382.5	383
	B0318	4-{[(trans)-4-{4-[(3R)-oxolan-3-yloxy]phenyl}piperidin-3-yl]methoxy}-N-(propan-2-yl)benzamide	438.56	439
	B0319	N-(propan-2-yl)-4-{[(trans)-4-(3-propoxyphenyl)-1-propylpiperidin-3-yl]methoxy}benzamide	452.63	453
	B0320	3-{[(trans)-4-(3-propoxyphenyl)-1-propylpiperidin-3-yl]methoxy}benzonitrile	392.53	393

Figure 1-Continued

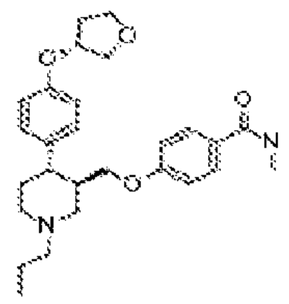
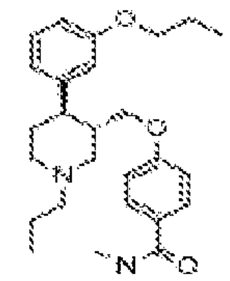
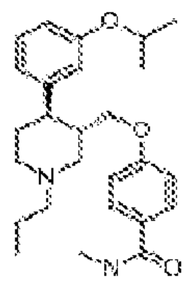
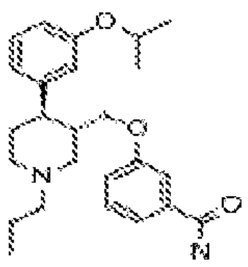
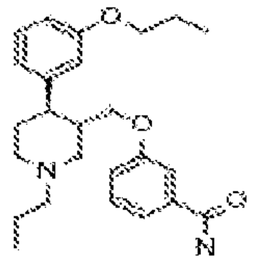
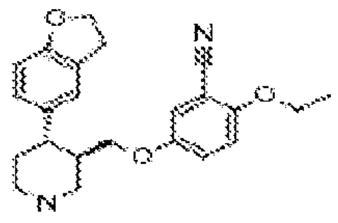
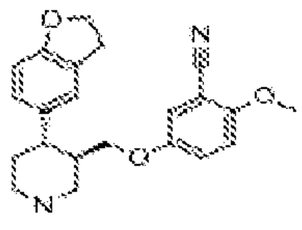
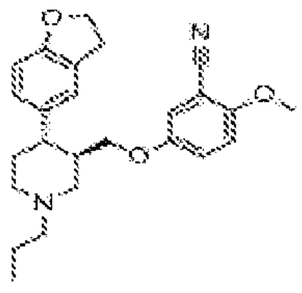
	B0321	N-methyl-4-{[(trans)-4-{4-[(3R)-oxolan-3-yloxy]phenyl}-1-propylpiperidin-3-yl]methoxy}benzamide	452.59	453
	B0322	N-methyl-4-{[(trans)-4-(3-propoxyphenyl)-1-propylpiperidin-3-yl]methoxy}benzamide	424.58	425
	B0323	N-methyl-4-{[(trans)-4-[3-(propan-2-yloxy)phenyl]-1-propylpiperidin-3-yl]methoxy}benzamide	424.58	425
	B0324	3-{[(trans)-4-[3-(propan-2-yloxy)phenyl]-1-propylpiperidin-3-yl]methoxy}benzamide	410.55	411
	B0325	3-{[(trans)-4-(3-propoxyphenyl)-1-propylpiperidin-3-yl]methoxy}benzamide	410.55	411
	B0326	5-{[(trans)-4-(2,3-dihydro-1-benzofuran-5-yl)piperidin-3-yl]methoxy}-2-ethoxybenzonitrile	378.46	379
	B0327	5-{[(trans)-4-(2,3-dihydro-1-benzofuran-5-yl)piperidin-3-yl]methoxy}-2-methoxybenzonitrile	364.44	365
	B0328	5-{[(trans)-4-(2,3-dihydro-1-benzofuran-5-yl)-1-propylpiperidin-3-yl]methoxy}-2-methoxybenzonitrile	406.52	407

Figure 1-Continued

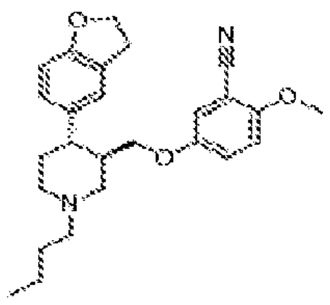
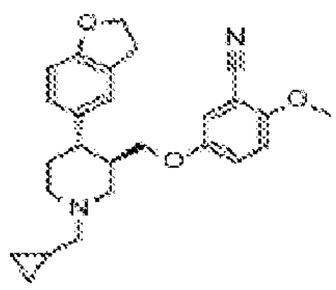
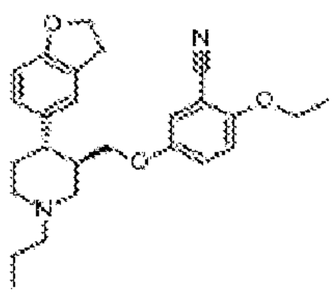
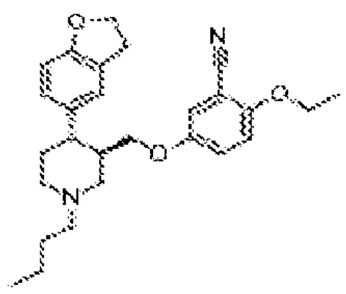
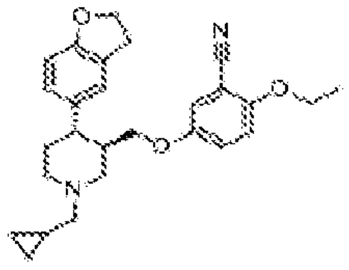
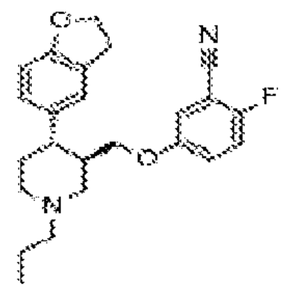
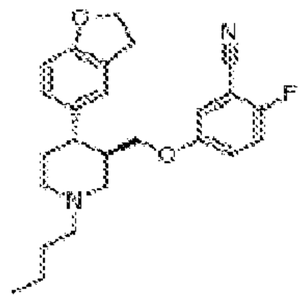
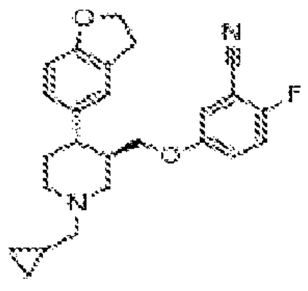
	B0329	5-{[(trans)-1-butyl-4-(2,3-dihydro-1-benzofuran-5-yl)piperidin-3-yl]methoxy}-2-methoxybenzonitrile	420.54	421
	B0330	5-{[(trans)-1-(cyclopropylmethyl)-4-(2,3-dihydro-1-benzofuran-5-yl)piperidin-3-yl]methoxy}-2-methoxybenzonitrile	418.53	419
	B0331	5-{[(trans)-4-(2,3-dihydro-1-benzofuran-5-yl)-1-propylpiperidin-3-yl]methoxy}-2-ethoxybenzonitrile	420.54	421
	B0332	5-{[(trans)-1-butyl-4-(2,3-dihydro-1-benzofuran-5-yl)piperidin-3-yl]methoxy}-2-ethoxybenzonitrile	434.57	435
	B0333	5-{[(trans)-1-(cyclopropylmethyl)-4-(2,3-dihydro-1-benzofuran-5-yl)piperidin-3-yl]methoxy}-2-ethoxybenzonitrile	432.55	433
	B0334	5-{[(trans)-4-(2,3-dihydro-1-benzofuran-5-yl)-1-propylpiperidin-3-yl]methoxy}-2-fluorobenzonitrile	394.48	395
	B0335	5-{[(trans)-1-butyl-4-(2,3-dihydro-1-benzofuran-5-yl)piperidin-3-yl]methoxy}-2-fluorobenzonitrile	408.51	409
	B0336	5-{[(trans)-1-(cyclopropylmethyl)-4-(2,3-dihydro-1-benzofuran-5-yl)piperidin-3-yl]methoxy}-2-fluorobenzonitrile	406.49	407

Figure 1-Continued

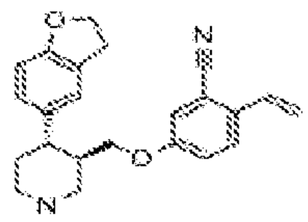
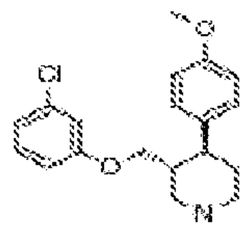
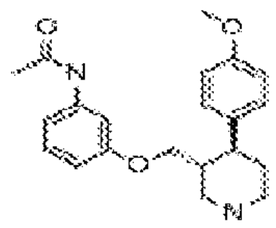
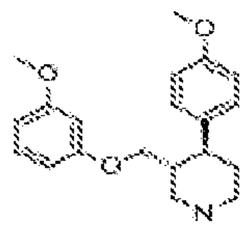
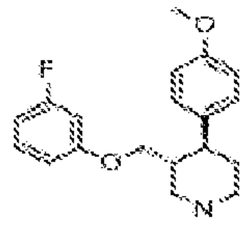
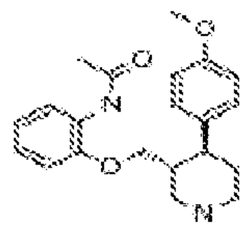
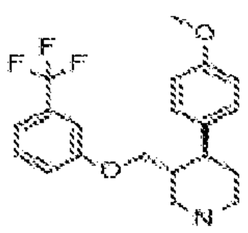
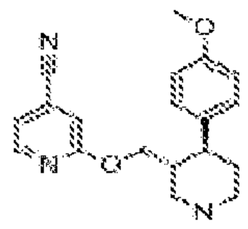
	B0337	5-{[(trans)-4-(2,3-dihydro-1-benzofuran-5-yl)piperidin-3-yl]methoxy}-2-ethenylbenzonitrile	360.45	361
	B0338	trans-3-[(3-Chlorophenoxy)methyl]-4-(4-methoxyphenyl)piperidine	331.84	332
	B0339	N-(3-{[(trans)-4-(4-Methoxyphenyl)piperidin-3-yl]methoxy}phenyl)acetamide	354.44	355
	B0340	trans-3-[(3-Methoxyphenoxy)methyl]-4-(4-methoxyphenyl)piperidine	327.42	328
	B0341	trans-3-[(3-Fluorophenoxy)methyl]-4-(4-methoxyphenyl)piperidine	315.38	316
	B0342	N-(2-{[trans-4-(4-Methoxyphenyl)piperidin-3-yl]methoxy}phenyl)acetamide	354.44	355
	B0343	trans-4-(4-Methoxyphenyl)-3-{[3-(trifluoromethyl)phenoxy]methyl}piperidine	365.39	366
	B0344	2-{[(trans)-4-(4-Methoxyphenyl)piperidin-3-yl]methoxy}isonicotinonitrile	323.39	324

Figure 1-Continued

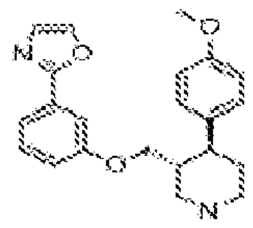
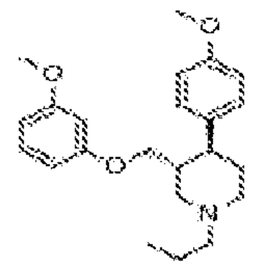
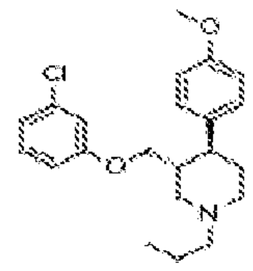
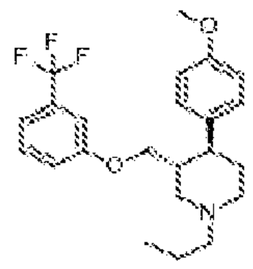
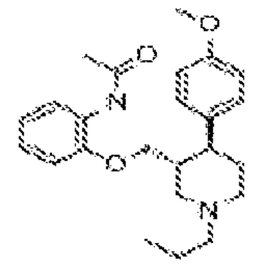
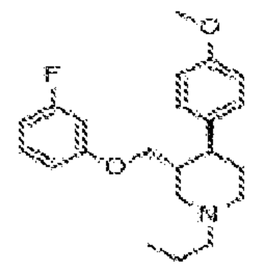
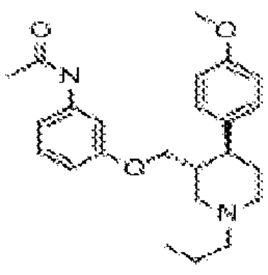
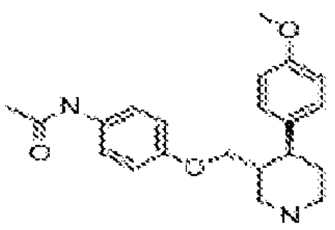
	B0345	2-(3-{[(trans)-4-(4-Methoxyphenyl)piperidin-3-yl]methoxy}phenyl)oxazole	364.44	365
	B0346	trans-3-[(3-Methoxyphenoxy)methyl]-4-(4-methoxyphenyl)-1-propylpiperidine	369.5	370
	B0347	trans-3-[(3-Chlorophenoxy)methyl]-4-(4-methoxyphenyl)-1-propylpiperidine	373.92	374
	B0348	trans-4-(4-Methoxyphenyl)-1-propyl-3-[(3-(trifluoromethyl)phenoxy]methyl)piperidine	407.47	408
	B0349	N-(2-{[trans-4-(4-Methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}phenyl)acetamide	396.52	397
	B0350	trans-3-[(3-Fluorophenoxy)methyl]-4-(4-methoxyphenyl)-1-propylpiperidine	357.46	358
	B0351	N-(3-{[trans-4-(4-Methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}phenyl)acetamide	396.52	397
	B0352	N-(4-{[trans-4-(4-Methoxyphenyl)piperidin-3-yl]methoxy}phenyl)acetamide	354.44	355

Figure 1-Continued

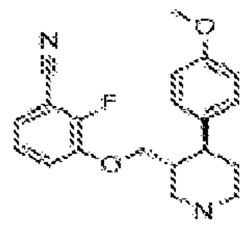
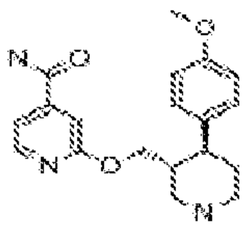
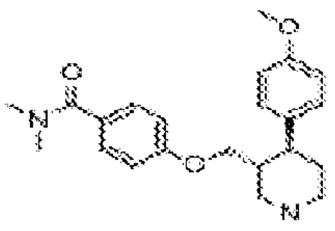
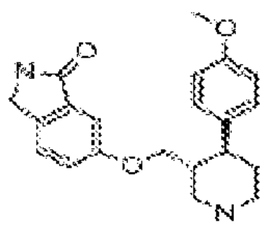
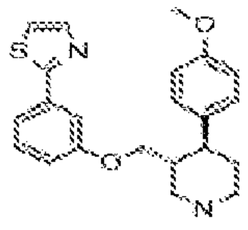
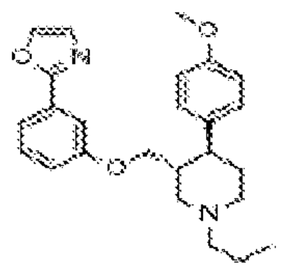
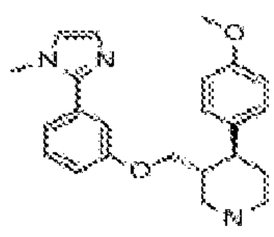
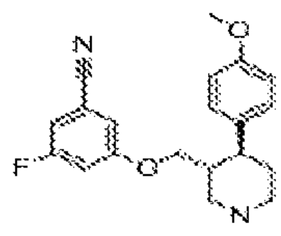
	B0353	2-Fluoro-3-{[trans-4-(4-methoxyphenyl)piperidin-3-yl]methoxy}benzonitrile	340.39	341
	B0354	2-{[trans-4-(4-Methoxyphenyl)piperidin-3-yl]methoxy}isonicotinamide	341.4	342
	B0355	4-{[trans-4-(4-Methoxyphenyl)piperidin-3-yl]methoxy}-N,N-dimethylbenzamide	368.47	369
	B0356	6-{[trans-4-(4-methoxyphenyl)piperidin-3-yl]methoxy}isoindolin-1-one	352.43	353
	B0357	2-(3-{[trans-4-(4-Methoxyphenyl)piperidin-3-yl]methoxy}phenyl)thiazole	380.5	381
	B0358	2-(3-{[trans-4-(4-Methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}phenyl)oxazole	406.52	407
	B0359	trans-4-(4-Methoxyphenyl)-3-{[3-(1-methyl-1H-imidazol-2-yl)phenoxy]methyl}piperidine	377.48	378
	B0360	3-Fluoro-5-{[trans-4-(4-methoxyphenyl)piperidin-3-yl]methoxy}benzonitrile	340.39	341

Figure 1-Continued

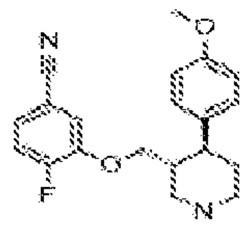
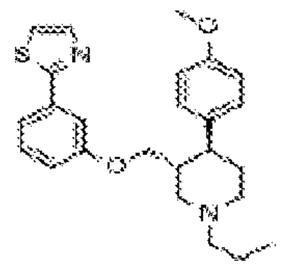
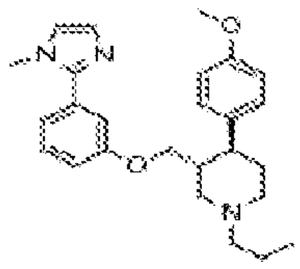
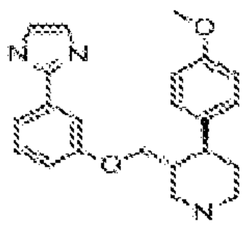
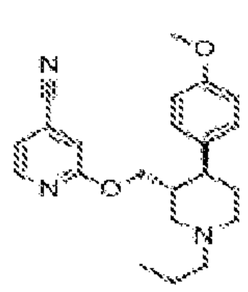
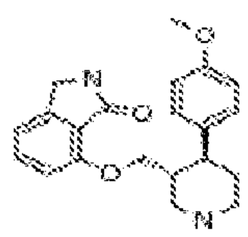
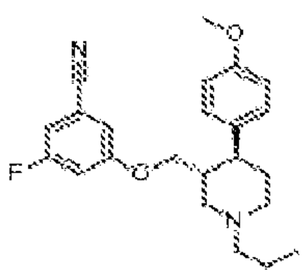
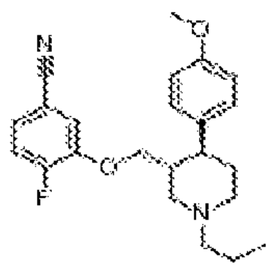
	B0361	4-Fluoro-3-{[trans-4-(4-methoxyphenyl)piperidin-3-yl]methoxy}benzonitrile	340.39	341
	B0362	2-(3-{[trans-4-(4-Methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}phenyl)thiazole	422.58	423
	B0363	trans-4-(4-Methoxyphenyl)-3-{[3-(1-methyl-1H-imidazol-2-yl)phenoxy]methyl}-1-propylpiperidine	419.56	420
	B0364	trans-3-[(3-(1H-Imidazol-2-yl)phenoxy]methyl)-4-(4-methoxyphenyl)piperidine	363.45	364
	B0365	2-{[trans-4-(4-Methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}isonicotinonitrile	365.47	366
	B0366	7-{[trans-4-(4-Methoxyphenyl)piperidin-3-yl]methoxy}isoindolin-1-one	352.43	353
	B0367	3-Fluoro-5-{[trans-4-(4-methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}benzonitrile	382.47	383
	B0368	4-Fluoro-3-{[trans-4-(4-methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}benzonitrile	382.47	383

Figure 1-Continued

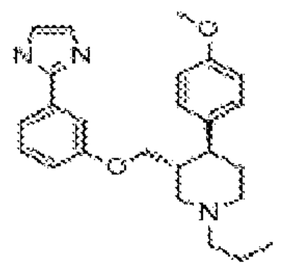
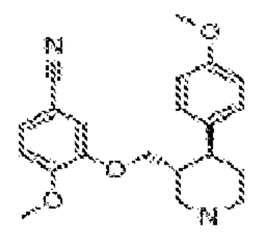
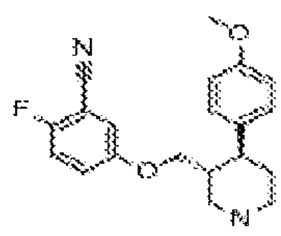
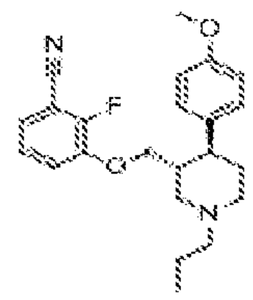
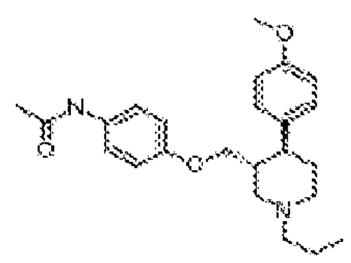
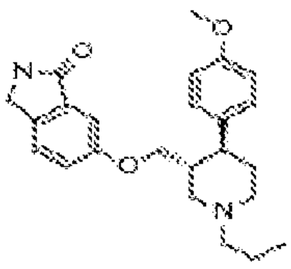
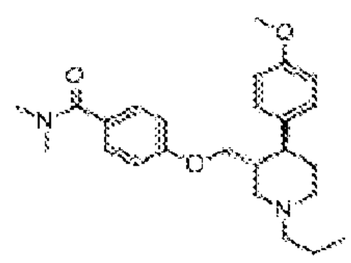
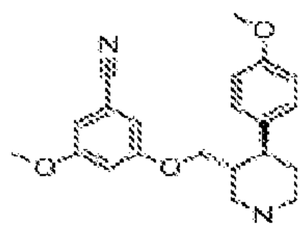
	B0369	trans-3-{[3-(1H-Imidazol-2-yl)phenoxy]methyl}-4-(4-methoxyphenyl)-1-propylpiperidine	405.53	406
	B0370	4-Methoxy-3-{[trans-4-(4-methoxyphenyl)piperidin-3-yl]methoxy}benzonitrile	352.43	353
	B0371	2-Fluoro-5-{[trans-4-(4-methoxyphenyl)piperidin-3-yl]methoxy}benzonitrile	340.39	341
	B0372	2-Fluoro-3-{[trans-4-(4-methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}benzonitrile	382.47	383
	B0373	N-(4-{[trans-4-(4-Methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}phenyl)acetamide	396.52	397
	B0374	6-{[trans-4-(4-Methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}isoindolin-1-one	394.51	395
	B0375	4-{[trans-4-(4-Methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}-N,N-dimethylbenzamide	410.55	411
	B0376	3-Methoxy-5-{[trans-4-(4-methoxyphenyl)piperidin-3-yl]methoxy}benzonitrile	352.43	353

Figure 1-Continued

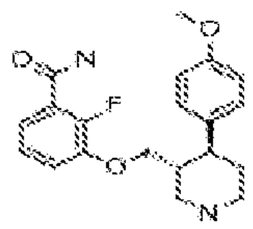
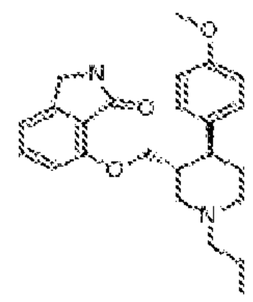
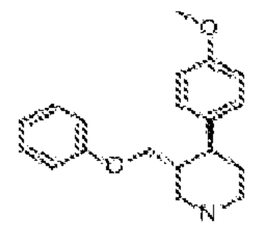
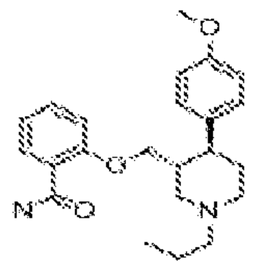
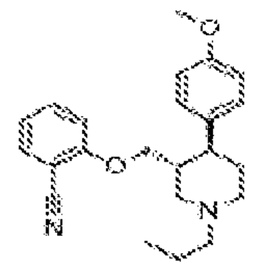
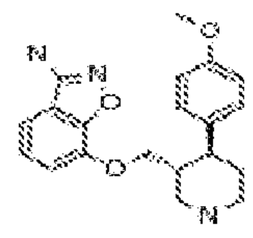
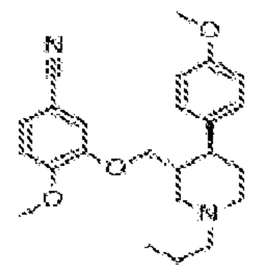
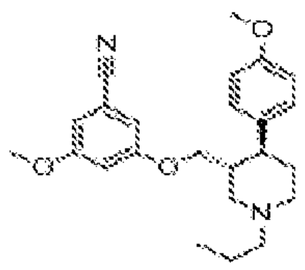
	B0377	2-Fluoro-3-{[trans-4-(4-methoxyphenyl)piperidin-3-yl]methoxy}benzamide	358.41	359
	B0378	7-{[trans-4-(4-Methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}isoindolin-1-one	394.51	395
	B0379	trans-4-(4-Methoxyphenyl)-3-(phenoxymethyl)piperidine	297.39	298
	B0380	2-{[trans-4-(4-Methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}benzamide	382.5	383
	B0381	2-{[trans-4-(4-Methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}benzonitrile	364.48	365
	B0382	7-{[trans-4-(4-Methoxyphenyl)piperidin-3-yl]methoxy}benzo[d]isoxazol-3-amine	353.41	354
	B0383	4-Methoxy-3-{[trans-4-(4-methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}benzonitrile	394.51	395
	B0384	3-Methoxy-5-{[trans-4-(4-methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}benzonitrile	394.51	395

Figure 1-Continued

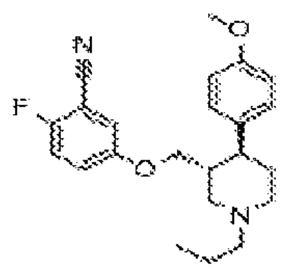
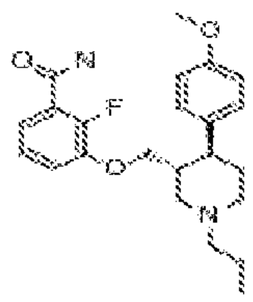
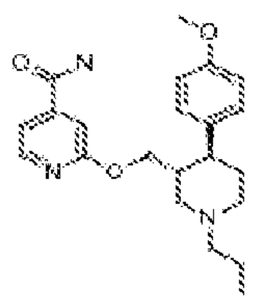
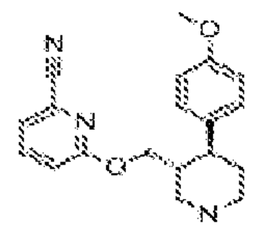
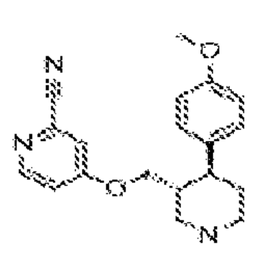
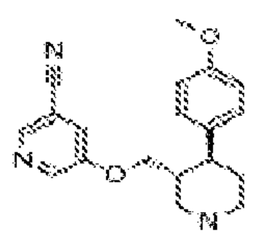
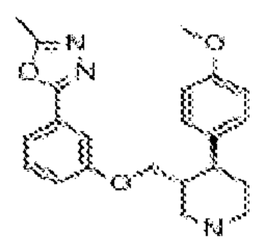
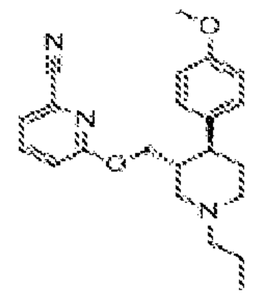
	B0385	2-Fluoro-5-{[trans-4-(4-methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}benzonitrile	382.47	383
	B0386	2-Fluoro-3-{[trans-4-(4-methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}benzamide	400.49	401
	B0387	2-{[trans-4-(4-Methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}isonicotinamide	383.48	384
	B0388	6-{[trans-4-(4-Methoxyphenyl)piperidin-3-yl]methoxy}picolinonitrile	323.39	324
	B0389	4-{[trans-4-(4-Methoxyphenyl)piperidin-3-yl]methoxy}picolinonitrile	323.39	324
	B0390	5-{[trans-4-(4-Methoxyphenyl)piperidin-3-yl]methoxy}nicotinonitrile	323.39	324
	B0391	2-(3-{[trans-4-(4-Methoxyphenyl)piperidin-3-yl]methoxy}phenyl)-5-methyl-1,3,4-oxadiazole	379.45	380
	B0392	6-{[trans-4-(4-Methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}picolinonitrile	365.47	366

Figure 1-Continued

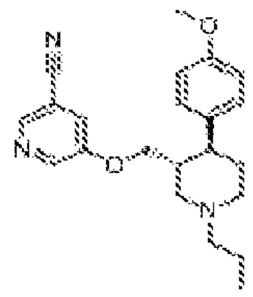
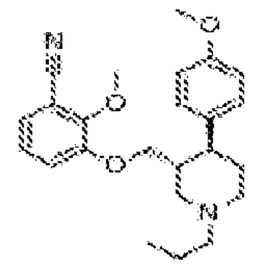
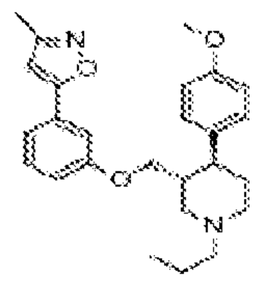
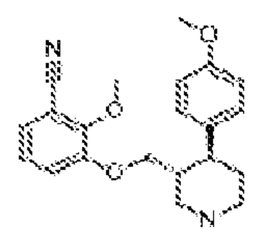
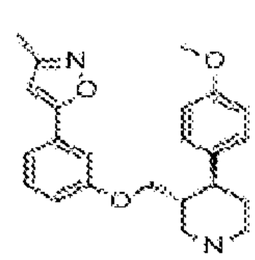
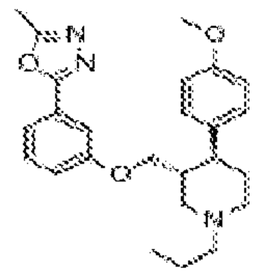
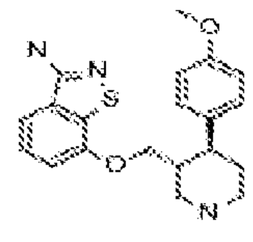
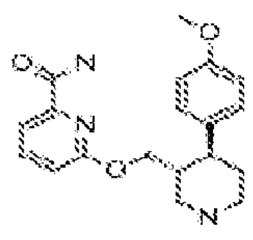
	B0393	5-{[trans-4-(4-Methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}nicotinonitrile	365.47	366
	B0394	2-methoxy-3-{[trans-4-(4-Methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}benzonitrile	394.51	395
	B0395	5-(3-{[trans-4-(4-Methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}phenyl)-3-methylisoxazole	420.54	421
	B0396	2-Methoxy-3-{[trans-4-(4-methoxyphenyl)piperidin-3-yl]methoxy}benzonitrile	352.43	353
	B0397	5-(3-{[trans-4-(4-Methoxyphenyl)piperidin-3-yl]methoxy}phenyl)-3-methylisoxazole	378.46	379
	B0398	2-(3-{[trans-4-(4-Methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}phenyl)-5-methyl-1,3,4-oxadiazole	421.53	422
	B0399	7-{[trans-4-(4-Methoxyphenyl)piperidin-3-yl]methoxy}benzo[d]isothiazol-3-amine	369.48	370
	B0400	6-{[trans-4-(4-Methoxyphenyl)piperidin-3-yl]methoxy}picolinamide	341.4	342

Figure 1-Continued

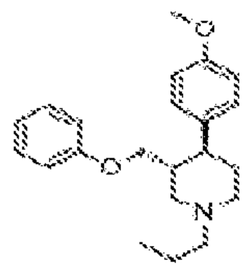
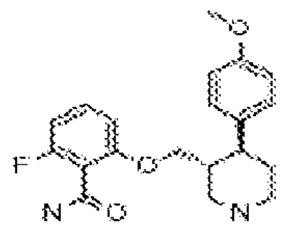
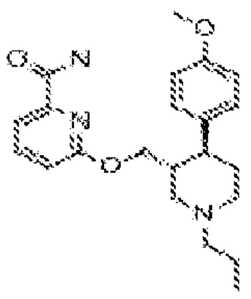
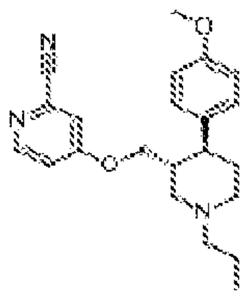
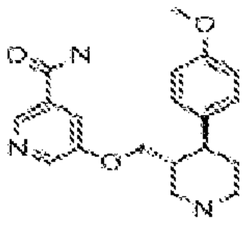
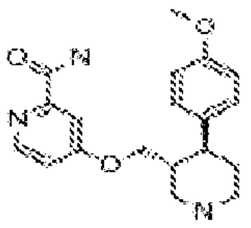
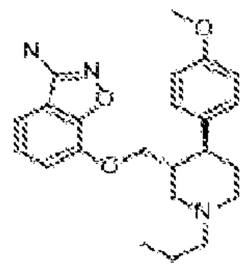
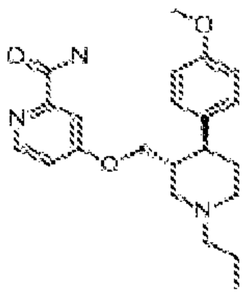
	B0401	trans-4-(4-Methoxyphenyl)-3-(phenoxymethyl)-1-propylpiperidine	339.47	440
	B0402	2-Fluoro-6-{[trans-4-(4-methoxyphenyl)piperidin-3-yl]methoxy}benzamide	358.41	359
	B0403	6-{[trans-4-(4-Methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}picolinamide	383.48	384
	B0404	4-{[trans-4-(4-Methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}picolinonitrile	365.47	366
	B0405	5-{[trans-4-(4-Methoxyphenyl)piperidin-3-yl]methoxy}nicotinamide	341.4	342
	B0406	4-{[trans-4-(4-Methoxyphenyl)piperidin-3-yl]methoxy}picolinamide	341.4	342
	B0407	7-{[trans-4-(4-Methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}benzo[d]isoxazol-3-amine	395.49	396
	B0408	4-{[trans-4-(4-Methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}picolinamide	383.48	384

Figure 1-Continued

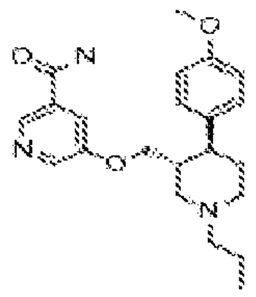
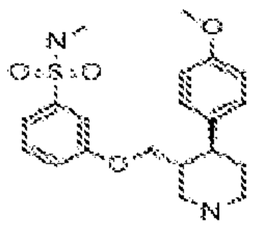
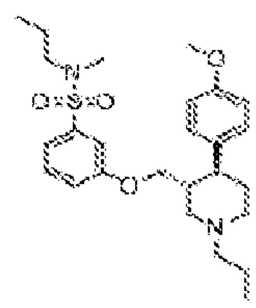
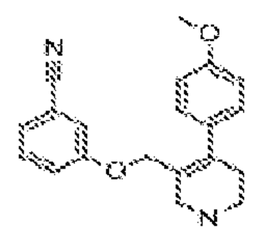
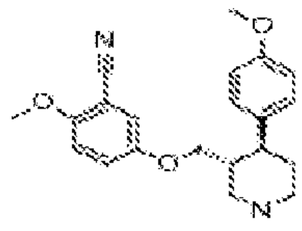
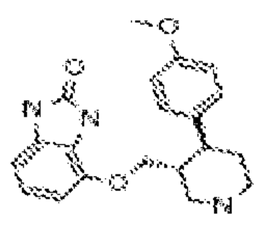
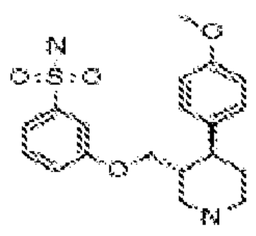
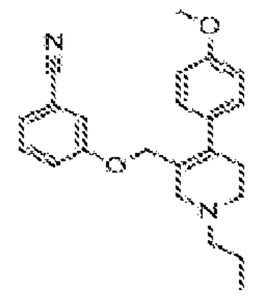
	B0409	5-{[trans-4-(4-Methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}nicotinamide	383.48	384
	B0410	3-{[trans-4-(4-Methoxyphenyl)piperidin-3-yl]methoxy}-N-methylbenzenesulfonamide	390.5	391
	B0411	3-{[trans-4-(4-Methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}-N-methyl-N-propylbenzenesulfonamide	474.66	475
	B0412	3-{[4-(4-Methoxyphenyl)-1,2,5,6-tetrahydropyridin-3-yl]methoxy}benzonitrile	320.39	321
	B0413	2-Methoxy-5-{[trans-4-(4-methoxyphenyl)piperidin-3-yl]methoxy}benzonitrile	352.43	353
	B0414	4-{[trans-4-(4-Methoxyphenyl)piperidin-3-yl]methoxy}-1H-benzo[d]imidazol-2(3H)-one	353.41	354
	B0415	3-{[trans-4-(4-Methoxyphenyl)piperidin-3-yl]methoxy}benzenesulfonamide	376.47	377
	B0416	3-{[4-(4-Methoxyphenyl)-1-propyl-1,2,5,6-tetrahydropyridin-3-yl]methoxy}benzonitrile	362.46	363

Figure 1-Continued

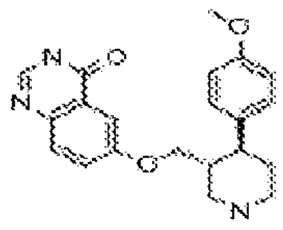
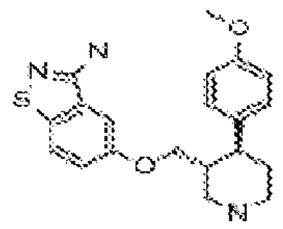
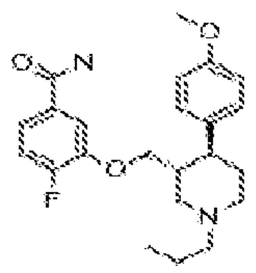
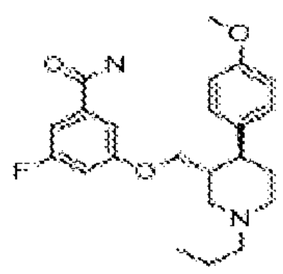
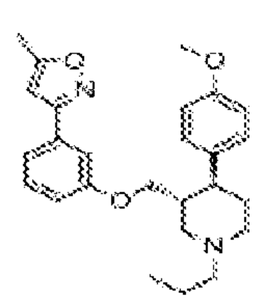
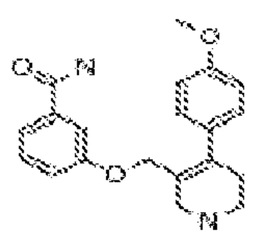
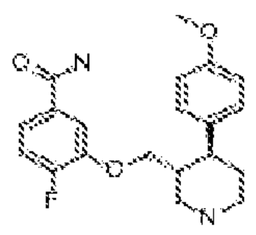
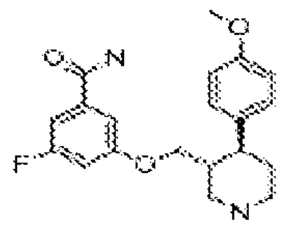
	B0417	6-{[trans-4-(4-Methoxyphenyl)piperidin-3-yl]methoxy}quinazolin-4(3H)-one	365.43	366
	B0418	5-{[trans-4-(4-Methoxyphenyl)piperidin-3-yl]methoxy}benzo[d]isothiazol-3-amine	369.48	370
	B0419	4-Fluoro-3-{[trans-4-(4-methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}benzamide	400.49	401
	B0420	3-Fluoro-5-{[trans-4-(4-methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}benzamide	400.49	401
	B0421	3-(3-{[trans-4-(4-Methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}phenyl)-5-methylisoxazole	420.54	421
	B0422	3-{[4-(4-Methoxyphenyl)-1,2,5,6-tetrahydropyridin-3-yl]methoxy}benzamide	338.4	339
	B0423	4-Fluoro-3-{[trans-4-(4-methoxyphenyl)piperidin-3-yl]methoxy}benzamide	358.41	359
	B0424	3-fluoro-5-{[(trans)-4-(4-methoxyphenyl)piperidin-3-yl]methoxy}benzamide	358.41	359

Figure 1-Continued

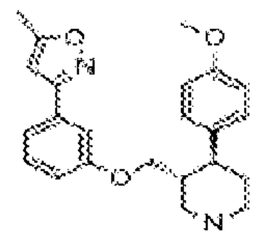
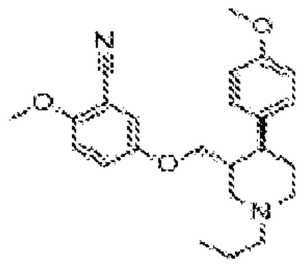
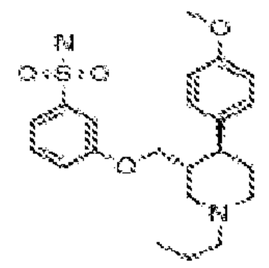
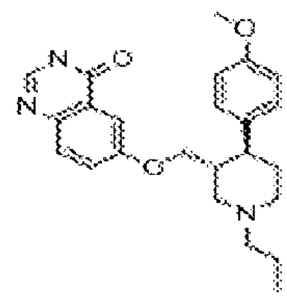
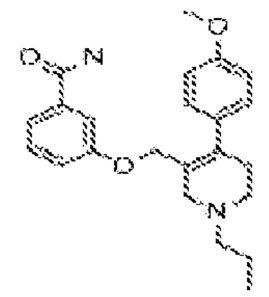
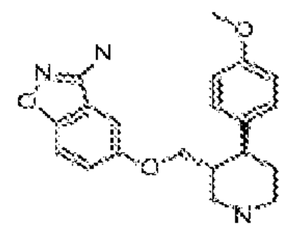
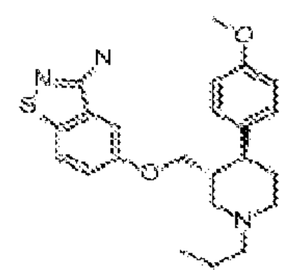
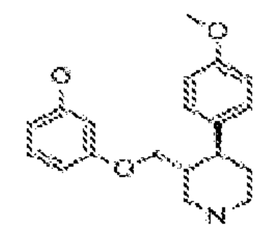
	B0425	3-(3-{[trans-4-(4-Methoxyphenyl)piperidin-3-yl]methoxy}phenyl)-5-methylisoxazole	378.46	379
	B0426	2-methoxy-5-{[(trans)-4-(4-methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}benzonitrile	394.51	395
	B0427	3-{[trans-4-(4-Methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}benzenesulfonamide	418.55	419
	B0428	6-{[trans-4-(4-Methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}quinazolin-4(3H)-one	407.51	408
	B0429	3-{[4-(4-Methoxyphenyl)-1-propyl-1,2,5,6-tetrahydropyridin-3-yl]methoxy}benzamide	380.48	381
	B0430	5-{[trans-4-(4-Methoxyphenyl)piperidin-3-yl]methoxy}benzo[d]isoxazol-3-amine	353.41	354
	B0431	5-{[trans-4-(4-Methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}benzo[d]isothiazol-3-amine	411.56	412
	B0432	3-{[trans-4-(4-Methoxyphenyl)piperidin-3-yl]methoxy}phenol	313.39	314

Figure 1-Continued

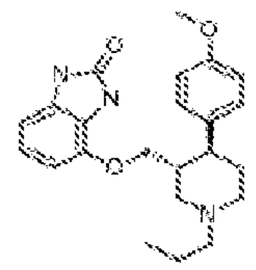
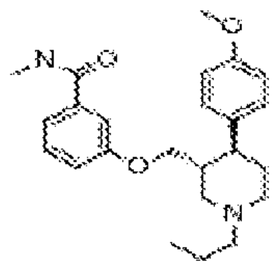
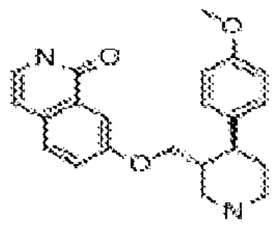
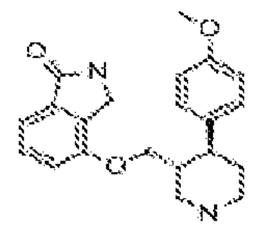
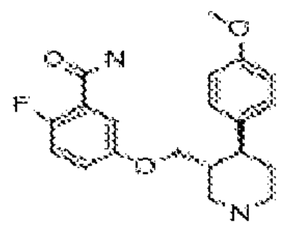
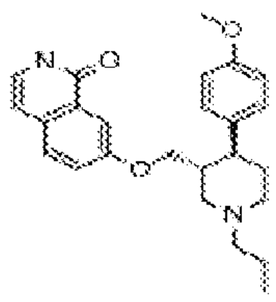
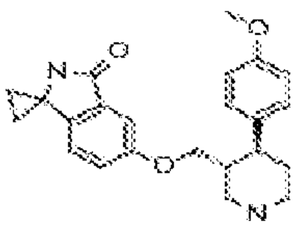
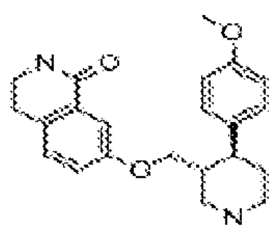
	B0433	4-{[trans-4-(4-Methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}-1H-benzo[d]imidazol-2(3H)-one	395.49	396
	B0434	3-{[trans-4-(4-Methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}-N-methylbenzamide	396.52	397
	B0435	7-{[trans-4-(4-Methoxyphenyl)piperidin-3-yl]methoxy}isoquinolin-1(2H)-one	364.44	365
	B0436	4-{[trans-4-(4-Methoxyphenyl)piperidin-3-yl]methoxy}isoindolin-1-one	352.43	353
	B0437	2-Fluoro-5-{[trans-4-(4-methoxyphenyl)piperidin-3-yl]methoxy}benzamide	358.41	359
	B0438	7-{[trans-4-(4-Methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}isoquinolin-1(2H)-one	406.52	407
	B0439	5'-{[trans-4-(4-Methoxyphenyl)piperidin-3-yl]methoxy}spiro[cyclopropane-1,1'-isoindolin]-3'-one	378.46	379
	B0440	7-{[(trans)-4-(4-methoxyphenyl)piperidin-3-yl]methoxy}-1,2,3,4-tetrahydroisoquinolin-1-one	366.45	367

Figure 1-Continued

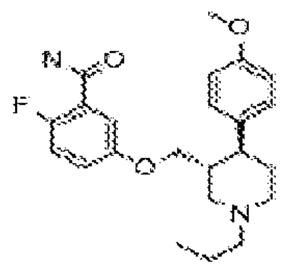
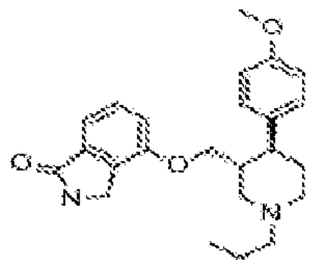
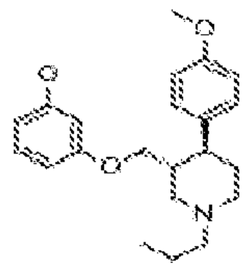
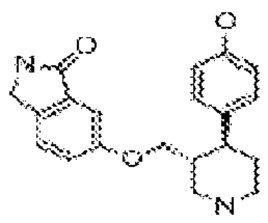
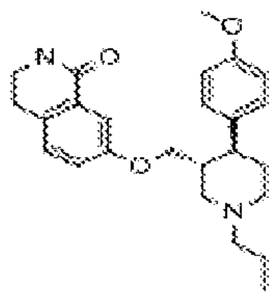
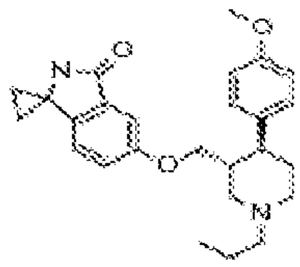
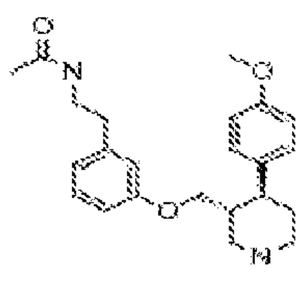
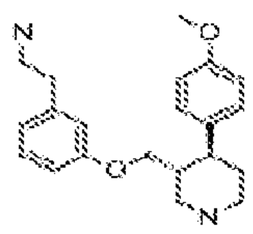
	B0441	2-Fluoro-5-{[trans-4-(4-methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}benzamide	400.49	401
	B0442	4-{[trans-4-(4-Methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}isoindolin-1-one	394.51	395
	B0443	3-{[trans-4-(4-Methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}phenol	355.47	356
	B0444	6-{[trans-4-(4-Hydroxyphenyl)piperidin-3-yl]methoxy}isoindolin-1-one	338.4	339
	B0445	7-{[trans-4-(4-Methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}-3,4-dihydroisoquinolin-1(2H)-one	408.53	409
	B0446	5'-{[trans-4-(4-Methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}spiro[cyclopropane-1,1'-isoindolin]-3'-one	420.54	421
	B0447	N-(3-{[trans-4-(4-Methoxyphenyl)piperidin-3-yl]methoxy}phenethyl)acetamide	382.5	383
	B0448	2-(3-{[trans-4-(4-Methoxyphenyl)piperidin-3-yl]methoxy}phenyl)ethanamine	340.46	341

Figure 1-Continued

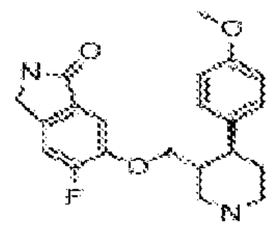
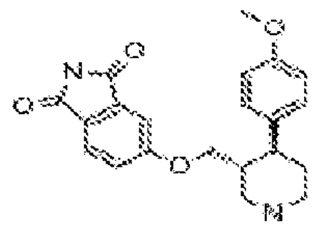
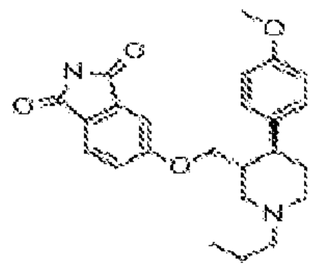
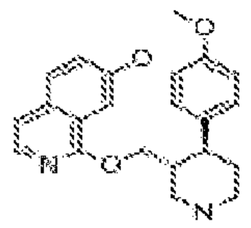
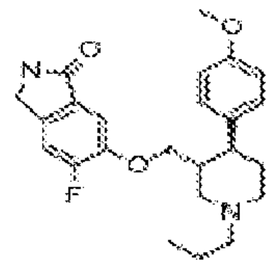
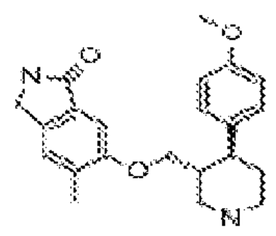
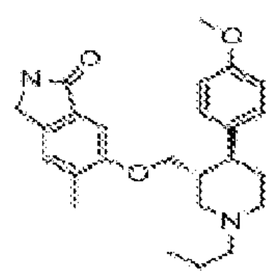
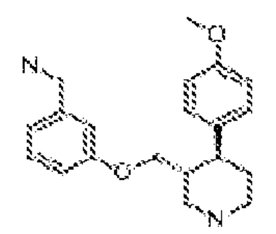
	B0449	5-Fluoro-6-{[trans-4-(4-methoxyphenyl)piperidin-3-yl]methoxy}isoindolin-1-one	370.42	371
	B0450	5-{[trans-4-(4-Methoxyphenyl)piperidin-3-yl]methoxy}isoindoline-1,3-dione	366.41	367
	B0451	5-{[trans-4-(4-Methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}isoindoline-1,3-dione	408.49	409
	B0452	1-{[(trans)-4-(4-methoxyphenyl)piperidin-3-yl]methoxy}isoquinolin-7-ol	364.44	365
	B0453	5-Fluoro-6-{[trans-4-(4-methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}isoindolin-1-one	412.5	413
	B0454	6-{[trans-4-(4-Methoxyphenyl)piperidin-3-yl]methoxy}-5-methylisoindolin-1-one	366.45	367
	B0455	6-{[trans-4-(4-Methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}-5-methylisoindolin-1-one	408.53	409
	B0456	(3-{[trans-4-(4-Methoxyphenyl)piperidin-3-yl)methoxy]phenyl}methanamine	326.43	327

Figure 1-Continued

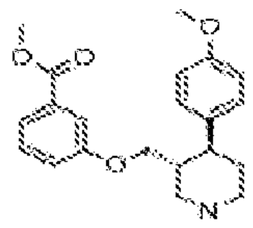
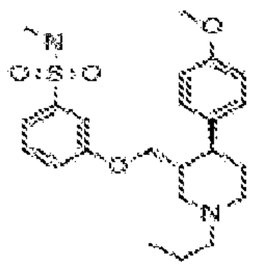
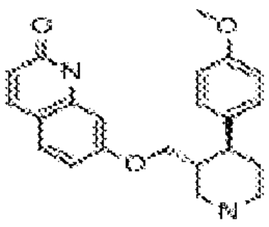
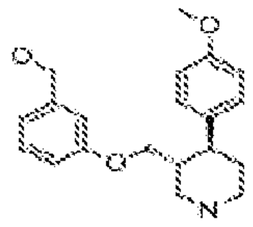
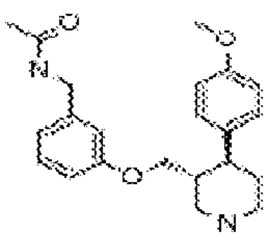
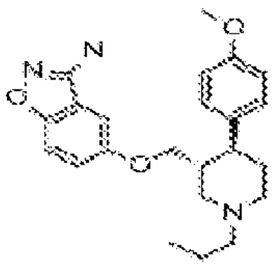
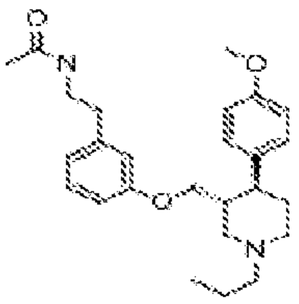
	B0457	Methyl 3-{[trans-4-(4-Methoxyphenyl)piperidin-3-yl]methoxy}benzoate	355.43	356
	B0458	3-{[trans-4-(4-Methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}-N-methylbenzenesulfonamide	432.58	433
	B0459	7-{[trans-4-(4-Methoxyphenyl)piperidin-3-yl]methoxy}quinolin-2(1H)-one	364.44	365
	B0460	(3-{[trans-4-(4-Methoxyphenyl)piperidin-3-yl)methoxy]phenyl}methanol	327.42	328
	B0461	Methyl 3-{[trans-4-(4-Methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}benzoate	397.51	398
	B0462	N-(3-{[trans-4-(4-Methoxyphenyl)piperidin-3-yl]methoxy}benzyl)acetamide	368.47	369
	B0463	5-{[trans-4-(4-Methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}benzo[d]isoxazol-3-amine	395.49	396
	B0464	N-(3-{[trans-4-(4-Methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}phenethyl)acetamide	424.58	425

Figure 1-Continued

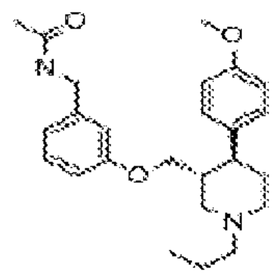
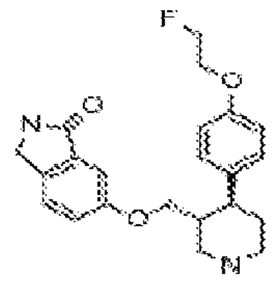
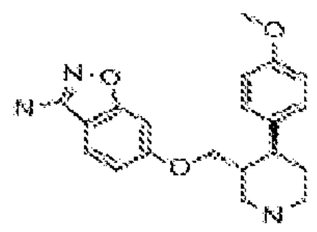
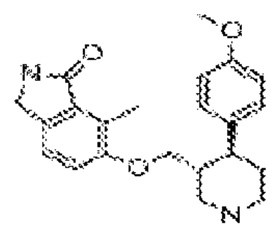
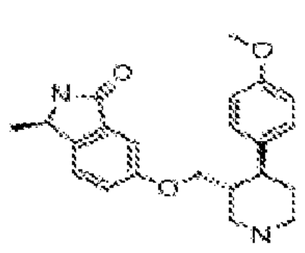
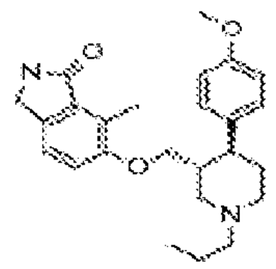
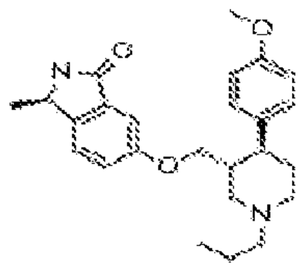
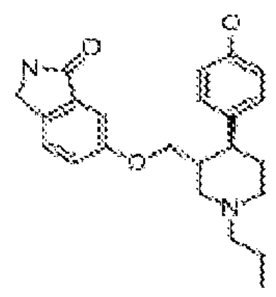
	B0465	N-(3-{[trans-4-(4-Methoxyphenyl)-1-propylpiperidin-3-yl)methoxy]benzyl}acetamide	410.55	411
	B0466	6-{[trans-4-[4-(2-Fluoroethoxy)phenyl]piperidin-3-yl]methoxy}isoindolin-1-one	384.44	385
	B0467	6-{[trans-4-(4-Methoxyphenyl)piperidin-3-yl]methoxy}benzo[d]isoxazol-3-amine	353.41	354
	B0468	6-{[trans-4-(4-Methoxyphenyl)piperidin-3-yl]methoxy}-7-methylisoindolin-1-one	366.45	367
	B0469	6-{[trans-4-(4-Methoxyphenyl)piperidin-3-yl]methoxy}-3-methylisoindolin-1-one	366.45	367
	B0470	6-{[trans-4-(4-Methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}-7-methylisoindolin-1-one	408.53	409
	B0471	6-{[trans-4-(4-Methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}-3-methylisoindolin-1-one	408.53	409
	B0472	6-{[trans-4-(4-Hydroxyphenyl)-1-propylpiperidin-3-yl]methoxy}isoindolin-1-one	380.48	381

Figure 1-Continued

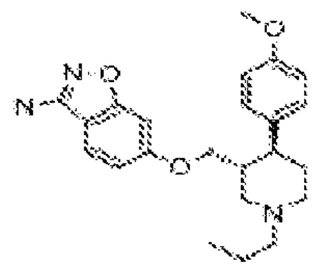
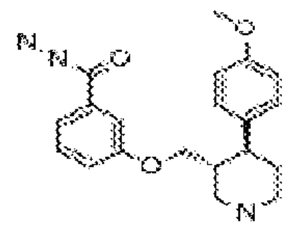
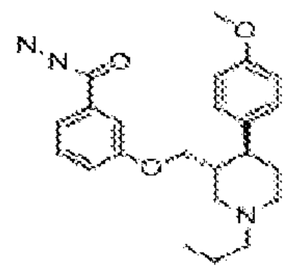
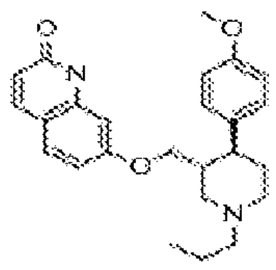
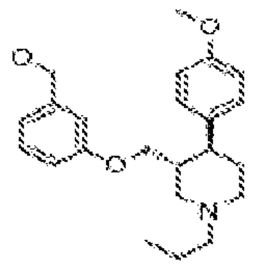
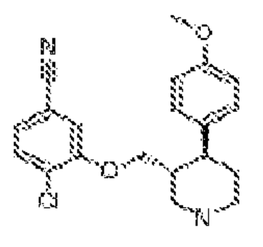
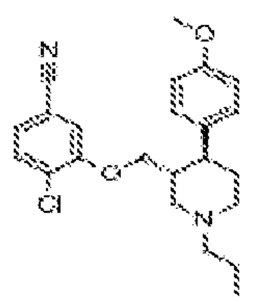
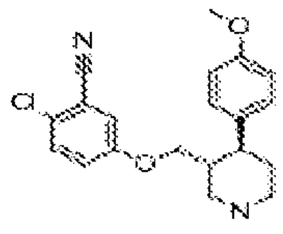
	B0473	6-{[trans-4-(4-Methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}benzo[d]isoxazol-3-amine	395.49	396
	B0474	3-{[trans-4-(4-Methoxyphenyl)piperidin-3-yl]methoxy}benzohydrazide	355.43	356
	B0475	3-{[trans-4-(4-Methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}benzohydrazide	397.51	398
	B0476	7-{[trans-4-(4-Methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}quinolin-2(1H)-one	406.52	407
	B0477	(3-{[trans-4-(4-Methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}phenyl)methanol	369.5	370
	B0478	4-Chloro-3-{[trans-4-(4-methoxyphenyl)piperidin-3-yl]methoxy}benzonitrile	356.85	357
	B0479	4-Chloro-3-{[trans-4-(4-methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}benzonitrile	398.93	399
	B0480	2-Chloro-5-{[trans-4-(4-methoxyphenyl)piperidin-3-yl]methoxy}benzonitrile	356.85	357

Figure 1-Continued

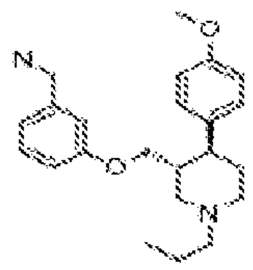
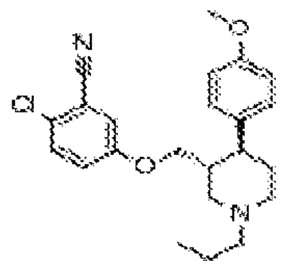
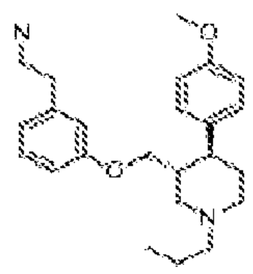
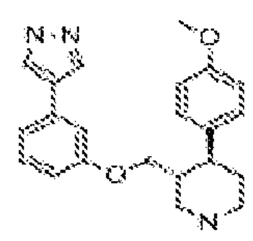
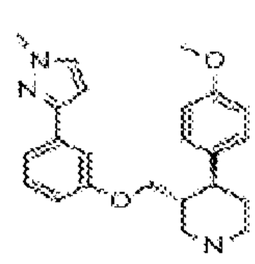
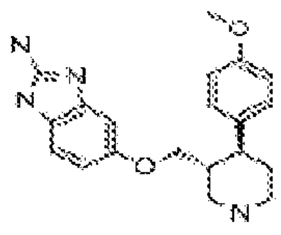
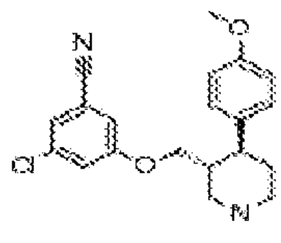
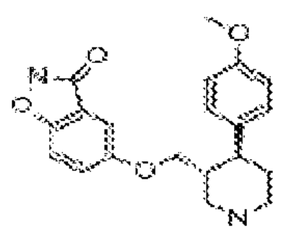
	B0481	(3-{[trans-4-(4-Methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}phenyl)methanamine	368.51	369
	B0482	2-Chloro-5-{[trans-4-(4-methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}benzonitrile	398.93	399
	B0483	2-(3-{[trans-4-(4-Methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}phenyl)ethanamine	382.54	383
	B0484	trans-3-{[3-(1H-Pyrazol-4-yl)phenoxy]methyl}-4-(4-methoxyphenyl)piperidine	363.45	364
	B0485	trans-4-(4-Methoxyphenyl)-3-{[3-(1-methyl-1H-pyrazol-3-yl)phenoxy]methyl}piperidine	377.48	378
	B0486	5-{[trans-4-(4-Methoxyphenyl)piperidin-3-yl]methoxy}-1H-benzo[d]imidazol-2-amine	352.43	353
	B0487	3-Chloro-5-{[trans-4-(4-methoxyphenyl)piperidin-3-yl]methoxy}benzonitrile	356.85	357
	B0488	5-{[trans-4-(4-Methoxyphenyl)piperidin-3-yl]methoxy}benzo[d]isoxazol-3(2H)-one	354.4	355

Figure 1-Continued

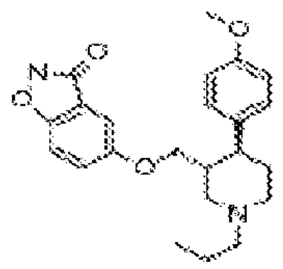
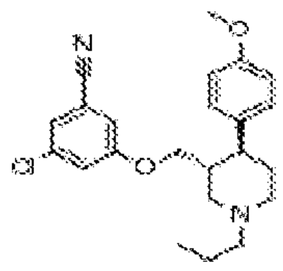
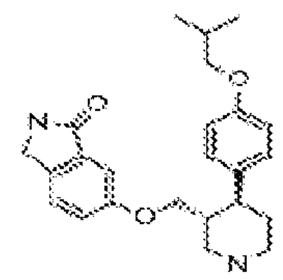
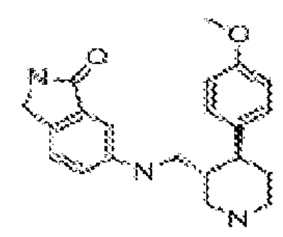
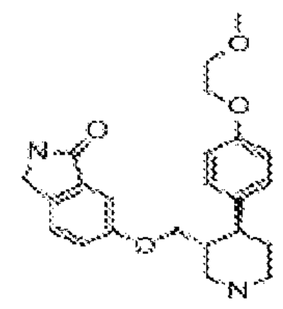
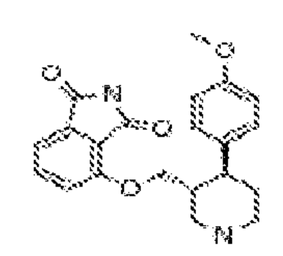
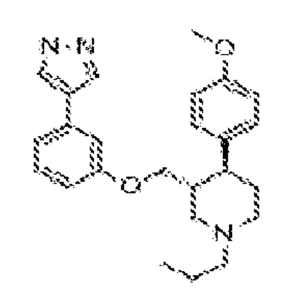
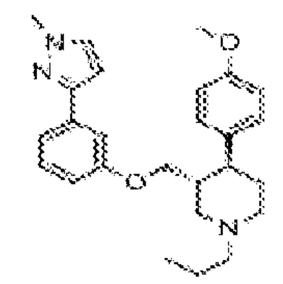
	B0489	5-{[trans-4-(4-Methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}benzo[d]isoxazol-3(2H)-one	396.48	397
	B0490	3-Chloro-5-{[trans-4-(4-methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}benzonitrile	398.93	399
	B0491	6-{[trans-4-(4-Isobutoxyphenyl)piperidin-3-yl]methoxy}isoindolin-1-one	394.51	395
	B0492	6-{[trans-4-(4-Methoxyphenyl)piperidin-3-yl)methyl]amino}isoindolin-1-one	351.44	352
	B0493	6-{[trans-4-[4-(2-Methoxyethoxy)phenyl]piperidin-3-yl]methoxy}isoindolin-1-one	396.48	397
	B0494	4-{[trans-4-(4-Methoxyphenyl)piperidin-3-yl]methoxy}isoindoline-1,3-dione	366.41	367
	B0495	trans-3-{[3-(1H-Pyrazol-4-yl)phenoxy]methyl}-4-(4-methoxyphenyl)-1-propylpiperidine	405.53	406
	B0496	trans-4-(4-Methoxyphenyl)-3-{[3-(1-methyl-1H-pyrazol-3-yl)phenoxy]methyl}-1-propylpiperidine	419.56	420

Figure 1-Continued

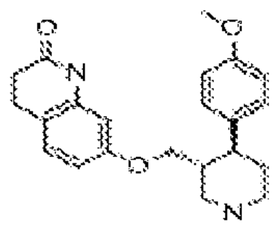
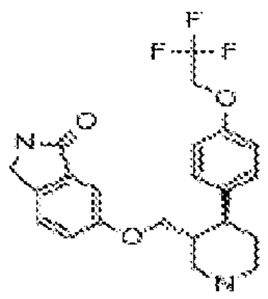
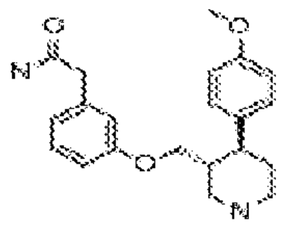
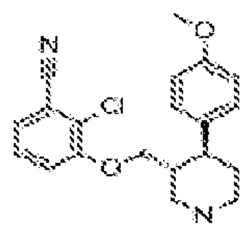
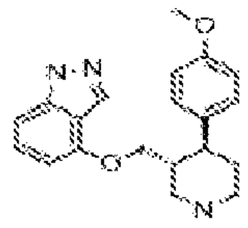
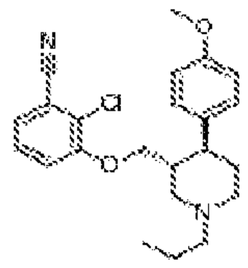
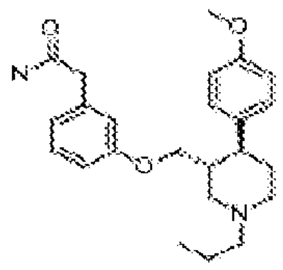
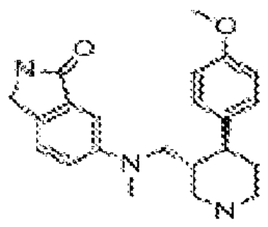
	B0497	7-{[trans-4-(4-Methoxyphenyl)piperidin-3-yl]methoxy}-3,4-dihydroquinolin-2(1H)-one	366.45	367
	B0498	6-{[trans-4-[4-(2,2,2-Trifluoroethoxy)phenyl]piperidin-3-yl]methoxy}isoindolin-1-one	420.42	421
	B0499	2-(3-{[trans-4-(4-Methoxyphenyl)piperidin-3-yl]methoxy}phenyl)acetamide	354.44	355
	B0500	2-Chloro-3-{[trans-4-(4-methoxyphenyl)piperidin-3-yl]methoxy}benzonitrile	356.85	357
	B0501	4-{[trans-4-(4-Methoxyphenyl)piperidin-3-yl]methoxy}-1H-indazole	337.42	338
	B0502	2-Chloro-3-{[trans-4-(4-methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}benzonitrile	398.93	399
	B0503	2-(3-{[trans-4-(4-Methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}phenyl)acetamide	396.52	397
	B0504	6-{[(trans-4-(4-Methoxyphenyl)piperidin-3-yl)methyl](methyl)-amino}isoindolin-1-one	365.47	366

Figure 1-Continued

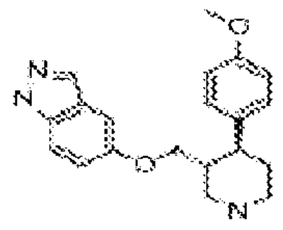
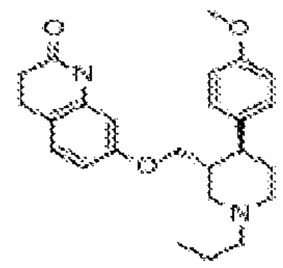
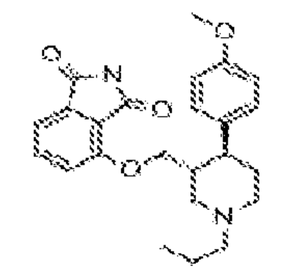
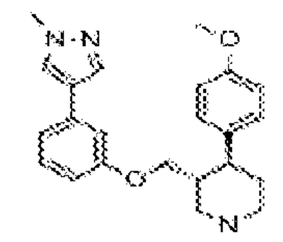
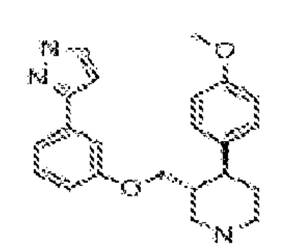
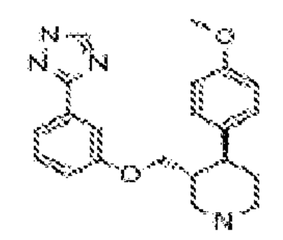
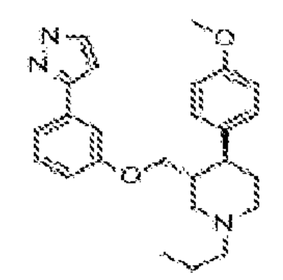
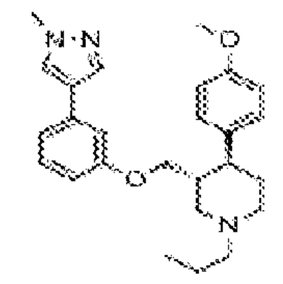
	B0505	5-{[trans-4-(4-Methoxyphenyl)piperidin-3-yl]methoxy}-1H-indazole	337.42	338
	B0506	7-{[trans-4-(4-Methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}-3,4-dihydroquinolin-2(1H)-one	408.53	409
	B0507	4-{[trans-4-(4-Methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}isoindoline-1,3-dione	408.49	409
	B0508	trans-4-(4-Methoxyphenyl)-3-{[3-(1-methyl-1H-pyrazol-4-yl)phenoxy]methyl}piperidine	377.48	378
	B0509	trans-3-{[3-(1H-Pyrazol-3-yl)phenoxy]methyl}-4-(4-methoxyphenyl)piperidine	363.45	364
	B0510	trans-3-{[3-(1H-1,2,4-Triazol-3-yl)phenoxy]methyl}-4-(4-methoxyphenyl)piperidine	364.44	365
	B0511	trans-3-{[3-(1H-Pyrazol-3-yl)phenoxy]methyl}-4-(4-methoxyphenyl)-1-propylpiperidine	405.53	406
	B0512	trans-4-(4-Methoxyphenyl)-3-{[3-(1-methyl-1H-pyrazol-4-yl)phenoxy]methyl}-1-propylpiperidine	419.56	420

Figure 1-Continued

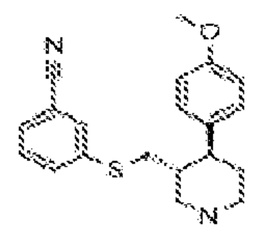
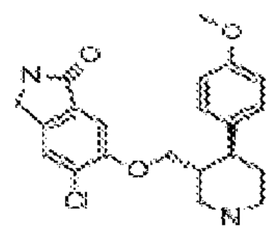
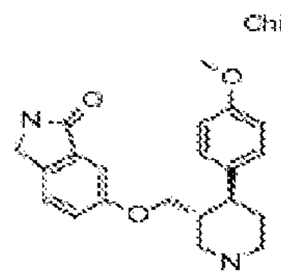
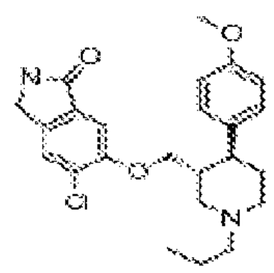
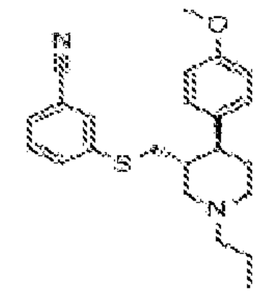
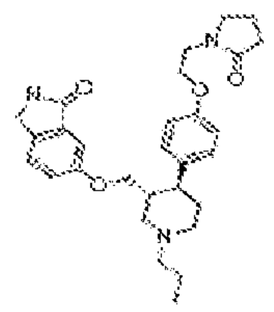
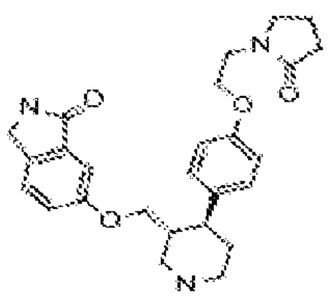
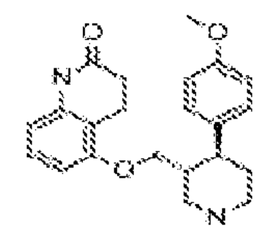
	B0513	3-({[trans-4-(4-Methoxyphenyl)piperidin-3-yl]methyl}thio)benzonitrile	338.47	339
	B0514	5-Chloro-6-{[trans-4-(4-methoxyphenyl)piperidin-3-yl]methoxy}isoindolin-1-one	386.87	387
Chiral 	B0515	(-)-6-{[(trans)-4-(4-methoxyphenyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	352.43	353
	B0516	5-Chloro-6-{[trans-4-(4-methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}isoindolin-1-one	428.95	429
	B0517	6-({[trans-4-(4-Methoxyphenyl)-1-propylpiperidin-3-yl]methyl}thio)isoindolin-1-one	380.55	381
	B0518	6-{[trans-4-(4-(2-(2-Oxopyrrolidin-1-yl)ethoxy]phenyl}-1-propylpiperidin-3-yl)methoxy)isoindolin-1-one	491.62	492
	B0519	6-{[trans-4-{4-[2-(2-Oxopyrrolidin-1-yl)ethoxy]phenyl}piperidin-3-yl]methoxy}isoindolin-1-one	449.54	450
	B0520	5-{[trans-4-(4-Methoxyphenyl)piperidin-3-yl)]ethoxy}-3,4-dihydroquinolin-2(1H)-one	366.45	367

Figure 1-Continued

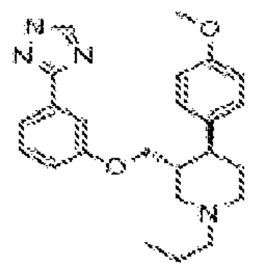
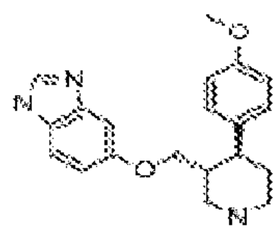
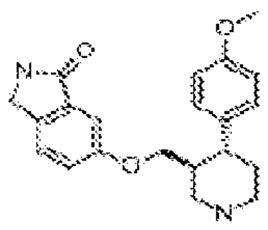
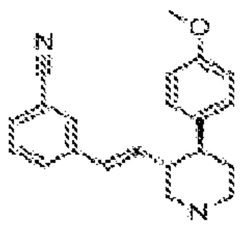
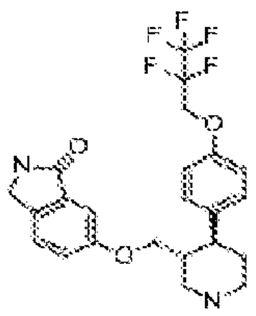
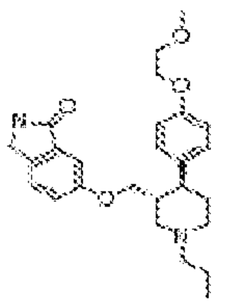
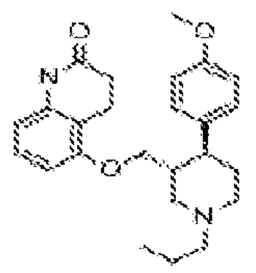
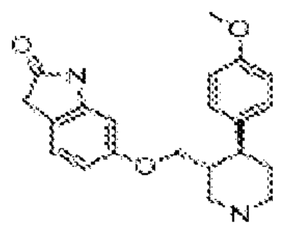
	B0521	trans-3-{[3-(1H-1,2,4-Triazol-3-yl)phenoxy]methyl}-4-(4-methoxyphenyl)-1-propylpiperidine	406.52	407
	B0522	5-{[trans-4-(4-Methoxyphenyl)piperidin-3-yl]methoxy}-1H-benzo[d]imidazole	337.42	338
Chiral 	B0523	(–)-6-{[trans-4-(4-Methoxyphenyl)piperidin-3-yl]methoxy}isoindolin-1-one	352.43	353
	B0524	3-{(E)-2-[trans-4-(4-Methoxyphenyl)piperidin-3-yl]vinyl}benzonitrile	318.41	319
	B0525	6-{[trans-4-[4-(2,2,3,3,3-Pentafluoropropoxy)phenyl]piperidin-3-yl]methoxy}isoindolin-1-one	470.43	471
	B0526	6-{[trans-4-[4-(2-Methoxyethoxy)phenyl]-1-propylpiperidin-3-yl]methoxy}isoindolin-1-one	438.56	439
	B0527	5-{[trans-4-(4-Methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}-3,4-dihydroquinolin-2(1H)-one	408.53	409
	B0528	6-{[trans-4-(4-Methoxyphenyl)piperidin-3-yl]methoxy}indolin-2-one	352.43	353

Figure 1-Continued

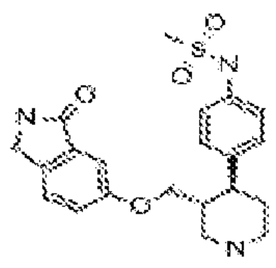
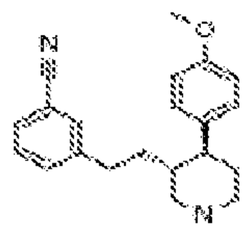
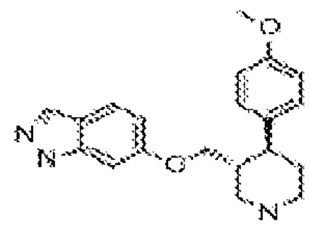
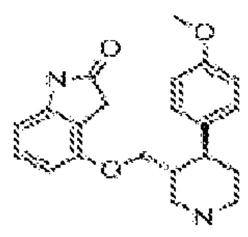
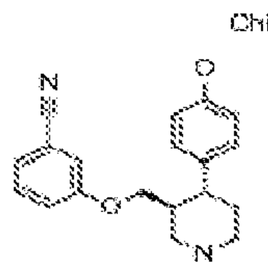
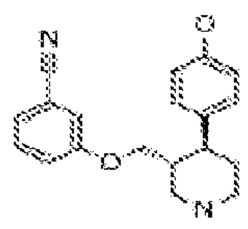
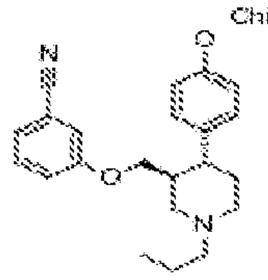
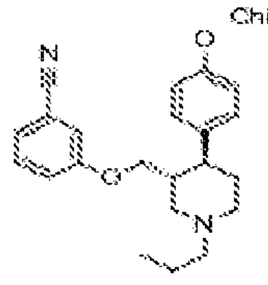
	B0529	N-{4-[trans-3-{[(3-Oxoisoindolin-5-yl)oxy]methyl}piperidin-4-yl]phenyl}methanesulfonamide	415.51	416
	B0530	3-{2-[trans-4-(4-Methoxyphenyl)piperidin-3-yl]ethyl}benzonitrile	320.43	321
	B0531	6-{[trans-4-(4-Methoxyphenyl)piperidin-3-yl]methoxy}-1H-indazole	337.42	338
	B0532	4-{[trans-4-(4-Methoxyphenyl)piperidin-3-yl]methoxy}indolin-2-one	352.43	353
Chiral 	B0533	(–)-3-{[trans-4-(4-Hydroxyphenyl)piperidin-3-yl]methoxy}benzonitrile	308.37	309
Chiral 	B0534	(+)-3-{[trans-4-(4-Hydroxyphenyl)piperidin-3-yl]methoxy}benzonitrile	308.37	309
Chiral 	B0535	(–)-3-{[trans-4-(4-Hydroxyphenyl)-1-propylpiperidin-3-yl]methoxy}benzonitrile	350.45	351
Chiral 	B0536	(+)-3-{[trans-4-(4-Hydroxyphenyl)-1-propylpiperidin-3-yl]methoxy}benzonitrile	350.45	351

Figure 1-Continued

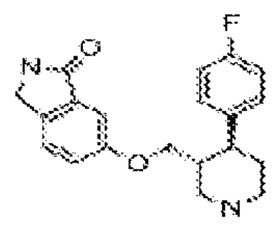
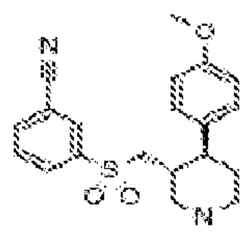
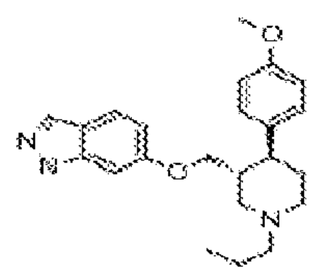
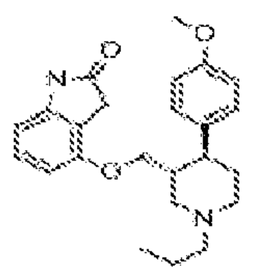
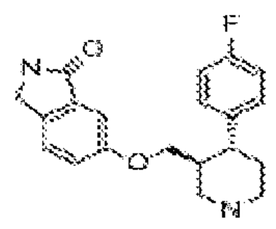
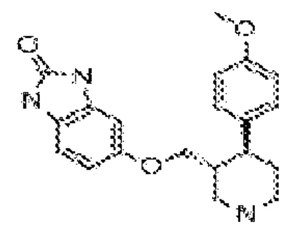
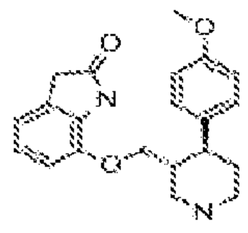
	B0537	6-{[trans-4-(4-Fluorophenyl)piperidin-3-yl]methoxy}isoindolin-1-one	340.39	341
	B0538	3-({[trans-4-(4-Methoxyphenyl)piperidin-3-yl]methyl}sulfonyl)-benzonitrile	370.47	371
	B0539	6-{[trans-4-(4-Methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}-1H-indazole	379.5	380
	B0540	4-{[trans-4-(4-Methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}indolin-2-one	394.51	395
	B0541	2-(4-{[trans-4-(4-Methoxyphenyl)piperidin-3-yl]methoxy}phenyl)acetamide	354.44	355
Chiral 	B0542	(–)-6-{[trans-4-(4-Fluorophenyl)piperidin-3-yl]methoxy}isoindolin-1-one	340.39	341
	B0543	5-{[trans-4-(4-Methoxyphenyl)piperidin-3-yl]methoxy}-1H-benzo[d]imidazol-2(3H)-one	353.41	354
	B0544	7-{[trans-4-(4-Methoxyphenyl)piperidin-3-yl]methoxy}indolin-2-one	352.43	353

Figure 1-Continued

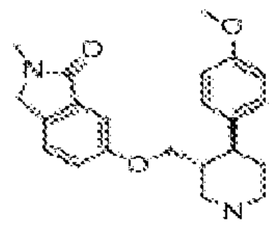
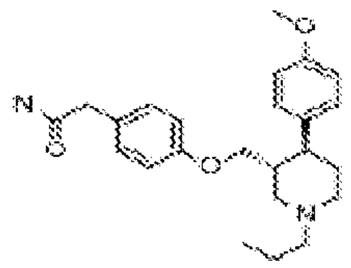
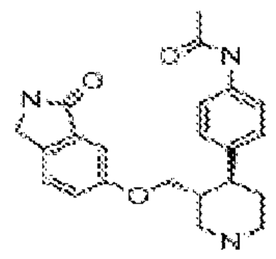
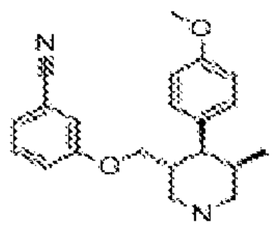
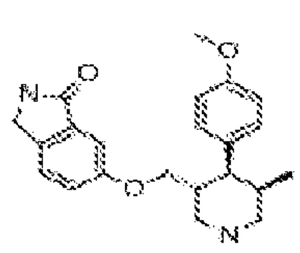
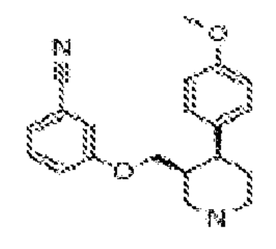
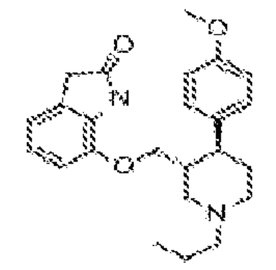
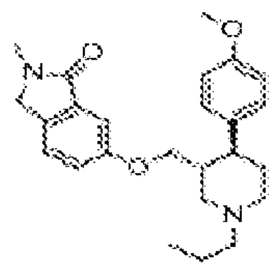
	B0545	6-{[trans-4-(4-Methoxyphenyl)piperidin-3-yl]methoxy}-2-methylisoindolin-1-one	366.45	367
	B0546	2-(4-{[trans-4-(4-Methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}phenyl)acetamide	396.52	397
	B0547	N-{4-[trans-3-{[(3-Oxoisoindolin-5-yl)oxy]methyl}piperidin-4-yl]phenyl}acetamide	379.45	380
	B0548	3-{[trans,cis-4-(4-Methoxyphenyl)-5-methylpiperidin-3-yl]methoxy}benzonitrile	336.43	337
	B0549	6-{[trans,cis-4-(4-Methoxyphenyl)-5-methylpiperidin-3-yl]methoxy}isoindolin-1-one	366.45	367
	B0550	3-{[cis-4-(4-Methoxyphenyl)piperidin-3-yl]methoxy}benzonitrile	322.4	323
	B0551	7-{[trans-4-(4-Methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}indolin-2-one	394.51	395
	B0552	6-{[trans-4-(4-Methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}-2-methylisoindolin-1-one	408.53	409

Figure 1-Continued

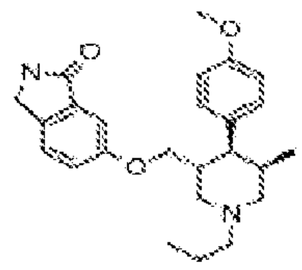
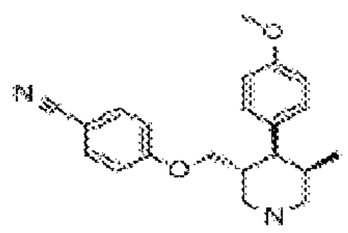
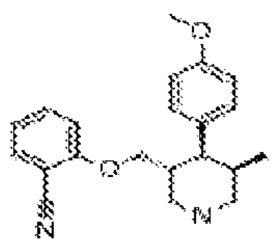
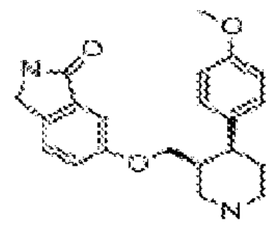
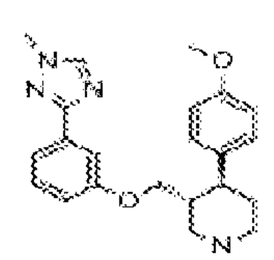
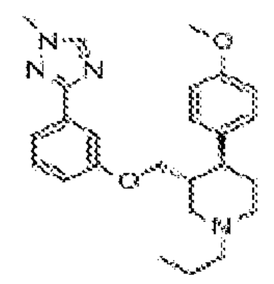
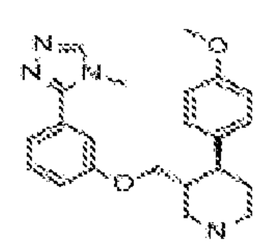
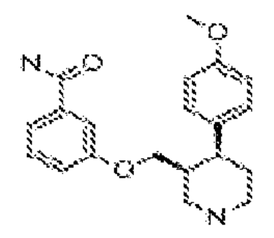
	B0553	6-{[trans,cis-4-(4-Methoxyphenyl)-5-methyl-1-propylpiperidin-3-yl]methoxy}isoindolin-1-one	408.53	409
	B0554	4-{[trans,cis-4-(4-Methoxyphenyl)-5-methylpiperidin-3-yl]methoxy}benzonitrile	336.43	337
	B0555	2-{[trans,cis-4-(4-Methoxyphenyl)-5-methylpiperidin-3-yl]methoxy}benzonitrile	336.43	337
	B0556	6-{[cis-4-(4-Methoxyphenyl)piperidin-3-yl]methoxy}isoindolin-1-one	352.43	353
	B0557	trans-4-(4-Methoxyphenyl)-3-{[3-(1-methyl-1H-1,2,4-triazol-3-yl)phenoxy]methyl}piperidine	378.47	379
	B0558	trans-4-(4-Methoxyphenyl)-3-{[3-(1-methyl-1H-1,2,4-triazol-3-yl)phenoxy]methyl}-1-propylpiperidine	420.55	421
	B0559	trans-4-(4-Methoxyphenyl)-3-{[3-(4-methyl-4H-1,2,4-triazol-3-yl)phenoxy]methyl}piperidine	378.47	379
	B0560	3-{[cis-4-(4-Methoxyphenyl)piperidin-3-yl]methoxy}benzamide	340.42	341

Figure 1-Continued

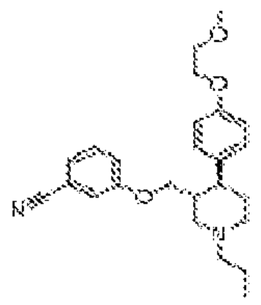
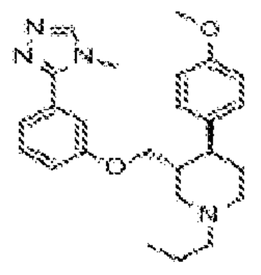
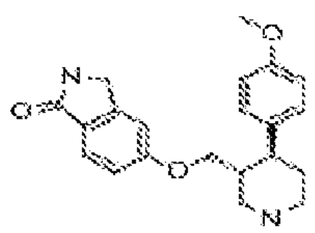
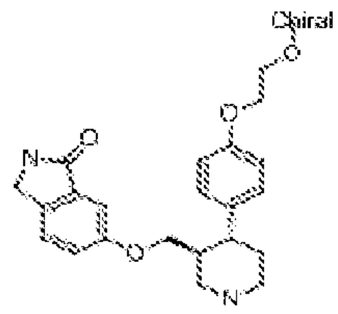
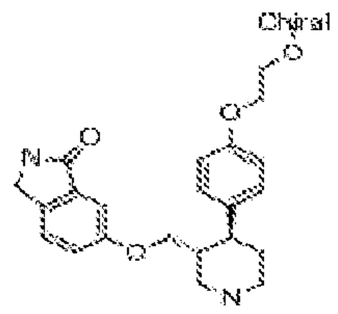
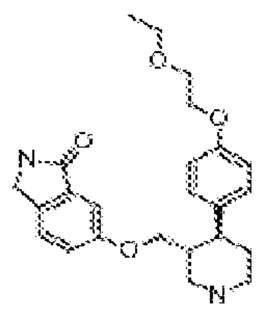
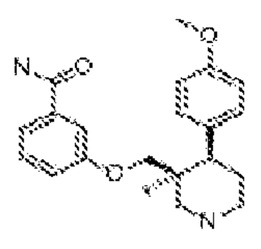
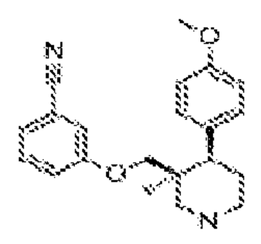
	B0561	3-{[trans-4-[4-(2-Methoxyethoxy)phenyl]-1-propylpiperidin-3-yl]methoxy}benzonitrile	408.53	409
	B0562	trans-4-(4-Methoxyphenyl)-3-{[3-(4-methyl-4H-1,2,4-triazol-3-yl)phenoxy]methyl}-1-propylpiperidine	420.55	421
	B0563	5-{[trans-4-(4-Methoxyphenyl)piperidin-3-yl]methoxy}isoindolin-1-one	352.43	353
	B0564	(–)-6-{[(trans)-4-[4-(2-Methoxyethoxy)phenyl]piperidin-3-yl]methoxy}isoindolin-1-one	396.48	397
	B0565	(+)-6-{[(trans)-4-[4-(2-Methoxyethoxy)phenyl]piperidin-3-yl]methoxy}isoindolin-1-one	396.48	397
	B0566	6-{[trans-4-[4-(2-Ethoxyethoxy)phenyl]piperidin-3-yl]methoxy}isoindolin-1-one	410.51	411
	B0567	3-{[cis-4-(4-Methoxyphenyl)-3-methylpiperidin-3-yl]methoxy}benzamide	354.44	355
	B0568	3-{[cis-4-(4-Methoxyphenyl)-3-methylpiperidin-3-yl]methoxy}benzonitrile	336.43	337

Figure 1-Continued

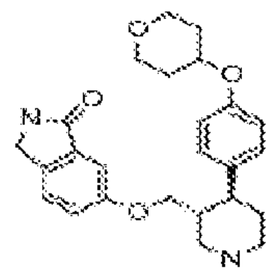
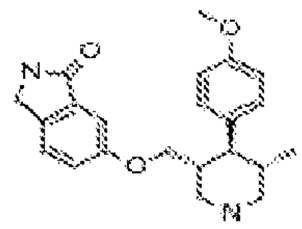
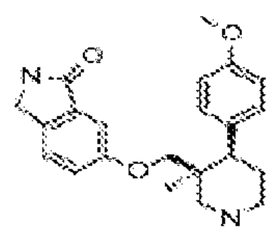
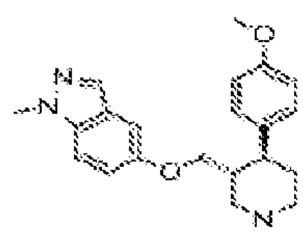
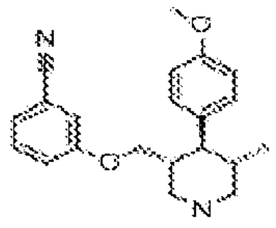
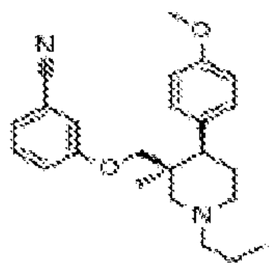
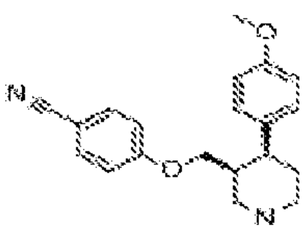
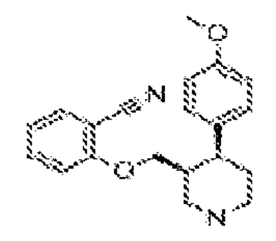
	B0569	6-{[trans-4-{4-[(Tetrahydro-2H-pyran-4-yl)oxy]phenyl}piperidin-3-yl]methoxy}isoindolin-1-one	422.52	423
	B0570	6-{[trans,trans-4-(4-Methoxyphenyl)-5-methylpiperidin-3-yl]methoxy}isoindolin-1-one	366.45	367
	B0571	6-{[cis-4-(4-Methoxyphenyl)-3-methylpiperidin-3-yl]methoxy}isoindolin-1-one	366.45	367
	B0572	5-{[trans-4-(4-Methoxyphenyl)piperidin-3-yl]methoxy}-1-methyl-1H-indazole	351.44	352
	B0573	3-{[trans,trans-4-(4-Methoxyphenyl)-5-methylpiperidin-3-yl]methoxy}benzonitrile	336.43	337
	B0574	3-{[trans-4-(4-Methoxyphenyl)-3-methyl-1-propylpiperidin-3-yl]methoxy}benzonitrile	378.51	379
	B0575	4-{[cis-4-(4-Methoxyphenyl)piperidin-3-yl]methoxy}benzonitrile	322.4	323
	B0576	2-{[cis-4-(4-Methoxyphenyl)piperidin-3-yl]methoxy}benzonitrile	322.4	323

Figure 1-Continued

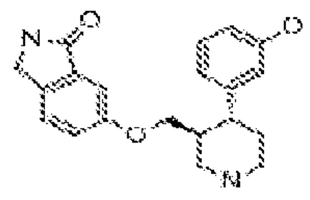
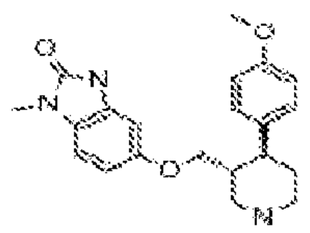
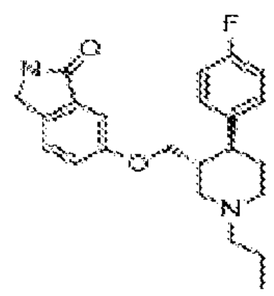
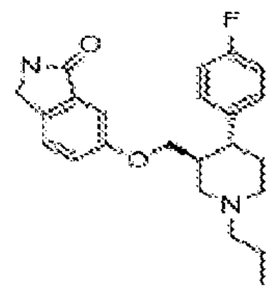
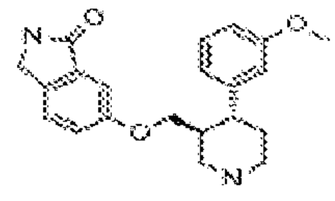
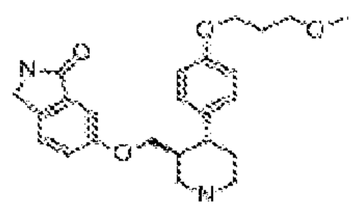
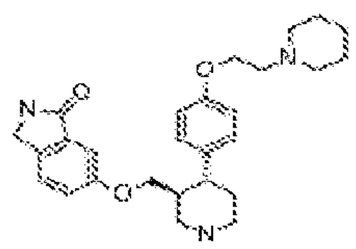
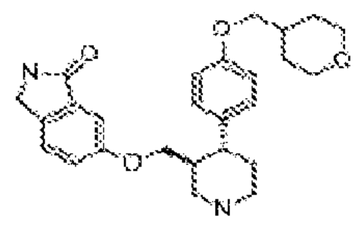
	B0577	6-{[trans-4-(3-Hydroxyphenyl)piperidin-3-yl]methoxy}isoindolin-1-one	338.4	339
	B0578	5-{[trans-4-(4-Methoxyphenyl)piperidin-3-yl]methoxy}-1-methyl-1H-benzo[d]imidazol-2(3H)-one	367.44	368
	B0579	6-{[trans-4-(4-Fluorophenyl)-1-propylpiperidin-3-yl]methoxy}isoindolin-1-one	382.47	383
	B0580	(–)-6-{[(trans)-4-(4-Fluorophenyl)-1-propylpiperidin-3-yl]methoxy}isoindolin-1-one	382.47	383
	B0581	6-{[trans-4-(3-Methoxyphenyl)piperidin-3-yl]methoxy}isoindolin-1-one	352.43	353
	B0582	6-{[trans-4-[4-(3-Methoxypropoxy)phenyl]piperidin-3-yl]methoxy}isoindolin-1-one	410.51	411
	B0583	6-{[trans-4-{4-[2-(Piperidin-1-yl)ethoxy]phenyl}piperidin-3-yl]methoxy}isoindolin-1-one	449.59	450
	B0584	6-{[trans-4-{4-[(Tetrahydro-2H-pyran-4-yl)methoxy]phenyl}piperidin-3-yl]methoxy}isoindolin-1-one	436.54	437

Figure 1-Continued

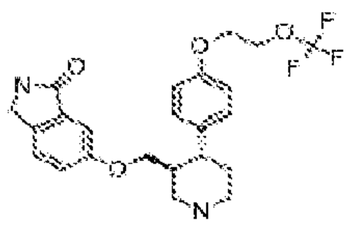
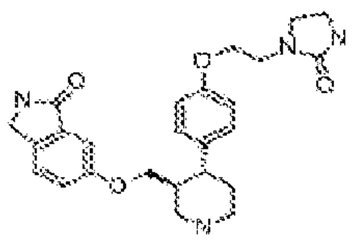
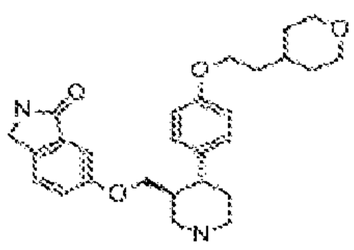
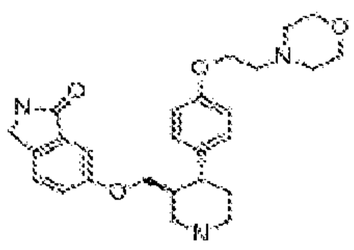
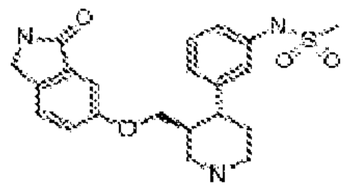
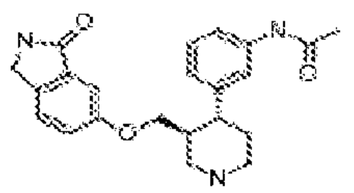
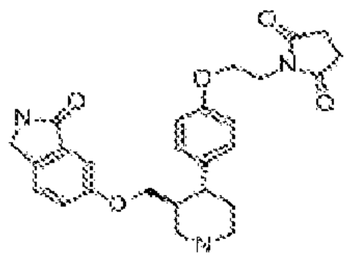
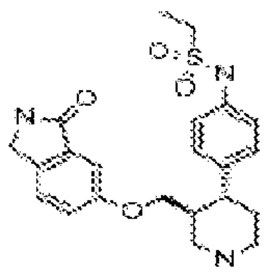
	B0585	6-{[trans-4-{4-[2-(Trifluoromethoxy)ethoxy]phenyl}piperidin-3-yl]methoxy}isoindolin-1-one	450.45	451
	B0586	6-{[trans-4-{4-[2-(2-Oxoimidazolidin-1-yl)ethoxy]phenyl}piperidin-3-yl]methoxy}isoindolin-1-one	450.53	451
	B0587	6-{[trans-4-{4-[2-(Tetrahydro-2H-pyran-4-yl)ethoxy]phenyl}piperidin-3-yl]methoxy}isoindolin-1-one	450.57	451
	B0588	6-{[trans-4-[4-(2-Morpholinoethoxy)phenyl]piperidin-3-yl]methoxy}isoindolin-1-one	451.56	452
	B0589	N-{3-[trans-3-{[(3-Oxoisoindolin-5-yl)oxy]methyl}piperidin-4-yl]phenyl}methanesulfonamide	415.51	416
	B0590	N-{3-[trans-3-{[(3-Oxoisoindolin-5-yl)oxy]methyl}piperidin-4-yl]phenyl}acetamide	379.45	380
	B0591	1-(2-{4-[trans-3-{[(3-Oxoisoindolin-5-yl)oxy]methyl}piperidin-4-yl]phenoxy}ethyl)pyrrolidine-2,5-dione	463.53	464
	B0592	N-{4-[trans-3-{[(3-Oxoisoindolin-5-yl)oxy]methyl}piperidin-4-yl]phenyl}ethanesulfonamide	429.53	430

Figure 1-Continued

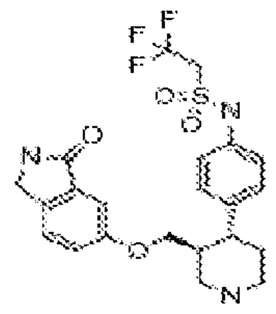
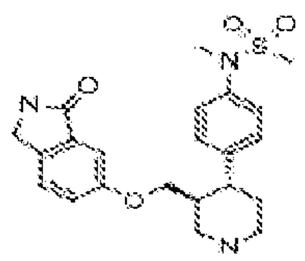
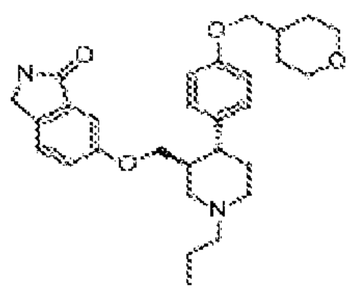
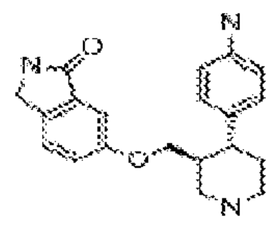
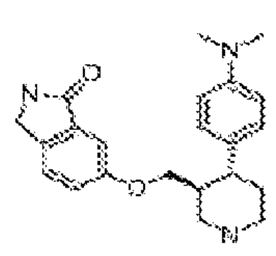
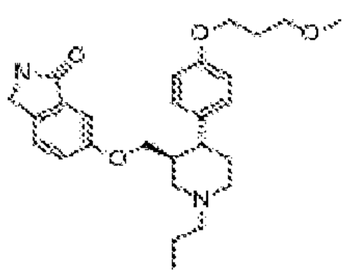
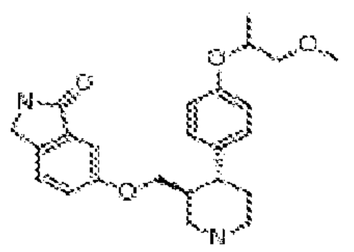
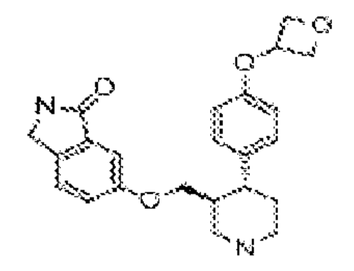
	B0593	2,2,2-Trifluoro-N-{4-[trans-3-{[(3-oxoisoindolin-5-yl)oxy]methyl}piperidin-4-yl]phenyl}ethanesulfonamide	483.5	484
	B0594	N-Methyl-N-{4-[trans-3-{[(3-oxoisoindolin-5-yl)oxy]methyl}piperidin-4-yl]phenyl}methanesulfonamide	429.53	430
	B0595	6-{[trans-1-Propyl-4-{4-[(tetrahydro-2H-pyran-4-yl)methoxy]phenyl}piperidin-3-yl]methoxy}isoindolin-1-one	478.62	479
	B0596	6-{[trans-4-(4-Aminophenyl)piperidin-3-yl]methoxy}isoindolin-1-one	337.42	338
	B0597	6-{[trans-4-[4-(Dimethylamino)phenyl]piperidin-3-yl]methoxy}isoindolin-1-one	365.47	366
	B0598	6-{[trans-4-[4-(3-Methoxypropoxy)phenyl]-1-propylpiperidin-3-yl]methoxy}isoindolin-1-one	452.59	453
	B0599	6-{[trans-4-{4-[(1-Methoxypropan-2-yl)oxy]phenyl}piperidin-3-yl]methoxy}isoindolin-1-one	410.51	411
	B0600	6-{[trans-4-[4-(Oxetan-3-yloxy)phenyl]piperidin-3-yl]methoxy}isoindolin-1-one	394.46	395

Figure 1-Continued

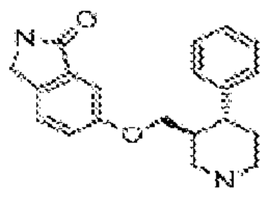
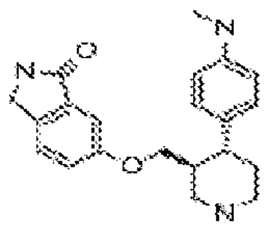
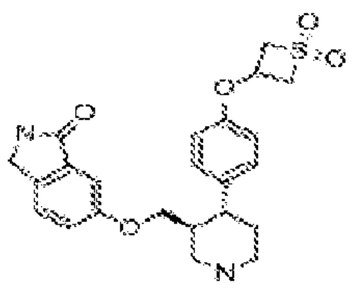
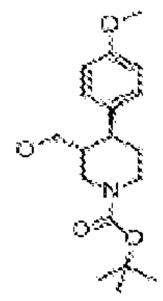
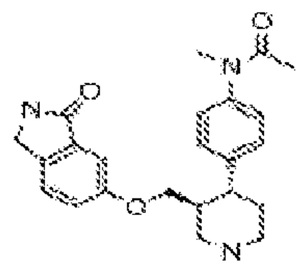
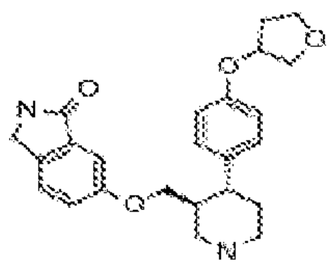
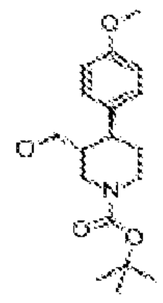
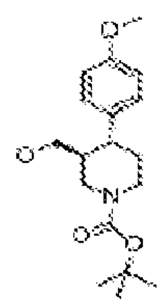
	B0601	6-{[trans-4-Phenylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	322.4	323
	B0602	6-{[trans-4-[4-(Methylamino)phenyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	351.44	352
	B0603	6-{[trans-4-{4-[(1,1-Dioxidothietan-3-yl)oxy]phenyl}piperidin-3-yl]methoxy}isoindolin-1-one	442.53	443
	B0604	tert-butyl (trans)-3-(hydroxymethyl)-4-(4-methoxyphenyl)piperidine-1-carboxylate	321.41	322
	B0605	N-Methyl-N-{4-[trans-3-{[(3-oxo-2,3-dihydro-1H-isoindol-5-yl)oxy]methyl}piperidin-4-yl]phenyl}acetamide	393.48	394
	B0606	6-{[trans-4-[4-(Oxolan-3-yloxy)phenyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	408.49	409
	B0607	(+)-tert-butyl (trans)-3-(hydroxymethyl)-4-(4-methoxyphenyl)piperidine-1-carboxylate	321.41	322
	B0608	(-)-tert-butyl (trans)-3-(hydroxymethyl)-4-(4-methoxyphenyl)piperidine-1-carboxylate	321.41	322

Figure 1-Continued

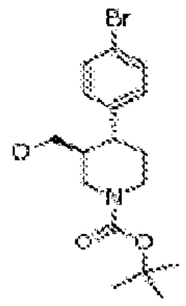
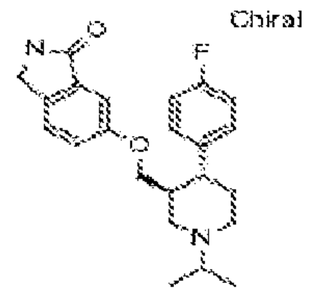
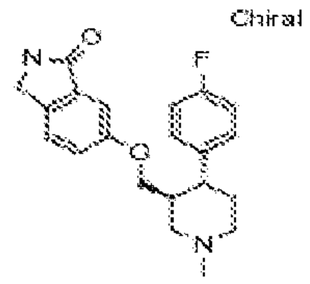
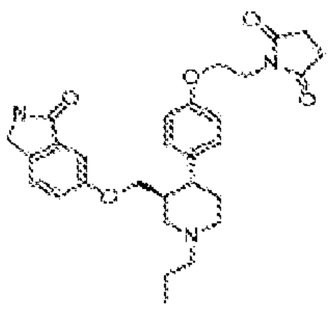
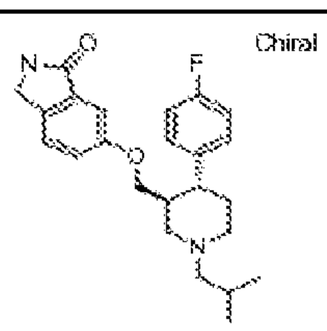
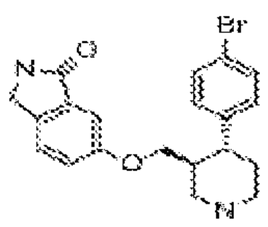
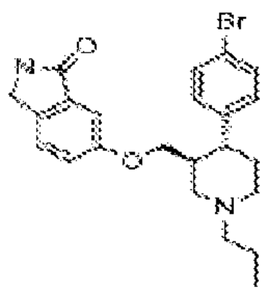
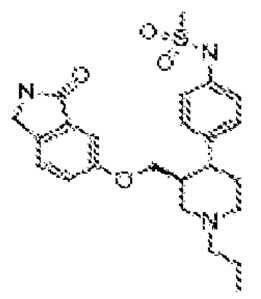
	B0609	tert-butyl (trans)-4-(4-bromophenyl)-3-(hydroxymethyl)piperidine-1-carboxylate	370.28	370
	B0610	(–)-6-{[trans-4-(4-Fluorophenyl)-1-(propan-2-yl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	382.47	383
	B0611	(–)-6-{[trans-4-(4-Fluorophenyl)-1-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	354.42	355
	B0612	1-(2-{4-[trans-3-{[(3-Oxo-2,3-dihydro-1H-isoindol-5-yl)oxy]methyl}-1-propylpiperidin-4-yl]phenoxy}ethyl)pyrrolidine-2,5-dione	505.61	506
	B0613	(–)-6-{[trans-4-(4-Fluorophenyl)-1-(2-methylpropyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	396.5	397
	B0614	6-{[trans-4-(4-Bromophenyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	401.3	401
	B0615	6-{[trans-4-(4-Bromophenyl)-1-propylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-on	443.38	443
	B0616	N-{4-[trans-3-{[(3-Oxo-2,3-dihydro-1H-isoindol-5-yl)oxy]methyl}-1-propylpiperidin-4-yl]phenyl}methanesulfonamide	457.59	458

Figure 1-Continued

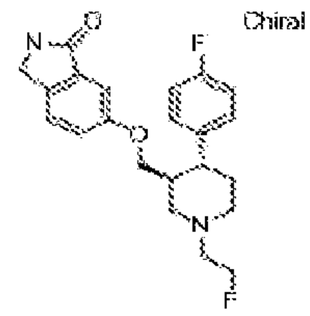
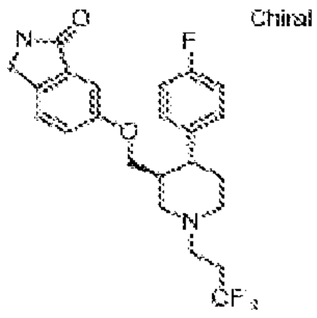
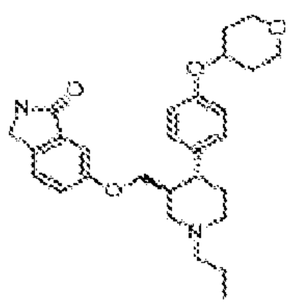
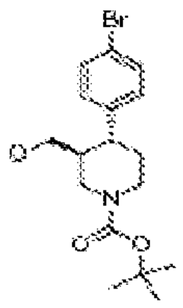
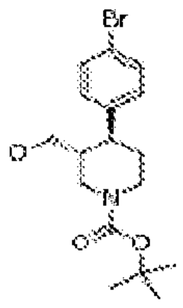
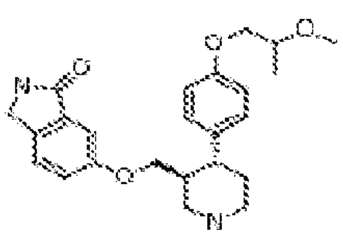
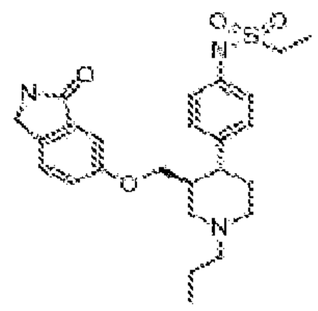
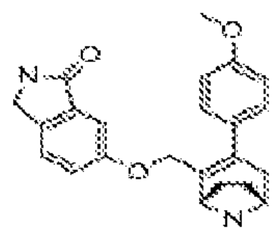
	B0617	(–)-6-{[trans-1-(2-Fluoroethyl)-4-(4-fluorophenyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	386.43	387
	B0618	(–)-6-{[trans-4-(4-Fluorophenyl)-1-(3,3,3-trifluoropropyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	436.44	437
	B0619	6-{[trans-4-[4-(Oxan-4-yloxy)phenyl]-1-propylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	464.6	465
	B0620	(+)-tert-butyl (trans)-4-(4-bromophenyl)-3-(hydroxymethyl)piperidine-1-carboxylate	370.28	370
	B0621	(-)-tert-butyl (trans)-4-(4-bromophenyl)-3-(hydroxymethyl)piperidine-1-carboxylate	370.28	370
	B0622	6-{[trans-4-[4-(2-Methoxypropoxy)phenyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	410.51	411
	B0623	N-{4-[trans-3-{[(3-Oxo-2,3-dihydro-1H-isoindol-5-yl)oxy]methyl}-1-propylpiperidin-4-yl]phenyl}ethane-1-sulfonamide	471.61	472
	B0624	6-{[3-(4-methoxyphenyl)-8-azabicyclo[3.2.1]oct-2-en-2-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	376.45	N.D.

Figure 1-Continued

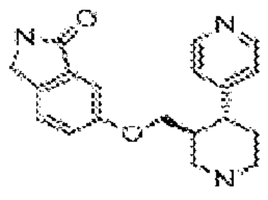
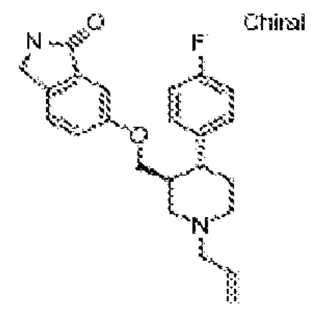
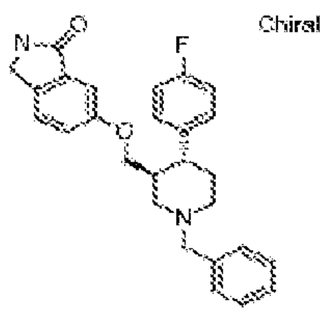
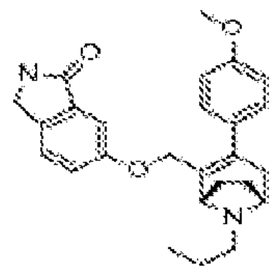
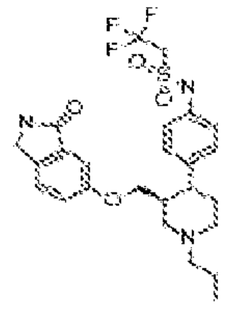
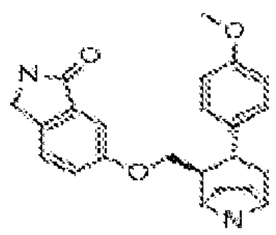
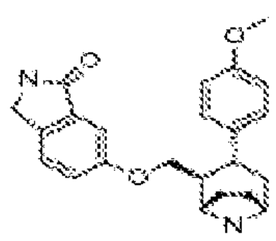
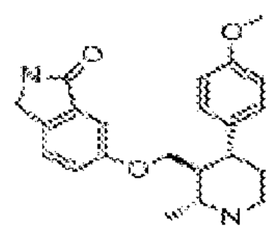
	B0625	6-{[trans-4-(Pyridin-4-yl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	323.39	324
 Chiral	B0626	(–)-6-{[trans-4-(4-Fluorophenyl)-1-(prop-2-en-1-yl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	380.46	381
 Chiral	B0627	(–)-6-{[trans-1-Benzyl-4-(4-fluorophenyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	430.51	431
	B0628	(+/-)-6-{[3-(4-Methoxyphenyl)-8-propyl-8-azabicyclo[3.2.1]oct-2-en-2-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	418.53	419
	B0629	2,2,2-Trifluoro-N-{4-[trans-3-({[3-oxoisoindolin-5-yl]oxy}methyl)-1-propylpiperidin-4-yl]phenyl}ethanesulfonamide	525.58	526
	B0630	(+/-)-endo-trans-6-{[3-(4-Methoxyphenyl)-8-azabicyclo[3.2.1]octan-2-yl]methoxy}isoindolin-1-one	378.46	379
	B0631	(+/-)-exo-trans-6-{[3-(4-Methoxyphenyl)-8-azabicyclo[3.2.1]octan-2-yl]methoxy}isoindolin-1-one	378.46	379
	B0632	(+/-)-6-{[cis,trans-4-(4-Methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}isoindolin-1-one	366.45	367

Figure 1-Continued

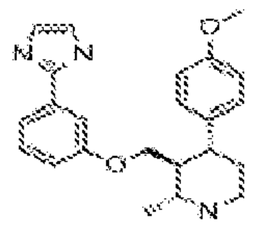
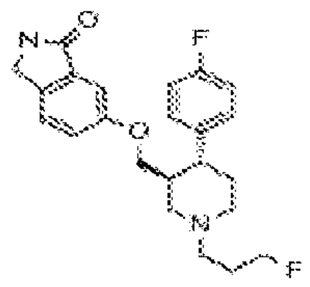
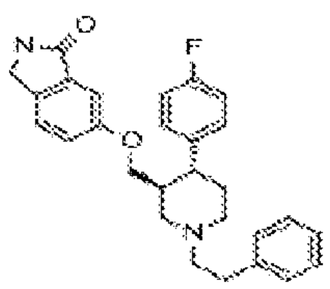
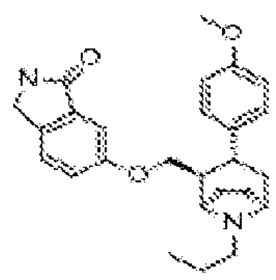
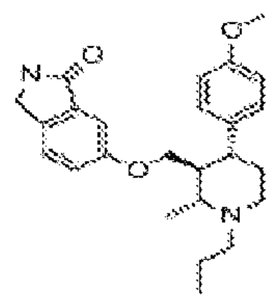
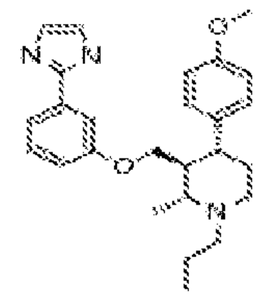
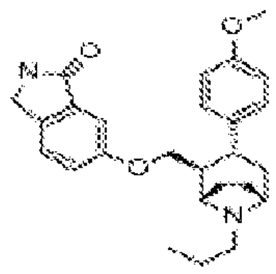
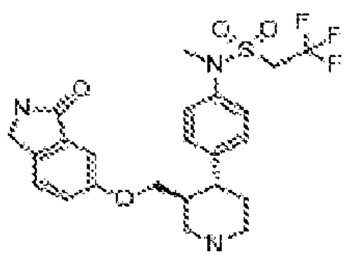
	B0633	(+/-)-cis,trans-3-{[3-(1H-Imidazol-2-yl)phenoxy]methyl}-4-(4-methoxyphenyl)-2-methylpiperidine	377.48	378
	B0634	(–)-6-{[trans-4-(4-Fluorophenyl)-1-(3-fluoropropyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	400.46	401
	B0635	(–)-6-{[trans-4-(4-Fluorophenyl)-1-phenethylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	444.54	445
	B0636	(+/-)-endo-6-{[trans-3-(4-Methoxyphenyl)-8-propyl-8-azabicyclo[3.2.1]octan-2-yl]methoxy}isoindolin-1-one	420.54	421
	B0637	(+/-)-6-{[cis,trans-4-(4-Methoxyphenyl)-2-methyl-1-propylpiperidin-3-yl)methoxy)isoindolin-1-one	408.53	409
	B0638	(+/-)-cis,trans-3-{[3-(1H-Imidazol-2-yl)phenoxy]methyl}-4-(4-methoxyphenyl)-2-methyl-1-propylpiperidine	419.56	420
	B0639	(+/-)-exo-6-{[trans-3-(4-Methoxyphenyl)-8-propyl-8-azabicyclo[3.2.1]octan-2-yl]methoxy}isoindolin-1-one	420.54	421.1
	B0640	2,2,2-Trifluoro-N-methyl-N-{4-[trans-3-{[(3-oxoisoindolin-5-yl)oxy]methyl}piperidin-4-yl]phenyl}ethanesulfonamide	497.53	498

Figure 1-Continued

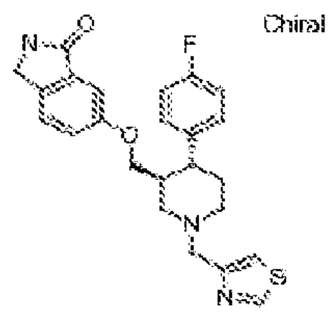
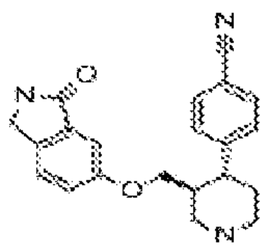
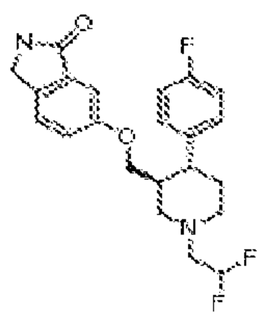
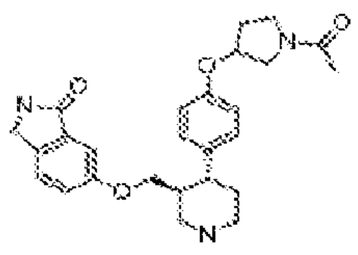
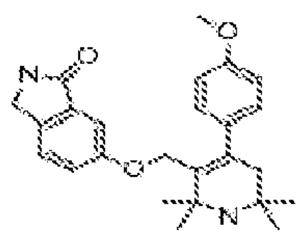
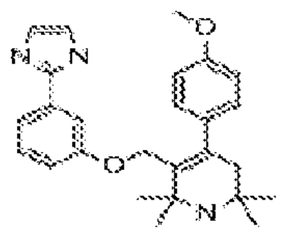
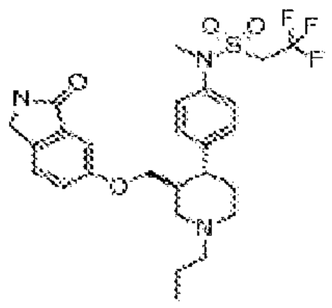
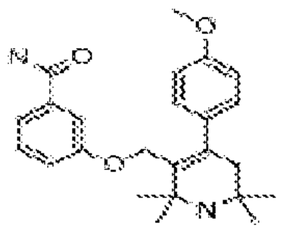
	B0641	(–)-6-{[trans-4-(4-Fluorophenyl)-1-(thiazol-4-ylmethyl)piperidin-3-yl]methoxy}isoindolin-1-one	437.53	438
	B0642	4-[trans-3-{[(3-Oxoisoindolin-5-yl)oxy]methyl}piperidin-4-yl]benzonitrile	347.41	348
	B0643	(–)-6-{[trans-1-(2,2-Difluoroethyl)-4-(4-fluorophenyl)piperidin-3-yl]methoxy}isoindolin-1-one	404.43	405
	B0644	6-{[trans-4-(4-{[1-Acetylpyrrolidin-3-yl]oxy}phenyl)piperidin-3-yl]methoxy}isoindolin-1-one	449.54	450
	B0645	6-{[4-(4-Methoxyphenyl)-2,2,6,6-tetramethyl-1,2,5,6-tetrahydropyridin-3-yl]methoxy}isoindolin-1-one	406.52	407
	B0646	5-{[3-(1H-Imidazol-2-yl)phenoxy]methyl}-4-(4-methoxyphenyl)-2,2,6,6-tetramethyl-1,2,3,6-tetrahydropyridine	417.54	418
	B0647	2,2,2-Trifluoro-N-methyl-N-{4-[trans-3-({[3-oxoisoindolin-5-yl]oxy}methyl)-1-propylpiperidin-4-yl]phenyl}ethanesulfonamide	539.61	540
	B0648	3-{[4-(4-Methoxyphenyl)-2,2,6,6-tetramethyl-1,2,5,6-tetrahydropyridin-3-yl]methoxy}benzamide	394.51	395

Figure 1-Continued

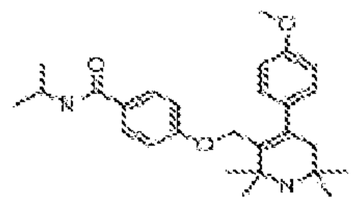
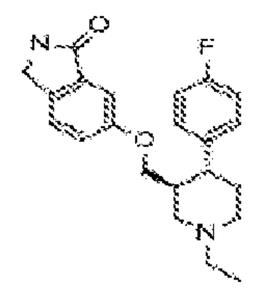
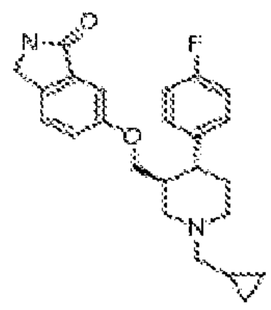
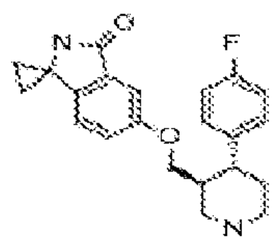
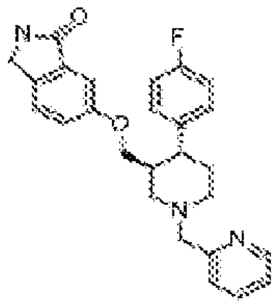
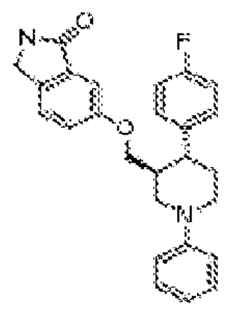
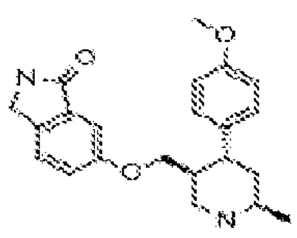
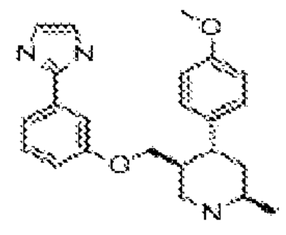
	B0649	N-Isopropyl-4-{[4-(4-methoxyphenyl)-2,2,6,6-tetramethyl-1,2,5,6-tetrahydropyridin-3-yl]methoxy}benzamide	436.59	437
	B0650	(–)-6-{[trans-1-Ethyl-4-(4-fluorophenyl)piperidin-3-yl]methoxy}isoindolin-1-one	368.44	369
	B0651	(–)-6-{[trans-1-(Cyclopropylmethyl)-4-(4-fluorophenyl)piperidin-3-yl]methoxy}isoindolin-1-one	394.48	395
	B0652	(–)-5'-{[trans-4-(4-Fluorophenyl)piperidin-3-yl]methoxy}spiro[cyclopropane-1,1'-isoindolin]-3'-one	366.43	367
	B0653	(–)-6-{[trans-4-(4-Fluorophenyl)-1-(pyridin-2-ylmethyl)piperidin-3-yl]methoxy}isoindolin-1-one	431.5	432
	B0654	6-{[(–)-trans-4-(4-Fluorophenyl)-1-phenylpiperidin-3-yl]methoxy}isoindolin-1-one	416.49	417
	B0655	(+/-)-6-{[trans,trans-4-(4-Methoxyphenyl)-6-methylpiperidin-3-yl]methoxy}isoindolin-1-one	366.45	367
	B0656	trans,trans-3-{[3-(1H-Imidazol-2-yl)phenoxy]methyl}-4-(4-methoxyphenyl)-6-methylpiperidine	377.48	378

Figure 1-Continued

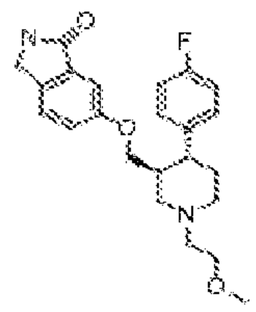
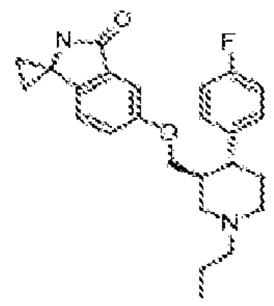
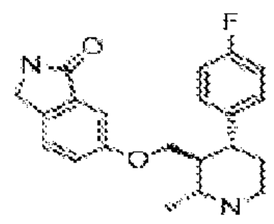
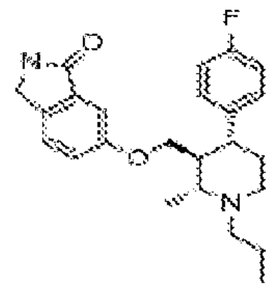
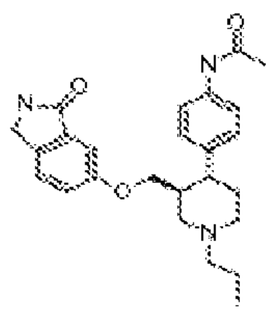
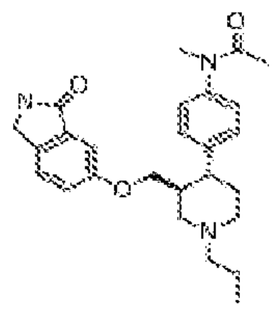
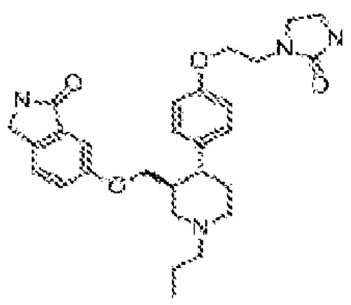
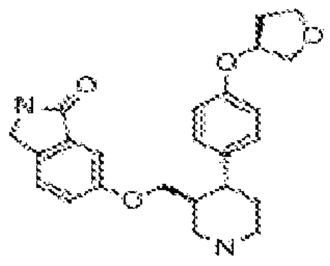
	B0657	(–)-6-{[trans-4-(4-Fluorophenyl)-1-(2-methoxyethyl)piperidin-3-yl]methoxy}isoindolin-1-one	398.47	399
	B0658	(–)-5'-{[trans-4-(4-Fluorophenyl)-1-propylpiperidin-3-yl]methoxy}spiro[cyclopropane-1,1'-isoindolin]-3'-one	408.51	409
	B0659	6-{[trans,trans-4-(4-Fluorophenyl)-2-methylpiperidin-3-yl]methoxy}isoindolin-1-one	354.42	355
	B0660	6-{[trans,trans-4-(4-Fluorophenyl)-2-methyl-1-propylpiperidin-3-yl)methoxy)isoindolin-1-one	396.5	397
	B0661	N-{4-[trans-3-{[(3-Oxoisoindolin)oxy]methyl}-1-propylpiperidin-4-yl]phenyl}acetamide	421.53	422
	B0662	N-methyl-N-{4-[trans-3-{[(3-Oxoisoindolin)oxy]methyl}-1-propylpiperidin-4-yl]phenyl}acetamide	435.56	436
	B0663	6-{[trans-4-{4-[2-(2-Oxoimidazolidin-1-yl)ethoxy]phenyl}-1-propylpiperidin-3-yl]methoxy}isoindolin-1-one	492.61	493
	B0664	6-{[trans-4-(4-{[(R)-Tetrahydrofuran-3-yl]oxy}phenyl)piperidin-3-yl]methoxy}isoindolin-1-one	408.49	409

Figure 1-Continued

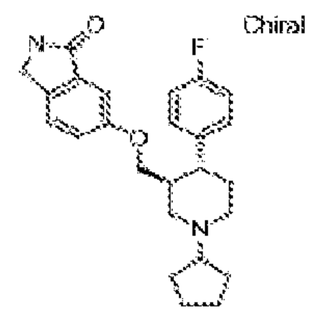
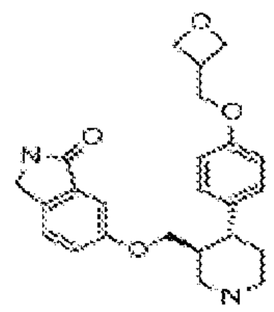
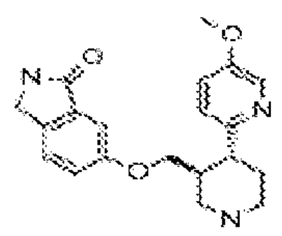
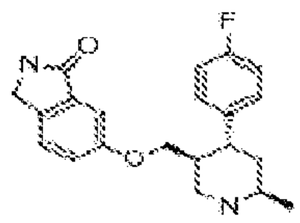
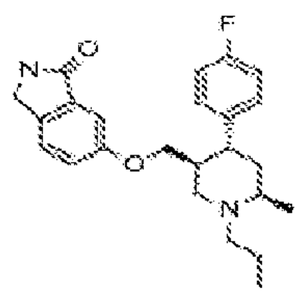
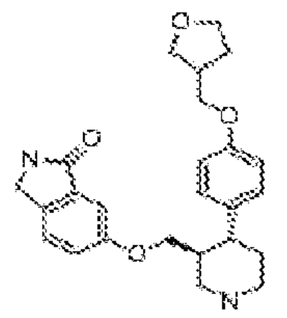
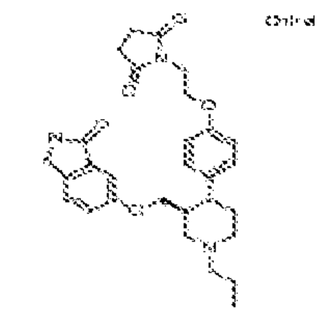
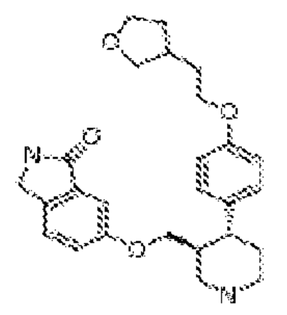
	B0665	(–)-6-{[trans-1-Cyclopentyl-4-(4-fluorophenyl)piperidin-3-yl]methoxy}isoindolin-1-one	408.51	409
	B0666	6-{[trans-4-(4-[Oxetan-3-ylmethoxy]phenyl)piperidin-3-yl]methoxy}isoindolin-1-one	408.49	409
	B0667	6-{[trans-4-(5-Methoxypyridin-2-yl)piperidin-3-yl]methoxy}isoindolin-1-one	353.41	354
	B0668	6-{[trans,trans-4-(4-Fluorophenyl)-6-methylpiperidin-3-yl]methoxy}isoindolin-1-one	354.42	355
	B0669	6-{[trans,trans-4-(4-Fluorophenyl)-6-methyl-1-propylpiperidin-3-yl)methoxy)isoindolin-1-one	396.5	397
	B0670	6-{[trans-4-(4-{[Tetrahydrofuran-3-yl]methoxy}phenyl)piperidin-3-yl]methoxy}isoindolin-1-one	422.52	423
	B0671	(–)-1-(2-{4-[trans-3-{[(3-Oxo-2,3-dihydro-1H-isoindol-5-yl)oxy]methyl}-1-propylpiperidin-4-yl]phenoxy}ethyl)pyrrolidine-2,5-dione	505.61	506
	B0672	6-{[trans-4-(4-{[Tetrahydrofuran-3-yl]ethoxy}phenyl)piperidin-3-yl]methoxy}isoindolin-1-one	436.54	437

Figure 1-Continued

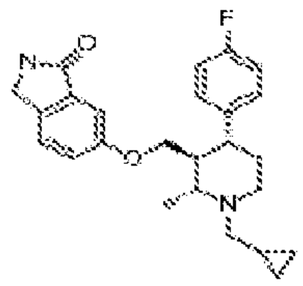
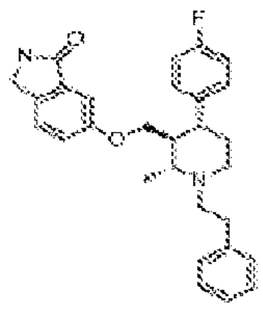
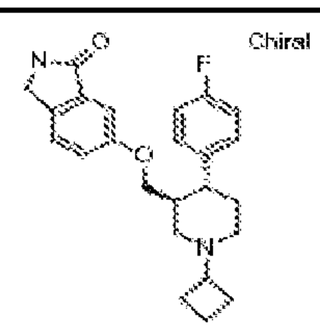
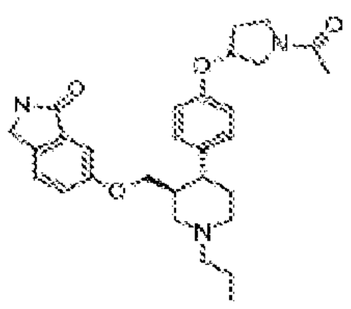
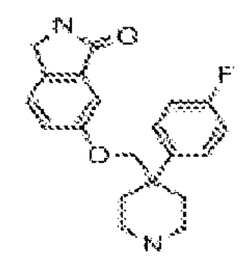
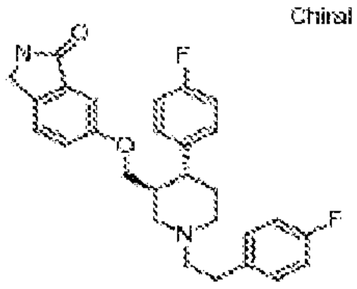
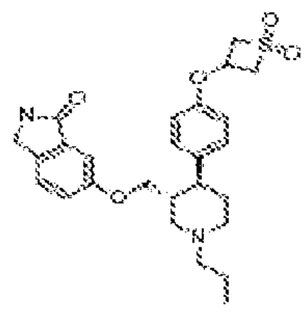
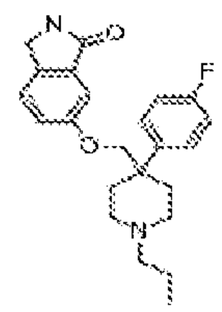
	B0673	6-{[trans,trans-1-(Cyclopropylmethyl)-4-(4-fluorophenyl)-2-methylpiperidin-3-yl]methoxy}isoindolin-1-one	408.51	409
	B0674	6-{[trans,trans-4-(4-Fluorophenyl)-2-methyl-1-phenethylpiperidin-3-yl)methoxy)isoindolin-1-one	458.57	459
	B0675	(–)-6-{[trans-1-Cyclobutyl-4-(4-fluorophenyl)piperidin-3-yl]methoxy}isoindolin-1-one	394.48	395
	B0676	6-{[trans-4-(4-{[(R)-1-Acetylpyrrolidin-3-yl]oxy}phenyl)-1-propylpiperidin-3-yl)methoxy)isoindolin-1-one	491.62	492
	B0677	6-{[4-(4-fluorophenyl)piperidin-4-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	340.39	341.1
	B0678	(–)-6-{[trans-1-(4-Fluorophenethyl)-4-(4-fluorophenyl)piperidin-3-yl]methoxy}isoindolin-1-one	462.53	463
	B0679	6-{[trans-4-(4-{[1,1-Dioxidothietan-3-yl]oxy}phenyl)-1-propylpiperidin-3-yl]methoxy}isoindolin-1-one	484.61	485
	B0680	6-{[4-(4-fluorophenyl)-1-propylpiperidin-4-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	382.47	383.1

Figure 1-Continued

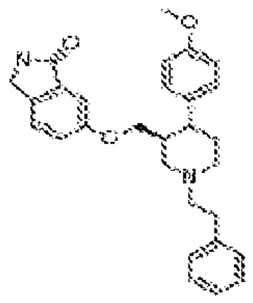
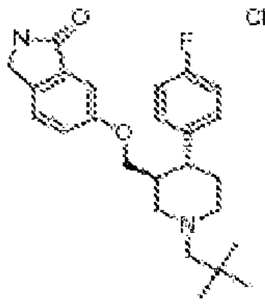
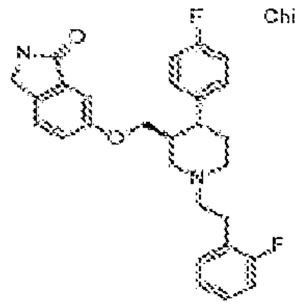
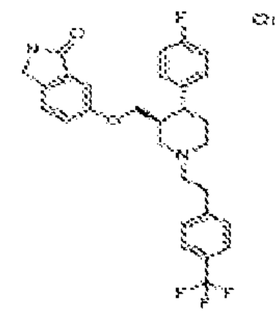
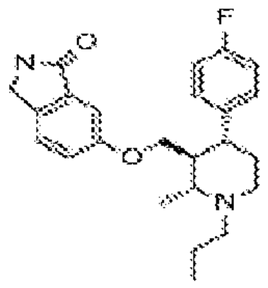
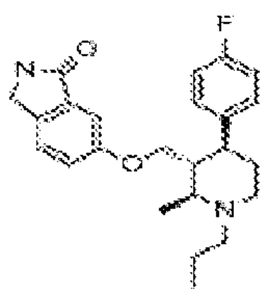
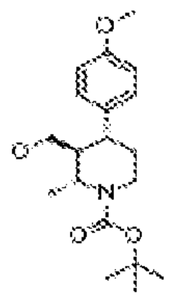
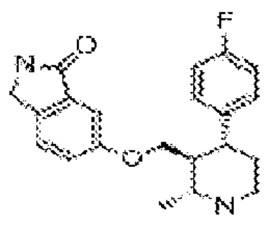
	B0681	6-{[trans-4-(4-Methoxyphenyl)-1-phenethylpiperidin-3-yl]methoxy}isoindolin-1-one	456.58	457
Chiral 	B0682	(–)-6-{[trans-4-(4-Fluorophenyl)-1-neopentylpiperidin-3-yl]methoxy}isoindolin-1-one	410.52	411
Chiral 	B0683	(–)-6-{[trans-1-(2-Fluorophenethyl)-4-(4-fluorophenyl)piperidin-3-yl]methoxy}isoindolin-1-one	462.53	463
Chiral 	B0684	(–)-6-{[trans-1-(4-Trifluorophenethyl)-4-(4-fluorophenyl)piperidin-3-yl]methoxy}isoindolin-1-one	512.54	513
	B0685	(–)-6-{[trans,trans-4-(4-Fluorophenyl)-2-methyl-1-propylpiperidin-3-yl)methoxy)isoindolin-1-one	396.5	397
	B0686	(+)-6-{[cis,trans-4-(4-Fluorophenyl)-2-methyl-1-propylpiperidin-3-yl)methoxy)isoindolin-1-one	396.5	397
	B0687	tert-butyl (trans, trans-3-(hydroxymethyl)-4-(4-methoxyphenyl)-2-methylpiperidine-1-carboxylate	335.44	336
Chiral 	B0688	(–)-6-{[trans,trans-4-(4-Fluorophenyl)-2-methylpiperidin-3-yl]methoxy}isoindolin-1-one	354.42	355

Figure 1-Continued

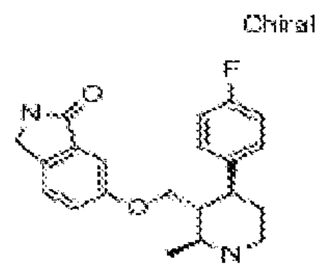
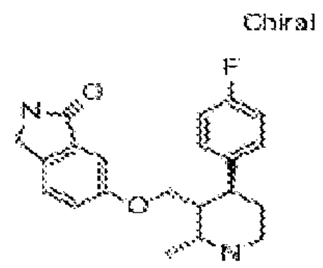
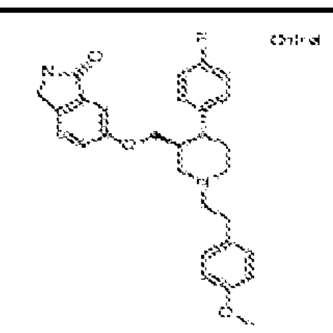
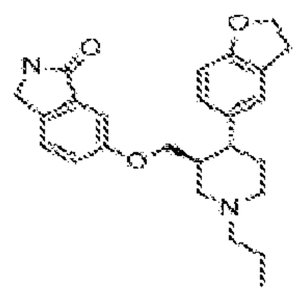
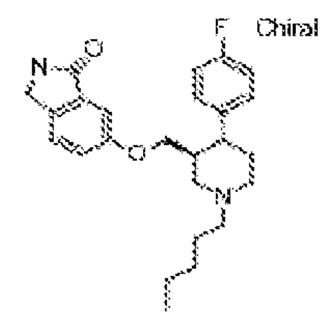
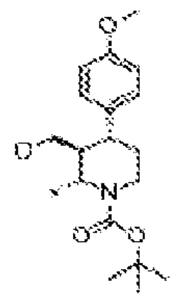
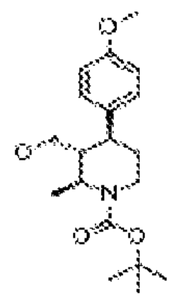
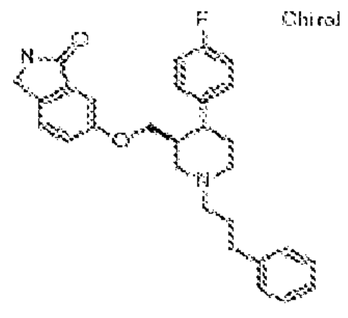
	B0689	(+)-6-{[trans,trans-4-(4-Fluorophenyl)-2-methylpiperidin-3-yl]methoxy}isoindolin-1-one	354.42	355
	B0690	(+)-6-{[cis,trans-4-(4-Fluorophenyl)-2-methylpiperidin-3-yl]methoxy}isoindolin-1-one	354.42	355
	B0691	(–)-6-{[trans-1-(4-Methoxyphenethyl)-4-(4-fluorophenyl)piperidin-3-yl]methoxy}isoindolin-1-one	474.57	475
	B0692	6-{[trans-4-(2,3-Dihydrobenzofuran-5-yl)-1-propylpiperidin-3-yl]methoxy}isoindolin-1-one	406.52	407
	B0693	(–)-6-{[trans-4-(4-Fluorophenyl)-1-pentylpiperidin-3-yl]methoxy}isoindolin-1-one	410.52	411
	B0694	(-)-tert-butyl (trans, trans-3-(hydroxymethyl)-4-(4-methoxyphenyl)-2-methylpiperidine-1-carboxylate	335.44	336
	B0695	(+)-tert-butyl (trans, trans-3-(hydroxymethyl)-4-(4-methoxyphenyl)-2-methylpiperidine-1-carboxylate	335.44	336
	B0696	(–)-6-{[trans-4-(4-Fluorophenyl)-1-(3-phenylpropyl)piperidin-3-yl]methoxy}isoindolin-1-one	458.57	459

Figure 1-Continued

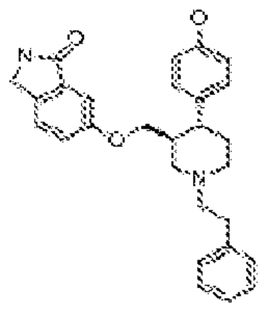
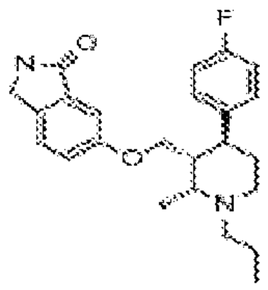
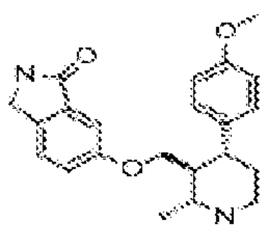
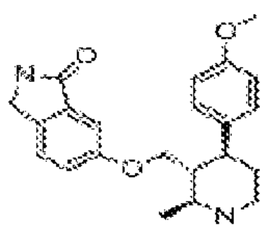
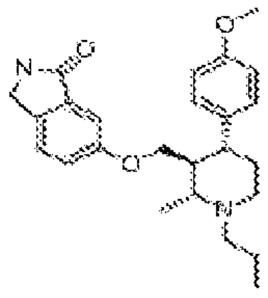
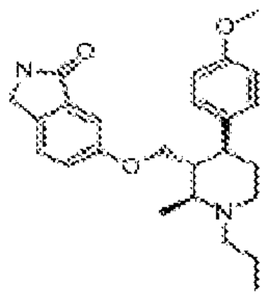
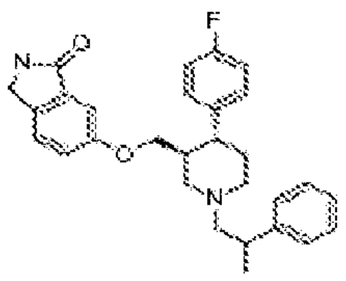
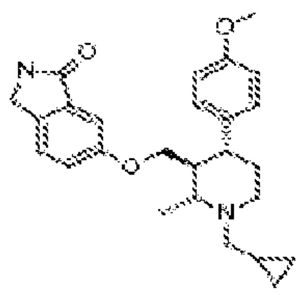
	B0697	6-{[trans-4-(4-Hydroxyphenyl)-1-phenethylpiperidin-3-yl]methoxy}isoindolin-1-one	442.55	443
	B0698	(+)-6-{[trans,trans-4-(4-Fluorophenyl)-2-methyl-1-propylpiperidin-3-yl)methoxy)isoindolin-1-one	396.5	397
	B0699	(-)-6-{[trans, trans-4-(4-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	366.45	367.2
	B0700	(+)-6-{[trans, trans-4-(4-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	366.45	367.2
	B0701	(-)-6-{[trans, trans-4-(4-methoxyphenyl)-2-methyl-1-propylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	408.53	409.3
	B0702	(+)-6-{[trans, trans-4-(4-methoxyphenyl)-2-methyl-1-propylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	408.53	409.3
	B0703	6-{[(trans)-4-(4-fluorophenyl)-1-(2-phenylpropyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	458.57	459.3
	B0704	(-)-6-{[trans, trans-1-(cyclopropylmethyl)-4-(4-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	420.54	421.3

Figure 1-Continued

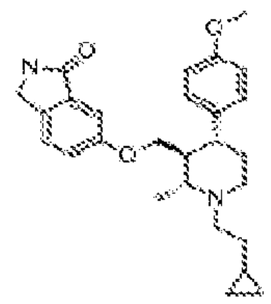
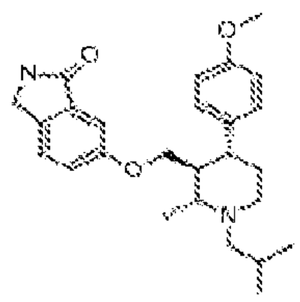
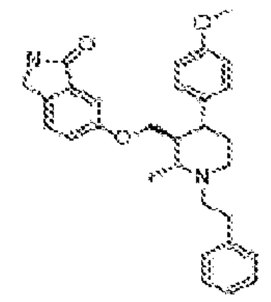
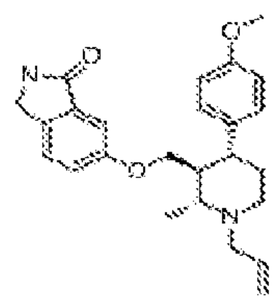
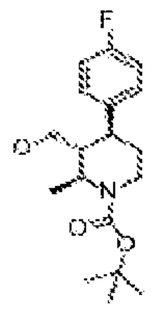
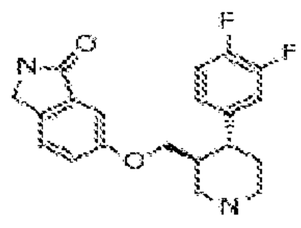
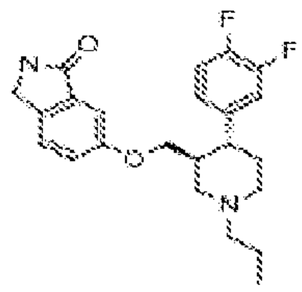
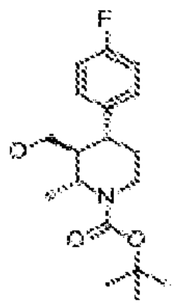
	B0705	(-)-6-{[trans, trans-1-(2-cyclopropylethyl)-4-(4-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	434.57	435.3
	B0706	(-)-6-{[trans, trans-4-(4-methoxyphenyl)-2-methyl-1-(2-methylpropyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	422.56	423.3
	B0707	(-)-6-{[trans, trans-4-(4-methoxyphenyl)-2-methyl-1-(2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	470.6	471.3
	B0708	(-)-6-{[trans, trans-4-(4-methoxyphenyl)-2-methyl-1-(prop-2-en-1-yl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	406.52	407.2
	B0709	tert-butyl (trans, trans)-4-(4-fluorophenyl)-3-(hydroxymethyl)-2-methylpiperidine-1-carboxylate	323.4	268
	B0710	6-{[(trans)-4-(3,4-difluorophenyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	358.38	359
	B0711	6-{[(trans)-4-(3,4-difluorophenyl)-1-propylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	400.46	401
	B0712	(-)-tert-butyl (trans, trans)-4-(4-fluorophenyl)-3-(hydroxymethyl)-2-methylpiperidine-1-carboxylate	323.4	346

Figure 1-Continued

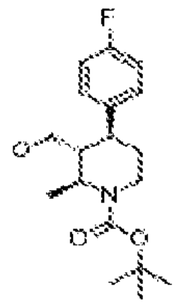
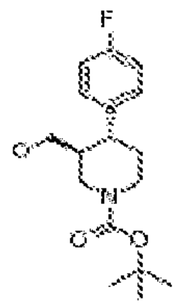
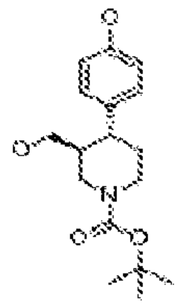
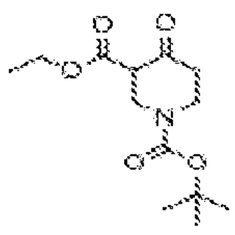
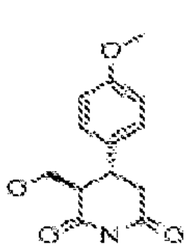
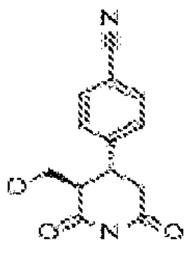
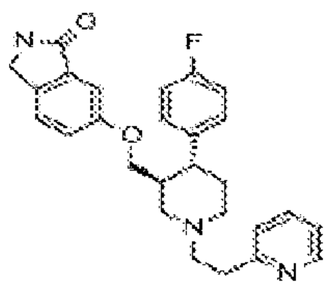
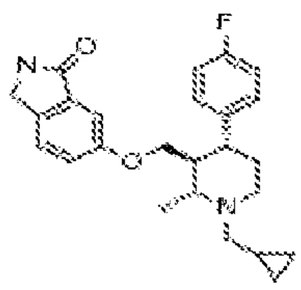
	B0713	(+)-tert-butyl (trans, trans)-4-(4-fluorophenyl)-3-(hydroxymethyl)-2-methylpiperidine-1-carboxylate	323.4	346
	B0714	(-)-tert-butyl (trans)-4-(4-fluorophenyl)-3-(hydroxymethyl)piperidine-1-carboxylate	309.38	254
	B0715	tert-butyl (trans)-3-(hydroxymethyl)-4-(4-hydroxyphenyl)piperidine-1-carboxylate	307.38	N.D.
	B0716	1-tert-butyl 3-ethyl 4-oxopiperidine-1,3-dicarboxylate	271.31	N.D.
	B0717	3-(hydroxymethyl)-4-(4-methoxyphenyl)piperidine-2,6-dione	249.26	N.D.
	B0718	4-[3-(hydroxymethyl)-2,6-dioxopiperidin-4-yl]benzonitrile	244.25	N.D.
	B0719	(-)-6-{[trans-4-(4-fluorophenyl)-1-[2-(pyridin-2-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	445.53	446.2
	B0720	(-)-6-{[trans, trans-1-(cyclopropylmethyl)-4-(4-fluorophenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	408.51	409.3

Figure 1-Continued

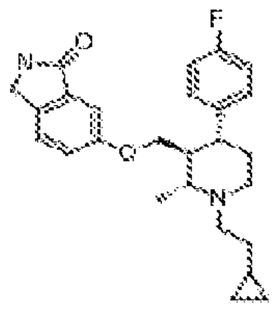
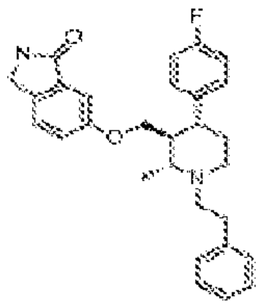
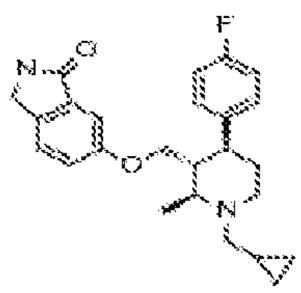
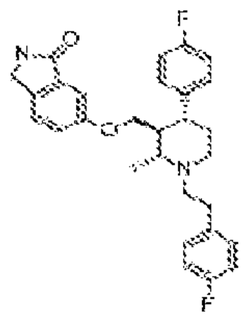
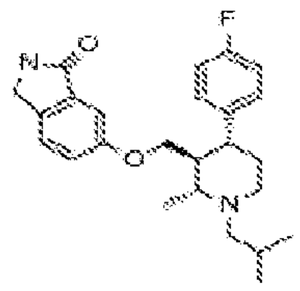
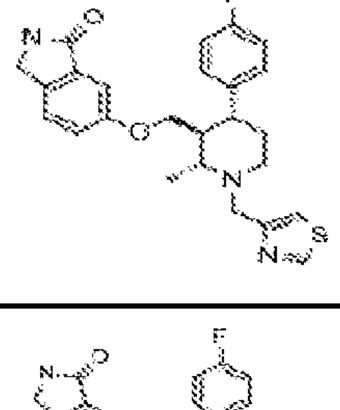
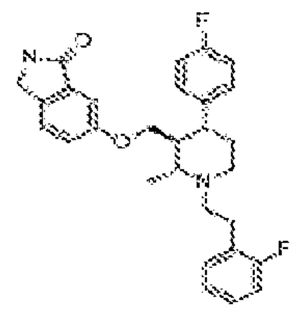
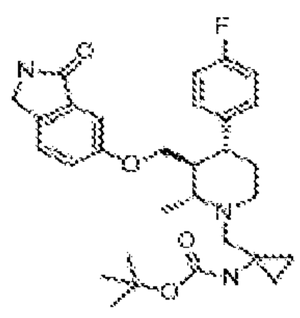
	B0721	(-)-6-{[trans, trans-1-(2-cyclopropylethyl)-4-(4-fluorophenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	422.53	423.3
	B0722	(-)-6-{[trans, trans-4-(4-fluorophenyl)-2-methyl-1-(2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	458.57	459.3
	B0723	(-)-6-{[trans, trans-1-(cyclopropylmethyl)-4-(4-fluorophenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	408.51	409.2
	B0724	(-)-6-{[trans, trans-4-(4-fluorophenyl)-1-[2-(4-fluorophenyl)ethyl]-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	476.56	477.3
	B0725	(-)-6-{[trans, trans-4-(4-fluorophenyl)-2-methyl-1-(2-methylpropyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	410.52	411.3
	B0726	(-)-6-{[trans, trans-4-(4-fluorophenyl)-2-methyl-1-(1,3-thi ol-4-ylmethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	451.56	452.2
	B0727	(-)-6-{[trans, trans-4-(4-fluorophenyl)-1-[2-(2-fluorophenyl)ethyl]-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	476.56	477.2
	B0728	(-)-N-(1-{[trans, trans-4-(4-fluorophenyl)-2-methyl-3-{[(3-oxo-2,3-dihydro-1H-isoindol-5-yl)oxy]methyl}piperidin-1-yl]methyl}cyclopropyl)carbamate	523.64	524.3

Figure 1-Continued

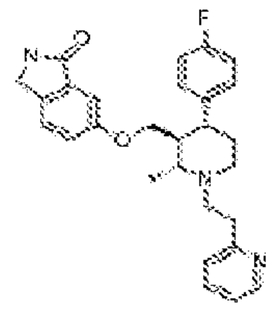
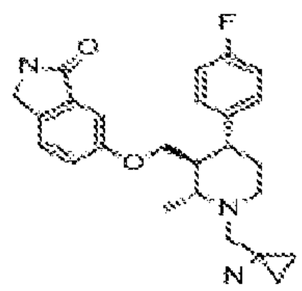
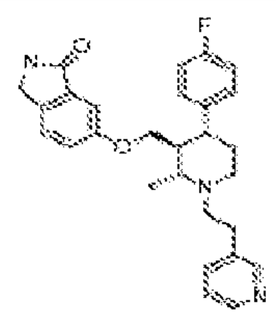
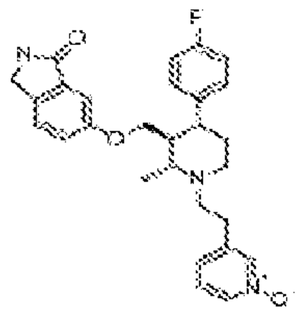
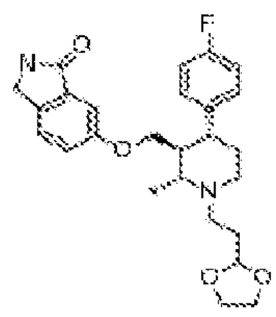
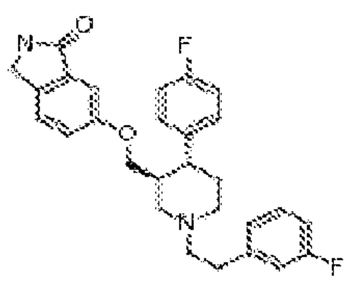
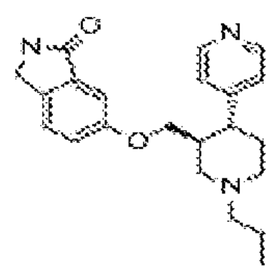
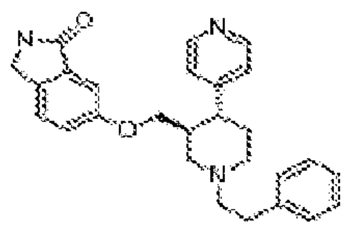
	B0729	(-)-6-{[trans, trans-4-(4-fluorophenyl)-2-methyl-1-[2-(pyridin-2-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	459.56	460.3
	B0730	(-)-6-{[trans, trans-1-[(1-minocyclopropyl)methyl]-4-(4-fluorophenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	423.52	424.3
	B0731	(-)-6-{[trans, trans4-(4-fluorophenyl)-2-methyl-1-[2-(pyridin-3-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	459.56	460.3
	B0732	(-)-3-{2-[trans, trans-4-(4-fluorophenyl)-2-methyl-3-{[(3-oxo-2,3-dihydro-1H-isoindol-5-yl)oxy]methyl}piperidin-1-yl]ethyl}pyridin-1-ium-1-olate	475.55	476.3
	B0733	(-)-6-{[trans, trans-1-[2-(1,3-dioxoln-2-yl)ethyl]-4-(4-fluorophenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	454.53	455.3
	B0734	(-)-6-{[trans-4-(4-fluorophenyl)-1-[2-(3-fluorophenyl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	462.53	463.2
	B0735	6-{[trans-1-propyl-4-(pyridin-4-yl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	365.47	366.2
	B0736	6-{[trans-1-(2-phenylethyl)-4-(pyridin-4-yl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	427.54	428.3

Figure 1-Continued

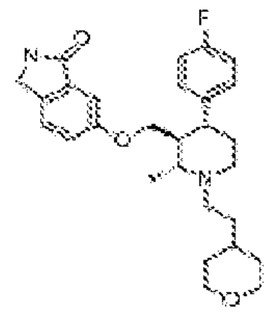
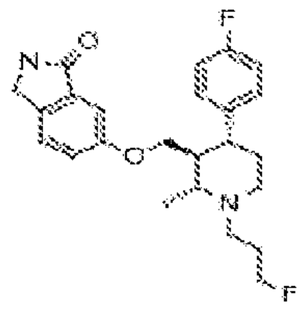
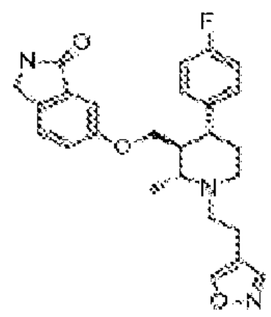
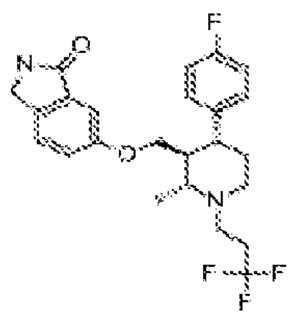
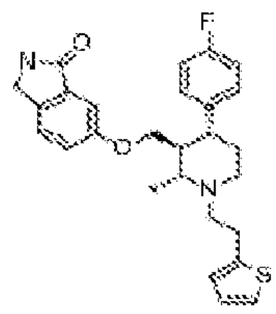
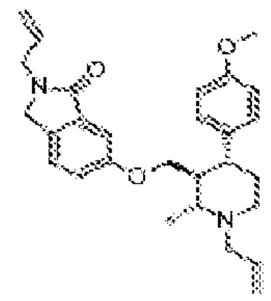
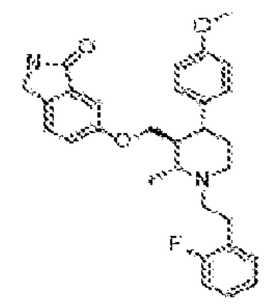
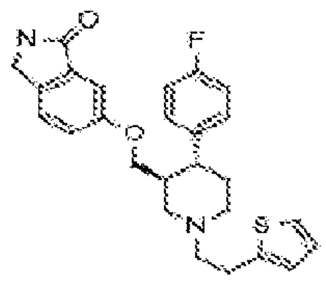
	B0737	(-)-6-{[trans, trans-4-(4-fluorophenyl)-2-methyl-1-[2-(oxn-4-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	466.59	467.3
	B0738	(-)-6-{[trans, trans-4-(4-fluorophenyl)-1-(3-fluoropropyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	414.49	415.2
	B0739	(-)-6-{[trans, trans-4-(4-fluorophenyl)-2-methyl-1-[2-(1,2-oxzol-4-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	449.52	450.2
	B0740	(-)-6-{[trans, trans-4-(4-fluorophenyl)-2-methyl-1-(3,3,3-trifluoropropyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	450.47	451.2
	B0741	(-)-6-{[trans, trans-4-(4-fluorophenyl)-2-methyl-1-[2-(thiophen-2-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	464.59	465.2
	B0742	(-)-6-{[trans, trans-4-(4-methoxyphenyl)-2-methyl-1-(prop-2-en-1-yl)piperidin-3-yl]methoxy}-2-(prop-2-en-1-yl)-2,3-dihydro-1H-isoindol-1-one	446.58	447.3
	B0743	(-)-6-{[trans, trans-1-[2-(2-fluorophenyl)ethyl]-4-(4-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	488.59	489.3
	B0744	(-)-6-{[trans-4-(4-fluorophenyl)-1-[2-(thiophen-2-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	450.57	451.2

Figure 1-Continued

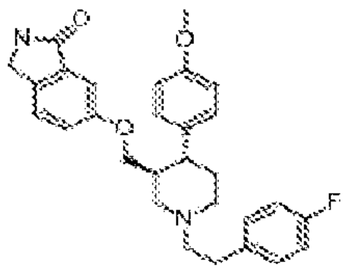
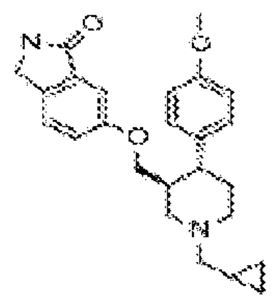
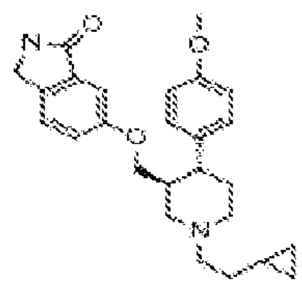
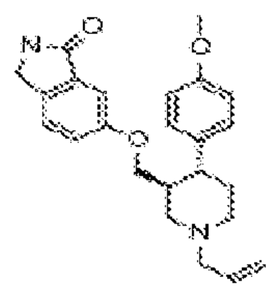
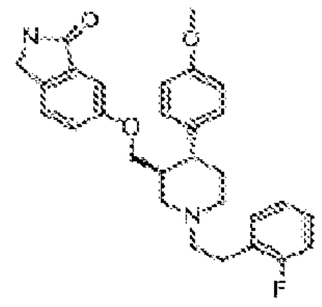
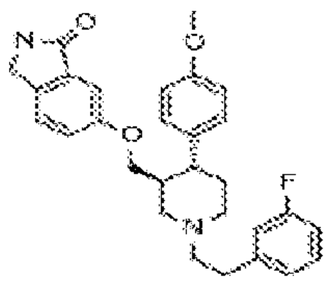
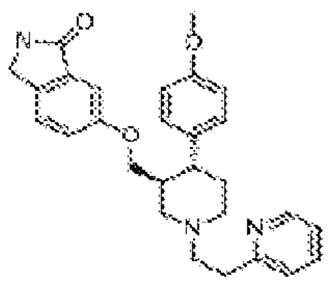
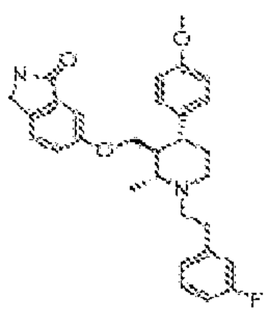
	B0745	6-{[trans-1-[2-(4-fluorophenyl)ethyl]-4-(4-methoxyphenyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	474.57	475.2
	B0746	6-{[trans-1-(cyclopropylmethyl)-4-(4-methoxyphenyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	406.52	407.2
	B0747	6-{[trans-1-(2-cyclopropylethyl)-4-(4-methoxyphenyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	420.54	421.3
	B0748	6-{[trans-4-(4-methoxyphenyl)-1-(prop-2-en-1-yl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	392.49	393.2
	B0749	6-{[trans-1-[2-(2-fluorophenyl)ethyl]-4-(4-methoxyphenyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	474.57	475.3
	B0750	6-{[trans-1-[2-(3-fluorophenyl)ethyl]-4-(4-methoxyphenyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	474.57	475.3
	B0751	6-{[trans-4-(4-methoxyphenyl)-1-[2-(pyridin-2-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	457.56	458.3
	B0752	(-)-6-{[trans-1-[2-(3-fluorophenyl)ethyl]-4-(4-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	488.59	489.3

Figure 1-Continued

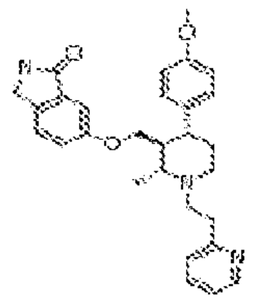
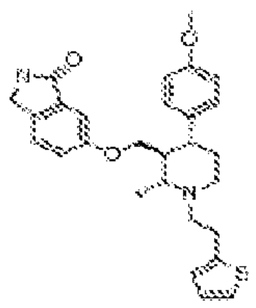
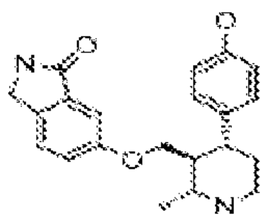
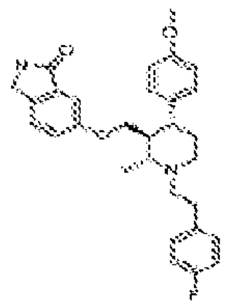
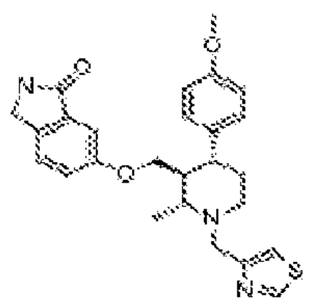
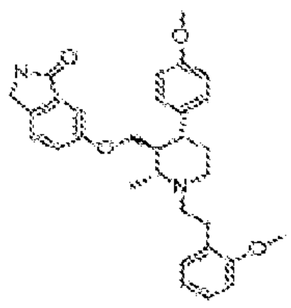
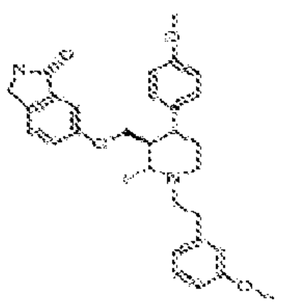
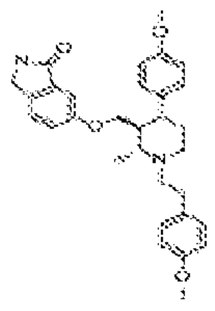
	B0753	(-)-6-{[trans-4-(4-methoxyphenyl)-2-methyl-1-[2-(pyridin-2-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	471.59	472.3
	B0754	(-)-6-{[trans, trans-4-(4-methoxyphenyl)-2-methyl-1-[2-(thiophen-2-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	476.63	477.2
	B0755	(-)-6-{[trans-4-(4-hydroxyphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	352.43	353.2
	B0756	(-)-6-{[trans, trans-1-[2-(4-fluorophenyl)ethyl]-4-(4-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	488.59	489.3
	B0757	(-)-6-{[trans, trans-4-(4-methoxyphenyl)-2-methyl-1-(1,3-thizol-4-ylmethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	463.59	464.2
	B0758	(-)-6-{[trans, trans-4-(4-methoxyphenyl)-1-[2-(2-methoxyphenyl)ethyl]-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	500.63	501.3
	B0759	(-)-6-{[trans, trans-4-(4-methoxyphenyl)-1-[2-(3-methoxyphenyl)ethyl]-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	500.63	501.3
	B0760	(-)-6-{[trans, trans-4-(4-methoxyphenyl)-1-[2-(4-methoxyphenyl)ethyl]-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	500.63	501.3

Figure 1-Continued

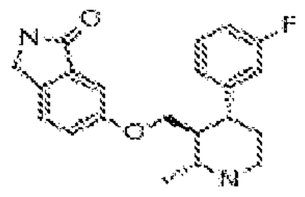
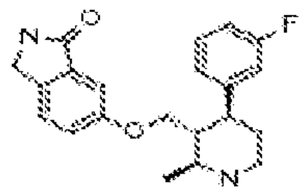
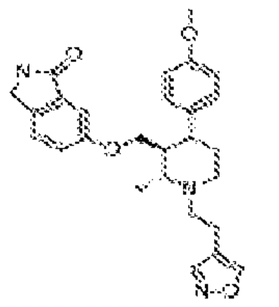
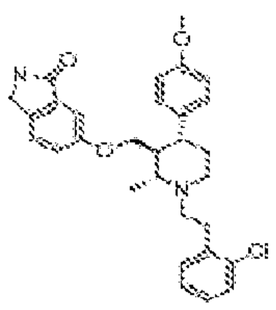
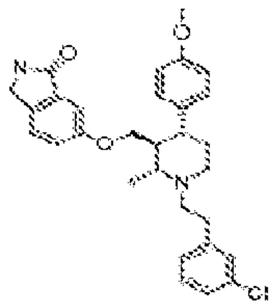
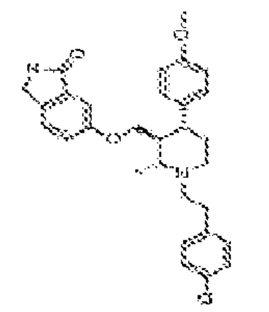
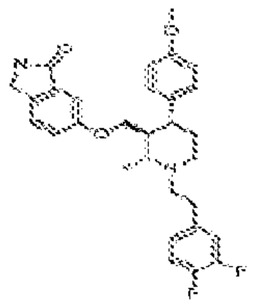
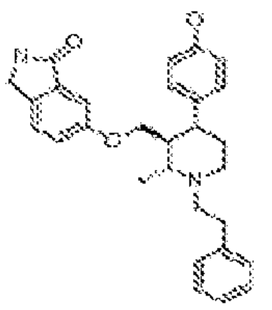
	B0761	(-)-6-{[trans, trans-4-(3-fluorophenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	354.42	355.2
	B0762	(+)-6-{[trans, trans-4-(3-fluorophenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	354.42	355.2
	B0763	(-)-6-{[trans, trans-4-(4-methoxyphenyl)-2-methyl-1-[2-(1,2-ox ol-4-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	461.55	462.3
	B0764	(-)-6-{[trans, trans-1-[2-(2-chlorophenyl)ethyl]-4-(4-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	505.05	505.2
	B0765	(-)-6-{[trans, trans-1-[2-(3-chlorophenyl)ethyl]-4-(4-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	505.05	505.2
	B0766	(-)-6-{[trans, trans-1-[2-(4-chlorophenyl)ethyl]-4-(4-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	505.05	505.3
	B0767	(-)-6-{[trans, trans-1-[2-(3,4-difluorophenyl)ethyl]-4-(4-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	506.58	507.3
	B0768	(-)-6-{[trans, trans-4-(4-hydroxyphenyl)-2-methyl-1-(2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	456.58	457.3

Figure 1-Continued

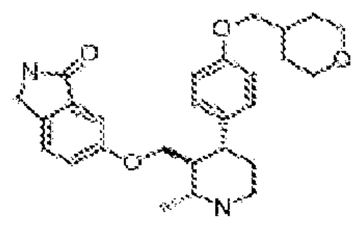
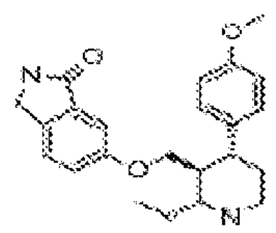
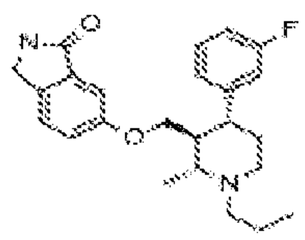
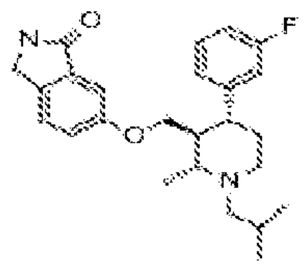
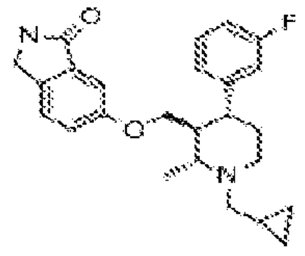
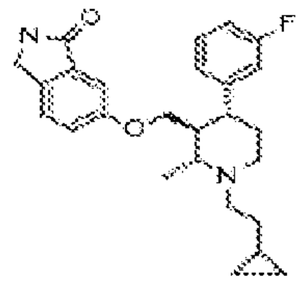
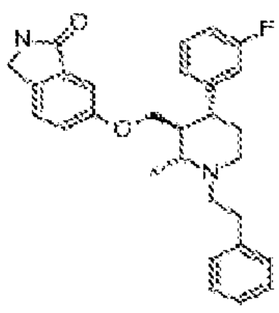
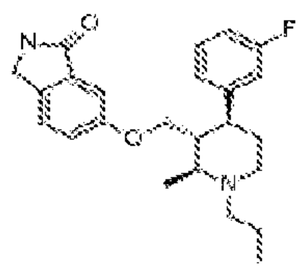
	B0769	(-)-6-{[trans, trans-2-methyl-4-[4-(oxn-4-ylmethoxy)phenyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	450.57	451.3
	B0770	(-)-6-{[trans, trans-2-ethyl-4-(4-methoxyphenyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	380.48	381.2
	B0771	(-)-6-{[trans, trans-4-(3-fluorophenyl)-2-methyl-1-propylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	396.5	397.2
	B0772	(-)-6-{[trans, trans-4-(3-fluorophenyl)-2-methyl-1-(2-methylpropyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	410.52	411.3
	B0773	(-)-6-{[trans, trans-1-(cyclopropylmethyl)-4-(3-fluorophenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	408.51	409.2
	B0774	(-)-6-{[trans, trans-1-(2-cyclopropylethyl)-4-(3-fluorophenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	422.54	423.3
	B0775	(-)-6-{[trans, trans-4-(3-fluorophenyl)-2-methyl-1-(2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	458.57	459.3
	B0776	(+)-6-{[trans, trans-4-(3-fluorophenyl)-2-methyl-1-propylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	396.5	397.2

Figure 1-Continued

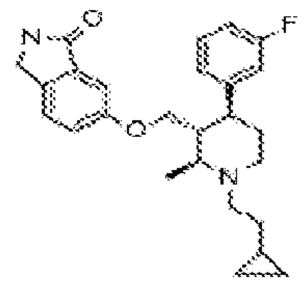
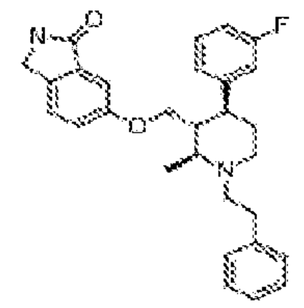
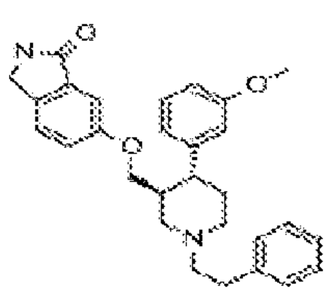
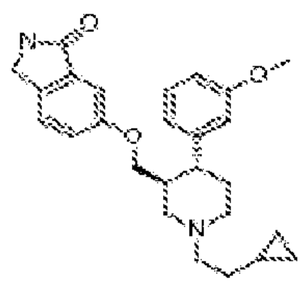
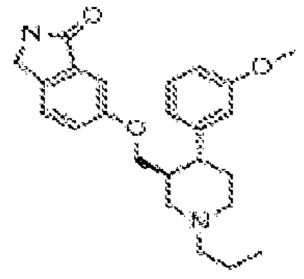
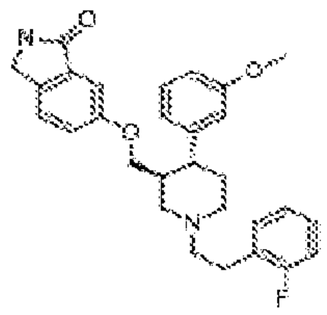
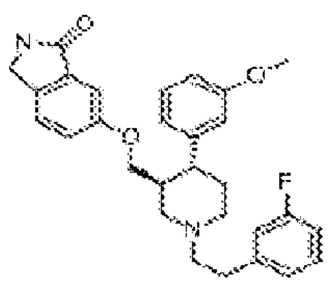
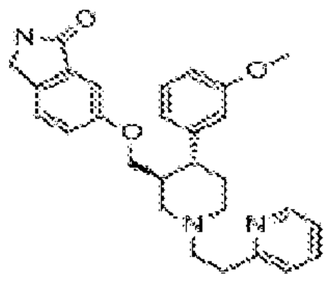
	B0777	(+)-6-{[trans, trans-1-(2-cyclopropylethyl)-4-(3-fluorophenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	422.53	423.3
	B0778	(+)-6-{[trans, trans-4-(3-fluorophenyl)-2-methyl-1-(2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	458.57	459.3
	B0779	6-{[trans-4-(3-methoxyphenyl)-1-(2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	456.58	457.3
	B0780	6-{[trans-1-(2-cyclopropylethyl)-4-(3-methoxyphenyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	420.54	421.3
	B0781	6-{[trans-4-(3-methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	394.51	395.2
	B0782	6-{[trans-1-[2-(2-fluorophenyl)ethyl]-4-(3-methoxyphenyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	474.57	475.3
	B0783	6-{[trans-1-[2-(3-fluorophenyl)ethyl]-4-(3-methoxyphenyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	474.57	475.3
	B0784	6-{[trans-4-(3-methoxyphenyl)-1-[2-(pyridin-2-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	457.56	458.3

Figure 1-Continued

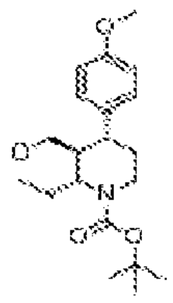
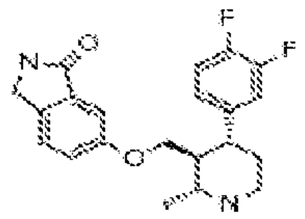
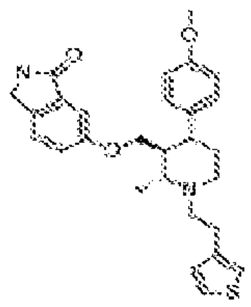
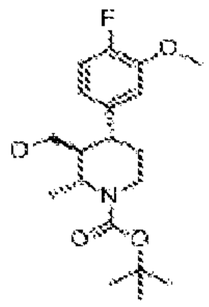
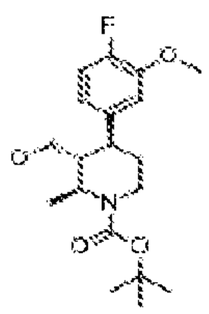
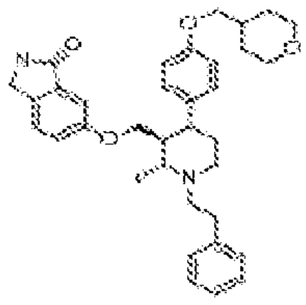
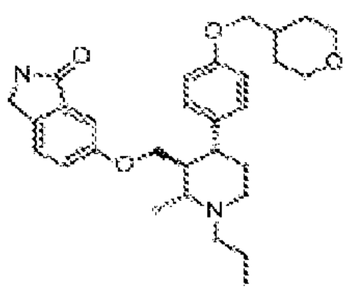
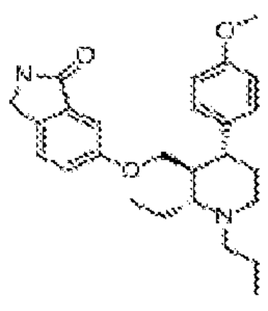
	B0785	(+)-tert-butyl (trans, trans)-2-ethyl-3-(hydroxymethyl)-4-(4-methoxyphenyl)piperidine-1-carboxylate	349.46	294.2
	B0786	(-)-6-{[trans, trans-4-(3,4-difluorophenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	372.41	373.2
	B0787	(-)-6-{[trans, trans-4-(4-methoxyphenyl)-2-methyl-1-[2-(thiophen-3-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	476.63	477.2
	B0788	(-)-tert-butyl (trans, trans)-4-(4-fluoro-3-methoxyphenyl)-3-(hydroxymethyl)-2-methylpiperidine-1-carboxylate	353.43	298.1
	B0789	(+)-tert-butyl (trans, trans)-4-(4-fluoro-3-methoxyphenyl)-3-(hydroxymethyl)-2-methylpiperidine-1-carboxylate	353.43	298.1
	B0790	(-)-6-{[trans, trans-2-methyl-4-[4-(oxn-4-ylmethoxy)phenyl]-1-(2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	554.72	555.4
	B0791	(-)-6-{[trans, trans-2-methyl-4-[4-(oxn-4-ylmethoxy)phenyl]-1-propylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	492.65	493.3
	B0792	(-)-6-{[trans, trans-2-ethyl-4-(4-methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	422.56	423.3

Figure 1-Continued

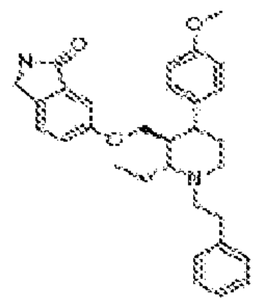
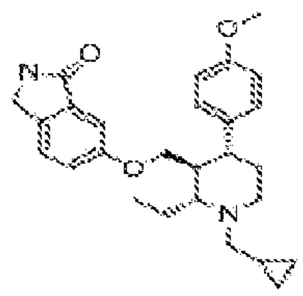
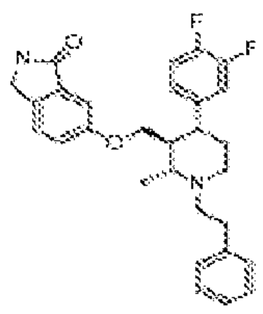
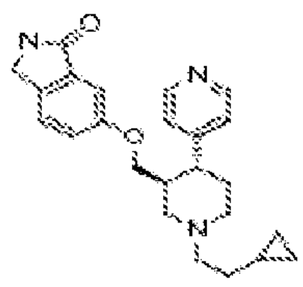
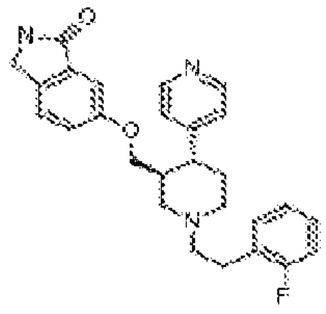
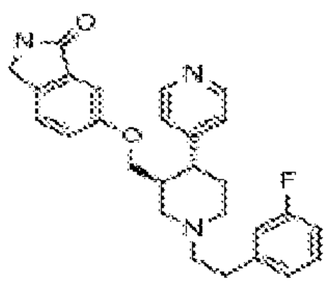
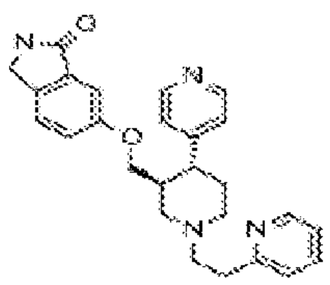
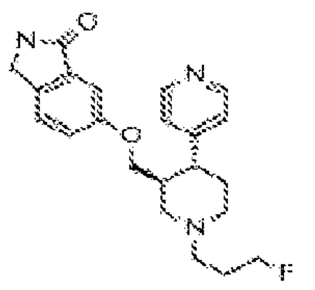
	B0793	(-)-6-{[trans, trans-2-ethyl-4-(4-methoxyphenyl)-1-(2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	484.63	485.3
	B0794	(-)-6-{[trans, trans-1-(cyclopropylmethyl)-2-ethyl-4-(4-methoxyphenyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	434.57	435.3
	B0795	(-)-6-{[trans, trans-4-(3,4-difluorophenyl)-2-methyl-1-(2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	476.56	477.3
	B0796	6-{[trans-1-(2-cyclopropylethyl)-4-(pyridin-4-yl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	391.51	392.3
	B0797	6-{[trans-1-[2-(2-fluorophenyl)ethyl]-4-(pyridin-4-yl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	445.53	446.2
	B0798	6-{[trans-1-[2-(3-fluorophenyl)ethyl]-4-(pyridin-4-yl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	445.53	446.2
	B0799	6-{[trans-1-[2-(pyridin-2-yl)ethyl]-4-(pyridin-4-yl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	428.53	429.2
	B0800	6-{[trans-1-(3-fluoropropyl)-4-(pyridin-4-yl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	383.46	384.2

Figure 1-Continued

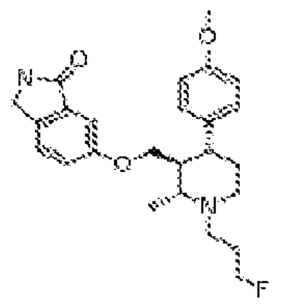
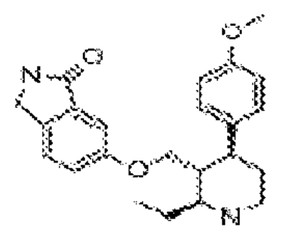
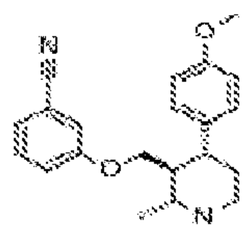
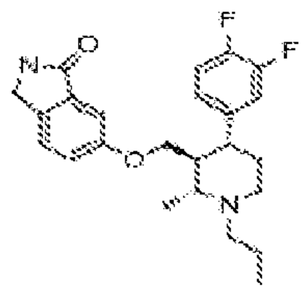
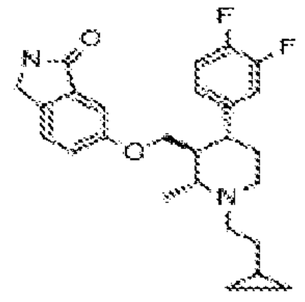
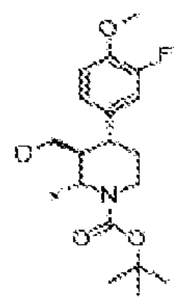
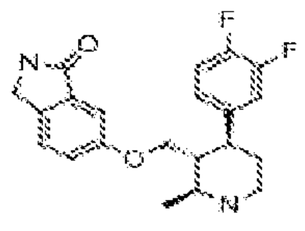
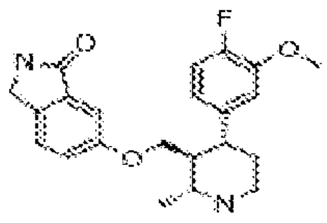
	B0801	(-)-6-{[trans, trans-1-(3-fluoropropyl)-4-(4-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	426.52	427.3
	B0802	(+)-6-{[trans, trans-2-ethyl-4-(4-methoxyphenyl)piperidin-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	380.48	381.2
	B0803	(-)-3-{[(trans)-4-(4-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}benzonitrile	336.43	337.2
	B0804	(-)-6-{[trans, trans-4-(3,4-difluorophenyl)-2-methyl-1-propylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	414.49	415.2
	B0805	(-)-6-{[trans, trans-1-(2-cyclopropylethyl)-4-(3,4-difluorophenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	440.53	441.2
	B0806	(+)-tert-butyl (trans, trans)-4-(3-fluoro-4-methoxyphenyl)-3-(hydroxymethyl)-2-methylpiperidine-1-carboxylate	353.43	376
	B0807	(+)-6-{[trans, trans-4-(3,4-difluorophenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	372.41	373.2
	B0808	(-)-6-{[trans, trans-4-(4-fluoro-3-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	384.44	385.2

Figure 1-Continued

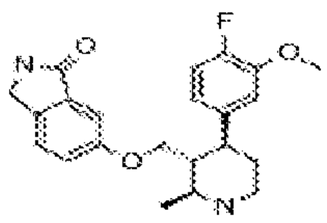
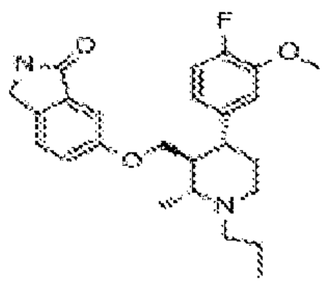
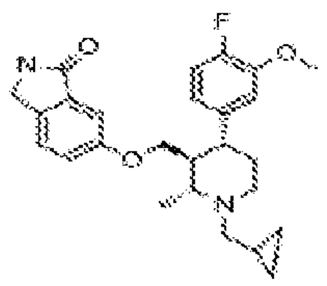
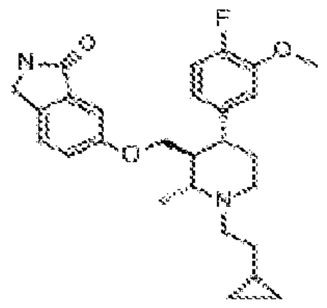
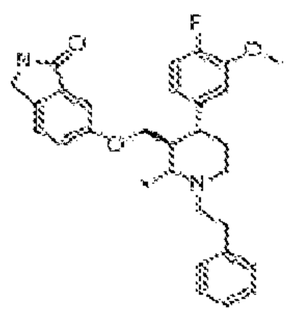
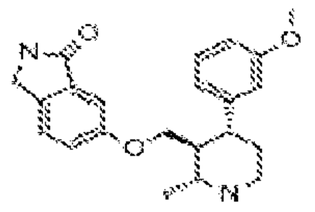
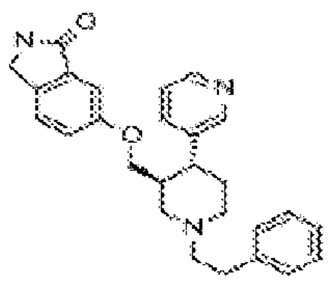
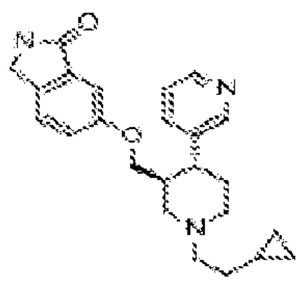
	B0809	(+)-6-{[trans, trans-4-(4-fluoro-3-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	384.44	385.2
	B0810	(-)-6-{[trans, trans-4-(4-fluoro-3-methoxyphenyl)-2-methyl-1-propylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	426.52	427.3
	B0811	(-)-6-{[trans, trans-1-(cyclopropylmethyl)-4-(4-fluoro-3-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	438.53	439.2
	B0812	(-)-6-{[trans, trans-1-(2-cyclopropylethyl)-4-(4-fluoro-3-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	452.56	453.3
	B0813	(-)-6-{[trans, trans-4-(4-fluoro-3-methoxyphenyl)-2-methyl-1-(2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	488.59	489.3
	B0814	(-)-6-{[trans, trans-4-(3-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	366.45	367.2
	B0815	6-{[trans-1-(2-phenylethyl)-4-(pyridin-3-yl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	427.54	428.3
	B0816	6-{[trans-1-(2-cyclopropylethyl)-4-(pyridin-3-yl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	391.51	392.2

Figure 1-Continued

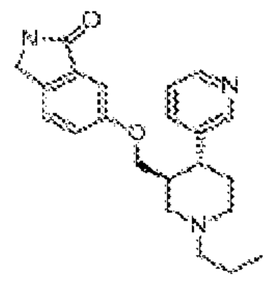
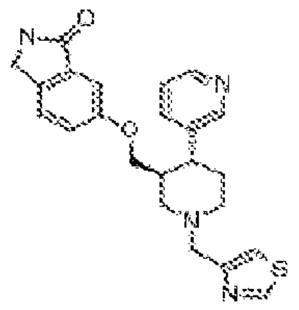
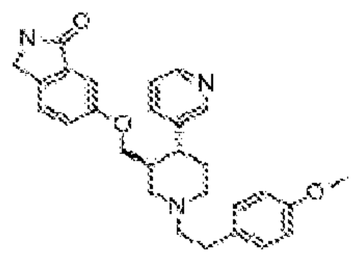
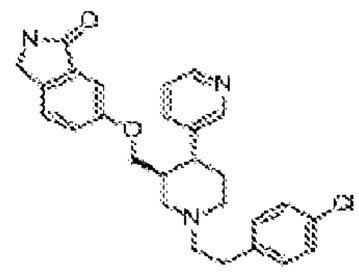
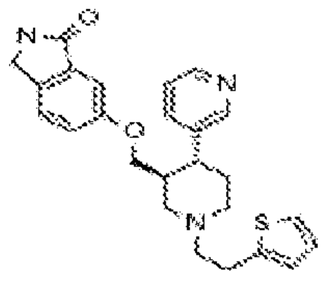
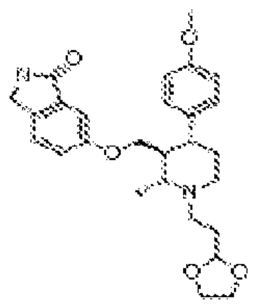
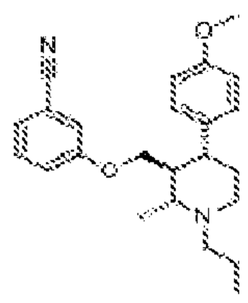
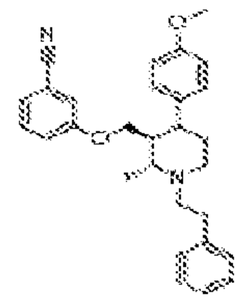
	B0817	6-{[trans-1-propyl-4-(pyridin-3-yl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	365.47	366.2
	B0818	6-{[trans-4-(pyridin-3-yl)-1-(1,3-thizol-4-ylmethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	420.53	421.1
	B0819	6-{[trans-1-[2-(4-methoxyphenyl)ethyl]-4-(pyridin-3-yl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	457.56	458.3
	B0820	6-{[trans-1-[2-(4-chlorophenyl)ethyl]-4-(pyridin-3-yl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	461.98	462.2
	B0821	6-{[trans-4-(pyridin-3-yl)-1-[2-(thiophen-2-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	433.57	434.2
	B0822	(-)-6-{[trans, trans-1-[2-(1,3-dioxolan-2-yl)ethyl]-4-(4-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	466.57	467.3
	B0823	(-)-3-{[trans, trans-4-(4-methoxyphenyl)-2-methyl-1-propylpiperidin-3-yl]methoxy}benzonitrile	378.51	379.3
	B0824	(-)-3-{[trans, trans-4-(4-methoxyphenyl)-2-methyl-1-(2-phenylethyl)piperidin-3-yl]methoxy}benzonitrile	440.58	441.3

Figure 1-Continued

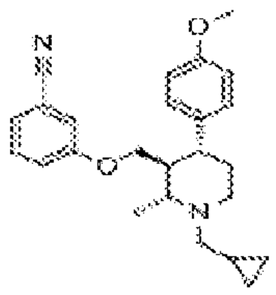
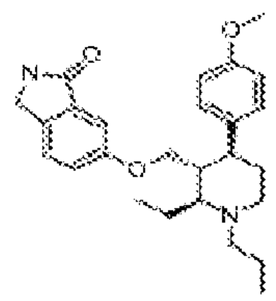
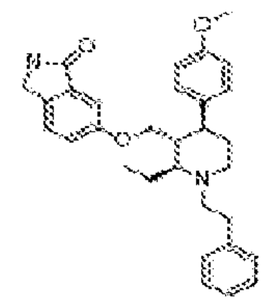
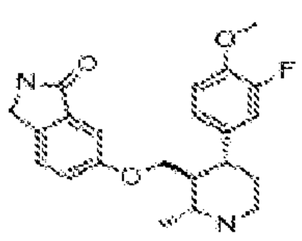
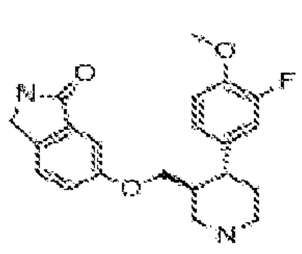
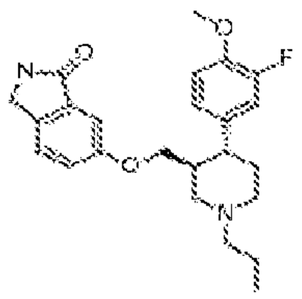
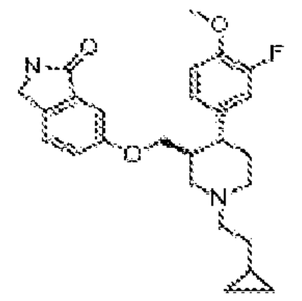
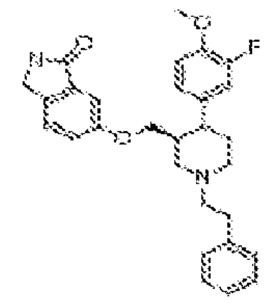
	B0825	(-)-3-{[trans, trans-1-(cyclopropylmethyl)-4-(4-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}benzonitrile	390.52	391.2
	B0826	(+)-6-{[trans, trans-2-ethyl-4-(4-methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	422.56	423.3
	B0827	(+)-6-{[trans, trans-2-ethyl-4-(4-methoxyphenyl)-1-(2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	484.63	485.3
	B0828	(-)-6-{[trans, trans-4-(3-fluoro-4-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	384.44	385.2
	B0829	6-{[trans-4-(3-fluoro-4-methoxyphenyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	370.42	371.2
	B0830	6-{[trans-4-(3-fluoro-4-methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	412.5	413.2
	B0831	6-{[trans-1-(2-cyclopropylethyl)-4-(3-fluoro-4-methoxyphenyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	438.53	439.3
	B0832	6-{[trans-4-(3-fluoro-4-methoxyphenyl)-1-(2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	474.57	475.3

Figure 1-Continued

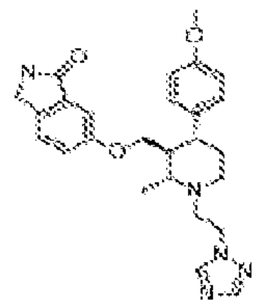
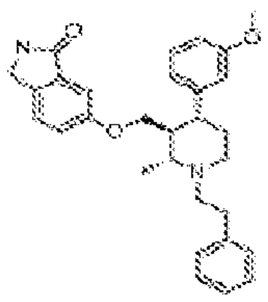
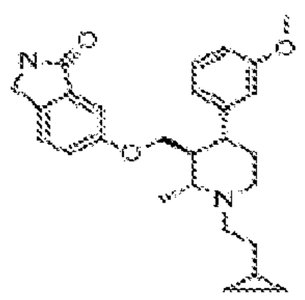
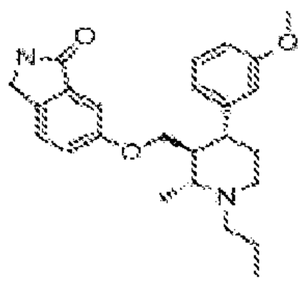
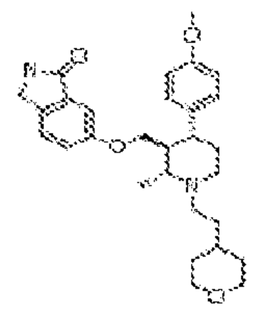
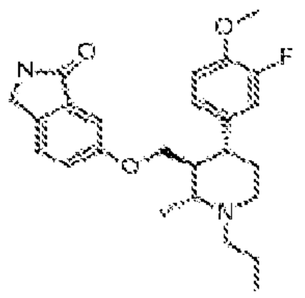
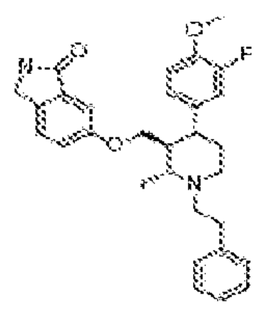
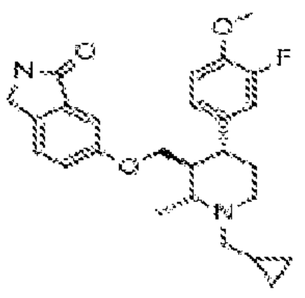
	B0833	(-)-6-{[trans-4-(4-methoxyphenyl)-2-methyl-1-[2-(1H-1,2,4-trizol-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	461.56	462.3
	B0834	(-)- 6-{[trans, trans-4-(3-methoxyphenyl)-2-methyl-1-(2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	470.6	471.3
	B0835	(-)-6-{[trans, trans-1-(2-cyclopropylethyl)-4-(3-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	434.57	435.3
	B0836	(-)-6-{[trans, trans-4-(3-methoxyphenyl)-2-methyl-1-propylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	408.53	409.3
	B0837	(-)-6-{[trans, trans-4-(4-methoxyphenyl)-2-methyl-1-[2-(oxn-4-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	478.62	479.3
	B0838	(-)-6-{[trans, trans-4-(3-fluoro-4-methoxyphenyl)-2-methyl-1-propylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	426.52	427.2
	B0839	(-)-6-{[trans, trans-4-(3-fluoro-4-methoxyphenyl)-2-methyl-1-(2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	488.59	489.3
	B0840	(-)-6-{[trans, trans-1-(cyclopropylmethyl)-4-(3-fluoro-4-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	438.53	439.3

Figure 1-Continued

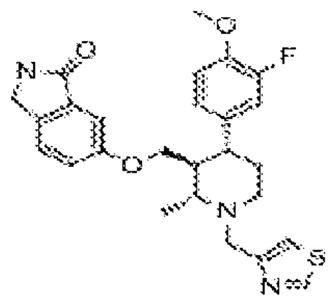
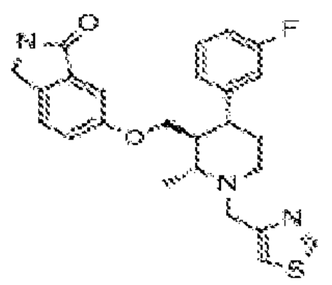
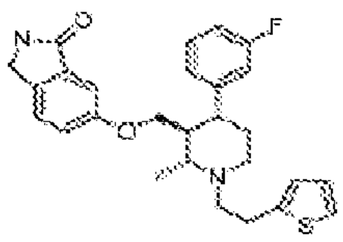
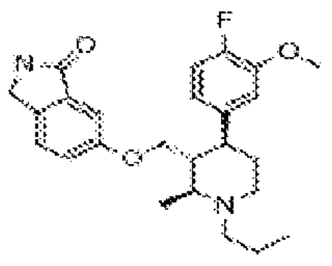
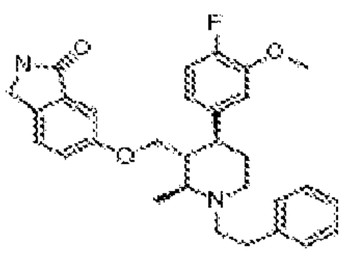
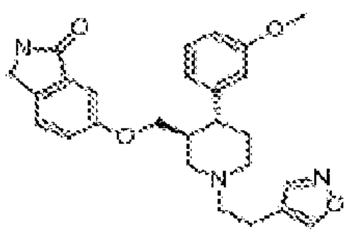
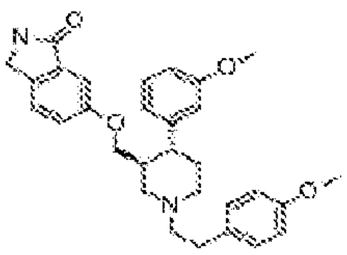
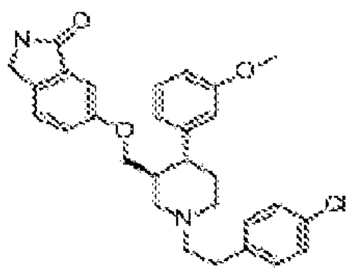
	B0841	(-)-6-{[trans, trans-4-(3-fluoro-4-methoxyphenyl)-2-methyl-1-(1,3-thizol-4-ylmethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	481.58	482.2
	B0842	(-)-6-{[trans, trans-4-(3-fluorophenyl)-2-methyl-1-(1,3-thizol-4-ylmethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	451.56	452.2
	B0843	(-)-6-{[trans, trans-4-(3-fluorophenyl)-2-methyl-1-[2-(thiophen-2-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	464.59	465.2
	B0844	(+)-6-{[trans, trans-4-(4-fluoro-3-methoxyphenyl)-2-methyl-1-propylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	426.52	427.3
	B0845	(+)-6-{[trans, trans-4-(4-fluoro-3-methoxyphenyl)-2-methyl-1-(2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	488.59	489.3
	B0846	6-{[trans-4-(3-methoxyphenyl)-1-[2-(1,2-oxazol-4-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	447.53	448.3
	B0847	6-{[trans-4-(3-methoxyphenyl)-1-[2-(4-methoxyphenyl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	486.6	487.3
	B0848	6-{[trans-1-[2-(4-chlorophenyl)ethyl]-4-(3-methoxyphenyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	491.02	491.2

Figure 1-Continued

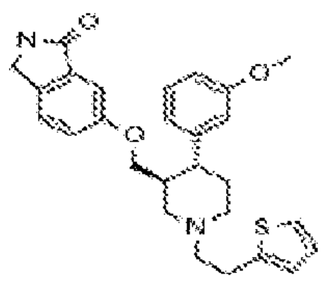
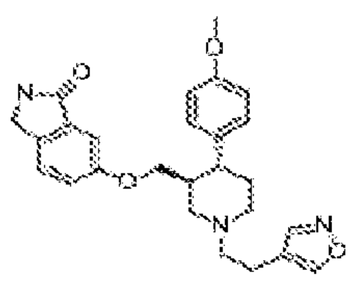
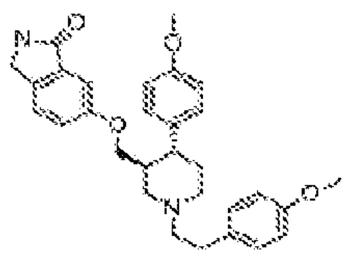
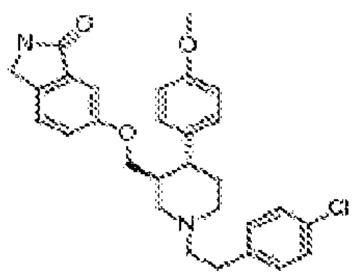
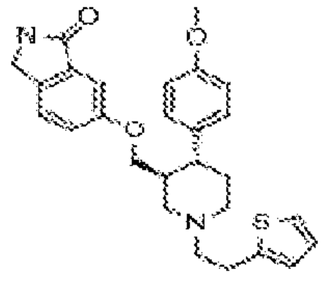
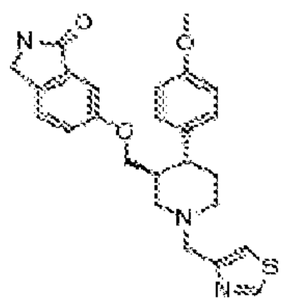
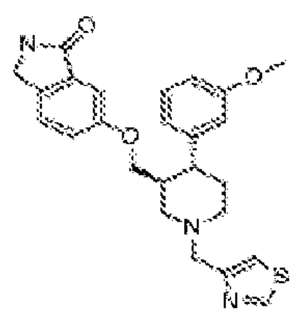
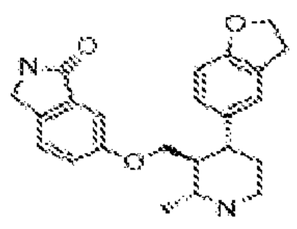
	B0849	6-{[trans-4-(3-methoxyphenyl)-1-[2-(thiophen-2-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	462.6	463.2
	B0850	6-{[trans-4-(4-methoxyphenyl)-1-[2-(1,2-oxzol-4-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	447.53	448.3
	B0851	6-{[trans-4-(4-methoxyphenyl)-1-[2-(4-methoxyphenyl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	486.6	487.3
	B0852	6-{[trans-1-[2-(4-chlorophenyl)ethyl]-4-(4-methoxyphenyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	491.02	491.2
	B0853	6-{[trans-4-(4-methoxyphenyl)-1-[2-(thiophen-2-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	462.6	463.2
	B0854	6-{[trans-4-(4-methoxyphenyl)-1-(1,3-thizol-4-ylmethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	449.57	450.2
	B0855	6-{[trans-4-(3-methoxyphenyl)-1-(1,3-thizol-4-ylmethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	449.57	450.2
	B0856	(-)6-{[trans, trans-4-(2,3-dihydro-1-benzofuran-5-yl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	378.46	379.2

Figure 1-Continued

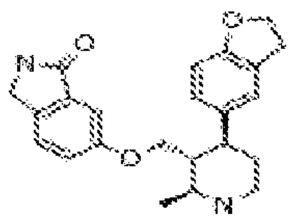
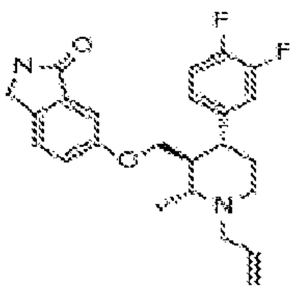
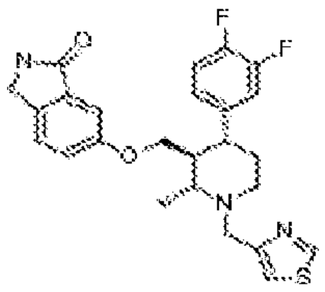
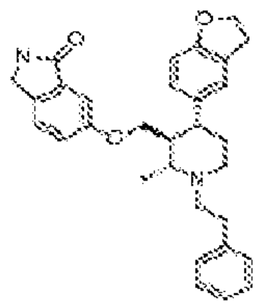
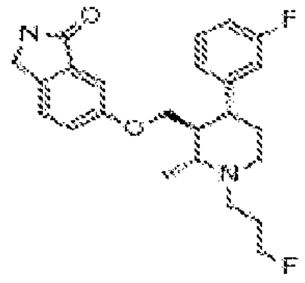
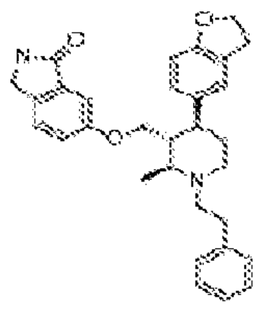
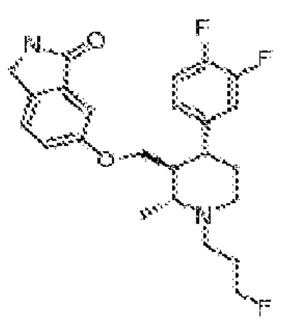
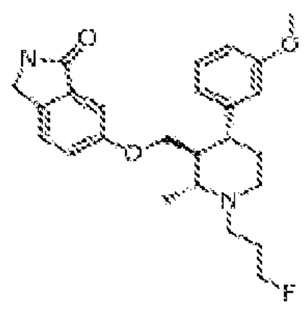
	B0857	(+)-6-{[trans, trans-4-(2,3-dihydro-1-benzofuran-5-yl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	378.46	379.2
	B0858	(-)-6-{[trans, trans-4-(3,4-difluorophenyl)-2-methyl-1-(prop-2-en-1-yl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	412.47	413.2
	B0859	(-)-6-{[trans, trans-4-(3,4-difluorophenyl)-2-methyl-1-(1,3-thizol-4-ylmethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	469.55	470.2
	B0860	(-)-6-{[trans, trans-4-(2,3-dihydro-1-benzofuran-5-yl)-2-methyl-1-(2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	482.61	483.3
	B0861	(-)-6-{[trans, trans-4-(3-fluorophenyl)-1-(3-fluoropropyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	414.49	415.2
	B0862	(-)-6-{[trans, trans-4-(2,3-dihydro-1-benzofuran-5-yl)-2-methyl-1-(2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	482.61	483.3
	B0863	(-)-6-{[trans, trans-4-(3,4-difluorophenyl)-1-(3-fluoropropyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	432.48	433.3
	B0864	(-)-6-{[trans, trans-1-(3-fluoropropyl)-4-(3-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	426.52	427.3

Figure 1-Continued

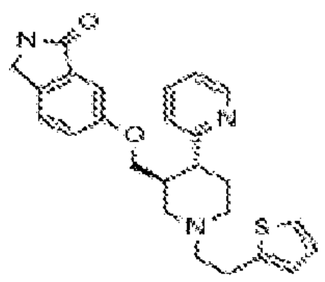
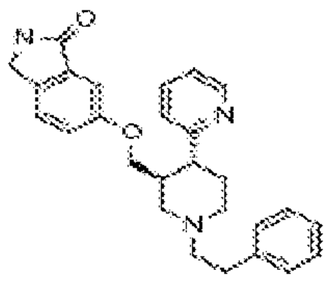
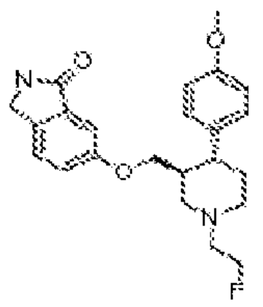
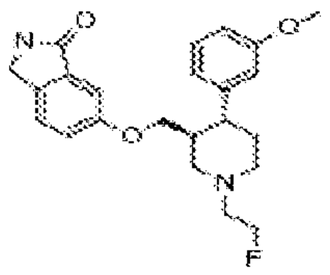
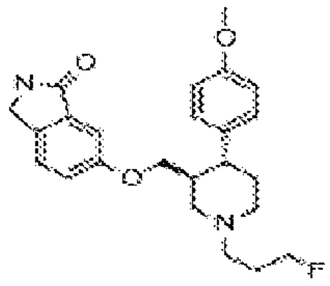
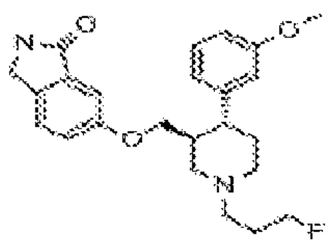
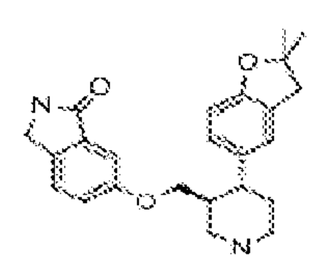
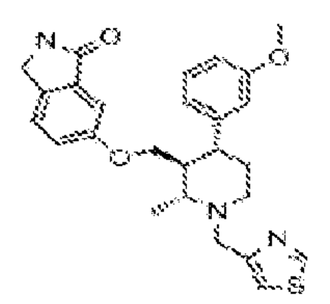
	B0865	6-{[trans-4-(pyridin-2-yl)-1-[2-(thiophen-2-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	433.57	434.2
	B0866	6-{[trans-1-(2-phenylethyl)-4-(pyridin-2-yl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	427.54	428.3
	B0867	6-{[trans-1-(2-fluoroethyl)-4-(4-methoxyphenyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	398.47	399.2
	B0868	6-{[trans-1-(2-fluoroethyl)-4-(3-methoxyphenyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	398.47	399.2
	B0869	6-{[trans-1-(3-fluoropropyl)-4-(4-methoxyphenyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	412.5	413.2
	B0870	6-{[trans-1-(3-fluoropropyl)-4-(3-methoxyphenyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	412.5	413.2
	B0871	6-{[(trans)-4-(2,2-dimethyl-2,3-dihydro-1-benzofuran-5-yl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	392.49	393.2
	B0872	(-)-6-{[trans, trans-4-(3-methoxyphenyl)-2-methyl-1-(1,3-thizol-4-ylmethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	463.59	464.2

Figure 1-Continued

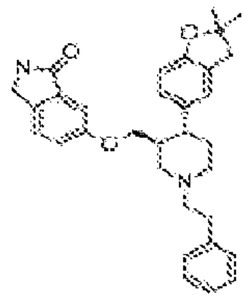
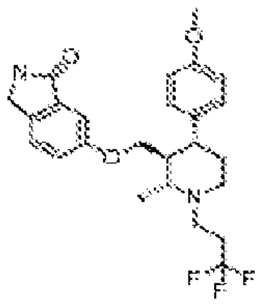
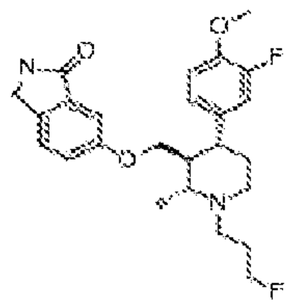
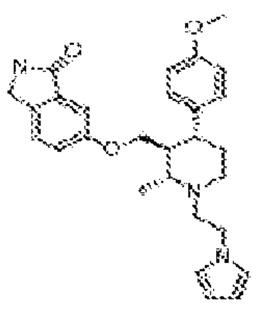
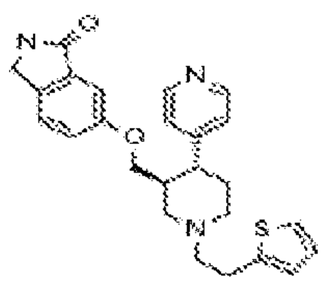
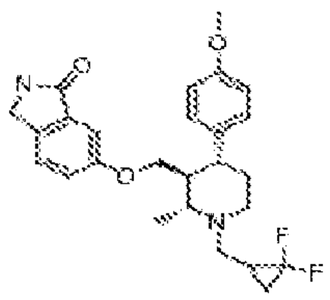
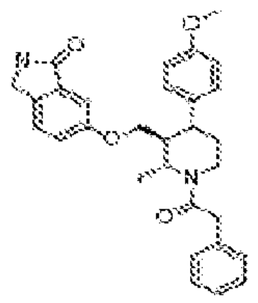
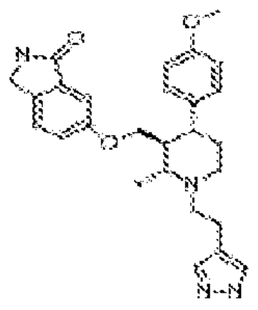
	B0873	6-{[(trans)-4-(2,2-dimethyl-2,3-dihydro-1-benzofuran-5-yl)-1-(2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	496.64	497.3
	B0874	(-)-6-{[trans, trans-4-(4-methoxyphenyl)-2-methyl-1-(3,3,3-trifluoropropyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	462.5	463.2
	B0875	(-)-6-{[trans, trans-4-(3-fluoro-4-methoxyphenyl)-1-(3-fluoropropyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	444.51	445.3
	B0876	(-)-6-{[trans, trans-4-(4-methoxyphenyl)-2-methyl-1-[2-(1H-pyrrol-1-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	459.58	460.3
	B0877	6-{[trans-4-(pyridin-4-yl)-1-[2-(thiophen-2-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	433.57	434.2
	B0878	(-)-6-{[trans, trans-1-[(2,2-difluorocyclopropyl)methyl]-4-(4-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	456.52	457.3
	B0879	(-)-6-{[trans, trans-4-(4-methoxyphenyl)-2-methyl-1-(2-phenylacetyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	484.59	485.3
	B0880	(-)-6-{[trans, trans-4-(4-methoxyphenyl)-2-methyl-1-[2-(1H-pyrrol-4-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	460.57	461.3

Figure 1-Continued

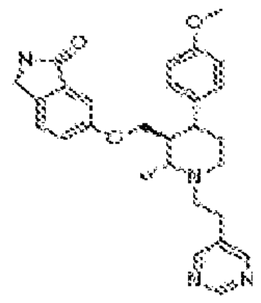
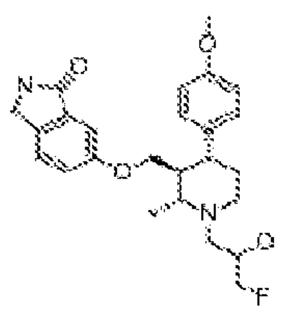
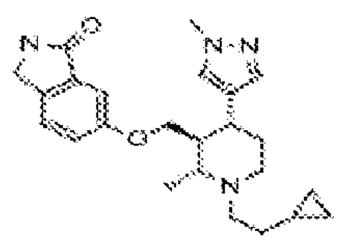
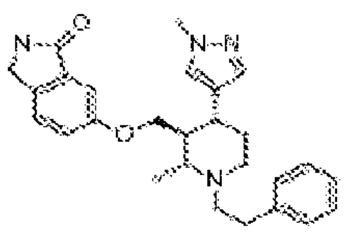
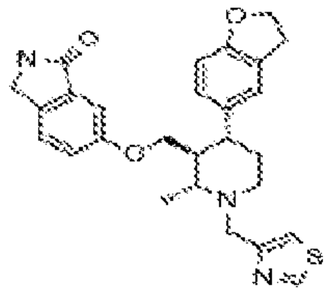
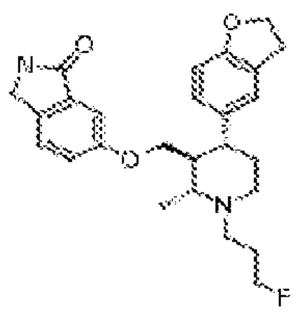
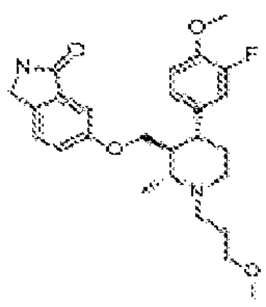
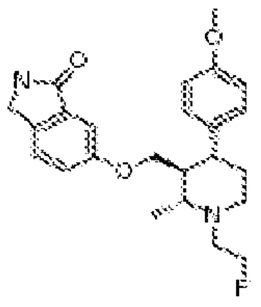
	B0881	(-)-6-{[trans, trans-4-(3-fluoro-4-methoxyphenyl)-2-methyl-1-[2-(pyrimidin-5-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	472.58	473.3
	B0882	(-)-6-{[trans, trans-1-(3-fluoro-2-hydroxypropyl)-4-(4-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	442.52	443.3
	B0883	6-{[(trans,trans)-1-(2-cyclopropylethyl)-2-methyl-4-(1-methyl-1H-pyrrol-4-yl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	408.54	409.1
	B0884	6-{[(trans, trans)-2-methyl-4-(1-methyl-1H-pyrrol-4-yl)-1-(2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	444.57	445.3
	B0885	(-)-6-{[trans, trans-4-(2,3-dihydro-1-benzofuran-5-yl)-2-methyl-1-(1,3-thi ol-4-ylmethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	475.6	476.2
	B0886	(-)-6-{[trans, trans-4-(2,3-dihydro-1-benzofuran-5-yl)-1-(3-fluoropropyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	438.53	439.3
	B0887	(-)-6-{[trans, trans-4-(3-fluoro-4-methoxyphenyl)-1-(3-methoxypropyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	456.55	457.3
	B0888	(-)-6-{[trans, trans-1-(2-fluoroethyl)-4-(4-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	412.5	413.2

Figure 1-Continued

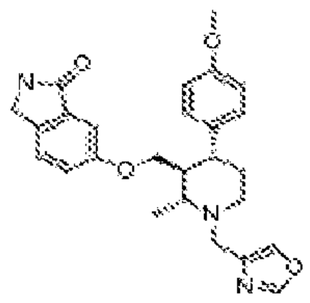
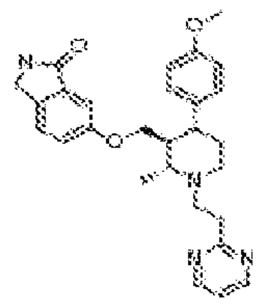
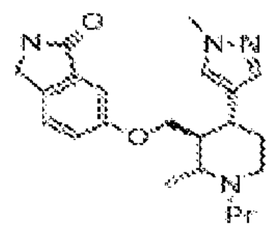
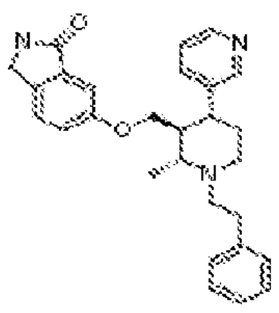
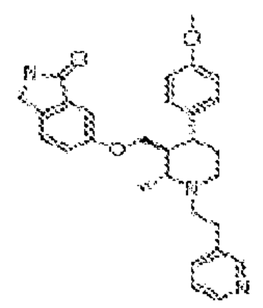
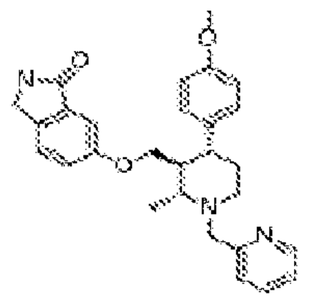
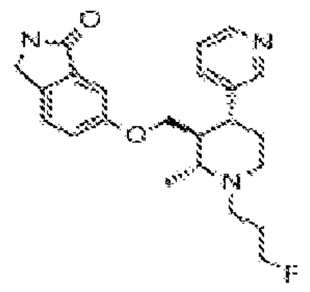
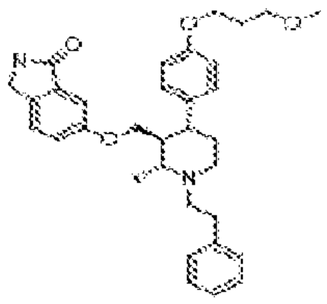
	B0889	(-)-6-{[trans, trans-4-(4-methoxyphenyl)-2-methyl-1-(1,3-ox ol-4-ylmethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	447.53	448.3
	B0890	(-)-6-{[trans, trans-4-(4-methoxyphenyl)-2-methyl-1-[2-(pyrimidin-2-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	472.58	473.3
	B0891	6-{[(trans, trans)-2-methyl-4-(1-methyl-1H-pyrrol-4-yl)-1-propylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	382.5	383.3
	B0892	(-)-6-{[trans, trans-2-methyl-1-(2-phenylethyl)-4-(pyridin-3-yl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	441.56	442.2
	B0893	(-)-6-{[trans, trans-4-(4-methoxyphenyl)-2-methyl-1-[2-(pyridin-3-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	471.59	472.3
	B0894	(-)-6-{[trans, trans-4-(4-methoxyphenyl)-2-methyl-1-(pyridin-2-ylmethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	457.56	458.3
	B0895	(-)-6-{[trans, trans-1-(3-fluoropropyl)-2-methyl-4-(pyridin-3-yl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	397.49	398.2
	B0896	(-)-6-{[trans, trans-4-[4-(3-methoxypropoxy)phenyl]-2-methyl-1-(2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	528.68	529.3

Figure 1-Continued

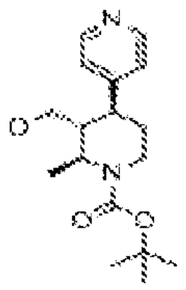
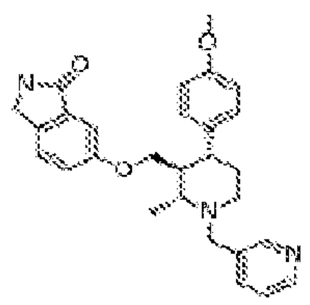
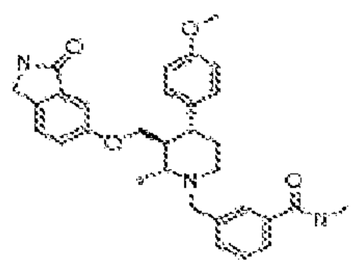
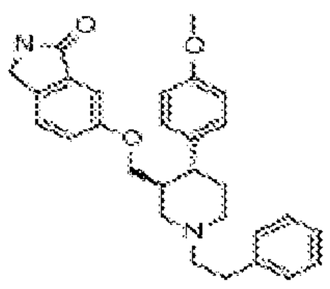
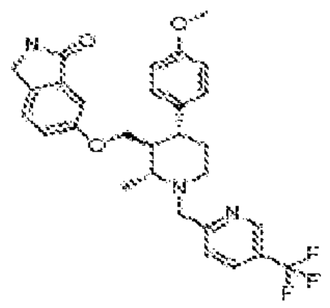
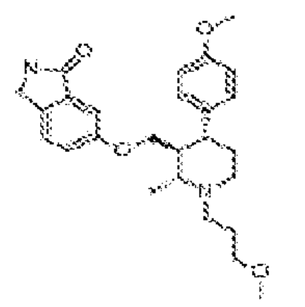
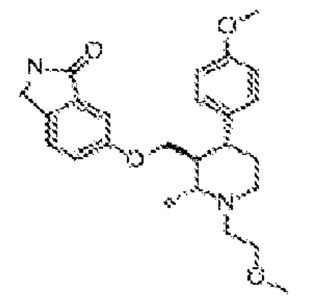
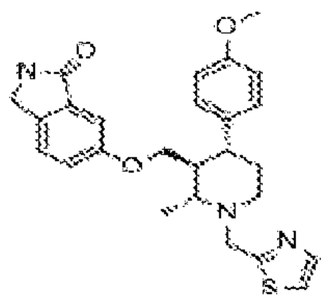
	B0897	(+)-tert-butyl (trans, trans)-3-(hydroxymethyl)-2-methyl-4-(pyridin-4-yl)piperidine-1-carboxylate	306.4	307.2
	B0898	(-)-6-{[trans, trans-4-(4-methoxyphenyl)-2-methyl-1-(pyridin-3-ylmethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	457.56	458.3
	B0899	(-)-3-{[trans, trans-4-(4-methoxyphenyl)-2-methyl-3-{[(3-oxo-2,3-dihydro-1H-isoindol-5-yl)oxy]methyl}piperidin-1-yl]methyl}-N-methylbenzamide	513.63	514.3
	B0900	(-)-6-{[trans, trans-4-(4-methoxyphenyl)-1-(2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	456.58	457.3
	B0901	(-)-6-{[trans, trans-4-(4-methoxyphenyl)-2-methyl-1-{[5-(trifluoromethyl)pyridin-2-yl]methyl}piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	525.56	526.3
	B0902	(-)-6-{[trans, trans-4-(4-methoxyphenyl)-1-(3-methoxypropyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	438.56	439.3
	B0903	(-)-6-{[trans, trans-1-(2-methoxyethyl)-4-(4-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	424.53	425.3
	B0904	(-)-6-{[trans, trans-4-(4-methoxyphenyl)-2-methyl-1-(1,3-thizol-2-ylmethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	463.59	464.2

Figure 1-Continued

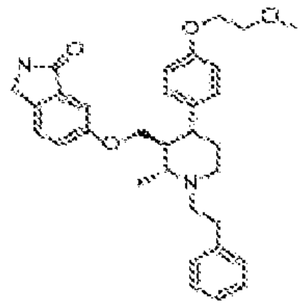
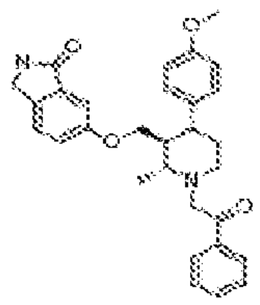
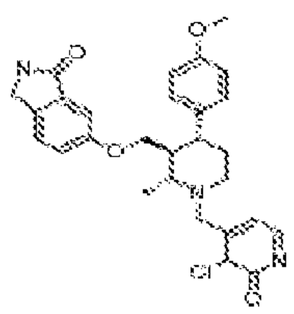
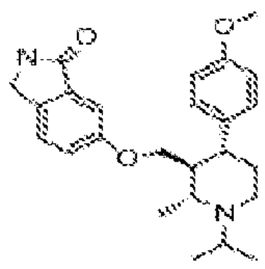
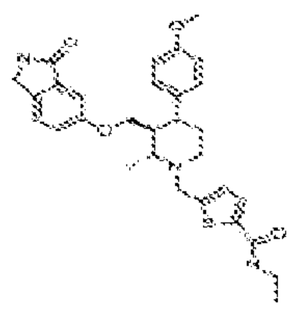
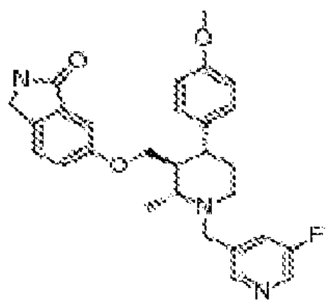
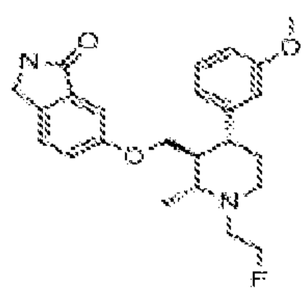
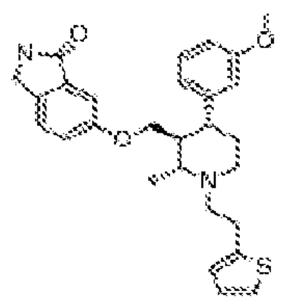
	B0905	(-)-6-{[trans, trans-4-[4-(2-methoxyethoxy)phenyl]-2-methyl-1-(2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	514.66	515.3
	B0906	(-)-6-{[trans, trans-4-(4-methoxyphenyl)-2-methyl-1-(2-oxo-2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	484.59	485
	B0907	(-)-6-{[trans, trans-1-[(3-chloro-2-oxo-2,3-dihydropyridin-4-yl)methyl]-4-(4-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	508.01	508.2
	B0908	6-{[(trans, trans-4-(4-methoxyphenyl)-2-methyl-1-(propn-2-yl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	408.53	409.3
	B0909	(-)-N-ethyl-5-{[trans, trans-4-(4-methoxyphenyl)-2-methyl-3-{[(3-oxo-2,3-dihydro-1H-isoindol-5-yl)oxy]methyl}piperidin-1-yl]methyl}thiophene-2-carboxamide	533.68	534.3
	B0910	(-)-6-{[trans, trans-1-[(5-fluoropyridin-3-yl)methyl]-4-(4-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	475.55	476.3
	B0911	(-)-6-{[trans, trans-1-(2-fluoroethyl)-4-(3-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	412.5	413.3
	B0912	(-)-6-{[trans, trans-4-(3-methoxyphenyl)-2-methyl-1-[2-(thiophen-2-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	476.63	477.3

Figure 1-Continued

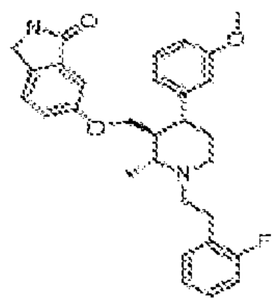
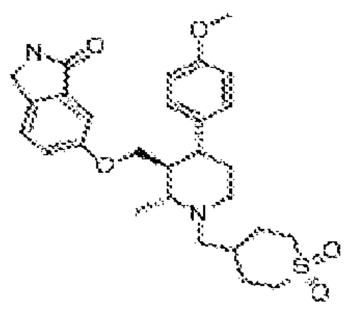
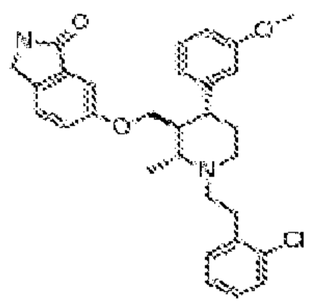
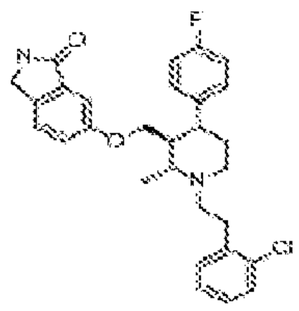
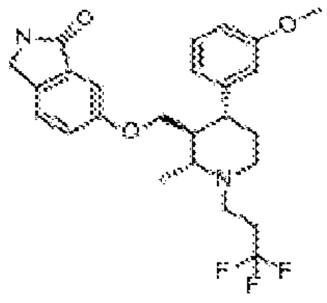
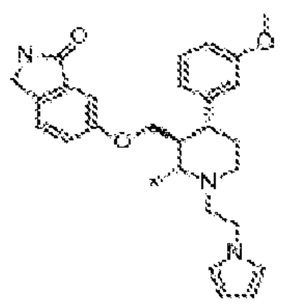
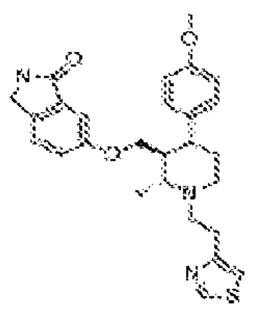
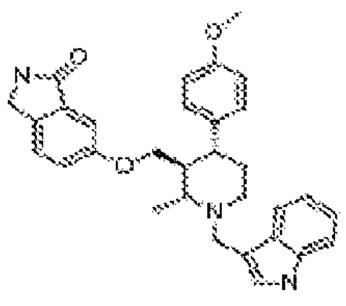
	B0913	(-)-6-{[trans, trans-1-[2-(2-fluorophenyl)ethyl]-4-(3-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	488.59	489.3
	B0914	(-)-4-{[trans, trans-4-(4-methoxyphenyl)-2-methyl-3-{[(3-oxo-2,3-dihydro-1H-isoindol-5-yl)oxy]methyl}piperidin-1-yl]methyl}-1λ^6-thine-1,1-dione	512.66	513.3
	B0915	(-)-6-{[trans, trans-1-[2-(2-chlorophenyl)ethyl]-4-(3-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	505.05	505.3
	B0916	(-)-6-{[trans, trans-1-[2-(2-chlorophenyl)ethyl]-4-(4-fluorophenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	493.01	493.3
	B0917	(-)-6-{[trans, trans-4-(3-methoxyphenyl)-2-methyl-1-(3,3,3-trifluoropropyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	462.5	463.2
	B0918	(-)-6-{[trans, trans-4-(3-methoxyphenyl)-2-methyl-1-[2-(1H-pyrrol-1-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	459.58	460.3
	B0919	(-)-6-{[trans, trans-4-(4-methoxyphenyl)-2-methyl-1-[2-(1,3-thizol-4-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	477.62	478.2
	B0920	(-)-6-{[trans, trans-1-(1H-indol-3-ylmethyl)-4-(4-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	495.61	496.3

Figure 1-Continued

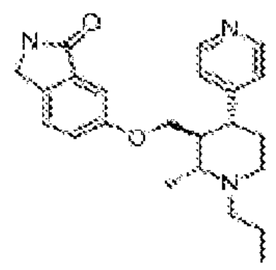
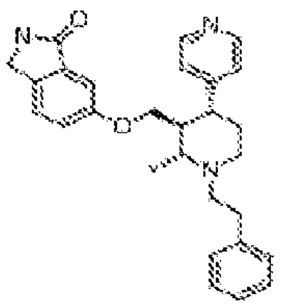
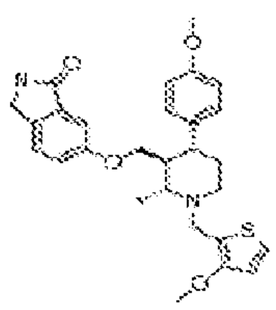
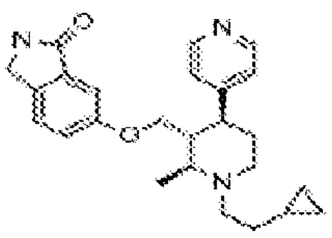
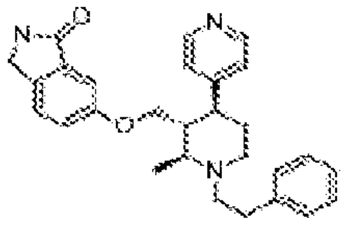
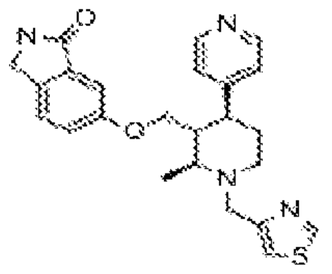
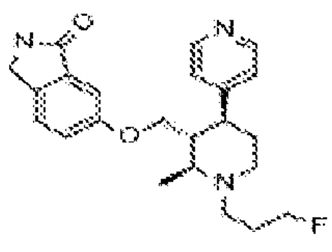
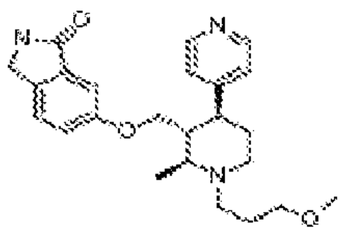
	B0921	(-)-6-{[trans, trans-2-methyl-1-propyl-4-(pyridin-4-yl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	379.5	380.3
	B0922	(-)-6-{[trans, trans-2-methyl-1-(2-phenylethyl)-4-(pyridin-4-yl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	441.56	442.3
	B0923	(-)-6-{[trans, trans-4-(4-methoxyphenyl)-1-[(3-methoxythiophen-2-yl)methyl]-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	492.63	493.2
	B0924	(+)-6-{[trans, trans-1-(2-cyclopropylethyl)-2-methyl-4-(pyridin-4-yl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	405.53	406.3
	B0925	(+)-6-{[trans, trans-2-methyl-1-(2-phenylethyl)-4-(pyridin-4-yl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	441.56	442.3
	B0926	(+)-6-{[trans, trans-2-methyl-4-(pyridin-4-yl)-1-(1,3-thiazol-4-ylmethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	434.55	435.2
	B0927	(+)-6-{[trans, trans-1-(3-fluoropropyl)-2-methyl-4-(pyridin-4-yl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	397.49	398.3
	B0928	(+)-6-{[trans, trans-1-(3-methoxypropyl)-2-methyl-4-(pyridin-4-yl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	409.52	410.3

Figure 1-Continued

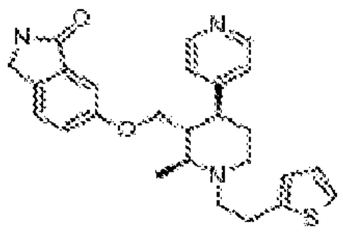
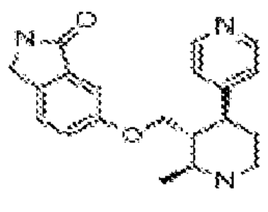
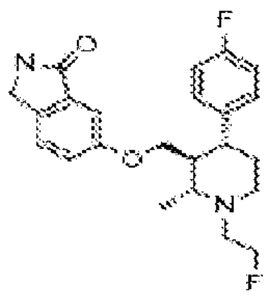
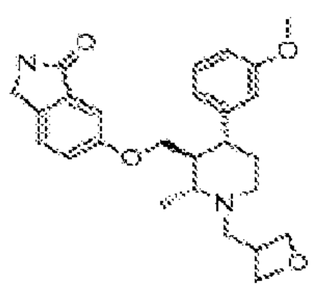
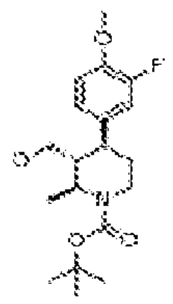
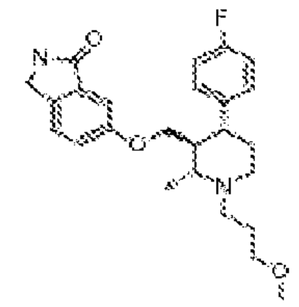
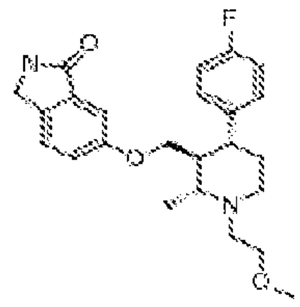
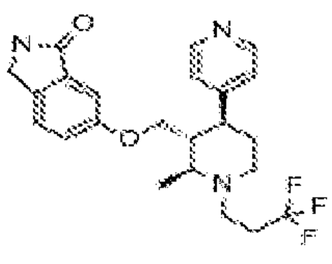
	B0929	(+)-6-{[trans, trans-2-methyl-4-(pyridin-4-yl)-1-[2-(thiophen-2-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	447.59	448.2
	B0930	(+)-6-{[trans, trans-2-methyl-4-(pyridin-4-yl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	337.42	338.2
	B0931	(-)-6-{[trans, trans-1-(2-fluoroethyl)-4-(4-fluorophenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	400.46	401.2
	B0932	(-)-6-{[trans, trans-4-(3-methoxyphenyl)-2-methyl-1-(oxetan-3-ylmethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	436.54	437.3
	B0933	(-)-tert-butyl (trans, trans)-4-(3-fluoro-4-methoxyphenyl)-3-(hydroxymethyl)-2-methylpiperidine-1-carboxylate	353.43	376
	B0934	(-)-6-{[trans, trans-4-(4-fluorophenyl)-1-(3-methoxypropyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	426.52	427.2
	B0935	(-)-6-{[trans, trans-4-(4-fluorophenyl)-1-(2-methoxyethyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	412.5	413.2
	B0936	(+)-6-{[trans, trans-2-methyl-4-(pyridin-4-yl)-1-(3,3,3-trifluoropropyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	433.47	434.3

Figure 1-Continued

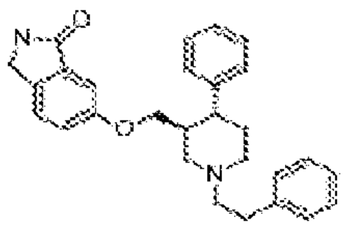
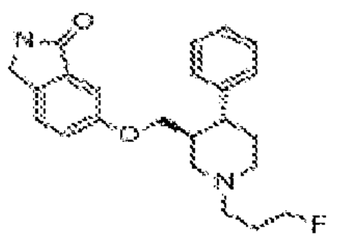
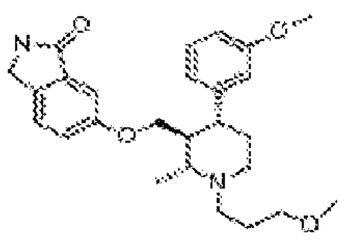
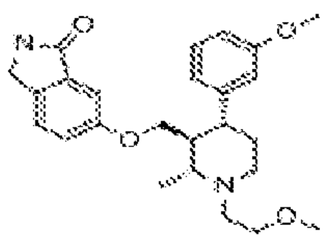
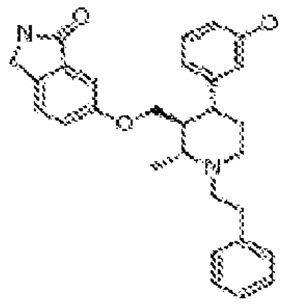
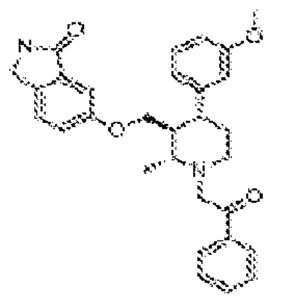
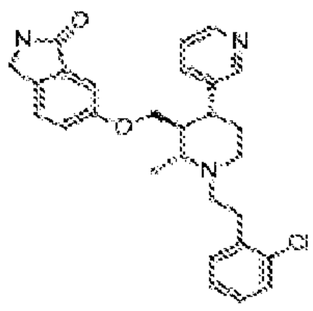
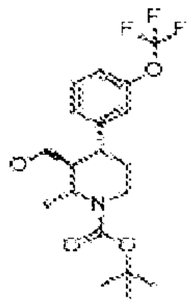
	B0937	(-)-6-{[trans, trans-4-phenyl-1-(2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	426.55	427.3
	B0938	(-)-6-{[trans, trans-1-(3-fluoropropyl)-4-phenylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	382.47	383.3
	B0939	(-)-6-{[trans, trans-4-(3-methoxyphenyl)-1-(3-methoxypropyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	438.56	439.3
	B0940	(-)-6-{[trans, trans-1-(2-methoxyethyl)-4-(3-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	424.53	425.3
	B0941	(-)-6-{[trans, trans-4-(3-hydroxyphenyl)-2-methyl-1-(2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	456.58	457.3
	B0942	(-)-6-{[trans, trans-4-(3-methoxyphenyl)-2-methyl-1-(2-oxo-2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	484.59	485.3
	B0943	(-)-6-{[trans, trans-1-[2-(2-chlorophenyl)ethyl]-2-methyl-4-(pyridin-3-yl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	476.01	476.3
	B0944	(-)-tert-butyl (trans, trans)-3-(hydroxymethyl)-2-methyl-4-[3-(trifluoromethoxy)phenyl]piperidine-1-carboxylate	389.41	334.1

Figure 1-Continued

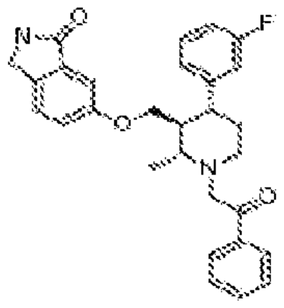
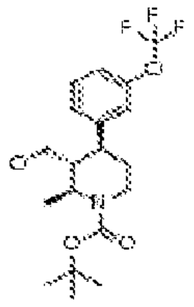
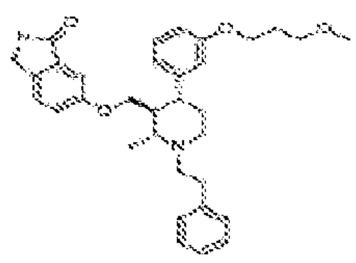
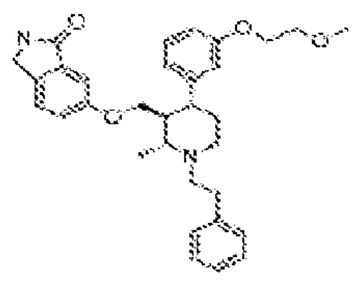
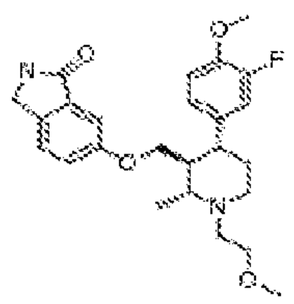
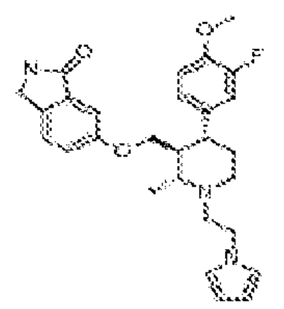
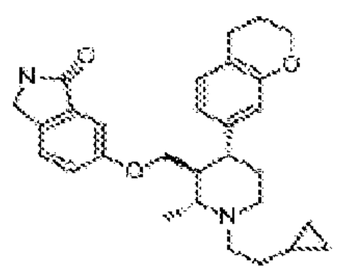
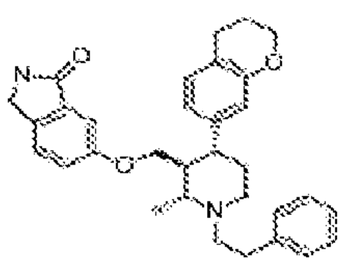
	B0945	(-)-6-{[trans, trans-4-(3-fluorophenyl)-2-methyl-1-(2-oxo-2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	472.55	473.2
	B0946	(+)-tert-butyl (trans, trans)-3-(hydroxymethyl)-2-methyl-4-[3-(trifluoromethoxy)phenyl]piperidine-1-carboxylate	389.41	334.1
	B0947	(-)-6-{[trans, trans-4-[3-(3methoxypropoxy)phenyl]-2-methyl-1-(2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	528.68	529.3
	B0948	(-)-6-{[trans, trans-4-[3-(2-methoxyethoxy)phenyl]-2-methyl-1-(2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	514.66	515.1
	B0949	(-)-6-{[trans, trans-4-(3-fluoro-4-methoxyphenyl)-1-(2-methoxyethyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	442.52	443.3
	B0950	(-)-6-{[trans, trans-4-(3-fluoro-4-methoxyphenyl)-2-methyl-1-(2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	477.57	478.3
	B0951	6-{[(trans, trans)-1-(2-cyclopropylethyl)-4-(3,4-dihydro-2H-1-benzopyran-7-yl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	460.61	461.5
	B0952	6-{[(trans, trans)-4-(3,4-dihydro-2H-1-benzopyran-7-yl)-2-methyl-1-(2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	496.64	497.5

Figure 1-Continued

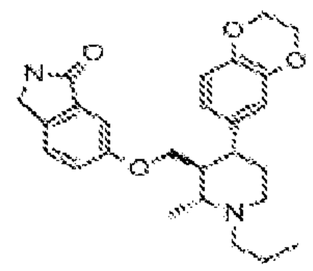
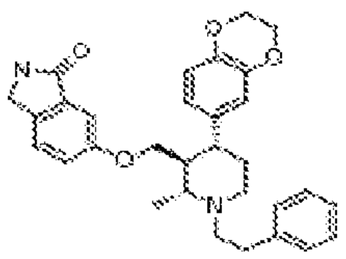
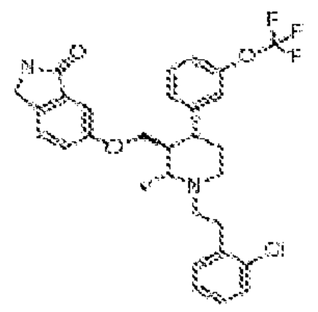
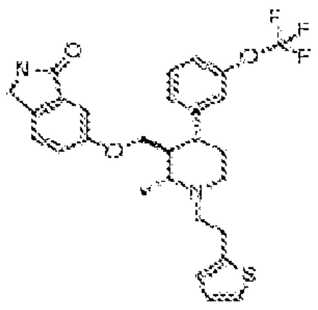
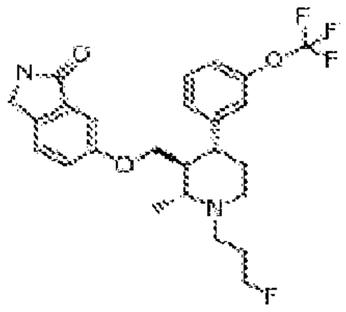
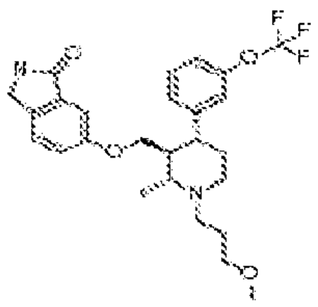
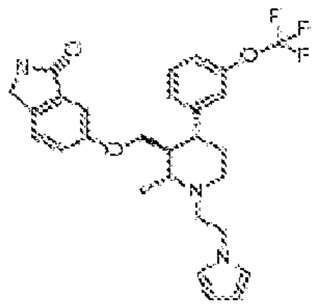
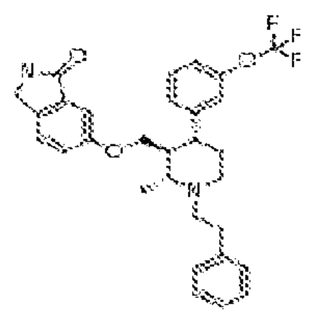
	B0953	6-{[(trans, trans)-4-(2,3-dihydro-1,4-benzodioxin-6-yl)-2-methyl-1-propylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	436.54	437.4
	B0954	6-{[(trans, trans)-4-(2,3-dihydro-1,4-benzodioxin-6-yl)-2-methyl-1-(2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	498.61	499.5
	B0955	(-)-6-{[trans, trans-1-[2-(2-chlorophenyl)ethyl]-2-methyl-4-[3-(trifluoromethoxy)phenyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	559.02	559.2
	B0956	(-)-6-{[trans, trans-2-methyl-1-[2-(thiophen-2-yl)ethyl]-4-[3-(trifluoromethoxy)phenyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	530.6	531.2
	B0957	(-)-6-{[trans, trans-1-(3-fluoropropyl)-2-methyl-4-[3-(trifluoromethoxy)phenyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	480.5	481.3
	B0958	(-)-6-{[trans, trans-1-(3-methoxypropyl)-2-methyl-4-[3-(trifluoromethoxy)phenyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	492.53	493.3
	B0959	(-)-6-{[trans, trans-2-methyl-1-[2-(1H-pyrrol-1-yl)ethyl]-4-[3-(trifluoromethoxy)phenyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	513.55	514.3
	B0960	(-)-6-{[trans, trans-2-methyl-1-(2-phenylethyl)-4-[3-(trifluoromethoxy)phenyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	524.57	525.3

Figure 1-Continued

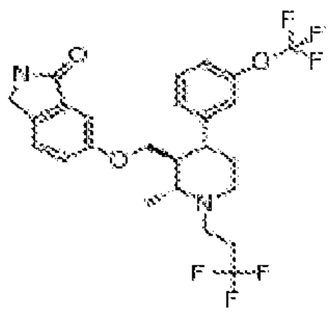
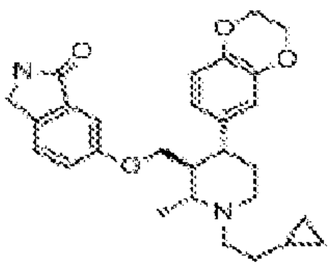
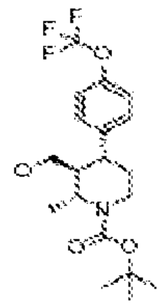
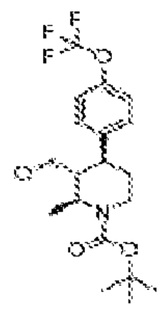
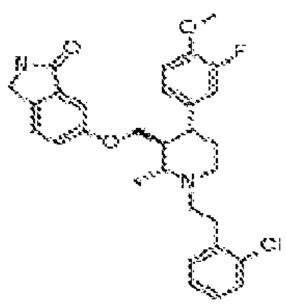
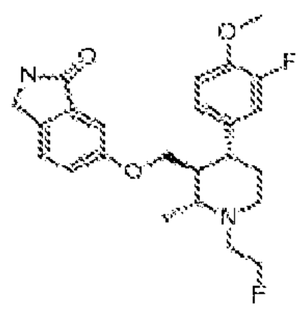
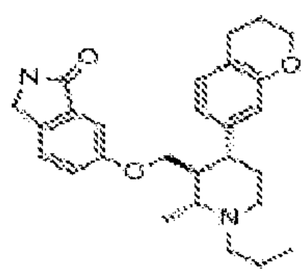
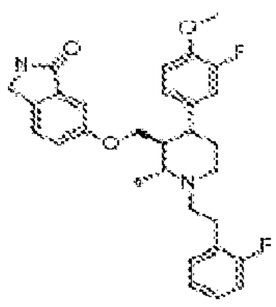
	B0961	(-)-6-{[trans, trans-2-methyl-4-[3-(trifluoromethoxy)phenyl]-1-(3,3,3-trifluoropropyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	516.48	517.2
	B0962	6-{[(trans, trans)-1-(2-cyclopropylethyl)-4-(2,3-dihydro-1,4-benzodioxin-6-yl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	462.58	463.4
	B0963	(-)-tert-butyl (trans, trans)-3-(hydroxymethyl)-2-methyl-4-[4-(trifluoromethoxy)phenyl]piperidine-1-carboxylate	389.41	334.1
	B0964	(+)-tert-butyl (trans, trans)-3-(hydroxymethyl)-2-methyl-4-[4-(trifluoromethoxy)phenyl]piperidine-1-carboxylate	389.41	334.1
	B0965	(-)-6-{[trans, trans-ethyl]-4-(3-fluoro-4-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	523.04	523.3
	B0966	(-)-6-{[trans, trans-4-(3-fluoro-4-methoxyphenyl)-1-(2-fluoroethyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	430.49	431.3
	B0967	6-{[(trans, trans)-4-(3,4-dihydro-2H-1-benzopyran-7-yl)-2-methyl-1-propylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	434.57	435.4
	B0968	(-)-6-{[trans, trans-4-(3-fluoro-4-methoxyphenyl)-1-[2-(2-fluorophenyl)ethyl]-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	506.58	507.3

Figure 1-Continued

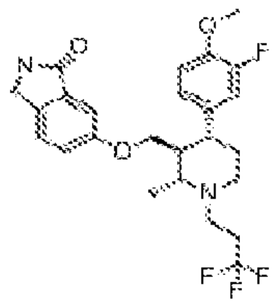
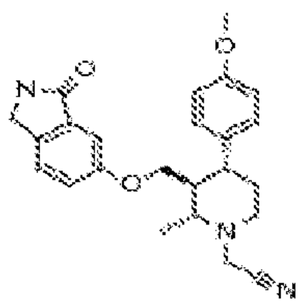
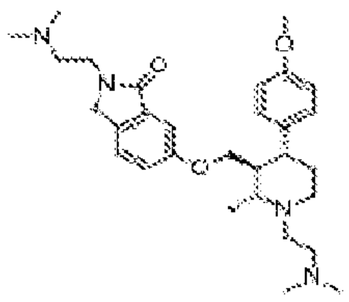
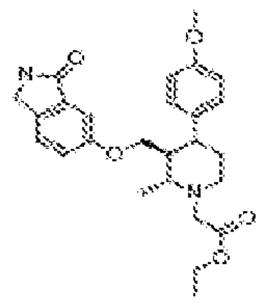
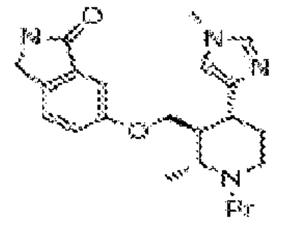
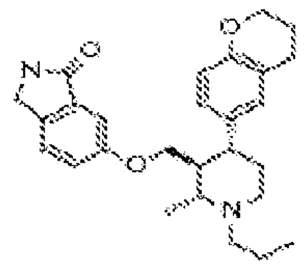
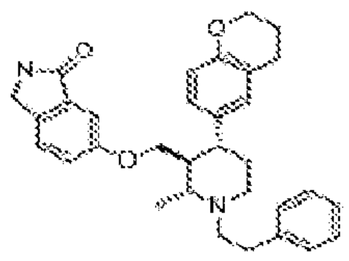
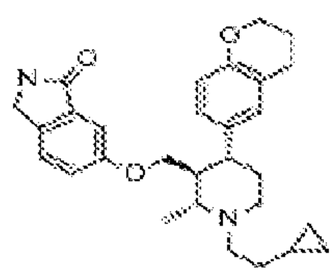
	B0969	(-)-6-{[trans, trans-4-(3-fluoro-4-methoxyphenyl)-2-methyl-1-(3,3,3trifluoropropyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	480.5	481.3
	B0970	(-)-2-[trans, trans-4-(4-methoxyphenyl)-2-methyl-3-{[(3-oxo-2,3-dihydro-1H-isoindol-5-yl)oxy]methyl}piperidin-1yl]acetonitrile	405.49	406.2
	B0971	(-)-2-[2-(dimethylamino)ethyl]-6-{[(trans, trans)-1-[2-(dimethylamino)ethyl]-4-(4-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	508.7	509.1
	B0972	(-)-2-[trans, trans-4-(4-methoxyphenyl)-2-methyl-3-{[(3-oxo-2,3-dihydro-1H-isoindol-5-yl)oxy]methyl}piperidin-1-yl]acetate	452.54	453.3
	B0973	6-{[(trans, trans)-2-methyl-4-(1-methyl-1H-imidazol-4-yl)-1-propylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	382.5	383.2
	B0974	6-{[(trans, trans)-4-(3,4-dihydro-2H-1-benzopyran-6-yl)-2-methyl-1-propylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	434.57	435.4
	B0975	6-{[(trans, trans)-4-(3,4-dihydro-2H-1-benzopyran-6-yl)-2-methyl-1-(2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	496.64	497.5
	B0976	6-{[(trans, trans)-1-(2-cyclopropylethyl)-4-(3,4-dihydro-2H-1-benzopyran-6-yl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	460.61	461.5

Figure 1-Continued

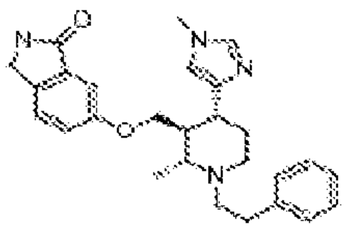
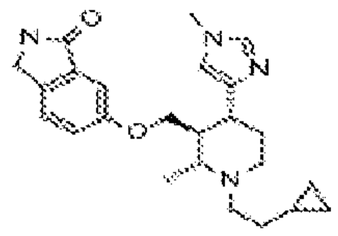
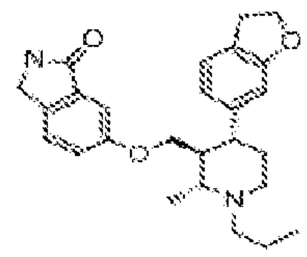
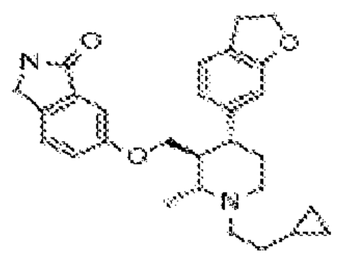
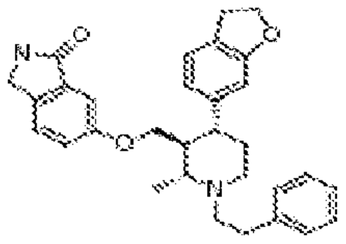
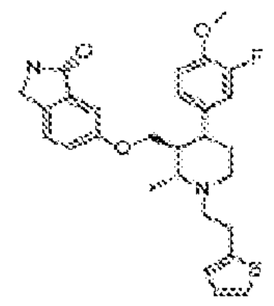
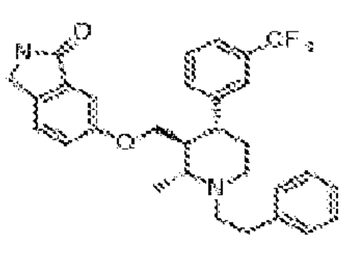
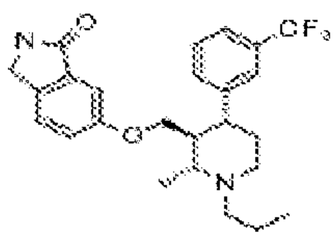
	B0977	6-{[(trans, trans)-2-methyl-4-(1-methyl-1H-imidazol-4-yl)-1-(2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	444.57	445.4
	B0978	6-{[(trans, trans)-1-(2-cyclopropylethyl)-2-methyl-4-(1-methyl-1H-imidazol-4-yl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	408.54	409.4
	B0979	6-{[(trans, trans)-4-(2,3-dihydro-1-benzofuran-6-yl)-2-methyl-1-propylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	420.54	421.4
	B0980	6-{[(trans, trans)-1-(2-cyclopropylethyl)-4-(2,3-dihydro-1-benzofuran-6-yl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	446.58	447.4
	B0981	6-{[(trans, trans)-4-(2,3-dihydro-1-benzofuran-6-yl)-2-methyl-1-(2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	482.61	483.5
	B0982	6-{[(trans, trans)-4-(3-fluoro-4-methoxyphenyl)-2-methyl-1-[2-(thiophen-2-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	494.62	495.2
	B0983	6-{[(trans, trans)-2-methyl-1-(2-phenylethyl)-4-[3-(trifluoromethyl)phenyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	508.57	509.5
	B0984	6-{[(trans, trans)-2-methyl-1-propyl-4-[3-(trifluoromethyl)phenyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	446.51	447.4

Figure 1-Continued

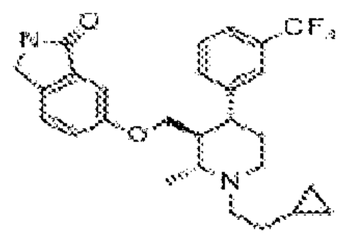
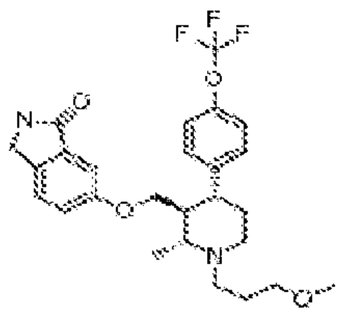
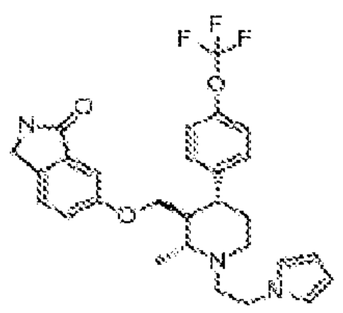
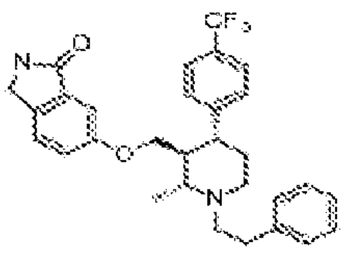
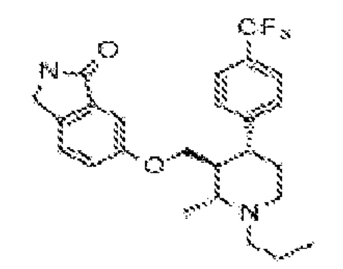
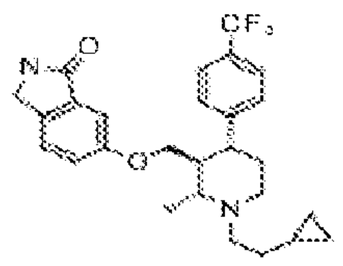
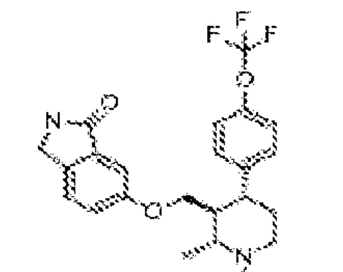
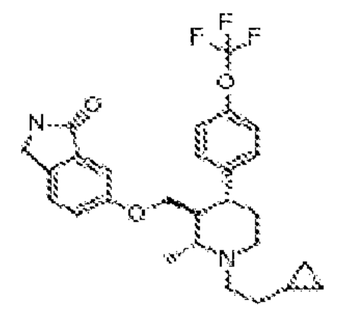
	B0985	6-{[(trans, trans)-1-(2-cyclopropylethyl)-2-methyl-4-[3-(trifluoromethyl)phenyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	472.54	473.4
	B0986	(-)-6-{[trans, trans-1-(3-methoxypropyl)-2-methyl-4-[4-(trifluoromethoxy)phenyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	492.53	493.3
	B0987	(-)-6-{[trans, trans-2-methyl-1-[2-(1H-pyrrol-1-yl)ethyl]-4-[4-(trifluoromethoxy)phenyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	513.55	514.3
	B0988	6-{[(trans, trans)-2-methyl-1-(2-phenylethyl)-4-[4-(trifluoromethyl)phenyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	508.57	509.4
	B0989	6-{[(trans, trans)-2-methyl-1-propyl-4-[4-(trifluoromethyl)phenyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	446.51	447.4
	B0990	6-{[(trans, trans)-1-(2-cyclopropylethyl)-2-methyl-4-[4-(trifluoromethyl)phenyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	472.54	473.4
	B0991	(-)-6-{[trans, trans-2-methyl-1-propyl-4-[4-(trifluoromethoxy)phenyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	462.5	463.3
	B0992	(-)-6-{[trans, trans-1-(2-cyclopropylethyl)-2-methyl-4-[4-(trifluoromethoxy)phenyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	488.54	489.3

Figure 1-Continued

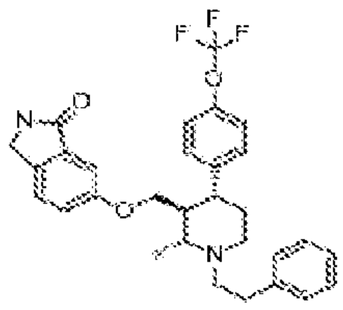
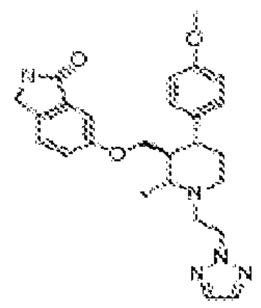
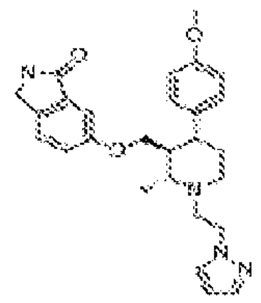
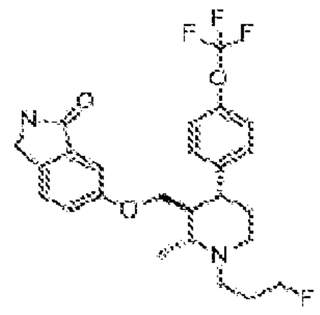
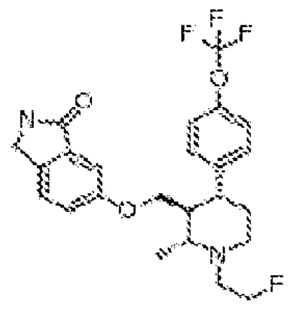
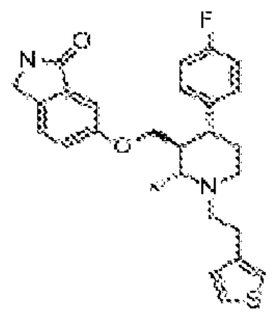
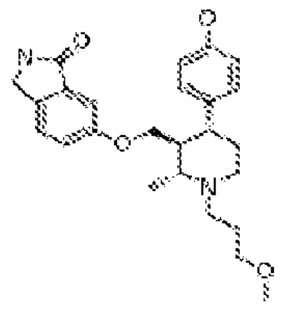
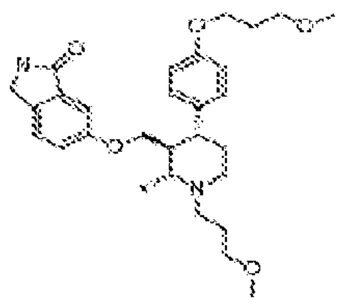
	B0993	(-)-6-{[trans, trans-2-methyl-1-(2-phenylethyl)-4-[4-(trifluoromethoxy)phenyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	524.57	525.3
	B0994	(-)-6-{[trans, trans-4-(4-methoxyphenyl)-2-methyl-1-[2-(2H-1,2,3-trizol-2-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	461.56	462.3
	B0995	(-)-6-{[trans, trans-4-(4-methoxyphenyl)-2-methyl-1-[2-(1H-pyr ol-1-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	460.57	461.3
	B0996	(-)-6-{[trans, trans-1-(3-fluoropropyl)-2-methyl-4-[4-(trifluoromethoxy)phenyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	480.5	481.2
	B0997	(-)-6-{[trans, trans-1-(2-fluoroethyl)-2-methyl-4-[4-(trifluoromethoxy)phenyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	466.47	467.2
	B0998	(-)-6-{[trans, trans-4-(4-fluorophenyl)-2-methyl-1-[2-(thiophen-3-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	464.59	465.2
	B0999	(-)-6-{[trans, trans-4-(4-hydroxyphenyl)-1-(3-methoxypropyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	424.53	425.3
	B1000	(-)-6-{[trans, trans-4-{4-[(3-methoxypropoxy)methyl]phenyl}-1-(3-methoxypropyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	496.64	497.4

Figure 1-Continued

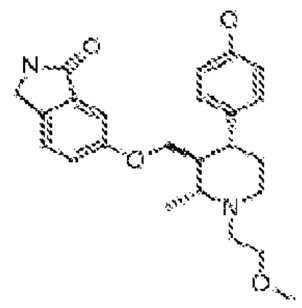
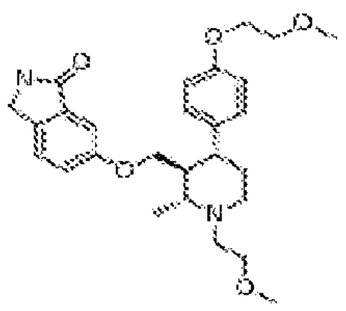
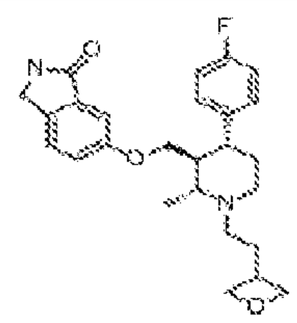
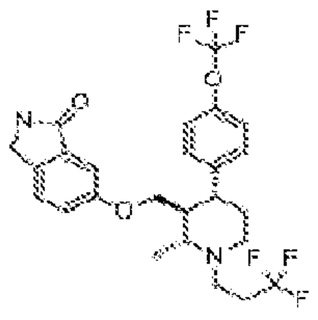
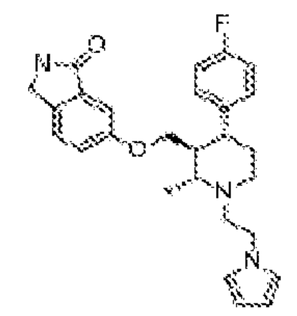
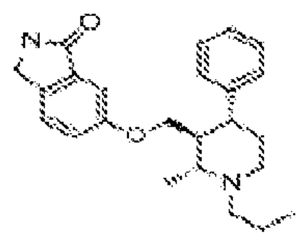
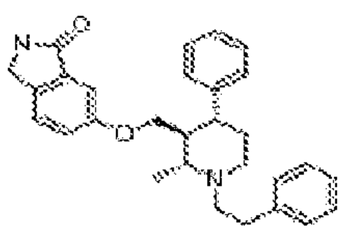
	B1001	(-)-6-{[trans, trans-4-(4-hydroxyphenyl)-1-(2-methoxyethyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	410.51	411.3
	B1002	(-)-6-{[trans, trans-4-[4-(2-methoxyethoxy)phenyl]-1-(2-methoxyethyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	468.59	469.3
	B1003	(-)-6-{[trans, trans-4-(4-fluorophenyl)-2-methyl-1-[2-(oxetan-3-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	438.53	439.2
	B1004	(-)-6-{[trans, trans-2-methyl-4-[4-(trifluoromethoxy)phenyl]-1-(3,3,3-trifluoropropyl)piperidin-3yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	516.48	517.2
	B1005	(-)-6-{[trans, trans-4-(4-fluorophenyl)-2-methyl-1-[2-(1H-pyrrol-1-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	447.54	448.3
	B1006	6-{[(trans, trans)-2-methyl-4-phenyl-1-propylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	378.51	379.4
	B1007	6-{[(trans, trans)-1-(2-cyclopropylethyl)-2-methyl-4-phenylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	404.54	405.4
	B1008	6-{[(trans, trans)-2-methyl-4-phenyl-1-(2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	440.58	441.4

Figure 1-Continued

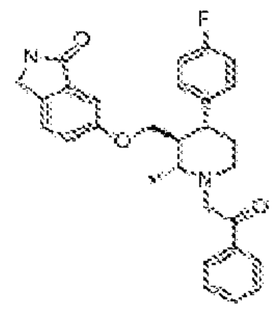
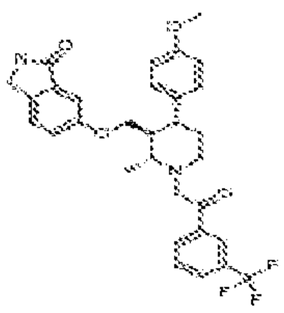
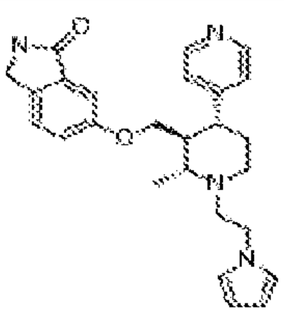
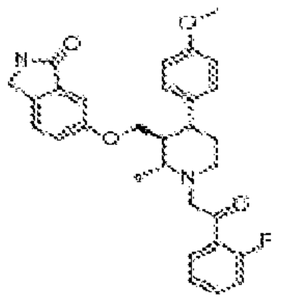
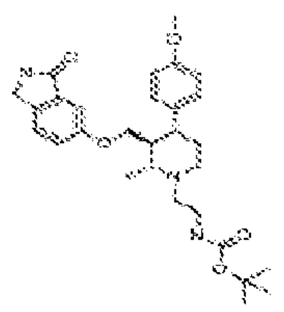
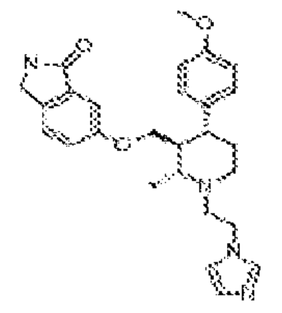
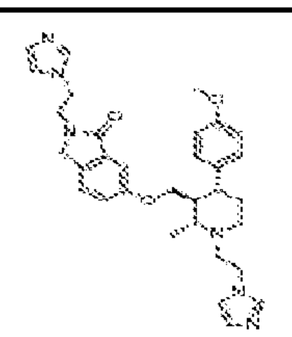
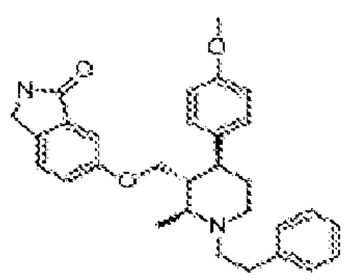
	B1009	(-)-6-{[trans, trans-4-(4-fluorophenyl)-2-methyl-1-(2-oxo-2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	472.55	473.3
	B1010	(-)-6-{[trans, trans-4-(4-methoxyphenyl)-2-methyl-1-{2-oxo-2-[3-(trifluoromethyl)phenyl]ethyl}piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	552.58	553.3
	B1011	(-)-6-{[trans, trans-2-methyl-4-(pyridin-4-yl)-1-[2-(1H-pyrrol-1-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	430.54	431.3
	B1012	(-)-6-{[trans, trans-1-[2-(2-fluorophenyl)-2-oxoethyl]-4-(4-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	502.58	503.3
	B1013	tert-butyl N-{2-[(trans, trans)-4-(4-methoxyphenyl)-2-methyl-3-{[(3-oxo-2,3-dihydro-1H-isoindol-5-yl)oxy]methyl}piperidin-1-yl]ethyl}carbamate	509.64	510.4
	B1014	(-)-6-{[trans, trans-1-[2-(1H-imidazol-1-yl)ethyl]-4-(4-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	460.57	461.3
	B1015	2-[2-(1H-imidazol-1-yl)ethyl]-6-{[(trans, trans)-1-[2-(1H-imidazol-1-yl)ethyl]-4-(4-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	554.68	555.4
	B1016	(+)-6-{[trans, trans-4-(4-methoxyphenyl)-2-methyl-1-(2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	470.6	471.3

Figure 1-Continued

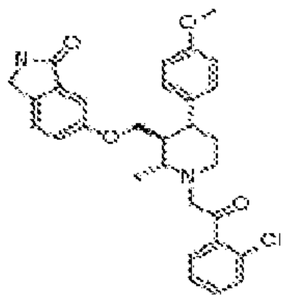
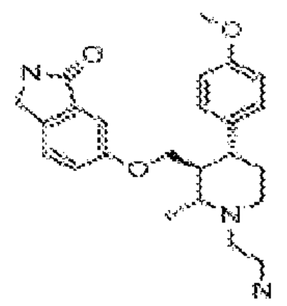
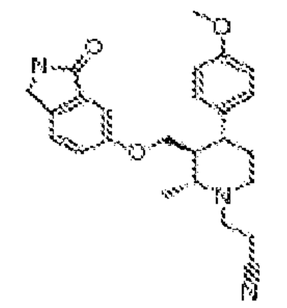
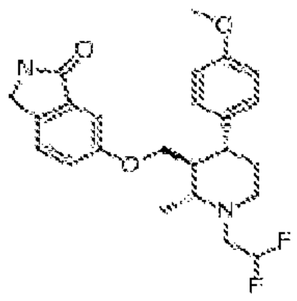
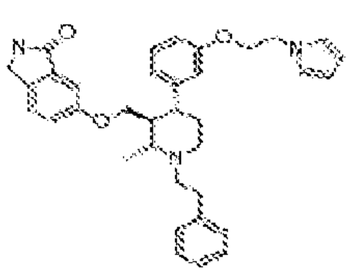
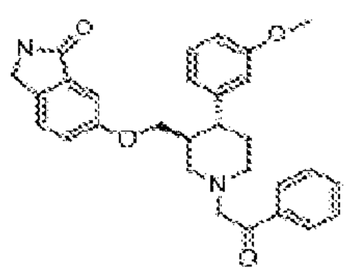
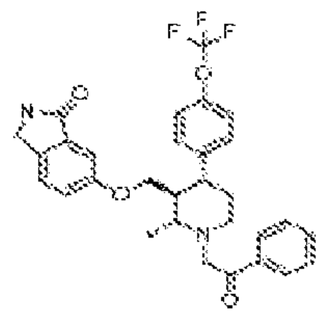
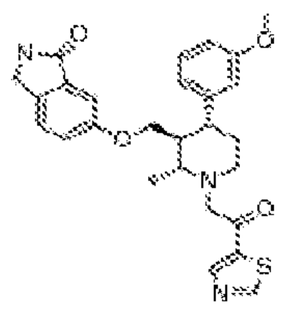
	B1017	(-)-6-{[trans, trans-1-[2-(2-chlorophenyl)-2-oxoethyl]-4-(4-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	519.03	519.2
	B1018	(-)-6-{[trans, trans-1-(2-aminoethyl)-4-(4-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	409.52	410.1
	B1019	(-)-3-[trans, trans-4-(4-methoxyphenyl)-2-methyl-3-{[(3-oxo-2,3-dihydro-1H-isoindol-5-yl)oxy]methyl}piperidin-1-yl]propanenitrile	419.52	420
	B1020	(-)-6-{[trans, trans-1-(2,2-difluoroethyl)-4-(4-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	430.49	431
	B1021	(-)-6-{[trans, trans-2-methyl-1-(2-phenylethyl)-4-{3-[2-(1H-pyrrol-1-yl)ethoxy]phenyl}piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	549.7	550.1
	B1022	6-{[trans-4-(3-methoxyphenyl)-1-(2-oxo-2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	470.56	471
	B1023	6-{[(trans, trans)-2-methyl-1-(2-oxo-2-phenylethyl)-4-[4-(trifluoromethoxy)phenyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	538.56	539
	B1024	(-)-6-{[trans, trans-4-(3-methoxyphenyl)-2-methyl-1-[2-oxo-2-(1,3-thi ol-5-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	491.6	492

Figure 1-Continued

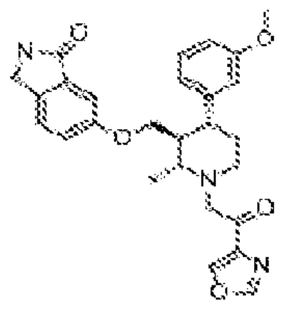
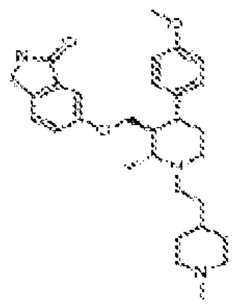
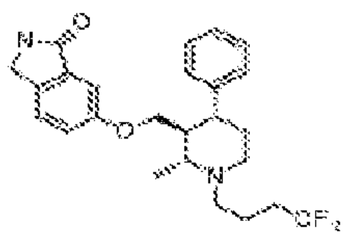
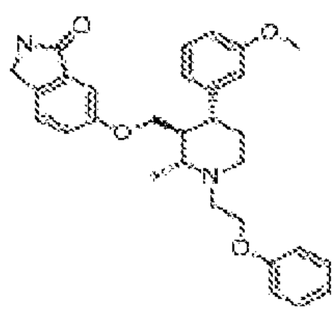
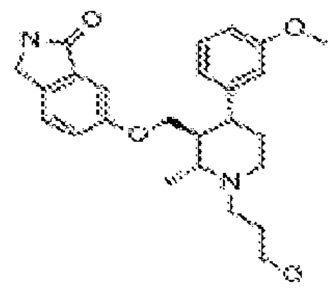
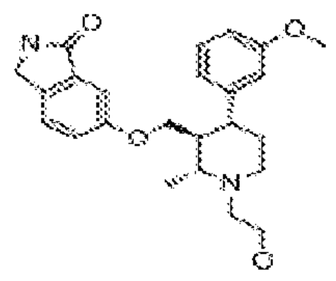
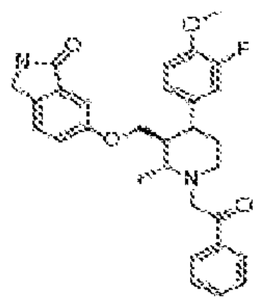
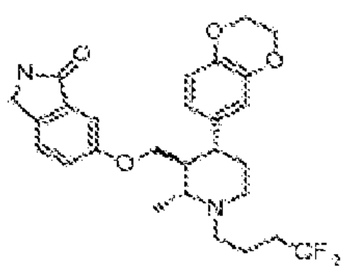
	B1025	(-)-6-{[trans, trans-4-(3-methoxyphenyl)-2-methyl-1-[2-(1,3-oxazol-4-yl)-2-oxoethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	475.54	476
	B1026	(-)-6-{[trans, trans-4-(4-methoxyphenyl)-2-methyl-1-[2-(1-methylpiperidin-4-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	491.66	492.1
	B1027	6-{[(trans, trans)-2-methyl-4-phenyl-1-(4,4,4-trifluorobutyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	446.51	447.2
	B1028	(-)-6-{[trans, trans-4-(3-methoxyphenyl)-2-methyl-1-(2-phenoxyethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	486.6	487
	B1029	(-)-6-{[trans, trans-1-(3-hydroxypropyl)-4-(3-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	424.53	425
	B1030	(-)-6-{[trans, trans-1-(2-hydroxyethyl)-4-(3-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	410.51	411
	B1031	(-)-6-{[trans, trans-4-(3-fluoro-4-methoxyphenyl)-2-methyl-1-(2-oxo-2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	502.58	503
	B1032	6-{[(trans, trans)-4-(2,3-dihydro-1,4-benzodioxin-6-yl)-2-methyl-1-(4,4,4-trifluorobutyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	504.54	505.5

Figure 1-Continued

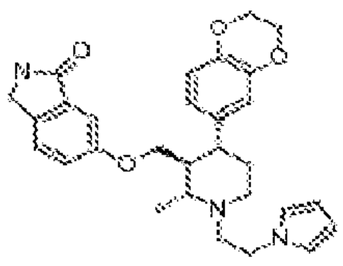
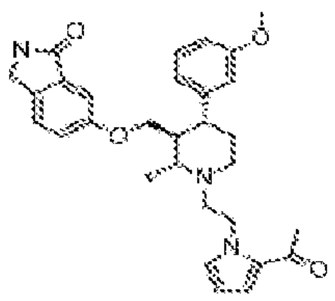
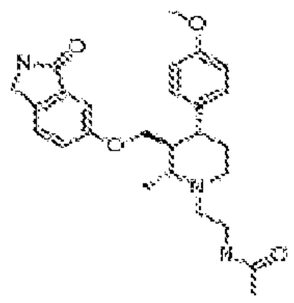
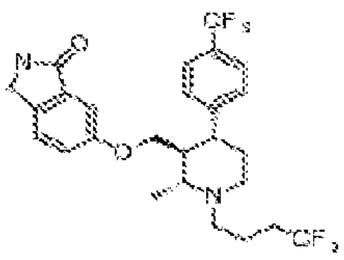
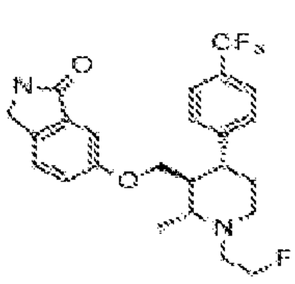
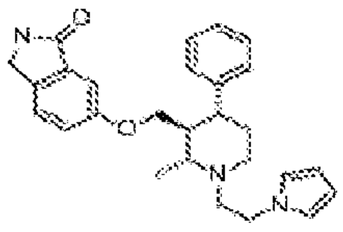
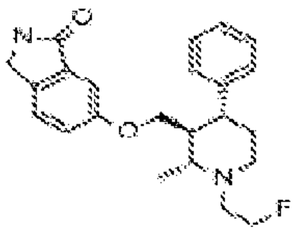
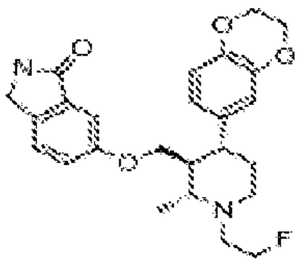
	B1033	6-{[(trans, trans)-4-(2,3-dihydro-1,4-benzodioxin-6-yl)-2-methyl-1-[2-(1H-pyrrol-1-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	487.59	488.5
	B1034	(-)-6-{[trans, trans-1-[2-(2-acetyl-1H-pyrrol-1-yl)ethyl]-4-(3-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	501.62	502.1
	B1035	(-)-N-{trans, trans-2-[4-(4-methoxyphenyl)-2-methyl-3-{[(3-oxo-2,3-dihydro-1H-isoindol-5-yl)oxy]methyl}piperidin-1-yl]ethyl}acetamide	451.56	452
	B1036	6-{[(trans, trans)-2-methyl-1-(4,4,4-trifluorobutyl)-4-[4-(trifluoromethyl)phenyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	514.5	515.5
	B1037	6-{[(trans, trans)-1-(2-fluoroethyl)-2-methyl-4-[4-(trifluoromethyl)phenyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	450.47	451.4
	B1038	6-{[(trans, trans)-2-methyl-4-phenyl-1-[2-(1H-pyrrol-1-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	429.55	430.5
	B1039	6-{(trans, trans)-[1-(2-fluoroethyl)-2-methyl-4-phenylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	382.47	383.3
	B1040	6-{[(trans, trans)-4-(2,3-dihydro-1,4-benzodioxin-6-yl)-1-(2-fluoroethyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	440.51	441.4

Figure 1-Continued

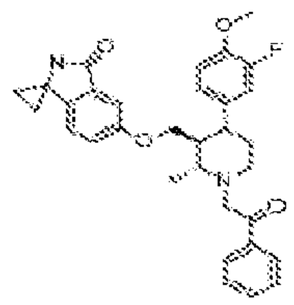
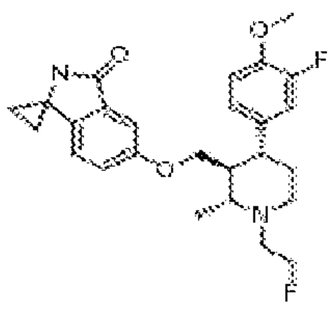
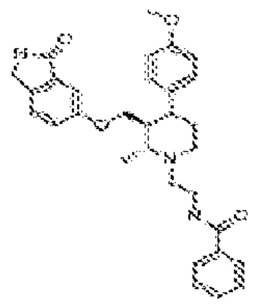
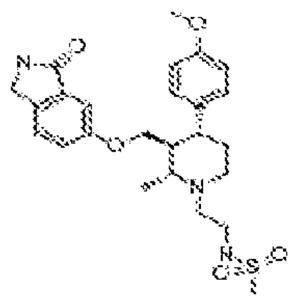
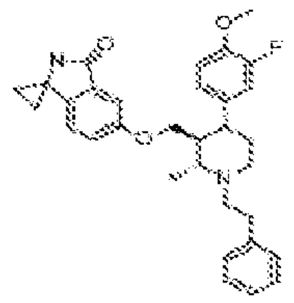
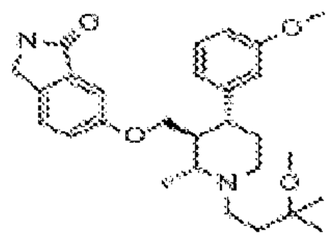
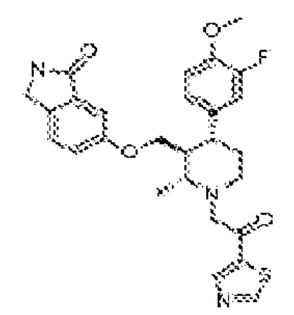
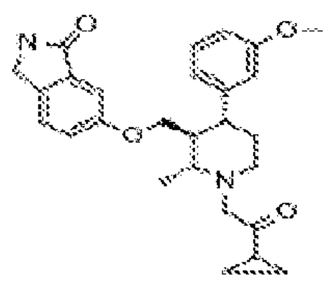
	B1041	(-)-5'-{[trans, trans-4-(3-fluoro-4-methoxyphenyl)-2-methyl-1-(2-oxo-2-phenylethyl)piperidin-3-yl]methoxy}-2',3'-dihydrospiro[cyclopropne-1,1'-isoindole]-3'-one	528.61	529
	B1042	(-)-5'-{[trans, trans-4-(3-fluoro-4-methoxyphenyl)-1-(2-fluoroethyl)-2-methylpiperidin-3-yl]methoxy}-2',3'-dihydrospiro[cyclopropne-1,1'-isoindole]-3'-one	456.52	457
	B1043	(-)-N-{2-[trans,trans-4-(4-methoxyphenyl)-2-methyl-3-{[(3-oxo-2,3-dihydro-1H-isoindol-5-yl)oxy]methyl}piperidin-1-yl]ethyl}benzamide	513.63	514
	B1044	(-)-N-{2-[trans, trans-4-(4-methoxyphenyl)-2-methyl-3-{[(3-oxo-2,3-dihydro-1H-isoindol-5-yl)oxy]methyl}piperidin-1-yl]ethyl}methnesulfonmide	487.61	488
	B1045	5'-{[(trans, trans)-4-(3-fluoro-4-methoxyphenyl)-2-methyl-1-(2-phenylethyl)piperidin-3-yl]methoxy}-2',3'-dihydrospiro[cyclopropne-1,1'-isoindole]-3'-one	514.63	515.1
	B1046	(-)-6-{[trans, trans-1-(3-methoxy-3-methyl utyl)-4-(3-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	466.61	467.1
	B1047	(-)-6-{[trans, trans-4-(3-fluoro-4-methoxyphenyl)-2-methyl-1-[2-oxo-2-(1,3-thizol-5-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	509.59	510
	B1048	(-)-6-{[trans, trans-1-(2-cyclopropyl-2-oxoethyl)-4-(3-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	448.55	449

Figure 1-Continued

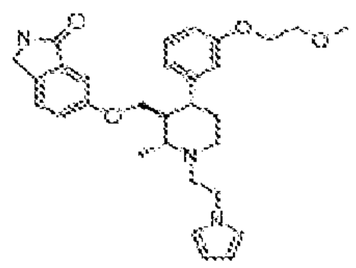
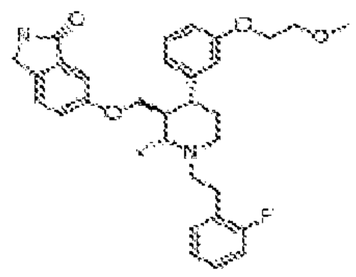
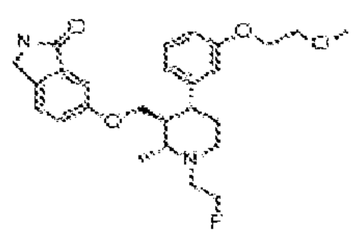
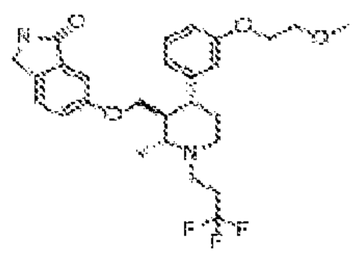
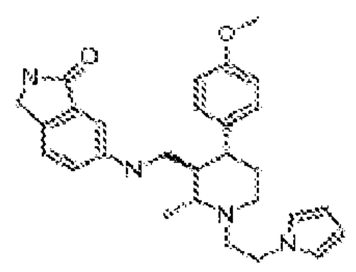
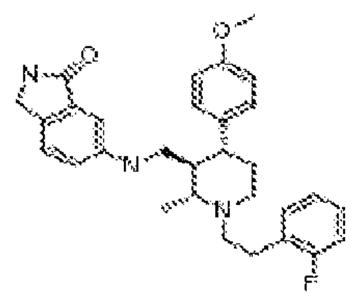
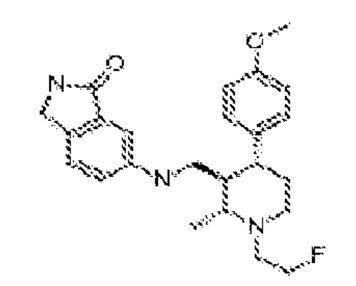
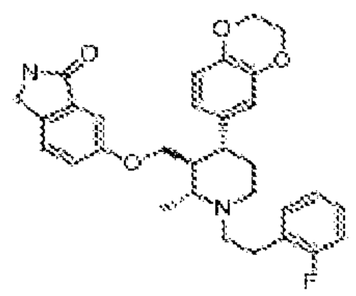
	B1049	(-)-6-{[trans, trans-4-[3-(2-methoxyethoxy)phenyl]-2-methyl-1-[2-(1H-pyrrol-1-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	503.63	504.1
	B1050	(-)-6-{[trans, trans-1-[2-(2-fluorophenyl)ethyl]-4-[3-(2-methoxyethoxy)phenyl]-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	532.65	533
	B1051	(-)-6-{[trans, trans-1-(2-fluoroethyl)-4-[3-(2-methoxyethoxy)phenyl]-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	456.55	457
	B1052	(-)-6-{[trans, trans-4-[3-(2-methoxyethoxy)phenyl]-2-methyl-1-(3,3,3-trifluoropropyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	506.56	507
	B1053	6-({[(trans, trans)-4-(4-methoxyphenyl)-2-methyl-1-[2-(1H-pyrrol-1-yl)ethyl]piperidin-3-yl]methyl}amino)-2,3-dihydro-1H-isoindol-1-one	458.6	459.2
	B1054	6-({[(trans, trans)-1-[2-(2-fluorophenyl)ethyl]-4-(4-methoxyphenyl)-2-methylpiperidin-3-yl]methyl}amino)-2,3-dihydro-1H-isoindol-1-one	487.61	488.3
	B1055	6-({[(trans, trans)-1-(2-fluoroethyl)-4-(4-methoxyphenyl)-2-methylpiperidin-3-yl]methyl}amino)-2,3-dihydro-1H-isoindol-1-one	411.51	412.2
	B1056	6-{[(trans, trans)-4-(2,3-dihydro-1,4-benzodioxin-6-yl)-1-[2-(2-fluorophenyl)ethyl]-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	516.6	517.2

Figure 1-Continued

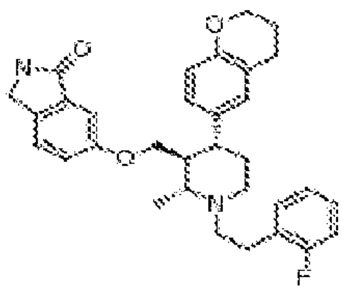
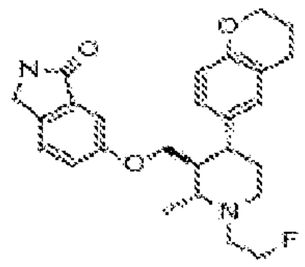
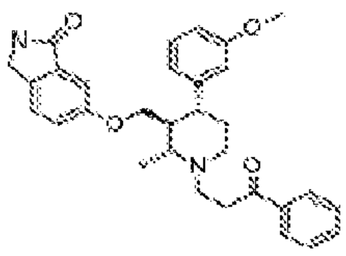
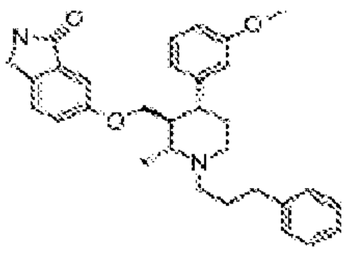
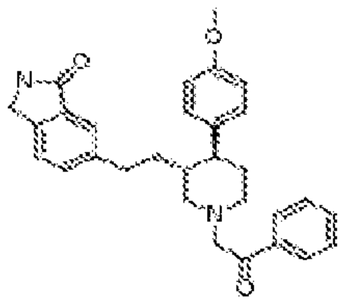
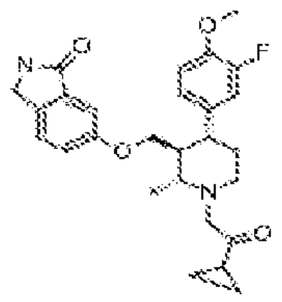
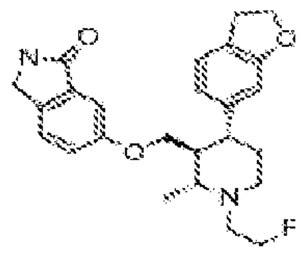
	B1057	6-{[(trans, trans)-4-(3,4-dihydro-2H-1-benzopyran-6-yl)-1-[2-(2-fluorophenyl)ethyl]-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	514.63	515.2
	B1058	6-{[(trans, trans)-4-(3,4-dihydro-2H-1-benzopyran-6-yl)-1-(2-fluoroethyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	438.53	439.2
	B1059	(-)-6-{[trans, trans-4-(3-methoxyphenyl)-2-methyl-1-(3-oxo-3-phenylpropyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	498.61	499
	B1060	(-)-6-{[trans, trans-4-(3-methoxyphenyl)-2-methyl-1-(3-phenylpropyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	484.63	485.1
	B1061	6-{2-[(trans)-4-(4-methoxyphenyl)-1-(2-phenylethyl)piperidin-3-yl]ethyl}-2,3-dihydro-1H-isoindol-1-one	454.6	455.1
	B1062	6-{2-[(trans)-4-(4-methoxyphenyl)-1-(2-oxo-2-phenylethyl)piperidin-3-yl]ethyl}-2,3-dihydro-1H-isoindol-1-one	468.59	469
	B1063	(-)-6-{[trans, trans-1-(2-cyclopropyl-2-oxoethyl)-4-(3-fluoro-4-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	466.54	467
	B1064	6-{[(trans, trans)-4-(2,3-dihydro-1-benzofuran-6-yl)-1-(2-fluoroethyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	424.51	425.1

Figure 1-Continued

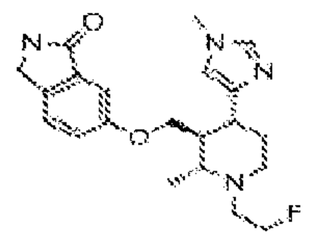
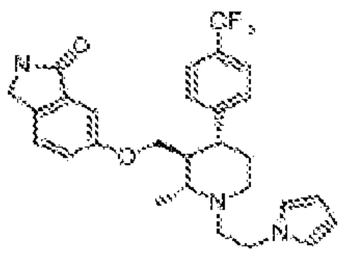
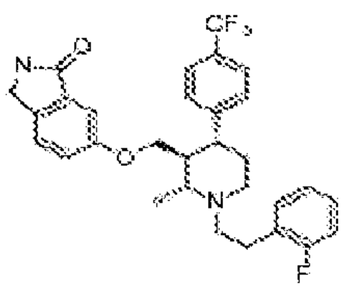
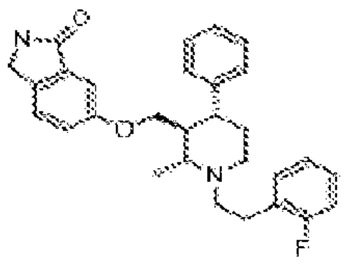
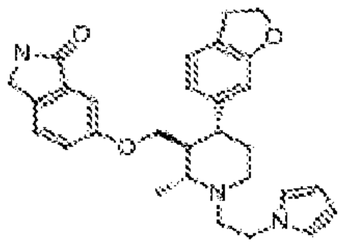
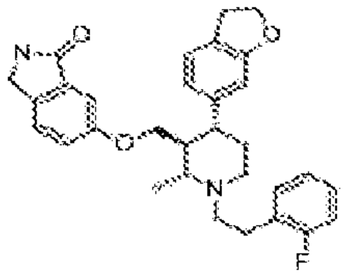
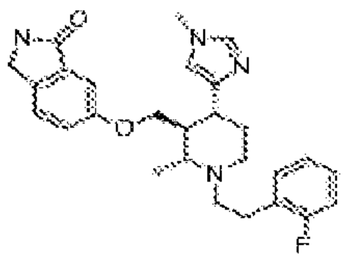
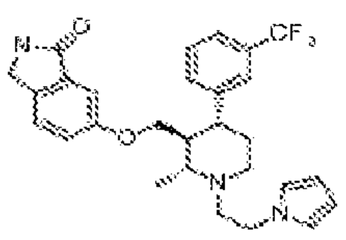
	B1065	6-{[(trans, trans)-1-(2-fluoroethyl)-2-methyl-4-(1-methyl-1H-imidazol-4-yl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	386.46	387.4
	B1066	6-{[(trans, trans)-2-methyl-1-[2-(1H-pyrrol-1-yl)ethyl]-4-[4-(trifluoromethyl)phenyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	497.55	498.1
	B1067	6-{[(trans, trans)-1-[2-(2-fluorophenyl)ethyl]-2-methyl-4-[4-(trifluoromethyl)phenyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	526.57	525.15
	B1068	6-{[(trans, trans)-1-[2-(2-fluorophenyl)ethyl]-2-methyl-4-phenylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	458.57	459.15
	B1069	6-{[(trans, trans)-4-(2,3-dihydro-1-benzofuran-6-yl)-2-methyl-1-[2-(1H-pyrrol-1-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	471.59	472
	B1070	6-{[(trans, trans)-4-(2,3-dihydro-1-benzofuran-6-yl)-1-[2-(2-fluorophenyl)ethyl]-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	500.6	501
	B1071	6-{[(trans, trans)-1-[2-(2-fluorophenyl)ethyl]-2-methyl-4-(1-methyl-1H-imidzol-4-yl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	462.56	463
	B1072	6-{[(trans, trans)-2-methyl-1-[2-(1H-pyrrol-1-yl)ethyl]-4-[3-(trifluoromethyl)phenyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	497.55	498.4

Figure 1-Continued

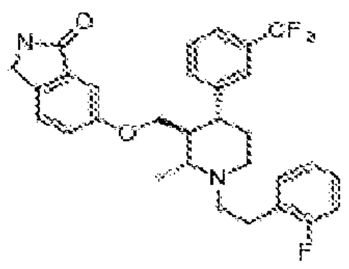
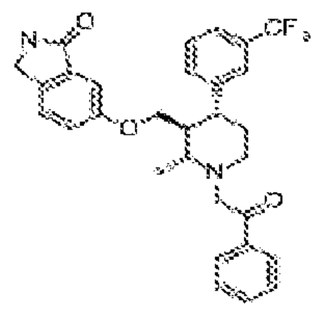
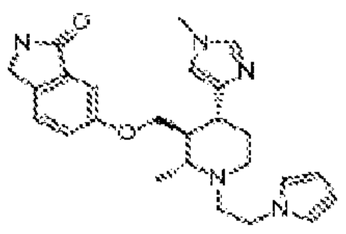
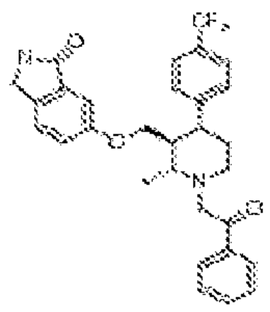
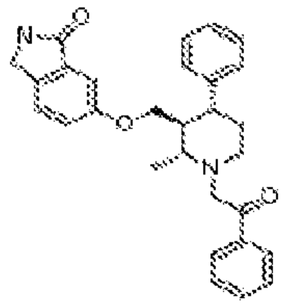
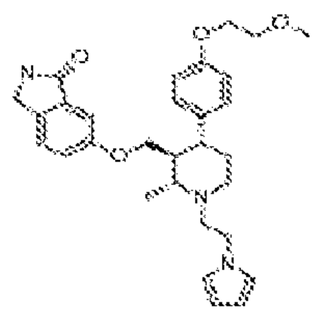
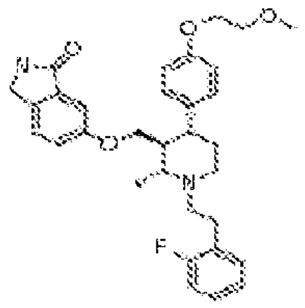
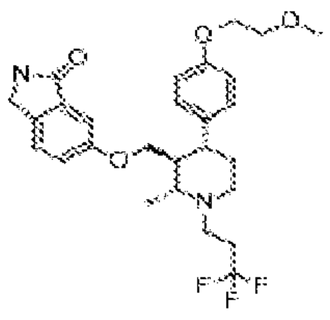
	B1073	6-{[(trans, trans)-1-[2-(2-fluorophenyl)ethyl]-2-methyl-4-[3-(trifluoromethyl)phenyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	526.57	527.3
	B1074	6-{[(trans, trans)-2-methyl-1-(2-oxo-2-phenylethyl)-4-[3-(trifluoromethyl)phenyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	522.56	523.4
	B1075	6-{[(trans, trans)-2-methyl-4-(1-methyl-1H-imidazol-4-yl)-1-[2-(1H-pyrrol-1-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	433.55	434
	B1076	6-{[(trans, trans)-2-methyl-1-(2-oxo-2-phenylethyl)-4-[4-(trifluoromethyl)phenyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	522.56	523.4
	B1077	6-{[(trans, trans)-2-methyl-1-(2-oxo-2-phenylethyl)-4-phenylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	454.56	455.15
	B1078	(-)-6-{[trans, trans-4-[4-(2-methoxyethoxy)phenyl]-2-methyl-1-[2-(1H-pyrrol-1-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	503.63	504.2
	B1079	(-)-6-{[trans, trans-1-[2-(2-fluorophenyl)ethyl]-4-[4-(2-methoxyethoxy)phenyl]-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	532.65	533.2
	B1080	(-)-6-{[(trans, trans)-4-[4-(2-methoxyethoxy)phenyl]-2-methyl-1-(3,3,3-trifluoropropyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	506.56	507

Figure 1-Continued

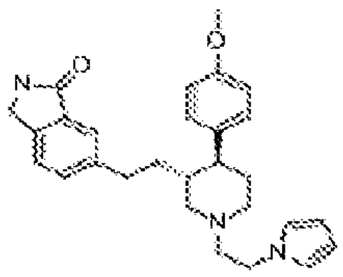
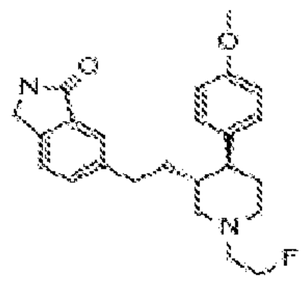
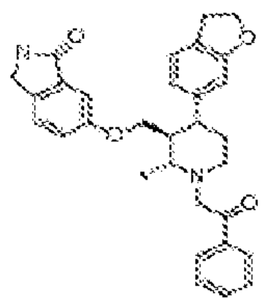
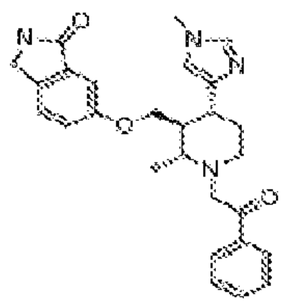
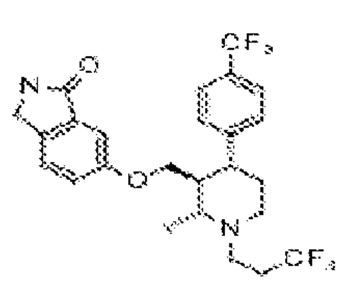
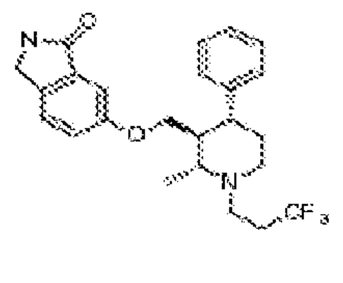
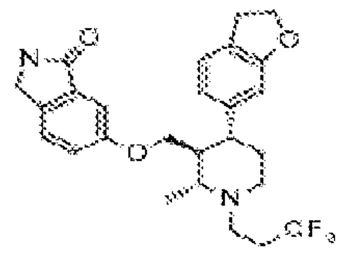
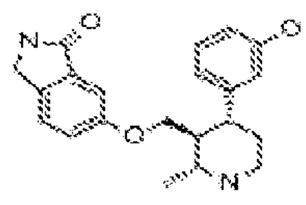
	B1081	6-{2-[(trans)-4-(4-methoxyphenyl)-1-[2-(1H-pyrrol-1-yl)ethyl]piperidin-3-yl]ethyl}-2,3-dihydro-1H-isoindol-1-one	443.58	444.2
	B1082	6-{2-[(trans)-1-(2-fluoroethyl)-4-(4-methoxyphenyl)piperidin-3-yl]ethyl}-2,3-dihydro-1H-isoindol-1-one	396.5	397.2
	B1083	6-{[(trans, trans)-4-(2,3-dihydro-1-benzofuran-6-yl)-2-methyl-1-(2-oxo-2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	496.6	497.1
	B1084	6-{[(trans, trans)-2-methyl-4-(1-methyl-1H-imidazol-4-yl)-1-(2-oxo-2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	458.55	459
	B1085	6-{[(trans, trans)-2-methyl-4-[4-(trifluoromethyl)phenyl]-1-(3,3,3-trifluoropropyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	500.48	501.1
	B1086	6-{[(trans, trans)-2-methyl-4-phenyl-1-(3,3,3-trifluoropropyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	432.48	433.1
	B1087	6-{[(trans, trans)-4-(2,3-dihydro-1-benzofuran-6-yl)-2-methyl-1-(3,3,3-trifluoropropyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	474.52	475.1
	B1088	6-{[(trans, trans)-4-(3-hydroxyphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	352.43	353.1

Figure 1-Continued

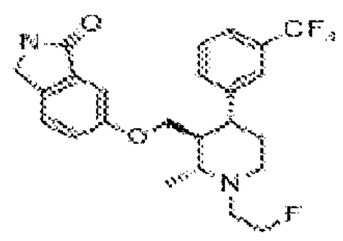
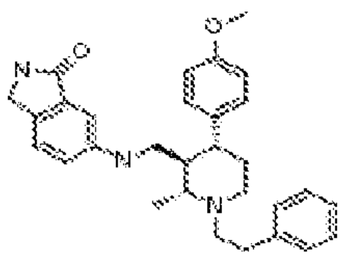
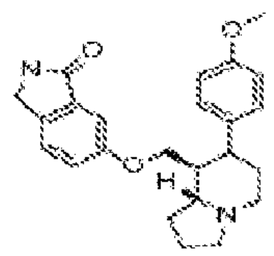
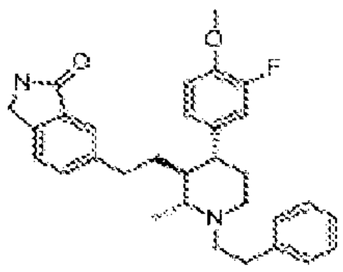
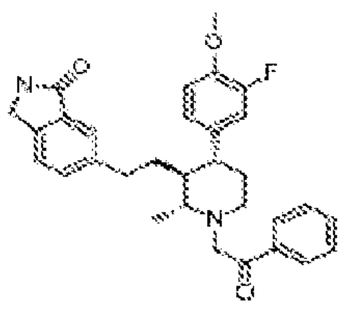
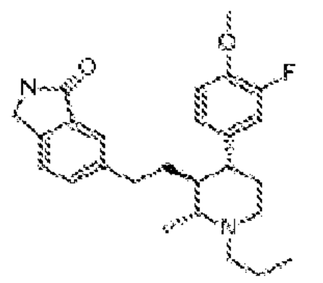
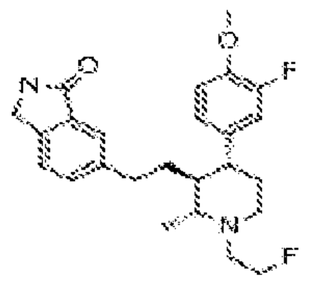
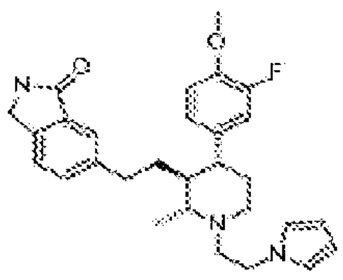
	B1089	6-{[(trans, trans)-1-(2-fluoroethyl)-2-methyl-4-[3-(trifluoromethyl)phenyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	450.47	451.2
	B1090	6-({[(trans, trans)-4-(4-methoxyphenyl)-2-methyl-1-(2-phenylethyl)piperidin-3-yl]methyl}amino)-2,3-dihydro-1H-isoindol-1-one	469.62	470.2
	B1091	6-{[7-(4-methoxyphenyl)-octahydroindolizin-8-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	392.49	393.1
	B1092	(-)-6-{2-[trans, trans-4-(3-fluoro-4-methoxyphenyl)-2-methyl-1-(2-phenylethyl)piperidin-3-yl]ethyl}-2,3-dihydro-1H-isoindol-1-one	486.62	487.2
	B1093	(-)-6-{2-[trans, trans-4-(3-fluoro-4-methoxyphenyl)-2-methyl-1-(2-oxo-2-phenylethyl)piperidin-3-yl]ethyl}-2,3-dihydro-1H-isoindol-1-one	500.6	501.2
	B1094	(-)-6-{2-[trans, trans-4-(3-fluoro-4-methoxyphenyl)-2-methyl-1-propylpiperidin-3-yl]ethyl}-2,3-dihydro-1H-isoindol-1-one	424.55	425.2
	B1095	(-)-6-{2-[trans, trans-4-(3-fluoro-4-methoxyphenyl)-1-(2-fluoroethyl)-2-methylpiperidin-3-yl]ethyl}-2,3-dihydro-1H-isoindol-1-one	428.51	429.2
	B1096	(-)-6-{2-[trans, trans-4-(3-fluoro-4-methoxyphenyl)-2-methyl-1-[2-(1H-pyrrol-1-yl)ethyl]piperidin-3-yl]ethyl}-2,3-dihydro-1H-isoindol-1-one	475.6	476.2

Figure 1-Continued

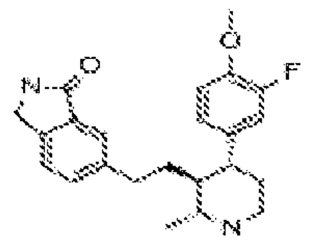
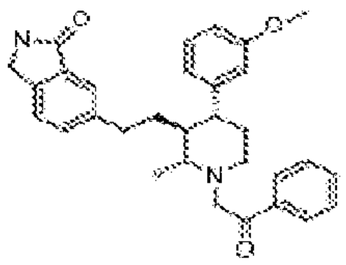
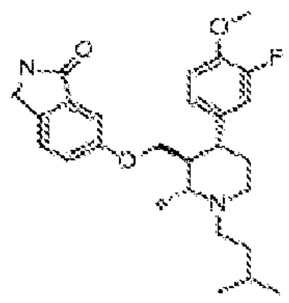
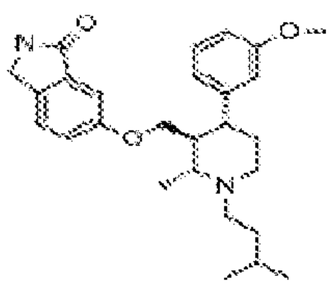
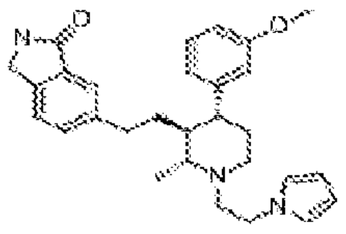
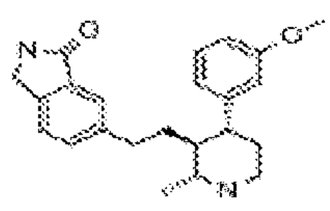
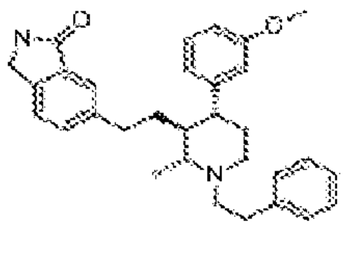
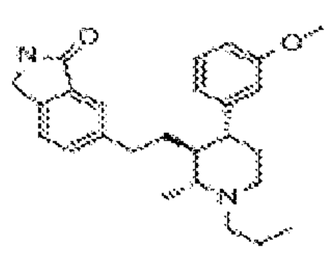
	B1097	(-)-6-{2-[trans, trans-4-(3-fluoro-4-methoxyphenyl)-2-methylpiperidin-3-yl]ethyl}-2,3-dihydro-1H-isoindol-1-one	382.47	383.2
	B1098	(-)-6-{2-[trans, trans-4-(3-methoxyphenyl)-2-methyl-1-(2-oxo-2-phenylethyl)piperidin-3-yl]ethyl}-2,3-dihydro-1H-isoindol-1-one	482.61	483.2
	B1099	(-)-6-{[trans, trans-4-(3-fluoro-4-methoxyphenyl)-2-methyl-1-(3-methylbutyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	454.58	455.2
	B1100	(-)-6-{[trans, trans-4-(3-methoxyphenyl)-2-methyl-1-(3-methylbutyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	436.59	437.2
	B1101	(-)-6-{2-[trans, trans-4-(3-methoxyphenyl)-2-methyl-1-[2-(1H-pyrrol-1-yl)ethyl]piperidin-3-yl]ethyl}-2,3-dihydro-1H-isoindol-1-one	457.61	458.2
	B1102	(-)-6-{2-[trans, trans-4-(3-methoxyphenyl)-2-methylpiperidin-3-yl]ethyl}-2,3-dihydro-1H-isoindol-1-one	364.48	365.2
	B1103	(-)-6-{2-[trans, trans-4-(3-methoxyphenyl)-2-methyl-1-(2-phenylethyl)piperidin-3-yl]ethyl}-2,3-dihydro-1H-isoindol-1-one	468.63	469.2
	B1104	(-)-6-{2-[trans, trans-4-(3-methoxyphenyl)-2-methyl-1-propylpiperidin-3-yl]ethyl}-2,3-dihydro-1H-isoindol-1-one	406.56	407.2

Figure 1-Continued

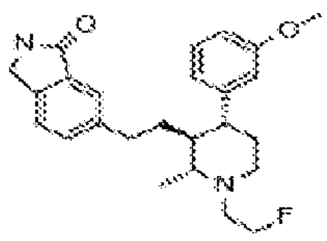
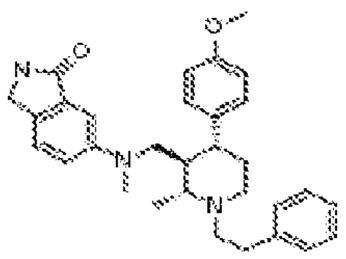
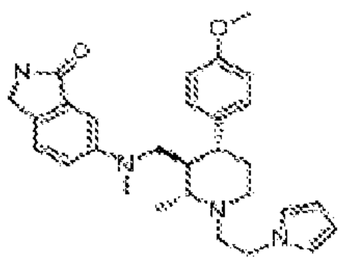
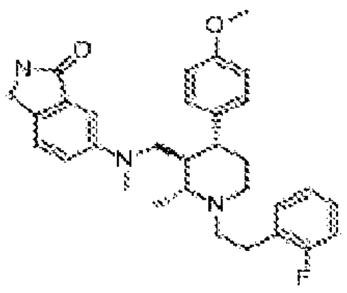
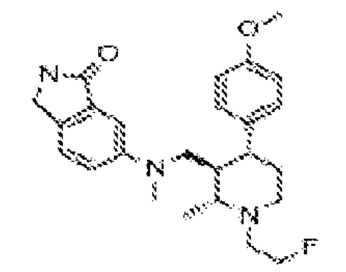
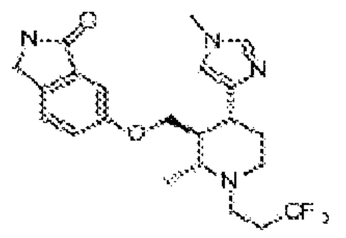
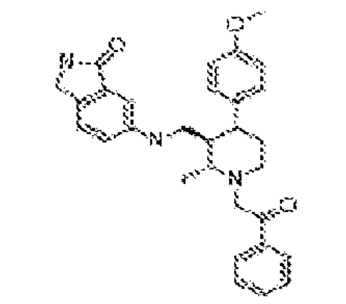
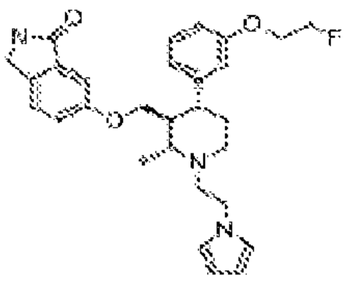
	B1105	(-)-6-{2-[trans,trans-1-(2-fluoroethyl)-4-(3-methoxyphenyl)-2-methylpiperidin-3-yl]ethyl}-2,3-dihydro-1H-isoindol-1-one	410.52	411.2
	B1106	6-({[(trans, trans)-4-(4-methoxyphenyl)-2-methyl-1-(2-phenylethyl)piperidin-3-yl]methyl}(methyl)amino)-2,3-dihydro-1H-isoindol-1-one	483.64	484.2
	B1107	6-({[(trans, trans)-4-(4-methoxyphenyl)-2-methyl-1-[2-(1H-pyrrol-1-yl)ethyl]piperidin-3-yl]methyl}(methyl)amino)-2,3-dihydro-1H-isoindol-1-one	472.62	473.2
	B1108	6-({[(trans, trans)-1-[2-(2-fluorophenyl)ethyl]-4-(4-methoxyphenyl)-2-methylpiperidin-3-yl]methyl}(methyl)amino)-2,3-dihydro-1H-isoindol-1-one	501.63	502.2
	B1109	6-({[(trans, trans)-1-(2-fluoroethyl)-4-(4-methoxyphenyl)-2-methylpiperidin-3-yl]methyl}(methyl)amino)-2,3-dihydro-1H-isoindol-1-one	425.54	426.2
	B1110	6-{[(trans, trans)-2-methyl-4-(1-methyl-1H-imidazol-4-yl)-1-(3,3,3-trifluoropropyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	436.47	437.2
	B1111	6-({[(trans, trans)-4-(4-methoxyphenyl)-2-methyl-1-(2-oxo-2-phenylethyl)piperidin-3-yl]methyl}amino)-2,3-dihydro-1H-isoindol-1-one	483.6	484.2
	B1112	(-)-6-{[trans, trans-4-[3-(2-fluoroethoxy)phenyl]-2-methyl-1-[2-(1H-pyrrol-1-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	491.6	492.2

Figure 1-Continued

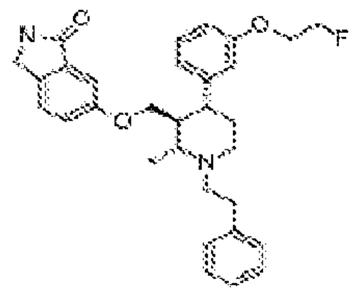
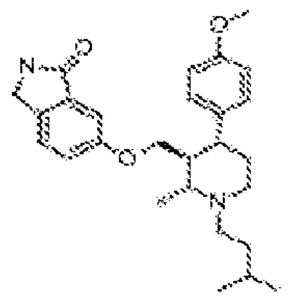
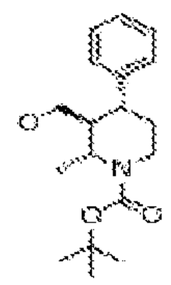
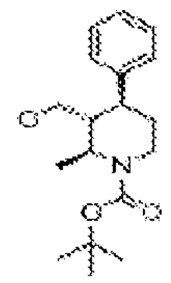
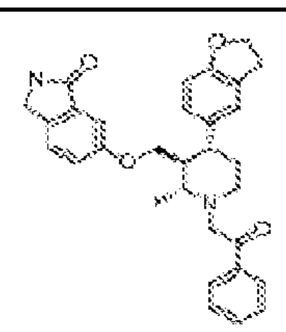
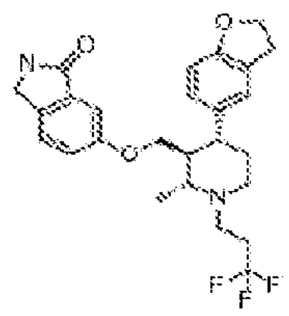
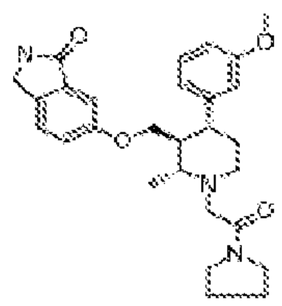
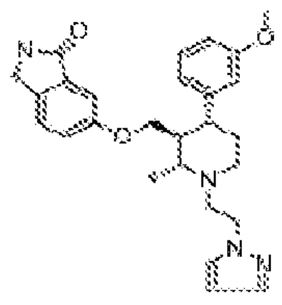
	B1113	(-)-6-{[trans, trans-4-[3-(2-fluoroethoxy)phenyl]-2-methyl-1-(2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	502.62	503.2
	B1114	(-)-6-{[trans, trans-4-(4-methoxyphenyl)-2-methyl-1-(3-methylbutyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	436.59	437.2
	B1115	(-)-tert-butyl (trans, trans)-3-(hydroxymethyl)-2-methyl-4-phenylpiperidine-1-carboxylate	305.41	250.2
	B1116	(+)-tert-butyl (trans, trans)-3-(hydroxymethyl)-2-methyl-4-phenylpiperidine-1-carboxylate	305.41	250.2
	B1117	(-)-6-{[trans, trans-4-(2,3-dihydro-1-benzofuran-5-yl)-2-methyl-1-(2-oxo-2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	496.6	497.2
	B1118	(-)-6-{[trans, trans-4-(2,3-dihydro-1-benzofuran-5-yl)-2-methyl-1-(3,3,3-trifluoropropyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	474.52	475.2
	B1119	(-)-6-{[trans, trans-4-(3-methoxyphenyl)-2-methyl-1-[2-oxo-2-(pyrrolidin-1-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	477.6	478.2
	B1120	(-)-6-{[trans, trans-4-(3-methoxyphenyl)-2-methyl-1-[2-(1H-pyr ol-1-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	460.57	461.2

Figure 1-Continued

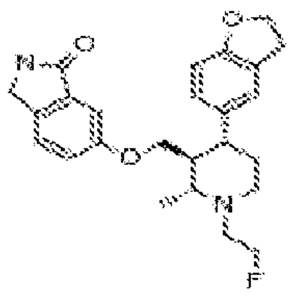
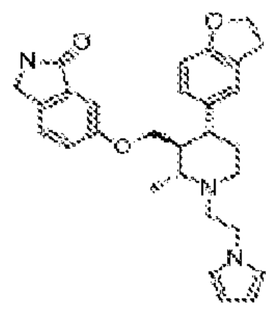
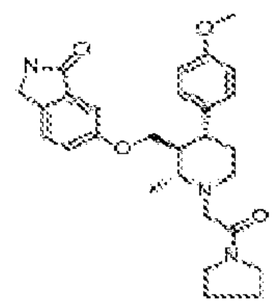
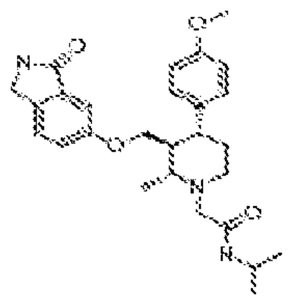
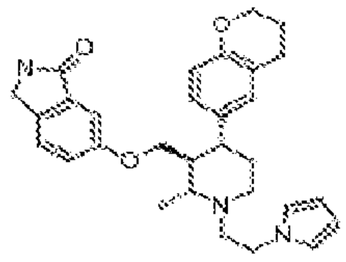
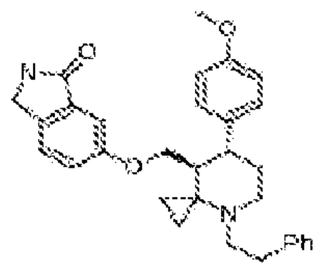
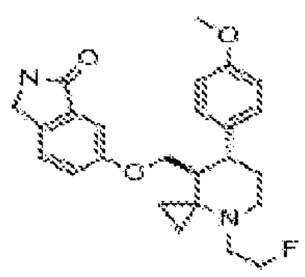
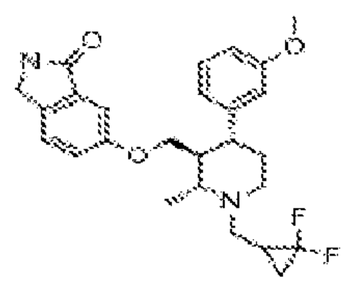
	B1121	(-)-6-{[trans, trans-4-(2,3-dihydro-1-benzofuran-5-yl)-1-(2-fluoroethyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	424.51	425.2
	B1122	(-)-6-{[trans, trans-4-(2,3-dihydro-1-benzofuran-5-yl)-2-methyl-1-[2-(1H-pyrrol-1-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1	471.59	472.2
	B1123	(-)-6-{[trans, trans-4-(4-methoxyphenyl)-2-methyl-1-[2-oxo-2-(pyrrolidin-1-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	477.6	478.2
	B1124	(-)-2-[trans, trans-4-(4-methoxyphenyl)-2-methyl-3-{[(3-oxo-2,3-dihydro-1H-isoindol-5-yl)oxy]methyl}piperidin-1-yl]-N-(propan-2-yl)acetamide	465.58	466.2
	B1125	6-{[(trans, trans)-4-(3,4-dihydro-2H-1-benzopyran-6-yl)-2-methyl-1-[2-(1H-pyrrol-1-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	485.62	486.2
	B1126	6-{[(trans)-7-(4-methoxyphenyl)-4-(2-phenylethyl)-4-azaspiro[2.5]octan-8-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	482.61	483.2
	B1127	6-{[(trans)-4-(2-fluoroethyl)-7-(4-methoxyphenyl)-4-azaspiro[2.5]octan-8-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	424.51	425.3
	B1128	6-{[(trans, trans)-1-[(2,2-difluorocyclopropyl)methyl]-4-(3-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	456.52	457.2

Figure 1-Continued

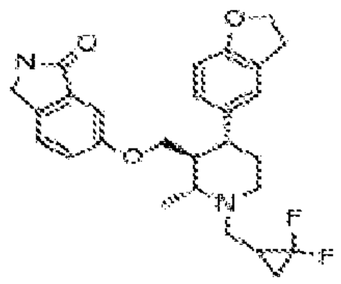
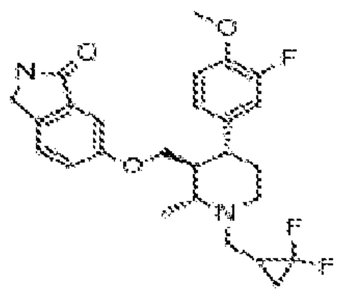
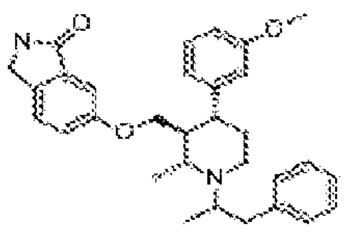
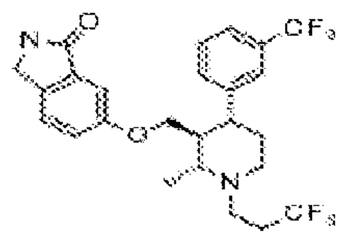
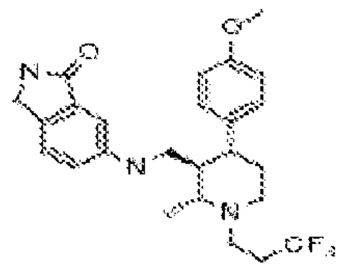
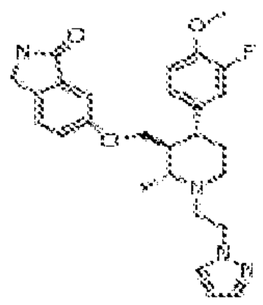
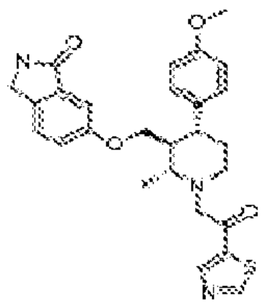
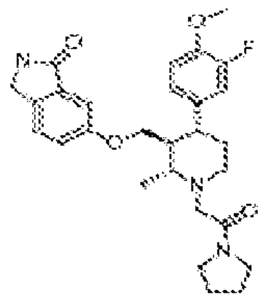
	B1129	6-{[(trans, trans)-1-[(2,2-difluorocyclopropyl)methyl]-4-(2,3-dihydro-1-benzofuran-5-yl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	468.54	469.1
	B1130	6-{[(trans, trans)-1-[(2,2-difluorocyclopropyl)methyl]-4-(3-fluoro-4-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	474.52	475.2
	B1131	(-)-6-{[trans, trans-4-(3-methoxyphenyl)-2-methyl-1-(1-phenylpropn-2-yl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	484.63	485.2
	B1132	6-{[(trans, trans)-2-methyl-4-[3-(trifluoromethyl)phenyl]-1-(3,3,3-trifluoropropyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	500.48	501.1
	B1133	6-({[(trans, trans)-4-(4-methoxyphenyl)-2-methyl-1-(3,3,3-trifluoropropyl)piperidin-3-yl]methyl}amino)-2,3-dihydro-1H-isoindol-1-one	461.52	462.2
	B1134	(-)-6-{[trans, trans-4-(3-fluoro-4-methoxyphenyl)-2-methyl-1-[2-(1H-pyrrol-1-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	478.56	479.2
	B1135	(-)-6-{[trans, trans-4-(4-methoxyphenyl)-2-methyl-1-[2-oxo-2-(1,3-thizol-5-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	491.6	492.1
	B1136	(-)-6-{[trans, trans-4-(3-fluoro-4-methoxyphenyl)-2-methyl-1-[2-oxo-2-(pyrrolidin-1-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	495.59	496.2

Figure 1-Continued

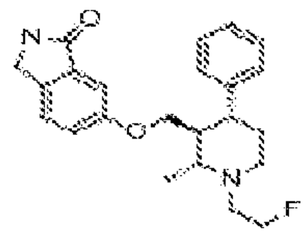
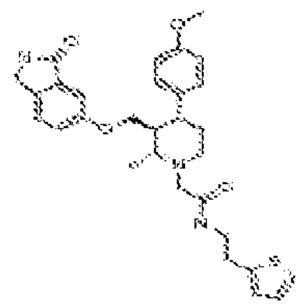
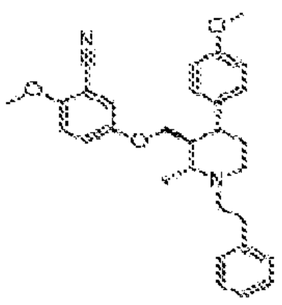
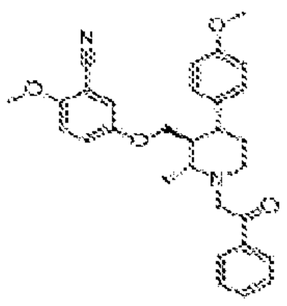
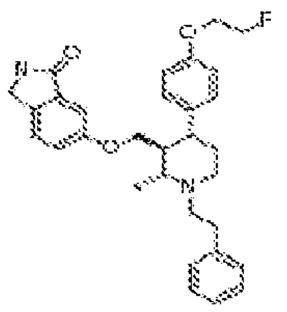
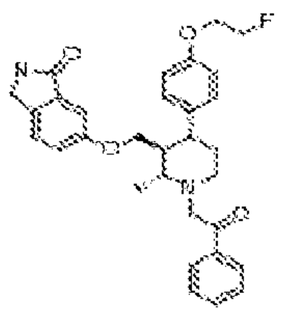
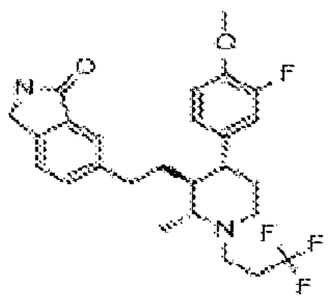
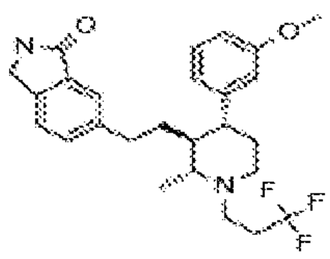
	B1137	(-)-6-{[trans, trans-1-(2-fluoroethyl)-2-methyl-4-phenylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	382.47	383.2
	B1138	(-)-2-[trans, trans-4-(4-methoxyphenyl)-2-methyl-3-{[(3-methylidene-2,3-dihydro-1H-isoindol-5-yl)oxy]methyl}piperidin-1-yl]-N-[2-(thiophen-2-yl)ethyl]acetmide	533.68	534.2
	B1139	(-)-2-methoxy-5-{[trans, trans-4-(4-methoxyphenyl)-2-methyl-1-(2-phenylethyl)piperidin-3-yl]methoxy}benzonitrile	470.6	471.2
	B1140	(-)-2-methoxy-5-{[trans, trans-4-(4-methoxyphenyl)-2-methyl-1-(2-oxo-2-phenylethyl)piperidin-3-yl]methoxy}benzonitrile	484.59	485.2
	B1141	(-)-6-{[trans, trans-4-[4-(2-fluoroethoxy)phenyl]-2-methyl-1-(2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	502.62	503.2
	B1142	(-)-6-{[trans, trans-4-[4-(2-fluoroethoxy)phenyl]-2-methyl-1-(2-oxo-2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	516.6	517.2
	B1143	6-{2-[(trans, trans)-4-(3-fluoro-4-methoxyphenyl)-2-methyl-1-(3,3,3-trifluoropropyl)piperidin-3-yl]ethyl}-2,3-dihydro-1H-isoindol-1-one	478.52	479.2
	B1144	6-{2-[(trans, trans)-4-(3-methoxyphenyl)-2-methyl-1-(3,3,3-trifluoropropyl)piperidin-3-yl]ethyl}-2,3-dihydro-1H-isoindol-1-one	460.53	461.2

Figure 1-Continued

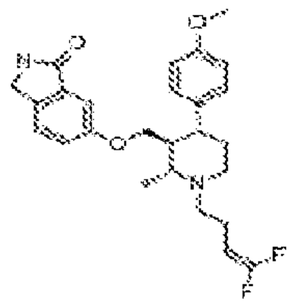
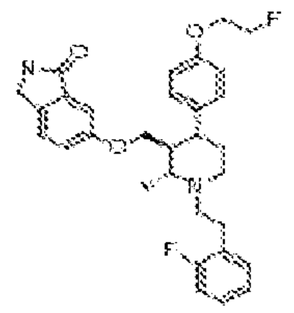
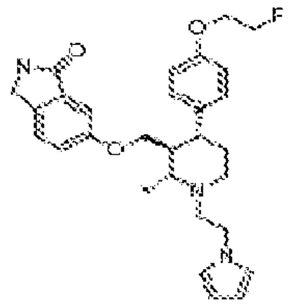
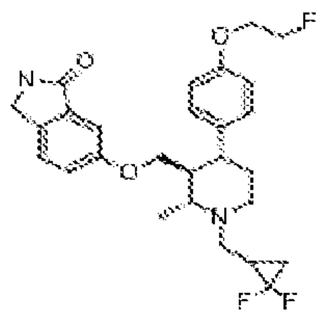
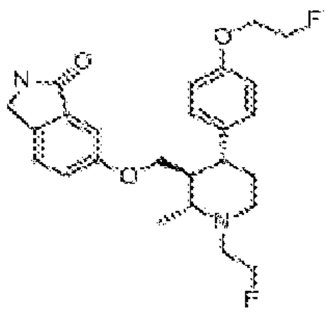
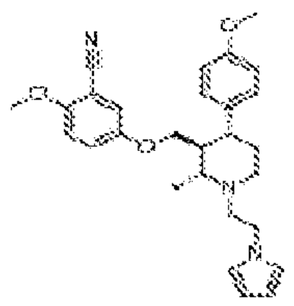
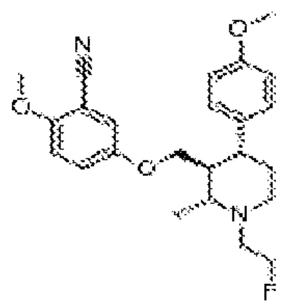
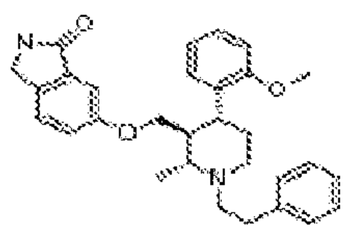
	B1145	(-)-6-{[trans, trans-1-(4,4-difluorobut-3-en-1-yl)-4-(4-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	456.52	457.2
	B1146	(-)-6-{[trans, trans-4-[4-(2-fluoroethoxy)phenyl]-1-[2-(2-fluorophenyl)ethyl]-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	520.61	521.2
	B1147	(-)-6-{[trans, trans-4-[4-(2-fluoroethoxy)phenyl]-2-methyl-1-[2-(1H-pyrrol-1-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	491.6	492.2
	B1148	(-)-6-{[trans, trans-1-[(2,2-difluorocyclopropyl)methyl]-4-[4-(2-fluoroethoxy)phenyl]-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	488.54	489.2
	B1149	(-)-6-{[trans, trans-4-[4-(2-fluoroethoxy)phenyl]-1-(2-fluoroethyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	444.51	445.2
	B1150	2-methoxy-5-{[(-)-4-(4-methoxyphenyl)-2-methyl-1-[2-(1H-pyrrol-1-yl)ethyl]piperidin-3-yl]methoxy}benzonitrile	459.58	460.2
	B1151	(-)-5-{[trans, trans-1-(2-fluoroethyl)-4-(4-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}-2-methoxybenzonitrile	412.5	413.2
	B1152	6-{[(trans, trans)-4-(2-methoxyphenyl)-2-methyl-1-(2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	470.6	471.3

Figure 1-Continued

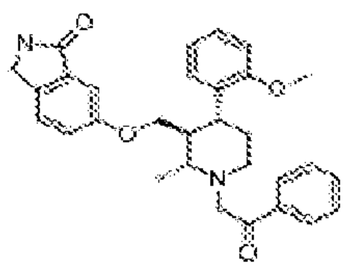
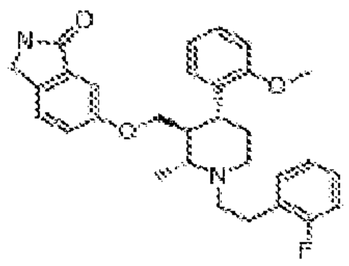
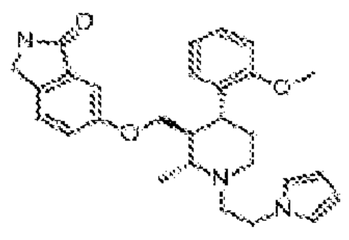
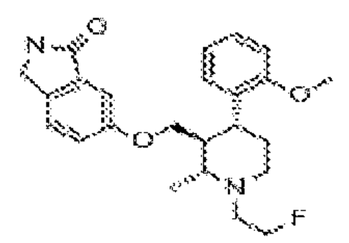
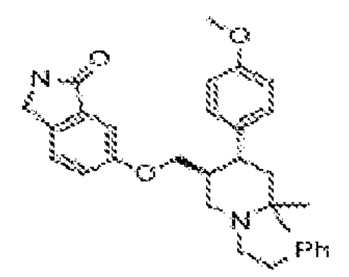
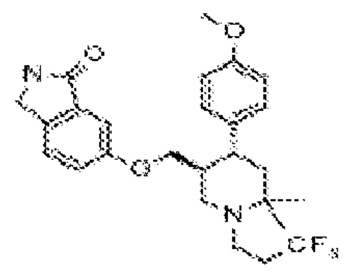
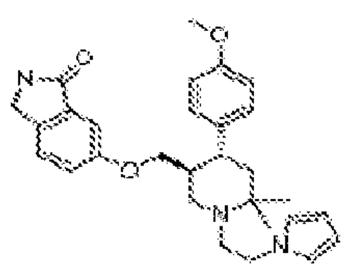
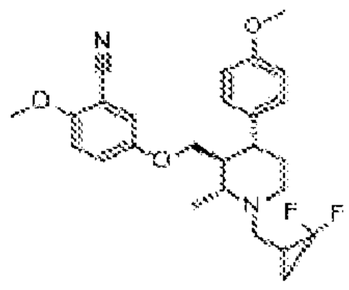
	B1153	6-{[(trans, trans)-4-(2-methoxyphenyl)-2-methyl-1-(2-oxo-2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	484.59	485.3
	B1154	6-{[(trans, trans)-1-[2-(2-fluorophenyl)ethyl]-4-(2-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	488.59	489.2
	B1155	6-{[(trans, trans)-4-(2-methoxyphenyl)-2-methyl-1-[2-(1H-pyrrol-1-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	459.58	460.4
	B1156	6-{[(trans, trans)-1-(2-fluoroethyl)-4-(2-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	412.5	413.1
	B1157	6-{[(trans)-4-(4-methoxyphenyl)-6,6-dimethyl-1-(2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	484.63	485.3
	B1158	6-{[(trans)-4-(4-methoxyphenyl)-6,6-dimethyl-1-(3,3,3-trifluoropropyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	476.53	477.3
	B1159	6-{[(trans, trans)-4-(4-methoxyphenyl)-6,6-dimethyl-1-[2-(1H-pyrrol-1-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	473.61	474.3
	B1160	(-)-5-{[1-[(2,2-difluorocyclopropyl)methyl]-4-(4-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}-2-methoxybenzonitrile	456.52	457.2

Figure 1-Continued

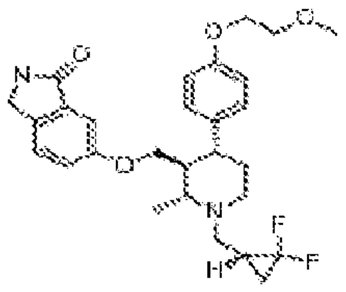
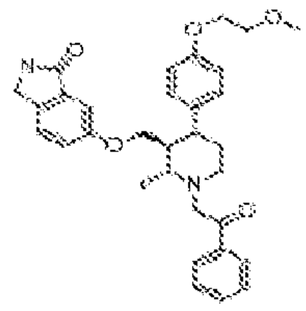
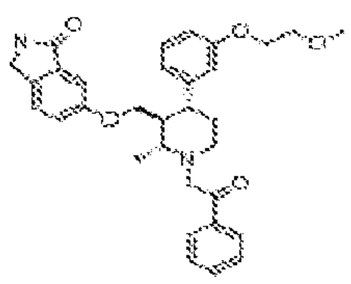
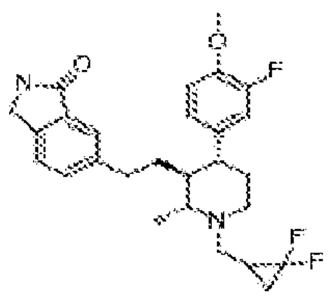
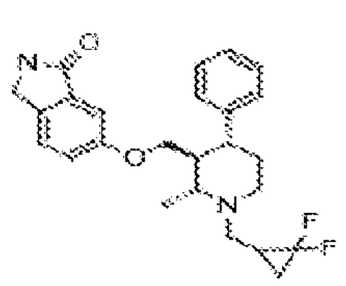
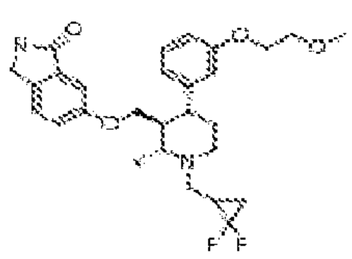
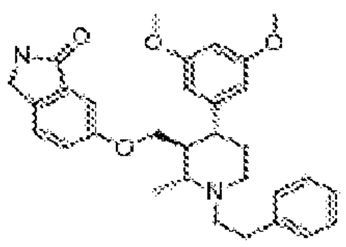
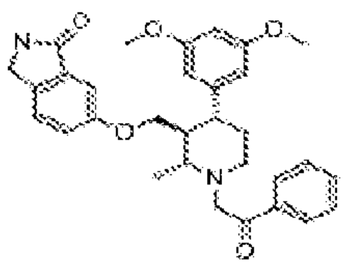
	B1161	6-{[(trans, trans)-1-[(2,2-difluorocyclopropyl)methyl]-4-[4-(2-methoxyethoxy)phenyl]-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	500.58	501.2
	B1162	(-)-6-{[trans, trans-4-[4-(2-methoxyethoxy)phenyl]-2-methyl-1-(2-oxo-2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	528.64	529.2
	B1163	(-)-6-{[trans, trans-4-[3-(2-methoxyethoxy)phenyl]-2-methyl-1-(2-oxo-2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	528.64	529.2
	B1164	6-{2-[(trans, trans)-1-[(2,2-difluorocyclopropyl)methyl]-4-(3-fluoro-4-methoxyphenyl)-2-methylpiperidin-3-yl]ethyl}-2,3-dihydro-1H-isoindol-1-one	472.54	473.2
	B1165	6-{[(trans, trans)-1-[(2,2-difluorocyclopropyl)methyl]-2-methyl-4-phenylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	426.5	427.2
	B1166	(-)-6-{[trans, trans-1-[(2,2-difluorocyclopropyl)methyl]-4-[3-(2-methoxyethoxy)phenyl]-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	500.58	501.2
	B1167	6-{[(trans, trans)-4-(3,5-dimethoxyphenyl)-2-methyl-1-(2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	500.63	501.3
	B1168	6-{[(trans, trans)-4-(3,5-dimethoxyphenyl)-2-methyl-1-(2-oxo-2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	514.61	515.2

Figure 1-Continued

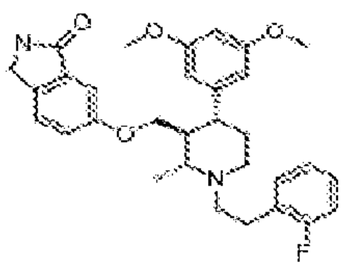
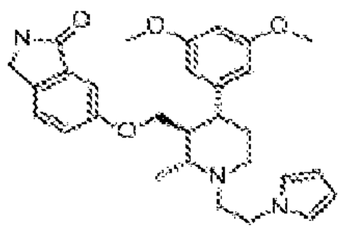
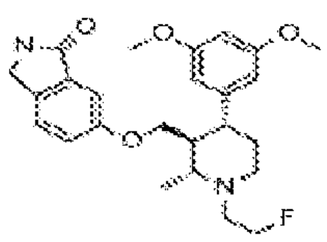
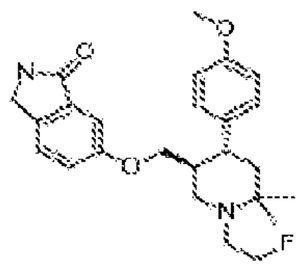
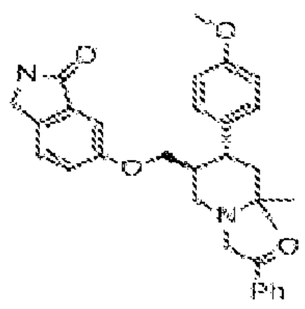
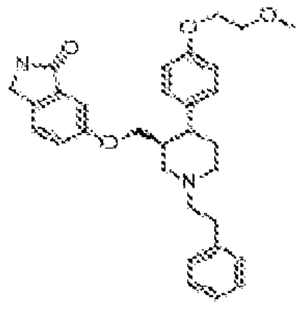
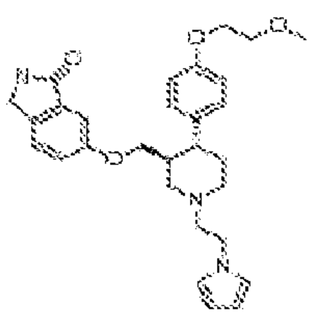
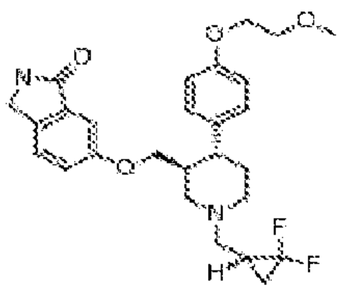
	B1169	6-{[(trans, trans)-4-(3,5-dimethoxyphenyl)-1-[2-(2-fluorophenyl)ethyl]-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	518.62	519.1
	B1170	6-{[(trans, trans)-4-(3,5-dimethoxyphenyl)-2-methyl-1-[2-(1H-pyrrol-1-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	489.61	490.3
	B1171	6-{[(trans, trans)-4-(3,5-dimethoxyphenyl)-1-(2-fluoroethyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	442.52	443.2
	B1172	6-{[(trans)-1-(2-fluoroethyl)-4-(4-methoxyphenyl)-6,6-dimethylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	426.52	427.2
	B1173	6-{[(trans)-4-(4-methoxyphenyl)-6,6-dimethyl-1-(2-oxo-2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	498.61	499.3
	B1174	6-((trans, trans){4-[4-(2-methoxyethoxy)phenyl]-1-(2-phenylethyl)piperidin-3-yl}methoxy)-2,3-dihydro-1H-isoindol-1-one	500.63	501.2
	B1175	6-({trans-4-[4-(2-methoxyethoxy)phenyl]-1-[2-(1H-pyrrol-1-yl)ethyl]piperidin-3-yl}methoxy)-2,3-dihydro-1H-isoindol-1-one	489.61	490.2
	B1176	6-({trans-1-[(2,2-difluorocyclopropyl)methyl]-4-[4-(2-methoxyethoxy)phenyl]piperidin-3-yl}methoxy)-2,3-dihydro-1H-isoindol-1-one	486.55	487.2

Figure 1-Continued

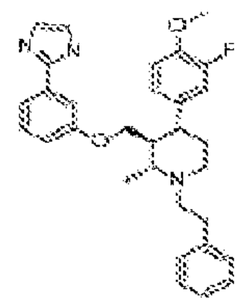
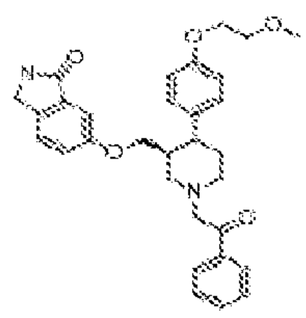
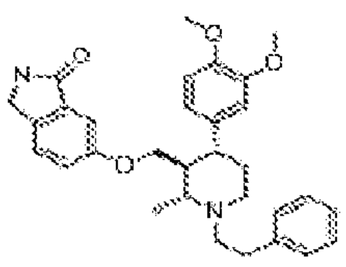
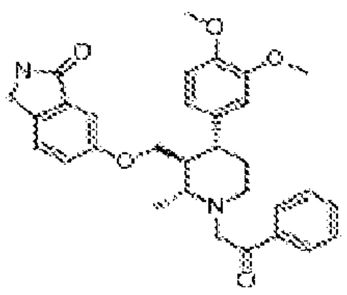
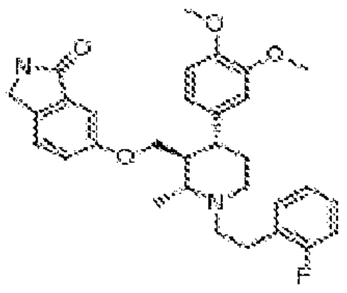
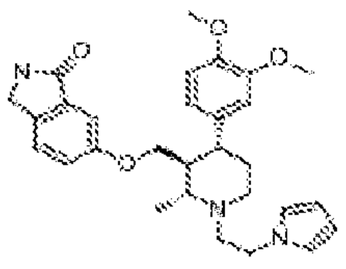
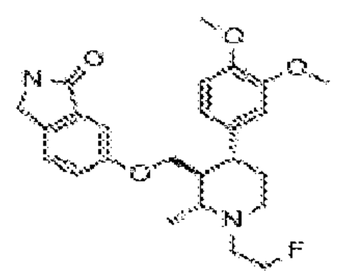
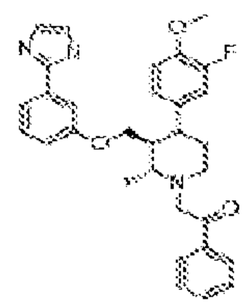
	B1177	(-)-4-(3-fluoro-4-methoxyphenyl)-3-[3-(1H-imidzol-2-yl)phenoxymethyl]-2-methyl-1-(2-phenylethyl)piperidine	499.62	500.2
	B1178	6-{(trans)-4-[4-(2-methoxyethoxy)phenyl]-1-(2-oxo-2-phenylethyl)piperidin-3-yl}methoxy)-2,3-dihydro-1H-isoindol-1-one	514.61	515.2
	B1179	6-{[(trans, trans)-4-(3,4-dimethoxyphenyl)-2-methyl-1-(2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	500.63	501.4
	B1180	6-{[(trans, trans)-4-(3,4-dimethoxyphenyl)-2-methyl-1-(2-oxo-2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	514.61	515.3
	B1181	6-{[(trans, trans)-4-(3,4-dimethoxyphenyl)-1-[2-(2-fluorophenyl)ethyl]-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	518.62	519.5
	B1182	6-{[(trans, trans)-4-(3,4-dimethoxyphenyl)-2-methyl-1-[2-(1H-pyrrol-1-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	489.61	490.4
	B1183	6-{[(trans, trans)-4-(3,4-dimethoxyphenyl)-1-(2-fluoroethyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	442.52	443.2
	B1184	(-)-2-[trans, trans-4-(3-fluoro-4-methoxyphenyl)-3-[3-(1H-imid ol-2-yl)phenoxymethyl]-2-methylpiperidin-1-yl]-1-phenylethn-1-one	513.6	514.2

Figure 1-Continued

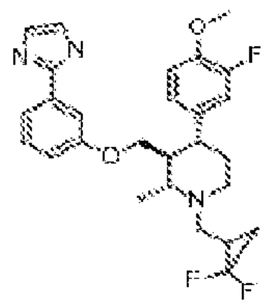
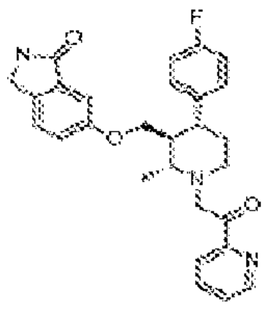
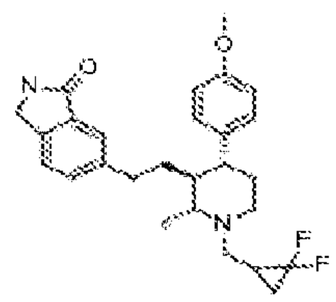
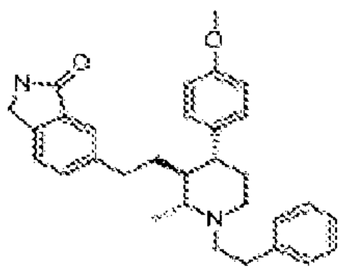
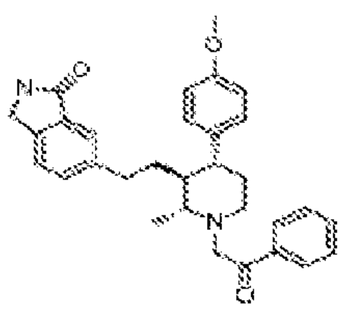
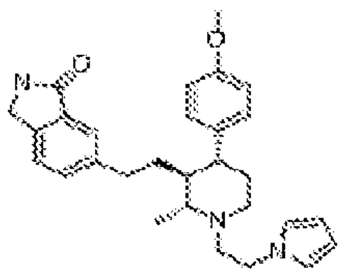
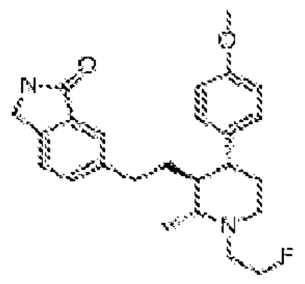
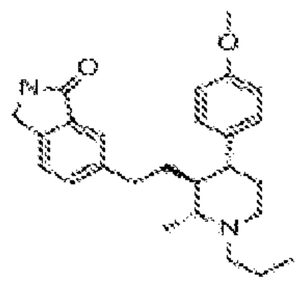
	B1185	1-[(2,2-difluorocyclopropyl)methyl]-trans, trans-4-(3-fluoro-4-methoxyphenyl)-3-[3-(1H-imidzol-2-yl)phenoxymethyl]-2-methylpiperidine	485.54	486.1
	B1186	(-)-6-{[trans, trans-4-(4-fluorophenyl)-2-methyl-1-[2-oxo-2-(pyridin-2-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	473.54	474.2
	B1187	6-{2-[(trans, trans)-1-[(2,2-difluorocyclopropyl)methyl]-4-(4-methoxyphenyl)-2-methylpiperidin-3-yl]ethyl}-2,3-dihydro-1H-isoindol-1-one	454.55	455.2
	B1188	6-{2-[(trans, trans)-4-(4-methoxyphenyl)-2-methyl-1-(2-phenylethyl)piperidin-3-yl]ethyl}-2,3-dihydro-1H-isoindol-1-one	468.63	469.2
	B1189	6-{2-[(trans, trans)-4-(4-methoxyphenyl)-2-methyl-1-(2-oxo-2-phenylethyl)piperidin-3-yl]ethyl}-2,3-dihydro-1H-isoindol-1-one	482.61	483.2
	B1190	6-{2-[(trans, trans)-4-(4-methoxyphenyl)-2-methyl-1-[2-(1H-pyrrol-1-yl)ethyl]piperidin-3-yl]ethyl}-2,3-dihydro-1H-isoindol-1-one	457.61	458.2
	B1191	6-{2-[(trans, trans)-1-(2-fluoroethyl)-4-(4-methoxyphenyl)-2-methylpiperidin-3-yl]ethyl}-2,3-dihydro-1H-isoindol-1-one	410.52	411.2
	B1192	6-{2-[(trans, trans)-4-(4-methoxyphenyl)-2-methyl-1-propylpiperidin-3-yl]ethyl}-2,3-dihydro-1H-isoindol-1-one	406.56	407.2

Figure 1-Continued

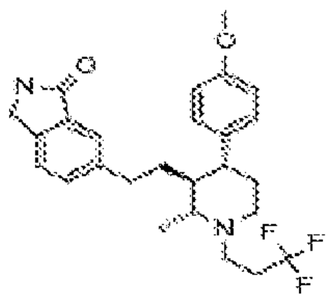
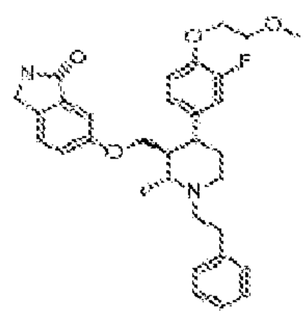
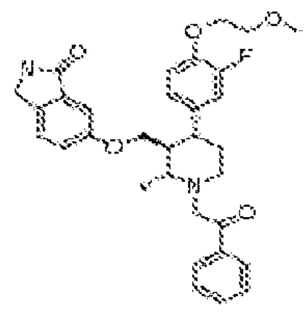
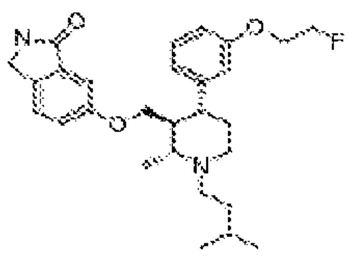
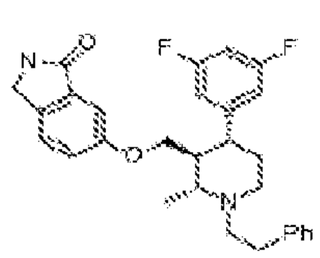
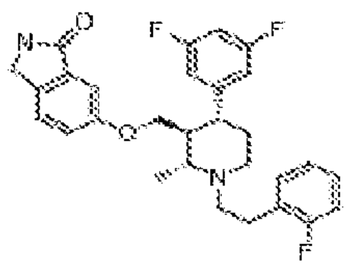
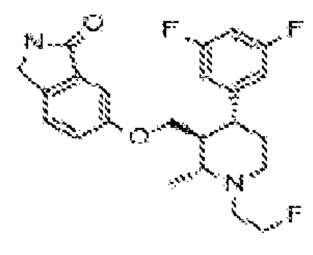
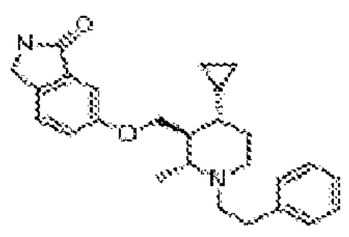
	B1193	6-{2-[(trans, trans)-4-(4-methoxyphenyl)-2-methyl-1-(3,3,3-trifluoropropyl)piperidin-3-yl]ethyl}-2,3-dihydro-1H-isoindol-1-one	460.53	461.2
	B1194	(-)-6-{[trans, trans-4-[3-fluoro-4-(2-methoxyethoxy)phenyl]-2-methyl-1-(2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	532.65	533.2
	B1195	(-)-6-{[trans, trans-4-[3-fluoro-4-(2-methoxyethoxy)phenyl]-2-methyl-1-(2-oxo-2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	546.63	547.2
	B1196	(-)-6-{[trans, trans-4-[3-(2-fluoroethoxy)phenyl]-2-methyl-1-(3-methylbutyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	468.6	469.2
	B1197	6-{[(trans, trans)-4-(3,5-difluorophenyl)-2-methyl-1-(2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	476.56	477
	B1198	6-{[(trans, trans)-4-(3,5-difluorophenyl)-1-[2-(2-fluorophenyl)ethyl]-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	494.55	495
	B1199	6-{[(trans, trans)-4-(3,5-difluorophenyl)-1-(2-fluoroethyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	418.45	418.95
	B1200	6-{[(trans, trans)-4-cyclopropyl-2-methyl-1-(2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	404.54	405.2

Figure 1-Continued

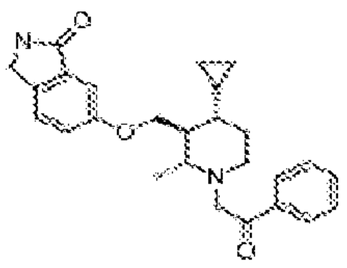
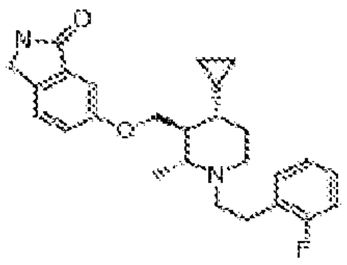
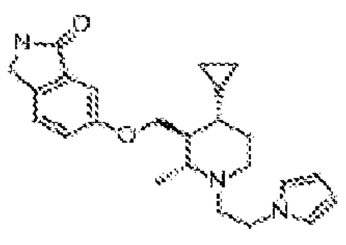
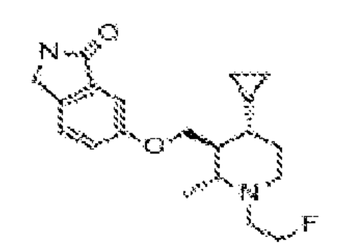
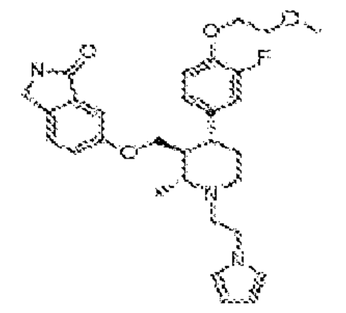
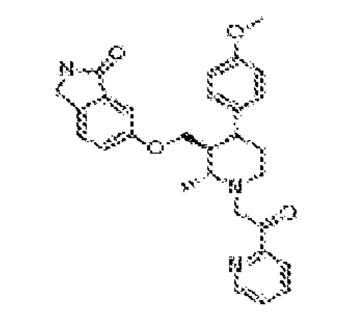
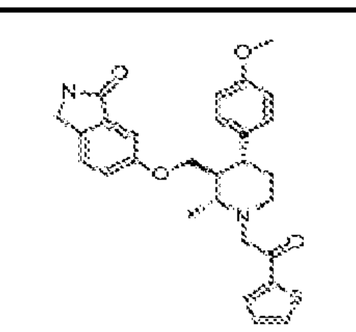
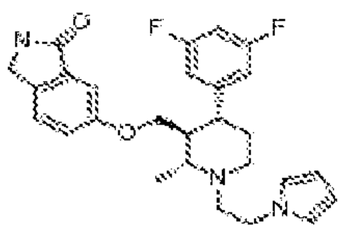
	B1201	6-{[(trans, trans)-4-cyclopropyl-2-methyl-1-(2-oxo-2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	418.53	419.3
	B1202	6-{[(trans, trans)-4-cyclopropyl-1-[2-(2-fluorophenyl)ethyl]-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	422.54	423.2
	B1203	6-{[(trans, trans)-4-cyclopropyl-2-methyl-1-[2-(1H-pyrrol-1-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	393.52	394.3
	B1204	6-{[(trans, trans)-4-cyclopropyl-1-(2-fluoroethyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	346.44	347.2
	B1205	(-)-6-{[trans, trans-4-[3-fluoro-4-(2-methoxyethoxy)phenyl]-2-methyl-1-[2-(1H-pyrrol-1-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	521.62	522.2
	B1206	(-)-6-{[trans, trans-4-(4-methoxyphenyl)-2-methyl-1-[2-oxo-2-(pyridin-2-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	485.57	486.1
	B1207	(-)-6-{[trans, trans-4-(4-methoxyphenyl)-2-methyl-1-[2-oxo-2-(thiophen-2-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	490.61	491.1
	B1208	6-{[(trans, trans)-4-(3,5-difluorophenyl)-2-methyl-1-[2-(1H-pyrrol-1-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	465.53	466.3

Figure 1-Continued

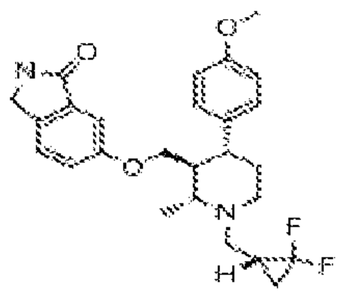
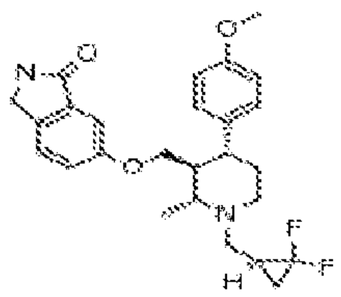
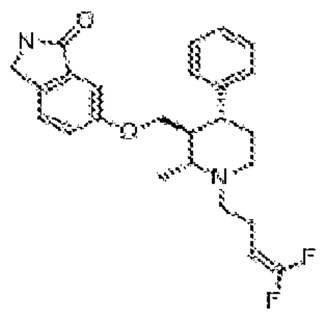
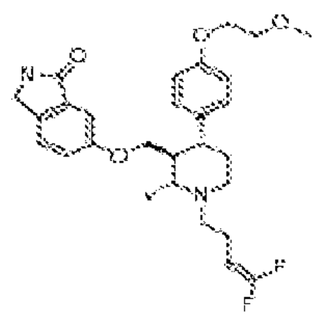
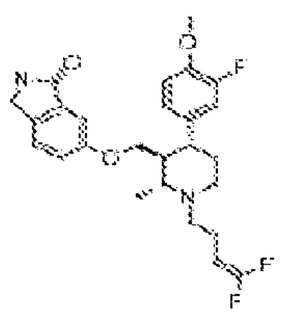
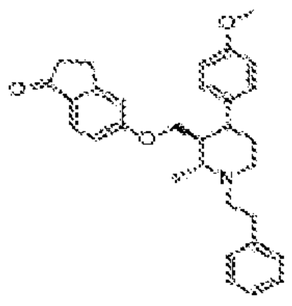
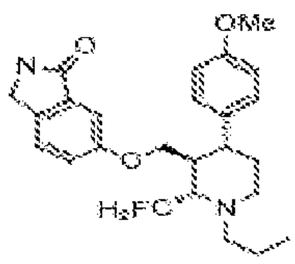
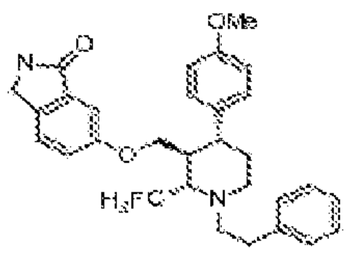
	B1209	(-)-6-{[(trans, trans)-1-{[2,2-difluorocyclopropyl]methyl}-4-(4-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	456.52	457.2
	B1210	(-)-6-{[(trans, trans)-1-{[2,2-difluorocyclopropyl]methyl}-4-(4-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	456.52	457.2
	B1211	(-)-6-{[trans, trans-1-(4,4-difluorobut-3-en-1-yl)-2-methyl-4-phenylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	426.5	427.1
	B1212	(-)-6-{[trans, trans-1-(4,4-difluorobut-3-en-1-yl)-4-[4-(2-methoxyethoxy)phenyl]-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	500.58	501.2
	B1213	(-)-6-{[trans, trans-1-(4,4-difluorobut-3-en-1-yl)-4-(3-fluoro-4-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	474.52	475.2
	B1214	(-)-5-{[trans, trans-4-(4-methoxyphenyl)-2-methyl-1-(2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-inden-1-one	469.61	470.2
	B1215	6-{[(trans, trans)-2-(fluoromethyl)-4-(4-methoxyphenyl)-1-propylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	426.52	427.4
	B1216	6-{[(trans, trans)-2-(fluoromethyl)-4-(4-methoxyphenyl)-1-(2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	488.59	489.1

Figure 1-Continued

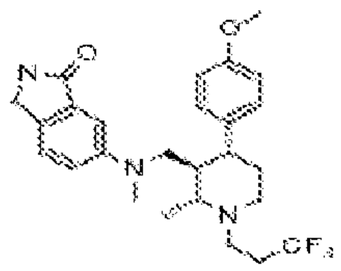
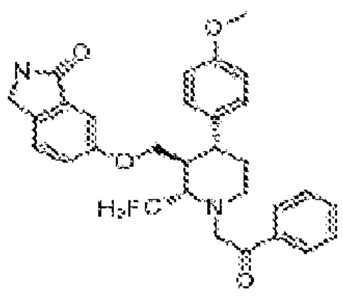
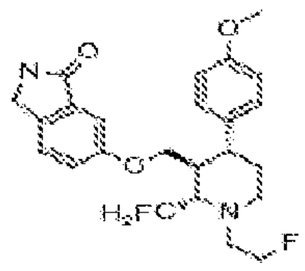
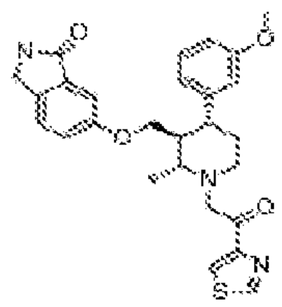
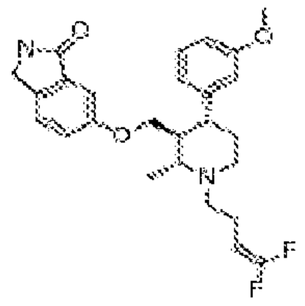
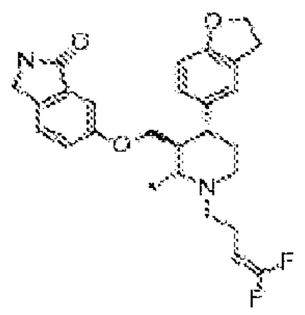
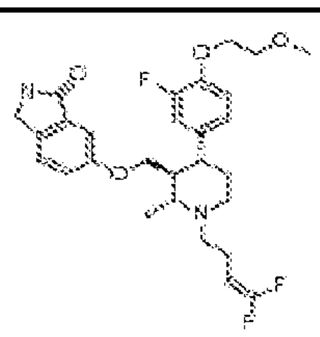
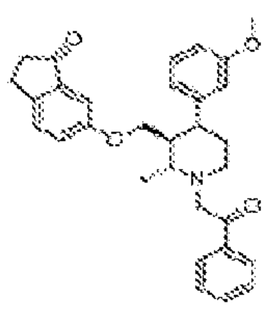
	B1217	6-({[(trans, trans)-4-(4-methoxyphenyl)-2-methyl-1-(3,3,3-trifluoropropyl)piperidin-3-yl]methyl}(methyl)amino)-2,3-dihydro-1H-isoindol-1-one	475.55	476.1
	B1218	6-{[(trans, trans)-2-(fluoromethyl)-4-(4-methoxyphenyl)-1-(2-oxo-2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	502.58	503.1
	B1219	6-{[(trans, trans)-1-(2-fluoroethyl)-2-(fluoromethyl)-4-(4-methoxyphenyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	430.49	431.3
	B1220	(-)-6-{[trans, trans-4-(3-methoxyphenyl)-2-methyl-1-[2-oxo-2-(1,3-thizol-4-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	491.6	492.1
	B1221	(-)-6-{[trans, trans-1-(4,4-difluorobut-3-en-1-yl)-4-(3-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	456.52	457.2
	B1222	(-)-6-{[trans, trans-1-(4,4-difluoro ut-3-en-1-yl)-4-(2,3-dihydro-1-benzofuran-5-yl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	468.54	469.1
	B1223	(-)-6-{[trans, trans-1-(4,4-difluorobut-3-en-1-yl)-4-[3-fluoro-4-(2-methoxyethoxy)phenyl]-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	518.57	519.2
	B1224	(-)-6-{[trans, trans-4-(3-methoxyphenyl)-2-methyl-1-(2-oxo-2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-inden-1-one	483.6	484.2

Figure 1-Continued

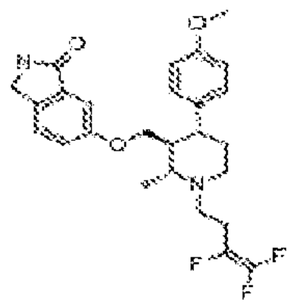
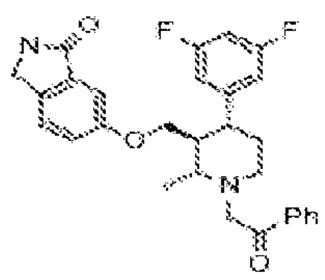
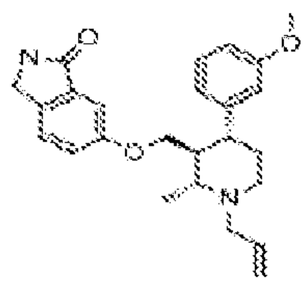
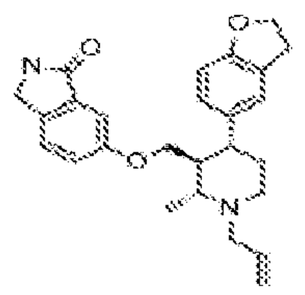
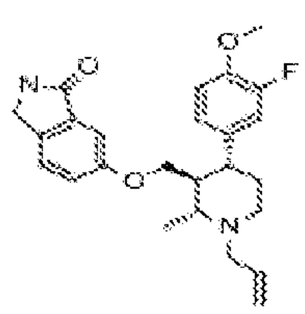
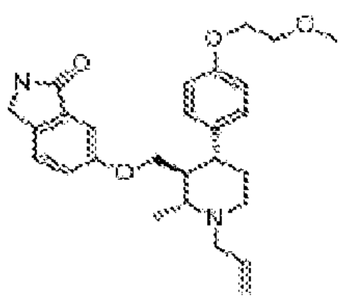
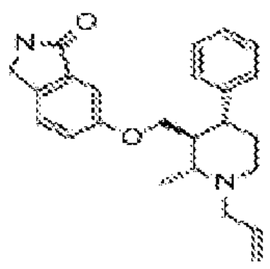
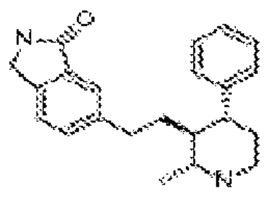
	B1225	(-)-6-{[trans, trans-4-(4-methoxyphenyl)-2-methyl-1-(3,4,4-trifluorobut-3-en-1-yl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	474.52	475.2
	B1226	6-{[(trans, trans)-4-(3,5-difluorophenyl)-2-methyl-1-(2-oxo-2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	490.54	491.2
	B1227	(-)-6-{[trans, trans-4-(3-methoxyphenyl)-2-methyl-1-(prop-2-en-1-yl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	406.52	407.2
	B1228	(-)-6-{[trans, trans-4-(2,3-dihydro-1-benzofuran-5-yl)-2-methyl-1-(prop-2-en-1-yl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	418.53	419.2
	B1229	(-)-6-{[trans, trans-4-(3-fluoro-4-methoxyphenyl)-2-methyl-1-(prop-2-en-1-yl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	424.51	425.1
	B1230	(-)-6-{[trans, trans-4-[4-(2-methoxyethoxy)phenyl]-2-methyl-1-(prop-2-en-1-yl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	450.57	451.2
	B1231	6-{[(trans, trans)-2-methyl-4-phenyl-1-(prop-2-en-1-yl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	376.49	377.1
	B1232	6-{2-[(trans, trans)-2-methyl-4-phenylpiperidin-3-yl]ethyl}-2,3-dihydro-1H-isoindol-1-one	334.45	335.1

Figure 1-Continued

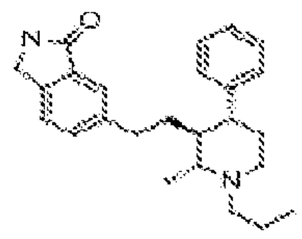
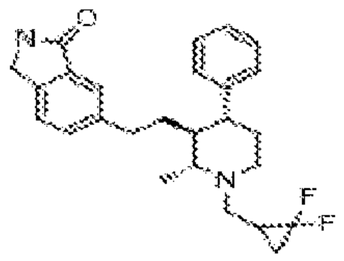
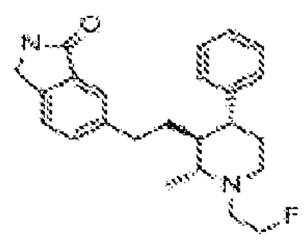
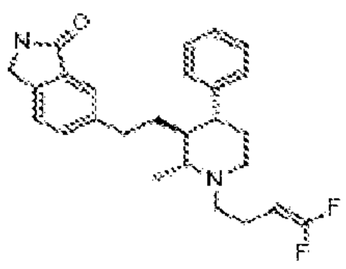
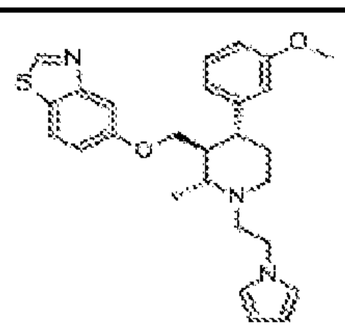
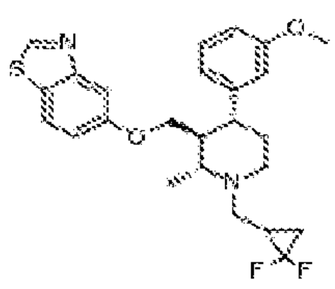
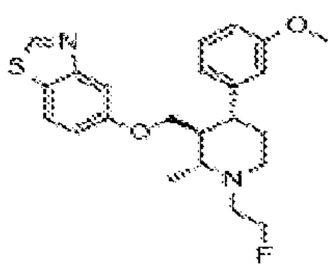
	B1233	6-{2-[(trans, trans)-2-methyl-4-phenyl-1-propylpiperidin-3-yl]ethyl}-2,3-dihydro-1H-isoindol-1-one	376.53	377.2
	B1234	6-{2-[(trans, trans)-1-[(2,2-difluorocyclopropyl)methyl]-2-methyl-4-phenylpiperidin-3-yl]ethyl}-2,3-dihydro-1H-isoindol-1-one	424.53	425.2
	B1235	6-{2-[(trans, trans)-1-(2-fluoroethyl)-2-methyl-4-phenylpiperidin-3-yl]ethyl}-2,3-dihydro-1H-isoindol-1-one	380.5	381.2
	B1236	(-)-6-{2-[trans, trans-1-(4,4-difluorobut-3-en-1-yl)-2-methyl-4-phenylpiperidin-3-yl]ethyl}-2,3-dihydro-1H-isoindol-1-one	424.53	425.1
	B1237	6-{2-[(trans, trans)-2-methyl-4-phenyl-1-(prop-2-en-1-yl)piperidin-3-yl]ethyl}-2,3-dihydro-1H-isoindol-1-one	374.52	375.2
	B1238	(-)-5-{[trans, trans-4-(3-methoxyphenyl)-2-methyl-1-[2-(1H-pyrrol-1-yl)ethyl]piperidin-3-yl]methoxy}-1,3-benzothizole	461.62	462.1
	B1239	(-)-5-{[trans, trans-1-[(2,2-difluorocyclopropyl)methyl]-4-(3-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}-1,3-benzothizole	458.56	459.1
	B1240	(-)-5-{[trans, trans-1-(2-fluoroethyl)-4-(3-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}-1,3-benzothizole	414.54	415.1

Figure 1-Continued

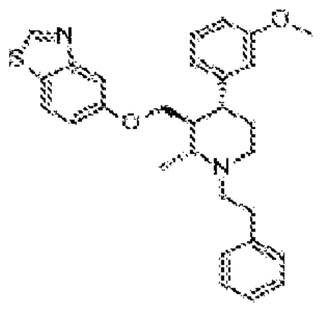
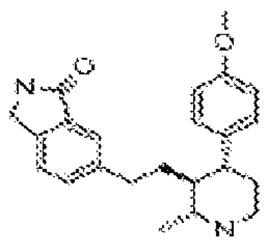
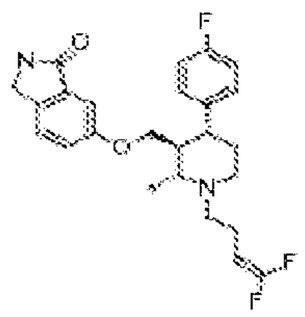
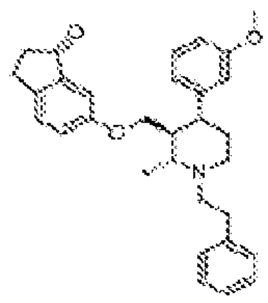
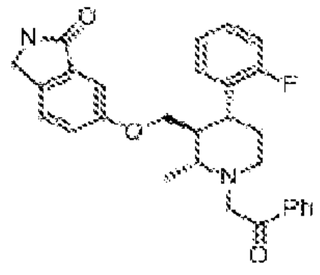
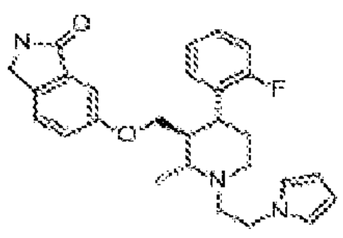
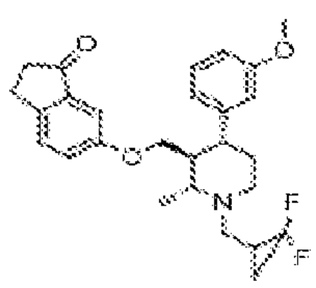
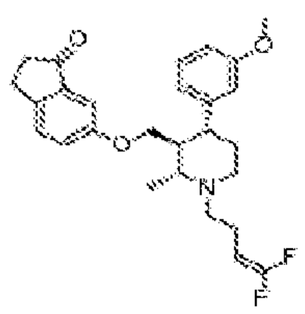
	B1241	(-)-5-{[trans, trans-4-(3-methoxyphenyl)-2-methyl-1-(2-phenylethyl)piperidin-3-yl]methoxy}-1,3-benzothiazole	472.64	473.1
	B1242	6-{2-[(trans, trans)-4-(4-methoxyphenyl)-2-methylpiperidin-3-yl]ethyl}-2,3-dihydro-1H-isoindol-1-one	364.48	365.2
	B1243	(-)-6-{[trans, trans-1-(4,4-difluorobut-3-en-1-yl)-4-(4-fluorophenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	444.49	445.1
	B1244	(-)-6-{[trans, trans-4-(3-methoxyphenyl)-2-methyl-1-(2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-inden-1-one	469.61	470.2
	B1245	6-{[(trans, trans)-4-(2-fluorophenyl)-2-methyl-1-(2-oxo-2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	472.55	473.3
	B1246	6-{[(trans, trans)-4-(2-fluorophenyl)-2-methyl-1-[2-(1H-pyrrol-1-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	447.54	448.1
	B1247	(-)-6-{[trans, trans-1-[(2,2-difluorocyclopropyl)methyl]-4-(3-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-inden-1-one	455.54	456.1
	B1248	(-)-6-{[trans, trans-1-(4,4-difluorobut-3-en-1-yl)-4-(3-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-inden-1-one	455.54	456.2

Figure 1-Continued

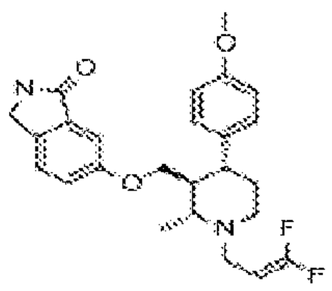
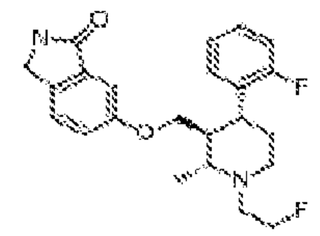
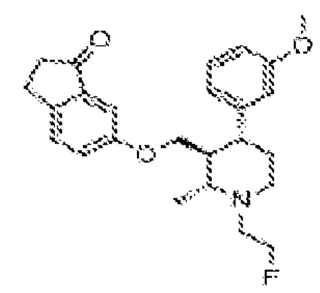
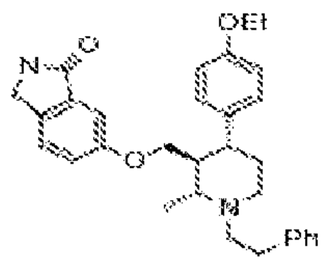
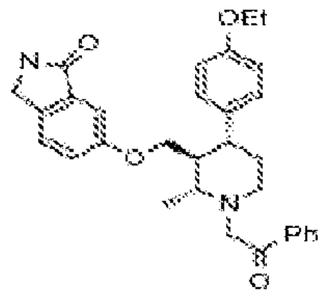
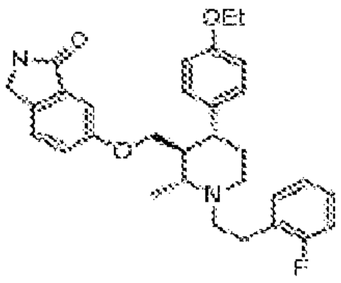
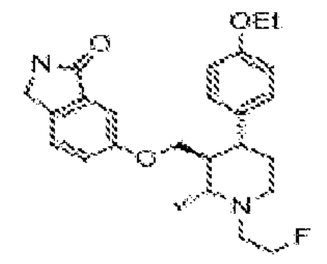
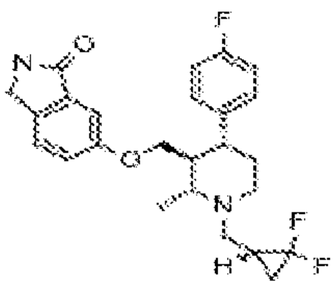
	B1249	(-)-6-{[trans, trans-1-(3,3-difluoroprop-2-en-1-yl)-4-(4-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	442.5	443.1
	B1250	6-{[(trans, trans)-1-(2-fluoroethyl)-4-(2-fluorophenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	400.46	401.1
	B1251	(-)-6-{[trans, trans-1-(2-fluoroethyl)-4-(3-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-inden-1-one	411.51	412.2
	B1252	6-{[(trans, trans)-4-(4-ethoxyphenyl)-2-methyl-1-(2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	484.63	485.1
	B1253	6-{[(trans, trans)-4-(4-ethoxyphenyl)-2-methyl-1-(2-oxo-2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	498.61	499.3
	B1254	6-{[(trans, trans)-4-(4-ethoxyphenyl)-1-[2-(2-fluorophenyl)ethyl]-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	502.62	503.1
	B1255	6-{[(trans, trans)-4-(4-ethoxyphenyl)-1-(2-fluoroethyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	426.52	427
	B1256	(-)-6-{[trans, trans-1-[(2,2-difluorocyclopropyl)methyl]-4-(4-fluorophenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	444.49	445.1

Figure 1-Continued

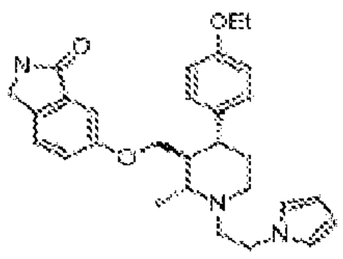
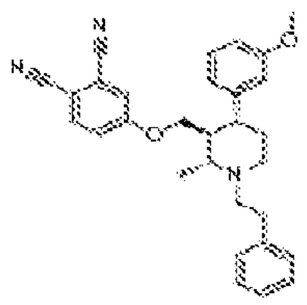
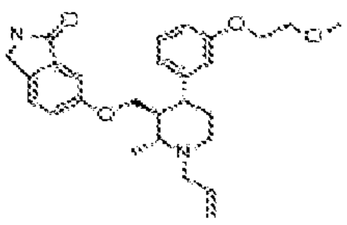
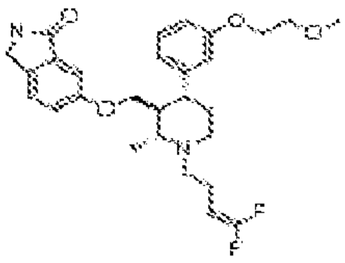
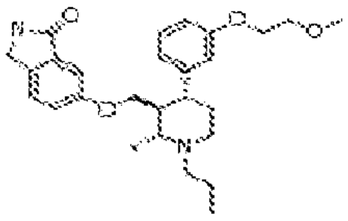
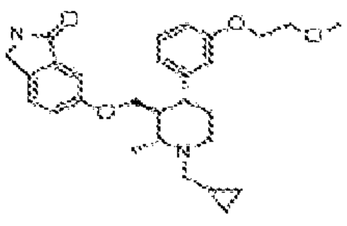
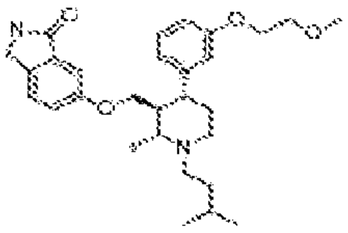
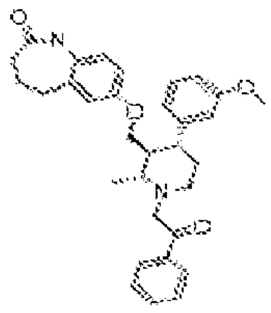
	B1257	6-{[(trans, trans)-4-(4-ethoxyphenyl)-2-methyl-1-[2-(1H-pyrrol-1-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	473.61	474.25
	B1258	(-)-4-{[trans-trans-4-(3-methoxyphenyl)-2-methyl-1-(2-phenylethyl)piperidin-3-yl]methoxy}benzene-1,2-dicarbonitrile	465.59	466.2
	B1259	(-)-6-{[trans, trans-4-[3-(2-methoxyethoxy)phenyl]-2-methyl-1-(prop-2-en-1-yl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	450.57	451.2
	B1260	(-)-6-{[trans, trans-1-(4,4-difluorobut-3-en-1-yl)-4-[3-(2-methoxyethoxy)phenyl]-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	500.58	501.2
	B1261	(-)-6-{[trans, trans-4-[3-(2-methoxyethoxy)phenyl]-2-methyl-1-propylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	452.59	453.2
	B1262	(-)-6-{[trans, trans-1-(cyclopropylmethyl)-4-[3-(2-methoxyethoxy)phenyl]-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	464.6	465.2
	B1263	(-)-6-{[trans, trans-4-[3-(2-methoxyethoxy)phenyl]-2-methyl-1-(3-methylbutyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	480.64	481.3
	B1264	(-)-7-{[trans, trans-4-(3-methoxyphenyl)-2-methyl-1-(2-oxo-2-phenylethyl)piperidin-3-yl]methoxy}-2,3,4,5-tetrahydro-1H-1-benzazepin-2-one	512.64	513.2

Figure 1-Continued

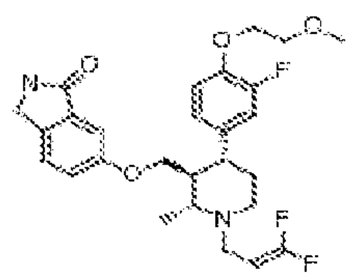
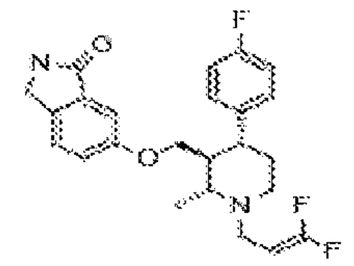
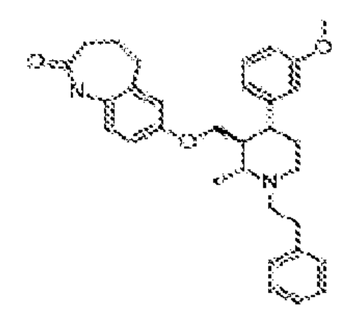
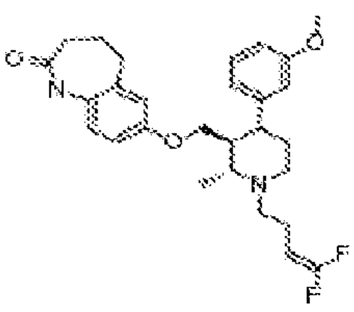
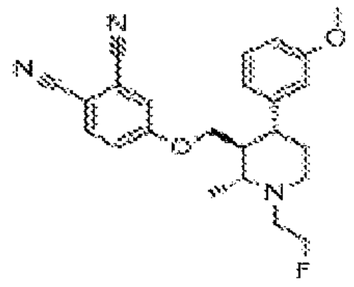
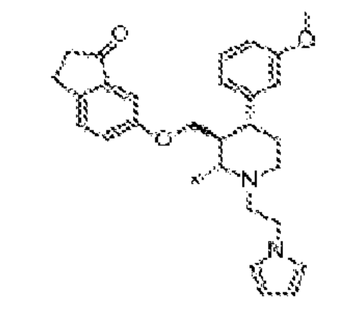
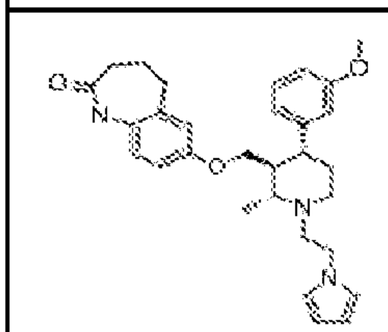
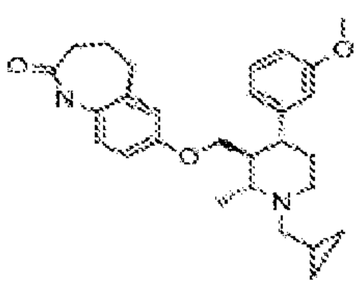
	B1265	(-)-6-{[trans, trans-1-(3,3-difluoroprop-2-en-1-yl)-4-[3-fluoro-4-(2-methoxyethoxy)phenyl]-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	504.54	505.1
	B1266	(-)-6-{[trans, trans-1-(3,3-difluoroprop-2-en-1-yl)-4-(4-fluorophenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	430.46	431.1
	B1267	(-)-7-{[trans, trans-4-(3-methoxyphenyl)-2-methyl-1-(2-phenylethyl)piperidin-3-yl]methoxy}-2,3,4,5-tetrahydro-1H-1-benzazepin-2-one	498.66	499.2
	B1268	(-)-7-{trans, trans-[1-(4,4-difluorobut-3-en-1-yl)-4-(3-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3,4,5-tetrahydro-1H-1-benzazepin-2-one	484.58	485.2
	B1269	(-)-4-{[trans, trans-1-(2-fluoroethyl)-4-(3-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}benzene-1,2-dicarbonitrile	407.48	408.1
	B1270	(-)-6-{[trans, trans-4-(3-methoxyphenyl)-2-methyl-1-[2-(1H-pyrrol-1-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-inden-1-one	458.59	459.2
	B1271	(-)-7-{[trans, trans-4-(3-methoxyphenyl)-2-methyl-1-[2-(1H-pyrrol-1-yl)ethyl]piperidin-3-yl]methoxy}-2,3,4,5-tetrahydro-1H-1-benzazepin-2-one	487.63	488.2
	B1272	(-)-7-{[trans, trans-1-(cyclopropylmethyl)-4-(3-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3,4,5-tetrahydro-1H-1-benzazepin-2-one	448.6	449.2

Figure 1-Continued

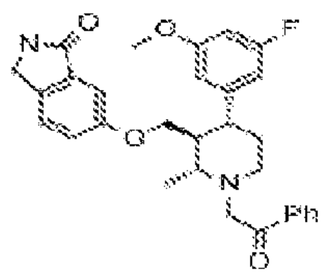
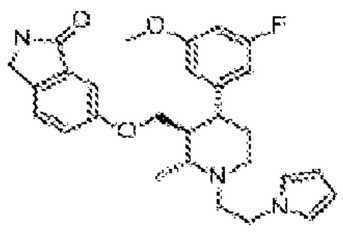
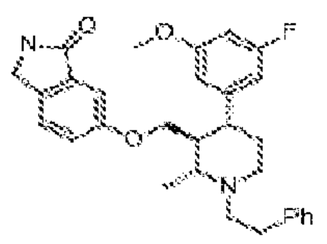
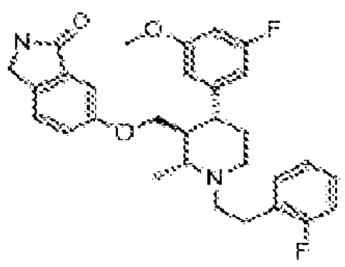
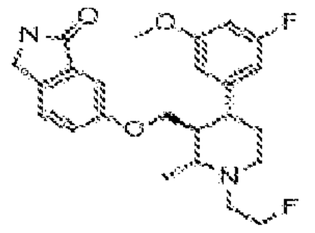
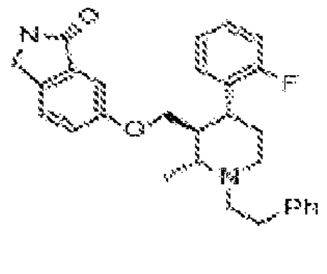
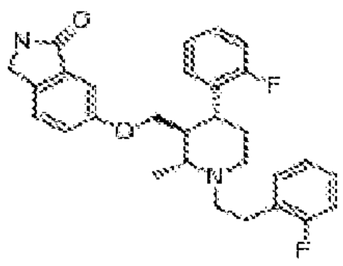
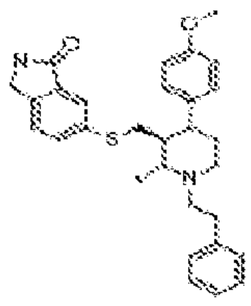
	B1273	6-{[(trans, trans)-4-(3-fluoro-5-methoxyphenyl)-2-methyl-1-(2-oxo-2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	502.58	503.4
	B1274	6-{[(trans, trans)-4-(3-fluoro-5-methoxyphenyl)-2-methyl-1-[2-(1H-pyrrol-1-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	477.57	478.3
	B1275	6-{[(trans, trans)-4-(3-fluoro-5-methoxyphenyl)-2-methyl-1-(2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	488.59	489.3
	B1276	6-{[(trans, trans)-4-(3-fluoro-5-methoxyphenyl)-1-[2-(2-fluorophenyl)ethyl]-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	506.58	507.35
	B1277	6-{[(trans, trans)-4-(3-fluoro-5-methoxyphenyl)-1-(2-fluoroethyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	430.49	431.1
	B1278	6-{[(trans, trans)-4-(2-fluorophenyl)-2-methyl-1-(2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	458.57	459.3
	B1279	6-{[(trans, trans)-4-(2-fluorophenyl)-1-[2-(2-fluorophenyl)ethyl]-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	476.56	477.25
	B1280	(-)-6-({[trans, trans-4-(4-methoxyphenyl)-2-methyl-1-(2-phenylethyl)piperidin-3-yl]methyl}sulfanyl)-2,3-dihydro-1H-isoindol-1-one	486.67	487.2

Figure 1-Continued

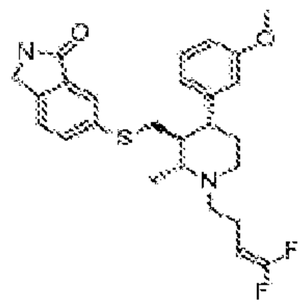
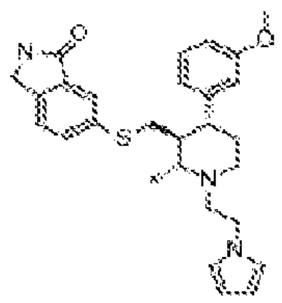
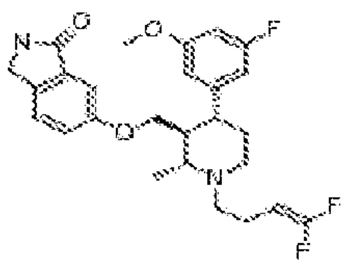
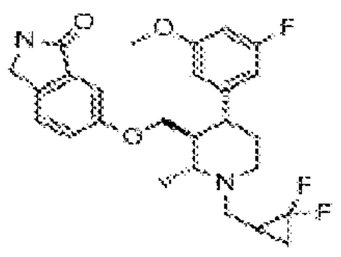
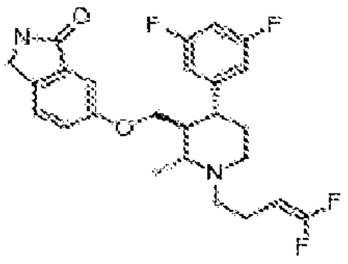
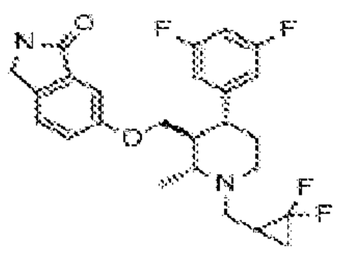
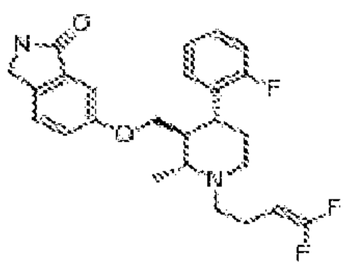
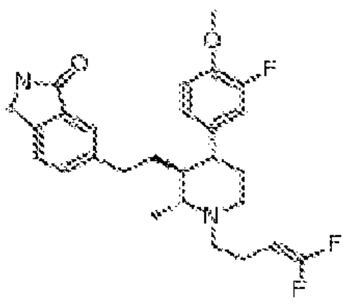
	B1281	(-)-6-({[trans, trans-1-(4,4-difluorobut-3-en-1-yl)-4-(3-methoxyphenyl)-2-methylpiperidin-3-yl]methyl}sulfanyl)-2,3-dihydro-1H-isoindol-1-one	472.59	473.1
	B1282	(-)-6-({[trans, trans-4-(3-methoxyphenyl)-2-methyl-1-[2-(1H-pyrrol-1-yl)ethyl]piperidin-3-yl]methyl}sulfanyl)-2,3-dihydro-1H-isoindol-1-one	475.65	476.2
	B1283	6-{[(trans, trans)-1-(4,4-difluorobut-3-en-1-yl)-4-(3-fluoro-5-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	474.52	475.3
	B1284	6-{[(trans, trans)-1-[(2,2-difluorocyclopropyl)methyl]-4-(3-fluoro-5-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	474.52	475.3
	B1285	6-{[(trans, trans)-1-(4,4-difluorobut-3-en-1-yl)-4-(3,5-difluorophenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	462.48	463.2
	B1286	6-{[(trans, trans)-1-[(2,2-difluorocyclopropyl)methyl]-4-(3,5-difluorophenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	462.48	463.2
	B1287	6-{[(trans, trans)-1-(4,4-difluorobut-3-en-1-yl)-4-(2-fluorophenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	444.49	445.2
	B1288	(-)-6-{2-[trans, trans-1-(4,4-difluorobut-3-en-1-yl)-4-(3-fluoro-4-methoxyphenyl)-2-methylpiperidin-3-yl]ethyl}-2,3-dihydro-1H-isoindol-1-one	472.54	473.2

Figure 1-Continued

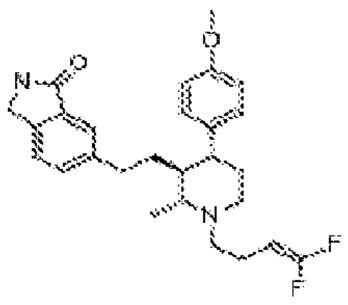
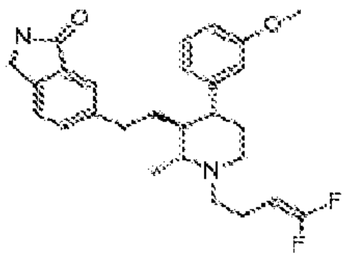
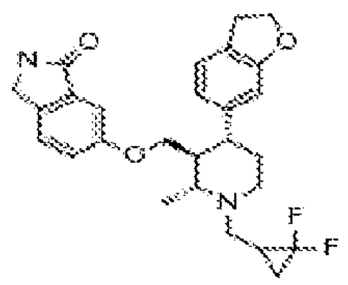
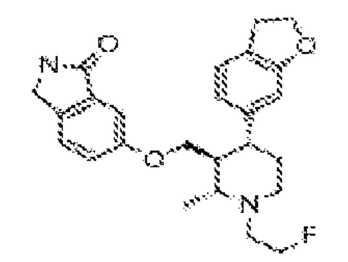
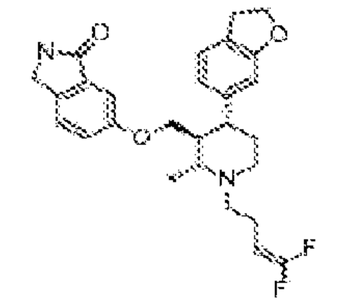
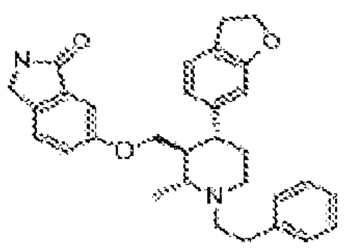
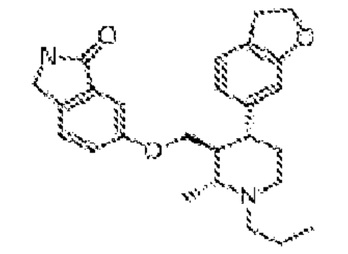
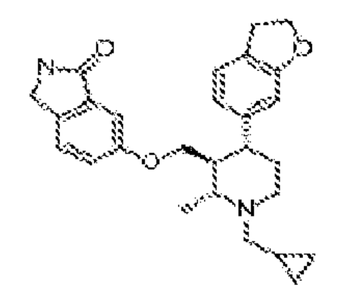
	B1289	6-{2-[(trans, trans)-1-(4,4-difluorobut-3-en-1-yl)-4-(4-methoxyphenyl)-2-methylpiperidin-3-yl]ethyl}-2,3-dihydro-1H-isoindol-1-one	454.55	455.2
	B1290	(-)-6-{2-[trans, trans-1-(4,4-difluorobut-3-en-1-yl)-4-(3-methoxyphenyl)-2-methylpiperidin-3-yl]ethyl}-2,3-dihydro-1H-isoindol-1-one	454.55	455.2
	B1291	(-)-6-{[trans, trans-1-[(2,2-difluorocyclopropyl)methyl]-4-(2,3-dihydro-1-benzofuran-6-yl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	468.54	469.2
	B1292	(-)-6-{[trans, trans-4-(2,3-dihydro-1-benzofuran-6-yl)-1-(2-fluoroethyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	424.51	425.1
	B1293	(-)-6-{[trans, trans-1-(4,4-difluorobut-3-en-1-yl)-4-(2,3-dihydro-1-benzofuran-6-yl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	468.54	469.1
	B1294	(-)-6-{[trans, trans-4-(2,3-dihydro-1-benzofurn-6-yl)-2-methyl-1-(2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	482.61	483.2
	B1295	(-)-6-{[trans, trans-4-(2,3-dihydro-1-benzofuran-6-yl)-2-methyl-1-propylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	420.54	421.2
	B1296	(-)-6-{[trans, trans-1-(cyclopropylmethyl)-4-(2,3-dihydro-1-benzofuran-6-yl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	432.55	433.2

Figure 1-Continued

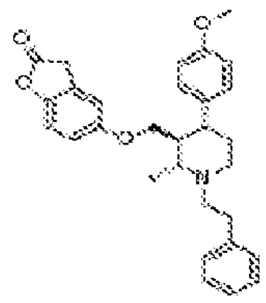
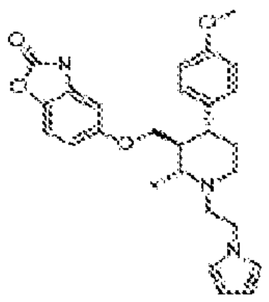
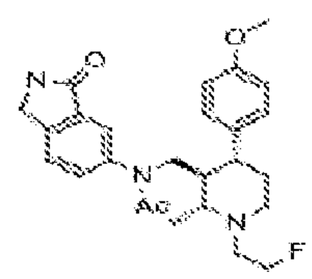
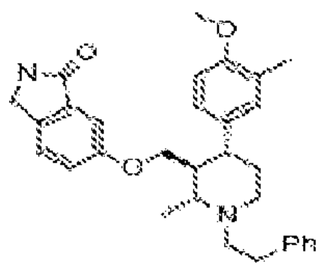
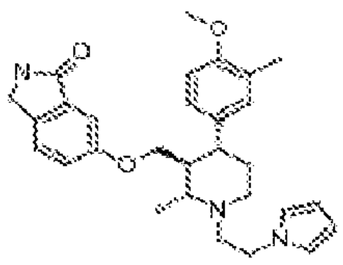
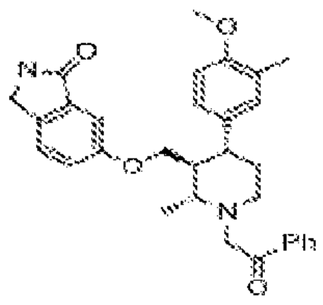
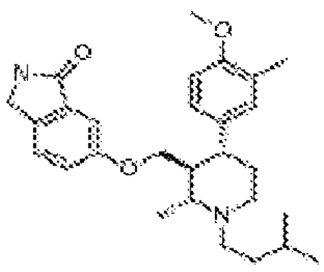
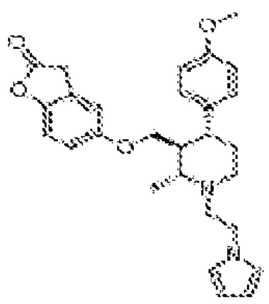
	B1297	(-)-5-{[trans, trans-4-(4-methoxyphenyl)-2-methyl-1-(2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1-benzofuran-2-one	471.59	472.3
	B1298	(-)-5-{[trans, trans-4-(4-methoxyphenyl)-2-methyl-1-[2-(1H-pyrrol-1-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1,3-benzoxazol-2-one	461.55	462.2
	B1299	N-{[(trans, trans)-1-(2-fluoroethyl)-4-(4-methoxyphenyl)-2-methylpiperidin-3-yl]methyl}-N-(3-oxo-2,3-dihydro-1H-isoindol-5-yl)acetamide	453.55	454.4
	B1300	6-{[(trans, trans)-4-(4-methoxy-3-methylphenyl)-2-methyl-1-(2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	484.63	485.5
	B1301	6-{[(trans, trans)-4-(4-methoxy-3-methylphenyl)-2-methyl-1-[2-(1H-pyrrol-1-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	473.61	474.4
	B1302	6-{[(trans, trans)-4-(4-methoxy-3-methylphenyl)-2-methyl-1-(2-oxo-2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	498.61	499.5
	B1303	6-{[(trans, trans)-4-(4-methoxy-3-methylphenyl)-2-methyl-1-(3-methylbutyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	450.61	451.4
	B1304	(-)-5-{[trans, trans-4-(4-methoxyphenyl)-2-methyl-1-[2-(1H-pyrrol-1-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1-benzofuran-2-one	460.56	461.3

Figure 1-Continued

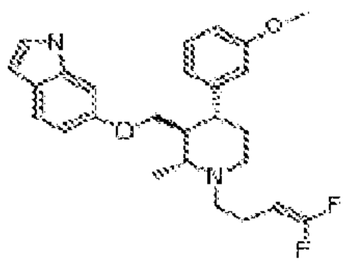
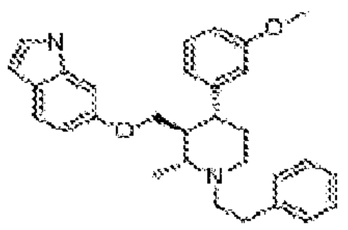
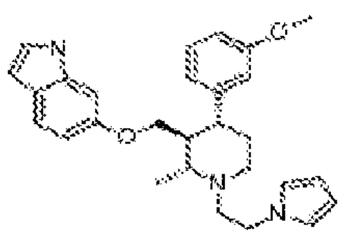
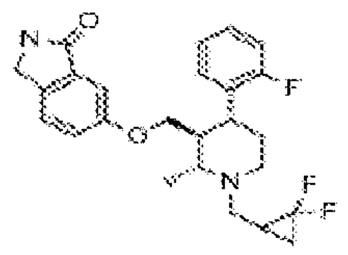
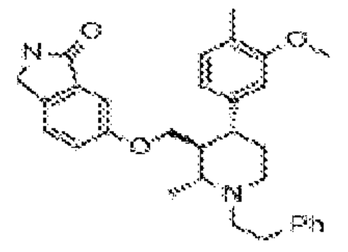
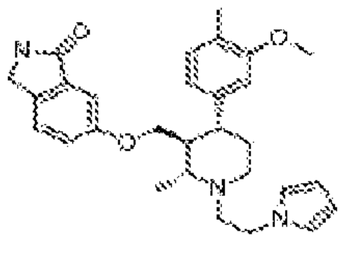
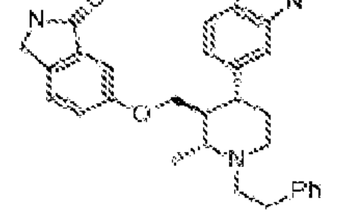
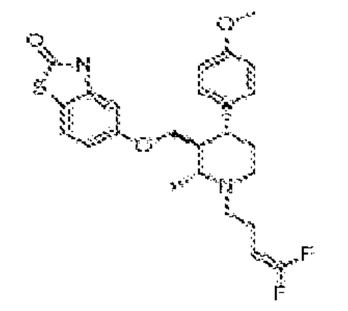
	B1305	6-{[(trans, trans)-1-(4,4-difluorobut-3-en-1-yl)-4-(3-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}-1H-indole	440.53	441.3
	B1306	(-)-6-{[trans, trans-4-(3-methoxyphenyl)-2-methyl-1-(2-phenylethyl)piperidin-3-yl]methoxy}-1H-indole	454.6	455.2
	B1307	(-)-6-{[trans, trans-4-(3-methoxyphenyl)-2-methyl-1-[2-(1H-pyrrol-1-yl)ethyl]piperidin-3-yl]methoxy}-1H-indole	443.58	444.1
	B1308	6-{[(trans, trans)-1-[(2,2-difluorocyclopropyl)methyl]-4-(2-fluorophenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	444.49	445.2
	B1309	6-{[(trans, trans)-4-(3-methoxy-4-methylphenyl)-2-methyl-1-(2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	484.63	485.35
	B1310	6-{[(trans, trans)-4-(3-methoxy-4-methylphenyl)-2-methyl-1-[2-(1H-pyrrol-1-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	473.61	474.5
	B1311	6-{[(trans, trans)-4-(1H-indol-6-yl)-2-methyl-1-(2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	479.61	480.2
	B1312	(-)-5-{[trans, trans-1-(4,4-difluorobut-3-en-1-yl)-4-(4-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1,3-benzothizol-2-one	474.56	475.1

Figure 1-Continued

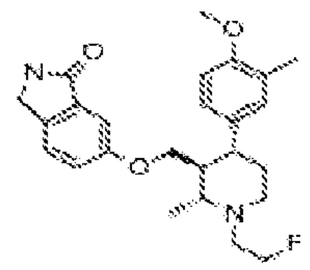
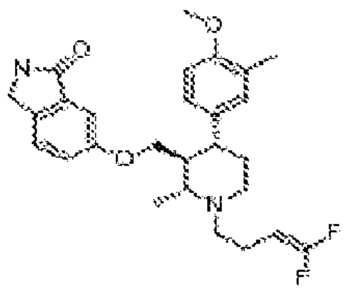
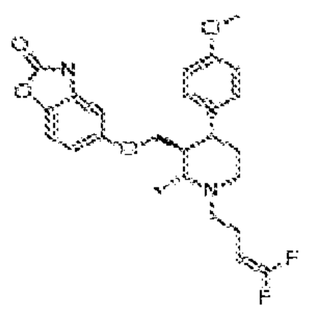
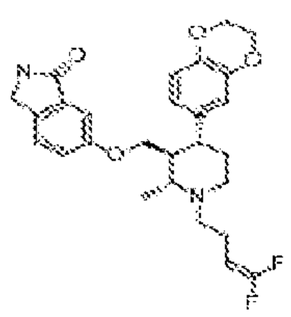
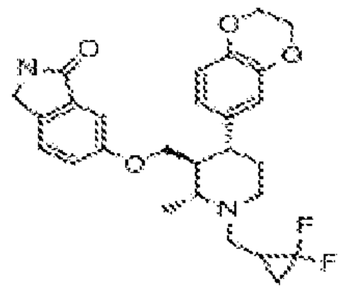
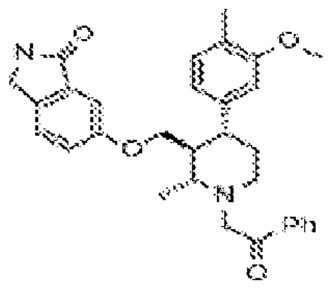
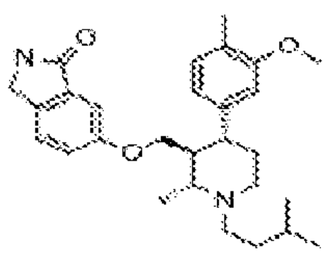
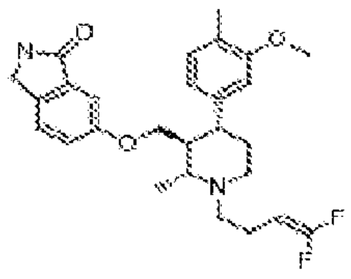
	B1313	6-{[(trans, trans)-1-(2-fluoroethyl)-4-(4-methoxy-3-methylphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	426.52	427.2
	B1314	6-{[(trans, trans)-1-(4,4-difluorobut-3-en-1-yl)-4-(4-methoxy-3-methylphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	470.55	471.2
	B1315	(-)-5-{[trans, trans-1-(4,4-difluorobut-3-en-1-yl)-4-(4-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1,3-benzoxzol-2-one	458.5	459.2
	B1316	(-)-6-{[trans, trans-1-(4,4-difluorobut-3-en-1-yl)-4-(2,3-dihydro-1,4-benzodioxin-6-yl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	484.53	485.2
	B1317	6-{[(trans, trans)-1-[(2,2-difluorocyclopropyl)methyl]-4-(2,3-dihydro-1,4-benzodioxin-6-yl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	484.53	485.2
	B1318	6-{[(trans, trans)-4-(3-methoxy-4-methylphenyl)-2-methyl-1-(2-oxo-2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	498.61	499.2
	B1319	6-{[(trans, trans)-4-(3-methoxy-4-methylphenyl)-2-methyl-1-(3-methylbutyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	450.61	451.2
	B1320	6-{[(trans, trans)-1-(4,4-difluorobut-3-en-1-yl)-4-(3-methoxy-4-methylphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	470.55	471.2

Figure 1-Continued

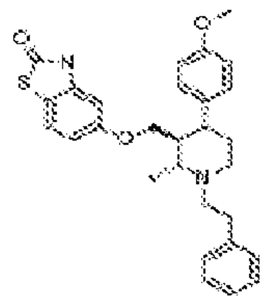
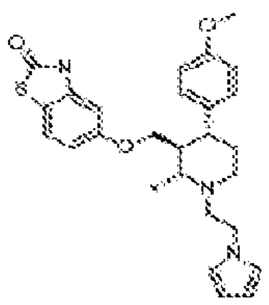
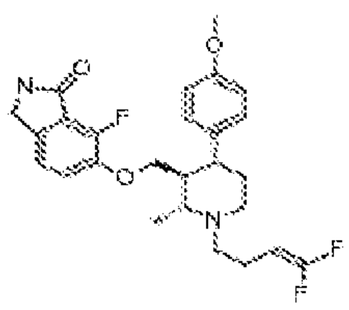
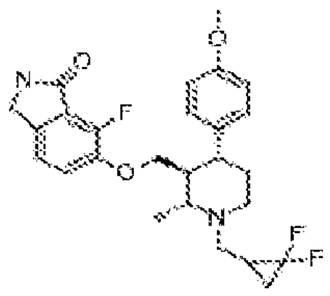
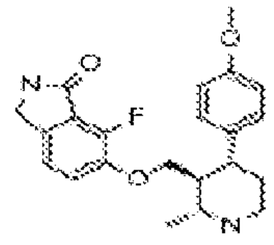
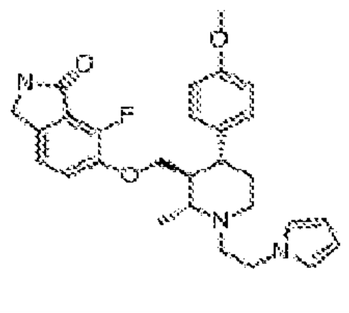
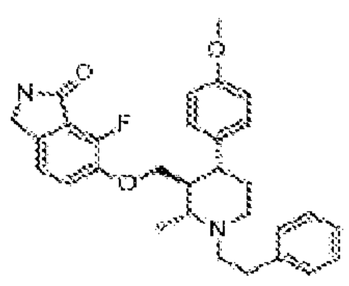
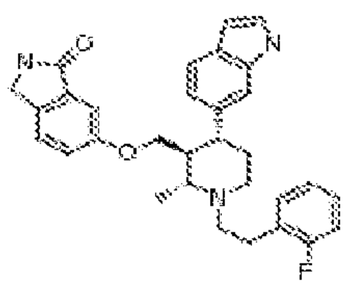
	B1321	(-)-5-{[trans, trans-4-(4-methoxyphenyl)-2-methyl-1-(2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1,3-benzothiazol-2-one	488.64	489.1
	B1322	(-)-5-{[trans, trans-4-(4-methoxyphenyl)-2-methyl-1-[2-(1H-pyrrol-1-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1,3-benzothizol-2-one	477.62	478.1
	B1323	(-)-6-{[trans, trans-1-(4,4-difluorobut-3-en-1-yl)-4-(4-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}-7-fluoro-2,3-dihydro-1H-isoindol-1-one	474.52	475.1
	B1324	(-)-6-{[trans, trans-1-[(2,2-difluorocyclopropyl)methyl]-4-(4-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}-7-fluoro-2,3-dihydro-1H-isoindol-1-one	474.52	475.2
	B1325	(-)-7-fluoro-6-{[trans, trans-4-(4-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	384.44	385.1
	B1326	(-)-7-fluoro-6-{[trans, trans-4-(4-methoxyphenyl)-2-methyl-1-[2-(1H-pyrrol-1-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	477.57	478.2
	B1327	(-)-7-fluoro-6-{[trans, trans-4-(4-methoxyphenyl)-2-methyl-1-(2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	488.59	489.2
	B1328	6-{[(trans, trans)-1-[2-(2-fluorophenyl)ethyl]-4-(1H-indol-6-yl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	497.6	498.5

Figure 1-Continued

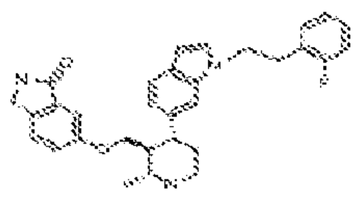
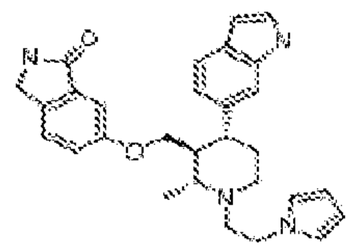
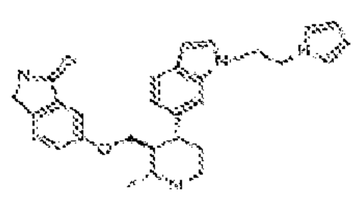
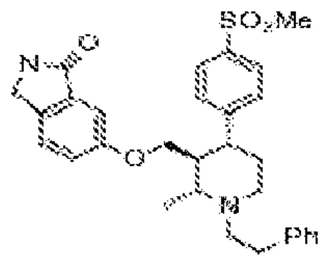
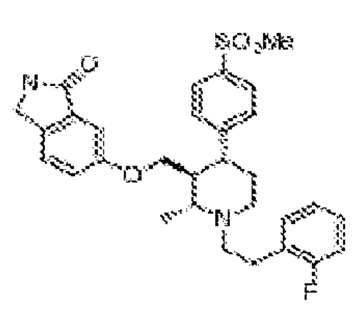
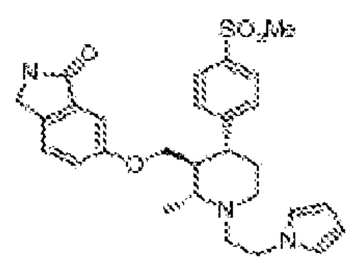
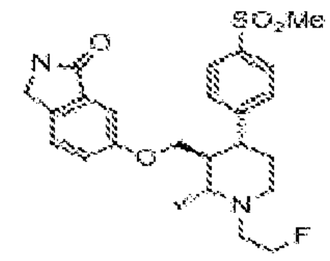
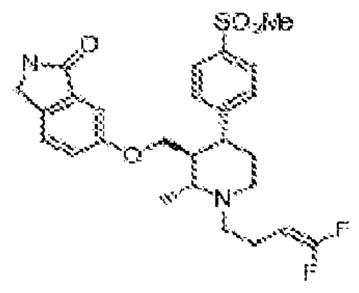
	B1329	6-{[(trans, trans)-4-{1-[2-(2-fluorophenyl)ethyl]-1H-indol-6-yl}-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	497.6	498.5
	B1330	6-{[(trans, trans)-4-(1H-indol-6-yl)-2-methyl-1-[2-(1H-pyrrol-1-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	468.59	469.4
	B1331	6-{[(trans, trans)-2-methyl-4-{1-[2-(1H-pyrrol-1-yl)ethyl]-1H-indol-6-yl}piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	468.59	469.5
	B1332	6-{[(trans, trans)-4-(4-methanesulfonylphenyl)-2-methyl-1-(2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	518.67	519.2
	B1333	6-{[(trans, trans)-1-[2-(2-fluorophenyl)ethyl]-4-(4-methnesulfonylphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	536.66	537.25
	B1334	6-{[(trans, trans)-4-(4-methnesulfonylphenyl)-2-methyl-1-[2-(1H-pyrrol-1-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	507.64	508.25
	B1335	6-{[(trans, trans)-1-(2-fluoroethyl)-4-(4-methnesulfonylphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	460.56	461.2
	B1336	6-{[(trans, trans)-1-(4,4-difluorobut-3-en-1-yl)-4-(4-methnesulfonylphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	504.59	505.25

Figure 1-Continued

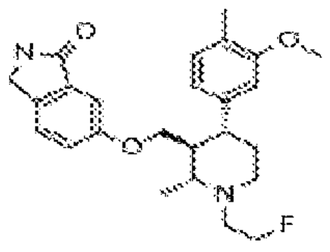
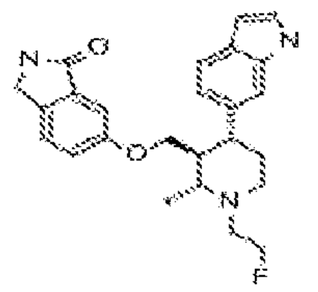
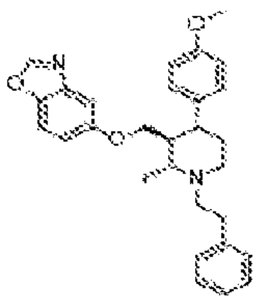
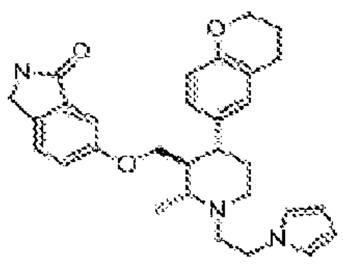
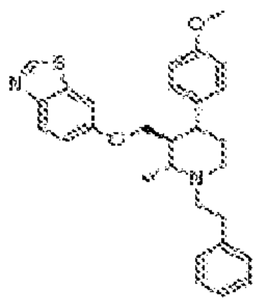
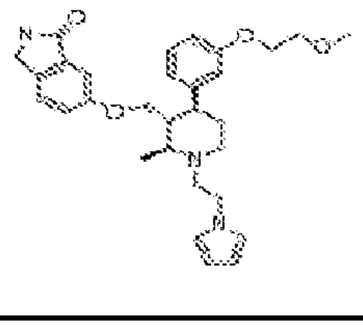
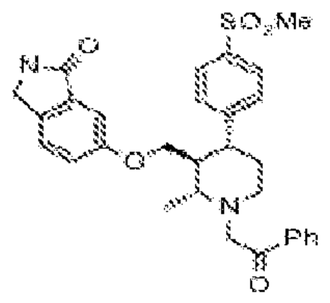
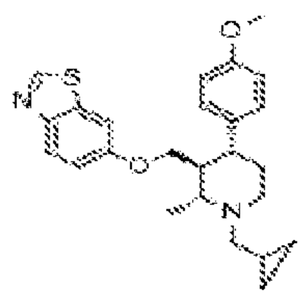
	B1337	6-{[(trans, trans)-1-(2-fluoroethyl)-4-(3-methoxy-4-methylphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	426.52	427.2
	B1338	6-{[(trans, trans)-1-(2-fluoroethyl)-4-(1H-indol-6-yl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	421.51	422.5
	B1339	(-)-5-{[trans, trans-4-(4-methoxyphenyl)-2-methyl-1-(2-phenylethyl)piperidin-3-yl]methoxy}-1,3-benzoxazole	456.58	457.2
	B1340	(-)-6-{[trans, trans-4-(3,4-dihydro-2H-1-benzopyran-6-yl)-2-methyl-1-[2-(1H-pyrrol-1-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	485.62	486.2
	B1341	(-)-6-{[trans, trans-4-(4-methoxyphenyl)-2-methyl-1-(2-phenylethyl)piperidin-3-yl]methoxy}-1,3-benzothizole	472.64	473.2
	B1342	(+)-6-{[(trans, trans)-4-[3-(2-methoxyethoxy)phenyl]-2-methyl-1-[2-(1H-pyrrol-1-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	503.63	504.2
	B1343	6-{[(trans, trans)-4-(4-methnesulfonylphenyl)-2-methyl-1-(2-oxo-2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	532.65	533.2
	B1344	(-)-6-{[trans, trans-1-(cyclopropylmethyl)-4-(4-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}-1,3- benzothiazole	422.58	423.1

Figure 1-Continued

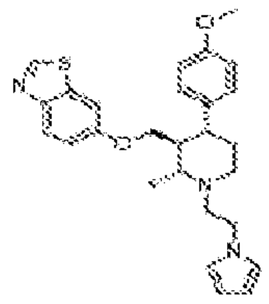
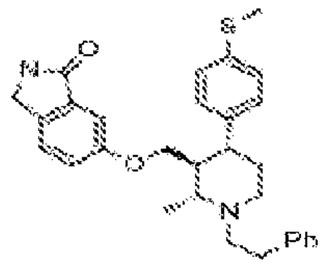
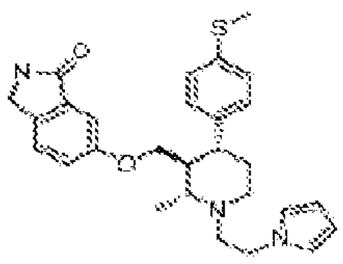
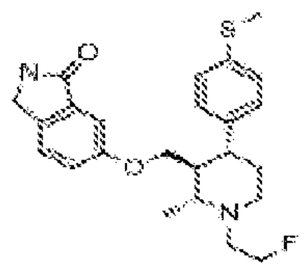
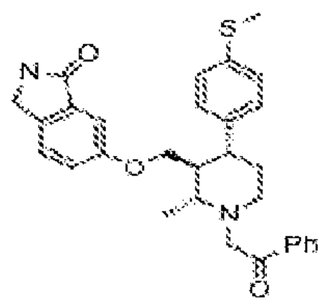
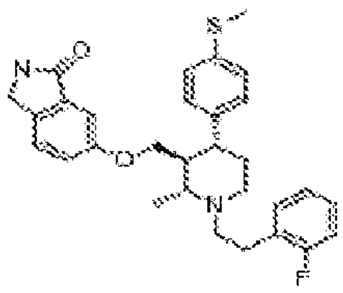
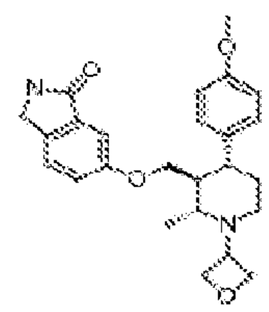
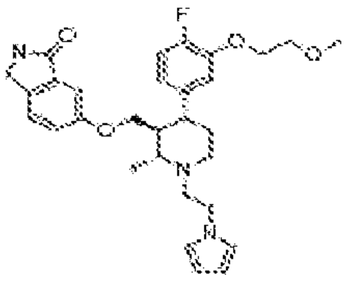
	B1345	(-)-6-{[trans, trans-4-(4-methoxyphenyl)-2-methyl-1-[2-(1H-pyrrol-1-yl)ethyl]piperidin-3-yl]methoxy}-1,3-benzothiazole	461.62	462.2
	B1346	6-{[(trans, trans)-2-methyl-4-[4-(methylsulfanyl)phenyl]-1-(2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	486.67	487.2
	B1347	6-{[(trans, trans)-2-methyl-4-[4-(methylsulfanyl)phenyl]-1-[2-(1H-pyrrol-1-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	475.65	476.1
	B1348	6-{[(trans, trans)-1-(2-fluoroethyl)-2-methyl-4-[4-(methylsulfanyl)phenyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	428.56	429.1
	B1349	6-{[(trans, trans)-2-methyl-4-[4-(methylsulfanyl)phenyl]-1-(2-oxo-2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	500.65	501.3
	B1350	6-{[(trans, trans)-1-[2-(2-fluorophenyl)ethyl]-2-methyl-4-[4-(methylsulfanyl)phenyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	504.66	505.2
	B1351	(-)-6-{[trans, trans-4-(4-methoxyphenyl)-2-methyl-1-(oxetan-3-yl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	422.52	423.1
	B1352	(-)-6-{[trans, trans-4-[4-fluoro-3-(2-methoxyethoxy)phenyl]-2-methyl-1-[2-(1H-pyrrol-1-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	521.62	522.2

Figure 1-Continued

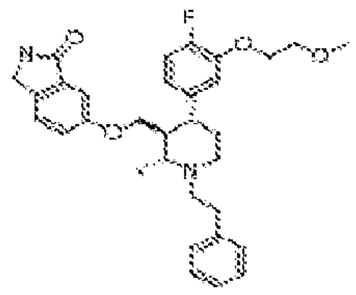
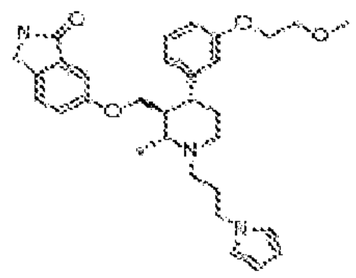
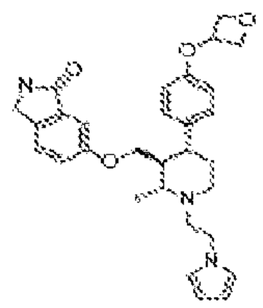
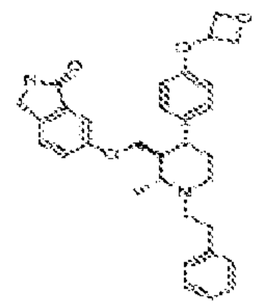
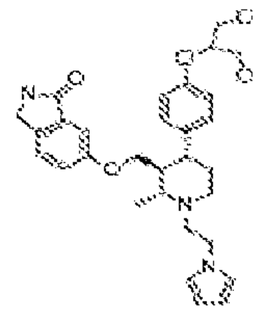
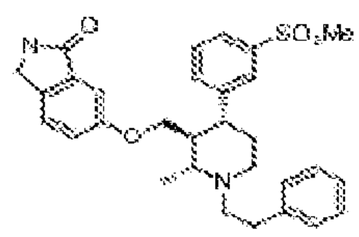
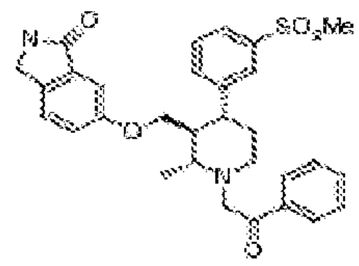
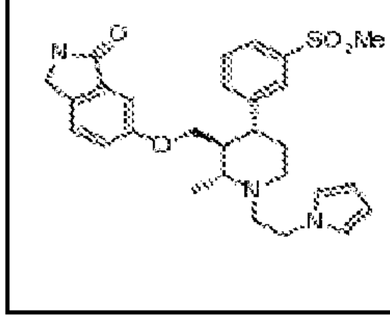
	B1353	(-)-6-{[trans, trans-4-[4-fluoro-3-(2-methoxyethoxy)phenyl]-2-methyl-1-(2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	532.65	533.2
	B1354	(-)-6-{[trans, trans-4-[3-(2-methoxyethoxy)phenyl]-2-methyl-1-[3-(1H-pyrrol-1-yl)propyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	517.66	518.2
	B1355	(-)-6-{[trans, trans-2-methyl-4-[4-(oxetan-3-yloxy)phenyl]-1-[2-(1H-pyrrol-1-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	501.62	502.2
	B1356	(-)-6-{[trans, trans-2-methyl-4-[4-(oxetan-3-yloxy)phenyl]-1-(2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	512.64	513.2
	B1357	(-)-6-{[trans, trans-4-{4-[(1,3-dihydroxypropan-2-yl)oxy]phenyl}-2-methyl-1-[2-(1H-pyrrol-1-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	519.63	520.2
	B1358	6-{[(trans, trans)-4-(3-methanesulfonylphenyl)-2-methyl-1-(2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	518.67	519.3
	B1359	6-{[(trans, trans)-4-(3-methanesulfonylphenyl)-2-methyl-1-(2-oxo-2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	532.65	533.3
	B1360	6-{[(trans, trans)-4-(3-methanesulfonylphenyl)-2-methyl-1-[2-(1H-pyrrol-1-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	507.64	508.2

Figure 1-Continued

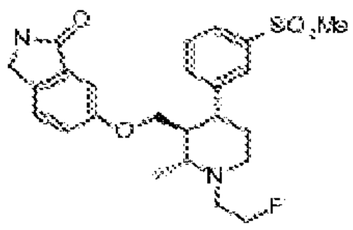
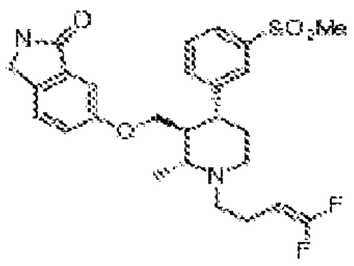
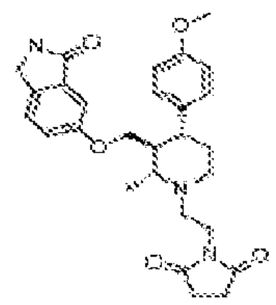
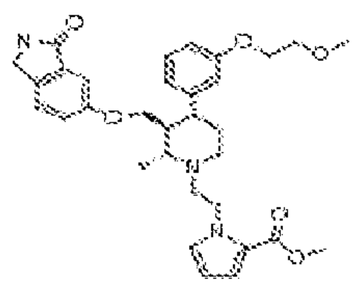
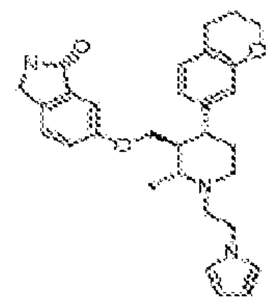
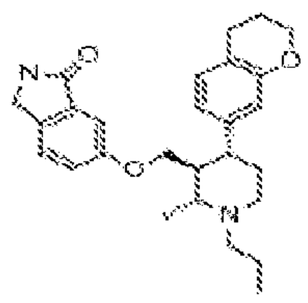
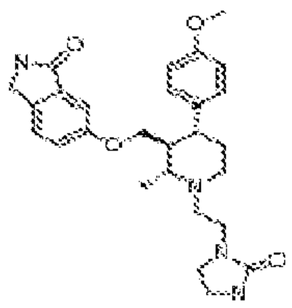
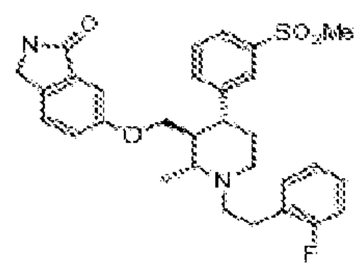
	B1361	6-{[(trans, trans)-1-(2-fluoroethyl)-4-(3-methanesulfonylphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	460.56	461.2
	B1362	6-{[(trans, trans)-1-(4,4-difluorobut-3-en-1-yl)-4-(3-methanesulfonylphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	504.59	505.1
	B1363	(-)-1-{2-[trans, trans-4-(4-methoxyphenyl)-2-methyl-3-{[(3-oxo-2,3-dihydro-1H-isoindol-5-yl)oxy]methyl}piperidin-1-yl]ethyl}pyrrolidine-2,5-dione	491.58	492.1
	B1364	(-)-methyl 1-{2-[trans, trans-4-[3-(2-methoxyethoxy)phenyl]-2-methyl-3-{[(3-oxo-2,3-dihydro-1H-isoindol-5-yl)oxy]methyl}piperidin-1-yl]ethyl}-1H-pyrrole-2-carboxylate	561.67	562.2
	B1365	(-)-6-{[trans, trans-4-(3,4-dihydro-2H-1-benzopyran-7-yl)-2-methyl-1-[2-(1H-pyrrol-1-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	485.62	486.2
	B1366	(-)-6-{[trans, trans-4-(3,4-dihydro-2H-1-benzopyran-7-yl)-2-methyl-1-propylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	434.57	435.2
	B1367	(-)-6-{[trans, trans-4-(4-methoxyphenyl)-2-methyl-1-[2-(2-oxoimidazolidin-1-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	478.58	479.2
	B1368	6-{[(trans, trans)-1-[2-(2-fluorophenyl)ethyl]-4-(3-methanesulfonylphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	536.66	537.3

Figure 1-Continued

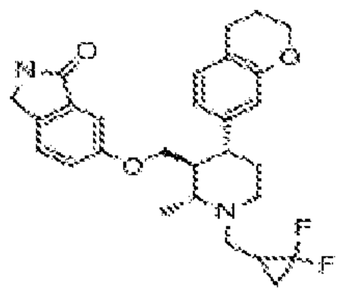
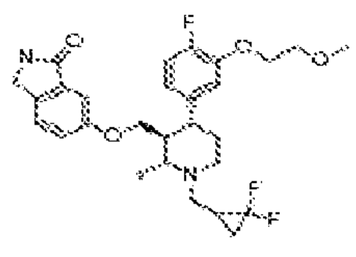
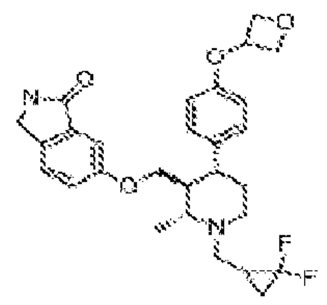
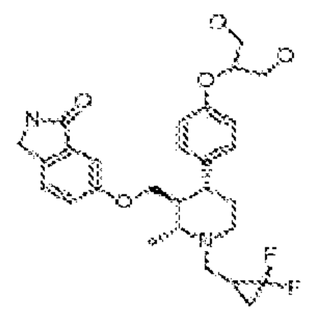
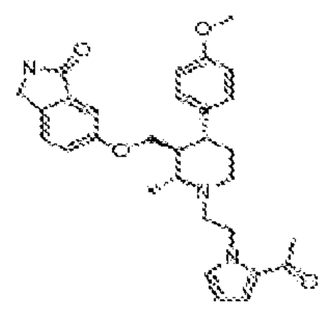
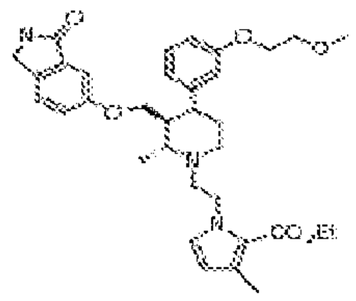
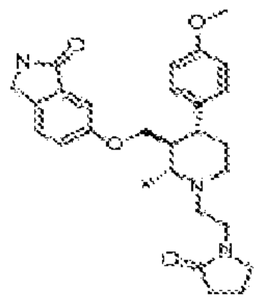
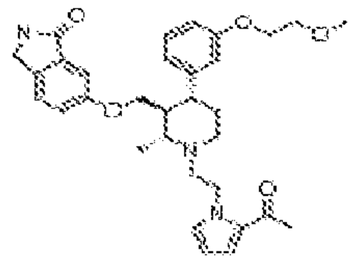
	B1369	(-)-6-{[trans, trans-1-[(2,2-difluorocyclopropyl)methyl]-4-(3,4-dihydro-2H-1-benzopyran-7-yl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	482.56	483.2
	B1370	6-{[(trans, trans)-1-[(2,2-difluorocyclopropyl)methyl]-4-[4-fluoro-3-(2-methoxyethoxy)phenyl]-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	518.57	519.2
	B1371	(-)-6-{[trans, trans-1-[(2,2-difluorocyclopropyl)methyl]-2-methyl-4-[4-(oxetan-3-yloxy)phenyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	498.56	499.1
	B1372	6-{[(trans, trans)-1-[(2,2-difluorocyclopropyl)methyl]-4-{4-[(1,3-dihydroxypropan-2-yl)oxy]phenyl}-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	516.58	517.2
	B1373	(-)-6-{[trans, trans-1-[2-(2-acetyl-1H-pyrrol-1-yl)ethyl]-4-(4-methoxyphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	501.62	502.2
	B1374	(-)-ethyl 1-{2-[trans, trans-4-[3-(2-methoxyethoxy)phenyl]-2-methyl-3-{[(3-oxo-2,3-dihydro-1H-isoindol-5-yl)oxy]methyl}piperidin-1-yl]ethyl}-3-methyl-1H-pyrrole-2-carboxylate	589.72	590.2
	B1375	6-{[(trans, trans)-4-(4-methoxyphenyl)-2-methyl-1-[2-(2-oxopyrrolidin-1-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	477.6	478.2
	B1376	(-)-6-{[trans, trans-1-[2-(2-acetyl-1H-pyrrol-1-yl)ethyl]-4-[3-(2-methoxyethoxy)phenyl]-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	545.67	546.2

Figure 1-Continued

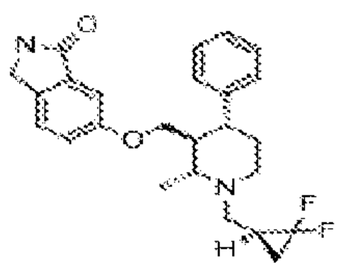
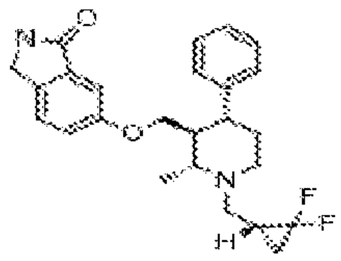
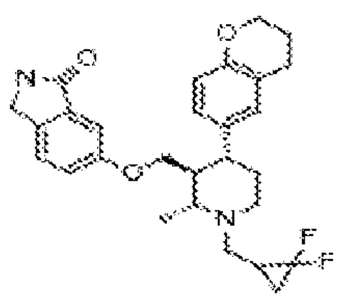
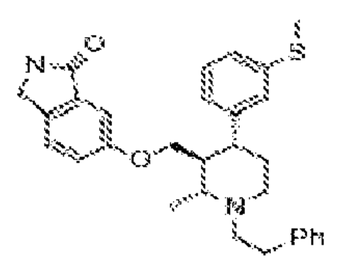
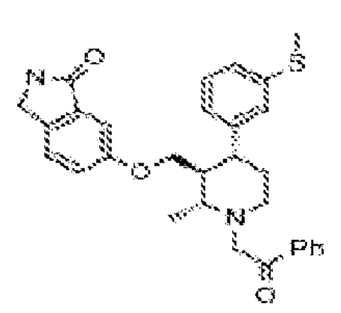
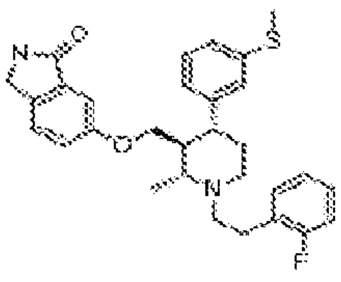
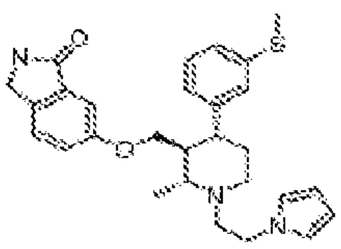
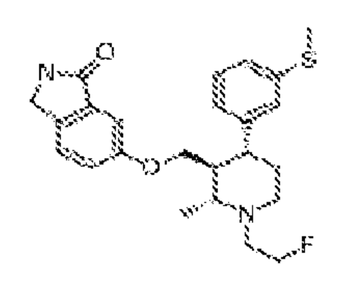
	B1377	(-)-6-{[(trans, trans)-1-{[2,2-difluorocyclopropyl]methyl}-2-methyl-4-phenylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	426.5	427.2
	B1378	(-)-6-{[(trans, trans)-1-{[2,2-difluorocyclopropyl]methyl}-2-methyl-4-phenylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	426.5	427.2
	B1379	6-{[(trans, trans)-1-[(2,2-difluorocyclopropyl)methyl]-4-(3,4-dihydro-2H-1-benzopyran-6-yl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	482.56	483.2
	B1380	6-{[(trans, trans)-2-methyl-4-[3-(methylsulfanyl)phenyl]-1-(2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	486.67	487.2
	B1381	6-{[(trans, trans)-2-methyl-4-[3-(methylsulfanyl)phenyl]-1-(2-oxo-2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	500.65	501.1
	B1382	6-{[(trans, trans)-1-[2-(2-fluorophenyl)ethyl]-2-methyl-4-[3-(methylsulfanyl)phenyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	504.66	505.2
	B1383	6-{[(trans, trans)-2-methyl-4-[3-(methylsulfanyl)phenyl]-1-[2-(1H-pyrrol-1-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	475.65	476.2
	B1384	6-{[(trans, trans)-1-(2-fluoroethyl)-2-methyl-4-[3-(methylsulfanyl)phenyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	428.56	429.1

Figure 1-Continued

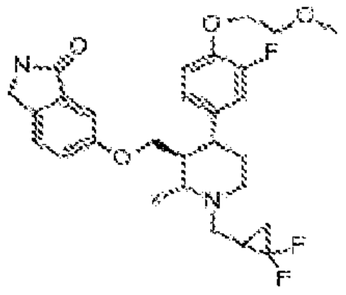
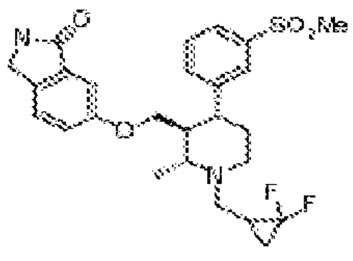
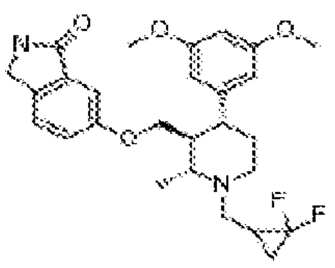
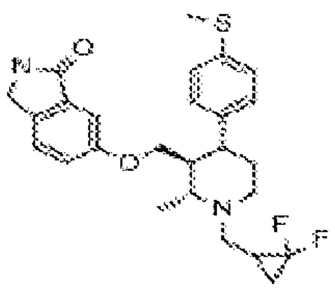
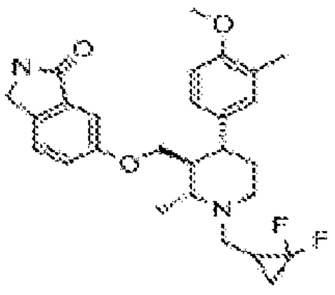
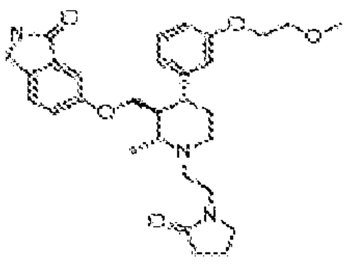
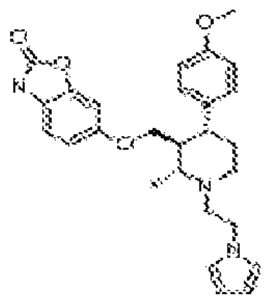
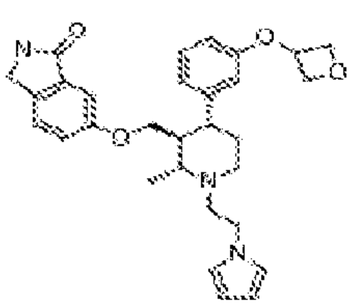
	B1385	(-)-6-{[trans, trans-1-[(2,2-difluorocyclopropyl)methyl]-4-[3-fluoro-4-(2-methoxyethoxy)phenyl]-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	518.57	519.2
	B1386	(-)-6-{[trans, trans-1-[(2,2-difluorocyclopropyl)methyl]-4-(3-methanesulfonylphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	504.59	505.1
	B1387	6-{[(trans, trans)-1-[(2,2-difluorocyclopropyl)methyl]-4-(3,5-dimethoxyphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	486.55	487.2
	B1388	6-{[(trans, trans)-1-[(2,2-difluorocyclopropyl)methyl]-2-methyl-4-[4-(methylsulfanyl)phenyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	472.59	473.2
	B1389	6-{[(trans, trans)-1-[(2,2-difluorocyclopropyl)methyl]-4-(4-methoxy-3-methylphenyl)-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	470.55	471.2
	B1390	(-)-6-{[trans, trans-4-[3-(2-methoxyethoxy)phenyl]-2-methyl-1-[2-(2-oxopyrrolidin-1-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	521.65	522.2
	B1391	(-)-6-{[trans, trans-4-(4-methoxyphenyl)-2-methyl-1-[2-(1H-pyrrol-1-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1,3-benzoxazol-2-one	461.55	462.2
	B1392	(-)-6-{[trans, trans-2-methyl-4-[3-(oxetan-3-yloxy)phenyl]-1-[2-(1H-pyrrol-1-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	501.62	502.2

Figure 1-Continued

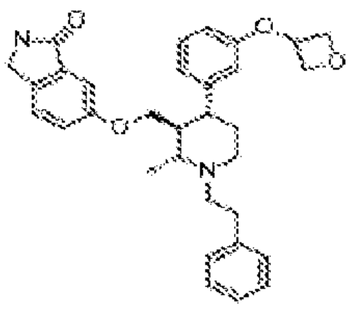
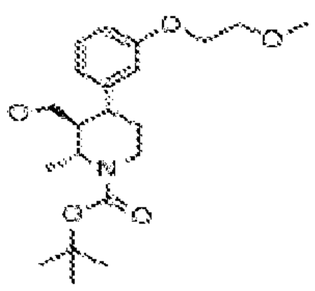
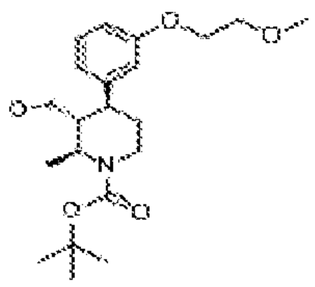
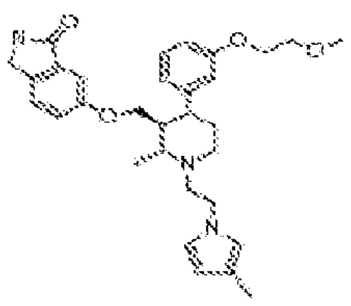
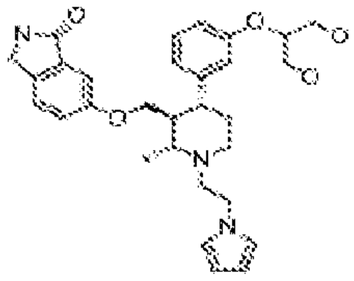
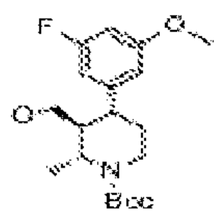
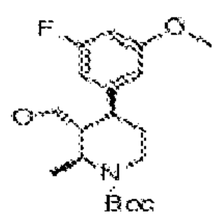
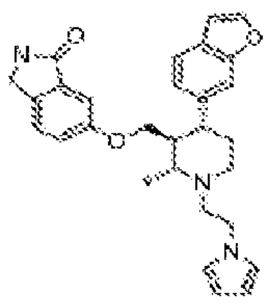
	B1393	(-)-6-{[trans, trans-2-methyl-4-[3-(oxetan-3-yloxy)phenyl]-1-(2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	512.64	513.2
	B1394	(-)-tert-butyl trans,trans-3-(hydroxymethyl)-4-[3-(2-methoxyethoxy)phenyl]-2-methylpiperidine-1-carboxylate	379.49	324.1
	B1395	(+)-tert-butyl trans, trans-3-(hydroxymethyl)-4-[3-(2-methoxyethoxy)phenyl]-2-methylpiperidine-1-carboxylate	379.49	324.1
	B1396	(-)-6-{[trans, trans-4-[3-(2-methoxyethoxy)phenyl]-2-methyl-1-[2-(3-methyl-1H-pyrrol-1-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	517.66	518.2
	B1397	(-)-6-{[trans, trans-4-{3-[(1,3-dihydroxypropan-2-yl)oxy]phenyl}-2-methyl-1-[2-(1H-pyrrol-1-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	519.63	520.4
	B1398	(-)-tert-butyl trans, trans-4-(3-fluoro-5-methoxyphenyl)-3-(hydroxymethyl)-2-methylpiperidine-1-carboxylate	353.43	354.2
	B1399	(+)-tert-butyl trans, trans-4-(3-fluoro-5-methoxyphenyl)-3-(hydroxymethyl)-2-methylpiperidine-1-carboxylate	353.43	354.2
	B1400	(-)-6-{[trans, trans-4-(1-benzofuran-6-yl)-2-methyl-1-[2-(1H-pyrrol-1-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	469.57	471.2

Figure 1-Continued

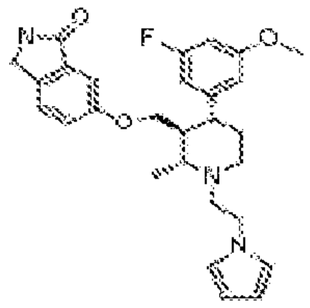
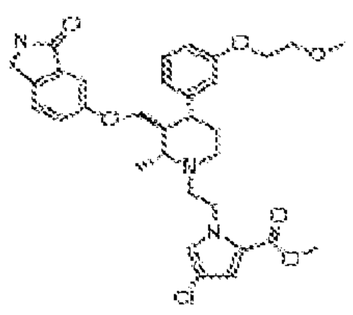
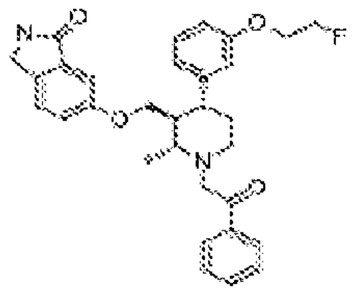
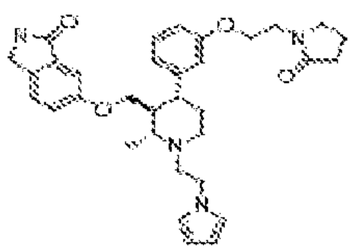
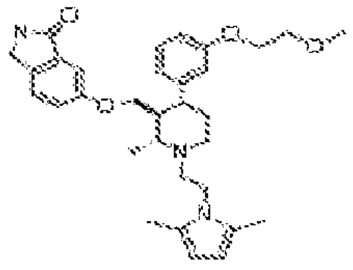
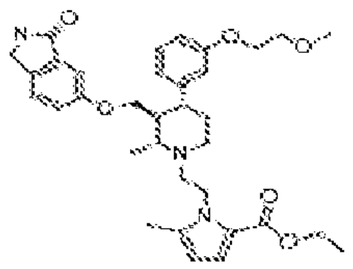
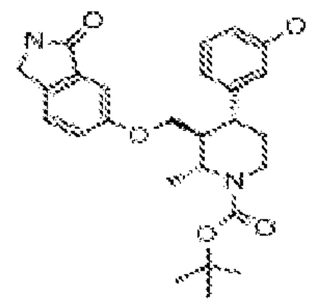
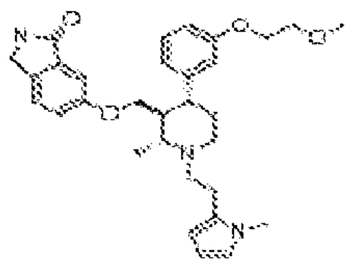
	B1401	(-)-6-{[trans, trans-4-(3-fluoro-5-methoxyphenyl)-2-methyl-1-[2-(1H-pyrrol-1-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	477.57	478.2
	B1402	(-)-methyl 4-chloro-1-{2-[trans, trans-4-[3-(2-methoxyethoxy)phenyl]-2-methyl-3-{[(3-oxo-2,3-dihydro-1H-isoindol-5-yl)oxy]methyl}piperidin-1-yl]ethyl}-1H-pyrrole-2-carboxylate	593.69	596.2
	B1403	(-)-6-{[trans, trans-4-[3-(2-fluoroethoxy)phenyl]-2-methyl-1-(2-oxo-2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	516.6	517.2
	B1404	(-)-6-{[trans, trans-2-methyl-4-{3-[2-(2-oxopyrrolidin-1-yl)ethoxy]phenyl}-1-[2-(1H-pyrrol-1-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	556.7	557.3
	B1405	(-)-6-{[trans, trans-1-[2-(2,5-dimethyl-1H-pyrrol-1-yl)ethyl]-4-[3-(2-methoxyethoxy)phenyl]-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	531.69	532.3
	B1406	(-)-ethyl 1-{2-[trans, trans-4-[3-(2-methoxyethoxy)phenyl]-2-methyl-3-{[(3-oxo-2,3-dihydro-1H-isoindol-5-yl)oxy]methyl}piperidin-1-yl]ethyl}-5-methyl-1H-pyrrole-2-carboxylate	589.72	590.3
	B1407	(-)-tert-butyl trans, trans-4-(3-hydroxyphenyl)-2-methyl-3-{[(3-oxo-2,3-dihydro-1H-isoindol-5-yl)oxy]methyl}piperidine-1-carboxylate	452.54	397
	B1408	(-)-6-{[trans, trans-4-[3-(2-methoxyethoxy)phenyl]-2-methyl-1-[2-(1-methyl-1H-pyrrol-2-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	517.66	518.2

Figure 1-Continued

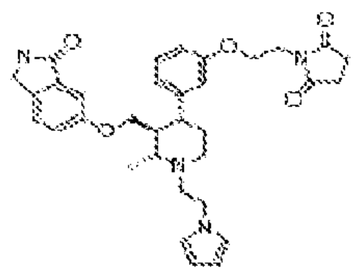
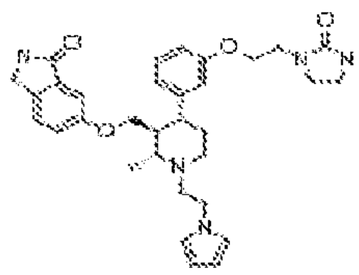
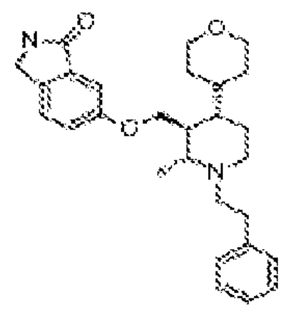
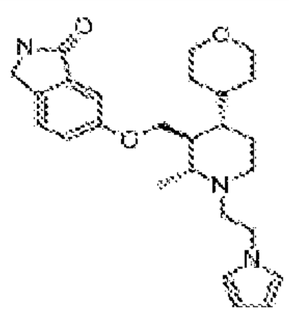
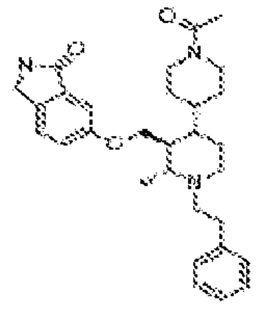
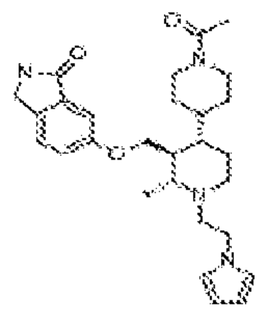
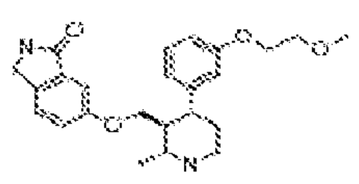
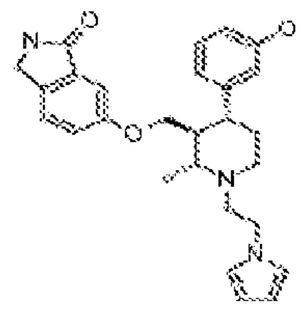
	B1409	(-)-1-(2-{3-[trans, trans-2-methyl-3-{[(3-oxo-2,3-dihydro-1H-isoindol-5-yl)oxy]methyl}-1-[2-(1H-pyrrol-1-yl)ethyl]piperidin-4-yl]phenoxy}ethyl)pyrrolidine-2,5-dione	570.68	571.2
	B1410	(-)-6-{[trans, trans-2-methyl-4-{3-[2-(2-oxoimidazolidin-1-yl)ethoxy]phenyl}-1-[2-(1H-pyrrol-1-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	557.68	558.3
	B1411	6-{[trans,trans)-2-methyl-4-(oxan-4-yl)-1-(2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	448.6	449.1
	B1412	6-{[(trans,trans)-2-methyl-4-(oxan-4-yl)-1-[2-(1H-pyrrol-1-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	437.57	438.1
	B1413	6-{[(trans, trans)-4-(1-acetylpiperidin-4-yl)-2-methyl-1-(2-phenylethyl)piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	489.65	490.2
	B1414	6-{[(trans, trans)-4-(1-acetylpiperidin-4-yl)-2-methyl-1-[2-(1H-pyrrol-1-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	478.63	479.2
	B1415	(-)-6-{[trans, trans-4-[3-(2-methoxyethoxy)phenyl]-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	410.51	411.1
	B1416	(-)-6-{[trans, trans-4-(3-hydroxyphenyl)-2-methyl-1-[2-(1H-pyrrol-1-yl)ethyl]piperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	445.55	446.2

Figure 1-Continued

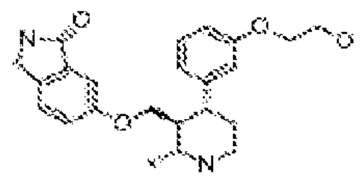
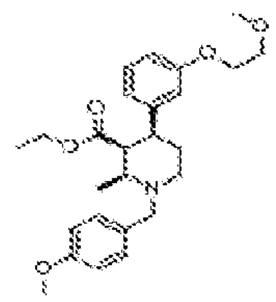
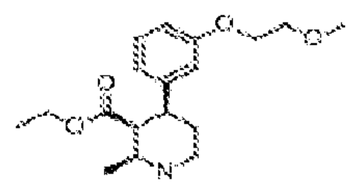
	B1417	(-)-6-{[trans, trans-4-[3-(2-hydroxyethoxy)phenyl]-2-methylpiperidin-3-yl]methoxy}-2,3-dihydro-1H-isoindol-1-one	396.48	397.1
	B1418	(cis, cis)-4-[3-(2-methoxyethoxy)phenyl]-1-[(4-methoxyphenyl)methyl]-2-methylpiperidine-3-carboxylate	441.56	442.2
Chiral 	B1419	(cis, cis)-4-[3-(2-methoxyethoxy)phenyl]-2-methylpiperidine-3-carboxylate	321.41	322.1

Figure 2

Compd.	hDOR				hMOR				hKOR			
	G-protein pEC_{50}	G-protein %eff	βarr2 pEC_{50}	βarr2 %eff	G-protein pEC_{50}	G-protein %eff	βarr2 pEC_{50}	βarr2 %eff	G-protein pEC_{50}	G-protein %eff	βarr2 pEC_{50}	βarr2 %eff
B0001	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	≥ 50
B0002	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0003	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0004	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0005	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0006	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0007	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0008	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0009	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0010	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0011	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0012	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0013	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0014	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0015	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0016	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0017	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0018	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0019	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0020	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0021	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0022	< 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0023	< 7	≥ 50	< 7	< 50	< 7	< 50	≥ 7	< 50	< 7	≥ 50	< 7	< 50
B0024	< 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0025	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0026	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0027	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B0028	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0029	≥ 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0030	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0031	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0032	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	≥ 50
B0033	< 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0034	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0035	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0036	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0037	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0038	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0039	≥ 7	≥ 50	≥ 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0040	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0041	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0042	≥ 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0043	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0044	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0045	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0046	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0047	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0048	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0049	≥ 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0050	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0051	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0052	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0053	< 7	≥ 50	≥ 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0054	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50

Figure 2-Continued

B0055	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0056	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0057	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	≥ 50
B0058	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0059	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	≥ 50
B0060	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0061	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0062	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0063	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0064	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0065	< 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0066	< 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0067	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0068	< 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0069	< 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0070	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0071	< 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0072	< 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0073	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0074	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0075	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0076	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0077	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0078	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0079	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50
B0080	≥ 7	≥ 50	≥ 7	≥ 50	< 7	≥ 50	< 7	< 50	N.D.	N.D.	N.D.	N.D.
B0081	< 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0082	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0083	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0084	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	≥ 50
B0085	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0086	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0087	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0088	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0089	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0090	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0091	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0092	≥ 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0093	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0094	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0095	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0096	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0097	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0098	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0099	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0100	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0101	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0102	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0103	< 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0104	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0105	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0106	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0107	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0108	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0109	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0110	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0111	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0112	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0113	< 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50

Figure 2-Continued

B0114	< 7	≥ 50	< 7	< 50	N.D.	N.D.	N.D.	N.D.	< 7	< 50	< 7	< 50
B0115	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0116	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0117	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0118	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0119	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0120	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0121	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0122	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0123	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0124	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0125	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0126	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0127	< 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0128	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0129	< 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0130	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0131	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0132	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0133	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0134	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0135	< 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0136	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0137	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0138	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0139	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0140	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0141	< 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0142	< 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0143	< 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0144	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0145	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0146	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0147	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0148	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0149	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0150	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0151	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0152	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0153	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0154	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0155	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0156	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0157	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0158	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0159	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0160	< 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0161	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0162	≥ 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0163	< 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0164	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0165	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0166	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0167	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0168	≥ 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0169	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0170	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0171	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0172	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50

Figure 2-Continued

B0173	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0174	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0175	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	≥ 50
B0176	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0177	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0178	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0179	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0180	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0181	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0182	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0183	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0184	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0185	≥ 7	≥ 50	≥ 7	≥ 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	≥ 50
B0186	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0187	< 7	≥ 50	< 7	< 50	N.D.	N.D.	N.D.	N.D.	< 7	≥ 50	< 7	< 50
B0188	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B0189	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0190	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0191	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0192	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50
B0193	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0194	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0195	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0196	< 7	< 50	≥ 7	< 50	N.D.	N.D.	N.D.	N.D.	< 7	< 50	< 7	< 50
B0197	< 7	≥ 50	< 7	≥ 50	N.D.	N.D.	N.D.	N.D.	< 7	< 50	< 7	< 50
B0198	< 7	≥ 50	< 7	≥ 50	N.D.	N.D.	N.D.	N.D.	< 7	≥ 50	< 7	< 50
B0199	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0200	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0201	< 7	≥ 50	< 7	< 50	< 7	< 50	≥ 7	< 50	< 7	≥ 50	< 7	< 50
B0202	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0203	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0204	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0205	≥ 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0206	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0207	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0208	< 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0209	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0210	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0211	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0212	< 7	≥ 50	< 7	< 50	< 7	≥ 50	≥ 7	< 50	< 7	≥ 50	< 7	< 50
B0213	< 7	≥ 50	< 7	≥ 50	< 7	≥ 50	≥ 7	< 50	< 7	≥ 50	< 7	< 50
B0214	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0215	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0216	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0217	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0218	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0219	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0220	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0221	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0222	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0223	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0224	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0225	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0226	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0227	< 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50
B0228	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0229	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0230	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0231	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50

Figure 2-Continued

B0232	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0233	< 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50
B0234	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0235	< 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	< 50	≥ 7	< 50
B0236	< 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	< 50	≥ 7	< 50
B0237	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	≥ 7	< 50
B0238	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	≥ 7	< 50
B0239	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0240	< 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0241	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0242	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0243	< 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50
B0244	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0245	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0246	< 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0247	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0248	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0249	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0250	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0251	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0252	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0253	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0254	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0255	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0256	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0257	< 7	≥ 50	< 7	≥ 50	< 7	< 50	≥ 7	< 50	< 7	< 50	≥ 7	< 50
B0258	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	≥ 7	< 50
B0259	< 7	≥ 50	≥ 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0260	< 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0261	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0262	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0263	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0264	< 7	≥ 50	< 7	≥ 50	< 7	≥ 50	≥ 7	< 50	< 7	≥ 50	< 7	< 50
B0265	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0266	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	≥ 7	< 50
B0267	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0268	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0269	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0270	< 7	≥ 50	< 7	< 50	< 7	< 50	≥ 7	< 50	< 7	≥ 50	< 7	< 50
B0271	≥ 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0272	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0273	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0274	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0275	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0276	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0277	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	≥ 50	≥ 7	< 50
B0278	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0279	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0280	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0281	≥ 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0282	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0283	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50
B0284	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0285	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0286	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50
B0287	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0288	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0289	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	≥ 7	< 50
B0290	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50

Figure 2-Continued

B0291	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0292	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0293	< 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0294	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0295	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0296	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0297	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0298	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0299	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0300	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0301	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0302	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0303	< 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0304	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0305	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0306	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0307	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0308	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0309	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0310	< 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0311	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0312	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	≥ 50
B0313	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0314	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	≥ 50
B0315	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0316	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0317	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0318	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0319	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0320	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0321	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0322	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0323	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0324	≥ 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0325	< 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0326	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0327	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0328	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B0329	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0330	≥ 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B0331	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0332	< 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0333	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0334	< 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50
B0335	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0336	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0337	< 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0338	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50
B0339	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50
B0340	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0341	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0342	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0343	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0344	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0345	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50
B0346	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0347	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0348	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0349	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50

Figure 2-Continued

B0350	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0351	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0352	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0353	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0354	< 7	< 50	≥ 7	< 50	< 7	< 50	< 7	< 50	≥ 7	< 50	< 7	< 50
B0355	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0356	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0357	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0358	< 7	≥ 50	< 7	< 50	< 7	< 50	≥ 7	< 50	< 7	< 50	< 7	< 50
B0359	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0360	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0361	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0362	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0363	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0364	≥ 7	≥ 50	≥ 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0365	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0366	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0367	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0368	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	≥ 50
B0369	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0370	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0371	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0372	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0373	≥ 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0374	≥ 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0375	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0376	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0377	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0378	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0379	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0380	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0381	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0382	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0383	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0384	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0385	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0386	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0387	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0388	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0389	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0390	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0391	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0392	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0393	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0394	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0395	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0396	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	≥ 7	< 50
B0397	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0398	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0399	< 7	≥ 50	≥ 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0400	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0401	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0402	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0403	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	≥ 7	< 50
B0404	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0405	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0406	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0407	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0408	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50

Figure 2-Continued

B0409	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0410	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0411	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0412	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0413	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0414	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0415	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0416	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0417	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0418	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0419	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0420	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0421	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0422	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0423	≥ 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0424	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	≥ 7	< 50	< 7	< 50
B0425	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0426	≥ 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	≥ 50
B0427	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0428	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0429	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0430	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0431	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0432	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0433	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0434	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0435	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0436	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0437	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0438	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0439	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0440	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0441	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0442	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	≥ 50
B0443	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0444	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0445	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0446	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0447	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0448	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0449	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0450	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0451	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0452	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0453	≥ 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B0454	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0455	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0456	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0457	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0458	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0459	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0460	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0461	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0462	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0463	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0464	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0465	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0466	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0467	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	≥ 50

Figure 2-Continued

B0468	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0469	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0470	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0471	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0472	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0473	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	≥ 50
B0474	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0475	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0476	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0477	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0478	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0479	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0480	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0481	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0482	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0483	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0484	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0485	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0486	< 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0487	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0488	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0489	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0490	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0491	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0492	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0493	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0494	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0495	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0496	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0497	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0498	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0499	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0500	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0501	< 7	< 50	< 7	< 50	≥ 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0502	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0503	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0504	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50
B0505	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0506	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0507	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0508	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0509	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0510	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0511	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0512	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0513	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0514	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0515	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0516	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0517	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0518	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	≥ 50
B0519	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0520	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0521	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0522	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0523	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0524	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0525	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0526	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50

Figure 2-Continued

B0527	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0528	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0529	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0530	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0531	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0532	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0533	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0534	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0535	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0536	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0537	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0538	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0539	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0540	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0541	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0542	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0543	< 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0544	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0545	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0546	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0547	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0548	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0549	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0550	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0551	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0552	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0553	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0554	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0555	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50
B0556	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0557	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0558	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0559	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0560	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0561	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0562	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0563	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0564	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0565	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0566	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0567	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0568	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0569	≥ 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0570	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0571	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0572	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0573	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0574	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0575	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0576	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0577	≥ 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0578	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0579	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0580	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B0581	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0582	≥ 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0583	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0584	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0585	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50

Figure 2-Continued

B0586	≥ 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0587	≥ 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0588	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0589	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0590	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0591	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0592	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0593	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0594	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0595	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0596	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0597	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0598	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0599	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0600	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0601	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0602	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0603	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0604	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
B0605	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0606	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0607	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
B0608	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
B0609	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
B0610	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	≥ 50
B0611	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0612	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0613	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	≥ 50
B0614	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0615	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0616	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B0617	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	≥ 50
B0618	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0619	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0620	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
B0621	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
B0622	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0623	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	≥ 50
B0624	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0625	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0626	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0627	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50
B0628	≥ 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0629	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	≥ 50
B0630	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0631	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0632	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0633	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0634	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0635	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0636	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0637	≥ 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0638	≥ 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0639	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0640	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0641	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0642	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0643	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0644	≥ 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50

Figure 2-Continued

B0645	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0646	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0647	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	≥ 50
B0648	≥ 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0649	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50
B0650	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	≥ 50
B0651	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	≥ 50
B0652	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0653	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50
B0654	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0655	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0656	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0657	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0658	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0659	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0660	≥ 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0661	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
B0662	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
B0663	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0664	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0665	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	≥ 50
B0666	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0667	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0668	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0669	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0670	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0671	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B0672	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0673	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B0674	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0675	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	≥ 50
B0676	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0677	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0678	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0679	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0680	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0681	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0682	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0683	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0684	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50
B0685	≥ 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B0686	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0687	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
B0688	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0689	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0690	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0691	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50
B0692	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B0693	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0694	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
B0695	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
B0696	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0697	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0698	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0699	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0700	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0701	≥ 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B0702	≥ 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0703	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50

Figure 2-Continued

B0704	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B0705	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0706	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B0707	≥ 7	≥ 50	≥ 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0708	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B0709	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
B0710	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0711	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B0712	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
B0713	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
B0714	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
B0715	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
B0716	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
B0717	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
B0718	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
B0719	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0720	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B0721	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0722	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0723	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0724	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0725	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B0726	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0727	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0728	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0729	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0730	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0731	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50
B0732	≥ 7	≥ 50	< 7	< 50	N.D.	N.D.	< 7	< 50	< 7	≥ 50	< 7	< 50
B0733	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0734	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0735	< 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	≥ 50
B0736	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0737	≥ 7	≥ 50	≥ 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0738	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0739	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0740	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0741	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0742	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0743	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0744	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0745	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0746	≥ 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B0747	≥ 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0748	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0749	≥ 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0750	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0751	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0752	≥ 7	≥ 50	≥ 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0753	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0754	≥ 7	≥ 50	≥ 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0755	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0756	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0757	≥ 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0758	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0759	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0760	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0761	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0762	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50

Figure 2-Continued

B0763	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0764	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0765	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50
B0766	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0767	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50
B0768	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0769	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0770	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0771	≥ 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B0772	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B0773	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B0774	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0775	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0776	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0777	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0778	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50
B0779	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0780	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0781	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	≥ 50
B0782	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50
B0783	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50
B0784	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50
B0785	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
B0786	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0787	≥ 7	≥ 50	≥ 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0788	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
B0789	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
B0790	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0791	≥ 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0792	≥ 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0793	≥ 7	≥ 50	≥ 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0794	≥ 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0795	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0796	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0797	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0798	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0799	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0800	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	≥ 50
B0801	≥ 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0802	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0803	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0804	≥ 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B0805	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0806	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
B0807	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0808	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0809	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0810	≥ 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B0811	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B0812	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0813	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0814	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0815	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0816	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0817	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	≥ 50
B0818	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0819	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0820	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0821	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50

Figure 2-Continued

B0822	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0823	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0824	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0825	≥ 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0826	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0827	≥ 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0828	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0829	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0830	≥ 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B0831	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0832	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0833	≥ 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0834	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0835	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0836	≥ 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B0837	≥ 7	≥ 50	≥ 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0838	≥ 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B0839	≥ 7	≥ 50	≥ 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0840	≥ 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B0841	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0842	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0843	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0844	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0845	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50
B0846	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0847	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0848	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	≥ 50
B0849	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0850	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0851	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0852	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0853	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0854	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0855	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0856	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	N.D.	N.D.	< 7	≥ 50	< 7	< 50
B0857	< 7	≥ 50	< 7	< 50	< 7	≥ 50	N.D.	N.D.	< 7	≥ 50	< 7	< 50
B0858	≥ 7	≥ 50	< 7	< 50	< 7	< 50	N.D.	N.D.	≥ 7	≥ 50	< 7	< 50
B0859	< 7	≥ 50	< 7	< 50	< 7	< 50	N.D.	N.D.	< 7	≥ 50	< 7	< 50
B0860	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0861	≥ 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B0862	< 7	≥ 50	< 7	< 50	< 7	≥ 50	N.D.	N.D.	< 7	< 50	< 7	< 50
B0863	≥ 7	≥ 50	< 7	< 50	< 7	< 50	N.D.	N.D.	≥ 7	≥ 50	< 7	< 50
B0864	≥ 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0865	< 7	≥ 50	< 7	< 50	< 7	≥ 50	N.D.	N.D.	< 7	≥ 50	< 7	< 50
B0866	< 7	≥ 50	< 7	< 50	< 7	≥ 50	N.D.	N.D.	< 7	≥ 50	< 7	< 50
B0867	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	N.D.	N.D.	< 7	≥ 50	< 7	≥ 50
B0868	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	N.D.	N.D.	< 7	≥ 50	< 7	< 50
B0869	≥ 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0870	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	N.D.	N.D.	< 7	≥ 50	< 7	< 50
B0871	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	N.D.	N.D.	< 7	≥ 50	< 7	< 50
B0872	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	N.D.	N.D.	< 7	≥ 50	< 7	< 50
B0873	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	N.D.	N.D.	< 7	≥ 50	< 7	< 50
B0874	≥ 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0875	≥ 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0876	≥ 7	≥ 50	≥ 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0877	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0878	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B0879	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0880	≥ 7	≥ 50	≥ 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50

Figure 2-Continued

B0881	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50
B0882	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0883	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0884	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0885	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0886	≥ 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0887	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0888	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B0889	≥ 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0890	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0891	≥ 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B0892	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0893	≥ 7	≥ 50	≥ 7	< 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50
B0894	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0895	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B0896	≥ 7	≥ 50	≥ 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0897	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
B0898	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0899	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50
B0900	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0901	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50
B0902	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0903	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0904	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0905	≥ 7	≥ 50	≥ 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0906	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0907	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0908	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0909	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0910	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0911	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B0912	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0913	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0914	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0915	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50
B0916	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0917	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0918	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0919	≥ 7	≥ 50	≥ 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0920	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0921	≥ 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0922	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0923	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0924	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0925	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50
B0926	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0927	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0928	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0929	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0930	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0931	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	≥ 50
B0932	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0933	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
B0934	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0935	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0936	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0937	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0938	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0939	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50

Figure 2-Continued

B0940	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0941	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0942	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0943	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0944	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
B0945	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0946	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
B0947	≥ 7	≥ 50	≥ 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0948	≥ 7	≥ 50	≥ 7	< 50	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0949	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0950	≥ 7	≥ 50	≥ 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0951	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0952	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0953	≥ 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0954	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0955	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0956	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0957	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0958	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0959	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0960	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0961	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0962	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0963	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
B0964	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
B0965	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0966	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B0967	≥ 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0968	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0969	≥ 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0970	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0971	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0972	≥ 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B0973	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0974	≥ 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B0975	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0976	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0977	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0978	≥ 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0979	≥ 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0980	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0981	≥ 7	≥ 50	≥ 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0982	≥ 7	≥ 50	≥ 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0983	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50
B0984	≥ 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B0985	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0986	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0987	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0988	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50
B0989	≥ 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0990	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0991	≥ 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0992	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0993	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0994	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0995	≥ 7	≥ 50	≥ 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0996	≥ 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B0997	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	≥ 50
B0998	≥ 7	≥ 50	≥ 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50

Figure 2-Continued

B0999	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1000	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1001	≥ 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1002	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1003	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1004	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1005	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1006	≥ 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B1007	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1008	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1009	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1010	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1011	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1012	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1013	≥ 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B1014	≥ 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B1015	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B1016	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
B1017	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1018	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50
B1019	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B1020	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1021	≥ 7	≥ 50	≥ 7	< 50	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1022	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1023	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1024	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1025	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1026	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B1027	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1028	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1029	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1030	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	≥ 50
B1031	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1032	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1033	≥ 7	≥ 50	≥ 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1034	≥ 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1035	≥ 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1036	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1037	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	≥ 50
B1038	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1039	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B1040	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	≥ 50
B1041	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B1042	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1043	≥ 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B1044	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1045	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1046	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B1047	≥ 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1048	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1049	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B1050	≥ 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1051	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	≥ 50
B1052	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1053	≥ 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1054	≥ 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B1055	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1056	≥ 7	≥ 50	< 7	< 50	N.D.	N.D.	< 7	< 50	< 7	< 50	< 7	< 50
B1057	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50

Figure 2-Continued

B1058	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B1059	≥ 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50
B1060	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50
B1061	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1062	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1063	≥ 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1064	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B1065	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1066	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1067	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50
B1068	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50
B1069	≥ 7	≥ 50	≥ 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1070	≥ 7	≥ 50	≥ 7	< 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50
B1071	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1072	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1073	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50
B1074	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1075	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1076	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1077	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1078	≥ 7	≥ 50	≥ 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1079	≥ 7	≥ 50	≥ 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1080	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1081	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1082	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1083	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1084	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1085	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1086	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1087	≥ 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1088	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1089	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B1090	≥ 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B1091	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1092	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1093	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1094	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1095	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1096	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1097	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1098	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1099	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1100	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1101	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1102	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50
B1103	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1104	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1105	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1106	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50
B1107	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B1108	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50
B1109	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1110	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1111	≥ 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B1112	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1113	≥ 7	≥ 50	≥ 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1114	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1115	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
B1116	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.

Figure 2-Continued

B1117	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1118	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1119	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B1120	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1121	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B1122	≥ 7	≥ 50	≥ 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1123	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B1124	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B1125	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1126	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B1127	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B1128	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	≥ 50
B1129	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B1130	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B1131	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1132	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1133	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1134	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1135	≥ 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1136	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1137	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	≥ 50
B1138	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1139	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50
B1140	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B1141	≥ 7	≥ 50	≥ 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1142	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1143	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1144	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1145	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B1146	≥ 7	≥ 50	≥ 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1147	≥ 7	≥ 50	≥ 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1148	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B1149	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B1150	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50
B1151	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B1152	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50
B1153	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1154	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50
B1155	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1156	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1157	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B1158	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B1159	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B1160	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1161	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B1162	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50
B1163	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1164	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1165	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	≥ 50
B1166	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B1167	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50
B1168	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50
B1169	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50
B1170	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1171	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	≥ 50
B1172	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1173	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B1174	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50
B1175	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50

Figure 2-Continued

B1176	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1177	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1178	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50
B1179	≥ 7	≥ 50	≥ 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1180	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1181	≥ 7	≥ 50	≥ 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1182	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1183	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1184	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50
B1185	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1186	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1187	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1188	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1189	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1190	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1191	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1192	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1193	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1194	≥ 7	≥ 50	≥ 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1195	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1196	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1197	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1198	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1199	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B1200	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1201	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1202	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50
B1203	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	≥ 50
B1204	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	≥ 50
B1205	≥ 7	≥ 50	≥ 7	< 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B1206	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1207	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1208	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1209	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B1210	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B1211	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	≥ 50
B1212	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B1213	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B1214	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1215	≥ 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1216	≥ 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1217	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1218	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1219	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1220	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1221	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B1222	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	≥ 50
B1223	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B1224	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50
B1225	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1226	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1227	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B1228	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B1229	≥ 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B1230	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B1231	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B1232	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50
B1233	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1234	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50

Figure 2-Continued

B1235	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1236	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1237	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1238	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1239	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1240	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1241	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1242	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
B1243	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	≥ 50
B1244	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50
B1245	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1246	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	≥ 50
B1247	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1248	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1249	≥ 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1250	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B1251	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1252	≥ 7	≥ 50	≥ 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1253	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1254	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1255	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	≥ 50
B1256	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	≥ 50
B1257	≥ 7	≥ 50	≥ 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1258	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50
B1259	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	≥ 50
B1260	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	≥ 50
B1261	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B1262	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	≥ 50
B1263	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1264	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1265	≥ 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1266	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1267	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50
B1268	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1269	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1270	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1271	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1272	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B1273	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1274	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1275	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1276	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1277	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B1278	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B1279	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1280	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B1281	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1282	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1283	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B1284	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B1285	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B1286	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B1287	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B1288	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1289	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1290	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1291	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B1292	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	≥ 50
B1293	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50

Figure 2-Continued

B1294	≥ 7	≥ 50	≥ 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1295	≥ 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B1296	≥ 7	≥ 50	< 7	≥ 50	≥ 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B1297	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1298	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B1299	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1300	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1301	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1302	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1303	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1304	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B1305	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1306	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50
B1307	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1308	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	≥ 50
B1309	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1310	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1311	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1312	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1313	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	≥ 50
B1314	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	≥ 50
B1315	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1316	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B1317	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B1318	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1319	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1320	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	≥ 50
B1321	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1322	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1323	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1324	≥ 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1325	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1326	≥ 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1327	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1328	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1329	≥ 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1330	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1331	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1332	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1333	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1334	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	≥ 50
B1335	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	≥ 50
B1336	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	≥ 50
B1337	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B1338	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1339	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1340	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1341	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1342	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
B1343	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1344	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1345	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1346	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1347	≥ 7	≥ 50	≥ 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1348	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	≥ 50
B1349	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1350	≥ 7	≥ 50	< 7	< 50	N.D.	N.D.	< 7	< 50	< 7	< 50	< 7	< 50
B1351	≥ 7	≥ 50	< 7	< 50	N.D.	N.D.	< 7	< 50	< 7	≥ 50	< 7	< 50
B1352	≥ 7	≥ 50	< 7	< 50	N.D.	N.D.	< 7	< 50	< 7	≥ 50	< 7	< 50

Figure 2-Continued

B1353	≥ 7	≥ 50	< 7	< 50	N.D.	N.D.	< 7	< 50	< 7	≥ 50	< 7	< 50
B1354	≥ 7	≥ 50	< 7	< 50	N.D.	N.D.	< 7	< 50	< 7	< 50	< 7	< 50
B1355	≥ 7	≥ 50	< 7	< 50	N.D.	N.D.	< 7	< 50	< 7	≥ 50	< 7	< 50
B1356	≥ 7	≥ 50	< 7	< 50	N.D.	N.D.	< 7	< 50	< 7	≥ 50	< 7	< 50
B1357	≥ 7	≥ 50	≥ 7	< 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B1358	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1359	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1360	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1361	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B1362	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B1363	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B1364	≥ 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1365	≥ 7	≥ 50	≥ 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1366	≥ 7	≥ 50	< 7	< 50	≥ 7	< 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B1367	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1368	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50
B1369	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B1370	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B1371	≥ 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B1372	≥ 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B1373	≥ 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1374	≥ 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1375	≥ 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1376	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1377	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B1378	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	≥ 50
B1379	≥ 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B1380	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1381	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1382	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50
B1383	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1384	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B1385	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B1386	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B1387	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	≥ 50
B1388	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	≥ 50
B1389	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B1390	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1391	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	< 50
B1392	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1393	≥ 7	≥ 50	≥ 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1394	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
B1395	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
B1396	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1397	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1398	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
B1399	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
B1400	≥ 7	≥ 50	≥ 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1401	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1402	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
B1403	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1404	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
B1405	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1406	< 7	≥ 50	< 7	< 50	< 7	< 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1407	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
B1408	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1409	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B1410	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1411	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50

Figure 2-Continued

B1412	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B1413	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50
B1414	≥ 7	≥ 50	< 7	< 50	N.D.	N.D.	N.D.	N.D.	< 7	≥ 50	< 7	< 50
B1415	≥ 7	≥ 50	< 7	≥ 50	< 7	≥ 50	N.D.	N.D.	< 7	≥ 50	< 7	< 50
B1416	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	< 7	< 50	≥ 7	≥ 50	< 7	< 50
B1417	≥ 7	≥ 50	< 7	< 50	< 7	≥ 50	N.D.	N.D.	< 7	≥ 50	< 7	< 50
B1418	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
B1419	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.

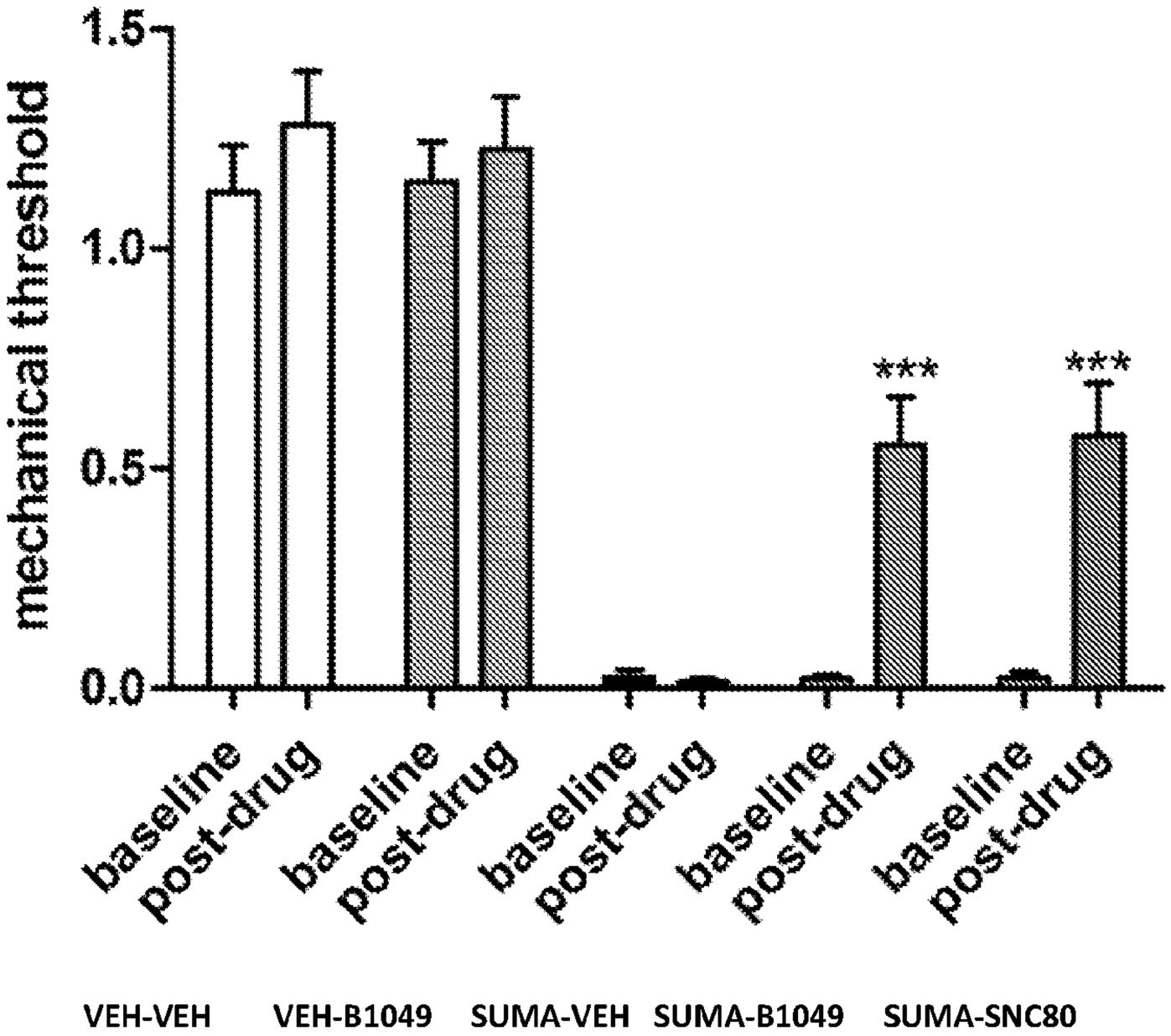

mechanical threshold
1.5
1.0
0.5
0.0
***
***
baseline
post-drug
baseline
post-drug
baseline
post-drug
baseline
post-drug
baseline
post-drug
VEH-VEH
VEH-B1049
SUMA-VEH
SUMA-B1049
SUMA-SNC80

Figure 3

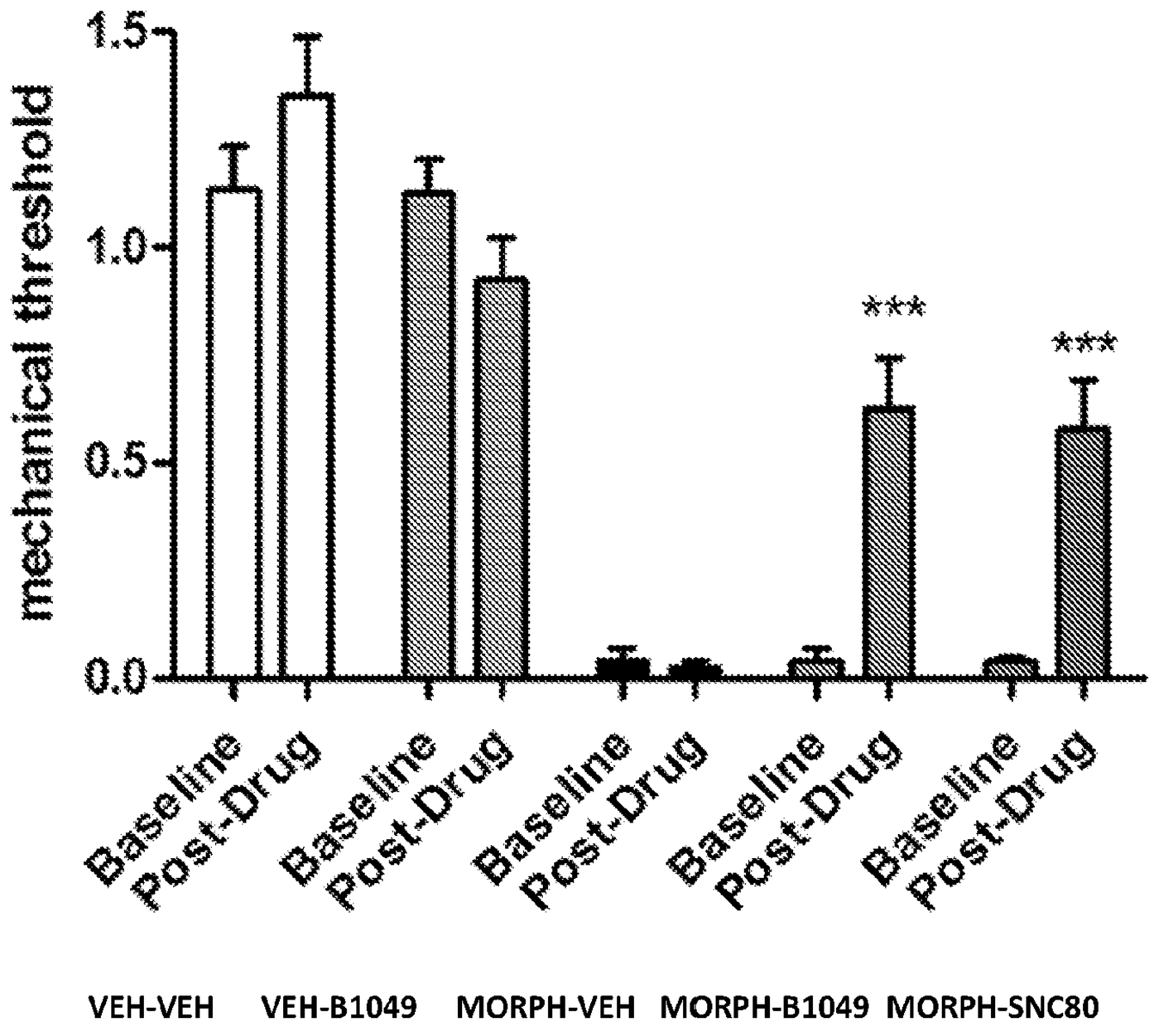

mechanical threshold
1.5
1.0
0.5
0.0
***
***
Baseline
Post-Drug
Baseline
Post-Drug
Baseline
Post-Drug
Baseline
Post-Drug
Baseline
Post-Drug
VEH-VEH
VEH-B1049
MORPH-VEH
MORPH-B1049
MORPH-SNC80

Figure 4

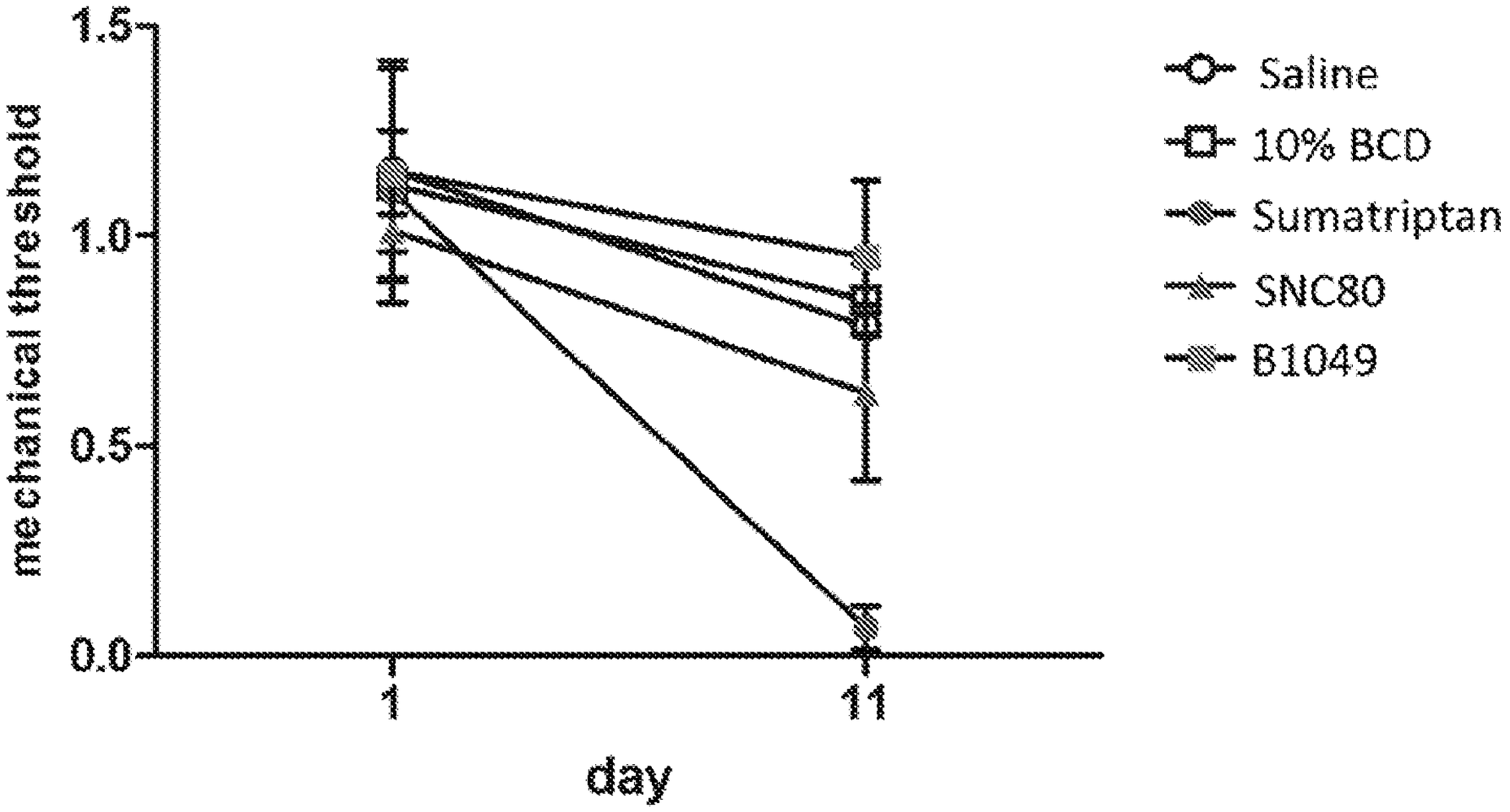

mechanical threshold
1.5
1.0
0.5
0.0
1
11
day
Saline
10% BCD
Sumatriptan
SNC80
B1049

Figure 5