HISTONE DEACETYLASE INHIBITORS

FIELD OF THE INVENTION

[0001] The present invention relates to compounds that may be used to inhibit histone deacetylases (HDACs), as well as compositions of matter and kits comprising these compounds. The invention also relates to methods for inhibiting HDACs and treatment methods using compounds according to the present invention. In particular, the present invention relates to compounds, compositions of matter, kits and methods used to inhibit Class I HDACs, such as HDAC1, HDAC2, HDAC6 and HDAC8.

BACKGROUND OF THE INVENTION

[0002] DNA in eukaryotic cells is tightly complexed with proteins (histones) to form chromatin. Histones are small, positively charged proteins that are rich in basic amino acids (positively charged at physiological pH), which contact the phosphate groups (negatively charged at physiological pH) of DNA. There are five main classes of histones H1, H2A, H2B, H3, and H4. The amino acid sequences of H2A, H2B, H3, and H4 show remarkable conservation between species, wherein H1 varies somewhat and in some cases is replaced by another histone, *e.g.*, H5. Four pairs of each of H2A, H2B, H3 and H4 together form a disk-shaped octomeric protein core, around which DNA (about 140 base pairs) is wound to form a nucleosome. Individual nucleosomes are connected by short stretches of linker DNA associated with another histone molecule to form a structure resembling a beaded string, which is itself arranged in a helical stack, known as a solenoid.

[0003] The majority of histones are synthesized during the S phase of the cell cycle, and newly synthesized histones quickly enter the nucleus to become associated with DNA. Within minutes of its synthesis, new DNA becomes associated with histones in nucleosomal structures.

[0004] A small fraction of histones, more specifically, the amino acid side chains thereof, are enzymatically modified by post-translational addition of methyl, acetyl, or phosphate groups, neutralizing the positive charge of the side chain, or converting it to a negative charge. For example, lysine and arginine groups may be methylated, lysine

groups may be acetylated, and serine groups may be phosphorylated. For lysine, the -$(CH_2)_4$-NH_2 sidechain may be acetylated, for example by an acetyltransferase enzyme to give the amide -$(CH_2)_4$-NHC(=O)CH_3. Methylation, acetylation, and phosphorylation of amino termini of histones that extend from the nucleosomal core affects chromatin structure and gene expression. Spencer and Davie 1999. Gene 240:1 1-12.

[0005] Acetylation and deacetylation of histones is associated with transcriptional events leading to cell proliferation and/or differentiation. Regulation of the function of transcriptional factors is also mediated through acetylation. Recent reviews on histone deacetylation include Kouzarides *et al.*, 1999, Curr. Opin. Genet. Dev. 9:1, 40-48 and Pazin *et al.*, 1997, 89:3 325-328.

[0006] The correlation between acetylation status of histones and the transcription of genes has been known for quite some time. Certain enzymes, specifically acetylases (*e.g.*, histone acetyltransferases (HAT) and deacetylases (histone deacetylases or HDACs), which regulate the acetylation state of histones have been identified in many organisms and have been implicated in the regulation of numerous genes, confirming a link between acetylation and transcription. In general, histone acetylation is believed to correlate with transcriptional activation, whereas histone deacetylation is believed to be associated with gene repression.

[0007] A growing number of histone deacetylases (HDACs) have been identified. HDACs function as part of large multiprotein complexes, which are tethered to the promoter and repress transcription. Well characterized transcriptional repressors such as MAD, nuclear receptors and YY1 associate with HDAC complexes to exert their repressor function.

[0008] Studies of HDAC inhibitors have shown that these enzymes play an important role in cell proliferation and differentiation. HDACs are believed to be associated with a variety of different disease states including, but not limited to cell proliferative diseases and conditions (Marks, P.A., Richon, V.M., Breslow, R. and Rifkind, R.A., J. Natl. Cancer Inst. (Bethesda) 92, 1210-1215, 2000) such as leukemia (Lin *et al.*, 1998. Nature 391: 811-814; Grignani *et al.*1998. Nature 391: 815-818; Warrell *et al.*, 1998, J. Natl. Cancer Inst. 90:1621-1625; Gelmetti *et al.*, 1998, Mol. Cell Biol. 18:7185-7191; Wang *et al.*, 1998, PNAS 951 0860-10865), melanomas/squamous cell carcinomas (Gillenwater *et al.*, 1998,

Int. J. Cancer 75217-224; Saunders *et al.*, 1999, Cancer Res. 59:399-404), breast cancer, prostrate cancer, bladder cancer (Gelmetti *et al.*, 1998, Mol. Cell Biol. 18:7185-7191; Wang *et al.*, 1998, PNAS 951 0860-10865), lung cancer, ovarian cancer, colon cancer (Hassig *et al.*, 1997, Chem. Biol. 4:783-789; Archer *et al.*, 1998, PNAS, 956791-6796; Swendeman *et al.*, 1999, Proc. Amer. Assoc. Cancer Res. 40, Abstract #3836), and hyperproliferative skin disease such as cancerous and precancerous skin lesions, as well as inflammatory cutaneous disorders.

[0009] Histone deacetylase inhibitors are potent inducers of growth arrest, differentiation, or apoptotic cell death in a variety of transformed cells in culture and in tumor bearing animals (*Histone deacetylase inhibitors as new cancer drugs*, Marks, P.A., Richon, V.M., Breslow, R. and Rifkind, R.A., Current Opinions in Oncology, 2001, Nov. 13 (6): 477-83; *Histone deacetylases and cancer: causes and therapies,* Marks, P., Rifkind, R.A., Richon, V.M., Breslow, R., Miller, T. and Kelly, W.K., Nat. Rev. Cancer 2001 Dec.1 (3):194-202). In addition, HDAC inhibitors are useful in the treatment or prevention of protozoal diseases (US Patent 5,922,837) and psoriasis (PCT Publication No. WO 02/26696).

[0010] Accordingly, despite the various HDAC inhibitors that have been reported to date, a need continues to exist for new and more effective inhibitors of HDACs.

SUMMARY OF THE INVENTION

[0011] The present invention relates to compounds that have activity for inhibiting histone deacetylases (HDACs). The present invention also provides compositions, articles of manufacture and kits comprising these compounds.

[0012] In one embodiment, a pharmaceutical composition is provided that comprises an HDAC inhibitor according to the present invention as an active ingredient. Pharmaceutical compositions according to the invention may optionally comprise 0.001%-100% of one or more HDAC inhibitors of this invention. These pharmaceutical compositions may be administered or coadministered by a wide variety of routes, including for example, orally, parenterally, intraperitoneally, intravenously, intraarterially, transdermally, sublingually, intramuscularly, rectally, transbuccally, intranasally, liposomally, via inhalation, vaginally, intraoccularly, via local delivery (for example by

catheter or stent), subcutaneously, intraadiposally, intraarticularly, or intrathecally. The compositions may also be administered or co-administered in slow release dosage forms.

[0013] The invention is also directed to kits and other articles of manufacture for treating disease states associated with one or more HDAC.

[0014] In one embodiment, a kit is provided that comprises a composition comprising at least one HDAC inhibitor of the present invention in combination with instructions. The instructions may indicate the disease state for which the composition is to be administered, storage information, dosing information and/or instructions regarding how to administer the composition. The kit may also comprise packaging materials. The packaging material may comprise a container for housing the composition. The kit may also optionally comprise additional components, such as syringes for administration of the composition. The kit may comprise the composition in single or multiple dose forms.

[0015] In another embodiment, an article of manufacture is provided that comprises a composition comprising at least one HDAC inhibitor of the present invention in combination with packaging materials. The packaging material may comprise a container for housing the composition. The container may optionally comprise a label indicating the disease state for which the composition is to be administered, storage information, dosing information and/or instructions regarding how to administer the composition. The kit may also optionally comprise additional components, such as syringes for administration of the composition. The kit may comprise the composition in single or multiple dose forms.

[0016] Also provided are methods for preparing compounds, compositions and kits according to the present invention. For example, several synthetic schemes are provided herein for synthesizing compounds according to the present invention. In still another embodiment, reactive intermediates are provided for use in conjunction with the synthetic schemes.

[0017] Also provided are methods for using compounds, compositions, kits and articles of manufacture according to the present invention.

[0018] In one embodiment, the compounds, compositions, kits and articles of manufacture are used to inhibit one or more HDAC.

[0019] In another embodiment, the compounds, compositions, kits and articles of manufacture are used to treat a disease state for which one or more HDAC possesses activity that contributes to the pathology and/or symptomology of the disease state.

[0020] In another embodiment, a compound is administered to a subject wherein HDAC activity within the subject is altered, preferably reduced.

[0021] In another embodiment, a prodrug of a compound is administered to a subject that is converted to the compound *in vivo* where it inhibits one or more HDAC.

[0022] In another embodiment, a method of inhibiting one or more HDAC is provided that comprises contacting an HDAC with a compound according to the present invention.

[0023] In another embodiment, a method of inhibiting one or more HDAC is provided that comprises causing a compound according to the present invention to be present in a subject in order to inhibit the HDAC *in vivo*.

[0024] In another embodiment, a method of inhibiting an HDAC is provided that comprises administering a first compound to a subject that is converted *in vivo* to a second compound wherein the second compound inhibits the HDAC *in vivo*. It is noted that the compounds of the present invention may be the first or second compounds.

[0025] In another embodiment, a therapeutic method is provided that comprises administering a compound according to the present invention.

[0026] In another embodiment, a method of treating a condition in a patient which is known to be mediated by one or more HDAC, or which is known to be treated by HDAC inhibitors, comprising administering to the patient a therapeutically effective amount of a compound according to the present invention.

[0027] In another embodiment, a method is provided for treating a disease state for which one or more HDAC possesses activity that contributes to the pathology and/or symptomology of the disease state, the method comprising: causing a compound according to the present invention to be present in a subject in a therapeutically effective amount for the disease state.

[0028] In another embodiment, a method is provided for treating a disease state for which one or more HDAC possesses activity that contributes to the pathology and/or symptomology of the disease state, the method comprising: administering a first compound to a subject that is converted *in vivo* to a second compound such that the second

compound is present in the subject in a therapeutically effective amount for the disease state. It is noted that the compounds of the present invention may be the first or second compounds.

[0029] In another embodiment, a method is provided for treating a disease state for which one or more HDAC possesses activity that contributes to the pathology and/or symptomology of the disease state, the method comprising: administering a compound according to the present invention to a subject such that the compound is present in the subject in a therapeutically effective amount for the disease state.

[0030] In another embodiment, a method is provided for using a compound according to the present invention in order to manufacture a medicament for use in the treatment of a disease state that is known to be mediated by one or more HDAC, or that is known to be treated by HDAC inhibitors.

[0031] It is noted in regard to all of the above embodiments that the present invention is intended to encompass all pharmaceutically acceptable ionized forms (*e.g.*, salts) and solvates (*e.g.*, hydrates) of the compounds, regardless of whether such ionized forms and solvates are specified since it is well know in the art to administer pharmaceutical agents in an ionized or solvated form. It is also noted that unless a particular stereochemistry is specified, recitation of a compound is intended to encompass all possible stereoisomers (*e.g.*, enantiomers or diastereomers depending on the number of chiral centers), independent of whether the compound is present as an individual isomer or a mixture of isomers. Further, unless otherwise specified, recitation of a compound is intended to encompass all possible resonance forms and tautomers. With regard to the claims, the language "compound comprising the formula" is intended to encompass the compound and all pharmaceutically acceptable ionized forms and solvates, all possible stereoisomers, and all possible resonance forms and tautomers unless otherwise specifically specified in the particular claim.

[0032] It is further noted that prodrugs may also be administered which are altered *in vivo* and become a compound according to the present invention. The various methods of using the compounds of the present invention are intended, regardless of whether prodrug delivery is specified, to encompass the administration of a prodrug that is converted *in vivo* to a compound according to the present invention. It is also noted that certain

compounds of the present invention may be altered *in vivo* prior to inhibiting kinases and thus may themselves be prodrugs for another compound. Such prodrugs of another compound may or may not themselves independently have kinase inhibitory activity.

BRIEF DESCRIPTION OF THE FIGURES

[0033] Figure 1 illustrates residues 1-482 of HDAC1 and a Flag tag at both the N- and C- terminus (SEQ ID NO: 1).

[0034] Figure 2 illustrates the DNA sequence (SEQ ID NO: 2) that was used to encode SEQ ID NO: 1.

[0035] Figure 3 illustrates residues 1-488 of HDAC2 and a 6-histidine tag at the C-terminus (SEQ ID NO: 3).

[0036] Figure 4 illustrates the DNA sequence (SEQ ID NO: 4) that was used to encode SEQ ID NO: 3.

[0037] Figure 5 illustrates residues 73-845 of HDAC6 and a 6-histidine tag at the C-terminus (SEQ ID NO: 5).

[0038] Figure 6 illustrates the DNA sequence (SEQ ID NO: 6) that was used to encode SEQ ID NO: 5.

[0039] Figure 7 illustrates residues 1-377 of HDAC8 and a 6-histidine tag at the N-terminus (SEQ ID NO: 7).

[0040] Figure 8 illustrates the DNA sequence (SEQ ID NO: 8) that was used to encode SEQ ID NO: 7.

DEFINITIONS

[0041] Unless otherwise stated, the following terms used in the specification and claims shall have the following meanings for the purposes of this Application.

[0042] "Alicyclic" means a moiety comprising a non-aromatic ring structure. Alicyclic moieties may be saturated or partially unsaturated with one, two or more double or triple bonds. Alicyclic moieties may also optionally comprise heteroatoms such as nitrogen, oxygen and sulfur. The nitrogen atoms can be optionally quaternerized or oxidized and the sulfur atoms can be optionally oxidized. Examples of alicyclic moieties include, but are not limited to moieties with C_{3-8} rings such as cyclopropyl, cyclohexane, cyclopentane,

cyclopentene, cyclopentadiene, cyclohexane, cyclohexene, cyclohexadiene, cycloheptane, cycloheptene, cycloheptadiene, cyclooctane, cyclooctene, and cyclooctadiene.

[0043] "Aliphatic" means a moiety characterized by a straight or branched chain arrangement of constituent carbon atoms and may be saturated or partially unsaturated with one, two or more double or triple bonds.

[0044] "Alkoxy" means an oxygen moiety having a further alkyl substituent. The alkoxy groups of the present invention can be optionally substituted.

[0045] "Alkyl" represented by itself means a straight or branched, saturated or unsaturated, aliphatic radical having a chain of carbon atoms, optionally with oxygen (See "oxaalkyl") or nitrogen atoms (See "aminoalkyl") between the carbon atoms. C_X alkyl and C_{X-Y} alkyl are typically used where X and Y indicate the number of carbon atoms in the chain. For example, C_{1-6} alkyl includes alkyls that have a chain of between 1 and 6 carbons (*e.g.*, methyl, ethyl, propyl, isopropyl, butyl, *sec*-butyl, isobutyl, *tert*-butyl, vinyl, allyl, 1-propenyl, isopropenyl, 1-butenyl, 2-butenyl, 3-butenyl, 2-methylallyl, ethynyl, 1-propynyl, 2-propynyl, and the like). Alkyl represented along with another radical (*e.g.*, as in arylalkyl, heteroarylalkyl) means a straight or branched, saturated or unsaturated aliphatic divalent radical having the number of atoms indicated or when no atoms are indicated means a bond (*e.g.*, (C_{6-10})aryl(C_{1-3})alkyl includes, benzyl, phenethyl, 1-phenylethyl, 3-phenylpropyl, 2-thienylmethyl, 2-pyridinylmethyl and the like).

[0046] "Alkenyl" means a straight or branched, carbon chain that contains at least one carbon-carbon double bond. Examples of alkenyl include vinyl, allyl, isopropenyl, pentenyl, hexenyl, heptenyl, 1-propenyl, 2-butenyl, 2-methyl-2-butenyl, and the like.

[0047] "Alkynyl" means a straight or branched, carbon chain that contains at least one carbon-carbon triple bond. Examples of alkynyl include ethynyl, propargyl, 3-methyl-1-pentynyl, 2-heptynyl and the like.

[0048] "Alkylene", unless indicated otherwise, means a straight or branched, saturated or unsaturated, aliphatic, divalent radical. C_X alkylene and C_{X-Y} alkylene are typically used where X and Y indicate the number of carbon atoms in the chain. For example, C_{1-6} alkylene includes methylene ($-CH_2-$), ethylene ($-CH_2CH_2-$), trimethylene ($-CH_2CH_2CH_2-$), tetramethylene ($-CH_2CH_2CH_2CH_2-$) 2-butenylene ($-CH_2CH=CHCH_2-$),

2-methyltetramethylene (-$CH_2CH(CH_3)CH_2CH_2$-), pentamethylene (-$CH_2CH_2CH_2CH_2CH_2$-) and the like.

[0049] "Alkenylene" means a straight or branched, divalent carbon chain having one or more carbon-carbon double bonds. Examples of alkenylene include ethene-1,2-diyl, propene-1,3-diyl, methylene-1,1-diyl, and the like.

[0050] "Alkynylene" means a straight or branched, divalent carbon chain having one or more carbon-carbon triple bonds. Examples of alkynylene include ethyne-1,2-diyl, propyne-1,3-diyl, and the like.

[0051] "Alkylidene" means a straight or branched saturated or unsaturated, aliphatic radical connected to the parent molecule by a double bond. C_X alkylidene and C_{X-Y} alkylidene are typically used where X and Y indicate the number of carbon atoms in the chain. For example, C_{1-6} alkylidene includes methylene (=CH_2), ethylidene (=$CHCH_3$), isopropylidene (=$C(CH_3)_2$), propylidene (=$CHCH_2CH_3$), allylidene (=CH-CH=CH_2), and the like).

[0052] "Amido" means the radical –$NR_aC(O)R_b$ where the point of attachment to the molecule is at the nitrogen, and R_a and R_b are further substituents attached to the nitrogen and the carbon of the carbonyl, respectively.

[0053] "Amino" means a nitrogen moiety having two further substituents where, for example, a hydrogen or carbon atom is attached to the nitrogen. For example, representative amino groups include -NH_2, -$NHCH_3$, -$N(CH_3)_2$, -NHC_{1-10}-alkyl, -$N(C_{1-10}$-alkyl$)_2$, -NHaryl, -NHheteroaryl, -N(aryl)$_2$, -N(heteroaryl)$_2$, and the like. Optionally, the two substituents together with the nitrogen may also form a ring. Unless indicated otherwise, the compounds of the invention containing amino moieties may include protected derivatives thereof. Suitable protecting groups for amino moieties include acetyl, *tert*-butoxycarbonyl, benzyloxycarbonyl, and the like.

[0054] "Aminoalkyl" means an alkyl, as defined above, except where one or more substituted or unsubstituted nitrogen atoms (-N-) are positioned between carbon atoms of the alkyl. For example, an (C_{2-6}) aminoalkyl refers to a chain comprising between 2 and 6 carbons and one or more nitrogen atoms positioned between the carbon atoms.

[0055] "Animal" includes humans, non-human mammals (*e.g.*, dogs, cats, rabbits, cattle, horses, sheep, goats, swine, deer, and the like) and non-mammals (*e.g.*, birds, and the like).

[0056] "Aromatic" means a moiety wherein the constituent atoms make up an unsaturated ring system, all atoms in the ring system are sp^2 hybridized and the total number of pi electrons is equal to 4n+2. An aromatic ring may be such that the ring atoms are only carbon atoms or may include carbon and non-carbon atoms (see Heteroaryl).

[0057] "Aryl" means a monocyclic or polycyclic ring assembly wherein each ring is aromatic or when fused with one or more rings forms an aromatic ring assembly. If one or more ring atoms is not carbon (*e.g.*, N, S), the aryl is a heteroaryl. C_X aryl and C_{X-Y} aryl are typically used where X and Y indicate the number of atoms in the ring.

[0058] "Bicycloalkyl" means a saturated or partially unsaturated fused bicyclic or bridged polycyclic ring assembly.

[0059] "Bicycloaryl" means a bicyclic ring assembly wherein the rings are linked by a single bond or fused and at least one of the rings comprising the assembly is aromatic. C_X bicycloaryl and C_{X-Y} bicycloaryl are typically used where X and Y indicate the number of carbon atoms in the bicyclic ring assembly and directly attached to the ring.

[0060] "Bridging ring" as used herein refers to a ring that is bonded to another ring to form a compound having a bicyclic structure where two ring atoms that are common to both rings are not directly bound to each other. Non-exclusive examples of common compounds having a bridging ring include borneol, norbornane, 7-oxabicyclo[2.2.1]heptane, and the like. One or both rings of the bicyclic system may also comprise heteroatoms.

[0061] "Carbamoyl" means the radical $-OC(O)NR_aR_b$ where R_a and R_b are each independently two further substituents where a hydrogen or carbon atom is attached to the nitrogen.

[0062] "Carbocycle" means a ring consisting of carbon atoms.

[0063] "Carbocyclic ketone derivative" means a carbocyclic derivative wherein the ring contains a -CO– moiety.

[0064] "Carbonyl" means the radical -CO-. It is noted that the carbonyl radical may be further substituted with a variety of substituents to form different carbonyl groups including acids, acid halides, aldehydes, amides, esters, and ketones.

[0065] "Carboxamido" means the radical $-C(O)NR_aR_b$ where the point of attachment to the molecule is at the carbon of the carbonyl, and R_a and R_b are each independently two further substituents on the nitrogen.

[0066] "Carboxy" means the radical $-CO_2-$. It is noted that compounds of the invention containing carboxy moieties may include protected derivatives thereof, *i.e.*, where the oxygen is substituted with a protecting group. Suitable protecting groups for carboxy moieties include benzyl, *tert*-butyl, and the like.

[0067] "Cyano" means the radical -CN.

[0068] "Cycloalkyl" means a non-aromatic, saturated or partially unsaturated, monocyclic, fused bicyclic or bridged polycyclic ring assembly. C_X cycloalkyl and C_{X-Y} cycloalkyl are typically used where X and Y indicate the number of carbon atoms in the ring assembly. For example, C_{3-10} cycloalkyl includes cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cyclohexenyl, 2,5-cyclohexadienyl, bicyclo[2.2.2]octyl, adamantan-1-yl, decahydronaphthyl, oxocyclohexyl, dioxocyclohexyl, thiocyclohexyl, 2-oxobicyclo[2.2.1]hept-1-yl, and the like.

[0069] "Cycloalkylene" means a divalent saturated or partially unsaturated, monocyclic or polycyclic ring assembly. C_X cycloalkylene and C_{X-Y} cycloalkylene are typically used where X and Y indicate the number of carbon atoms in the ring assembly.

[0070] "Disease" specifically includes any unhealthy condition of an animal or part thereof and includes an unhealthy condition that may be caused by, or incident to, medical or veterinary therapy applied to that animal, *i.e.*, the "side effects" of such therapy.

[0071] "Fused ring" as used herein refers to a ring that is bonded to another ring to form a compound having a bicyclic structure when the ring atoms that are common to both rings are directly bound to each other. Non-exclusive examples of common fused rings include decalin, naphthalene, anthracene, phenanthrene, indole, furan, benzofuran, quinoline, and the like. Compounds having fused ring systems may be saturated, partially saturated, carbocyclics, heterocyclics, aromatics, heteroaromatics, and the like.

[0072] "Halo" means fluoro, chloro, bromo or iodo.

[0073] "Halo-substituted alkyl", as an isolated group or part of a larger group, means "alkyl" substituted by one or more "halo" atoms, as such terms are defined in this Application. Halo-substituted alkyl includes haloalkyl, dihaloalkyl, trihaloalkyl, perhaloalkyl and the like (*e.g.*, halo-substituted (C_{1-3})alkyl includes chloromethyl, dichloromethyl, difluoromethyl, trifluoromethyl, 2,2,2-trifluoroethyl, perfluoroethyl, 2,2,2-trifluoro-1,1-dichloroethyl, and the like).

[0074] "Heteroatom" refers to an atom that is not a carbon atom. Particular examples of heteroatoms include, but are not limited to nitrogen, oxygen, and sulfur.

[0075] "Heteroatom moiety" includes a moiety where the atom by which the moiety is attached is not a carbon. Examples of heteroatom moieties include -N=, -NR_c-, -$N^+(O^-)$=, -O-, -S- or -$S(O)_2$-, wherein R_c is further substituent.

[0076] "Heterobicycloalkyl" means bicycloalkyl, as defined in this Application, provided that one or more of the atoms within the ring is a heteroatom. For example hetero(C_{9-12})bicycloalkyl as used in this application includes, but is not limited to, 3-aza-bicyclo[4.1.0]hept-3-yl, 2-aza-bicyclo[3.1.0]hex-2-yl , 3-aza-bicyclo[3.1.0]hex-3-yl, and the like.

[0077] "Heterocycloalkylene" means cycloalkylene, as defined in this Application, provided that one or more of the ring member carbon atoms is replaced by a heteroatom.

[0078] "Heteroaryl" means a cyclic aromatic group having five or six ring atoms, wherein at least one ring atom is a heteroatom and the remaining ring atoms are carbon. The nitrogen atoms can be optionally quaternerized and the sulfur atoms can be optionally oxidized. Heteroaryl groups of this invention include, but are not limited to, those derived from furan, imidazole, isothiazole, isoxazole, oxadiazole, oxazole, 1,2,3-oxadiazole, pyrazine, pyrazole, pyridazine, pyridine, pyrimidine, pyrroline, thiazole, 1,3,4-thiadiazole, triazole and tetrazole. "Heteroaryl" also includes, but is not limited to, bicyclic or tricyclic rings, wherein the heteroaryl ring is fused to one or two rings independently selected from the group consisting of an aryl ring, a cycloalkyl ring, a cycloalkenyl ring, and another monocyclic heteroaryl or heterocycloalkyl ring. These bicyclic or tricyclic heteroaryls include, but are not limited to, those derived from benzo[b]furan, benzo[b]thiophene, benzimidazole, imidazo[4,5-c]pyridine, quinazoline, thieno[2,3-c]pyridine, thieno[3,2-b]pyridine, thieno[2,3-b]pyridine, indolizine, imidazo[1,2a]pyridine, quinoline,

isoquinoline, phthalazine, quinoxaline, naphthyridine, quinolizine, indole, isoindole, indazole, indoline, benzoxazole, benzopyrazole, benzothiazole, imidazo[1,5-a]pyridine, pyrazolo[1,5-a]pyridine, imidazo[1,2-a]pyrimidine, imidazo[1,2-c]pyrimidine, imidazo[1,5-a]pyrimidine, imidazo[1,5-c]pyrimidine, pyrrolo[2,3-b]pyridine, pyrrolo[2,3-c]pyridine, pyrrolo[3,2-c]pyridine, pyrrolo[3,2-b]pyridine, pyrrolo[2,3-d]pyrimidine, pyrrolo[3,2-d]pyrimidine, pyrrolo[2,3-b]pyrazine, pyrazolo[1,5-a]pyridine, pyrrolo[1,2-b]pyridazine, pyrrolo[1,2-c]pyrimidine, pyrrolo[1,2-a]pyrimidine, pyrrolo[1,2-a]pyrazine, triazo[1,5-a]pyridine, pteridine, purine, carbazole, acridine, phenazine, phenothiazene, phenoxazine, 1,2-dihydropyrrolo[3,2,1-*hi*]indole, indolizine, pyrido[1,2-a]indole and 2(1H)-pyridinone. The bicyclic or tricyclic heteroaryl rings can be attached to the parent molecule through either the heteroaryl group itself or the aryl, cycloalkyl, cycloalkenyl or heterocycloalkyl group to which it is fused. The heteroaryl groups of this invention can be substituted or unsubstituted.

[0079] "Heterobicycloaryl" means bicycloaryl, as defined in this Application, provided that one or more of the atoms within the ring is a heteroatom. For example, hetero(C_{4-12})bicycloaryl as used in this Application includes, but is not limited to, 2-amino-4-oxo-3,4-dihydropteridin-6-yl, tetrahydroisoquinolinyl, and the like.

[0080] "Heterocycloalkyl" means cycloalkyl, as defined in this Application, provided that one or more of the atoms forming the ring is a heteroatom selected, independently from N, O, or S. Non-exclusive examples of heterocycloalkyl include piperidyl, 4-morpholyl, 4-piperazinyl, pyrrolidinyl, perhydropyrrolizinyl, 1,4-diazaperhydroepinyl, 1,3-dioxanyl, 1,4-dioxanyl and the like.

[0081] "Hydroxy" means the radical -OH.

[0082] "IC_{50}" means the molar concentration of an inhibitor that produces 50% inhibition of the target enzyme.

[0083] "Iminoketone derivative" means a derivative comprising the moiety -C(NR)-, wherein R comprises a hydrogen or carbon atom attached to the nitrogen.

[0084] "Isomers" mean any compound having an identical molecular formulae but differing in the nature or sequence of bonding of their atoms or in the arrangement of their atoms in space. Isomers that differ in the arrangement of their atoms in space are termed "stereoisomers." Stereoisomers that are not mirror images of one another are termed

"diastereomers" and stereoisomers that are nonsuperimposable mirror images are termed "enantiomers" or sometimes "optical isomers." A carbon atom bonded to four nonidentical substituents is termed a "chiral center." A compound with one chiral center has two enantiomeric forms of opposite chirality. A mixture of the two enantiomeric forms is termed a "racemic mixture." A compound that has more than one chiral center has 2^{n-1} enantiomeric pairs, where n is the number of chiral centers. Compounds with more than one chiral center may exist as ether an individual diastereomer or as a mixture of diastereomers, termed a "diastereomeric mixture." When one chiral center is present a stereoisomer may be characterized by the absolute configuration of that chiral center. Absolute configuration refers to the arrangement in space of the substituents attached to the chiral center. Enantiomers are characterized by the absolute configuration of their chiral centers and described by the *R*- and *S*-sequencing rules of Cahn, Ingold and Prelog. Conventions for stereochemical nomenclature, methods for the determination of stereochemistry and the separation of stereoisomers are well known in the art (*e.g.*, see "Advanced Organic Chemistry", 4th edition, March, Jerry, John Wiley & Sons, New York, 1992).

[0085] "Leaving group" means a moiety that can be displaced by another moiety, such as by nucleophilic attack, during a chemical reaction. Leaving groups are well known in the art and include, for example, halides and OSO_2R' where R' is, for example, alkyl, haloalkyl, or aryl optionally substituted by halo, alkyl, alkoxy, amino, and the like. Non-limiting examples of leaving groups include chloro, bromo, iodo, mesylate, tosylate, and other similar groups.

[0086] "Nitro" means the radical $-NO_2$.

[0087] "Oxo" means the radical =O.

[0088] "Oxaalkyl" means an alkyl, as defined above, except where one or more oxygen atoms (-O-) are positioned between carbon atoms of the alkyl. For example, an (C_{2-6})oxaalkyl refers to a chain comprising between 2 and 6 carbons and one or more oxygen atoms positioned between the carbon atoms.

[0089] "Oxoalkyl" means an alkyl, further substituted with a carbonyl group. The carbonyl group may be an aldehyde, ketone, ester, amide, acid or acid chloride.

[0090] "Pharmaceutically acceptable" means that which is useful in preparing a pharmaceutical composition that is generally safe, non-toxic and neither biologically nor otherwise undesirable and includes that which is acceptable for veterinary use as well as human pharmaceutical use.

[0091] "Pharmaceutically acceptable salts" means salts of compounds of the present invention which are pharmaceutically acceptable, as defined above, and which possess the desired pharmacological activity. Such salts include acid addition salts formed with inorganic acids such as hydrochloric acid, hydrobromic acid, sulfuric acid, nitric acid, phosphoric acid, and the like; or with organic acids such as acetic acid, propionic acid, hexanoic acid, heptanoic acid, cyclopentanepropionic acid, glycolic acid, pyruvic acid, lactic acid, malonic acid, succinic acid, malic acid, maleic acid, fumaric acid, tartaric acid, citric acid, benzoic acid, *o*-(4-hydroxybenzoyl)benzoic acid, cinnamic acid, mandelic acid, methanesulfonic acid, ethanesulfonic acid, 1,2-ethanedisulfonic acid, 2-hydroxyethanesulfonic acid, benzenesulfonic acid, *p*-chlorobenzenesulfonic acid, 2-naphthalenesulfonic acid, *p*-toluenesulfonic acid, camphorsulfonic acid, 4-methylbicyclo[2.2.2]oct-2-ene-1-carboxylic acid, glucoheptonic acid, 4,4'-methylenebis(3-hydroxy-2-ene-1-carboxylic acid), 3-phenylpropionic acid, trimethylacetic acid, tertiary butylacetic acid, lauryl sulfuric acid, gluconic acid, glutamic acid, hydroxynaphthoic acid, salicylic acid, stearic acid, muconic acid and the like.

[0092] Pharmaceutically acceptable salts also include base addition salts which may be formed when acidic protons present are capable of reacting with inorganic or organic bases. Acceptable inorganic bases include sodium hydroxide, sodium carbonate, potassium hydroxide, aluminum hydroxide and calcium hydroxide. Acceptable organic bases include ethanolamine, diethanolamine, triethanolamine, tromethamine, *N*-methylglucamine and the like.

[0093] "Prodrug" means a compound that is convertible *in vivo* metabolically into an inhibitor according to the present invention. The prodrug itself may or may not also have HDAC inhibitory activity. For example, an inhibitor comprising a hydroxy group may be administered as an ester that is converted by hydrolysis *in vivo* to the hydroxy compound. Suitable esters that may be converted *in vivo* into hydroxy compounds include acetates, citrates, lactates, tartrates, malonates, oxalates, salicylates, propionates, succinates,

fumarates, maleates, methylene-bis-b-hydroxynaphthoates, gentisates, isethionates, di-*p*-toluoyltartrates, methanesulfonates, ethanesulfonates, benzenesulfonates, p-toluenesulfonates, cyclohexylsulfamates, quinates, esters of amino acids, and the like. Similarly, an inhibitor comprising an amine group may be administered as an amide that is converted by hydrolysis *in vivo* to the amine compound.

[0094] "Protected derivatives" means derivatives of inhibitors in which a reactive site or sites are blocked with protecting groups. Protected derivatives are useful in the preparation of inhibitors or in themselves may be active as inhibitors. A comprehensive list of suitable protecting groups can be found in T.W. Greene, *Protecting Groups in Organic Synthesis*, 3rd edition, John Wiley & Sons, Inc. 1999.

[0095] "Ring" means a carbocyclic or a heterocyclic system.

[0096] "Substituted or unsubstituted" means that a given moiety may consist of only hydrogen substituents through available valencies (unsubstituted) or may further comprise one or more non-hydrogen substituents through available valencies (substituted) that are not otherwise specified by the name of the given moiety. For example, isopropyl is an example of an ethylene moiety that is substituted by $-CH_3$. In general, a non-hydrogen substituent may be any substituent that may be bound to an atom of the given moiety that is specified to be substituted. Examples of substituents include, but are not limited to, aldehyde, alicyclic, aliphatic, (C_{1-10})alkyl, alkylene, alkylidene, amide, amino, aminoalkyl, aromatic, aryl, bicycloalkyl, bicycloaryl, carbamoyl, carbocyclyl, carboxyl, carbonyl group, cycloalkyl, cycloalkylene, ester, halo, heterobicycloalkyl, heterocycloalkylene, heteroaryl, heterobicycloaryl, heterocycloalkyl, oxo, hydroxy, iminoketone, ketone, nitro, oxaalkyl, and oxoalkyl moieties, each of which may optionally also be substituted or unsubstituted.

[0097] "Sulfinyl" means the radical –SO-. It is noted that the sulfinyl radical may be further substituted with a variety of substituents to form different sulfinyl groups including sulfinic acids, sulfinamides, sulfinyl esters, and sulfoxides.

[0098] "Sulfonyl" means the radical $-SO_2-$. It is noted that the sulfonyl radical may be further substituted with a variety of substituents to form different sulfonyl groups including sulfonic acids, sulfonamides, sulfonate esters, and sulfones.

[0099] "Therapeutically effective amount" means that amount which, when administered to an animal for treating a disease, is sufficient to effect such treatment for the disease.

[0100] "Thiocarbonyl" means the radical -CS-. It is noted that the thiocarbonyl radical may be further substituted with a variety of substituents to form different thiocarbonyl groups including thioacids, thioamides, thioesters, and thioketones.

[0101] "Treatment" or "treating" means any administration of a compound of the present invention and includes:

(1) preventing the disease from occurring in an animal which may be predisposed to the disease but does not yet experience or display the pathology or symptomatology of the disease,

(2) inhibiting the disease in an animal that is experiencing or displaying the pathology or symptomatology of the diseased (*i.e.*, arresting further development of the pathology and/or symptomatology), or

(3) ameliorating the disease in an animal that is experiencing or displaying the pathology or symptomatology of the diseased (*i.e.*, reversing the pathology and/or symptomatology).

[0102] It is noted in regard to all of the definitions provided herein that the definitions should be interpreted as being open ended in the sense that further substituents beyond those specified may be included. Hence, a C_1 alkyl indicates that there is one carbon atom but does not indicate what are the substituents on the carbon atom. Hence, a C_1 alkyl comprises methyl (*i.e.*, $-CH_3$) as well as $-CR_aR_bR_c$ where R_a, R_b, and R_c may each independently be hydrogen or any other substituent where the atom attached to the carbon is a heteroatom or cyano. Hence, CF_3, CH_2OH and CH_2CN, for example, are all C_1 alkyls.

DETAILED DESCRIPTION OF THE INVENTION

[0103] The present invention relates to compounds, compositions, kits and articles of manufacture that may be used to inhibit histone deacetylases (HDACs) and, in particular, Class I HDACs such as HDAC1, HDAC2, HDAC6 and HDAC8.

[0104] At least seventeen human genes that encode proven or putative HDACs have been identified to date, some of which are described in Johnstone, R. W., "Histone-

Deacetylase Inhibitors: Novel Drugs for the Treatment of Cancer", Nature Reviews, Volume I, pp. 287-299, (2002) and PCT Publication Nos. 00/10583, 01/18045, 01/42437 and 02/08273.

[0105] HDACs have been categorized into three distinct classes based on their relative size and sequence homology. The different HDACs (Homo sapiens), HDAC classes, sequences and references describing the different HDACs are provided in Tables 1 - 3.

TABLE 1: CLASS I HDACs

HDAC	GenBank Accession Number	Reference
1	NP_004955	Histone deacetylase: a regulator of transcription, Wolffe, A.P., Science 272 (5260), 371-372 (1996)
2	NP_001518	Isolation and mapping of a human gene (RPD3L1) that is homologous to RPD3, a transcription factor in Saccharomyces cerevisiae; Furukawa,Y., Kawakami,T., Sudo,K., Inazawa,J., Matsumine,A., Akiyama,T. and Nakamura,Y., Cytogenet. Cell Genet. 73 (1-2), 130-133 (1996)
3	NP_003874	Isolation and characterization of cDNAs corresponding to an additional member of the human histone deacetylase gene family, Yang,W.M., Yao,Y.L., Sun,J.M., Davie,J.R. and Seto,E., J. Biol. Chem. 272 (44), 28001-28007 (1997)
8	NP_060956	Buggy,J.J., Sideris,M.L., Mak,P., Lorimer,D.D., McIntosh,B. and Clark,J.M. Biochem. J. 350 Pt 1, 199-205 (2000)
11	NP_079103	Cloning and Functional Characterization of HDAC11, a Novel Member of the Human Histone Deacetylase Family, Gao,L., Cueto,M.A., Asselbergs,F. and Atadja,P., J. Biol. Chem. 277 (28), 25748-25755 (2002)

TABLE 2: CLASS II HDACs

HDAC	GenBank Accession Number	Reference
4	NP_006028	Transcriptional control. Sinful repression, Wolffe,A.P., Nature 387 (6628), 16-17 (1997)

HDAC	GenBank Accession Number	Reference
5	NP_631944	Prediction of the coding sequences of unidentified human genes. IX. The complete sequences of 100 new cDNA clones from brain which can code for large proteins in vitro, Nagase,T., Ishikawa,K., Miyajima,N., Tanaka,A., Kotani,H., Nomura,N. and Ohara,O., DNA Res. 5 (1), 31-39 (1998)
6	NP_006035	Transcriptional control. Sinful repression, Wolffe,A.P., Nature 387 (6628), 16-17 (1997)
7	NP_057680	Isolation of a novel histone deacetylase reveals that class I and class II deacetylases promote SMRT-mediated repression, Kao,H.Y., Downes,M., Ordentlich,P. and Evans,R.M., Genes Dev. 14 (1), 55-66 (2000)
9	NP_478056	MEF-2 function is modified by a novel co-repressor, MITR, Sparrow,D.B., Miska,E.A., Langley,E., Reynaud-Deonauth,S., Kotecha,S., Towers,N., Spohr,G., Kouzarides,T. and Mohun,T.J., EMBO J. 18 (18), 5085-5098 (1999)
10	NP_114408	Isolation and characterization of mammalian HDAC10, a novel histone deacetylase, Kao,H.Y., Lee,C.H., Komarov,A., Han,C.C. and Evans,R.M., J. Biol. Chem. 277 (1), 187-193 (2002)

TABLE 3: CLASS III HDACs

HDAC	GenBank Accession Number	Reference
Sirtuin 1	NP_036370	Characterization of five human cDNAs with homology to the yeast SIR2 gene: Sir2-like proteins (sirtuins) metabolize NAD and may have protein ADP-ribosyltransferase activity; Frye,R.A.; Biochem. Biophys. Res. Commun. 260 (1), 273-279 (1999)
Sirtuin 2	NP_085096 / NP_036369	A 'double adaptor' method for improved shotgun library construction; Andersson,B., Wentland,M.A., Ricafrente,J.Y., Liu,W. and Gibbs,R.A.; Anal. Biochem. 236 (1), 107-113 (1996)
Sirtuin 3	NP_036371	Characterization of five human cDNAs with homology to the yeast SIR2 gene: Sir2-like proteins (sirtuins) metabolize NAD and may have protein ADP-ribosyltransferase activity; Frye,R.A.; Biochem. Biophys. Res. Commun. 260 (1), 273-279 (1999)

HDAC	GenBank Accession Number	Reference
Sirtuin 4	NP_036372	Characterization of five human cDNAs with homology to the yeast SIR2 gene: Sir2-like proteins (sirtuins) metabolize NAD and may have protein ADP-ribosyltransferase activity; Frye,R.A.; Biochem. Biophys. Res. Commun. 260 (1), 273-279 (1999)
Sirtuin 5	NP_112534 / NP_036373	Characterization of five human cDNAs with homology to the yeast SIR2 gene: Sir2-like proteins (sirtuins) metabolize NAD and may have protein ADP-ribosyltransferase activity; Frye,R.A.; Biochem. Biophys. Res. Commun. 260 (1), 273-279 (1999)
Sirtuin 6	NP_057623	Phylogenetic classification of prokaryotic and eukaryotic Sir2-like proteins; Frye,R.A.; Biochem. Biophys. Res. Commun. 273 (2), 793-798 (2000)
Sirtuin 7	NP_057622	Phylogenetic classification of prokaryotic and eukaryotic Sir2-like proteins; Frye,R.A.; Biochem. Biophys. Res. Commun. 273 (2), 793-798 (2000)

[0106] Of particular note are Class I HDACs. All Class I HDACs appear to be sensitive to inhibition by trichostatin A (TSA). Of particular note HDAC2 and HDAC8, proteins whose crystal structures Applicants determined and used in conjunction with arriving at the present invention.

[0107] HDAC2 is a 488 residue, 55 kDa protein localized to the nucleus of a wide array of tissues, as well as several human tumor cell lines. The wild-type form of full length HDAC2 is described in GenBank Accession Number NM 001527, Furukawa, Y. et al., Cryogenet. Cell Genet., 73 (1-2), 130-133 (1996). Zn^{2+} is likely native to the protein and required for HDAC2 activity.

[0108] HDAC8 is a 377 residue, 42kDa protein localized to the nucleus of a wide array of tissues, as well as several human tumor cell lines. The wild-type form of full length HDAC8 is described in GenBank Accession Number NP 060956; Buggy, J.J. et al., Biochem. J., 350 (Pt 1), 199-205 (2000). Zn^{2+} is likely native to the protein and required for HDAC8 activity.

[0109] It is noted that the compounds of the present invention may also possess inhibitory activity for other HDAC family members and thus may be used to address disease states associated with these other family members.

Crystal Structure of Histone Deacetylase

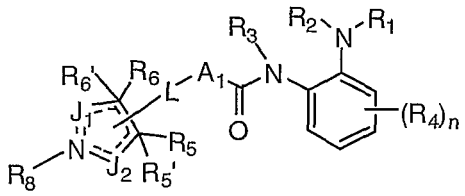
[0110] Syrrx, Inc. (now Takeda San Diego, Inc.) in San Diego, California solved the crystal structure for HDAC2. HDAC2 was found to adopt an open-faced α/β structure consisting of 8 central parallel β-sheets sandwiched between 12 α-helices. The ligand binding cleft lies almost in the plane of the central β-sheet, and is formed primarily by loops emanating from the carboxy-terminal ends of the β-strands comprising the sheet. Residues which form loop regions extending between β-strand 1 and α-helix 1 and between α-helix 4 and α-helix 5, provide key surface interactions with bound ligands. Residues which form loop regions extending between β-strand 3 and α-helix 6 and between β-strand 4 and α-helix 7 and between β-strand 8 and α-helix 10 play important roles in defining the shape of the ligand binding pocket, and are involved in a number of key interactions with the bound ligands.

[0111] HDAC8 was found to have a single domain structure belonging to the open α/β class of folds. The structure consists of a central 8-stranded parallel β-sheet sandwiched between layers of α-helices. The ligand binding clefts lie almost in the plane of the central β-sheet, and are formed primarily by loops emanating from the carboxy-terminal ends of the β-strands comprising the sheet. There are two large structural extensions, which occur beyond the core of the α/β motif, off the second and last β-strands of the central β-sheet. Residues contained in the extension off the second β-strand form a globular "cap" over the core of the protein, play an important role in defining the shape of the ligand binding pockets, and are involved in a number of key interactions with the bound ligands.

[0112] Knowledge of the crystal structures was used to guide the design of the HDAC inhibitors provided herein.

HDAC Inhibitors

[0113] In one embodiment, HDAC inhibitors of the present invention comprise:



wherein:

n is selected from the group consisting of 0, 1, 2, 3 and 4;

A_1 is selected from the group consisting of (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl, and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

L is a linker providing a 0-6 atom separation between the two ring atom to which L is attached;

J_1 is selected from the group consisting of $-CR_7R_7'$- and $-NR_{19}$-;

J_2 is selected from the group consisting of $-CR_{20}R_{20}'$ and $-NR_{10}$-;

R_1 and R_2 are each independently selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_1 and R_2 are taken together to form a substituted or unsubstituted ring;

R_3 is selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl,

aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

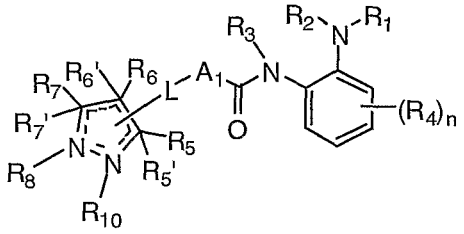
each R_4 is selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

R_5, R_5', R_6, R_6', R_7, and R_7', R_{20} and R_{20}' are each independently selected from the group consisting of hydrogen, halo, nitro, cyano, oxo, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or any two of R_5, R_5', R_6, R_6', R_7, R_7', R_{20} and R_{20}' may be taken together to form a substituted or unsubstituted ring, provided that R_5, R_6, R_7 and R_{20}, are each independently absent when the C to which they are bound is bound to L, and R_5', R_6', R_7' and R_{20}', are each independently absent when the C to which they are bound form part of a double bond; and

R_8, R_{10} and R_{19} are each individually selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl,

carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_8 and any one of R_5, R_5', R_6, R_6', R_7, R_7', R_{20}, R_{20}', R_{10} and R_{19} may be taken together to form a substituted or unsubstituted ring, or R_{10} and any one of R_5, R_5', R_6, R_6', R_7, R_7', R_{20}, R_{20}' and R_{19} may be taken together to form a substituted or unsubstituted ring, or R_{19} and any one of R_5, R_5', R_6, R_6', R_{20} and R_{20}', may be taken together to form a substituted or unsubstituted ring, provided that R_8, R_{10} and R_{19} are each independently absent when the N to which they are bound is bound to L, and R_8, R_{10} and R_{19} are each independently absent when the N to which they are bound form part of a double bond.

[0114] In another embodiment, HDAC inhibitors of the present invention comprise:



wherein:

n is selected from the group consisting of 0, 1, 2, 3 and 4;

A_1 is selected from the group consisting of (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl, and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

L is a linker providing a 0-6 atom separation between the two ring atoms to which L is attached;

R_1 and R_2 are each independently selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl,

hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_1 and R_2 may be taken together to form a substituted or unsubstituted ring;

R_3 is selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

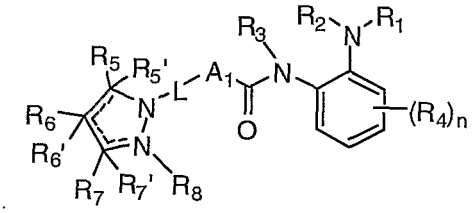
each R_4 is selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

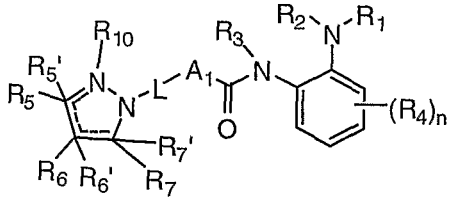
R_5, R_5', R_6, R_6', R_7 and R_7' are each independently selected from the group consisting of hydrogen, halo, nitro, cyano, oxo, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl,

(C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or any two of R_5, R_5', R_6, R_6', R_7 and R_7' may be taken together to form a substituted or unsubstituted ring, provided that R_5, R_6 and R_7 are each independently absent when the C to which they are bound is bound to L, and R_5', R_6' and R_7' are each independently absent when the C to which they are bound form part of a double bond; and

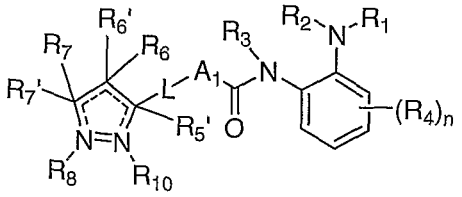
R_8 and R_{10} are each individually selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_8 and any one of R_5, R_5', R_6, R_6', R_7, R_7' and R_{10} may be taken together to form a substituted or unsubstituted ring, or R_{10} and any one of R_5, R_5', R_6, R_6', R_7 and R_7' may be taken together to form a substituted or unsubstituted ring, provided that R_8 and R_{10} are each independently absent when the N to which they are bound is bound to L, and R_8 and R_{10} are absent when the N to which they are bound form part of a double bond.

[0115] In another embodiment, HDAC inhibitors of the present invention comprise a compound selected from the group consisting of:





and



wherein:

n is selected from the group consisting of 0, 1, 2, 3 and 4;

A_1 is selected from the group consisting of (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl, and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

L is a linker providing a 0-6 atom separation between the two ring atoms to which L is attached;

R_1 and R_2 are each independently selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_1 and R_2 may be taken together to form a substituted or unsubstituted ring;

R_3 is selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

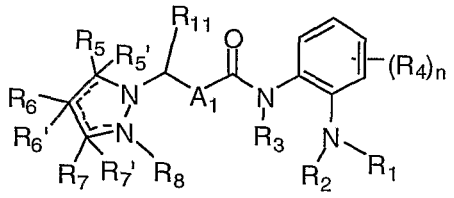
each R_4 is selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

R_5, R_5', R_6, R_6', R_7 and R_7' are each independently selected from the group consisting of hydrogen, halo, nitro, cyano, oxo, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or any two of R_5, R_5', R_6, R_6', R_7 and R_7' may be taken together to form a substituted or unsubstituted ring, provided that R_5', R_6' and R_7' are each independently absent when the C to which they are bound form part of a double bond; and

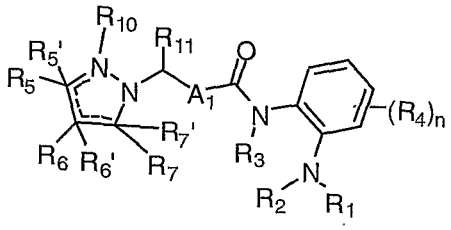
R_8 and R_{10} are each individually selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_8

and any one of R_5, R_5', R_6, R_6', R_7, R_7' and R_{10} may be taken together to form a substituted or unsubstituted ring, or R_{10} and any one of R_5, R_5', R_6, R_6', R_7 and R_7' may be taken together to form a substituted or unsubstituted ring, provided that R_8 and R_{10} are each independently absent when the N to which they are bound form part of a double bond.

[0116] In yet another embodiment, HDAC inhibitors of the present invention comprise a compound selected from the group consisting of:



and



wherein:

n is selected from the group consisting of 0, 1, 2, 3 and 4;

A_1 is selected from the group consisting of (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl, and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

R_1 and R_2 are each independently selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl,

(C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_1 and R_2 may be taken together to form a substituted or unsubstituted ring;

R_3 is selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

each R_4 is selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

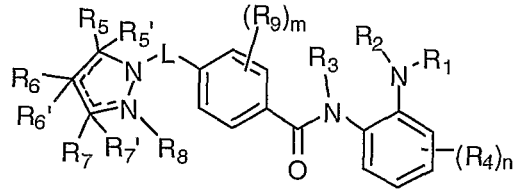
R_5, R_5', R_6, R_6', R_7 and R_7' are each independently selected from the group consisting of hydrogen, halo, nitro, cyano, oxo, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or any two of R_5, R_5', R_6, R_6', R_7 and R_7' may be taken together to form a substituted or unsubstituted ring,

provided that R_5', R_6' and R_7' are each independently absent when the C to which they are bound form part of a double bond;

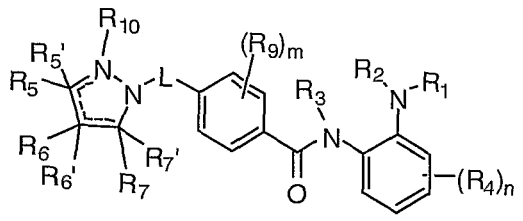
R_8 and R_{10} are each independently selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_8 and any one of R_5, R_5', R_6, R_6', R_7, R_7' and R_{10} may be taken together to form a substituted or unsubstituted ring, or R_{10} and any one of R_5, R_5', R_6, R_6', R_7 and R_7' may be taken together to form a substituted or unsubstituted ring, provided that R_8 and R_{10} are each independently absent when the N to which they are bound form part of a double bond; and

R_{11} is selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted.

[0117] In still another embodiment, HDAC inhibitors of the present invention comprise a compound selected from the group consisting of:



and



wherein:

m is selected from the group consisting of 0, 1, 2, 3 and 4;

n is selected from the group consisting of 0, 1, 2, 3 and 4;

L is a linker providing a 0-6 atom separation between the two ring atoms to which L is attached;

R_1 and R_2 are each independently selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_1 and R_2 may be taken together to form a substituted or unsubstituted ring;

R_3 is selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl,

hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

each R_4 is selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

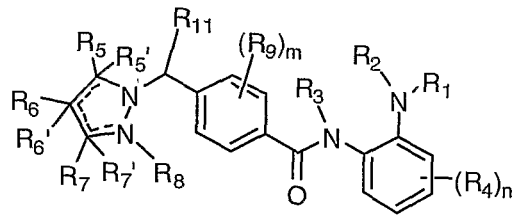
R_5, R_5', R_6, R_6', R_7 and R_7' are each independently selected from the group consisting of hydrogen, halo, nitro, cyano, oxo, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or any two of R_5, R_5', R_6, R_6', R_7 and R_7' may be taken together to form a substituted or unsubstituted ring, provided that R_5', R_6' and R_7' are each independently absent when the C to which they are bound form part of a double bond;

R_8 and R_{10} are independently selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl,

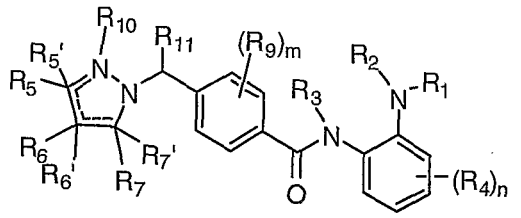
(C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_8 and any one of R_5, R_5', R_6, R_6', R_7, $R_7'$and R_{10} may be taken together to form a substituted or unsubstituted ring, or R_{10} and any one of R_5, R_5', R_6, R_6', R_7 and R_7' may be taken together to form a substituted or unsubstituted ring, provided that R_8 and R_{10} are absent when the N to which they are bound form part of a double bond; and

each R_9 is independently selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or any two R_9 or one R_9 and any one of R_3, R_5, R_5', R_7, R_7', R_8 and R_{10} may be taken together to form a substituted or unsubstituted ring.

[0118] In a further embodiment, HDAC inhibitors of the present invention comprise a compound selected from the group consisting of:



and



wherein:

m is selected from the group consisting of 0, 1, 2, 3 and 4;

n is selected from the group consisting of 0, 1, 2, 3 and 4;

R_1 and R_2 are each independently selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_1 and R_2 may be taken together to form a substituted or unsubstituted ring;

R_3 is selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

each R_4 is selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

R_5, R_5', R_6, R_6', R_7 and R_7' are each independently selected from the group consisting of hydrogen, halo, nitro, cyano, oxo, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or any two of R_5, R_5', R_6, R_6', R_7 and R_7' may be taken together to form a substituted or unsubstituted ring, provided that R_5', R_6' and R_7' are each independently absent when the C to which they are bound form part of a double bond;

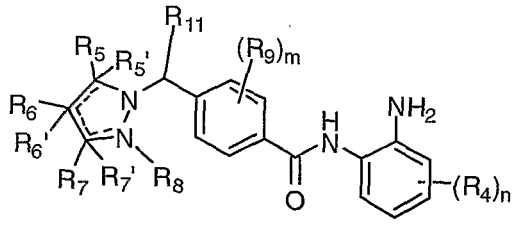
R_8 and R_{10} are each independently selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_8 and any one of R_5, R_5', R_6, R_6', R_7, R_7' and R_{10} may be taken together to form a substituted or unsubstituted ring, or R_{10} and any one of R_5, R_5', R_6, R_6', R_7 and R_7' may be taken together to form a substituted or unsubstituted ring, provided that R_8 or R_{10} are each independently absent when the N to which it is bound form part of a double bond;

each R_9 is independently selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl,

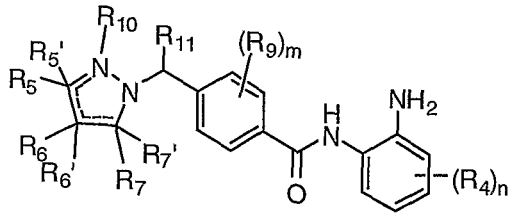
amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or any two R_9 or one R_9 and any one of R_3, R_5, R_5', R_7, R_7', R_8 and R_{10} may be taken together to form a substituted or unsubstituted ring; and

R_{11} is selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_{11} and R_9 may be taken together to form a substituted or unsubstituted ring.

[0119] In still a further embodiment, HDAC inhibitors of the present invention comprise a compound selected from the group consisting of:



and



wherein:

m is selected from the group consisting of 0, 1, 2, 3 and 4;

n is selected from the group consisting of 0, 1, 2, 3 and 4;

each R_4 is selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

R_5, R_5', R_6, R_6', R_7 and R_7' are each independently selected from the group consisting of hydrogen, halo, nitro, cyano, oxo, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or any two of R_5, R_5', R_6, R_6', R_7 and R_7' may be taken together to form a substituted or unsubstituted ring, provided that R_5', R_6' and R_7' are each independently absent when the C to which they are bound form part of a double bond;

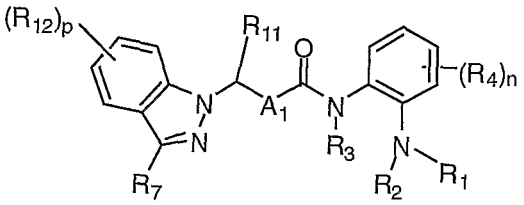
R_8 and R_{10} are each independently selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl,

hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_8 and any one of R_5, R_5', R_6, R_6', R_7, R_7' and R_{10} may be taken together to form a substituted or unsubstituted ring, or R_{10} and any one of R_5, R_5', R_6, R_6', R_7 and R_7' may be taken together to form a substituted or unsubstituted ring, provided that R_8 is absent when the N to which it is bound forms part of a double bond;

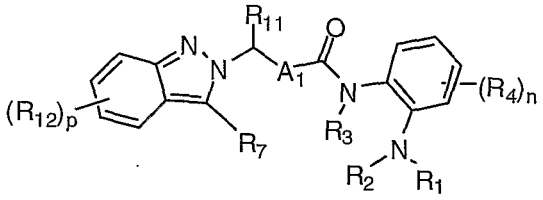
each R_9 is independently selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or any two R_9 or one R_9 and any one of R_5, R_5', R_7, R_7', R_8 and R_{10} may be taken together to form a substituted or unsubstituted ring; and

R_{11} is selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_{11} and R_9 may be taken together to form a substituted or unsubstituted ring.

[0120] In yet a further embodiment, HDAC inhibitors of the present invention comprise a compound selected from the group consisting of:



and



wherein:

n is selected from the group consisting of 0, 1, 2, 3 and 4;

p is selected from the group consisting of 0, 1, 2, 3 and 4;

A_1 is selected from the group consisting of (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl, and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

R_1 and R_2 are each independently selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_1 and R_2 may be taken together to form a substituted or unsubstituted ring;

R_3 is selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl,

aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

each R_4 is selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

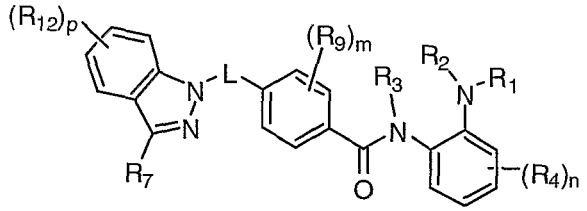
R_7 is selected from the group consisting of hydrogen, halo, nitro, cyano, oxo, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

R_{11} is selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl,

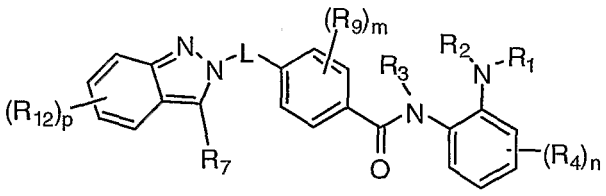
(C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_{11} and R_7 may be taken together to form a substituted or unsubstituted ring; and

each R_{12} is independently selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_{12} and R_7 or R_{11} may be taken together to form a substituted or unsubstituted ring.

[0121] In another embodiment, HDAC inhibitors of the present invention comprise a compound selected from the group consisting of:



and



wherein:

m is selected from the group consisting of 0, 1, 2, 3 and 4;

n is selected from the group consisting of 0, 1, 2, 3 and 4;

p is selected from the group consisting of 0, 1, 2, 3 and 4;

L is a linker providing a 0-6 atom separation between the two rings atoms to which L is attached;

R_1 and R_2 are each independently selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_1 and R_2 may be taken together to form a substituted or unsubstituted ring;

R_3 is selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

each R_4 is selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

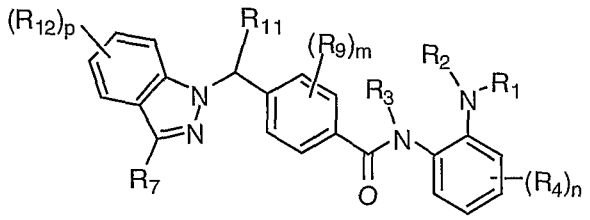
R_7 is selected from the group consisting of hydrogen, halo, nitro, cyano, oxo, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamido, imino, sulfonyl, sulfinyl,

(C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

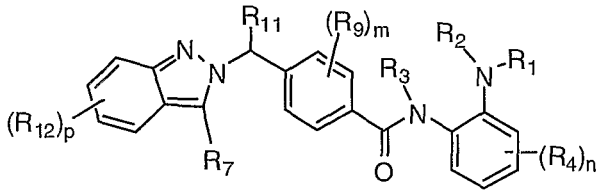
each R_9 is independently selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or any two R_9 or one R_9 and R_3 may be taken together to form a substituted or unsubstituted ring; and

each R_{12} is independently selected from the group consisting of hydrogen, halo, nitro, cyano, oxo, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_{12} and R_7 may be taken together to form a substituted or unsubstituted ring.

[0122] In still another embodiment, HDAC inhibitors of the present invention comprise a compound selected from the group consisting of:



and



wherein:

m is selected from the group consisting of 0, 1, 2, 3 and 4;

n is selected from the group consisting of 0, 1, 2, 3 and 4;

p is selected from the group consisting of 0, 1, 2, 3 and 4

R_1 and R_2 are each independently selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_1 and R_2 may be taken together to form a substituted or unsubstituted ring;

R_3 is selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl,

(C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

each R_4 is selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

R_7 is selected from the group consisting of hydrogen, halo, nitro, cyano, oxo, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

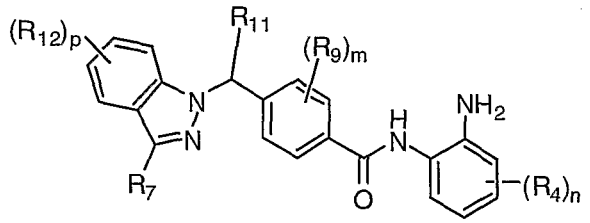
each R_9 is independently selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or

any two R_9 or one R_9 and R_3 may be taken together to form a substituted or unsubstituted ring;

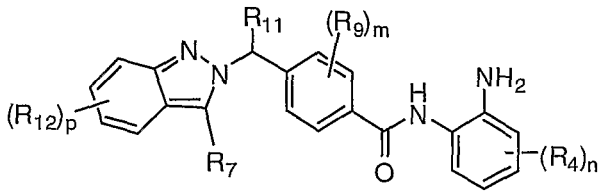
R_{11} is selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_{11} and R_9 may be taken together to form a substituted or unsubstituted ring; and

each R_{12} is independently selected from the group consisting of hydrogen, halo, nitro, cyano, oxo, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_{12} and R_7 or R_{11} may be taken together to form a substituted or unsubstituted ring.

[0123] In yet another embodiment, HDAC inhibitors of the present invention comprise a compound selected from the group consisting of:



and



wherein:

m is selected from the group consisting of 0, 1, 2, 3 and 4;

n is selected from the group consisting of 0, 1, 2, 3 and 4;

p is selected from the group consisting of 0, 1, 2, 3 and 4

each R_4 is selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

R_7 is selected from the group consisting of hydrogen, halo, nitro, cyano, oxo, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

each R_9 is independently selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl,

amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or any two R_9 may be taken together to form a substituted or unsubstituted ring;

R_{11} is selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_{11} and R_7 or R_9 may be taken together to form a substituted or unsubstituted ring; and

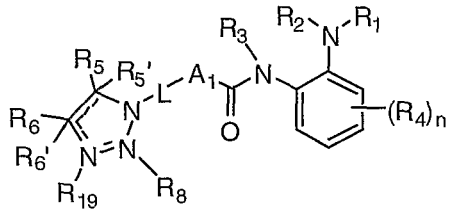
each R_{12} is independently selected from the group consisting of hydrogen, halo, nitro, cyano, oxo, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_{12} and R_7 or R_{11} may be taken together to form a substituted or unsubstituted ring.

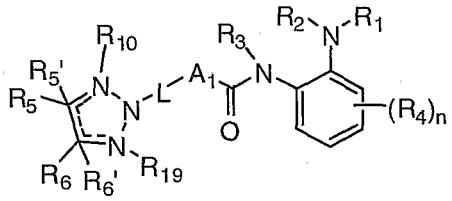
[0124] In one variation of each of the above embodiments, m is 0, R_{11} is hydrogen, and R_{12} is selected from the group consisting of hydroxy, alkoxy, halo, amido, carboxamido, and (C_{1-10})alkylamido, each substituted or unsubstituted.

[0125] In yet another variation, n is 0, p is 2, and R_{12} is selected from the group consisting of hydroxy, alkoxy, and halo.

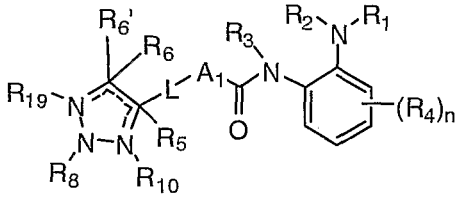
[0126] In still another variation, R_7 is hydrogen, and R_{12} is alkoxy.

[0127] In still another embodiment, HDAC inhibitors of the present invention comprise a compound selected from the group consisting of:





and



wherein:

n is selected from the group consisting of 0, 1, 2, 3 and 4;

A_1 is selected from the group consisting of (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl, and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

L is a linker providing a 0-6 atom separation between the two ring atoms to which L is attached;

R_1 and R_2 are each independently selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl,

(C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_1 and R_2 may be taken together to form a substituted or unsubstituted ring;

R_3 is selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

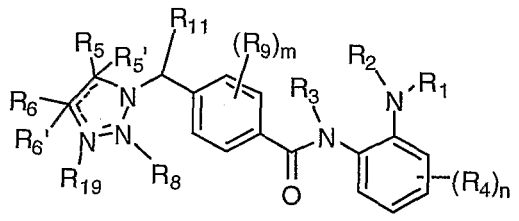
R_4 is selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

R_5, R_5', R_6 and R_6' are each independently selected from the group consisting of hydrogen, halo, nitro, cyano, oxo, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and

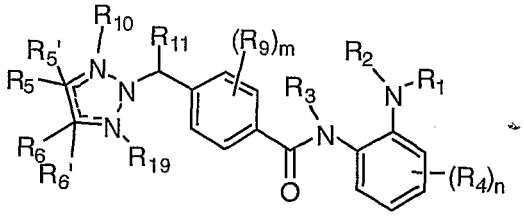
hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or any two of R_5, R_5', R_6, and R_6' may be taken together to form a substituted or unsubstituted ring, provided that R_5' andR_6' are each independently absent when the C to which they are bound form part of a double bond; and

R_8, R_{10} and R_{19}, are each individually selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_8 and any one of R_5, R_5', R_6, R_6', R_{10} and R_{19} may be taken together to form a substituted or unsubstituted ring, or R_{10} and any one of R_5, R_5', R_6, R_6' and R_{19} may be taken together to form a substituted or unsubstituted ring, or R_{19} and any one of R_5, R_5', R_6 and R_6' may be taken together to form a substituted or unsubstituted ring, provided that R_8, R_{10} and R_{19} are each independently absent when the N to which they are bound forms part of a double bond.

[0128] In still another embodiment, HDAC inhibitors of the present invention comprise a compound selected from the group consisting of:



and



wherein:

m is selected from the group consisting of 0, 1, 2, 3 and 4;

n is selected from the group consisting of 0, 1, 2, 3 and 4;

R_1 and R_2 are each independently selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_1 and R_2 may be taken together to form a substituted or unsubstituted ring;

R_3 is selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

R_4 is selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

R_5, R_5', R_6 and R_6' are each independently selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or any two of R_5, R_5', R_6 and R_6' may be taken together to form a substituted or unsubstituted ring, provided that R_5' and R_6' are each independently absent when the C to which they are bound form part of a double bond;

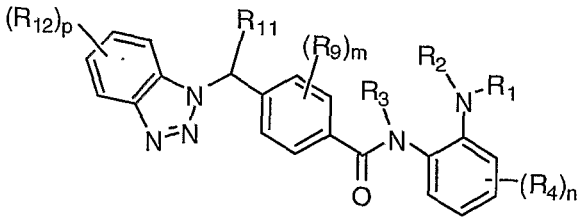
R_8, R_{10} and R_{19} are each independently selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_8 and any one of R_5, R_5', R_6, R_6', R_{10} and R_{19} may be taken together to form a substituted or unsubstituted ring, or R_{10} and any one of R_5, R_5', R_6, R_6' and R_{19} may be taken together to form a substituted or unsubstituted ring, or R_{19} and any one of R_5, R_5', R_6 and R_6' may be taken together to form a substituted or unsubstituted ring, provided that R_8, R_{10} and R_{19} are each independently absent when the N to which they are bound forms part of a double bond.

each R_9 is independently selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl,

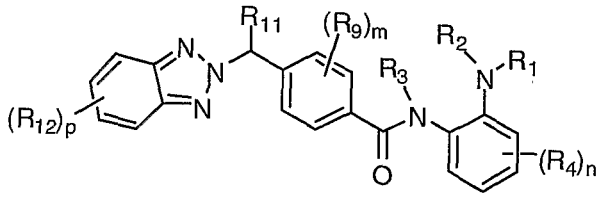
carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or any two R_9 or one R_9 and any one of R_3, R_5, R_5', R_8, R_{10} and R_{19} may be taken together to form a substituted or unsubstituted ring; and

R_{11} is selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_{11} and R_9 may be taken together to form a substituted or unsubstituted ring.

[0129] In still another embodiment, HDAC inhibitors of the present invention comprise a compound selected from the group consisting of:



and



wherein:

m is selected from the group consisting of 0, 1, 2, 3 and 4;

n is selected from the group consisting of 0, 1, 2, 3 and 4;

p is selected from the group consisting of 0, 1, 2, 3 and 4;

R_1 and R_2 are each independently selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_1 and R_2 may be taken together to form a substituted or unsubstituted ring;

R_3 is selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

R_4 is selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

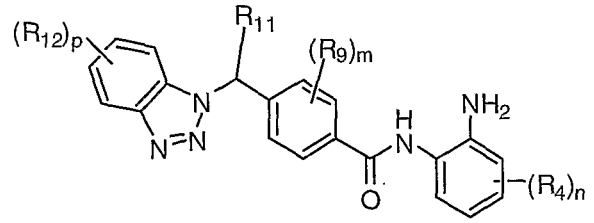
each R_9 is independently selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or any two R_9 or one R_9 and R_3 may be taken together to form a substituted or unsubstituted ring;

R_{11} is selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_{11} and R_9 may be taken together to form a substituted or unsubstituted ring; and

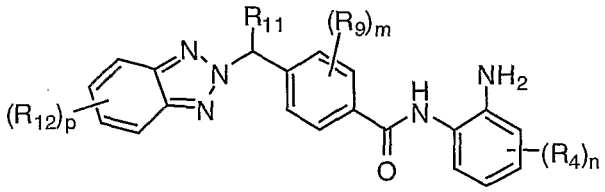
each R_{12} is independently selected from the group consisting of hydrogen, halo, nitro, cyano, oxo, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and

hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_{12} and R_{11} may be taken together to form a substituted or unsubstituted.

[0130] In still another embodiment, HDAC inhibitors of the present invention comprise a compound selected from the group consisting of:



and



wherein:

m is selected from the group consisting of 0, 1, 2, 3 and 4;

n is selected from the group consisting of 0, 1, 2, 3 and 4;

p is selected from the group consisting of 0, 1, 2, 3 and 4;

R_4 is selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

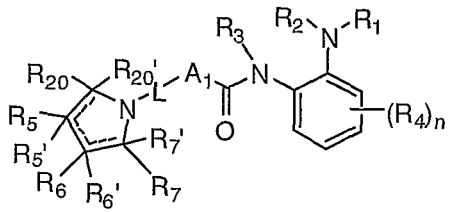
each R_9 is independently selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl,

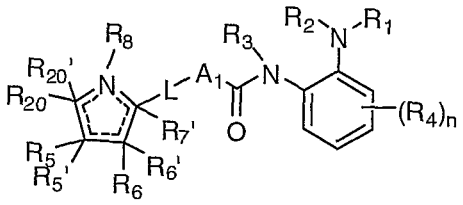
amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or any two R_9 may be taken together to form a substituted or unsubstituted ring;

R_{11} is selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_{11} and R_9 may be taken together to form a substituted or unsubstituted ring; and

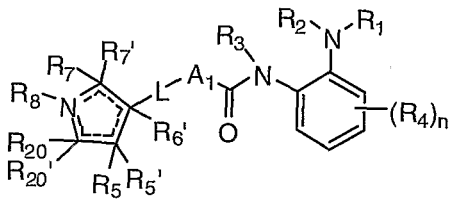
each R_{12} is independently selected from the group consisting of hydrogen, halo, nitro, cyano, oxo, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamide, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_{12} and R_{11} may be taken together to form a substituted or unsubstituted ring.

[0131] In still another embodiment, HDAC inhibitors of the present invention comprise a compound selected from the group consisting of:





and



wherein:

n is selected from the group consisting of 0, 1, 2, 3 and 4;

A_1 is selected from the group consisting of (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl, and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

L is a linker providing a 0-6 atom separation between the two ring atoms to which L is attached;

R_1 and R_2 are each independently selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_1 and R_2 may be taken together to form a substituted or unsubstituted ring;

R_3 is selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

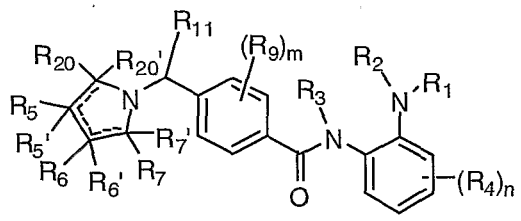
R_4 is selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

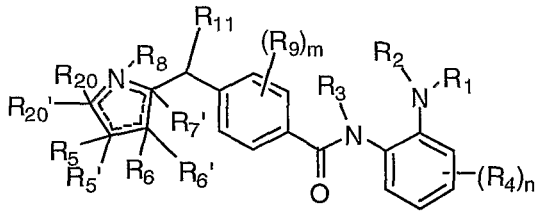
R_5, R_5', R_6, R_6', R_7, R_7', R_{20} and R_{20}' are each independently selected from the group consisting of hydrogen, halo, nitro, cyano, oxo, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or any two of R_5, R_5', R_6, R_6', R_7, R_7', R_{20} and R_{20}' may be taken together to form a substituted or unsubstituted ring, provided that R_5', R_6', R_7' and R_{20}', are each

independently absent when the C to which they are bound form part of a double bond; and

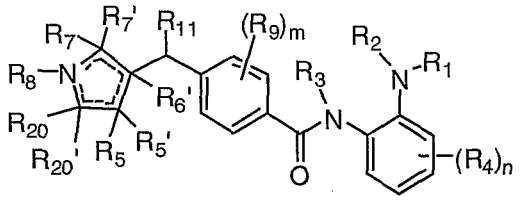
R_8 is selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_8 and any one of R_5, R_5', R_6, R_6', R_7, R_7', R_{20} and R_{20}' may be taken together to form a substituted or unsubstituted ring, provided that R_8 is absent when the N to which it is bound forms part of a double bond.

[0132] In still another embodiment, HDAC inhibitors of the present invention comprise a compound selected from the group consisting of:





and



wherein:

m is selected from the group consisting of 0, 1, 2, 3 and 4;

n is selected from the group consisting of 0, 1, 2, 3 and 4;

R_1 and R_2 are each independently selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_1 and R_2 may be taken together to form a substituted or unsubstituted ring;

R_3 is selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

R_4 is selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

R_5, R_5', R_6, R_6', R_7, R_7', R_{20} and R_{20}' are each independently selected from the group consisting of hydrogen, halo, nitro, cyano, oxo, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or any two of R_5, R_5', R_6, R_6', R_7, R_7', R_{20} and R_{20}' may be taken together to form a substituted or unsubstituted ring, provided that R_5', R_6', R_7' and R_{20}', are each independently absent when the C to which they are bound form part of a double bond; and

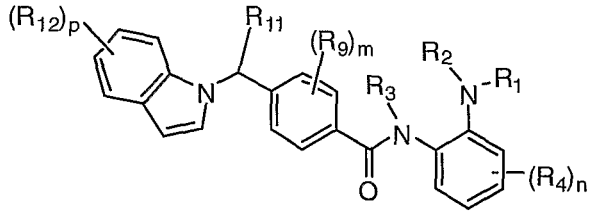
R_8 is selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_8 and any one of R_5, R_5', R_6, R_6', R_7, R_7', R_{20} and R_{20}' may be taken together to form a substituted or unsubstituted ring, provided that R_8 is absent when the N to which it is bound forms part of a double bond;

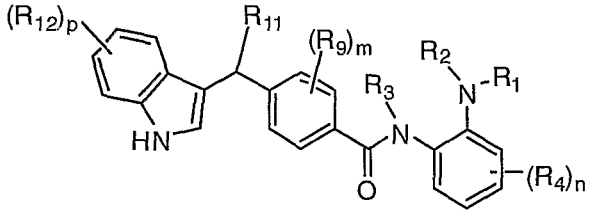
each R_9 is independently selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl,

hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or any two R_9 or one R_9 and any one of R_3, R_5, R_5', R_6, R_6', R_7, R_7', R_{20}, R_{20}' and R_8 may be taken together to form a substituted or unsubstituted ring; and

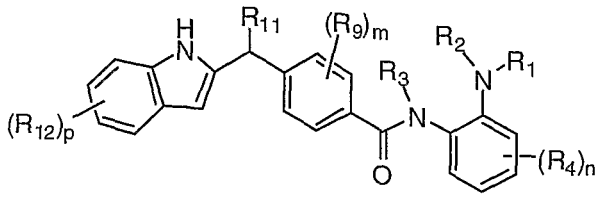
R_{11} is selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_{11} and R_9 may be taken together to form a substituted or unsubstituted ring.

[0133] In still another embodiment, HDAC inhibitors of the present invention comprise a compound selected from the group consisting of:





and



wherein:

m is selected from the group consisting of 0, 1, 2, 3 and 4;

n is selected from the group consisting of 0, 1, 2, 3 and 4;

p is selected from the group consisting of 0, 1, 2, 3 and 4;

R_1 and R_2 are each independently selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_1 and R_2 may be taken together to form a substituted or unsubstituted ring;

R_3 is selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

R_4 is selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl,

amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

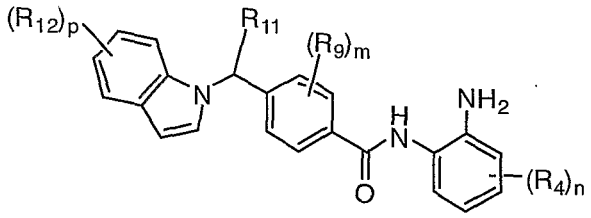
each R_9 is independently selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or any two R_9 or one R_9 and R_3 may be taken together to form a substituted or unsubstituted ring;

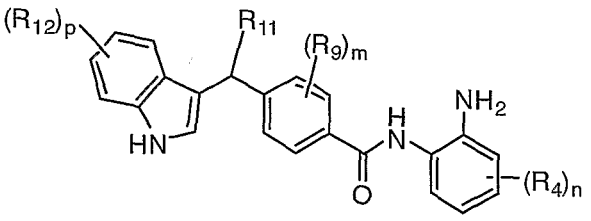
R_{11} is selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_{11} and R_9 may be taken together to form a substituted or unsubstituted ring; and

each R_{12} is independently selected from the group consisting of hydrogen, halo, nitro, cyano, oxo, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl,

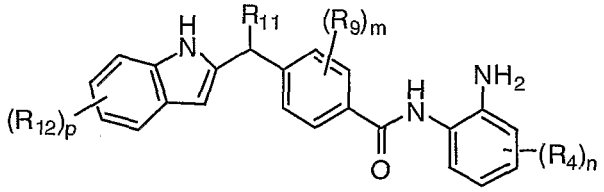
(C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_{12} and R_{11} may be taken together to form a substituted or unsubstituted ring.

[0134] In still another embodiment, HDAC inhibitors of the present invention comprise a compound selected from the group consisting of:





and



wherein:

m is selected from the group consisting of 0, 1, 2, 3 and 4;

n is selected from the group consisting of 0, 1, 2, 3 and 4;

p is selected from the group consisting of 0, 1, 2, 3 and 4;

R_4 is selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl,

carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

each R_9 is independently selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or any two R_9 may be taken together to form a substituted or unsubstituted ring;

R_{11} is selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_{11} and R_9 may be taken together to form a substituted or unsubstituted ring; and

each R_{12} is independently selected from the group consisting of hydrogen, halo, nitro, cyano, oxo, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl,

(C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_{12} and R_{11} may be taken together to form a substituted or unsubstituted ring.

[0135] In one variation of each of the above embodiments, R_1 and R_2 are each independently selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl and imino(C_{1-3})alkyl, each substituted or unsubstituted.

[0136] In another variation of each of the above embodiments and variations, R_1 is hydrogen or a substituent convertible in vivo to hydrogen. In still another variation of each of the above embodiments and variations, R_2 is hydrogen or a substituent convertible in vivo to hydrogen. In yet another variation of each of the above embodiments and variations, R_3 is hydrogen or a substituent convertible in vivo to hydrogen.

[0137] In a further variation of each of the above embodiments and variations, R_4 is selected from the group consisting of hydrogen, halo, aryl and heteroaryl, each substituted or unsubstituted. In yet a further variation of each of the above embodiments and variations, R_4 is selected from the group consisting of phenyl, oxazolyl, thiazolyl, morpholinyl and thiomorpholinyl, each substituted or unsubstituted.

[0138] In still a further variation of each of the above embodiments and variations, R_5, R_6, R_7 and R_{20} are independently selected from the group consisting of carbonyl, oxo, amino, (C_{1-10})alkylamino, amido, carboxamido, cyano, alkoxy, (C_{1-10})alkyl, aryl, and heteroaryl, each substituted or unsubstituted.

[0139] In another variation of each of the above embodiments and variations, R_5 and R_6 are taken together to form a substituted or unsubstituted ring. In one variation, the ring is an aryl or heteroaryl, each substituted or unsubstituted. In another variation, the ring is substituted with a substituent selected from the group consisting of halo, alkoxy, amino(C_{1-10})alkoxy, amino(C_{1-10})alkylamino, amino(C_{1-10})alkylsulfanyl, halo(C_{1-10})alkyl,

aryl and heteroaryl, each substituted or unsubstituted. In yet another variation, the ring is substituted with a substituent selected from the group consisting of thiopheneyl, pyridinyl, furanyl and pyrimidinyl, each substituted or unsubstituted.

[0140] In still another variation, the ring is substituted with -O-CH_2CH_2-$NR_{13}R_{14}$. In a further variation, the ring is substituted with -NH-CH_2CH_2-$NR_{13}R_{14}$. In yet a further variation, the ring is substituted with -S-CH_2CH_2-$NR_{13}R_{14}$. In each of these variations, R_{13} and R_{14} are each independently selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero (C_{8-12})bicycloaryl (C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_{13} and R_{14} may be taken together to form a substituted or unsubstituted ring. In other embodiments, R_{13} and R_{14} are each independently selected from the group consisting of hydrogen, (C_{1-10})alkyl, (C_{3-12})cycloalkyl, and heteroaryl, each substituted or unsubstituted. In still other embodiments, R_{13} and R_{14} are taken together to form a ring selected from the group consisting of morpholinyl, pyrrolidinyl, piperazinyl and thiomorpholinyl, each substituted or unsubstituted.

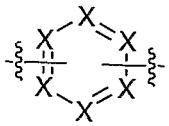
[0141] In another variation of each of the above embodiments and variations, R_8, R_{10} and R_{19} are selected from the group consisting of hydrogen and substituted or unsubstituted (C_{1-10})alkyl.

[0142] In still another variation of each of the above embodiments and variations, L is a linker providing a 1-5 atom separation between the two ring atoms to which L is attached. In yet another variation of each of the above embodiments and variations, L is a linker providing a 1-3 atom separation between the two ring atoms to which L is attached. In a further variation of each of the above embodiments and variations, L is a substituted or unsubstituted alkylene. In yet a further variation of each of the above embodiments and variations, wherein L is -CH_2-. In another variation of each of the above embodiments and

variations, L is selected from the group consisting of $-NR_{15}-$; $-NR_{15}-CH_2-$; $-O-CH_2-$; $-S-CH_2-$; $-CH_2-NR_{15}-$; $-CH_2-O-$ and $-CH_2-S-$, wherein R_{15} is selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted.

[0143] In still another variation of each of the above embodiments and variations, A_1 is selected from the group consisting of aryl and heteroaryl, each substituted or unsubstituted. In yet another variation of each of the above embodiments and variations, A_1 is a substituted or unsubstituted phenylene. In a further variation of each of the above embodiments and variations, A_1 is a substituted or unsubstituted 1,4-phenylene. In still a further variation of each of the above embodiments and variations, A_1 is selected from the group consisting of a thiophenediyl, furandiyl, pyrrolediyl, thiazolediyl, oxazolediyl, imidazolediyl and pyridinediyl, each substituted or unsubstituted.

[0144] In another variation of each of the above embodiments and variations, A_1 comprises:



wherein:

each X is independently selected from the group consisting of CR_{16} and N; and

each R_{16} is independently selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl,

heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_{16} is absent when the C to which it is bound is further bound to L or the carbonyl adjacent to A_1.

[0145] Particular examples of compounds according to the present invention include, but are not limited to:

4-((1H-indazol-1-yl)methyl)-N-(2-aminophenyl)benzamide;

4-((2H-indazol-2-yl)methyl)-N-(2-aminophenyl)benzamide;

4-((5-acetamido-1H-indazol-1-yl)methyl)-N-(2-aminophenyl)benzamide;

4-((5-acetamido-2H-indazol-2-yl)methyl)-N-(2-aminophenyl)benzamide;

N-(2-aminophenyl)-4-((5-nitro-1H-indazol-1-yl)methyl)benzamide;

4-((5-benzamido-1H-indazol-1-yl)methyl)-N-(2-aminophenyl)benzamide;

4-((5-amino-1H-indazol-1-yl)methyl)-N-(2-aminophenyl)benzamide;

N-(2-aminophenyl)-4-((5-nitro-2H-indazol-2-yl)methyl)benzamide;

4-((5-amino-2H-indazol-2-yl)methyl)-N-(2-aminophenyl)benzamide;

4-((5-benzamido-2H-indazol-1-yl)methyl)-N-(2-aminophenyl)benzamide;

2-Methoxyethyl 2-(4-((2-aminophenyl)carbamoyl)benzyl)-2H-indazol-5-ylcarbamate;

Methyl 2-(4-((2-aminophenyl)carbamoyl)benzyl)-2H-indazol-5-ylcarbamate;

2-Methoxyethyl 1-(4-((2-aminophenyl)carbamoyl)benzyl)-1H-indazol-5-ylcarbamate;

Methyl 1-(4-((2-aminophenyl)carbamoyl)benzyl)-1H-indazol-5-ylcarbamate;

Benzyl 1-(4-((2-aminophenyl)carbamoyl)benzyl)-1H-indazol-5-ylcarbamate;

Benzyl 2-(4-((2-aminophenyl)carbamoyl)benzyl)-2H-indazol-5-ylcarbamate;

N-(4-Amino-biphenyl-3-yl)-4-(5-nitro-indazol-2-ylmethyl)-benzamide;

N-(2-(4-((2-Aminophenyl)carbamoyl)benzyl)-2H-indazol-5-yl)morpholine-4-carboxamide;

5-((2H-Indazol-2-yl)methyl)-N-(2-aminophenyl)thiophene-2-carboxamide;

N-(2-Aminophenyl)-5-((5-nitro-2H-indazol-2-yl)methyl)thiophene-2-carboxamide;

N-(1-(4-((2-Aminophenyl)carbamoyl)benzyl)-1H-indazol-5-yl)morpholine-4-carboxamide;

2-Morpholinoethyl 1-(4-((2-aminophenyl)carbamoyl)benzyl)-1H-indazol-5-ylcarbamate;

Pyridin-3-ylmethyl 1-(4-((2-aminophenyl)carbamoyl)benzyl)-1H-indazol-5-ylcarbamate;

5-((1H-Indazol-1-yl)methyl)-N-(2-aminophenyl)thiophene-2-carboxamide;

4-((2H-Pyrazolo[3,4-b]pyridin-2-yl)methyl)-N-(2-aminophenyl)benzamide;

N-(4-Amino-biphenyl-3-yl)-4-pyrazolo[3,4-b]pyridin-2-ylmethyl-benzamide;

N-(4-Amino-biphenyl-3-yl)-4-indazol-2-ylmethyl-benzamide;

N-(2-Aminophenyl)-4-((3-methyl-1H-indazol-1-yl)methyl)benzamide;

N-(2-Aminophenyl)-4-((3-methyl-2H-indazol-2-yl)methyl)benzamide;

4-((1H-indazol-3-ylamino)methyl)-N-(2-aminophenyl)benzamide;

4-((1H-pyrazol-1-yl)methyl)-N-(2-aminophenyl)benzamide;

N-(2-(4-((2-Aminophenyl)carbamoyl)benzyl)-2H-indazol-5-yl)morpholine-4-carboxamide;

Methyl 3-(4-((2H-indazol-2-yl)methyl)benzamido)-4-aminobenzoate;

N-(2-aminophenyl)-4-((4-methyl-1H-pyrazol-1-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((6-fluoro-2H-indazol-2-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((6-fluoro-1H-indazol-1-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((5-fluoro-1H-indazol-1-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((5-fluoro-2H-indazol-2-yl)methyl)benzamide;

4-(1-(1H-indazol-1-yl)propan-2-yl)-N-(2-aminophenyl)benzamide;

4-(2-(1H-indazol-1-yl)ethyl)-N-(2-aminophenyl)benzamide;

4-(2-(2H-indazol-2-yl)ethyl)-N-(2-aminophenyl)benzamide;

N-(2-aminophenyl)-4-((4-chloro-1H-indazol-1-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((4-chloro-2H-indazol-2-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((4,6-difluoro-1H-indazol-1-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((4,6-difluoro-2H-indazol-2-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((7-fluoro-1H-indazol-1-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((7-fluoro-2H-indazol-2-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((4-fluoro-1H-indazol-1-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((4-fluoro-2H-indazol-2-yl)methyl)benzamide;

(R)-4-(1-(2H-indazol-2-yl)ethyl)-N-(2-aminophenyl)benzamide;

(S)-4-(1-(2H-indazol-2-yl)ethyl)-N-(2-aminophenyl)benzamide;

N-(2-aminophenyl)-4-((7-fluoro-3-methyl-1H-indazol-1-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((7-fluoro-3-methyl-2H-indazol-2-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((4-fluoro-3-methyl-1H-indazol-1-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((4-fluoro-3-methyl-2H-indazol-2-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((5,6-difluoro-3-methyl-1H-indazol-1-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((5,6-difluoro-3-methyl-2H-indazol-2-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((6-methoxy-1H-indazol-1-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((6-methoxy-2H-indazol-2-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((3-chloro-1H-indazol-1-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((3-chloro-2H-indazol-2-yl)methyl)benzamide;

4-((3-amino-5-(trifluoromethyl)-2H-indazol-2-yl)methyl)-N-(2-aminophenyl)benzamide;

4-((3-amino-5-(trifluoromethyl)-1H-indazol-1-yl)methyl)-N-(2-aminophenyl)benzamide;

N-(2-aminophenyl)-4-((3-oxo-2,3-dihydro-1H-indazol-1-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((3-oxo-1H-indazol-2(3H)-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((6-methoxy-3-methyl-1H-indazol-1-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((6-methoxy-3-methyl-2H-indazol-2-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((6-fluoro-3-methyl-1H-indazol-1-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((6-fluoro-3-methyl-2H-indazol-2-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((5-fluoro-3-methyl-1H-indazol-1-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((5-fluoro-3-methyl-2H-indazol-2-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((3-ethyl-1H-indazol-1-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((3-ethyl-2H-indazol-2-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((6-hydroxy-3-methyl-1H-indazol-1-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((6-hydroxy-3-methyl-2H-indazol-2-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((3-phenyl-1H-indazol-1-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((3-phenyl-2H-indazol-2-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((5-methoxy-1H-indazol-1-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((5-methoxy-2H-indazol-2-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((3,5-dimethyl-1H-indazol-1-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((3,5-dimethyl-2H-indazol-2-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((7-methoxy-2H-indazol-2-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((4-methoxy-2H-indazol-2-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((7-methoxy-1H-indazol-1-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((4-methoxy-1H-indazol-1-yl)methyl)benzamide;

4-((6-acetamido-3-methyl-2H-indazol-2-yl)methyl)-N-(2-aminophenyl)benzamide;

4-((6-acetamido-3-methyl-1H-indazol-1-yl)methyl)-N-(2-aminophenyl)benzamide;

4-((3-amino-2H-indazol-2-yl)methyl)-N-(2-aminophenyl)benzamide;

4-((6-acetamido-1H-indazol-1-yl)methyl)-N-(2-aminophenyl)benzamide;

4-((6-acetamido-2H-indazol-2-yl)methyl)-N-(2-aminophenyl)benzamide;

N-(2-aminophenyl)-4-((3-methyl-7-(trifluoromethyl)-2H-indazol-2-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((3-methyl-6-(trifluoromethyl)-2H-indazol-2-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((3-methyl-6-(trifluoromethyl)-1H-indazol-1-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((3-methyl-5-(trifluoromethyl)-1H-indazol-1-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((3-methyl-5-(trifluoromethyl)-2H-indazol-2-yl)methyl)benzamide;

4-((3-amino-1*H*-indazol-1-yl)methyl)-*N*-(2-aminophenyl)benzamide;

N-(2-aminophenyl)-4-((5-hydroxy-6-methoxy-2H-indazol-2-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((5,6-dimethoxy-2H-indazol-2-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((5,6-dimethoxy-1H-indazol-1-yl)methyl)benzamide;

4-((1*H*-benzo[*d*][1,2,3]triazol-1-yl)methyl)-*N*-(2-aminophenyl)benzamide;

4-((2*H*-benzo[*d*][1,2,3]triazol-2-yl)methyl)-*N*-(2-aminophenyl)benzamide;

4-((5-acetamido-1*H*-indazol-1-yl)methyl)-*N*-(2-aminophenyl)benzamide;

1-(4-(2-aminophenylcarbamoyl)benzyl)-N-(2-(piperazin-1-yl)ethyl)-1H-pyrazole-4-carboxamide;

4-((2*H*-indazol-2-yl)methyl)-*N*-(4-aminopyrimidin-5-yl)benzamide;

4-((5-acetamido-3-amino-1*H*-indazol-1-yl)methyl)-*N*-(2-aminophenyl)benzamide;

4-((5-acetamido-3-methyl-2*H*-indazol-2-yl)methyl)-*N*-(2-aminophenyl)benzamide;

4-((5-acetamido-3-methyl-1*H*-indazol-1-yl)methyl)-*N*-(2-aminophenyl)benzamide;

4-(1-(1*H*-indazol-1-yl)ethyl)-*N*-(2-aminophenyl)benzamide;

4-(1-(2*H*-indazol-2-yl)ethyl)-*N*-(2-aminophenyl)benzamide;

5-((5-acetamido-1*H*-indazol-1-yl)methyl)-*N*-(2-aminophenyl)thiophene-2-carboxamide;

4-((2*H*-indazol-2-yl)methyl)-*N*-(2-amino-5-(thiophen-2-yl)phenyl)benzamide;

N-(2-amino-5-(thiophen-2-yl)phenyl)-4-((4,6-difluoro-2*H*-indazol-2-yl)methyl)benzamide;

N-(2-amino-5-(thiophen-2-yl)phenyl)-4-((4,6-difluoro-1*H*-indazol-1-yl)methyl)benzamide;

N-(2-amino-5-(thiophen-2-yl)phenyl)-4-((6-methoxy-3-methyl-1*H*-indazol-1-yl)methyl)benzamide;

N-(2-amino-5-(thiophen-2-yl)phenyl)-4-((4-methyl-1*H*-pyrazol-1-yl)methyl)benzamide;

N-(2-amino-5-(thiophen-2-yl)phenyl)-4-((6-methoxy-3-methyl-2*H*-indazol-2-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((4-(trifluoromethyl)-1*H*-indazol-1-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((4-(trifluoromethyl)-2*H*-indazol-2-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((5-(trifluoromethyl)-1*H*-indazol-1-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((5-(trifluoromethyl)-2*H*-indazol-2-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((6-(trifluoromethyl)-2*H*-indazol-2-yl)methyl)benzamide;

1-(4-(2-aminophenylcarbamoyl)benzyl)-1H-pyrazole-4-carboxylic acid;

N-(2-aminophenyl)-4-((3-methyl-1H-pyrazol-1-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((3,5-dimethyl-1H-pyrazol-1-yl)methyl)benzamide;

Ethyl 1-(4-(2-aminophenylcarbamoyl)benzyl)-1H-pyrazole-4-carboxylate;

1-(4-(2-aminophenylcarbamoyl)benzyl)-N-(pyridin-2-ylmethyl)-1H-pyrazole-4-carboxamide;

1-(4-(2-aminophenylcarbamoyl)benzyl)-N-phenyl-1H-pyrazole-4-carboxamide;

1-(4-(2-aminophenylcarbamoyl)benzyl)-N-benzyl-1H-pyrazole-4-carboxamide;

N-(2-aminophenyl)-4-((4,5,6,7-tetrahydro-2H-indazol-2-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((4,5,6,7-tetrahydro-1H-indazol-1-yl)methyl)benzamide;

4-((1H-pyrazol-3-ylamino)methyl)-N-(2-aminophenyl)benzamide;

4-((5-amino-1H-pyrazol-1-yl)methyl)-N-(2-aminophenyl)benzamide;

4-((3-amino-1H-pyrazol-1-yl)methyl)-N-(2-aminophenyl)benzamide;

1-(4-(2-aminophenylcarbamoyl)benzyl)-N-methyl-1H-pyrazole-4-carboxamide;

1-(4-(2-aminophenylcarbamoyl)benzyl)-N-ethyl-1H-pyrazole-4-carboxamide;

1-(4-(2-aminophenylcarbamoyl)benzyl)-N,N-dimethyl-1H-pyrazole-4-carboxamide;

1-(4-(2-aminophenylcarbamoyl)benzyl)-N-isopropyl-1H-pyrazole-4-carboxamide;

1-(4-(2-aminophenylcarbamoyl)benzyl)-N-cyclopropyl-1H-pyrazole-4-carboxamide;

1-(4-(2-aminophenylcarbamoyl)benzyl)-N-(cyclopropylmethyl)-1H-pyrazole-4-carboxamide;

1-(4-(2-aminophenylcarbamoyl)benzyl)-N-(2-(dimethylamino)ethyl)-1H-pyrazole-4-carboxamide;

1-(4-(2-aminophenylcarbamoyl)benzyl)-1H-pyrazole-4-carboxamide;

1-(4-(2-aminophenylcarbamoyl)benzyl)-N-(2-hydroxyethyl)-1H-pyrazole-4-carboxamide;

1-(4-(2-aminophenylcarbamoyl)benzyl)-N-(3-(dimethylamino)propyl)-1H-pyrazole-4-carboxamide;

1-(4-(2-aminophenylcarbamoyl)benzyl)-N-(pyridin-3-ylmethyl)-1H-pyrazole-4-carboxamide;

1-(4-(2-aminophenylcarbamoyl)benzyl)-N-(pyridin-4-ylmethyl)-1H-pyrazole-4-carboxamide;

1-(4-(2-aminophenylcarbamoyl)benzyl)-N-(2-morpholinoethyl)-1H-pyrazole-4-carboxamide;

N-(2-aminophenyl)-4-((5-methyl-1H-pyrazol-1-yl)methyl)benzamide;

1-(4-(2-aminophenylcarbamoyl)benzyl)-N-propyl-1H-pyrazole-4-carboxamide;

1-(4-(2-aminophenylcarbamoyl)benzyl)-N-isobutyl-1H-pyrazole-4-carboxamide;

1-(4-(2-aminophenylcarbamoyl)benzyl)-N-(2-methoxyethyl)-1H-pyrazole-4-carboxamide;

1-(4-(2-aminophenylcarbamoyl)benzyl)-N-(3-methoxypropyl)-1H-pyrazole-4-carboxamide;

1-(4-(2-aminophenylcarbamoyl)benzyl)-N-(3-hydroxypropyl)-1H-pyrazole-4-carboxamide;

1-(4-(2-aminophenylcarbamoyl)benzyl)-N-(3-morpholinopropyl)-1H-pyrazole-4-carboxamide;

1-(4-(2-aminophenylcarbamoyl)benzyl)-N-(2-(piperidin-1-yl)ethyl)-1H-pyrazole-4-carboxamide;

1-(4-(2-aminophenylcarbamoyl)benzyl)-N-(3-(4-methylpiperazin-1-yl)propyl)-1H-pyrazole-4-carboxamide;

4-((1*H*-Pyrrolo[2,3-b]pyridin-1-yl)methyl)-N-(2-aminophenyl)benzamide;

4-((1*H*-Indol-3-yl)methyl)-N-(2-aminophenyl)benzamide;

4-((1H-indazol-1-yl)methyl)-N-(2-amino-5-fluorophenyl)benzamide;

4-((2H-indazol-2-yl)methyl)-N-(2-amino-5-fluorophenyl)benzamide;

4-((1H-indazol-1-yl)methyl)-N-(2-amino-5-fluorophenyl)-3-methylbenzamide;

4-((2H-indazol-2-yl)methyl)-N-(2-amino-5-fluorophenyl)-3-methylbenzamide;

N-(2-aminophenyl)-3-methyl-4-((3-methyl-1H-indazol-1-yl)methyl)benzamide;

N-(2-aminophenyl)-3-methyl-4-((3-methyl-2H-indazol-2-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((3-cyano-1H-indazol-1-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((3-cyano-2H-indazol-2-yl)methyl)benzamide;

1-(4-((2-aminophenyl)carbamoyl)benzyl)-1H-indazole-3-carboxylic acid;

2-(4-((2-aminophenyl)carbamoyl)benzyl)-2H-indazole-3-carboxylic acid;

N-(2-aminophenyl)-4-((5-cyano-1H-indazol-1-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((5-cyano-2H-indazol-2-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((3-(pyridin-2-yl)-1H-indazol-1-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((3-(pyridin-2-yl)-2H-indazol-2-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((3-(dimethylamino)-1H-indazol-1-yl)methyl)benzamide;
N-(2-aminophenyl)-4-((3-(dimethylamino)-2H-indazol-2-yl)methyl)benzamide;
4-((1H-indazol-1-yl)methyl)-N-(2-amino-5-(furan-2-yl)phenyl)benzamide;
4-((2H-indazol-2-yl)methyl)-N-(2-amino-5-(furan-2-yl)phenyl)benzamide;
N-(2-aminophenyl)-4-((3-methoxy-1H-indazol-1-yl)methyl)benzamide;
N-(2-aminophenyl)-4-((3-methoxy-2H-indazol-2-yl)methyl)benzamide;
N-(2-aminophenyl)-4-((3-(methoxymethylamino)-1H-indazol-1-yl)methyl)benzamide;
N-(2-aminophenyl)-4-((3-(methoxymethylamino)-2H-indazol-2-yl)methyl)benzamide;
4-((1H-pyrazol-1-yl)methyl)-N-(2-amino-5-fluorophenyl)benzamide;
N-(2-amino-5-fluorophenyl)-4-((4-methyl-1H-pyrazol-1-yl)methyl)benzamide;
4-((1H-pyrazol-1-yl)methyl)-N-(2-aminophenyl)-3-methylbenzamide;
N-(2-amino-5-fluorophenyl)-3-methyl-4-((4-methyl-1H-pyrazol-1-yl)methyl)benzamide;
N-(2-aminophenyl)-4-((4-(furan-2-yl)-1H-pyrazol-1-yl)methyl)benzamide;
1-(4-((2-aminophenyl)carbamoyl)benzyl)-1H-pyrazole-4-carboxylic acid;
N-(2-aminophenyl)-4-((3-ethyl-1H-pyrazol-1-yl)methyl)benzamide;
N-(2-aminophenyl)-4-((5-ethyl-1H-pyrazol-1-yl)methyl)benzamide;
N-(2-aminophenyl)-4-((4-phenyl-1H-pyrazol-1-yl)methyl)benzamide;
N-(2-aminophenyl)-3-methyl-4-((5-methyl-4-phenyl-1H-pyrazol-1-yl)methyl)benzamide;
N-(2-aminophenyl)-4-((3-cyano-1H-pyrazol-1-yl)methyl)benzamide;
N-(2-aminophenyl)-4-((5-(pyridin-2-yl)-1H-pyrazol-1-yl)methyl)benzamide;
4-((1H-pyrazol-1-yl)methyl)-N-(2-amino-5-(furan-2-yl)phenyl)benzamide;
N-(2-amino-5-(furan-2-yl)phenyl)-4-((4-methyl-1H-pyrazol-1-yl)methyl)benzamide;
(S)-4-(1-(1H-pyrazol-1-yl)ethyl)-N-(2-aminophenyl)benzamide;
(R)-4-(1-(1H-pyrazol-1-yl)ethyl)-N-(2-aminophenyl)benzamide;
N-(2-aminophenyl)-4-((3-(pyridin-2-yl)-1H-pyrazol-1-yl)methyl)benzamide;
N-(2-aminophenyl)-4-((5-methoxy-1H-pyrazol-1-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((3-(methoxymethylamino)-1H-pyrazol-1-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((5-(methoxymethylamino)-1H-pyrazol-1-yl)methyl)benzamide; and

N-(2-aminophenyl)-4-((3-methoxy-1H-pyrazol-1-yl)methyl)benzamide.

[0146] It is noted that the compounds of the present invention may be in the form of a pharmaceutically acceptable salt, biohydrolyzable ester, biohydrolyzable amide, biohydrolyzable carbamate, solvate, hydrate or prodrug thereof. For example, the compound optionally comprises a substituent that is convertible in vivo to a different substituent such as a hydrogen.

[0147] It is further noted that the compound may be present in a mixture of stereoisomers (including tautomers), or the compound may comprise a single stereoisomer.

[0148] The present invention also provides a pharmaceutical composition comprising as an active ingredient a compound according to any one of the above embodiments and variations. In one particular variation, the composition is a solid formulation adapted for oral administration. In another particular variation, the composition is a liquid formulation adapted for oral administration. In yet another particular variation, the composition is a tablet. In still another particular variation, the composition is a liquid formulation adapted for parenteral administration.

[0149] In another of its aspects, there is provided a pharmaceutical composition comprising a compound according to any one of the above embodiments and variations, wherein the composition is adapted for administration by a route selected from the group consisting of orally, parenterally, intraperitoneally, intravenously, intraarterially, transdermally, sublingually, intramuscularly, rectally, transbuccally, intranasally, liposomally, via inhalation, vaginally, intraoccularly, via local delivery (for example by catheter or stent), subcutaneously, intraadiposally, intraarticularly, and intrathecally.

[0150] In yet another of its aspects, there is provided a kit comprising a compound of any one of the above embodiments and variations; and instructions which comprise one or more forms of information selected from the group consisting of indicating a disease state for which the composition is to be administered, storage information for the composition,

dosing information and instructions regarding how to administer the composition. In one particular variation, the kit comprises the compound in a multiple dose form.

[0151] In still another of its aspects, there is provided an article of manufacture comprising a compound of any one of the above embodiments and variations; and packaging materials. In one variation, the packaging material comprises a container for housing the compound. In one particular variation, the container comprises a label indicating one or more members of the group consisting of a disease state for which the compound is to be administered, storage information, dosing information and/or instructions regarding how to administer the compound. In another variation, the article of manufacture comprises the compound in a multiple dose form.

[0152] In a further of its aspects, there is provided a therapeutic method comprising administering a compound of any one of the above embodiments and variations to a subject.

[0153] In another of its aspects, there is provided a method of inhibiting HDAC comprising contacting HDAC with a compound of any one of the above embodiments and variations.

[0154] In yet another of its aspects, there is provided a method of inhibiting HDAC comprising causing a compound of any one of the above embodiments and variations to be present in a subject in order to inhibit HDAC in vivo.

[0155] In a further of its aspects, there is provided a method of inhibiting HDAC comprising administering a first compound to a subject that is converted in vivo to a second compound wherein the second compound inhibits HDAC in vivo, the second compound being a compound according to any one of the above embodiments and variations.

[0156] In another of its aspects, there is provided a method of treating a disease state for which HDAC possesses activity that contributes to the pathology and/or symptomology of the disease state, the method comprising causing a compound of any one of the above embodiments and variations to be present in a subject in a therapeutically effective amount for the disease state.

[0157] In yet another of its aspects, there is provided a method of treating a disease state for which HDAC possesses activity that contributes to the pathology and/or

symptomology of the disease state, the method comprising administering a compound of any one of the above embodiments and variations to a subject, wherein the compound is present in the subject in a therapeutically effective amount for the disease state.

[0158] In a further of its aspects, there is provided a method of treating a disease state for which HDAC possesses activity that contributes to the pathology and/or symptomology of the disease state, the method comprising administering a first compound to a subject that is converted in vivo to a second compound wherein the second compound inhibits HDAC in vivo, the second compound being a compound according to any one of the above embodiments and variations.

[0159] In still another embodiment, the present invention relates to a method for treating cancer comprising administering a compound according to any one of the above embodiments and variations to a mammalian species in need thereof. In one variation, the cancer is selected from the group consisting of squamous cell carcinoma, astrocytoma, Kaposi's sarcoma, glioblastoma, non small-cell lung cancer, bladder cancer, head and neck cancer, melanoma, ovarian cancer, prostate cancer, breast cancer, small-cell lung cancer, glioma, colorectal cancer, genitourinary cancer and gastrointestinal cancer.

[0160] In another embodiment, the present invention relates to a method for treating inflammation, inflammatory bowel disease, psoriasis, or transplant rejection, comprising administering a compound according to any one of the above embodiments and variations to a mammalian species in need thereof.

[0161] In a further embodiment, the present invention relates to a method for treating arthritis comprising administering a compound according to any one of the above embodiments and variations to a mammalian species in need thereof.

[0162] In yet another embodiment, the present invention relates to a method for treating degenerative diseases of the eye comprising administering a compound according to any one of the above embodiments and variations to a mammalian species in need thereof.

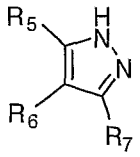
[0163] In still another embodiment, the present invention relates to a method for treating multiple sclerosis, amyotrophic lateral sclerosis, thyroid neoplasm or Alzheimer's disease comprising administering a compound according to any one of the above embodiments and variations to a mammalian species in need thereof.

[0164] In a further embodiment, the present invention relates to a method for treating hyperproliferative skin diseases or inflammatory cutaneous disorders comprising administering a compound according to any one of the above embodiments and variations to a mammalian species in need thereof.

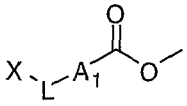
[0165] In each of the above embodiments and variations, the histone deacetylase is optionally a Class I histone deacetylase. In particular variations of each of the above embodiments and variations, the histone deacetylase is HDAC2 and/or HDAC8.

[0166] In still other of its aspects, the present invention relates to methods of making the HDAC inhibitors of the present invention, as well as intermediates useful for the preparation of such HDAC inhibitors. In one embodiment, the processes comprise:

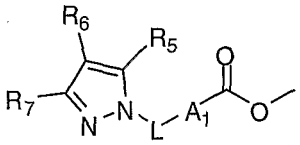
reacting a compound comprising the formula



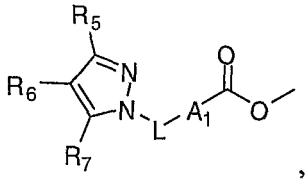
with a compound comprising the formula



under conditions that form a reaction product comprising a formula selected from the group consisting of



and



,

wherein

X is a leaving group;

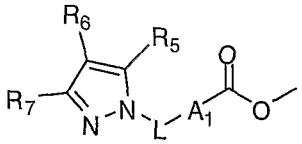
A_1 is selected from the group consisting of (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl, and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

L is a linker providing a 0-6 atom separation between the two ring atoms to which L is attached; and

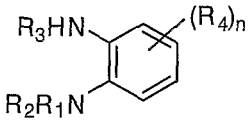
R_5, R_6 and R_7 are each independently selected from the group consisting of hydrogen, halo, nitro, cyano, oxo, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or any two of R_5, R_6 and R_7 may be taken together to form a substituted or unsubstituted ring.

[0167] In another embodiment, the processes comprise:

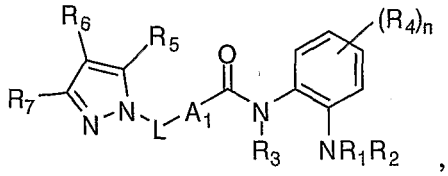
reacting a compound comprising the formula



with a compound comprising the formula



under conditions that form a reaction product comprising a formula



wherein

n is selected from the group consisting of 0, 1, 2, 3 and 4;

A_1 is selected from the group consisting of (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl, and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

L is a linker providing a 0-6 atom separation between the two ring atoms to which L is attached;

R_1 and R_2 are each independently selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_1 and R_2 may be taken together to form a substituted or unsubstituted ring;

R_3 is selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

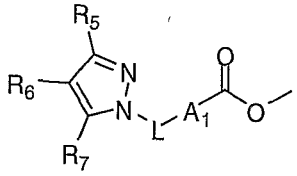
each R_4 is selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl,

hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted; and

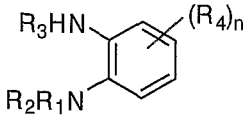
R_5, R_6 and R_7 are each independently selected from the group consisting of hydrogen, halo, nitro, cyano, oxo, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or any two of R_5, R_6 and R_7 may be taken together to form a substituted or unsubstituted ring.

[0168] In still another embodiment, the processes comprise:

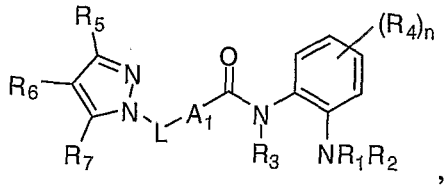
reacting a compound comprising the formula



with a compound comprising the formula



under conditions that form a reaction product comprising a formula



wherein

n is selected from the group consisting of 0, 1, 2, 3 and 4;

A_1 is selected from the group consisting of (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl, and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

L is a linker providing a 0-6 atom separation between the two ring atoms to which L is attached;

R_1 and R_2 are each independently selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_1 and R_2 may be taken together to form a substituted or unsubstituted ring;

R_3 is selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

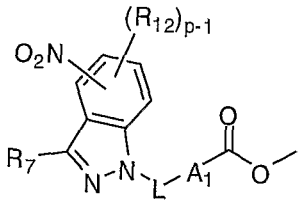
each R_4 is selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl,

hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted; and

R_5, R_6 and R_7 are each independently selected from the group consisting of hydrogen, halo, nitro, cyano, oxo, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or any two of R_5, R_6 and R_7 may be taken together to form a substituted or unsubstituted ring.

[0169] In yet another embodiment, the processes comprise:

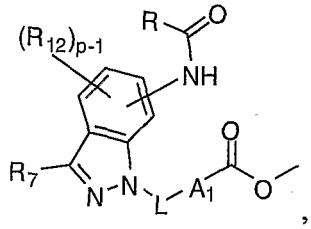
reacting a compound comprising the formula



with a compound comprising the formula

R-C(O)-X

under conditions that form a reaction product comprising a formula



,

wherein

p is selected from the group consisting of 0, 1, 2, 3 and 4;

A_1 is selected from the group consisting of (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl, and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

L is a linker providing a 0-6 atom separation between the two ring atoms to which L is attached;

R is selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

X is a leaving group;

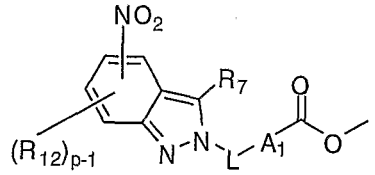
R_7 is selected from the group consisting of hydrogen, halo, nitro, cyano, oxo, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted; and

each R_{12} is independently selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl,

heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_{12} and R_7 or R_{11} may be taken together to form a substituted or unsubstituted ring.

[0170] In a further embodiment, the processes comprise:

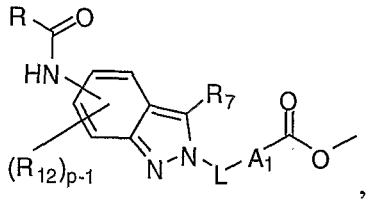
reacting a compound comprising the formula



with a compound comprising the formula

R-C(O)-X

under conditions that form a reaction product comprising a formula



,

wherein

p is selected from the group consisting of 0, 1, 2, 3 and 4;

A_1 is selected from the group consisting of (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl, and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

L is a linker providing a 0-6 atom separation between the two ring atoms to which L is attached;

R is selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl,

imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

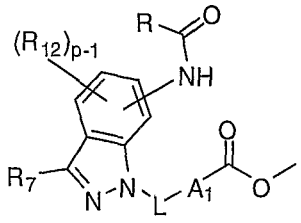
X is a leaving group;

R_7 is selected from the group consisting of hydrogen, halo, nitro, cyano, oxo, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted; and

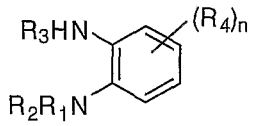
each R_{12} is independently selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_{12} and R_7 or R_{11} may be taken together to form a substituted or unsubstituted ring.

[0171] In still a further embodiment, the processes comprise:

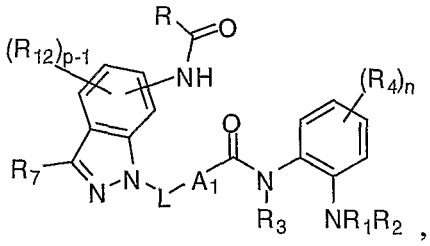
reacting a compound comprising the formula



with a compound comprising the formula



under conditions that form a reaction product comprising a formula



wherein

n is selected from the group consisting of 0, 1, 2, 3 and 4;

p is selected from the group consisting of 0, 1, 2, 3 and 4;

A_1 is selected from the group consisting of (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl, and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

L is a linker providing a 0-6 atom separation between the two ring atoms to which L is attached;

R is selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl,

(C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

R_1 and R_2 are each independently selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_1 and R_2 may be taken together to form a substituted or unsubstituted ring;

R_3 is selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

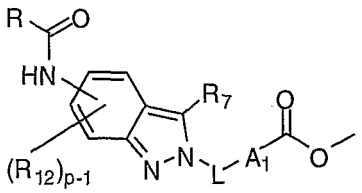
each R_4 is selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

R_7 is selected from the group consisting of hydrogen, halo, nitro, cyano, oxo, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted; and

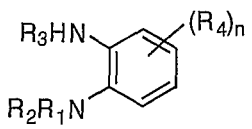
each R_{12} is independently selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_{12} and R_7 or R_{11} may be taken together to form a substituted or unsubstituted ring.

[0172] In yet a further embodiment, the processes comprise:

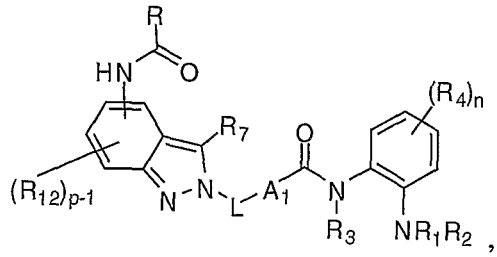
reacting a compound comprising the formula



with a compound comprising the formula



under conditions that form a reaction product comprising a formula



wherein

n is selected from the group consisting of 0, 1, 2, 3 and 4;

p is selected from the group consisting of 0, 1, 2, 3 and 4;

A_1 is selected from the group consisting of (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl, and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

L is a linker providing a 0-6 atom separation between the two ring atoms to which L is attached;

R is selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

R_1 and R_2 are each independently selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl,

hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_1 and R_2 may be taken together to form a substituted or unsubstituted ring;

R_3 is selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

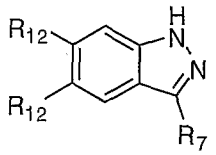
each R_4 is selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

R_7 is selected from the group consisting of hydrogen, halo, nitro, cyano, oxo, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted; and

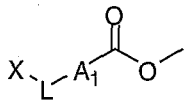
each R_{12} is independently selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_{12} and R_7 or R_{11} may be taken together to form a substituted or unsubstituted ring.

[0173] In another embodiment, the processes comprise:

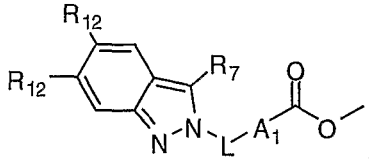
reacting a compound comprising the formula



with a compound comprising the formula

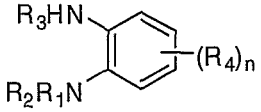


under conditions that form a first reaction product comprising a formula

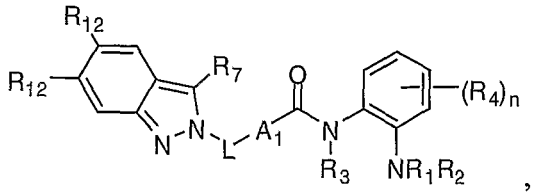


; and

reacting the first reaction product with a compound comprising the formula



under conditions that form a second reaction product comprising a formula



wherein

n is selected from the group consisting of 0, 1, 2, 3 and 4;

X is a leaving group;

A_1 is selected from the group consisting of (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl, and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

L is a linker providing a 0-6 atom separation between the two ring atoms to which L is attached;

R_1 and R_2 are each independently selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_1 and R_2 may be taken together to form a substituted or unsubstituted ring;

R_3 is selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

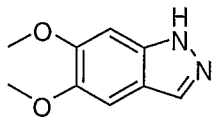
each R_4 is selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

R_7 is selected from the group consisting of hydrogen, halo, nitro, cyano, oxo, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted; and

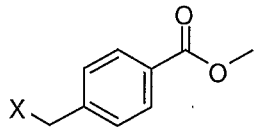
each R_{12} is independently selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_{12} and R_7 or R_{11} may be taken together to form a substituted or unsubstituted ring.

[0174] In another embodiment, the processes comprise:

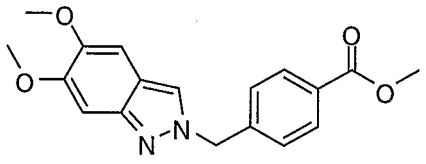
reacting a compound comprising the formula



with a compound comprising the formula

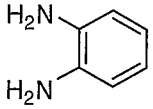


under conditions that form a first reaction product comprising a formula

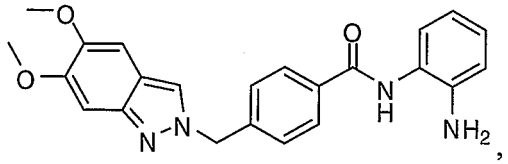


; and

reacting the first reaction product with a compound comprising the formula



under conditions that form a second reaction product comprising a formula



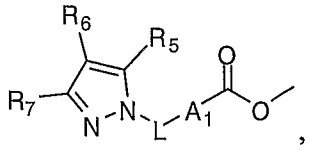
,

wherein

X is a leaving group.

[0175] In one variation of the above embodiments, X is halo. In one particular variation, X is bromo. In another particular variation, X is chloro.

[0176] In yet other of its aspects, the present invention relates to compounds useful in the preparation of the HDAC inhibitors of the present invention. In one embodiment, the compounds comprise:



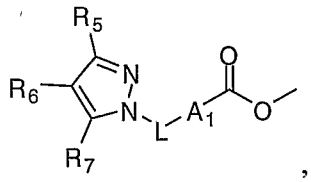
wherein

A_1 is selected from the group consisting of (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl, and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

L is a linker providing a 0-6 atom separation between the two ring atoms to which L is attached; and

R_5, R_6 and R_7 are each independently selected from the group consisting of hydrogen, halo, nitro, cyano, oxo, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or any two of R_5, R_6 and R_7 may be taken together to form a substituted or unsubstituted ring.

[0177] In another embodiment, the compounds comprise:



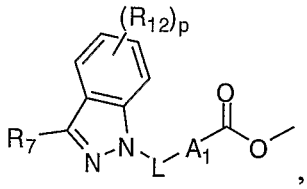
wherein

A_1 is selected from the group consisting of (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl, and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

L is a linker providing a 0-6 atom separation between the two ring atoms to which L is attached; and

R_5, R_6 and R_7 are each independently selected from the group consisting of hydrogen, halo, nitro, cyano, oxo, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or any two of R_5, R_6 and R_7 may be taken together to form a substituted or unsubstituted ring.

[0178] In still another embodiment, the compounds comprise:



wherein

p is selected from the group consisting of 0, 1, 2, 3 and 4;

A_1 is selected from the group consisting of (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl, and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

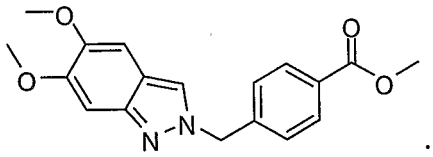
L is a linker providing a 0-6 atom separation between the two ring atoms to which L is attached;

R_7 is selected from the group consisting of hydrogen, halo, nitro, cyano, oxo, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl,

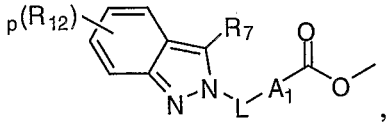
heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted; and

each R_{12} is independently selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_{12} and R_7 or R_{11} may be taken together to form a substituted or unsubstituted ring.

[0179] In one particular variation of the above embodiment, the compounds comprise:



[0180] In yet another embodiment, the compounds comprise:



wherein

p is selected from the group consisting of 0, 1, 2, 3 and 4;

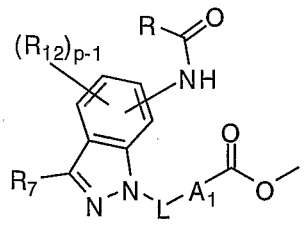
A_1 is selected from the group consisting of (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl, and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

L is a linker providing a 0-6 atom separation between the two ring atoms to which L is attached;

R_7 is selected from the group consisting of hydrogen, halo, nitro, cyano, oxo, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted; and

each R_{12} is independently selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_{12} and R_7 or R_{11} may be taken together to form a substituted or unsubstituted ring.

[0181] In a further embodiment, the compounds comprise:



,

wherein

p is selected from the group consisting of 0, 1, 2, 3 and 4;

A_1 is selected from the group consisting of (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl, and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

L is a linker providing a 0-6 atom separation between the two ring atoms to which L is attached;

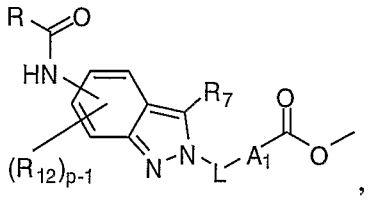
R is selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

R_7 is selected from the group consisting of hydrogen, halo, nitro, cyano, oxo, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted; and

each R_{12} is independently selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl,

(C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_{12} and R_7 or R_{11} may be taken together to form a substituted or unsubstituted ring.

[0182] In still a further embodiment, the compounds comprise:



wherein

p is selected from the group consisting of 0, 1, 2, 3 and 4;

A_1 is selected from the group consisting of (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl, and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

L is a linker providing a 0-6 atom separation between the two ring atoms to which L is attached;

R is selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

R_7 is selected from the group consisting of hydrogen, halo, nitro, cyano, oxo, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl,

(C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted; and

each R_{12} is independently selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_{12} and R_7 or R_{11} may be taken together to form a substituted or unsubstituted ring.

Salts, Hydrates, and Prodrugs of HDAC Inhibitors

[0183] It should be recognized that the compounds of the present invention may be present and optionally administered in the form of salts, hydrates and prodrugs that are converted in vivo into the compounds of the present invention. For example, it is within the scope of the present invention to convert the compounds of the present invention into and use them in the form of their pharmaceutically acceptable salts derived from various organic and inorganic acids and bases in accordance with procedures well known in the art.

[0184] When the compounds of the present invention possess a free base form, the compounds can be prepared as a pharmaceutically acceptable acid addition salt by reacting the free base form of the compound with a pharmaceutically acceptable inorganic or organic acid, e.g., hydrohalides such as hydrochloride, hydrobromide, hydroiodide; other mineral acids and their corresponding salts such as sulfate, nitrate, phosphate, etc.; and alkyl and monoarylsulfonates such as ethanesulfonate, toluenesulfonate and benzenesulfonate; and other organic acids and their corresponding salts such as acetate,

tartrate, maleate, succinate, citrate, benzoate, salicylate and ascorbate. Further acid addition salts of the present invention include, but are not limited to: adipate, alginate, arginate, aspartate, bisulfate, bisulfite, bromide, butyrate, camphorate, camphorsulfonate, caprylate, chloride, chlorobenzoate, cyclopentanepropionate, digluconate, dihydrogenphosphate, dinitrobenzoate, dodecylsulfate, fumarate, galacterate (from mucic acid), galacturonate, glucoheptaoate, gluconate, glutamate, glycerophosphate, hemisuccinate, hemisulfate, heptanoate, hexanoate, hippurate, hydrochloride, hydrobromide, hydroiodide, 2-hydroxyethanesulfonate, iodide, isethionate, iso-butyrate, lactate, lactobionate, malate, malonate, mandelate, metaphosphate, methanesulfonate, methylbenzoate, monohydrogenphosphate, 2-naphthalenesulfonate, nicotinate, nitrate, oxalate, oleate, pamoate, pectinate, persulfate, phenylacetate, 3-phenylpropionate, phosphate, phosphonate and phthalate. It should be recognized that the free base forms will typically differ from their respective salt forms somewhat in physical properties such as solubility in polar solvents, but otherwise the salts are equivalent to their respective free base forms for the purposes of the present invention.

[0185] When the compounds of the present invention possess a free acid form, a pharmaceutically acceptable base addition salt can be prepared by reacting the free acid form of the compound with a pharmaceutically acceptable inorganic or organic base. Examples of such bases are alkali metal hydroxides including potassium, sodium and lithium hydroxides; alkaline earth metal hydroxides such as barium and calcium hydroxides; alkali metal alkoxides, e.g., potassium ethanolate and sodium propanolate; and various organic bases such as ammonium hydroxide, piperidine, diethanolamine and N-methylglutamine. Also included are the aluminum salts of the compounds of the present invention. Further base salts of the present invention include, but are not limited to: copper, ferric, ferrous, lithium, magnesium, manganic, manganous, potassium, sodium and zinc salts. Organic base salts include, but are not limited to, salts of primary, secondary and tertiary amines, substituted amines including naturally occurring substituted amines, cyclic amines and basic ion exchange resins, e.g., arginine, betaine, caffeine, chloroprocaine, choline, N,N'-dibenzylethylenediamine (benzathine), dicyclohexylamine, diethanolamine, 2-diethylaminoethanol, 2-dimethylaminoethanol, ethanolamine, ethylenediamine, N-ethylmorpholine, N-ethylpiperidine, glucamine, glucosamine,

histidine, hydrabamine, iso-propylamine, lidocaine, lysine, meglumine, N-methyl-D-glucamine, morpholine, piperazine, piperidine, polyamine resins, procaine, purines, theobromine, triethanolamine, triethylamine, trimethylamine, tripropylamine and tris-(hydroxymethyl)-methylamine (tromethamine). It should be recognized that the free acid forms will typically differ from their respective salt forms somewhat in physical properties such as solubility in polar solvents, but otherwise the salts are equivalent to their respective free acid forms for the purposes of the present invention.

[0186] Compounds of the present invention that comprise basic nitrogen-containing groups may be quaternized with such agents as (C_{1-4}) alkyl halides, e.g., methyl, ethyl, iso-propyl and tert-butyl chlorides, bromides and iodides; di (C_{1-4}) alkyl sulfates, e.g., dimethyl, diethyl and diamyl sulfates; (C_{10-18}) alkyl halides, e.g., decyl, dodecyl, lauryl, myristyl and stearyl chlorides, bromides and iodides; and aryl (C_{1-4}) alkyl halides, e.g., benzyl chloride and phenethyl bromide. Such salts permit the preparation of both water-soluble and oil-soluble compounds of the present invention.

[0187] N-oxides of compounds according to the present invention can be prepared by methods known to those of ordinary skill in the art. For example, N-oxides can be prepared by treating an unoxidized form of the compound with an oxidizing agent (e.g., trifluoroperacetic acid, permaleic acid, perbenzoic acid, peracetic acid, meta-chloroperoxybenzoic acid, or the like) in a suitable inert organic solvent (e.g., a halogenated hydrocarbon such as dichloromethane) at approximately 0 °C. Alternatively, the N-oxides of the compounds can be prepared from the N-oxide of an appropriate starting material.

[0188] Prodrug derivatives of compounds according to the present invention can be prepared by modifying substituents of compounds of the present invention that are then converted in vivo to a different substituent. It is noted that in many instances, the prodrugs themselves also fall within the scope of the range of compounds according to the present invention. For example, prodrugs can be prepared by reacting a compound with a carbamylating agent (e.g., 1,1-acyloxyalkylcarbonochloridate, para-nitrophenyl carbonate, or the like) or an acylating agent. Further examples of methods of making prodrugs are described in Saulnier et al.(1994), Bioorganic and Medicinal Chemistry Letters, Vol. 4, p. 1985.

[0189] Protected derivatives of compounds of the present invention can also be made. Examples of techniques applicable to the creation of protecting groups and their removal can be found in T.W. Greene, Protecting Groups in Organic Synthesis, 3rd edition, John Wiley & Sons, Inc. 1999.

[0190] Compounds of the present invention may also be conveniently prepared, or formed during the process of the invention, as solvates (e.g., hydrates). Hydrates of compounds of the present invention may be conveniently prepared by recrystallization from an aqueous/organic solvent mixture, using organic solvents such as dioxin, tetrahydrofuran or methanol.

[0191] A "pharmaceutically acceptable salt", as used herein, is intended to encompass any compound according to the present invention that is utilized in the form of a salt thereof, especially where the salt confers on the compound improved pharmacokinetic properties as compared to the free form of compound or a different salt form of the compound. The pharmaceutically acceptable salt form may also initially confer desirable pharmacokinetic properties on the compound that it did not previously possess, and may even positively affect the pharmacodynamics of the compound with respect to its therapeutic activity in the body. An example of a pharmacokinetic property that may be favorably affected is the manner in which the compound is transported across cell membranes, which in turn may directly and positively affect the absorption, distribution, biotransformation and excretion of the compound. While the route of administration of the pharmaceutical composition is important, and various anatomical, physiological and pathological factors can critically affect bioavailability, the solubility of the compound is usually dependent upon the character of the particular salt form thereof, which it utilized. One of skill in the art will appreciate that an aqueous solution of the compound will provide the most rapid absorption of the compound into the body of a subject being treated, while lipid solutions and suspensions, as well as solid dosage forms, will result in less rapid absorption of the compound.

Preparation Of HDAC Inhibitors

[0192] Various methods may be developed for synthesizing compounds according to the present invention. Representative methods for synthesizing these compounds are

provided in the Examples. It is noted, however, that compounds of the present invention may also be synthesized by other synthetic routes that others may devise.

[0193] It will be readily recognized that certain compounds according to the present invention have atoms with linkages to other atoms that confer a particular stereochemistry to the compound (e.g., chiral centers). It is recognized that synthesis of compounds according to the present invention may result in the creation of mixtures of different stereoisomers (i.e., enantiomers and diastereomers). Unless a particular stereochemistry is specified, recitation of a compound is intended to encompass all of the different possible stereoisomers.

[0194] Various methods for separating mixtures of different stereoisomers are known in the art. For example, a racemic mixture of a compound may be reacted with an optically active resolving agent to form a pair of diastereoisomeric compounds. The diastereomers may then be separated in order to recover the optically pure enantiomers. Dissociable complexes may also be used to resolve enantiomers (e.g., crystalline diastereoisomeric salts). Diastereomers typically have sufficiently distinct physical properties (e.g., melting points, boiling points, solubilities, reactivity, etc.) that they can be readily separated by taking advantage of these dissimilarities. For example, diastereomers can typically be separated by chromatography or by separation/resolution techniques based upon differences in solubility. A more detailed description of techniques that can be used to resolve stereoisomers of compounds from their racemic mixture can be found in Jean Jacques Andre Collet, Samuel H. Wilen, Enantiomers, Racemates and Resolutions, John Wiley & Sons, Inc. (1981).

Compositions Comprising HDAC Inhibitors

[0195] A wide variety of compositions and administration methods may be used in conjunction with the compounds of the present invention. Such compositions may include, in addition to the compounds of the present invention, conventional pharmaceutical excipients, and other conventional, pharmaceutically inactive agents. Additionally, the compositions may include active agents in addition to the compounds of the present invention. These additional active agents may include additional compounds according to the invention, and/or one or more other pharmaceutically active agents.

[0196] The compositions may be in gaseous, liquid, semi-liquid or solid form, formulated in a manner suitable for the route of administration to be used. For oral administration, capsules and tablets are typically used. For parenteral administration, reconstitution of a lyophilized powder, prepared as described herein, is typically used.

[0197] Compositions comprising compounds of the present invention may be administered or coadministered orally, parenterally, intraperitoneally, intravenously, intraarterially, transdermally, sublingually, intramuscularly, rectally, transbuccally, intranasally, liposomally, via inhalation, vaginally, intraoccularly, via local delivery (for example by catheter or stent), subcutaneously, intraadiposally, intraarticularly, or intrathecally. The compounds and/or compositions according to the invention may also be administered or coadministered in slow release dosage forms.

[0198] The HDAC inhibitors and compositions comprising them may be administered or coadministered in any conventional dosage form. Co-administration in the context of this invention is intended to mean the administration of more than one therapeutic agent, one of which includes a HDAC inhibitor, in the course of a coordinated treatment to achieve an improved clinical outcome. Such co-administration may also be coextensive, that is, occurring during overlapping periods of time.

[0199] Solutions or suspensions used for parenteral, intradermal, subcutaneous, or topical application may optionally include one or more of the following components: a sterile diluent, such as water for injection, saline solution, fixed oil, polyethylene glycol, glycerine, propylene glycol or other synthetic solvent; antimicrobial agents, such as benzyl alcohol and methyl parabens; antioxidants, such as ascorbic acid and sodium bisulfite; chelating agents, such as ethylenediaminetetraacetic acid (EDTA); buffers, such as acetates, citrates and phosphates; agents for the adjustment of tonicity such as sodium chloride or dextrose, and agents for adjusting the acidity or alkalinity of the composition, such as alkaline or acidifying agents or buffers like carbonates, bicarbonates, phosphates, hydrochloric acid, and organic acids like acetic and citric acid. Parenteral preparations may optionally be enclosed in ampules, disposable syringes or single or multiple dose vials made of glass, plastic or other suitable material.

[0200] When compounds according to the present invention exhibit insufficient solubility, methods for solubilizing the compounds may be used. Such methods are

known to those of skill in this art, and include, but are not limited to, using cosolvents, such as dimethylsulfoxide (DMSO), using surfactants, such as TWEEN, or dissolution in aqueous sodium bicarbonate. Derivatives of the compounds, such as prodrugs of the compounds may also be used in formulating effective pharmaceutical compositions.

[0201] Upon mixing or adding compounds according to the present invention to a composition, a solution, suspension, emulsion or the like may be formed. The form of the resulting composition will depend upon a number of factors, including the intended mode of administration, and the solubility of the compound in the selected carrier or vehicle. The effective concentration needed to ameliorate the disease being treated may be empirically determined.

[0202] Compositions according to the present invention are optionally provided for administration to humans and animals in unit dosage forms, such as tablets, capsules, pills, powders, dry powders for inhalers, granules, sterile parenteral solutions or suspensions, and oral solutions or suspensions, and oil-water emulsions containing suitable quantities of the compounds, particularly the pharmaceutically acceptable salts, preferably the sodium salts, thereof. The pharmaceutically therapeutically active compounds and derivatives thereof are typically formulated and administered in unit-dosage forms or multiple-dosage forms. Unit-dose forms, as used herein, refers to physically discrete units suitable for human and animal subjects and packaged individually as is known in the art. Each unit-dose contains a predetermined quantity of the therapeutically active compound sufficient to produce the desired therapeutic effect, in association with the required pharmaceutical carrier, vehicle or diluent. Examples of unit-dose forms include ampoules and syringes individually packaged tablet or capsule. Unit-dose forms may be administered in fractions or multiples thereof. A multiple-dose form is a plurality of identical unit-dosage forms packaged in a single container to be administered in segregated unit-dose form. Examples of multiple-dose forms include vials, bottles of tablets or capsules or bottles of pint or gallons. Hence, multiple dose form is a multiple of unit-doses that are not segregated in packaging.

[0203] In addition to one or more compounds according to the present invention, the composition may comprise: a diluent such as lactose, sucrose, dicalcium phosphate, or carboxymethylcellulose; a lubricant, such as magnesium stearate, calcium stearate and

talc; and a binder such as starch, natural gums, such as gum acaciagelatin, glucose, molasses, polvinylpyrrolidine, celluloses and derivatives thereof, povidone, crospovidones and other such binders known to those of skill in the art. Liquid pharmaceutically administrable compositions can, for example, be prepared by dissolving, dispersing, or otherwise mixing an active compound as defined above and optional pharmaceutical adjuvants in a carrier, such as, for example, water, saline, aqueous dextrose, glycerol, glycols, ethanol, and the like, to form a solution or suspension. If desired, the pharmaceutical composition to be administered may also contain minor amounts of auxiliary substances such as wetting agents, emulsifying agents, or solubilizing agents, pH buffering agents and the like, for example, acetate, sodium citrate, cyclodextrine derivatives, sorbitan monolaurate, triethanolamine sodium acetate, triethanolamine oleate, and other such agents. Actual methods of preparing such dosage forms are known in the art, or will be apparent, to those skilled in this art; for example, see Remington's Pharmaceutical Sciences, Mack Publishing Company, Easton, Pa., 15th Edition, 1975. The composition or formulation to be administered will, in any event, contain a sufficient quantity of a inhibitor of the present invention to reduce HDAC activity in vivo, thereby treating the disease state of the subject.

[0204] Dosage forms or compositions may optionally comprise one or more compounds according to the present invention in the range of 0.005% to 100% (weight/weight) with the balance comprising additional substances such as those described herein. For oral administration, a pharmaceutically acceptable composition may optionally comprise any one or more commonly employed excipients, such as, for example pharmaceutical grades of mannitol, lactose, starch, magnesium stearate, talcum, cellulose derivatives, sodium crosscarmellose, glucose, sucrose, magnesium carbonate, sodium saccharin, talcum. Such compositions include solutions, suspensions, tablets, capsules, powders, dry powders for inhalers and sustained release formulations, such as, but not limited to, implants and microencapsulated delivery systems, and biodegradable, biocompatible polymers, such as collagen, ethylene vinyl acetate, polyanhydrides, polyglycolic acid, polyorthoesters, polylactic acid and others. Methods for preparing these formulations are known to those skilled in the art. The compositions may optionally

contain 0.01%-100% (weight/weight) of one or more HDAC inhibitors, optionally 0.1-95%, and optionally 1-95%.

[0205] Salts, preferably sodium salts, of the inhibitors may be prepared with carriers that protect the compound against rapid elimination from the body, such as time release formulations or coatings. The formulations may further include other active compounds to obtain desired combinations of properties.

Formulations For Oral Administration

[0206] Oral pharmaceutical dosage forms may be as a solid, gel or liquid. Examples of solid dosage forms include, but are not limited to tablets, capsules, granules, and bulk powders. More specific examples of oral tablets include compressed, chewable lozenges and tablets that may be enteric-coated, sugar-coated or film-coated. Examples of capsules include hard or soft gelatin capsules. Granules and powders may be provided in non-effervescent or effervescent forms. Each may be combined with other ingredients known to those skilled in the art.

[0207] In certain embodiments, compounds according to the present invention are provided as solid dosage forms, preferably capsules or tablets. The tablets, pills, capsules, troches and the like may optionally contain one or more of the following ingredients, or compounds of a similar nature: a binder; a diluent; a disintegrating agent; a lubricant; a glidant; a sweetening agent; and a flavoring agent.

[0208] Examples of binders that may be used include, but are not limited to, microcrystalline cellulose, gum tragacanth, glucose solution, acacia mucilage, gelatin solution, sucrose and starch paste.

[0209] Examples of lubricants that may be used include, but are not limited to, talc, starch, magnesium or calcium stearate, lycopodium and stearic acid.

[0210] Examples of diluents that may be used include, but are not limited to, lactose, sucrose, starch, kaolin, salt, mannitol and dicalcium phosphate.

[0211] Examples of glidants that may be used include, but are not limited to, colloidal silicon dioxide.

[0212] Examples of disintegrating agents that may be used include, but are not limited to, crosscarmellose sodium, sodium starch glycolate, alginic acid, corn starch, potato starch, bentonite, methylcellulose, agar and carboxymethylcellulose.

[0213] Examples of coloring agents that may be used include, but are not limited to, any of the approved certified water-soluble FD and C dyes, mixtures thereof; and water insoluble FD and C dyes suspended on alumina hydrate.

[0214] Examples of sweetening agents that may be used include, but are not limited to, sucrose, lactose, mannitol and artificial sweetening agents such as sodium cyclamate and saccharin, and any number of spray-dried flavors.

[0215] Examples of flavoring agents that may be used include, but are not limited to, natural flavors extracted from plants such as fruits and synthetic blends of compounds that produce a pleasant sensation, such as, but not limited to peppermint and methyl salicylate.

[0216] Examples of wetting agents that may be used include, but are not limited to, propylene glycol monostearate, sorbitan monooleate, diethylene glycol monolaurate and polyoxyethylene lauryl ether.

[0217] Examples of anti-emetic coatings that may be used include, but are not limited to, fatty acids, fats, waxes, shellac, ammoniated shellac and cellulose acetate phthalates.

[0218] Examples of film coatings that may be used include, but are not limited to, hydroxyethylcellulose, sodium carboxymethylcellulose, polyethylene glycol 4000 and cellulose acetate phthalate.

[0219] If oral administration is desired, the salt of the compound may optionally be provided in a composition that protects it from the acidic environment of the stomach. For example, the composition can be formulated in an enteric coating that maintains its integrity in the stomach and releases the active compound in the intestine. The composition may also be formulated in combination with an antacid or other such ingredient.

[0220] When the dosage unit form is a capsule, it may optionally additionally comprise a liquid carrier such as a fatty oil. In addition, dosage unit forms may optionally additionally comprise various other materials that modify the physical form of the dosage unit, for example, coatings of sugar and other enteric agents.

[0221] Compounds according to the present invention may also be administered as a component of an elixir, suspension, syrup, wafer, sprinkle, chewing gum or the like. A syrup may optionally comprise, in addition to the active compounds, sucrose as a sweetening agent and certain preservatives, dyes and colorings and flavors.

[0222] The compounds of the present invention may also be mixed with other active materials that do not impair the desired action, or with materials that supplement the desired action, such as antacids, H2 blockers, and diuretics. For example, if a compound is used for treating asthma or hypertension, it may be used with other bronchodilators and antihypertensive agents, respectively.

[0223] Examples of pharmaceutically acceptable carriers that may be included in tablets comprising compounds of the present invention include, but are not limited to binders, lubricants, diluents, disintegrating agents, coloring agents, flavoring agents, and wetting agents. Enteric-coated tablets, because of the enteric-coating, resist the action of stomach acid and dissolve or disintegrate in the neutral or alkaline intestines. Sugar-coated tablets may be compressed tablets to which different layers of pharmaceutically acceptable substances are applied. Film-coated tablets may be compressed tablets that have been coated with polymers or other suitable coating. Multiple compressed tablets may be compressed tablets made by more than one compression cycle utilizing the pharmaceutically acceptable substances previously mentioned. Coloring agents may also be used in tablets. Flavoring and sweetening agents may be used in tablets, and are especially useful in the formation of chewable tablets and lozenges.

[0224] Examples of liquid oral dosage forms that may be used include, but are not limited to, aqueous solutions, emulsions, suspensions, solutions and/or suspensions reconstituted from non-effervescent granules and effervescent preparations reconstituted from effervescent granules.

[0225] Examples of aqueous solutions that may be used include, but are not limited to, elixirs and syrups. As used herein, elixirs refer to clear, sweetened, hydroalcoholic preparations. Examples of pharmaceutically acceptable carriers that may be used in elixirs include, but are not limited to solvents. Particular examples of solvents that may be used include glycerin, sorbitol, ethyl alcohol and syrup. As used herein, syrups refer to

concentrated aqueous solutions of a sugar, for example, sucrose. Syrups may optionally further comprise a preservative.

[0226] Emulsions refer to two-phase systems in which one liquid is dispersed in the form of small globules throughout another liquid. Emulsions may optionally be oil-in-water or water-in-oil emulsions. Examples of pharmaceutically acceptable carriers that may be used in emulsions include, but are not limited to non-aqueous liquids, emulsifying agents and preservatives.

[0227] Examples of pharmaceutically acceptable substances that may be used in non-effervescent granules, to be reconstituted into a liquid oral dosage form, include diluents, sweeteners and wetting agents.

[0228] Examples of pharmaceutically acceptable substances that may be used in effervescent granules, to be reconstituted into a liquid oral dosage form, include organic acids and a source of carbon dioxide.

[0229] Coloring and flavoring agents may optionally be used in all of the above dosage forms.

[0230] Particular examples of preservatives that may be used include glycerin, methyl and propylparaben, benzoic add, sodium benzoate and alcohol.

[0231] Particular examples of non-aqueous liquids that may be used in emulsions include mineral oil and cottonseed oil.

[0232] Particular examples of emulsifying agents that may be used include gelatin, acacia, tragacanth, bentonite, and surfactants such as polyoxyethylene sorbitan monooleate.

[0233] Particular examples of suspending agents that may be used include sodium carboxymethylcellulose, pectin, tragacanth, Veegum and acacia. Diluents include lactose and sucrose. Sweetening agents include sucrose, syrups, glycerin and artificial sweetening agents such as sodium cyclamate and saccharin.

[0234] Particular examples of wetting agents that may be used include propylene glycol monostearate, sorbitan monooleate, diethylene glycol monolaurate and polyoxyethylene lauryl ether.

[0235] Particular examples of organic acids that may be used include citric and tartaric acid.

[0236] Sources of carbon dioxide that may be used in effervescent compositions include sodium bicarbonate and sodium carbonate. Coloring agents include any of the approved certified water soluble FD and C dyes, and mixtures thereof.

[0237] Particular examples of flavoring agents that may be used include natural flavors extracted from plants such fruits, and synthetic blends of compounds that produce a pleasant taste sensation.

[0238] For a solid dosage form, the solution or suspension, in for example propylene carbonate, vegetable oils or triglycerides, is preferably encapsulated in a gelatin capsule. Such solutions, and the preparation and encapsulation thereof, are disclosed in U.S. Pat. Nos. 4,328,245; 4,409,239; and 4,410,545. For a liquid dosage form, the solution, e.g., for example, in a polyethylene glycol, may be diluted with a sufficient quantity of a pharmaceutically acceptable liquid carrier, e.g., water, to be easily measured for administration.

[0239] Alternatively, liquid or semi-solid oral formulations may be prepared by dissolving or dispersing the active compound or salt in vegetable oils, glycols, triglycerides, propylene glycol esters (e.g., propylene carbonate) and other such carriers, and encapsulating these solutions or suspensions in hard or soft gelatin capsule shells. Other useful formulations include those set forth in U.S. Pat. Nos. Re 28,819 and 4,358,603.

Injectables, Solutions, and Emulsions

[0240] The present invention is also directed to compositions designed to administer the compounds of the present invention by parenteral administration, generally characterized by subcutaneous, intramuscular or intravenous injection. Injectables may be prepared in any conventional form, for example as liquid solutions or suspensions, solid forms suitable for solution or suspension in liquid prior to injection, or as emulsions.

[0241] Examples of excipients that may be used in conjunction with injectables according to the present invention include, but are not limited to water, saline, dextrose, glycerol or ethanol. The injectable compositions may also optionally comprise minor amounts of non-toxic auxiliary substances such as wetting or emulsifying agents, pH buffering agents, stabilizers, solubility enhancers, and other such agents, such as for

example, sodium acetate, sorbitan monolaurate, triethanolamine oleate and cyclodextrins. Implantation of a slow-release or sustained-release system, such that a constant level of dosage is maintained (see, e.g., U.S. Pat. No. 3,710,795) is also contemplated herein. The percentage of active compound contained in such parenteral compositions is highly dependent on the specific nature thereof, as well as the activity of the compound and the needs of the subject.

[0242] Parenteral administration of the formulations includes intravenous, subcutaneous and intramuscular administrations. Preparations for parenteral administration include sterile solutions ready for injection, sterile dry soluble products, such as the lyophilized powders described herein, ready to be combined with a solvent just prior to use, including hypodermic tablets, sterile suspensions ready for injection, sterile dry insoluble products ready to be combined with a vehicle just prior to use and sterile emulsions. The solutions may be either aqueous or nonaqueous.

[0243] When administered intravenously, examples of suitable carriers include, but are not limited to physiological saline or phosphate buffered saline (PBS), and solutions containing thickening and solubilizing agents, such as glucose, polyethylene glycol, and polypropylene glycol and mixtures thereof.

[0244] Examples of pharmaceutically acceptable carriers that may optionally be used in parenteral preparations include, but are not limited to aqueous vehicles, nonaqueous vehicles, antimicrobial agents, isotonic agents, buffers, antioxidants, local anesthetics, suspending and dispersing agents, emulsifying agents, sequestering or chelating agents and other pharmaceutically acceptable substances.

[0245] Examples of aqueous vehicles that may optionally be used include Sodium Chloride Injection, Ringers Injection, Isotonic Dextrose Injection, Sterile Water Injection, Dextrose and Lactated Ringers Injection.

[0246] Examples of nonaqueous parenteral vehicles that may optionally be used include fixed oils of vegetable origin, cottonseed oil, corn oil, sesame oil and peanut oil.

[0247] Antimicrobial agents in bacteriostatic or fungistatic concentrations may be added to parenteral preparations, particularly when the preparations are packaged in multiple-dose containers and thus designed to be stored and multiple aliquots to be removed. Examples of antimicrobial agents that may be used include phenols or cresols,

mercurials, benzyl alcohol, chlorobutanol, methyl and propyl p-hydroxybenzoic acid esters, thimerosal, benzalkonium chloride and benzethonium chloride.

[0248] Examples of isotonic agents that may be used include sodium chloride and dextrose. Examples of buffers that may be used include phosphate and citrate. Examples of antioxidants that may be used include sodium bisulfate. Examples of local anesthetics that may be used include procaine hydrochloride. Examples of suspending and dispersing agents that may be used include sodium carboxymethylcellulose, hydroxypropyl methylcellulose and polyvinylpyrrolidone. Examples of emulsifying agents that may be used include Polysorbate 80 (TWEEN 80). A sequestering or chelating agent of metal ions include EDTA.

[0249] Pharmaceutical carriers may also optionally include ethyl alcohol, polyethylene glycol and propylene glycol for water miscible vehicles and sodium hydroxide, hydrochloric acid, citric acid or lactic acid for pH adjustment.

[0250] The concentration of an inhibitor in the parenteral formulation may be adjusted so that an injection administers a pharmaceutically effective amount sufficient to produce the desired pharmacological effect. The exact concentration of an inhibitor and/or dosage to be used will ultimately depend on the age, weight and condition of the patient or animal as is known in the art.

[0251] Unit-dose parenteral preparations may be packaged in an ampoule, a vial or a syringe with a needle. All preparations for parenteral administration should be sterile, as is known and practiced in the art.

[0252] Injectables may be designed for local and systemic administration. Typically a therapeutically effective dosage is formulated to contain a concentration of at least about 0.1% w/w up to about 90% w/w or more, preferably more than 1% w/w of the HDAC inhibitor to the treated tissue(s). The inhibitor may be administered at once, or may be divided into a number of smaller doses to be administered at intervals of time. It is understood that the precise dosage and duration of treatment will be a function of the location of where the composition is parenterally administered, the carrier and other variables that may be determined empirically using known testing protocols or by extrapolation from in vivo or in vitro test data. It is to be noted that concentrations and dosage values may also vary with the age of the individual treated. It is to be further

understood that for any particular subject, specific dosage regimens may need to be adjusted over time according to the individual need and the professional judgment of the person administering or supervising the administration of the formulations. Hence, the concentration ranges set forth herein are intended to be exemplary and are not intended to limit the scope or practice of the claimed formulations.

[0253] The HDAC inhibitor may optionally be suspended in micronized or other suitable form or may be derivatized to produce a more soluble active product or to produce a prodrug. The form of the resulting mixture depends upon a number of factors, including the intended mode of administration and the solubility of the compound in the selected carrier or vehicle. The effective concentration is sufficient for ameliorating the symptoms of the disease state and may be empirically determined.

Lyophilized Powders

[0254] The compounds of the present invention may also be prepared as lyophilized powders, which can be reconstituted for administration as solutions, emulsions and other mixtures. The lyophilized powders may also be formulated as solids or gels.

[0255] Sterile, lyophilized powder may be prepared by dissolving the compound in a sodium phosphate buffer solution containing dextrose or other suitable excipient. Subsequent sterile filtration of the solution followed by lyophilization under standard conditions known to those of skill in the art provides the desired formulation. Briefly, the lyophilized powder may optionally be prepared by dissolving dextrose, sorbitol, fructose, corn syrup, xylitol, glycerin, glucose, sucrose or other suitable agent, about 1-20%, preferably about 5 to 15%, in a suitable buffer, such as citrate, sodium or potassium phosphate or other such buffer known to those of skill in the art at, typically, about neutral pH. Then, a HDAC inhibitor is added to the resulting mixture, preferably above room temperature, more preferably at about 30-35 oC, and stirred until it dissolves. The resulting mixture is diluted by adding more buffer to a desired concentration. The resulting mixture is sterile filtered or treated to remove particulates and to insure sterility, and apportioned into vials for lyophilization. Each vial may contain a single dosage or multiple dosages of the inhibitor.

Topical Administration

[0256] The compounds of the present invention may also be administered as topical mixtures. Topical mixtures may be used for local and systemic administration. The resulting mixture may be a solution, suspension, emulsions or the like and are formulated as creams, gels, ointments, emulsions, solutions, elixirs, lotions, suspensions, tinctures, pastes, foams, aerosols, irrigations, sprays, suppositories, bandages, dermal patches or any other formulations suitable for topical administration.

[0257] The HDAC inhibitors may be formulated as aerosols for topical application, such as by inhalation (see, U.S. Pat. Nos. 4,044,126, 4,414,209, and 4,364,923, which describe aerosols for delivery of a steroid useful for treatment of inflammatory diseases, particularly asthma). These formulations for administration to the respiratory tract can be in the form of an aerosol or solution for a nebulizer, or as a microfine powder for insufflation, alone or in combination with an inert carrier such as lactose. In such a case, the particles of the formulation will typically have diameters of less than 50 microns, preferably less than 10 microns.

[0258] The inhibitors may also be formulated for local or topical application, such as for topical application to the skin and mucous membranes, such as in the eye, in the form of gels, creams, and lotions and for application to the eye or for intracisternal or intraspinal application. Topical administration is contemplated for transdermal delivery and also for administration to the eyes or mucosa, or for inhalation therapies. Nasal solutions of the HDAC inhibitor alone or in combination with other pharmaceutically acceptable excipients can also be administered.

Formulations For Other Routes of Administrations

[0259] Depending upon the disease state being treated, other routes of administration, such as topical application, transdermal patches, and rectal administration, may also be used. For example, pharmaceutical dosage forms for rectal administration are rectal suppositories, capsules and tablets for systemic effect. Rectal suppositories are used herein mean solid bodies for insertion into the rectum that melt or soften at body temperature releasing one or more pharmacologically or therapeutically active ingredients. Pharmaceutically acceptable substances utilized in rectal suppositories are bases or

vehicles and agents to raise the melting point. Examples of bases include cocoa butter (theobroma oil), glycerin-gelatin, carbowax, (polyoxyethylene glycol) and appropriate mixtures of mono-, di- and triglycerides of fatty acids. Combinations of the various bases may be used. Agents to raise the melting point of suppositories include spermaceti and wax. Rectal suppositories may be prepared either by the compressed method or by molding. The typical weight of a rectal suppository is about 2 to 3 gm. Tablets and capsules for rectal administration may be manufactured using the same pharmaceutically acceptable substance and by the same methods as for formulations for oral administration.

Examples of Formulations

[0260] The following are particular examples of oral, intravenous and tablet formulations that may optionally be used with compounds of the present invention. It is noted that these formulations may be varied depending on the particular compound being used and the indication for which the formulation is going to be used.

ORAL FORMULATION

Compound of the Present Invention	10-100 mg
Citric Acid Monohydrate	105 mg
Sodium Hydroxide	18 mg
Flavoring	
Water	q.s. to 100 mL

INTRAVENOUS FORMULATION

Compound of the Present Invention	0.1-10 mg
Dextrose Monohydrate	q.s. to make isotonic
Citric Acid Monohydrate	1.05 mg
Sodium Hydroxide	0.18 mg
Water for Injection	q.s. to 1.0 mL

TABLET FORMULATION

Compound of the Present Invention	1%
Microcrystalline Cellulose	73%
Stearic Acid	25%
Colloidal Silica	1%.

Kits Comprising HDAC Inhibitors

[0261] The invention is also directed to kits and other articles of manufacture for treating diseases associated with HDACs. It is noted that diseases are intended to cover all

conditions for which the HDACs possess activity that contributes to the pathology and/or symptomology of the condition.

[0262] In one embodiment, a kit is provided that comprises a composition comprising at least one inhibitor of the present invention in combination with instructions. The instructions may indicate the disease state for which the composition is to be administered, storage information, dosing information and/or instructions regarding how to administer the composition. The kit may also comprise packaging materials. The packaging material may comprise a container for housing the composition. The kit may also optionally comprise additional components, such as syringes for administration of the composition. The kit may comprise the composition in single or multiple dose forms.

[0263] In another embodiment, an article of manufacture is provided that comprises a composition comprising at least one inhibitor of the present invention in combination with packaging materials. The packaging material may comprise a container for housing the composition. The container may optionally comprise a label indicating the disease state for which the composition is to be administered, storage information, dosing information and/or instructions regarding how to administer the composition. The kit may also optionally comprise additional components, such as syringes for administration of the composition. The kit may comprise the composition in single or multiple dose forms.

[0264] It is noted that the packaging material used in kits and articles of manufacture according to the present invention may form a plurality of divided containers such as a divided bottle or a divided foil packet. The container can be in any conventional shape or form as known in the art which is made of a pharmaceutically acceptable material, for example a paper or cardboard box, a glass or plastic bottle or jar, a re-sealable bag (for example, to hold a "refill" of tablets for placement into a different container), or a blister pack with individual doses for pressing out of the pack according to a therapeutic schedule. The container that is employed will depend on the exact dosage form involved, for example a conventional cardboard box would not generally be used to hold a liquid suspension. It is feasible that more than one container can be used together in a single package to market a single dosage form. For example, tablets may be contained in a bottle that is in turn contained within a box. Typically the kit includes directions for the administration of the separate components. The kit form is particularly advantageous

when the separate components are preferably administered in different dosage forms (e.g., oral, topical, transdermal and parenteral), are administered at different dosage intervals, or when titration of the individual components of the combination is desired by the prescribing physician.

[0265] One particular example of a kit according to the present invention is a so-called blister pack. Blister packs are well known in the packaging industry and are being widely used for the packaging of pharmaceutical unit dosage forms (tablets, capsules, and the like). Blister packs generally consist of a sheet of relatively stiff material covered with a foil of a preferably transparent plastic material. During the packaging process recesses are formed in the plastic foil. The recesses have the size and shape of individual tablets or capsules to be packed or may have the size and shape to accommodate multiple tablets and/or capsules to be packed. Next, the tablets or capsules are placed in the recesses accordingly and the sheet of relatively stiff material is sealed against the plastic foil at the face of the foil which is opposite from the direction in which the recesses were formed. As a result, the tablets or capsules are individually sealed or collectively sealed, as desired, in the recesses between the plastic foil and the sheet. Preferably the strength of the sheet is such that the tablets or capsules can be removed from the blister pack by manually applying pressure on the recesses whereby an opening is formed in the sheet at the place of the recess. The tablet or capsule can then be removed via said opening.

[0266] Another specific embodiment of a kit is a dispenser designed to dispense the daily doses one at a time in the order of their intended use. Preferably, the dispenser is equipped with a memory-aid, so as to further facilitate compliance with the regimen. An example of such a memory-aid is a mechanical counter that indicates the number of daily doses that has been dispensed. Another example of such a memory-aid is a battery-powered micro-chip memory coupled with a liquid crystal readout, or audible reminder signal which, for example, reads out the date that the last daily dose has been taken and/or reminds one when the next dose is to be taken.

Combination Therapy

[0267] A wide variety of therapeutic agents may have a therapeutic additive or synergistic effect with HDAC inhibitors according to the present invention. Such

therapeutic agents may additively or synergistically combine with the HDAC inhibitors to inhibit undesirable cell growth, such as inappropriate cell growth resulting in undesirable benign conditions or tumor growth.

[0268] In one embodiment, a method is provided for treating a cell proliferative disease state comprising treating cells with a compound according to the present invention in combination with an anti-proliferative agent, wherein the cells are treated with the compound according to the present invention before, at the same time, and/or after the cells are treated with the anti-proliferative agent, referred to herein as combination therapy. It is noted that treatment of one agent before another is referred to herein as sequential therapy, even if the agents are also administered together. It is noted that combination therapy is intended to cover when agents are administered before or after each other (sequential therapy) as well as when the agents are administered at the same time.

[0269] Examples of therapeutic agents that may be used in combination with HDAC inhibitors include, but are not limited to, anticancer agents, alkylating agents, antibiotic agents, antimetabolic agents, hormonal agents, plant-derived agents, and biologic agents.

[0270] Alkylating agents are polyfunctional compounds that have the ability to substitute alkyl groups for hydrogen ions. Examples of alkylating agents include, but are not limited to, bischloroethylamines (nitrogen mustards, e.g. chlorambucil, cyclophosphamide, ifosfamide, mechlorethamine, melphalan, uracil mustard), aziridines (e.g. thiotepa), alkyl alkone sulfonates (e.g. busulfan), nitrosoureas (e.g. carmustine, lomustine, streptozocin), nonclassic alkylating agents (altretamine, dacarbazine, and procarbazine), platinum compounds (carboplastin and cisplatin). These compounds react with phosphate, amino, hydroxyl, sulfihydryl, carboxyl, and imidazole groups. Under physiological conditions, these drugs ionize and produce positively charged ion that attach to susceptible nucleic acids and proteins, leading to cell cycle arrest and/or cell death. Combination therapy including a HDAC inhibitor and an alkylating agent may have therapeutic synergistic effects on cancer and reduce sides affects associated with these chemotherapeutic agents.

[0271] Antibiotic agents are a group of drugs that produced in a manner similar to antibiotics as a modification of natural products. Examples of antibiotic agents include,

but are not limited to, anthracyclines (e.g. doxorubicin, daunorubicin, epirubicin, idarubicin and anthracenedione), mitomycin C, bleomycin, dactinomycin, plicatomycin. These antibiotic agents interfere with cell growth by targeting different cellular components. For example, anthracyclines are generally believed to interfere with the action of DNA topoisomerase II in the regions of transcriptionally active DNA, which leads to DNA strand scissions. Bleomycin is generally believed to chelate iron and forms an activated complex, which then binds to bases of DNA, causing strand scissions and cell death. Combination therapy including a HDAC inhibitor and an antibiotic agent may have therapeutic synergistic effects on cancer and reduce sides affects associated with these chemotherapeutic agents.

[0272] Antimetabolic agents are a group of drugs that interfere with metabolic processes vital to the physiology and proliferation of cancer cells. Actively proliferating cancer cells require continuous synthesis of large quantities of nucleic acids, proteins, lipids, and other vital cellular constituents. Many of the antimetabolites inhibit the synthesis of purine or pyrimidine nucleosides or inhibit the enzymes of DNA replication. Some antimetabolites also interfere with the synthesis of ribonucleosides and RNA and/or amino acid metabolism and protein synthesis as well. By interfering with the synthesis of vital cellular constituents, antimetabolites can delay or arrest the growth of cancer cells. Examples of antimetabolic agents include, but are not limited to, fluorouracil (5-FU), floxuridine (5-FUdR), methotrexate, leucovorin, hydroxyurea, thioguanine (6-TG), mercaptopurine (6-MP), cytarabine, pentostatin, fludarabine phosphate, cladribine (2-CDA), asparaginase, and gemcitabine. Combination therapy including a HDAC inhibitor and a antimetabolic agent may have therapeutic synergistic effects on cancer and reduce sides affects associated with these chemotherapeutic agents.

[0273] Hormonal agents are a group of drug that regulate the growth and development of their target organs. Most of the hormonal agents are sex steroids and their derivatives and analogs thereof, such as estrogens, androgens, and progestins. These hormonal agents may serve as antagonists of receptors for the sex steroids to down regulate receptor expression and transcription of vital genes. Examples of such hormonal agents are synthetic estrogens (e.g. diethylstibestrol), antiestrogens (e.g. tamoxifen, toremifene, fluoxymesterol and raloxifene), antiandrogens (bicalutamide, nilutamide, flutamide),

aromatase inhibitors (e.g., aminoglutethimide, anastrozole and tetrazole), ketoconazole, goserelin acetate, leuprolide, megestrol acetate and mifepristone. Combination therapy including a HDAC inhibitor and a hormonal agent may have therapeutic synergistic effects on cancer and reduce sides affects associated with these chemotherapeutic agents.

[0274] Plant-derived agents are a group of drugs that are derived from plants or modified based on the molecular structure of the agents. Examples of plant-derived agents include, but are not limited to, vinca alkaloids (e.g., vincristine, vinblastine, vindesine, vinzolidine and vinorelbine), podophyllotoxins (e.g., etoposide (VP-16) and teniposide (VM-26)), taxanes (e.g., paclitaxel and docetaxel). These plant-derived agents generally act as antimitotic agents that bind to tubulin and inhibit mitosis. Podophyllotoxins such as etoposide are believed to interfere with DNA synthesis by interacting with topoisomerase II, leading to DNA strand scission. Combination therapy including a HDAC inhibitor and a plant-derived agent may have therapeutic synergistic effects on cancer and reduce sides affects associated with these chemotherapeutic agents.

[0275] Biologic agents are a group of biomolecules that elicit cancer/tumor regression when used alone or in combination with chemotherapy and/or radiotherapy. Examples of biologic agents include, but are not limited to, immuno-modulating proteins such as cytokines, monoclonal antibodies against tumor antigens, tumor suppressor genes, and cancer vaccines. Combination therapy including a HDAC inhibitor and a biologic agent may have therapeutic synergistic effects on cancer, enhance the patient's immune responses to tumorigenic signals, and reduce potential sides affects associated with this chemotherapeutic agent.

[0276] Cytokines possess profound immunomodulatory activity. Some cytokines such as interleukin-2 (IL-2, aldesleukin) and interferon have demonstrated antitumor activity and have been approved for the treatment of patients with metastatic renal cell carcinoma and metastatic malignant melanoma. IL-2 is a T-cell growth factor that is central to T-cell-mediated immune responses. The selective antitumor effects of IL-2 on some patients are believed to be the result of a cell-mediated immune response that discriminate between self and nonself. Examples of interleukins that may be used in conjunction with HDAC inhibitor include, but are not limited to, interleukin 2 (IL-2), and interleukin 4 (IL-4), interleukin 12 (IL-12).

[0277] Interferon include more than 23 related subtypes with overlapping activities, all of the IFN subtypes within the scope of the present invention. IFN has demonstrated activity against many solid and hematologic malignancies, the later appearing to be particularly sensitive.

[0278] Other cytokines that may be used in conjunction with a HDAC inhibitor include those cytokines that exert profound effects on hematopoiesis and immune functions. Examples of such cytokines include, but are not limited to erythropoietin, granulocyte-CSF (filgrastin), and granulocyte, macrophage-CSF (sargramostim). These cytokines may be used in conjunction with a HDAC inhibitor to reduce chemotherapy-induced myelopoietic toxicity.

[0279] Other immuno-modulating agents other than cytokines may also be used in conjunction with a HDAC inhibitor to inhibit abnormal cell growth. Examples of such immuno-modulating agents include, but are not limited to bacillus Calmette-Guerin, levamisole, and octreotide, a long-acting octapeptide that mimics the effects of the naturally occurring hormone somatostatin.

[0280] Monoclonal antibodies against tumor antigens are antibodies elicited against antigens expressed by tumors, preferably tumor-specific antigens. For example, monoclonal antibody HERCEPTIN® (Trastruzumab) is raised against human epidermal growth factor receptor2 (HER2) that is overexpressed in some breast tumors including metastatic breast cancer. Overexpression of HER2 protein is associated with more aggressive disease and poorer prognosis in the clinic. HERCEPTIN® is used as a single agent for the treatment of patients with metastatic breast cancer whose tumors over express the HER2 protein. Combination therapy including HDAC inhibitor and HERCEPTIN® may have therapeutic synergistic effects on tumors, especially on metastatic cancers.

[0281] Another example of monoclonal antibodies against tumor antigens is RITUXAN® (Rituximab) that is raised against CD20 on lymphoma cells and selectively deplete normal and malignant CD20+ pre-B and mature B cells. RITUXAN® is used as single agent for the treatment of patients with relapsed or refractory low-grade or follicular, CD20+, B cell non-Hodgkin's lymphoma. Combination therapy including

HDAC inhibitor and RITUXAN® may have therapeutic synergistic effects not only on lymphoma, but also on other forms or types of malignant tumors.

[0282] Tumor suppressor genes are genes that function to inhibit the cell growth and division cycles, thus preventing the development of neoplasia. Mutations in tumor suppressor genes cause the cell to ignore one or more of the components of the network of inhibitory signals, overcoming the cell cycle check points and resulting in a higher rate of controlled cell growth-cancer. Examples of the tumor suppressor genes include, but are not limited to, DPC-4, NF-1, NF-2, RB, p53, WT1, BRCA1 and BRCA2.

[0283] DPC-4 is involved in pancreatic cancer and participates in a cytoplasmic pathway that inhibits cell division. NF-1 codes for a protein that inhibits Ras, a cytoplasmic inhibitory protein. NF-1 is involved in neurofibroma and pheochromocytomas of the nervous system and myeloid leukemia. NF-2 encodes a nuclear protein that is involved in meningioma, schwanoma, and ependymoma of the nervous system. RB codes for the pRB protein, a nuclear protein that is a major inhibitor of cell cycle. RB is involved in retinoblastoma as well as bone, bladder, small cell lung and breast cancer. P53 codes for p53 protein that regulates cell division and can induce apoptosis. Mutation and/or inaction of p53 is found in a wide ranges of cancers. WT1 is involved in Wilms tumor of the kidneys. BRCA1 is involved in breast and ovarian cancer, and BRCA2 is involved in breast cancer. The tumor suppressor gene can be transferred into the tumor cells where it exerts its tumor suppressing functions. Combination therapy including a HDAC inhibitor and a tumor suppressor may have therapeutic synergistic effects on patients suffering from various forms of cancers.

[0284] Cancer vaccines are a group of agents that induce the body's specific immune response to tumors. Most of cancer vaccines under research and development and clinical trials are tumor-associated antigens (TAAs). TAA are structures (i.e. proteins, enzymes or carbohydrates) which are present on tumor cells and relatively absent or diminished on normal cells. By virtue of being fairly unique to the tumor cell, TAAs provide targets for the immune system to recognize and cause their destruction. Example of TAAs include, but are not limited to gangliosides (GM2), prostate specific antigen (PSA), alpha-fetoprotein (AFP), carcinoembryonic antigen (CEA) (produced by colon cancers and other adenocarcinomas, e.g. breast, lung, gastric, and pancreas cancer s), melanoma associated

antigens (MART-1, gp100, MAGE 1,3 tyrosinase), papillomavirus E6 and E7 fragments, whole cells or portions/lysates of antologous tumor cells and allogeneic tumor cells.

[0285] An adjuvant may be used to augment the immune response to TAAs. Examples of adjuvants include, but are not limited to, bacillus Calmette-Guerin (BCG), endotoxin lipopolysaccharides, keyhole limpet hemocyanin (GKLH), interleukin-2 (IL-2), granulocyte-macrophage colony-stimulating factor (GM-CSF) and cytoxan, a chemotherapeutic agent which is believe to reduce tumor-induced suppression when given in low doses.

EXAMPLES

Preparation of HDAC Inhibitors

[0286] Various methods may be developed for synthesizing compounds according to the present invention. Representative methods for synthesizing these compounds are provided in the Examples. It is noted, however, that the compounds of the present invention may also be synthesized by other synthetic routes that others may devise.

[0287] It will be readily recognized that certain compounds according to the present invention have atoms with linkages to other atoms that confer a particular stereochemistry to the compound (e.g., chiral centers). It is recognized that synthesis of compounds according to the present invention may result in the creation of mixtures of different stereoisomers (i.e., enantiomers and diastereomers). Unless a particular stereochemistry is specified, recitation of a compound is intended to encompass all of the different possible stereoisomers.

[0288] Various methods for separating mixtures of different stereoisomers are known in the art. For example, a racemic mixture of a compound may be reacted with an optically active resolving agent to form a pair of diastereoisomeric compounds. The diastereomers may then be separated in order to recover the optically pure enantiomers. Dissociable complexes may also be used to resolve enantiomers (e.g., crystalline diastereoisomeric salts). Diastereomers typically have sufficiently distinct physical properties (e.g., melting points, boiling points, solubilities, reactivity, etc.) and can be readily separated by taking advantage of these dissimilarities. For example, diastereomers can typically be separated by chromatography or by separation/resolution techniques based upon differences in solubility. A more detailed description of techniques that can be

used to resolve stereoisomers of compounds from their racemic mixture can be found in Jean Jacques Andre Collet, Samuel H. Wilen, Enantiomers, Racemates and Resolutions, John Wiley & Sons, Inc. (1981).

[0289] Compounds according to the present invention can also be prepared as a pharmaceutically acceptable acid addition salt by reacting the free base form of the compound with a pharmaceutically acceptable inorganic or organic acid. Alternatively, a pharmaceutically acceptable base addition salt of a compound can be prepared by reacting the free acid form of the compound with a pharmaceutically acceptable inorganic or organic base. Inorganic and organic acids and bases suitable for the preparation of the pharmaceutically acceptable salts of compounds are set forth in the definitions section of this Application. Alternatively, the salt forms of the compounds can be prepared using salts of the starting materials or intermediates.

[0290] The free acid or free base forms of the compounds can be prepared from the corresponding base addition salt or acid addition salt form. For example, a compound in an acid addition salt form can be converted to the corresponding free base by treating with a suitable base (e.g., ammonium hydroxide solution, sodium hydroxide, and the like). A compound in a base addition salt form can be converted to the corresponding free acid by treating with a suitable acid (e.g., hydrochloric acid, etc).

[0291] The N-oxides of compounds according to the present invention can be prepared by methods known to those of ordinary skill in the art. For example, N-oxides can be prepared by treating an unoxidized form of the compound with an oxidizing agent (e.g., trifluoroperacetic acid, permaleic acid, perbenzoic acid, peracetic acid, meta-chloroperoxybenzoic acid, or the like) in a suitable inert organic solvent (e.g., a halogenated hydrocarbon such as dichloromethane) at approximately 0 C. Alternatively, the N-oxides of the compounds can be prepared from the N-oxide of an appropriate starting material.

[0292] Compounds in an unoxidized form can be prepared from N-oxides of compounds by treating with a reducing agent (e.g., sulfur, sulfur dioxide, triphenyl phosphine, lithium borohydride, sodium borohydride, phosphorus trichloride, tribromide, or the like) in an suitable inert organic solvent (e.g., acetonitrile, ethanol, aqueous dioxane, or the like) at 0 to 80 oC.

[0293] Prodrug derivatives of the compounds can be prepared by methods known to those of ordinary skill in the art (e.g., for further details see Saulnier et al.(1994), Bioorganic and Medicinal Chemistry Letters, Vol. 4, p. 1985). For example, appropriate prodrugs can be prepared by reacting a non-derivatized compound with a suitable carbamylating agent (e.g., 1,1-acyloxyalkylcarbonochloridate, para-nitrophenyl carbonate, or the like).

[0294] Protected derivatives of the compounds can be made by methods known to those of ordinary skill in the art. A detailed description of the techniques applicable to the creation of protecting groups and their removal can be found in T.W. Greene, Protecting Groups in Organic Synthesis, 3rd edition, John Wiley & Sons, Inc. 1999.

[0295] Compounds according to the present invention may be conveniently prepared, or formed during the process of the invention, as solvates (e.g., hydrates). Hydrates of compounds of the present invention may be conveniently prepared by recrystallization from an aqueous/organic solvent mixture, using organic solvents such as dioxin, tetrahydrofuran or methanol.

[0296] Compounds according to the present invention can also be prepared as their individual stereoisomers by reacting a racemic mixture of the compound with an optically active resolving agent to form a pair of diastereoisomeric compounds, separating the diastereomers and recovering the optically pure enantiomer. While resolution of enantiomers can be carried out using covalent diastereomeric derivatives of compounds, dissociable complexes are preferred (e.g., crystalline diastereoisomeric salts). Diastereomers have distinct physical properties (e.g., melting points, boiling points, solubilities, reactivity, etc.) and can be readily separated by taking advantage of these dissimilarities. The diastereomers can be separated by chromatography or, preferably, by separation/resolution techniques based upon differences in solubility. The optically pure enantiomer is then recovered, along with the resolving agent, by any practical means that would not result in racemization. A more detailed description of the techniques applicable to the resolution of stereoisomers of compounds from their racemic mixture can be found in Jean Jacques Andre Collet, Samuel H. Wilen, Enantiomers, Racemates and Resolutions, John Wiley & Sons, Inc. (1981).

[0297] As used herein the symbols and conventions used in these processes, schemes and examples are consistent with those used in the contemporary scientific literature, for example, the Journal of the American Chemical Society or the Journal of Biological Chemistry. Standard single-letter or thee-letter abbreviations are generally used to designate amino acid residues, which are assumed to be in the L-configuration unless otherwise noted. Unless otherwise noted, all starting materials were obtained from commercial suppliers and used without further purification. Specifically, the following abbreviations may be used in the examples and throughout the specification:

μL (microliters)	Ac (acetyl)
atm (atmosphere)	ATP (Adenosine Triphophatase)
BOC (tert-butyloxycarbonyl)	BOP (bis(2-oxo-3-oxazolidinyl)phosphinic chloride)
BSA (Bovine Serum Albumin)	CBZ (benzyloxycarbonyl)
CDI (1,1-carbonyldiimidazole)	DCC (dicyclohexylcarbodiimide)
DCE (dichloroethane)	DCM (dichloromethane)
DMAP (4-dimethylaminopyridine)	DME (1,2-dimethoxyethane)
DMF (N,N-dimethylformamide)	DMPU (N,N'-dimethylpropyleneurea)
DMSO (dimethylsulfoxide)	EDCI (ethylcarbodiimide hydrochloride)
EDTA (Ethylenediaminetetraacetic acid)	Et (ethyl)
Et_2O (diethyl ether)	EtOAc (ethyl acetate)
FMOC (9-fluorenylmethoxycarbonyl)	g (grams)
h (hours)	HOAc or AcOH (acetic acid)
HOBT (1-hydroxybenzotriazole)	HOSu (N-hydroxysuccinimide)
HPLC (high pressure liquid chromatography)	Hz (Hertz)
i.v. (intravenous)	IBCF (isobutyl chloroformate)
i-PrOH (isopropanol)	L (liters)
M (molar)	mCPBA (meta-chloroperbenzoic acid)
Me (methyl)	MeOH (methanol)
mg (milligrams)	MHz (megahertz)
min (minutes)	mL (milliliters)
mM (millimolar)	mmol (millimoles)
mol (moles)	MOPS (Morpholinepropanesulfonic acid)
mp (melting point)	NaOAc (sodium acetate)
OMe (methoxy)	psi (pounds per square inch)
RP (reverse phase)	RT (ambient temperature)
SPA (Scintillation Proximity Assay)	TBAF (tetra-n-butylammonium fluoride)
TBS (t-butyldimethylsilyl)	tBu (tert-butyl)
TEA (triethylamine)	TFA (trifluoroacetic acid)

TFAA (trifluoroacetic anhydride)	THF (tetrahydrofuran)
TIPS (triisopropylsilyl)	TLC (thin layer chromatography)
TMS (trimethylsilyl)	TMSE (2-(trimethylsilyl)ethyl)
Tr (retention time)	

[0298] All references to ether or Et2O are to diethyl ether; and brine refers to a saturated aqueous solution of NaCl. Unless otherwise indicated, all temperatures are expressed in °C (degrees Centigrade). All reactions are conducted under an inert atmosphere at RT unless otherwise noted.

[0299] 1H NMR spectra were recorded on a Bruker Avance 400. Chemical shifts are expressed in parts per million (ppm). Coupling constants are in units of Hertz (Hz). Splitting patterns describe apparent multiplicities and are designated as s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), br (broad).

[0300] Low-resolution mass spectra (MS) and compound purity data were acquired on a Waters ZQ LC/MS single quadrupole system equipped with electrospray ionization (ESI) source, UV detector (220 and 254 nm), and evaporative light scattering detector (ELSD). Thin-layer chromatography was performed on 0.25 mm E. Merck silica gel plates (60F-254), visualized with UV light, 5% ethanolic phosphomolybdic acid, Ninhydrin or p-anisaldehyde solution. Flash column chromatography was performed on silica gel (230-400 mesh, Merck).

[0301] The starting materials and reagents used in preparing these compounds are either available from commercial suppliers such as the Aldrich Chemical Company (Milwaukee, WI), Bachem (Torrance, CA), Sigma (St. Louis, MO), or may be prepared by methods well known to a person of ordinary skill in the art, following procedures described in such standard references as Fieser and Fieser's Reagents for Organic Synthesis, vols. 1-17, John Wiley and Sons, New York, NY, 1991; Rodd's Chemistry of Carbon Compounds, vols. 1-5 and supps., Elsevier Science Publishers, 1989; Organic Reactions, vols. 1-40, John Wiley and Sons, New York, NY, 1991; March J.: Advanced Organic Chemistry, 4th ed., John Wiley and Sons, New York, NY; and Larock: Comprehensive Organic Transformations, VCH Publishers, New York, 1989.

[0302] The entire disclosure of all documents cited throughout this application are incorporated herein by reference.

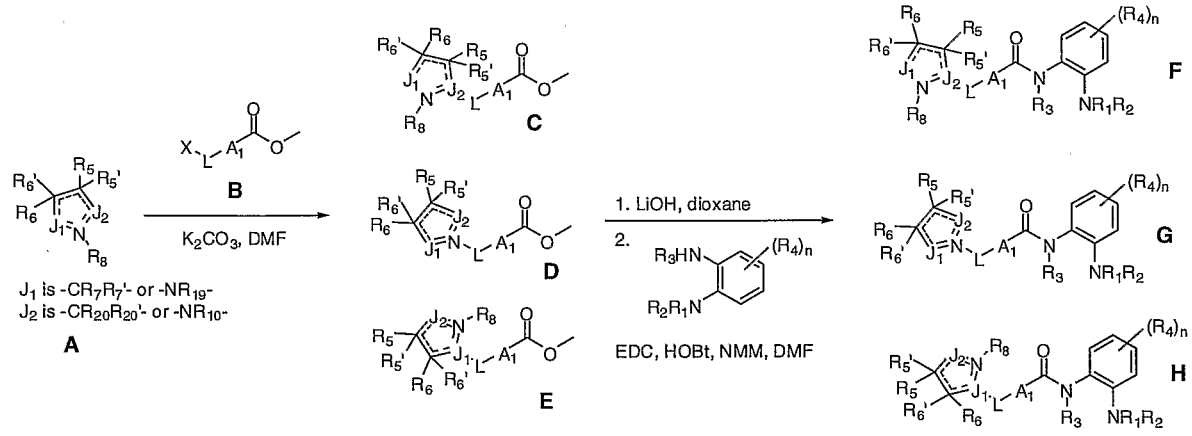
Synthetic Schemes For Compounds of the Present Invention

[0303] Compounds according to the present invention may be synthesized according to the reaction schemes shown below. Other reaction schemes could be readily devised by those skilled in the art. It should also be appreciated that a variety of different solvents, temperatures and other reaction conditions can be varied to optimize the yields of the reactions.

[0304] In the reactions described hereinafter it may be necessary to protect reactive functional groups, for example hydroxy, amino, imino, thio or carboxy groups, where these are desired in the final product, to avoid their unwanted participation in the reactions. Conventional protecting groups may be used in accordance with standard practice, for examples see T.W. Greene and P. G. M. Wuts in "Protective Groups in Organic Chemistry" John Wiley and Sons, 1991.

[0305] General synthetic routes for producing compounds of the present invention are shown in the schemes below.

Scheme 1



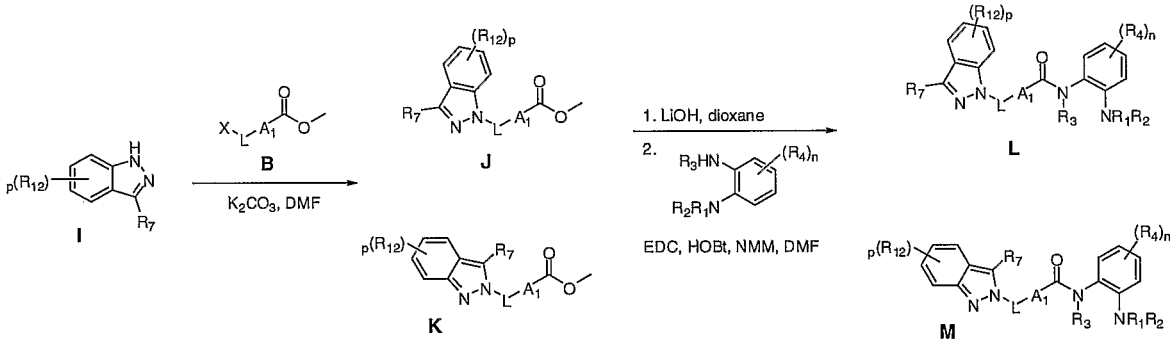
[0306] A solution of **B** (0.5 mmol) in DMF (2.5 mL) is treated with an appropriate heterocycle **A** (0.5 mmol) and solid K_2CO_3 (0.6 mmol). After stirring at 23 °C for 18 h, the reaction is poured into water (10 mL) and the resulting solid isolated by filtration. The filter cake can be rinsed with water and allowed to dry in vacuo to yield a mixture of regioisomeric alkylation products **C**, **D** and **E**, which can be separated by flash chromatography. If no solid is formed, the DMF/water mixture can be extracted with

ethylacetate. The combined extracts can be dried ($MgSO_4$), concentrated *in vacuo* and purified by flash chromatography.

[0307] A solution of the alkylation products **C**, **D** and/or **E** (0.25 mmol) in dioxane (1 mL) is treated with aqueous LiOH (1 M, 1.0 mL). After stirring at 23 °C for 2 h, the reaction is neutralized with aqueous HCl (1 M, 2.0 mL) and the resulting solid isolated by filtration. The filter cake can be rinsed with water and allowed to dry in vacuo to yield the corresponding carboxylic acid.

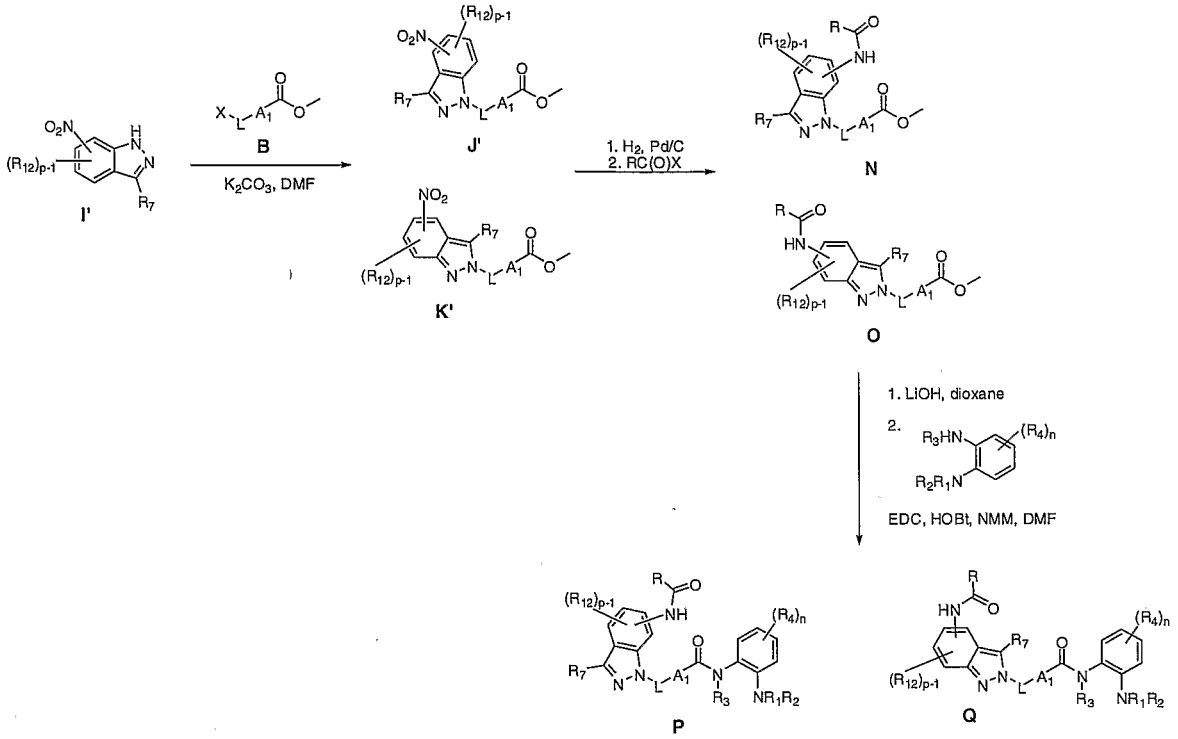
[0308] A solution of the carboxylic acid formed above (0.1 mmol) in DMF (1 mL) is sequentially treated with EDC (0.12 mmol), HOBt (0.12 mmol), a substituted or unsubstituted 1,2-phenylenediamine (0.12 mmol) and NMM (0.3 mmol). After stirring at 23 °C for 4 h, the reaction is poured into water (10 mL) and the resulting solid isolated by filtration. The filter cake can be rinsed with water and allowed to dry in vacuo to yield the corresponding amide **F**, **G** and/or **H**.

Scheme 2



[0309] In relation to Scheme 2, the alkylation of **I** with **B**, hydrolysis of **J** and/or **K**, and coupling with the 1,2-phenylenediamine to provide **L** and/or **M** proceed as described in Scheme 1.

Scheme 3



[0310] In relation to Scheme 3, nitrobenzenes **J'** and **K'** may be prepared as described in connection with Schemes 1 and 2.

[0311] A solution of the nitrobenzene (**J'** and/or **K'**) (1.0 mmol) in MeOH (10 mL) with Pd/C (10 wt%, 50 mg) is stirred vigorously under hydrogen for 4 h. The reaction is filtered and concentrated in vacuo to give the corresponding aniline that can be carried forward.

[0312] A solution of the aniline (1.0 mmol) in dichloromethane (10 mL) is treated sequentially with the appropriate acid chloride or chloroformate (RC(O)Cl, wherein R is, for example, an optionally substituted alkoxy, alkyl, heterocycloalkyl or aryl) (1.1 mmol) and triethylamine (2.2 mmol). After stirring at 23 °C for 4 h, the reaction is concentrated in vacuo to yield the corresponding acylation product (**N** and/or **O**). If necessary, purification can be carried out by flash chromatography or recrystallization.

[0313] Compounds **N** and/or **O** can be coupled with a substituted or unsubstituted 1,2-phenylenediamine to yield **P** and/or **Q**, as described in connection with Schemes 1 and 2.

[0314] Chiral components can be separated and purified using any of a variety of techniques known to those skilled in the art. For example, chiral components can be purified using supercritical fluid chromatography (SFC). In one particular variation, chiral analytical SFC/MS analyses are conducted using a Berger analytical SFC system (AutoChem, Newark, DE) which consists of a Berger SFC dual pump fluid control module with a Berger FCM 1100/1200 supercritical fluid pump and FCM 1200 modifier fluid pump, a Berger TCM 2000 oven, and an Alcott 718 autosampler. The integrated system can be controlled by BI-SFC Chemstation software version 3.4. Detection can be accomplished with a Watrers ZQ 2000 detector operated in positive mode with an ESI interface and a scan range from 200-800 Da with 0.5 second per scan. Chromatographic separations can be performed on a ChiralPak AD-H, ChiralPak AS-H, ChiralCel OD-H, or ChiralCel OJ-H column (5μ, 4.6 x 250 mm; Chiral Technologies, Inc. West Chester, PA) with 10 to 40% methanol as the modifier and with or without ammonium acetate (10 mM). Any of a variety of flow rates can be utilized including, for example, 1.5 or 3.5 mL/min with an inlet pressure set at 100 bar. Additionally, a variety of sample injection conditions can be used including, for example, sample injections of either 5 or 10μL in methanol at 0.1 mg/mL in concentration.

[0315] In another variation, preparative chiral separations are performed using a Berger MultiGram II SFC purification system. For example, samples can be loaded onto a ChiralPak AD column (21 x 250 mm, 10μ). In particular variations, the flow rate for separation can be 70 mL/min, the injection volume up to 2 mL, and the inlet pressure set at 130 bar. Stacked injections can be applied to increase the efficiency.

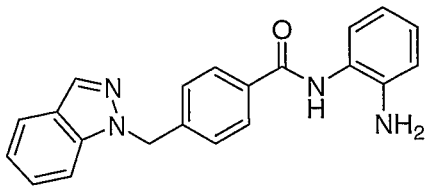
[0316] In each of the above reaction procedures or schemes, the various substituents may be selected from among the various substituents otherwise taught herein.

[0317] Descriptions of the syntheses of particular compounds according to the present invention based on the above reaction scheme are set forth herein.

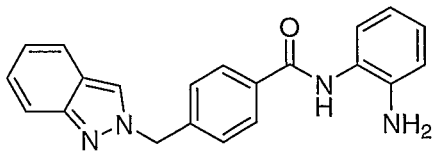
Examples of HDAC Inhibitors

[0318] The present invention is further exemplified, but not limited by, the following examples that describe the synthesis of particular compounds according to the invention.

Examples 1 and 2: 4-((1*H*-indazol-1-yl)methyl)-N-(2-aminophenyl)benzamide *and* 4-((2*H*-indazol-2-yl)methyl)-N-(2-aminophenyl)benzamide



Example 1



Example 2

[0319] The title compounds were prepared using the procedure described in Scheme 2. In particular, a solution of methyl 4-bromomethylbenzoate (0.5 mmol) in DMF (2.5 mL) was treated with the indazole (0.5 mmol) and solid K_2CO_3 (0.6 mmol). After stirring at 23 °C for 18 h, the reaction was poured into water (10 mL) and the resulting solid was isolated by filtration. The filter cake was rinsed with water and allowed to dry in vacuo to yield a mixture of regioisomeric alkylation products, which were separated by flash chromatography.

[0320] A solution of the methyl ester (0.25 mmol) in dioxane (1 mL) was treated with aqueous LiOH (1 M, 1.0 mL). After stirring at 23 °C for 2 h, the reaction was neutralized with aqueous HCl (1 M, 2.0 mL) and the resulting solid was isolated by filtration. The filter cake was rinsed with water and allowed to dry in vacuo to yield the corresponding benzoic acid.

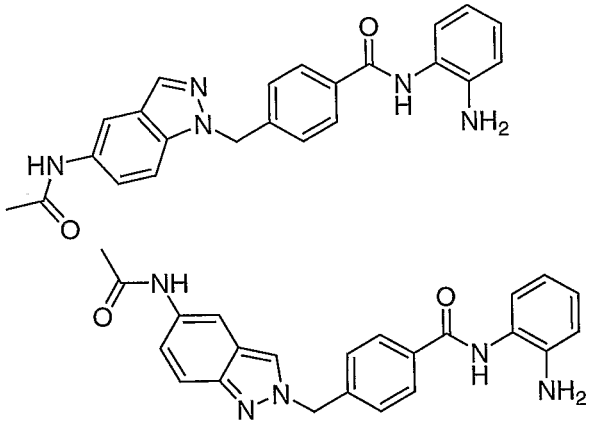
[0321] A solution of the appropriate benzoic acid (0.1 mmol) in DMF (1 mL) was sequentially treated with EDC (0.12 mmol), HOBt (0.12 mmol), 1,2-phenylenediame (0.12 mmol) and NMM (0.3 mmol). After stirring at 23 °C for 4 h, the reaction was poured into water (10 mL) and the resulting solid was isolated by filtration. The filter cake was rinsed with water and allowed to dry in vacuo to yield the corresponding amide.

[0322] Example 1: ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 4.85 (s, 2 H) 5.74 (s, 2 H) 6.53 - 6.58 (m, 1 H) 6.73 (dd, J=7.83, 1.26 Hz, 1 H) 6.91 - 6.96 (m, 1 H) 7.09 - 7.16 (m, 2 H) 7.28 - 7.39 (m, 3 H) 7.70 (d, J=8.34 Hz, 1 H) 7.77 (d, J=8.34 Hz, 1 H) 7.87 (d, J=8.08 Hz, 2 H) 8.13 (s, 1 H) 9.56 (s, 1 H). ESI-MS: m/z 343.4 $(M + H)^+$.

[0323] Example 2: ^{1}H NMR (400 MHz, DMSO-D6) δ ppm 4.94 (s, 2 H) 5.72 (s, 2 H) 6.57 (t, J=7.58 Hz, 1 H) 6.74 - 6.77 (m, 1 H) 6.95 (td, J=7.58, 1.52 Hz, 1 H) 7.00 - 7.05 (m, 1 H) 7.13 (d, J=7.58 Hz, 1 H) 7.22 (dd, J=8.21, 7.20 Hz, 1 H) 7.41 (d, J=8.08 Hz, 2 H)

7.58 (d, J=8.59 Hz, 1 H) 7.71 (d, J=8.59 Hz, 1 H) 7.93 (d, J=8.08 Hz, 2 H) 8.51 (s, 1 H) 9.62 (s, 1 H). ESI-MS: m/z 343.4 $(M + H)^+$.

Examples 3 and 4: 4-((5-acetamido-1*H*-indazol-1-yl)methyl)-N-(2-aminophenyl)benzamide *and* 4-((5-acetamido-2*H*-indazol-2-yl)methyl)-N-(2-aminophenyl)benzamide



Example 3 Example 4

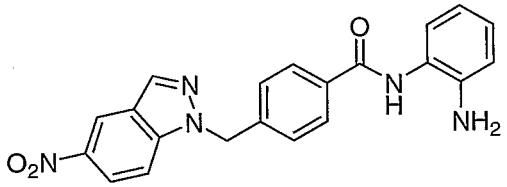
[0324] The title compounds were prepared using a procedure analogous to that described in Examples 1 and 2 except that the nitrobenzene was reduced and the aniline acylated as further described in Scheme 2. Specifically, the alkylation with methyl 4-bromomethylbenzoate, hydrolysis of methyl benzoate, and coupling with 1,2-phenylenediamine proceed as described in connection with Examples 1 and 2. A solution of the nitrobenzene (1.0 mmol) in MeOH (10 mL) with Pd/C (10 wt%, 50 mg) was then stirred vigorously under hydrogen for 4 h. The reaction was filtered and concentrated in vacuo to give the corresponding aniline that was carried forward. A solution of the aniline (1.0 mmol) in dichloromethane (10 mL) was treated sequentially with the appropriate acid chloride or chloroformate (1.1 mmol) and triethylamine (2.2 mmol). After stirring at 23 °C for 4 h, the reaction was concentrated in vacuo to yield the corresponding acylation product. If necessary, purification can be carried out by flash chromatography or recrystallization.

[0325] Example 3: ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 2.02 (s, 3 H) 4.85 (s, 2 H) 5.69 (s, 2 H) 6.49 - 6.60 (m, 1 H) 6.73 (d, J=8.08 Hz, 1 H) 6.87 - 6.99 (m, 2 H) 7.11 (d, J=8.08 Hz, 1 H) 7.29 (d, J=8.08 Hz, 2 H) 7.39 (dd, J=9.09, 1.77 Hz, 1 H) 7.61 (d, J=8.84

Hz, 1 H) 7.87 (d, J=8.08 Hz, 2 H) 8.06 (s, 1 H) 8.12 (s, 1 H) 9.56 (s, 1 H). ESI-MS: m/z 400.5 $(M + H)^+$.

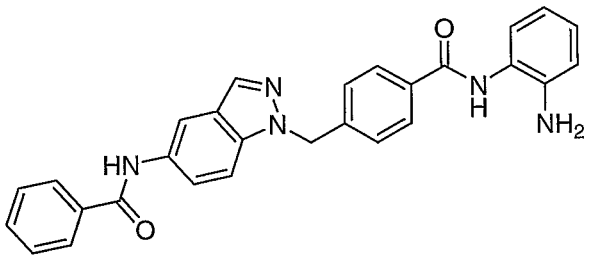
[0326] Example 4: ^{1}H NMR (400 MHz, DMSO-D6) δ ppm 2.03 (s, 3 H) 4.87 (s, 2 H) 5.67 (s, 2 H) 6.45 - 6.65 (m, 1 H) 6.74 (d, J=8.08 Hz, 1 H) 6.86 - 7.02 (m, 1 H) 7.13 (d, J=7.33 Hz, 1 H) 7.20 (dd, J=9.35, 1.77 Hz, 1 H) 7.39 (d, J=8.08 Hz, 2 H) 7.52 (d, J=9.09 Hz, 1 H) 7.92 (d, J=8.08 Hz, 2 H) 8.12 (s, 1 H) 8.41 (s, 1 H) 9.61 (s, 1 H) 9.85 (s, 1 H). ESI-MS: m/z 400.5 $(M + H)^+$.

Example 5: N-(2-aminophenyl)-4-((5-nitro-1H-indazol-1-yl)methyl)benzamide



[0327] The title compound was prepared using a procedure analogous to that described in Examples 1 and 2. ^{1}H NMR (400 MHz, DMSO-D6) of the trifluoroacetic acid salt: δ ppm 5.86 (s, 2 H) 6.96 (s, 1 H) 7.05 (d, J=7.58 Hz, 1 H) 7.13 (d, J=7.33 Hz, 1 H) 7.25 (d, J=7.83 Hz, 1 H) 7.37 (d, J=8.08 Hz, 2 H) 7.92 (d, J=8.34 Hz, 2 H) 7.96 (d, J=9.09 Hz, 1 H) 8.24 (dd, J=9.35, 2.27 Hz, 1 H) 8.47 (s, 1 H) 8.85 (d, J=2.02 Hz, 1 H) 9.99 (s, 1 H). ESI-MS: m/z 388.4 $(M + H)^+$.

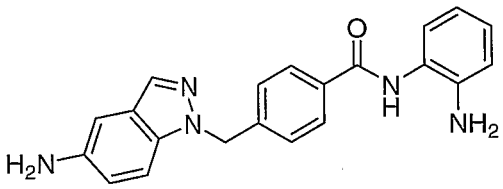
Example 6: 4-((5-benzamido-1*H*-indazol-1-yl)methyl)-N-(2-aminophenyl)benzamide



[0328] The title compound was prepared using a procedure analogous to that described in Examples 3 and 4. ^{1}H NMR (400 MHz, DMSO-D6) δ ppm 4.86 (s, 2 H) 5.73 (s, 2 H) 6.49 - 6.62 (m, 1 H) 6.73 (d, J=7.83 Hz, 1 H) 6.85 - 6.97 (m, 1 H) 7.11 (d, J=7.83 Hz, 1 H) 7.30 (d, J=8.08 Hz, 2 H) 7.45 - 7.62 (m, 3 H) 7.61 - 7.74 (m, 2 H) 7.88 (d, J=8.34 Hz, 2 H)

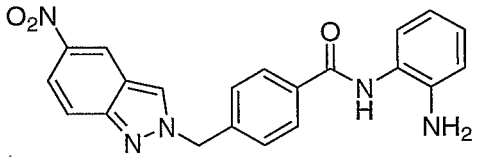
7.96 (d, J=6.82 Hz, 2 H) 8.12 (s, 1 H) 8.26 (s, 1 H) 9.57 (s, 1 H) 10.28 (s, 1 H). ESI-MS: m/z 462.5 $(M + H)^+$.

Example 7: 4-((5-amino-1*H*-indazol-1-yl)methyl)-N-(2-aminophenyl)benzamide



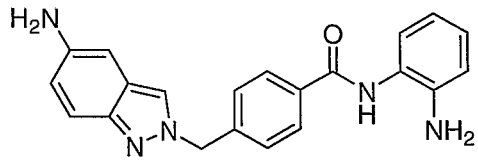
[0329] The title compound was prepared using a procedure analogous to that described in Examples 3 and 4. ^{1}H NMR (400 MHz, DMSO-D6) δ ppm 4.85 (bs, 4 H) 5.59 (s, 2 H) 6.55 (s, 1 H) 6.71 - 6.80 (m, 3 H) 6.93 (d, J=6.32 Hz, 1 H) 7.11 (d, J=6.82 Hz, 1 H) 7.26 (d, J=7.58 Hz, 2 H) 7.30 - 7.40 (m, 1 H) 7.73 - 7.83 (m, 1 H) 7.86 (d, J=7.58 Hz, 2 H) 9.56 (s, 1 H). ESI-MS: m/z 358.4 $(M + H)^+$.

Example 8: N-(2-aminophenyl)-4-((5-nitro-2*H*-indazol-2-yl)methyl)benzamide



[0330] The title compound was prepared using a procedure analogous to that described in Examples 1 and 2. ^{1}H NMR (400 MHz, DMSO-D6) δ ppm 4.87 (br. s., 2 H) 5.75 - 5.88 (m, 2 H) 6.51 - 6.61 (m, 1 H) 6.74 (d, J=7.33 Hz, 1 H) 6.90 - 6.98 (m, 1 H) 7.13 (d, J=7.58 Hz, 1 H) 7.46 (d, J=8.08 Hz, 2 H) 7.77 (d, J=9.60 Hz, 1 H) 7.94 (d, J=8.08 Hz, 2 H) 7.97 - 8.04 (m, 1 H) 8.91 (d, 1 H) 8.94 - 9.01 (m, 1 H) 9.62 (s, 1 H). ESI-MS: m/z 388.4 $(M + H)^+$.

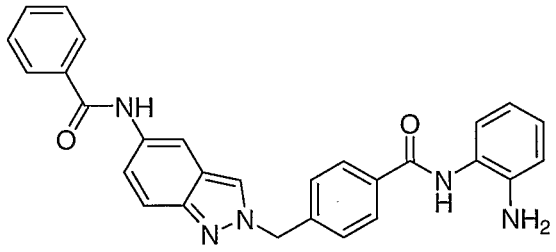
Example 9: 4-((5-amino-2*H*-indazol-2-yl)methyl)-N-(2-aminophenyl)benzamide



[0331] The title compound was prepared using a procedure analogous to that described in Examples 3 and 4. ^{1}H NMR (400 MHz, DMSO-D6) of the trifluoroacetic acid salt: δ

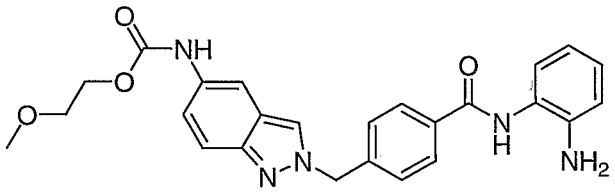
ppm 5.76 (s, 2 H) 6.84 - 6.95 (m, 1 H) 7.01 (d, J=7.83 Hz, 1 H) 7.08 - 7.20 (m, 2 H) 7.24 (s, 1 H) 7.44 (d, J=8.08 Hz, 2 H) 7.69 - 7.79 (m, 2 H) 7.96 (d, J=7.83 Hz, 2 H) 8.64 (s, 1 H) 9.96 (s, 1 H). ESI-MS: m/z 358.4 $(M + H)^+$

Example 10: 4-((5-benzamido-2*H*-indazol-1-yl)methyl)-N-(2-aminophenyl)benzamide



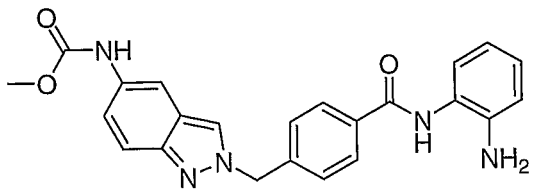
[0332] The title compound was prepared using a procedure analogous to that described in Examples 3 and 4. ^{1}H NMR (400 MHz, DMSO-D6) δ ppm 4.87 (s, 2 H) 5.61 - 5.76 (s, 2 H) 6.56 (t, J=7.33 Hz, 1 H) 6.75 (d, J=8.08 Hz, 1 H) 6.88 - 7.00 (m, 1 H) 7.13 (d, J=8.08 Hz, 1 H) 7.41 (d, J=7.07 Hz, 2 H) 7.45 - 7.63 (m, 3 H) 7.83 - 8.02 (m, 4 H) 8.26 (s, 1 H) 8.49 (s, 1 H) 9.61 (s, 1 H) 10.20 (s, 1 H). ESI-MS: m/z 462.5 $(M + H)^+$.

Example 11: 2-Methoxyethyl 2-(4-((2-aminophenyl)carbamoyl)benzyl)-2*H*-indazol-5-ylcarbamate



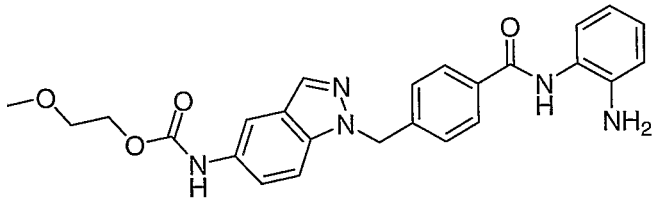
[0333] The title compound was prepared using a procedure analogous to that described in Examples 3 and 4. ^{1}H NMR (400 MHz, DMSO-D6) δ ppm 3.52 - 3.60 (m, 2 H) 4.13 - 4.22 (m, 2 H) 4.86 (bs, 2 H) 5.66 (s, 2 H) 6.56 (m, 1 H) 6.75 (m, 1 H) 6.93 (d, J=6.82 Hz, 1 H) 7.13 (m, 1 H) 7.21 (d, J=2.02 Hz, 1 H) 7.39 (d, J=7.83 Hz, 2 H) 7.52 (s, 1 H) 7.82 - 7.89 (m, 2 H) 7.91 (s, 1 H) 8.40 (s, 1 H) 9.60 (s, 1 H) 9.64 (s, 1 H). ESI-MS: m/z 460.5 $(M + H)^+$.

Example 12: Methyl 2-(4-((2-aminophenyl)carbamoyl)benzyl)-2*H*-indazol-5-ylcarbamate



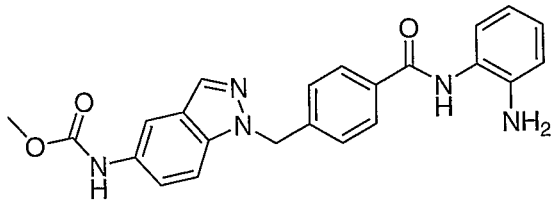
[0334] The title compound was prepared using a procedure analogous to that described in Examples 3 and 4. ^{1}H NMR (400 MHz, DMSO-D6) δ ppm 3.32 (s, 3 H) 4.87 (s, 2 H) 5.58 - 5.73 (m, 2 H) 6.48 - 6.62 (m, 1 H) 6.74 (d, J=8.08 Hz, 1 H) 6.88 - 7.00 (m, 1 H) 7.07 - 7.17 (m, 1 H) 7.18 - 7.24 (m, 1 H) 7.39 (dd, J=8.08, 4.55 Hz, 2 H) 7.46 - 7.57 (m, 1 H) 7.88 - 8.00 (m, 2 H) 8.39 (d, J=6.32 Hz, 1 H) 8.56 (s, 1 H) 9.54 (s, 1 H) 9.61 (s, 1 H). ESI-MS: m/z 416.5 $(M + H)^+$.

Example 13: 2-Methoxyethyl 1-(4-((2-aminophenyl)carbamoyl)benzyl)-1*H*-indazol-5-ylcarbamate



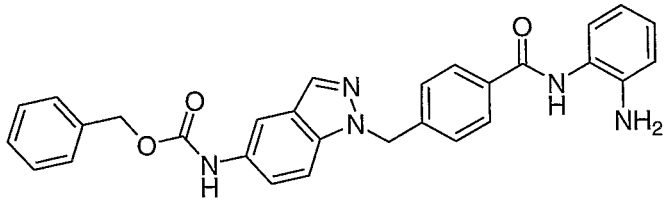
[0335] The title compound was prepared using a procedure analogous to that described in Examples 3 and 4. ^{1}H NMR (400 MHz, DMSO-D6) δ ppm 3.31 (s, 3 H) 3.47 - 3.61 (m, 2 H) 4.12 - 4.23 (m, 2 H) 4.85 (s, 2 H) 5.69 (s, 2 H) 6.55 (t, J=7.58 Hz, 1 H) 6.69 - 6.78 (m, 1 H) 6.86 - 7.01 (m, 1 H) 7.11 (d, J=7.83 Hz, 1 H) 7.28 (d, J=8.34 Hz, 2 H) 7.33 - 7.45 (m, 1 H) 7.61 (d, J=9.09 Hz, 1 H) 7.87 (m, 3 H) 8.05 (s, 1 H) 9.56 (s, 1 H) 9.71 (s, 1 H). ESI-MS: m/z 460.5 $(M + H)^+$.

Example 14: Methyl 1-(4-((2-aminophenyl)carbamoyl)benzyl)-1*H*-indazol-5-ylcarbamate



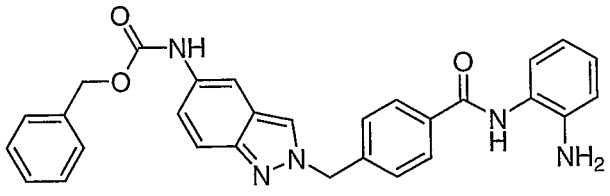
[0336] The title compound was prepared using a procedure analogous to that described in Examples 3 and 4. ^{1}H NMR (400 MHz, DMSO-D6) of the trifluoroacetic acid salt: δ ppm 3.65 (s, 3 H) 5.70 (s, 2 H) 6.90 (s, 1 H) 6.99 (s, 1 H) 7.11 (s, 1 H) 7.23 (d, J=7.83 Hz, 1 H) 7.31 (d, J=8.08 Hz, 2 H) 7.38 (s, 1 H) 7.61 (d, J=9.09 Hz, 1 H) 7.89 (d, J=7.83 Hz, 3 H) 8.06 (s, 1 H) 9.61 (s, 1 H) 9.91 (s, 1 H). ESI-MS: m/z 416.5 $(M + H)^+$.

Example 15: Benzyl 1-(4-((2-aminophenyl)carbamoyl)benzyl)-1*H*-indazol-5-ylcarbamate



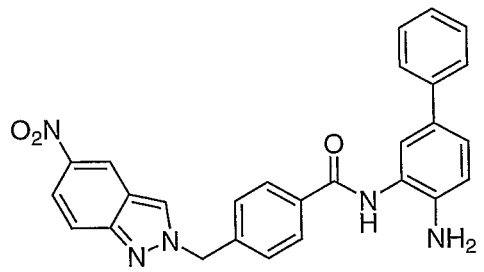
[0337] The title compound was prepared using a procedure analogous to that described in Examples 3 and 4. ^{1}H NMR (400 MHz, DMSO-D6) of the trifluoroacetic acid salt: δ ppm 4.85 (s, 2 H) 5.14 (s, 2 H) 5.69 (s, 2 H) 6.55 (s, 1 H) 6.73 (d, J=8.08 Hz, 1 H) 6.93 (s, 1 H) 7.04 - 7.18 (m, 1 H) 7.22 - 7.49 (m, 7 H) 7.61 (s, 1 H) 7.79 - 8.00 (m, 4 H) 8.05 (s, 1 H) 9.56 (s, 1 H) 9.74 (s, 1 H). ESI-MS: m/z 492.5 $(M + H)^+$.

Example 16: Benzyl 2-(4-((2-aminophenyl)carbamoyl)benzyl)-2*H*-indazol-5-ylcarbamate



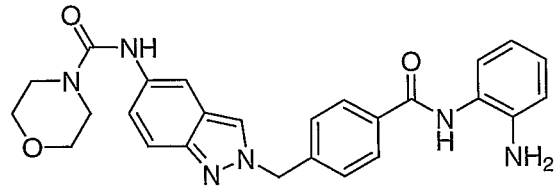
[0338] The title compound was prepared using a procedure analogous to that described in Examples 3 and 4. ^{1}H NMR (400 MHz, DMSO-D6) of the trifluoroacetic acid salt: δ ppm 5.14 (s, 2 H) 5.68 (s, 2 H) 6.81 - 6.94 (m, 1 H) 6.95 - 7.05 (m, 1 H) 7.10 (s, 1 H) 7.22 (dd, J=9.35, 1.77 Hz, 2 H) 7.29 - 7.47 (m, 7 H) 7.51 (d, J=9.35 Hz, 2 H) 7.94 (d, J=8.08 Hz, 2 H) 8.41 (s, 1 H) 9.68 (s, 1 H) 9.94 (s, 1 H). ESI-MS: m/z 492.5 $(M + H)^+$.

Example 17: *N*-(4-Amino-biphenyl-3-yl)-4-(5-nitro-indazol-2-ylmethyl)-benzamide



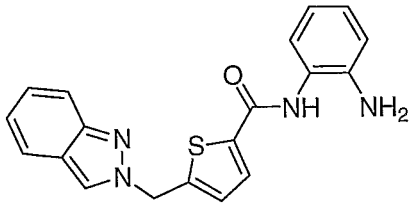
[0339] The title compound was prepared using a procedure analogous to that described in Examples 3 and 4. ^{1}H NMR (400 MHz, DMSO-D6) of the trifluoroacetic acid salt: δ ppm 5.84 (s, 2 H) 6.97 (s, 1 H) 7.25 (s, 1 H) 7.39 (s, 3 H) 7.44 - 7.62 (m, 5 H) 7.79 (s, 1 H) 7.99 (s, 3 H) 8.98 (s, 2 H) 9.89 (s, 1 H). ESI-MS: m/z 464.5 $(M + H)^+$.

Example 18: N-(2-(4-((2-Aminophenyl)carbamoyl)benzyl)-2*H*-indazol-5-yl)morpholine-4-carboxamide



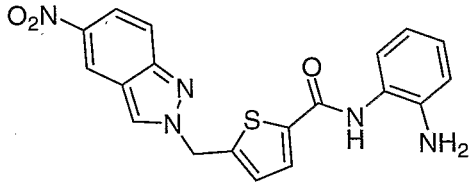
[0340] The title compound was prepared using a procedure analogous to that described in Examples 3 and 4. ^{1}H NMR (400 MHz, DMSO-D6) of the trifluoroacetic acid salt: δ ppm 3.34 - 3.45 (m, 4 H) 3.59 (m, 4 H) 4.86 (s, 2 H) 5.66 (s, 2 H) 6.75 (m, 1 H) 6.86 - 6.98 (m, 1 H) 7.06 - 7.16 (m, 1 H) 7.20 - 7.30 (m, 1 H) 7.38 (d, 2 H) 7.46 (m, 1 H) 7.78 (s, 1 H) 7.91 (d, 2 H) 8.36 (s, 1 H) 8.40 - 8.48 (m, 1 H) 9.61 (s, 1 H). ESI-MS: m/z 471.5 $(M + H)^+$.

Example 19: 5-((2*H*-Indazol-2-yl)methyl)-N-(2-aminophenyl)thiophene-2-carboxamide



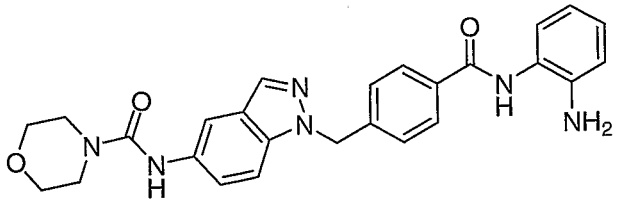
[0341] The title compound was prepared using a procedure analogous to that described in Examples 1 and 2. ^{1}H NMR (400 MHz, DMSO-D6) δ ppm 4.88 (s, 2 H) 5.89 (s, 2 H) 6.54 - 6.60 (m, 1 H) 6.75 (d, J=8.08 Hz, 1 H) 6.94 - 6.99 (m, 1 H) 7.02 - 7.10 (m, 2 H) 7.22 - 7.30 (m, 2 H) 7.62 (d, J=8.84 Hz, 1 H) 7.72 (d, J=8.59 Hz, 1 H) 7.83 (d, J=3.03 Hz, 1 H) 8.51 (s, 1 H) 9.68 (s, 1 H). ESI-MS: m/z 349.4 $(M + H)^+$.

Example 20: N-(2-Aminophenyl)-5-((5-nitro-2*H*-indazol-2-yl)methyl)thiophene-2-carboxamide



[0342] The title compound was prepared using a procedure analogous to that described in Examples 1 and 2. ^{1}H NMR (400 MHz, DMSO-D6) δ ppm 4.89 (s, 2 H) 6.01 (s, 2 H) 6.55 - 6.59 (m, 1 H) 6.75 (d, J=8.08 Hz, 1 H) 6.95 (d, J=7.83 Hz, 1H) 7.07 (d, J=7.83 Hz, 1 H) 7.30 (s, 1 H) 7.82 (d, J=9.35 Hz, 2 H) 8.01 - 8.05 (m, 1 H) 8.93 - 8.97 (m, 2 H) 9.70 (s, 1 H). ESI-MS: m/z 394.4 $(M + H)^+$.

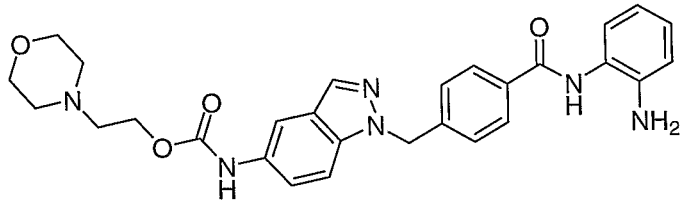
Example 21: N-(1-(4-((2-Aminophenyl)carbamoyl)benzyl)-1*H*-indazol-5-yl)morpholine-4-carboxamide



[0343] The title compound was prepared using a procedure analogous to that described in Examples 3 and 4. ^{1}H NMR (400 MHz, DMSO-D6) δ ppm 3.37 - 3.47 (m, 4 H) 3.50 -

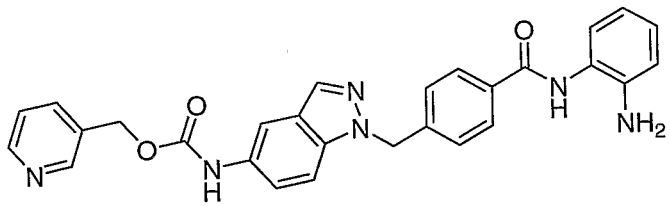
3.66 (m, 4 H) 5.62 (s, 2 H) 6.56 (m, 1 H) 6.74 (d, J=8.59 Hz, 1 H) 6.94 (m, 1 H) 7.11 (m, 1 H) 7.29 (d, J=8.08 Hz, 2 H) 7.39 (dd, J=9.09, 1.77 Hz, 1 H) 7.57 (d, J=9.09 Hz, 1 H) 7.74 - 7.89 (m, 3 H) 7.96 - 8.05 (m, 1 H) 8.52 (s, 1 H) 9.57 (s, 1 H). ESI-MS: m/z 471.5 $(M + H)^+$.

Example 22: 2-Morpholinoethyl 1-(4-((2-aminophenyl)carbamoyl)benzyl)-1*H*-indazol-5-ylcarbamate



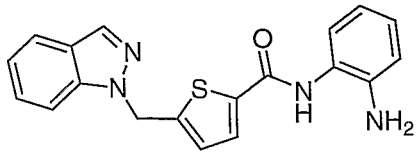
[0344] The title compound was prepared using a procedure analogous to that described in Examples 3 and 4. ^{1}H NMR (400 MHz, DMSO-D6) δ ppm 2.41 (m, 2 H) 2.56 (m, 2 H) 3.55 (m, 4 H) 4.18 (m, 4 H) 4.85 (s, 2 H) 5.68 (s, 2 H) 6.47 - 6.63 (m, 1 H) 6.73 (d, J=8.08 Hz, 1 H) 6.85 - 6.99 (m, 1 H) 7.10 (s, 1 H) 7.28 (d, J=8.34 Hz, 2 H) 7.39 (d, J=8.84 Hz, 1 H) 7.61 (d, J=9.09 Hz, 1 H) 7.87 (d, J=8.08 Hz, 3 H) 8.04 (s, 1 H) 9.55 (s, 1 H) 9.60 - 9.71 (m, 1 H). ESI-MS: m/z 515.6 $(M + H)^+$.

Example 23: Pyridin-3-ylmethyl 1-(4-((2-aminophenyl)carbamoyl)benzyl)-1*H*-indazol-5-ylcarbamate



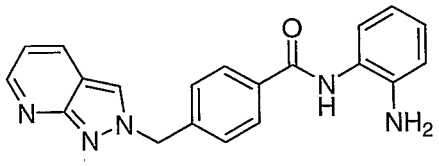
[0345] The title compound was prepared using a procedure analogous to that described in Examples 3 and 4. ^{1}H NMR (400 MHz, DMSO-D6) δ ppm 4.85 (bs, 2 H) 5.18 (s, 2 H) 5.69 (s, 2 H) 6.48 - 6.59 (m, 1 H) 6.73 (dd, J=8.08, 1.26 Hz, 1 H) 6.87 - 6.98 (m, 1 H) 7.11 (d, J=7.33 Hz, 1 H) 7.28 (d, J=8.34 Hz, 2 H) 7.34 - 7.47 (m, 2 H) 7.62 (d, J=9.09 Hz, 2 H) 7.77 - 7.94 (m, 3 H) 8.03 - 8.08 (m, 1 H) 8.54 (dd, J=4.80, 1.52 Hz, 1 H) 8.65 (d, J=1.77 Hz, 1 H) 9.56 (s, 1 H) 9.78 (s, 1 H). ESI-MS: m/z 493.5 $(M + H)^+$.

Example 24: 5-((1*H*-Indazol-1-yl)methyl)-N-(2-aminophenyl)thiophene-2-carboxamide



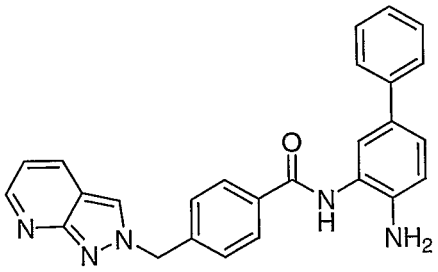
[0346] The title compound was prepared using a procedure analogous to that described in Examples 1 and 2. ^{1}H NMR (400 MHz, DMSO-D6) δ ppm 4.86 (s, 2 H) 5.90 (s, 2 H) 6.52 - 6.59 (m, 1 H) 6.74 (d, J=7.33 Hz, 1 H) 6.91 - 6.99 (m, 1 H) 7.05 (d, J=7.33 Hz, 1 H) 7.13 - 7.23 (m, 2 H) 7.42 (s, 1 H) 7.79 (m, 3 H) 8.15 (s, 1 H) 9.62 (s, 1 H). ESI-MS: m/z 349.4 $(M + H)^+$.

Example 25: 4-((2*H*-Pyrazolo[3,4-b]pyridin-2-yl)methyl)-N-(2-aminophenyl)benzamide



[0347] The title compound was prepared using a procedure analogous to that described in Examples 1 and 2. ^{1}H NMR (400 MHz, DMSO-D6) of the *bis*-trifluoroacetic acid salt: δ ppm 6.11 (s, 2 H) 6.79 (d, J=8.08 Hz, 1 H) 6.92 (d, J=8.08 Hz, 1 H) 7.02 - 7.10 (m, 1 H) 7.19 (d, J=7.58 Hz, 1 H) 7.63 (d, J=8.08 Hz, 2H) 7.79 (dd, J=8.08, 5.81 Hz, 1 H) 7.97 (d, J=8.34 Hz, 2 H) 9.11 - 9.19 (m, 1 H) 9.23 (d, J=7.83 Hz, 1 H) 9.40 (d, J=4.80 Hz, 1 H) 9.86 (s, 1 H). ESI-MS: m/z 344.4 $(M + H)^+$.

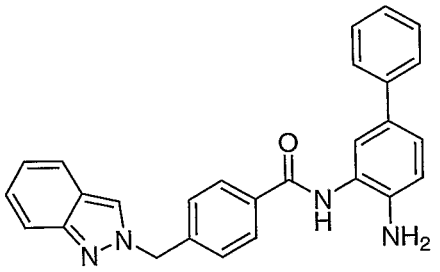
Example 26: *N*-(4-Amino-biphenyl-3-yl)-4-pyrazolo[3,4-*b*]pyridin-2-ylmethyl-benzamide



[0348] The title compound was prepared using a procedure analogous to that described in Examples 1 and 2. ^{1}H NMR (400 MHz, DMSO-D6) of the *bis*-trifluoroacetic acid salt:

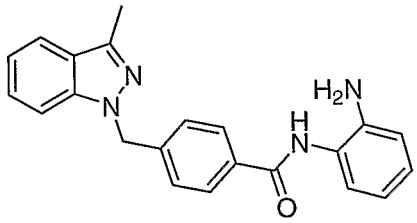
δ ppm 6.11 (s, 2H) 6.91 (d, J=8.34 Hz, 1 H) 7.24 (t, J=7.33 Hz, 1 H) 7.33 - 7.41 (m, 3 H) 7.48 - 7.56 (m, 3 H) 7.64 (d, J=8.34 Hz, 2 H) 7.79 (dd, J=8.08, 5.81 Hz, 1 H) 8.00 (d, J=8.34 Hz, 2 H) 9.16 (br. s., 1 H) 9.23 (d, J=7.83 Hz, 1 H) 9.35 - 9.45 (m, 1 H) 9.82 (s, 1 H). ESI-MS: m/z 420.5 $(M + H)^+$.

Example 27: *N*-(4-Amino-biphenyl-3-yl)-4-indazol-2-ylmethyl-benzamide



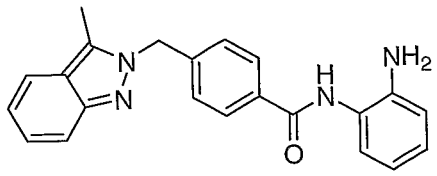
[0349] The title compound was prepared using a procedure analogous to that described in Examples 1 and 2. ^{1}H NMR (400 MHz, DMSO-D6) of the trifluoroacetic acid salt: δ ppm 5.74 (s, 2 H) 6.98 - 7.06 (m, 1 H) 7.08 (d, J=8.34 Hz, 1 H) 7.18 - 7.25 (m, 1 H) 7.28 (t, 1 H) 7.35 - 7.48 (m, 5 H) 7.58 (m, 4 H) 7.71 (d, J=8.34 Hz, 1 H) 7.98 (d, J=8.08 Hz, 2 H) 8.53 (s, 1 H) 10.02 (s, 1 H). ESI-MS: m/z 419.5 $(M + H)^+$.

Example 28: N-(2-Aminophenyl)-4-((3-methyl-1*H*-indazol-1-yl)methyl)benzamide



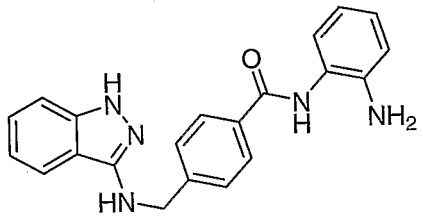
[0350] The title compound was prepared using a procedure analogous to that described in Examples 1 and 2. ^{1}H NMR (400 MHz, DMSO-D6) δ ppm 2.48 (s, 3 H) 4.87 (s, 2 H) 5.66 (s, 2 H) 6.54 - 6.61 (m, 1 H) 6.76 (dd, J=7.83, 1.26 Hz, 1 H) 6.91 - 6.99 (m, 1 H) 7.09 - 7.17 (m, 2 H) 7.31 (d, J=8.34 Hz, 2 H) 7.34 - 7.40 (m, 1 H) 7.64 (d, J=8.34 Hz, 1 H) 7.73 (d, J=8.08 Hz, 1 H) 7.89 (d, J=8.34 Hz, 2 H) 9.57 (s, 1 H). ESI-MS: m/z 357.4 $(M + H)^+$.

Example 29: N-(2-Aminophenyl)-4-((3-methyl-2*H*-indazol-2-yl)methyl)benzamide



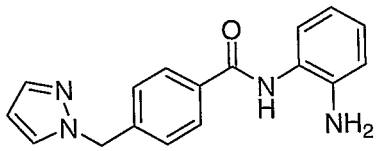
[0351] The title compound was prepared using a procedure analogous to that described in Examples 1 and 2. ^{1}H NMR (400 MHz, DMSO-D6) δ ppm 2.61 (s, 3 H) 4.88 (s, 2 H) 5.72 (s, 2 H) 6.50 - 6.64 (m, 1 H) 6.72 - 6.82 (m, 1 H) 6.93 - 7.03 (m, 2 H) 7.12 - 7.17 (m, 1 H) 7.20 - 7.31 (m, 3 H) 7.55 (d, J=8.59 Hz, 1 H) 7.68 (d, J=8.59 Hz, 1 H) 7.93 (d, J=8.08 Hz, 2 H) 9.62 (s, 1 H). ESI-MS: m/z 357.4 $(M + H)^+$.

Example 30: 4-((1H-indazol-3-ylamino)methyl)-N-(2-aminophenyl)benzamide



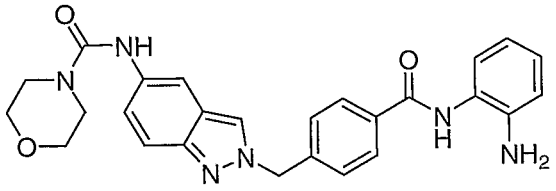
[0352] The title compound was prepared using a procedure analogous to that described in Examples 1 and 2. ^{1}H NMR (400 MHz, DMSO-D6) δ ppm 4.56 (d, J=6.15 Hz, 2 H) 4.88 (s, 2 H) 6.49 - 6.63 (m, 1 H) 6.63 - 6.73 (m, 1 H) 6.77 (d, J=7.98 Hz, 1 H) 6.84 - 7.01 (m, 2 H) 7.16 (d, J=7.48 Hz, 1 H) 7.20 - 7.29 (m, 2 H) 7.52 (d, J=8.14 Hz, 2 H) 7.77 (d, J=8.14 Hz, 1 H) 7.92 (d, J=8.14 Hz, 2 H) 9.60 (s, 1 H) 11.40 (s, 1 H). ESI-MS: m/z 358.4 $(M + H)^+$.

Example 31: 4-((1H-pyrazol-1-yl)methyl)-N-(2-aminophenyl)benzamide



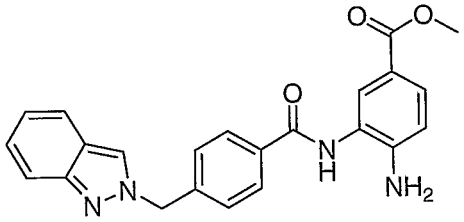
[0353] ^{1}H NMR (499 MHz, DMSO-d_6) of the trifluoroacetic acid salt: δ ppm 5.38 (s, 2 H), 6.25 - 6.33 (m, 2 H), 7.18 - 7.26 (m, 3 H), 7.31 - 7.38 (m, 3 H), 7.46 - 7.53 (m, 1 H), 7.84 - 7.89 (m, 1 H), 7.92 - 7.99 (m, 1 H), 10.09 (s, 1 H). ESI-MS: *m/z* 293.3 $(M + H)^+$.

Example 32: N-(2-(4-((2-Aminophenyl)carbamoyl)benzyl)-2*H*-indazol-5-yl)morpholine-4-carboxamide



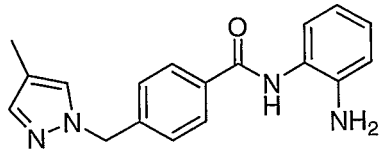
[0354] ^{1}H NMR (400 MHz, DMSO-D6) δ ppm 3.36 - 3.47 (m, 4 H) 3.61 (m, 4 H) 4.85 (s, 2 H) 5.69 (s, 2 H) 6.77 (m, 1 H) 6.94 (m, 1 H) 7.12 (m, 1 H) 7.27 (m, 1 H) 7.37 (d, 2 H) 7.46 (m, 1 H) 7.78 (s, 1 H) 7.87 (d, 2 H) 8.36 (s, 1 H) 8.46 (m, 1 H) 9.56 (s, 1 H). ESI-MS: *m/z* 471.5 $(M + H)^+$.

Example 33: Methyl 3-(4-((2H-indazol-2-yl)methyl)benzamido)-4-aminobenzoate



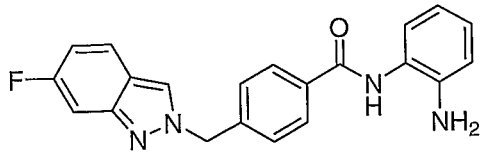
[0355] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 3.73 (s, 14 H), 5.72 (s, 10 H), 5.81 (s, 10 H), 6.74 (d, *J*=8.59 Hz, 6 H), 6.98 - 7.07 (m, 6 H), 7.17 - 7.26 (m, 6 H), 7.41 (d, *J*=8.34 Hz, 10 H), 7.51 - 7.61 (m, 11 H), 7.67 - 7.77 (m, 11 H), 7.94 (d, *J*=8.08 Hz, 10 H), 8.52 (s, 6 H), 9.60 (s, 1 H). ESI-MS: *m/z* 401.4 $(M + H)^+$.

Example 34: N-(2-aminophenyl)-4-((4-methyl-1H-pyrazol-1-yl)methyl)benzamide



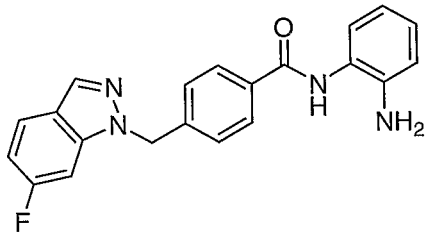
[0356] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 2.00 (s, 3 H), 4.87 (s, 2 H), 5.29 - 5.33 (m, 2 H), 6.54 - 6.60 (m, 1 H), 6.73 - 6.78 (m, 1 H), 6.92 - 6.97 (m, 1 H), 7.13 (d, *J*=7.58 Hz, 1 H), 7.25 - 7.30 (m, 3 H), 7.58 (s, 1 H), 7.91 (d, *J*=8.08 Hz, 2 H), 9.60 (s, 1 H). ESI-MS: *m/z* 307.4 $(M + H)^+$.

Example 35: N-(2-aminophenyl)-4-((6-fluoro-2H-indazol-2-yl)methyl)benzamide



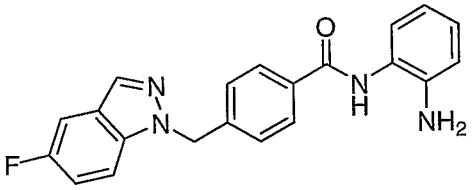
[0357] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 4.87 (s, 2 H), 5.70 (s, 2 H), 6.53 - 6.60 (m, 1 H), 6.75 (d, *J*=8.08 Hz, 1 H), 6.91 - 6.99 (m, 2 H), 7.13 (d, *J*=8.08 Hz, 1 H), 7.31 (d, *J*=10.36 Hz, 1 H), 7.41 (d, *J*=8.08 Hz, 2 H), 7.76 - 7.83 (m, 1 H), 7.93 (d, *J*=8.08 Hz, 2 H), 8.58 (s, 1 H), 9.61 (s, 1 H). ESI-MS: *m/z* 361.4 $(M + H)^+$.

Example 36: N-(2-aminophenyl)-4-((6-fluoro-1H-indazol-1-yl)methyl)benzamide



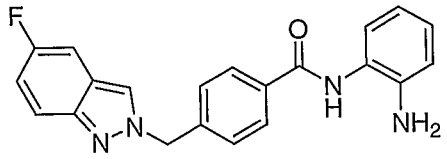
[0358] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 4.86 (s, 2 H), 5.67 - 5.72 (m, 2 H), 6.53 - 6.59 (m, 1 H), 6.74 (dd, *J*=8.08, 1.26 Hz, 1 H), 6.91 - 6.96 (m, 1 H), 6.99 - 7.06 (m, 1 H), 7.11 (d, *J*=7.33 Hz, 1 H), 7.33 (d, *J*=8.08 Hz, 2 H), 7.59 - 7.66 (m, 1 H), 7.81 (dd, *J*=8.84, 5.31 Hz, 1 H), 7.88 (d, *J*=8.08 Hz, 2 H), 8.13 - 8.16 (m, 1 H), 9.57 (s, 1 H). ESI-MS: *m/z* 361.4 $(M + H)^+$.

Example 37: N-(2-aminophenyl)-4-((5-fluoro-1H-indazol-1-yl)methyl)benzamide



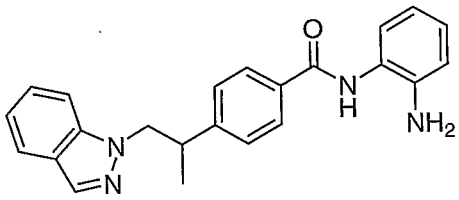
[0359] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 4.86 (s, 2 H), 5.75 (s, 2 H), 6.55 (s, 1 H), 6.74 (d, *J*=7.83 Hz, 1 H), 6.92 (d, *J*=7.58 Hz, 1 H), 7.10 (s, 1 H), 7.23 - 7.33 (m, 3 H), 7.49 - 7.59 (m, 1 H), 7.75 (s, 1 H), 7.87 (s, 2 H), 8.11 (s, 1 H), 9.57 (s, 1 H). ESI-MS: *m/z* 361.4 $(M + H)^+$.

Example 38: N-(2-aminophenyl)-4-((5-fluoro-2H-indazol-2-yl)methyl)benzamide



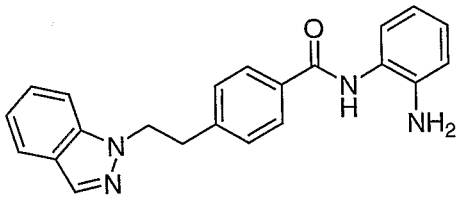
[0360] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 4.87 (s, 2 H), 5.68 (s, 2 H), 6.52 - 6.59 (m, 1 H), 6.71 - 6.77 (m, 1 H), 6.91 - 6.98 (m, 1 H), 7.09 - 7.17 (m, 2 H), 7.37 - 7.48 (m, 3 H), 7.62 - 7.68 (m, 1 H), 7.93 (d, *J*=8.34 Hz, 2 H), 8.50 (s, 1 H), 9.60 (s, 1 H). ESI-MS: *m/z* 361.4 $(M + H)^+$.

Example 39: 4-(1-(1H-indazol-1-yl)propan-2-yl)-N-(2-aminophenyl)benzamide



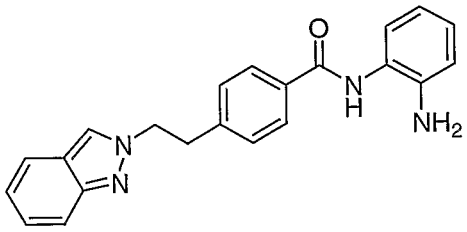
[0361] ^{1}H NMR (400 MHz, DMSO-d_6) of the trifluoroacetic acid salt: δ ppm 1.20 (d, *J*=6.82 Hz, 3 H), 3.51 - 3.62 (m, 1 H), 4.54 - 4.65 (m, 2 H), 6.95 (s, 2 H), 7.01 - 7.13 (m, 3 H), 7.25 (d, *J*=7.58 Hz, 1 H), 7.29 - 7.35 (m, 1 H), 7.44 (d, *J*=8.34 Hz, 2 H), 7.65 - 7.72 (m, 2 H), 7.85 (d, *J*=8.08 Hz, 2 H), 8.02 (s, 1 H), 9.84 - 10.01 (m, 1 H). ESI-MS: *m/z* 371.4 $(M + H)^+$.

Example 40: 4-(2-(1H-indazol-1-yl)ethyl)-N-(2-aminophenyl)benzamide



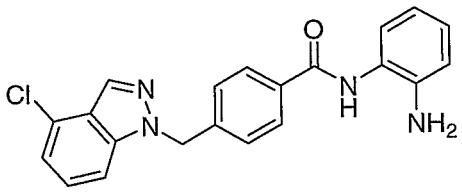
[0362] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 3.17 - 3.28 (m, 2 H), 4.68 (t, *J*=7.07 Hz, 2 H), 4.85 (s, 2 H), 6.51 - 6.62 (m, 1 H), 6.75 (dd, *J*=8.08, 1.26 Hz, 1 H), 6.88 - 7.00 (m, 1 H), 7.03 - 7.18 (m, 2 H), 7.26 - 7.38 (m, 3 H), 7.62 (d, *J*=8.34 Hz, 1 H), 7.72 (d, *J*=8.08 Hz, 1 H), 7.78 - 7.86 (m, 2 H), 8.04 (s, 1 H), 9.56 (s, 1 H). ESI-MS: *m/z* 357.4 $(M + H)^+$.

Example 41: 4-(2-(2H-indazol-2-yl)ethyl)-N-(2-aminophenyl)benzamide



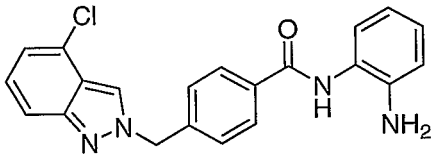
[0363] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 3.34 (t, *J*=7.07 Hz, 2 H), 4.72 (t, *J*=7.07 Hz, 2 H), 4.85 (s, 2 H), 6.51 - 6.62 (m, 1 H), 6.74 (dd, *J*=8.08, 1.26 Hz, 1 H), 6.88 - 7.03 (m, 2 H), 7.11 (d, *J*=7.33 Hz, 1 H), 7.15 - 7.25 (m, 1 H), 7.29 (d, *J*=8.08 Hz, 2 H), 7.54 - 7.68 (m, 2 H), 7.84 (d, *J*=8.08 Hz, 2 H), 8.19 - 8.30 (m, 1 H), 9.56 (s, 1 H). ESI-MS: *m/z* 357.4 $(M + H)^+$.

Example 42: N-(2-aminophenyl)-4-((4-chloro-1H-indazol-1-yl)methyl)benzamide



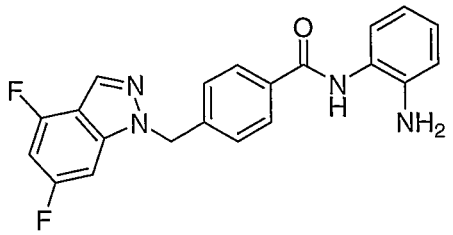
[0364] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 4.85 (s, 2 H), 5.74 - 5.81 (m, 2 H), 6.52 - 6.59 (m, 1 H), 6.71 - 6.77 (m, 1 H), 6.90 - 6.97 (m, 1 H), 7.11 (d, *J*=7.07 Hz, 1 H), 7.23 (d, *J*=7.58 Hz, 1 H), 7.31 (d, *J*=8.34 Hz, 2 H), 7.35 - 7.42 (m, 1 H), 7.74 (d, *J*=8.59 Hz, 1 H), 7.89 (d, *J*=8.08 Hz, 2 H), 8.18 - 8.23 (m, 1 H), 9.57 (s, 1 H). ESI-MS: *m/z* 377.8 $(M + H)^+$.

Example 43: N-(2-aminophenyl)-4-((4-chloro-2H-indazol-2-yl)methyl)benzamide



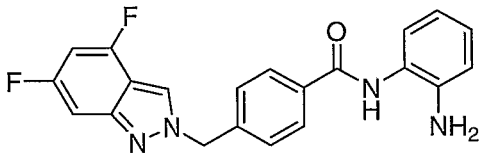
[0365] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 4.87 (s, 2 H), 5.70 - 5.78 (m, 2 H), 6.53 - 6.61 (m, 1 H), 6.75 (dd, *J*=8.08, 1.26 Hz, 1 H), 6.91 - 6.98 (m, 1 H), 7.13 (d, *J*=7.07 Hz, 2 H), 7.22 (dd, *J*=8.59, 7.07 Hz, 1 H), 7.41 - 7.49 (m, 2 H), 7.58 (d, *J*=8.59 Hz, 1 H), 7.93 (d, *J*=8.08 Hz, 2 H), 8.67 - 8.71 (m, 1 H), 9.61 (s, 1 H). ESI-MS: *m/z* 377.8 $(M + H)^+$.

Example 44: N-(2-aminophenyl)-4-((4,6-difluoro-1H-indazol-1-yl)methyl)benzamide



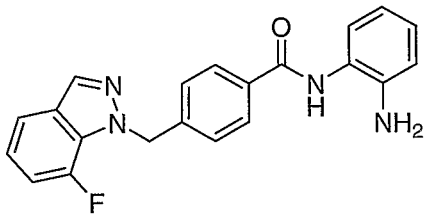
[0366] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 4.86 (s, 2 H), 5.67 - 5.75 (m, 2 H), 6.52 - 6.59 (m, 1 H), 6.74 (dd, *J*=8.08, 1.26 Hz, 1 H), 6.91 - 6.96 (m, 1 H), 7.00 - 7.07 (m, 1 H), 7.12 (d, *J*=7.58 Hz, 1 H), 7.34 (d, *J*=8.08 Hz, 2 H), 7.60 (d, *J*=9.35 Hz, 1 H), 7.89 (d, *J*=8.08 Hz, 2 H), 8.25 - 8.30 (m, 1 H), 9.58 (s, 1 H). ESI-MS: *m/z* 379.4 $(M + H)^+$.

Example 45: N-(2-aminophenyl)-4-((4,6-difluoro-2H-indazol-2-yl)methyl)benzamide



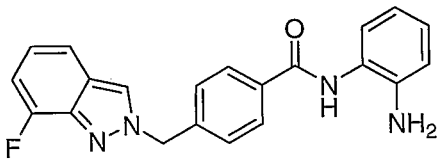
[0367] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 4.87 (s, 2 H), 5.67 - 5.74 (m, 2 H), 6.52 - 6.61 (m, 1 H), 6.75 (dd, *J*=7.83, 1.26 Hz, 1 H), 6.88 - 6.98 (m, 2 H), 7.13 (d, *J*=7.07 Hz, 1 H), 7.25 (d, *J*=8.84 Hz, 1 H), 7.44 (d, *J*=8.34 Hz, 2 H), 7.93 (d, *J*=8.08 Hz, 2 H), 8.82 (s, 1 H), 9.61 (s, 1 H). ESI-MS: *m/z* 379.4 $(M + H)^+$.

Example 46: N-(2-aminophenyl)-4-((7-fluoro-1H-indazol-1-yl)methyl)benzamide



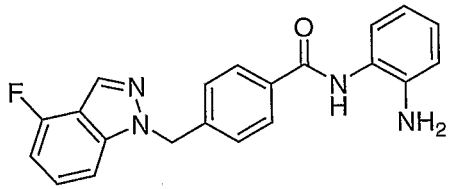
[0368] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 4.86 (s, 2 H), 5.78 (s, 2 H), 6.51 - 6.58 (m, 1 H), 6.71 - 6.76 (m, 1 H), 6.89 - 6.96 (m, 1 H), 7.07 - 7.14 (m, 2 H), 7.17 - 7.25 (m, 3 H), 7.61 (d, *J*=7.83 Hz, 1 H), 7.88 (d, *J*=8.08 Hz, 2 H), 8.24 (d, *J*=2.53 Hz, 1 H), 9.56 (s, 1 H). ESI-MS: *m/z* 361.4 $(M + H)^+$.

Example 47: N-(2-aminophenyl)-4-((7-fluoro-2H-indazol-2-yl)methyl)benzamide



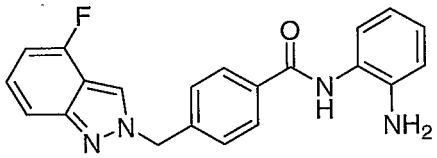
[0369] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 4.87 (s, 2 H), 5.72 - 5.78 (m, 2 H), 6.52 - 6.60 (m, 1 H), 6.75 (dd, *J*=8.08, 1.26 Hz, 1 H), 6.92 - 7.04 (m, 3 H), 7.13 (d, *J*=7.33 Hz, 1 H), 7.43 (d, *J*=8.08 Hz, 2 H), 7.51 - 7.57 (m, 1 H), 7.94 (d, *J*=8.08 Hz, 2 H), 8.66 (d, *J*=2.78 Hz, 1 H), 9.62 (s, 1 H). ESI-MS: *m/z* 361.4 $(M + H)^+$.

Example 48: N-(2-aminophenyl)-4-((4-fluoro-1H-indazol-1-yl)methyl)benzamide



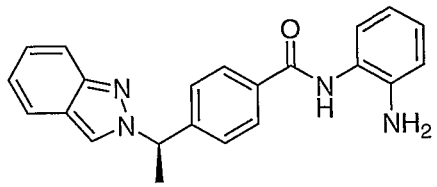
[0370] ^{1}H NMR (400 MHz, DMSO-d6) □ ppm 4.86 (s, 2 H), 5.77 (s, 2 H), 6.50 - 6.60 (m, 1 H), 6.73 (d, J=8.34 Hz, 1 H), 6.88 - 6.97 (m, 2 H), 7.11 (d, J=7.58 Hz, 1 H), 7.32 (d, J=8.08 Hz, 2 H), 7.34 - 7.42 (m, 1 H), 7.58 (d, J=8.34 Hz, 1 H), 7.89 (d, J=7.83 Hz, 2 H), 8.25 (s, 1 H), 9.57 (s, 1 H). ESI-MS: m/z 361.4 (M + H)+.

Example 49: N-(2-aminophenyl)-4-((4-fluoro-2H-indazol-2-yl)methyl)benzamide



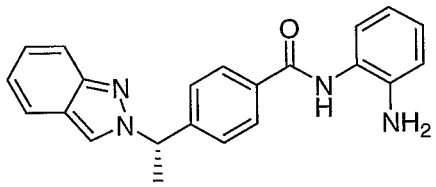
[0371] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 4.87 (s, 2 H), 5.69 - 5.75 (m, 2 H), 6.52 - 6.60 (m, 1 H), 6.72 - 6.82 (m, 2 H), 6.91 - 6.97 (m, 1 H), 7.12 (d, *J*=7.33 Hz, 1 H), 7.17 - 7.24 (m, 1 H), 7.39 - 7.46 (m, 3 H), 7.93 (d, *J*=8.08 Hz, 2 H), 8.74 (s, 1 H), 9.61 (s, 1 H). ESI-MS: *m/z* 361.4 $(M + H)^+$.

Example 50: (R)-4-(1-(2H-indazol-2-yl)ethyl)-N-(2-aminophenyl)benzamide



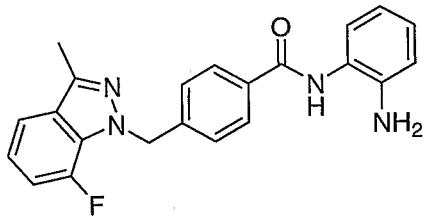
[0372] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 2.18 (d, J=7.07 Hz, 4 H), 3.36 (d, J=5.05 Hz, 2 H), 4.29 (q, 1 H), 5.07 (s, 2 H), 6.24 (d, J=7.07 Hz, 1 H), 6.76 (s, 1 H), 6.96 (s, 1 H), 7.13 (s, 1 H), 7.24 (d, J=8.59 Hz, 2 H), 7.32 (s, 1 H), 7.39 - 7.44 (m, 1 H), 7.63 (d, J=8.08 Hz, 3 H), 7.80 (d, J=8.84 Hz, 2 H), 7.90 (d, J=8.34 Hz, 1 H), 8.11 (d, J=8.34 Hz, 3 H), 8.75 (s, 1 H), 9.79 (s, 1 H). ESI-MS: m/z 357.4 $(M + H)^+$.

Example 51: (S)-4-(1-(2H-indazol-2-yl)ethyl)-N-(2-aminophenyl)benzamide



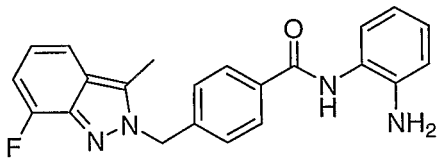
[0373] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 2.18 (d, J=7.07 Hz, 4 H), 3.36 (d, J=5.05 Hz, 2 H), 4.29 (q, 1 H), 5.07 (s, 2 H), 6.24 (d, J=7.07 Hz, 1 H), 6.76 (s, 1 H), 6.96 (s, 1 H), 7.13 (s, 1 H), 7.24 (d, J=8.59 Hz, 2 H), 7.32 (s, 1 H), 7.39 - 7.44 (m, 1 H), 7.63 (d, J=8.08 Hz, 3 H), 7.80 (d, J=8.84 Hz, 2 H), 7.90 (d, J=8.34 Hz, 1 H), 8.11 (d, J=8.34 Hz, 3 H), 8.75 (s, 1 H), 9.79 (s, 1 H). ESI-MS: m/z 357.4 $(M + H)^+$.

Example 52: N-(2-aminophenyl)-4-((7-fluoro-3-methyl-1H-indazol-1-yl)methyl)benzamide



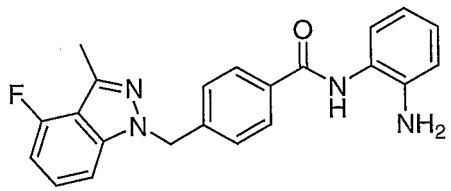
[0374] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 2.51 (s, 3 H), 4.86 (s, 2 H), 5.62 - 5.71 (m, 2 H), 6.51 - 6.59 (m, 1 H), 6.73 (d, J=7.83 Hz, 1 H), 6.89 - 6.97 (m, 1 H), 7.04 - 7.14 (m, 2 H), 7.15 - 7.25 (m, 3 H), 7.56 (d, J=8.08 Hz, 1 H), 7.87 (d, J=7.83 Hz, 2 H), 9.56 (s, 1 H). ESI-MS: m/z 375.4 $(M + H)^+$.

Example 53: N-(2-aminophenyl)-4-((7-fluoro-3-methyl-2H-indazol-2-yl)methyl)benzamide



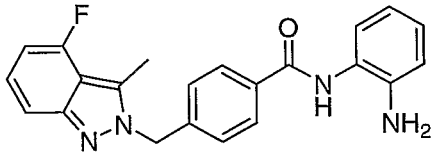
[0375] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 2.61 (s, 3 H), 4.87 (s, 2 H), 5.74 (s, 2 H), 6.53 - 6.59 (m, 1 H), 6.74 (dd, *J*=8.08, 1.26 Hz, 1 H), 6.91 - 7.02 (m, 3 H), 7.12 (d, *J*=7.58 Hz, 1 H), 7.29 (d, *J*=8.08 Hz, 2 H), 7.51 (d, *J*=8.34 Hz, 1 H), 7.93 (d, *J*=8.08 Hz, 2 H), 9.61 (s, 1 H). ESI-MS: *m/z* 375.4 $(M + H)^+$.

Example 54: N-(2-aminophenyl)-4-((4-fluoro-3-methyl-1H-indazol-1-yl)methyl)benzamide



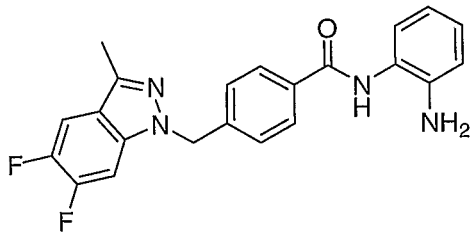
[0376] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 2.53 - 2.58 (m, 3 H), 4.86 (s, 2 H), 5.65 (s, 2 H), 6.51 - 6.59 (m, 1 H), 6.74 (dd, *J*=7.83, 1.26 Hz, 1 H), 6.84 (dd, *J*=10.86, 7.58 Hz, 1 H), 6.90 - 6.97 (m, 1 H), 7.11 (d, *J*=7.83 Hz, 1 H), 7.25 - 7.36 (m, 3 H), 7.48 (d, *J*=8.59 Hz, 1 H), 7.88 (d, *J*=8.08 Hz, 2 H), 9.56 (s, 1 H). ESI-MS: *m/z* 375.4 $(M + H)^+$.

Example 55: N-(2-aminophenyl)-4-((4-fluoro-3-methyl-2H-indazol-2-yl)methyl)benzamide



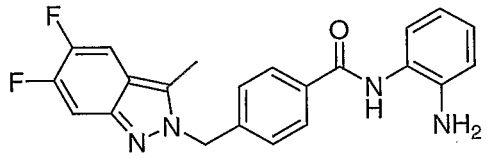
[0377] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 2.65 - 2.71 (m, 3 H), 4.87 (s, 2 H), 5.71 (s, 2 H), 6.53 - 6.60 (m, 1 H), 6.66 - 6.77 (m, 2 H), 6.91 - 6.98 (m, 1 H), 7.09 - 7.19 (m, 2 H), 7.29 (d, *J*=8.08 Hz, 2 H), 7.36 (d, *J*=8.59 Hz, 1 H), 7.92 (d, *J*=8.34 Hz, 2 H), 9.61 (s, 1 H). ESI-MS: *m/z* 375.4 $(M + H)^+$.

Example 56: N-(2-aminophenyl)-4-((5,6-difluoro-3-methyl-1H-indazol-1-yl)methyl)benzamide



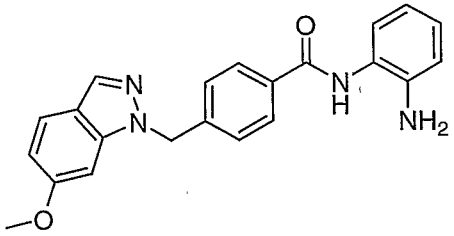
[0378] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 2.45 (s, 3 H), 4.86 (s, 2 H), 5.60 (s, 2 H), 6.51 - 6.60 (m, 1 H), 6.74 (d, *J*=8.08 Hz, 1 H), 6.89 - 6.98 (m, 1 H), 7.12 (d, *J*=7.83 Hz, 1 H), 7.32 (d, *J*=7.83 Hz, 2 H), 7.78 - 7.84 (m, 1 H), 7.85 - 7.91 (m, 3 H), 9.56 (s, 1 H). ESI-MS: *m/z* 393.4 $(M + H)^+$.

Example 57: N-(2-aminophenyl)-4-((5,6-difluoro-3-methyl-2H-indazol-2-yl)methyl)benzamide



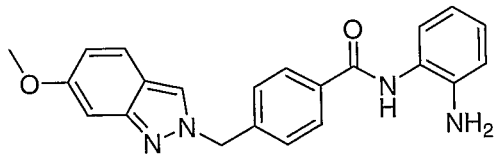
[0379] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 2.57 (s, 3 H), 4.98 (s, 1 H), 5.67 (s, 2 H), 6.58 (s, 1 H), 6.76 (s, 1 H), 6.95 (s, 1 H), 7.13 (s, 1 H), 7.27 (s, 2 H), 7.55 (s, 1 H), 7.75 (s, 1 H), 7.90 (s, 3 H), 9.62 (s, 1 H). ESI-MS: *m/z* 393.4 $(M + H)^+$.

Example 58: N-(2-aminophenyl)-4-((6-methoxy-1H-indazol-1-yl)methyl)benzamide



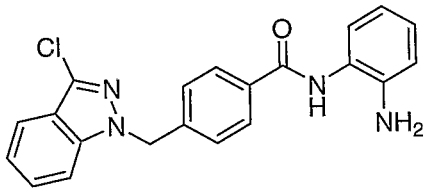
[0380] ^{1}H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 3.31 (s, 3 H), 4.85 (s, 2 H), 5.68 (s, 2 H), 6.56 (s, 1 H), 6.72 - 6.79 (m, 2 H), 6.93 (s, 1 H), 7.11 (s, 1 H), 7.20 (s, 1 H), 7.30 (d, *J*=8.08 Hz, 2 H), 7.61 (s, 1 H), 7.88 (d, *J*=8.08 Hz, 2 H), 7.98 (s, 1 H), 9.56 (s, 1 H). ESI-MS: *m/z* 373.4 $(M + H)^+$.

Example 59: N-(2-aminophenyl)-4-((6-methoxy-2H-indazol-2-yl)methyl)benzamide



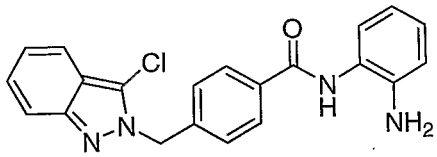
[0381] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 3.71 - 3.79 (m, 3 H), 4.87 (s, 2 H), 5.63 (s, 2 H), 6.51 - 6.62 (m, 1 H), 6.64 - 6.71 (m, 1 H), 6.72 - 6.78 (m, 1 H), 6.90 (d, *J*=1.77 Hz, 1 H), 6.91 - 6.97 (m, 1 H), 7.13 (d, *J*=7.83 Hz, 1 H), 7.38 (d, *J*=8.34 Hz, 2 H), 7.57 (d, *J*=9.09 Hz, 1 H), 7.92 (d, *J*=8.08 Hz, 2 H), 8.38 (s, 1 H), 9.60 (s, 1 H). ESI-MS: *m/z* 373.4 $(M + H)^+$.

Example 60: N-(2-aminophenyl)-4-((3-chloro-1H-indazol-1-yl)methyl)benzamide



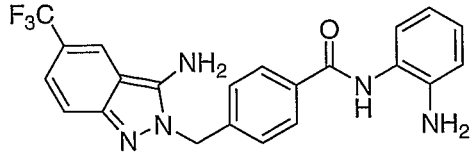
[0382] ^{1}H NMR (400 MHz, DMSO-d6) δ ppm 4.86 (s, 2 H), 5.72 (s, 2 H), 6.52 - 6.59 (m, 1 H), 6.74 (dd, *J*=8.08, 1.26 Hz, 1 H), 6.90 - 6.97 (m, 1 H), 7.11 (d, *J*=6.57 Hz, 1 H), 7.22 - 7.30 (m, 1 H), 7.35 (d, *J*=8.34 Hz, 2 H), 7.47 - 7.54 (m, 1 H), 7.68 (d, *J*=8.08 Hz, 1 H), 7.82 (d, J=8.59 Hz, 1 H), 7.89 (d, J=8.34 Hz, 2 H), 9.57 (s, 1 H). ESI-MS: m/z 377.8 (M + H)+.

Example 61: N-(2-aminophenyl)-4-((3-chloro-2H-indazol-2-yl)methyl)benzamide



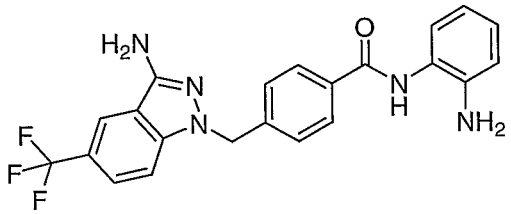
[0383] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 4.87 (s, 2 H), 5.73 - 5.82 (m, 2 H), 6.51 - 6.61 (m, 1 H), 6.74 (d, *J*=8.08 Hz, 1 H), 6.90 - 6.99 (m, 1 H), 7.10 - 7.19 (m, 2 H), 7.29 - 7.37 (m, 3 H), 7.53 (s, 1 H), 7.57 - 7.68 (m, 2 H), 7.93 (d, *J*=7.83 Hz, 2 H), 9.61 (s, 1 H). ESI-MS: *m/z* 377.8 $(M + H)^+$.

Example 62: 4-((3-amino-5-(trifluoromethyl)-2H-indazol-2-yl)methyl)-N-(2-aminophenyl)benzamide



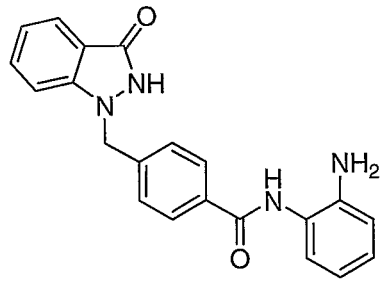
[0384] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 4.86 (s, 2 H), 5.47 (s, 2 H), 6.53 - 6.60 (m, 1 H), 6.73 - 6.80 (m, 3 H), 6.90 - 6.97 (m, 1 H), 7.13 (d, *J*=7.58 Hz, 1 H), 7.20 - 7.25 (m, 1 H), 7.25 - 7.34 (m, 3 H), 7.90 (d, *J*=8.08 Hz, 2 H), 8.17 (s, 1 H), 9.59 (s, 1 H). ESI-MS: *m/z* 425.5 $(M + H)^+$.

Example 63: 4-((3-amino-5-(trifluoromethyl)-1H-indazol-1-yl)methyl)-N-(2-aminophenyl)benzamide



[0385] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 4.85 (s, 2 H), 5.45 (s, 2 H), 5.85 (s, 2 H), 6.56 (td, *J*=7.58, 1.26 Hz, 1 H), 6.74 (dd, *J*=8.08, 1.26 Hz, 1 H), 6.89 - 6.97 (m, 1 H), 7.10 (s, 1 H), 7.28 (d, *J*=8.08 Hz, 2 H), 7.50 - 7.57 (m, 1 H), 7.66 (d, *J*=8.84 Hz, 1 H), 7.87 (d, *J*=8.08 Hz, 2 H), 8.20 (s, 1 H), 9.55 (s, 1 H). ESI-MS: *m/z* 425.5 $(M + H)^+$.

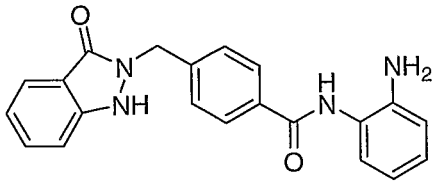
Example 64: N-(2-aminophenyl)-4-((3-oxo-2,3-dihydro-1H-indazol-1-yl)methyl)benzamide



[0386] ^{1}H NMR (400 MHz, DMSO-d_6) of the trifluoroacetic acid salt: δ ppm 5.46 (s, 2 H), 6.92 (s, 1 H), 7.01 (t, *J*=7.33 Hz, 2 H), 7.12 (s, 1 H), 7.25 (s, 1 H), 7.33 (d, *J*=7.83 Hz,

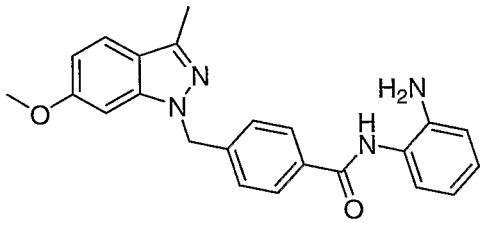
3 H), 7.55 (d, *J*=8.34 Hz, 1 H), 7.64 (d, *J*=8.08 Hz, 1 H), 7.90 (d, *J*=7.58 Hz, 2 H), 9.92 (s, 1 H). ESI-MS: *m/z* 359.3 $(M + H)^+$.

Example 65: N-(2-aminophenyl)-4-((3-oxo-1H-indazol-2(3H)-yl)methyl)benzamide



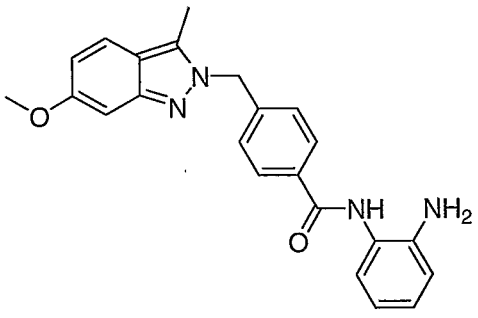
[0387] ^{1}H NMR (400 MHz, DMSO-d_6) of the trifluoroacetic acid salt: δ ppm 5.51 (s, 2 H), 6.89 (s, 1 H), 7.02 (s, 2 H), 7.15 (s, 1 H), 7.27 (s, 1 H), 7.37 (s, 2 H), 7.66 (s, 3 H), 8.02 (d, *J*=7.33 Hz, 2 H), 9.96 (s, 1 H), 11.98 (s, 1 H). ESI-MS: *m/z* 359.3 $(M + H)^+$.

Example 66: N-(2-aminophenyl)-4-((6-methoxy-3-methyl-1H-indazol-1-yl)methyl)benzamide



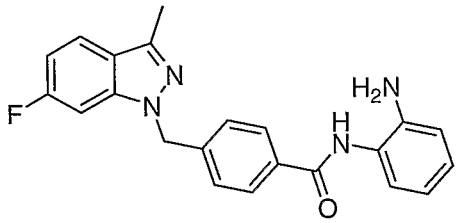
[0388] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 2.41 - 2.46 (m, 3 H), 3.78 - 3.84 (m, 3 H), 4.88 (s, 2 H), 5.60 (s, 2 H), 6.54 - 6.62 (m, 1 H), 6.72 - 6.79 (m, 2 H), 6.92 - 6.99 (m, 1 H), 7.11 - 7.18 (m, 2 H), 7.32 (d, *J*=8.34 Hz, 2 H), 7.58 (d, *J*=8.59 Hz, 1 H), 7.90 (d, *J*=8.34 Hz, 2 H), 9.58 (s, 1 H). ESI-MS: *m/z* 387.2 $(M + H)^+$.

Example 67: N-(2-aminophenyl)-4-((6-methoxy-3-methyl-2H-indazol-2-yl)methyl)benzamide



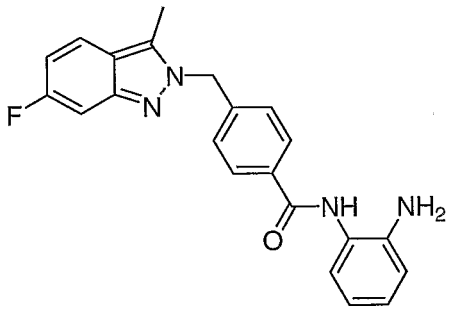
[0389] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 2.55 (s, 3 H), 3.79 (s, 3 H), 4.88 (s, 2 H), 5.63 (s, 2 H), 6.55 - 6.62 (m, 1 H), 6.62 - 6.68 (m, 1 H), 6.77 (dd, *J*=7.83, 1.26 Hz, 1 H), 6.86 (d, *J*=2.02 Hz, 1 H), 6.93 - 7.00 (m, 1 H), 7.14 (d, *J*=7.33 Hz, 1 H), 7.27 (d, *J*=8.34 Hz, 2 H), 7.55 (d, *J*=9.09 Hz, 1 H), 7.93 (d, *J*=8.08 Hz, 2 H), 9.62 (s, 1 H). ESI-MS: *m/z* 387.2 $(M + H)^+$.

Example 68: N-(2-aminophenyl)-4-((6-fluoro-3-methyl-1H-indazol-1-yl)methyl)benzamide



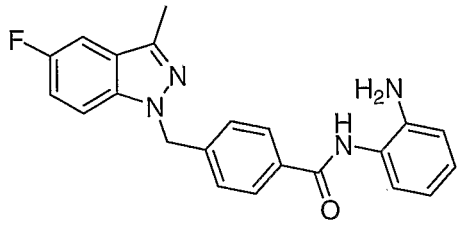
[0390] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 2.47 - 2.49 (m, 3 H), 4.87 (s, 2 H), 5.61 (s, 2 H), 6.55 - 6.61 (m, 1 H), 6.76 (dd, *J*=8.08, 1.52 Hz, 1 H), 6.93 - 7.02 (m, 2 H), 7.14 (d, *J*=7.83 Hz, 1 H), 7.34 (d, *J*=8.34 Hz, 2 H), 7.54 - 7.61 (m, 1 H), 7.77 (dd, *J*=8.84, 5.31 Hz, 1 H), 7.90 (d, *J*=8.34 Hz, 2 H), 9.57 (s, 1 H). ESI-MS: *m/z* 375.3 $(M + H)^+$.

Example 69: N-(2-aminophenyl)-4-((6-fluoro-3-methyl-2H-indazol-2-yl)methyl)benzamide



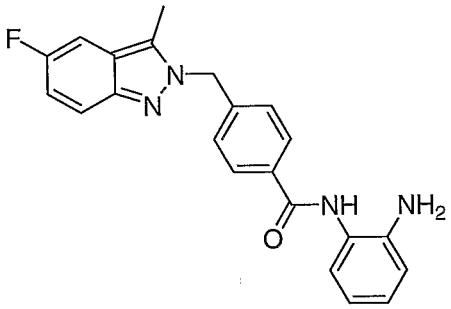
[0391] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 2.59 - 2.63 (m, 3 H), 4.88 (s, 2 H), 5.69 (s, 2 H), 6.53 - 6.62 (m, 1 H), 6.78 (dd, *J*=7.75, 1.52 Hz, 1 H), 6.87 - 6.99 (m, 2 H), 7.15 (d, *J*=7.33 Hz, 1 H), 7.24 - 7.35 (m, 3 H), 7.77 (dd, *J*=9.09, 5.56 Hz, 1 H), 7.94 (d, *J*=8.08 Hz, 2 H), 9.62 (s, 1 H). ESI-MS: *m/z* 375.3 $(M + H)^+$.

Example 70: N-(2-aminophenyl)-4-((5-fluoro-3-methyl-1H-indazol-1-yl)methyl)benzamide



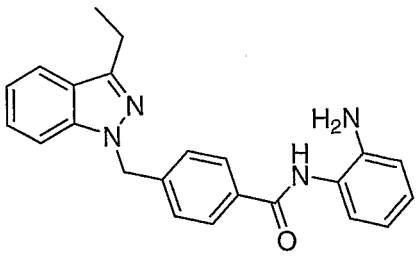
[0392] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 2.46 - 2.49 (m, 3 H), 4.87 (s, 2 H), 5.66 (s, 2 H), 6.53 - 6.62 (m, 1 H), 6.77 (d, *J*=1.26 Hz, 1 H), 6.91 - 7.01 (m, 1 H), 7.14 (d, *J*=7.07 Hz, 1 H), 7.25 - 7.35 (m, 3 H), 7.55 (d, *J*=2.27 Hz, 1 H), 7.70 (dd, *J*=9.09, 4.29 Hz, 1 H), 7.89 (d, *J*=8.08 Hz, 2 H), 9.57 (s, 1 H). ESI-MS: *m/z* 375.3 $(M + H)^+$.

Example 71: N-(2-aminophenyl)-4-((5-fluoro-3-methyl-2H-indazol-2-yl)methyl)benzamide



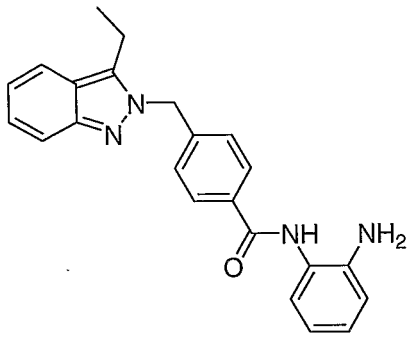
[0393] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 2.58 (s, 3 H), 4.88 (s, 2 H), 5.72 (s, 2 H), 6.55 - 6.62 (m, 1 H), 6.77 (dd, *J*=8.08, 1.26 Hz, 1 H), 6.93 - 7.00 (m, 1 H), 7.14 (td, *J*=9.35, 2.53 Hz, 2 H), 7.29 (d, *J*=8.34 Hz, 2 H), 7.46 (dd, *J*=9.60, 2.02 Hz, 1 H), 7.62 (dd, *J*=9.35, 4.55 Hz, 1 H), 7.94 (d, *J*=8.34 Hz, 2 H), 9.62 (s, 1 H). ESI-MS: *m/z* 375.4 $(M + H)^+$.

Example 72: N-(2-aminophenyl)-4-((3-ethyl-1H-indazol-1-yl)methyl)benzamide



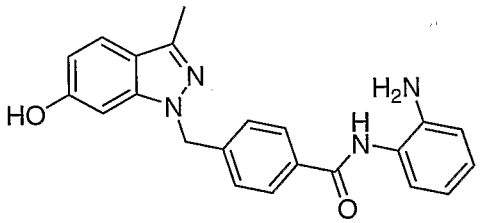
[0394] 1H NMR (400 MHz, DMSO-d_6) δ ppm 1.29 - 1.36 (m, 3 H), 2.95 (q, *J*=7.58 Hz, 2 H), 4.87 (s, 2 H), 5.67 (s, 2 H), 6.53 - 6.62 (m, 1 H), 6.72 - 6.81 (m, 1 H), 6.91 - 7.00 (m, 1 H), 7.08 - 7.18 (m, 2 H), 7.27 - 7.39 (m, 3 H), 7.63 (d, *J*=8.34 Hz, 1 H), 7.77 (d, *J*=8.08 Hz, 1 H), 7.89 (d, *J*=8.08 Hz, 1 H), 9.57 (s, 1 H). ESI-MS: *m/z* 371.4 $(M + H)^+$.

Example 73: N-(2-aminophenyl)-4-((3-ethyl-2H-indazol-2-yl)methyl)benzamide



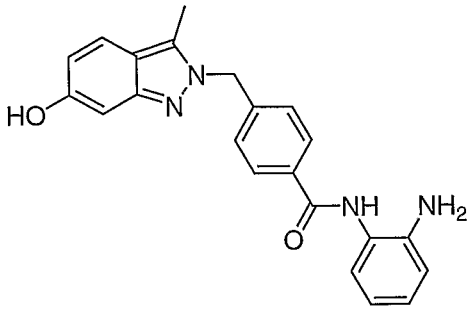
[0395] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 1.09 - 1.20 (m, 3 H), 3.09 (q, *J*=7.58 Hz, 2 H), 4.89 (s, 2 H), 5.75 (s, 2 H), 6.55 - 6.62 (m, 1 H), 6.74 - 6.80 (m, 1 H), 6.93 - 7.03 (m, 2 H), 7.14 (d, *J*=7.58 Hz, 1 H), 7.21 - 7.31 (m, 3 H), 7.56 (d, *J*=8.84 Hz, 1 H), 7.72 (d, *J*=8.59 Hz, 1 H), 7.93 (d, *J*=8.34 Hz, 2 H), 9.63 (s, 1 H). ESI-MS: *m/z* 371.4 $(M + H)^+$.

Example 74: N-(2-aminophenyl)-4-((6-hydroxy-3-methyl-1H-indazol-1-yl)methyl)benzamide



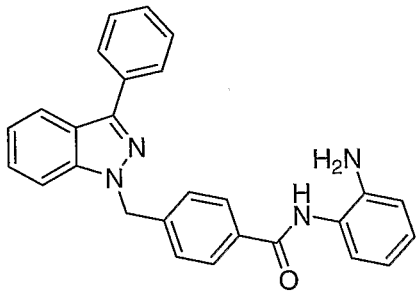
[0396] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 2.42 (s, 3 H), 5.52 (s, 2 H), 6.59 - 6.69 (m, 1 H), 6.74 (d, *J*=1.77 Hz, 1 H), 6.94 (s, 1 H), 7.04 (s, 1 H), 7.08 - 7.20 (m, 2 H), 7.23 - 7.34 (m, 3 H), 7.50 (d, *J*=8.84 Hz, 1 H), 7.92 (d, *J*=8.34 Hz, 2 H), 9.95 (s, 1 H). ESI-MS: *m/z* 373.3 $(M + H)^+$.

Example 75: N-(2-aminophenyl)-4-((6-hydroxy-3-methyl-2H-indazol-2-yl)methyl)benzamide



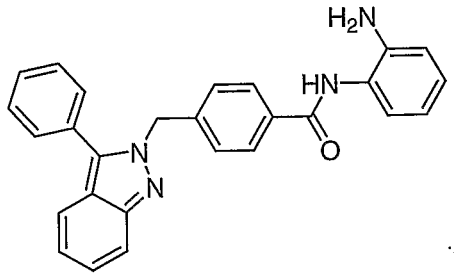
[0397] ^{1}H NMR (400 MHz, DMSO-d_6) of the trifluoroacetic acid salt: δ ppm 2.54 (s, 3 H), 3.97 (s, 1 H), 5.62 (s, 2 H), 6.56 - 6.65 (m, 1 H), 6.69 (d, *J*=1.52 Hz, 1 H), 7.01 (s, 1 H), 7.10 (d, *J*=7.83 Hz, 1 H), 7.14 - 7.23 (m, 1 H), 7.30 (d, *J*=8.08 Hz, 3 H), 7.52 (d, *J*=8.84 Hz, 1 H), 7.96 (d, *J*=8.34 Hz, 2 H), 10.07 (s, 1 H). ESI-MS: *m/z* 373.3 $(M + H)^+$.

Example 76: N-(2-aminophenyl)-4-((3-phenyl-1H-indazol-1-yl)methyl)benzamide



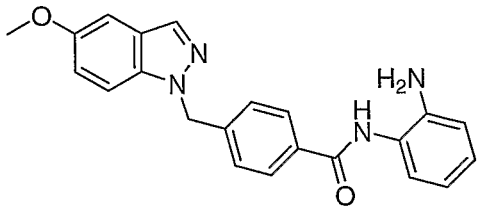
[0398] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 4.86 (s, 2 H), 5.78 - 5.87 (m, 2 H), 6.53 - 6.61 (m, 1 H), 6.75 (dd, *J*=8.08, 1.26 Hz, 1 H), 6.91 - 6.99 (m, 1 H), 7.13 (d, *J*=7.83 Hz, 1 H), 7.22 - 7.30 (m, 1 H), 7.38 - 7.49 (m, 3 H), 7.50 - 7.57 (m, 2 H), 7.80 (d, *J*=8.34 Hz, 1 H), 7.91 (d, *J*=8.34 Hz, 2 H), 8.00 (d, *J*=7.07 Hz, 2 H), 8.11 (d, *J*=8.08 Hz, 1 H), 9.57 (s, 1 H). ESI-MS: *m/z* 419.4 $(M + H)^+$.

Example 77: N-(2-aminophenyl)-4-((3-phenyl-2H-indazol-2-yl)methyl)benzamide



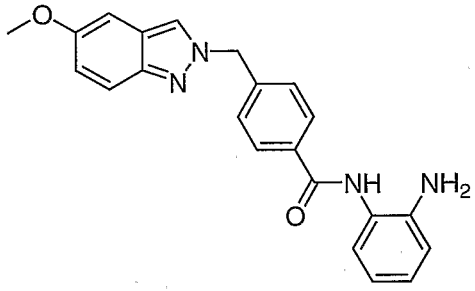
[0399] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 4.87 (s, 2 H), 5.77 (s, 2 H), 6.54 - 6.61 (m, 1 H), 6.76 (dd, *J*=8.08, 1.26 Hz, 1 H), 6.92 - 6.99 (m, 1 H), 7.09 - 7.17 (m, 3 H), 7.30 - 7.37 (m, 1 H), 7.52 - 7.63 (m, 3 H), 7.69 (d, *J*=8.84 Hz, 1 H), 7.89 (d, *J*=8.08 Hz, 2 H), 9.60 (s, 1 H). ESI-MS: *m/z* 419.4 $(M + H)^+$.

Example 78: N-(2-aminophenyl)-4-((5-methoxy-1H-indazol-1-yl)methyl)benzamide



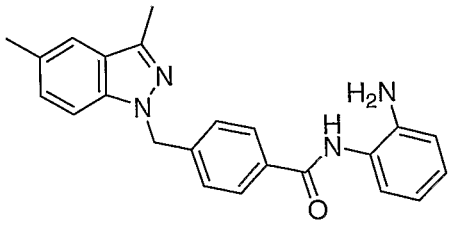
[0400] ^{1}H NMR (400 MHz, DMSO-d_6) of the trifluoroacetic acid salt: δ ppm 3.78 (s, 3 H), 5.71 (s, 2 H), 6.53 - 6.64 (m, 1 H), 6.78 (s, 1 H), 6.91 - 7.00 (m, 1 H), 7.01 - 7.08 (m, 1 H), 7.13 (s, 1 H), 7.20 (d, *J*=2.27 Hz, 1 H), 7.30 (d, *J*=8.08 Hz, 2 H), 7.61 (d, *J*=9.09 Hz, 1 H), 7.89 (d, *J*=8.08 Hz, 2 H), 8.01 (s, 1 H), 9.59 (s, 1 H). ESI-MS: *m/z* 373.3 $(M + H)^+$.

Example 79: N-(2-aminophenyl)-4-((5-methoxy-2H-indazol-2-yl)methyl)benzamide



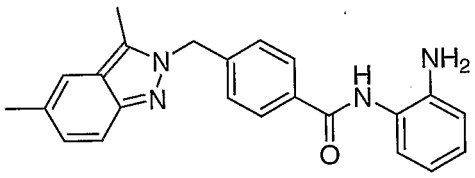
[0401] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 3.77 (s, 3 H), 5.69 (s, 2 H), 6.84 - 6.95 (m, 2 H), 6.95 - 7.05 (m, 2 H), 7.07 - 7.15 (m, 1 H), 7.26 (d, *J*=7.58 Hz, 1 H), 7.42 (d, *J*=8.34 Hz, 2 H), 7.51 (d, *J*=9.09 Hz, 1 H), 7.96 (d, *J*=8.34 Hz, 2 H), 8.35 (s, 1 H), 9.91 (s, 1 H). ESI-MS: *m/z* 373.3 $(M + H)^+$.

Example 80: N-(2-aminophenyl)-4-((3,5-dimethyl-1H-indazol-1-yl)methyl)benzamide



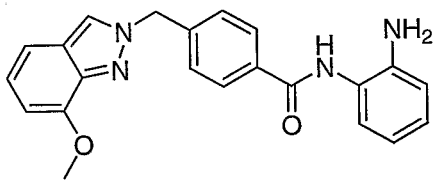
[0402] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 2.40 (s, 3 H), 2.44 - 2.48 (m, 3 H), 4.87 (s, 2 H), 5.62 (s, 2 H), 6.54 - 6.61 (m, 1 H), 6.76 (dd, *J*=8.08, 1.26 Hz, 1 H), 6.92 - 6.99 (m, 1 H), 7.13 (d, *J*=7.07 Hz, 1 H), 7.20 (dd, *J*=8.59, 1.26 Hz, 1 H), 7.28 (d, *J*=8.08 Hz, 2 H), 7.49 (s, 1 H), 7.52 (d, *J*=8.59 Hz, 1 H), 7.88 (d, *J*=8.08 Hz, 2 H), 9.57 (s, 1 H). ESI-MS: *m/z* 371.4 $(M + H)^+$.

Example 81: N-(2-aminophenyl)-4-((3,5-dimethyl-2H-indazol-2-yl)methyl)benzamide



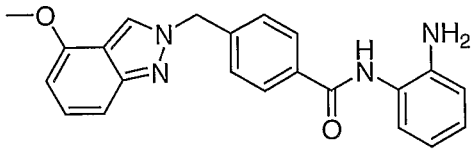
[0403] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 2.36 (s, 3 H), 2.56 (s, 3 H), 4.88 (s, 2 H), 5.69 (s, 2 H), 6.54 - 6.62 (m, 1 H), 6.77 (dd, *J*=8.08, 1.26 Hz, 1 H), 6.93 - 7.00 (m, 1 H), 7.07 (dd, *J*=8.84, 1.52 Hz, 1 H), 7.14 (d, *J*=7.07 Hz, 1 H), 7.26 (d, *J*=8.34 Hz, 2 H), 7.41 (s, 1 H), 7.45 (d, *J*=8.84 Hz, 1 H), 7.93 (d, *J*=8.08 Hz, 2 H), 9.62 (s, 1 H). ESI-MS: *m/z* 371.4 $(M + H)^+$.

Example 82: N-(2-aminophenyl)-4-((7-methoxy-2H-indazol-2-yl)methyl)benzamide



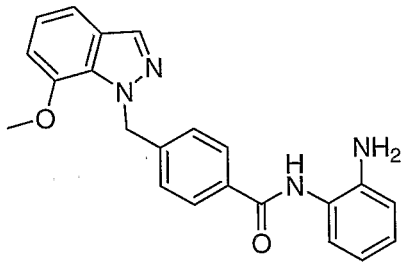
[0404] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 3.88 (s, 3 H), 4.89 (s, 2 H), 5.70 (s, 2 H), 6.54 - 6.65 (m, 2 H), 6.76 (d, *J*=7.58 Hz, 1 H), 6.90 - 7.01 (m, 2 H), 7.15 (s, 1 H), 7.24 (d, *J*=8.34 Hz, 1 H), 7.41 (d, *J*=7.58 Hz, 2 H), 7.95 (d, *J*=8.08 Hz, 2 H), 8.47 (s, 1 H), 9.62 (s, 1 H). ESI-MS: *m/z* 373.1 $(M + H)^+$.

Example 83: N-(2-aminophenyl)-4-((4-methoxy-2H-indazol-2-yl)methyl)benzamide



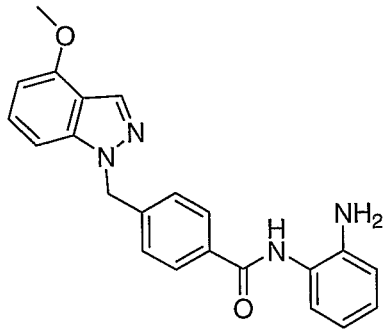
[0405] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 3.89 (s, 3 H), 4.89 (s, 2 H), 5.69 (s, 2 H), 6.36 - 6.46 (m, 1 H), 6.53 - 6.64 (m, 1 H), 6.76 (d, *J*=8.08 Hz, 1 H), 6.91 - 7.02 (m, 1 H), 7.11 - 7.20 (m, 3 H), 7.42 (d, *J*=7.83 Hz, 2 H), 7.94 (d, *J*=7.83 Hz, 2 H), 8.55 (s, 1 H), 9.62 (s, 1 H). ESI-MS: *m/z* 373.2 $(M + H)^+$.

Example 84: N-(2-aminophenyl)-4-((7-methoxy-1H-indazol-1-yl)methyl)benzamide



[0406] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 3.92 (s, 3 H), 4.87 (s, 2 H), 5.85 (s, 2 H), 6.54 - 6.61 (m, 1 H), 6.76 (d, *J*=7.83 Hz, 1 H), 6.87 (d, *J*=7.58 Hz, 1 H), 6.92 - 6.99 (m, 1 H), 7.03 - 7.10 (m, 1 H), 7.13 (d, *J*=7.83 Hz, 1 H), 7.24 (d, *J*=7.83 Hz, 2 H), 7.32 (d, *J*=8.08 Hz, 1 H), 7.88 (d, *J*=7.58 Hz, 2 H), 8.09 (s, 1 H), 9.56 (s, 1 H). ESI-MS: *m/z* 373.3 $(M + H)^+$.

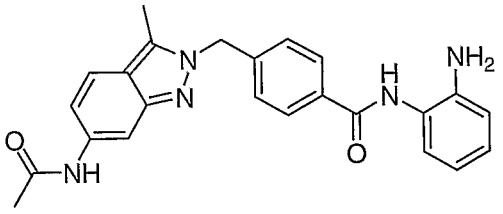
Example 85: N-(2-aminophenyl)-4-((4-methoxy-1H-indazol-1-yl)methyl)benzamide



[0407] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 3.93 (s, 3 H), 4.87 (s, 2 H), 5.72 (s, 2 H), 6.54 - 6.63 (m, 2 H), 6.76 (d, *J*=7.83 Hz, 1 H), 6.90 - 7.00 (m, 1 H), 7.13 (d, *J*=7.83 Hz, 1

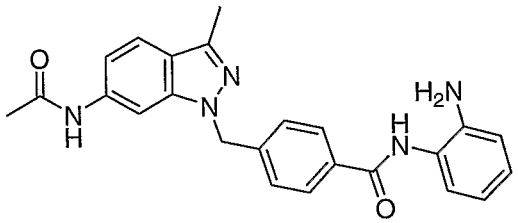
H), 7.23 - 7.33 (m, 4 H), 7.89 (d, *J*=7.83 Hz, 2 H), 8.10 (s, 1 H), 9.58 (s, 1 H). ESI-MS: *m/z* 373.3 $(M + H)^+$.

Example 86: 4-((6-acetamido-3-methyl-2H-indazol-2-yl)methyl)-N-(2-aminophenyl)benzamide



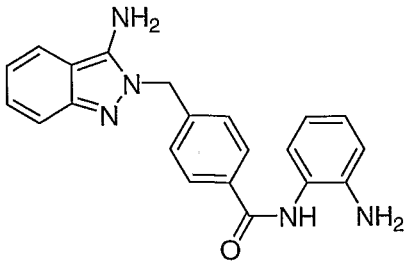
[0408] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 2.06 (s, 3 H), 2.53 - 2.57 (m, 2 H), 4.88 (s, 2 H), 5.66 (s, 2 H), 6.53 - 6.63 (m, 1 H), 6.76 (dd, *J*=8.08, 1.26 Hz, 1 H), 6.93 - 7.04 (m, 2 H), 7.14 (d, *J*=7.07 Hz, 1 H), 7.27 (d, *J*=8.08 Hz, 2 H), 7.59 (d, *J*=9.09 Hz, 1 H), 7.93 (d, *J*=8.08 Hz, 2 H), 7.99 (s, 1 H), 9.62 (s, 1 H), 9.91 (s, 1 H). ESI-MS: *m/z* 414.3 $(M + H)^+$.

Example 87: 4-((6-acetamido-3-methyl-1H-indazol-1-yl)methyl)-N-(2-aminophenyl)benzamide



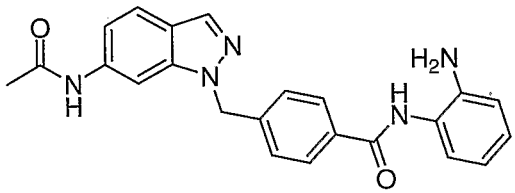
[0409] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 2.06 (s, 3 H), 2.44 - 2.48 (m, 3 H), 4.88 (s, 2 H), 5.56 (s, 2 H), 6.53 - 6.63 (m, 1 H), 6.73 - 6.81 (m, 1 H), 6.91 - 7.01 (m, 1 H), 7.08 - 7.19 (m, 2 H), 7.24 (d, *J*=8.08 Hz, 2 H), 7.63 (d, *J*=8.59 Hz, 1 H), 7.89 (d, *J*=8.08 Hz, 2 H), 8.01 (s, 1 H), 9.58 (s, 1 H), 10.09 (s, 1 H). ESI-MS: *m/z* 414.3 $(M + H)^+$.

Example 88: 4-((3-amino-2H-indazol-2-yl)methyl)-N-(2-aminophenyl)benzamide



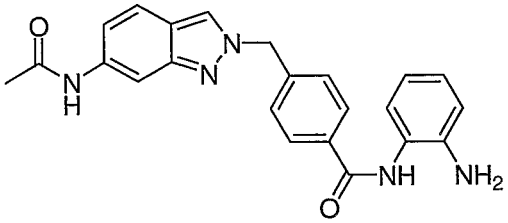
[0410] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 4.88 (s, 2 H), 5.46 (s, 2 H), 6.27 (s, 2 H), 6.58 (t, *J*=7.45 Hz, 1 H), 6.65 (t, *J*=7.33 Hz, 1 H), 6.76 (d, *J*=8.08 Hz, 1 H), 6.96 (t, *J*=7.58 Hz, 1 H), 7.05 (t, *J*=7.58 Hz, 1 H), 7.12 - 7.20 (m, 2 H), 7.29 (d, *J*=7.83 Hz, 2 H), 7.63 (d, *J*=8.34 Hz, 1 H), 7.91 (d, *J*=7.83 Hz, 2 H), 9.6 (s, 1H). ESI-MS: *m/z* 358.2 $(M + H)^+$.

Example 89: 4-((6-acetamido-1H-indazol-1-yl)methyl)-N-(2-aminophenyl)benzamide



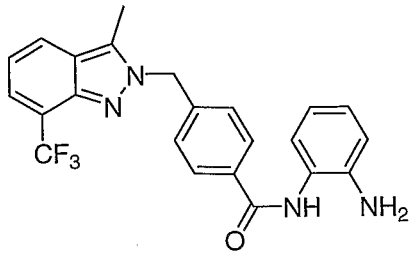
[0411] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 1.93 - 2.13 (m, 3 H), 4.87 (s, 2 H), 5.66 (s, 2 H), 6.53 - 6.61 (m, 1 H), 6.75 (dd, *J*=7.96, 1.39 Hz, 1 H), 6.91 - 6.98 (m, 1 H), 7.13 (dd, *J*=8.72, 1.64 Hz, 2 H), 7.24 (d, *J*=8.34 Hz, 2 H), 7.69 (d, *J*=8.59 Hz, 1 H), 7.90 (d, *J*=8.08 Hz, 2 H), 8.05 (s, 1 H), 8.08 (s, 1 H), 9.59 (s, 1 H), 10.11 (s, 1 H). ESI-MS: *m/z* 400.2 $(M + H)^+$.

Example 90: 4-((6-acetamido-2H-indazol-2-yl)methyl)-N-(2-aminophenyl)benzamide



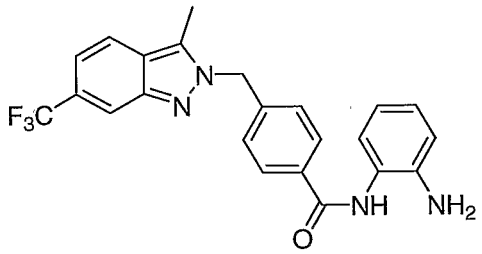
[0412] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 2.06 (s, 3 H), 4.88 (s, 2 H), 5.67 (s, 2 H), 6.51 - 6.65 (m, 1 H), 6.76 (dd, *J*=8.08, 1.26 Hz, 1 H), 6.89 - 7.00 (m, 1 H), 7.06 (dd, *J*=8.84, 1.77 Hz, 1 H), 7.14 (d, *J*=7.33 Hz, 1 H), 7.40 (d, *J*=8.08 Hz, 2 H), 7.63 (d, *J*=8.34 Hz, 1 H), 7.94 (d, *J*=8.08 Hz, 2 H), 8.04 (s, 1 H), 8.42 (s, 1 H), 9.62 (s, 1 H), 9.93 (s, 1 H). ESI-MS: *m/z* 400.2 $(M + H)^+$.

Example 91: N-(2-aminophenyl)-4-((3-methyl-7-(trifluoromethyl)-2H-indazol-2-yl)methyl)benzamide



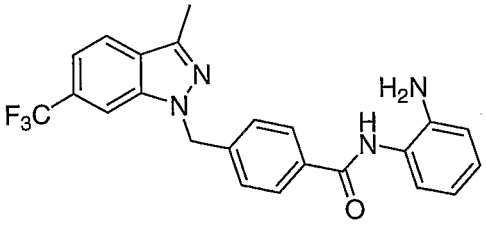
[0413] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 2.66 (s, 3 H), 4.89 (s, 2 H), 5.82 (s, 2 H), 6.58 (t, *J*=7.45 Hz, 1 H), 6.76 (d, *J*=7.83 Hz, 1 H), 6.96 (t, *J*=7.58 Hz, 1 H), 7.14 (ddd, *J*=7.26, 3.92, 3.73 Hz, 2 H), 7.28 (d, *J*=8.08 Hz, 2 H), 7.66 (d, *J*=6.82 Hz, 1 H), 7.94 (d, *J*=8.08 Hz, 2 H), 8.05 (d, *J*=8.34 Hz, 1 H), 9.62 (s, 1H). ESI-MS: *m/z* 425.2 $(M + H)^+$.

Example 92: N-(2-aminophenyl)-4-((3-methyl-6-(trifluoromethyl)-2H-indazol-2-yl)methyl)benzamide



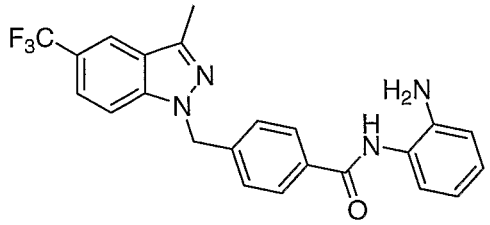
[0414] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 2.67 (s, 3 H), 4.88 (s, 2 H), 5.80 (s, 2 H), 6.58 (t, *J*=7.58 Hz, 1 H), 6.76 (d, *J*=7.83 Hz, 1 H), 6.96 (t, *J*=7.71 Hz, 1 H), 7.14 (d, *J*=7.83 Hz, 1 H), 7.22 (d, *J*=8.84 Hz, 1 H), 7.30 (d, *J*=8.08 Hz, 2 H), 7.92 - 8.02 (m, 4 H), 9.63 (s, 1H). ESI-MS: *m/z* 425.2 $(M + H)^+$.

Example 93: N-(2-aminophenyl)-4-((3-methyl-6-(trifluoromethyl)-1H-indazol-1-yl)methyl)benzamide



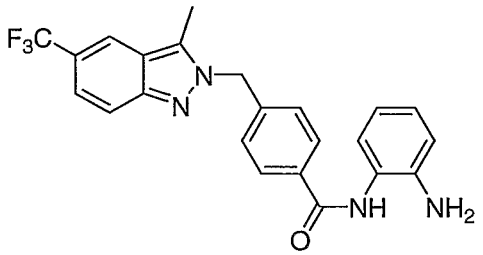
[0415] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 2.55 (s, 3 H), 4.87 (s, 2 H), 5.79 (s, 2 H), 6.57 (t, *J*=7.33 Hz, 1 H), 6.75 (d, *J*=8.08 Hz, 1 H), 6.95 (t, *J*=7.58 Hz, 1 H), 7.13 (d, *J*=7.58 Hz, 1 H), 7.33 (d, *J*=8.08 Hz, 2 H), 7.41 (d, *J*=8.59 Hz, 1 H), 7.90 (d, *J*=7.83 Hz, 2 H), 7.98 (d, *J*=8.34 Hz, 1 H), 8.24 (s, 1 H), 9.58 (s, 1H). ESI-MS: *m/z* 425.2 $(M + H)^+$.

Example 94: N-(2-aminophenyl)-4-((3-methyl-5-(trifluoromethyl)-1H-indazol-1-yl)methyl)benzamide



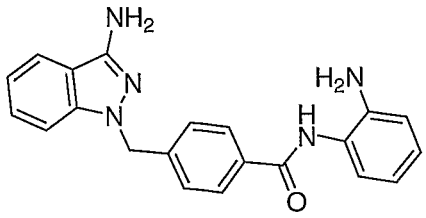
[0416] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 2.57 (s, 3 H), 4.87 (s, 2 H), 5.73 (s, 2 H), 6.57 (t, *J*=7.45 Hz, 1 H), 6.75 (d, *J*=7.83 Hz, 1 H), 6.95 (t, *J*=7.45 Hz, 1 H), 7.13 (d, *J*=7.58 Hz, 1 H), 7.33 (d, *J*=7.83 Hz, 2 H), 7.67 (d, *J*=8.84 Hz, 1 H), 7.90 (d, *J*=8.34 Hz, 3 H), 8.22 (s, 1 H), 9.58 (s, 1H). ESI-MS: *m/z* 425.2 $(M + H)^+$.

Example 95: N-(2-aminophenyl)-4-((3-methyl-5-(trifluoromethyl)-2H-indazol-2-yl)methyl)benzamide



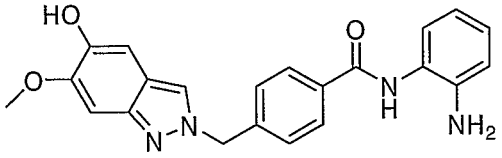
[0417] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 2.70 (s, 3 H), 4.88 (s, 2 H), 5.78 (s, 2 H), 6.58 (t, *J*=7.45 Hz, 1 H), 6.76 (d, *J*=8.08 Hz, 1 H), 6.93 - 6.99 (m, 1 H), 7.14 (d, *J*=7.33 Hz, 1 H), 7.31 (d, *J*=8.08 Hz, 2 H), 7.44 (d, *J*=8.84 Hz, 1 H), 7.75 (d, *J*=9.09 Hz, 1 H), 7.94 (d, *J*=8.08 Hz, 2 H), 8.25 (s, 1 H), 9.63 (s, 1H). ESI-MS: *m/z* 425.2 $(M + H)^+$.

Example 96: 4-((3-amino-1*H*-indazol-1-yl)methyl)-*N*-(2-aminophenyl)benzamide



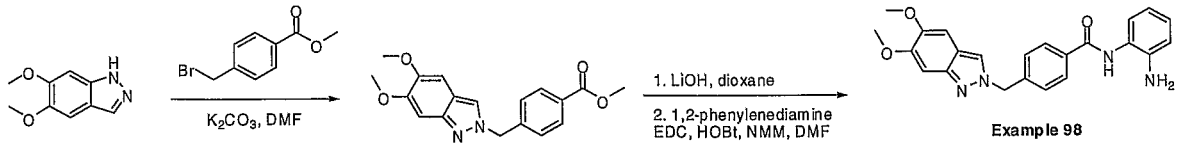
[0418] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 4.87 (s, 2 H), 5.39 (s, 2 H), 5.52 (s, 2 H), 6.57 (t, *J*=7.45 Hz, 1 H), 6.75 (d, *J*=7.83 Hz, 1 H), 6.94 (q, *J*=7.75 Hz, 2 H), 7.13 (d, *J*=7.58 Hz, 1 H), 7.27 (t, *J*=8.21 Hz, 3 H), 7.44 (d, *J*=8.34 Hz, 1 H), 7.70 (d, *J*=7.83 Hz, 1 H), 7.86 (d, *J*=7.83 Hz, 2 H), 9.55 (s, 1 H). ESI-MS: *m/z* 358.4 $(M + H)^+$.

Example 97: N-(2-aminophenyl)-4-((5-hydroxy-6-methoxy-2H-indazol-2-yl)methyl)benzamide



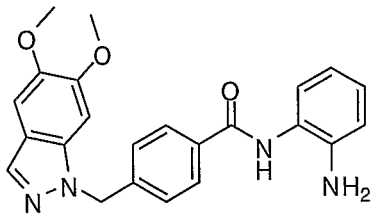
[0419] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 3.81 (s, 2 H) 4.89 (s, 2 H) 5.58 (s, 2 H) 6.59 (t, *J*=7.58 Hz, 1 H) 6.77 (dd, *J*=7.96, 1.39 Hz, 1 H) 6.85 (s, 1 H) 6.91 (s, 1 H) 6.96 (dd, *J*=15.16, 1.52 Hz, 1 H) 7.15 (d, *J*=7.33 Hz, 1 H) 7.36 (d, *J*=8.08 Hz, 2 H) 7.93 (d, *J*=8.08 Hz, 2 H) 8.11 (s, 1 H) 8.82 (s, 1 H) 9.62 (s, 1 H). ESI-MS: *m/z* 389.4 $(M + H)^+$.

Example 98: N-(2-aminophenyl)-4-((5,6-dimethoxy-2H-indazol-2-yl)methyl)benzamide



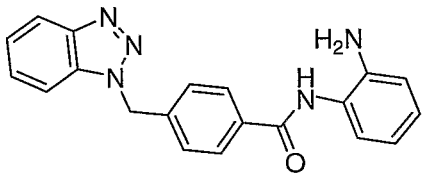
[0420] 5,6-dimethoxy-1H-indazole was prepared according to the procedure described in Dennler *et al.*, "Synthesis of indazoles using polyphosphoric acid- I" **Tetrahedron**, **22**(9): 3131-3141 (1966), which is hereby incorporated by reference in its entirety. The title compound was then prepared using a procedure analogous to that described in Scheme 1. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 3.78 (s, 3 H) 3.83 (s, 3 H) 4.88 (br. s., 2 H) 5.69 (s, 2 H) 6.58 (t, *J*=7.45 Hz, 1 H) 6.77 (d, *J*=1.01 Hz, 1 H) 6.96 (dd, *J*=15.16, 1.26 Hz, 1 H) 7.17 (s, 1 H) 7.13 (d, *J*=7.58 Hz, 1 H) 7.27 (s, 1 H) 7.30 (d, *J*=8.34 Hz, 2 H) 7.83 - 7.93 (m, 3 H) 9.59 (s, 1 H). ESI-MS: *m/z* 403.4 $(M + H)^+$.

Example 99: N-(2-aminophenyl)-4-((5,6-dimethoxy-1H-indazol-1-yl)methyl)benzamide



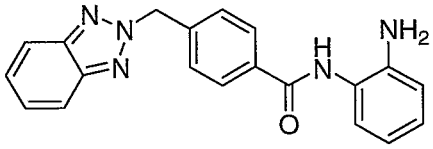
[0421] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 3.78 (s, 3 H) 3.83 (s, 3 H) 4.88 (br. s., 2 H) 5.69 (s, 2 H) 6.58 (s, 1 H) 6.77 (d, *J*=1.01 Hz, 1 H) 6.95 (d, *J*=7.33 Hz, 1 H) 7.17 (s, 1 H) 7.13 (d, *J*=7.58 Hz, 1 H) 7.27 (s, 1 H) 7.30 (d, *J*=8.34 Hz, 2 H) 7.82 - 7.94 (m, 3 H) 9.59 (s, 1 H). ESI-MS: *m/z* 403.4 $(M + H)^+$.

Example 100: 4-((1*H*-benzo[*d*][1,2,3]triazol-1-yl)methyl)-*N*-(2-aminophenyl)benzamide



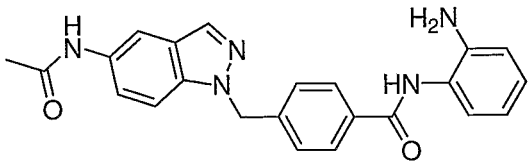
[0422] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 4.88 (s, 2 H), 6.08 (s, 2 H), 6.57 (t, *J*=7.58 Hz, 1 H), 6.74 - 6.78 (m, 1 H), 6.93 - 6.98 (m, 1 H), 7.13 (d, *J*=7.58 Hz, 1 H), 7.39 - 7.46 (m, 3 H), 7.55 (t, *J*=7.71 Hz, 1 H), 7.86 (d, *J*=8.34 Hz, 1 H), 7.94 (d, *J*=8.08 Hz, 2 H), 8.07 (d, *J*=8.34 Hz, 1 H), 9.60 (s, 1 H). ESI-MS: *m/z* 344.4 $(M + H)^+$.

Example 101: 4-((2*H*-benzo[*d*][1,2,3]triazol-2-yl)methyl)-*N*-(2-aminophenyl)benzamide



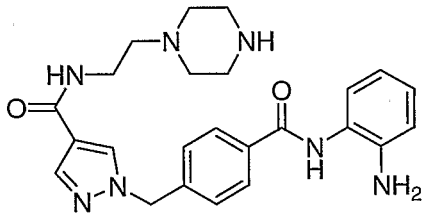
[0423] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 4.88 (s, 2 H), 6.07 (s, 2 H), 6.55 - 6.61 (m, 1 H), 6.77 (dd, *J*=8.08, 1.26 Hz, 1 H), 6.93 - 6.99 (m, 1 H), 7.15 (d, *J*=7.58 Hz, 1 H), 7.43 - 7.48 (m, 2 H), 7.50 (d, *J*=8.34 Hz, 2 H), 7.91 - 7.99 (m, 4 H), 9.63 (s, 1 H). ESI-MS: *m/z* 344.4 $(M + H)^+$.

Example 102: 4-((5-acetamido-1*H*-indazol-1-yl)methyl)-*N*-(2-aminophenyl)benzamide



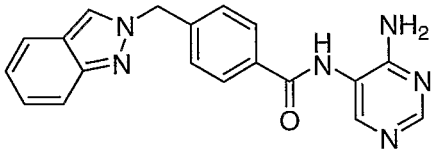
[0424] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 2.05 (s, 3 H), 5.70 (s, 2 H), 6.95 - 7.03 (m, 4 H), 7.06 - 7.13 (m, 1 H), 7.30 - 7.40 (m, 5 H), 7.64 (d, *J*=9.09 Hz, 1 H), 7.75 (d, *J*=8.84 Hz, 2 H), 7.86 (d, *J*=8.08 Hz, 2 H), 8.11 (d, *J*=17.68 Hz, 2 H), 9.96 (s, 1 H), 10.21 (s, 1 H). ESI-MS: *m/z* 477.3 $(M + H)^+$.

Example 103: 1-(4-(2-aminophenylcarbamoyl)benzyl)-N-(2-(piperazin-1-yl)ethyl)-1H-pyrazole-4-carboxamide



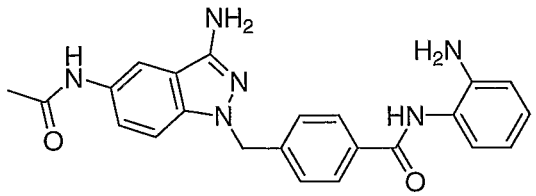
[0425] ^{1}H NMR (400 MHz, DMSO-d_6) of the *bis*-trifluoroacetic acid salt: δ ppm 3.06 (s, 2 H), 3.22 (s, 4 H), 3.30 (s, 4 H), 3.44 - 3.52 (m, 2 H), 5.46 (s, 2 H), 6.79 (t, *J*=7.33 Hz, 1 H), 6.93 (d, *J*=7.07 Hz, 1 H), 7.07 (td, *J*=7.64, 1.39 Hz, 1 H), 7.22 (d, *J*=8.59 Hz, 1 H), 7.38 (d, *J*=8.34 Hz, 2 H), 7.90 (d, *J*=0.51 Hz, 1 H), 7.97 (d, *J*=8.08 Hz, 2 H), 8.29 - 8.32 (m, 1 H), 8.32 - 8.35 (m, 1 H), 9.85 (s, 1 H). ESI-MS: *m/z* 448.4 $(M + H)^+$.

Example 104: 4-((2*H*-indazol-2-yl)methyl)-*N*-(4-aminopyrimidin-5-yl)benzamide



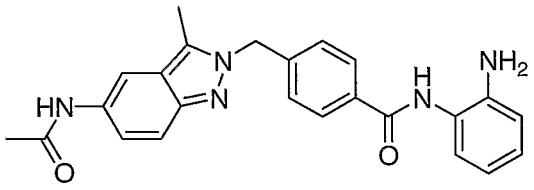
[0426] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 5.74 (s, 2 H), 6.82 (s, 2 H), 7.00 - 7.08 (m, 1 H), 7.23 (dd, *J*=8.72, 6.69 Hz, 1 H), 7.43 (d, *J*=8.34 Hz, 2 H), 7.59 (d, *J*=8.84 Hz, 1 H), 7.72 (d, *J*=8.34 Hz, 1 H), 7.95 (d, *J*=8.08 Hz, 2 H), 8.15 (s, 1 H), 8.26 (s, 1 H), 8.53 (s, 1 H), 9.64 (s, 1 H). ESI-MS: *m/z* 345.3 $(M + H)^+$.

Example 105: 4-((5-acetamido-3-amino-1H-indazol-1-yl)methyl)-N-(2-aminophenyl)benzamide



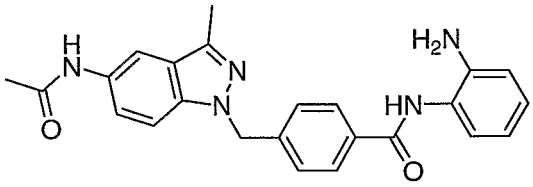
[0427] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 2.03 (s, 3 H), 4.86 (s, 2 H), 5.35 (s, 2 H), 5.43 (s, 2 H), 6.57 (t, *J*=7.45 Hz, 1 H), 6.75 (d, *J*=7.07 Hz, 1 H), 6.92 - 6.98 (m, 1 H), 7.13 (d, *J*=7.33 Hz, 1 H), 7.24 - 7.31 (m, 3 H), 7.35 - 7.41 (m, 1 H), 7.86 (d, *J*=7.83 Hz, 2 H), 7.96 (s, 1 H), 9.55 (s, 1 H), 9.81 (s, 1 H). ESI-MS: *m/z* 415.3 $(M + H)^+$.

Example 106: 4-((5-acetamido-3-methyl-2*H*-indazol-2-yl)methyl)-*N*-(2-aminophenyl)benzamide



[0428] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 2.05 (s, 3 H), 2.53 (s, 3 H), 4.88 (s, 2 H), 5.68 (s, 2 H), 6.58 (t, *J*=7.45 Hz, 1 H), 6.76 (d, *J*=7.83 Hz, 1 H), 6.93 - 6.98 (m, 1 H), 7.14 (d, *J*=7.83 Hz, 1 H), 7.20 (dd, *J*=9.22, 1.64 Hz, 1 H), 7.27 (d, *J*=8.34 Hz, 2 H), 7.49 (d, *J*=9.09 Hz, 1 H), 7.93 (d, *J*=8.08 Hz, 2 H), 8.05 (s, 1 H), 9.62 (s, 1 H), 9.85 (s, 1 H). ESI-MS: *m/z* 414.3 $(M + H)^+$.

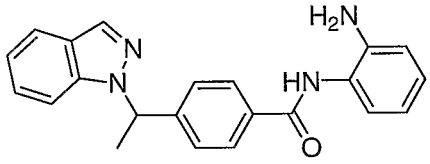
Example 107: 4-((5-acetamido-3-methyl-1*H*-indazol-1-yl)methyl)-*N*-(2-aminophenyl)benzamide



[0429] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 2.04 (s, 3 H), 2.45 (s, 3 H), 4.87 (s, 2 H), 5.61 (s, 2 H), 6.54 - 6.60 (m, 1 H), 6.75 (dd, *J*=7.96, 1.39 Hz, 1 H), 6.92 - 6.98 (m, 1 H), 7.13 (d, *J*=7.33 Hz, 1 H), 7.30 (d, *J*=8.34 Hz, 2 H), 7.38 (dd, *J*=9.09, 1.77 Hz, 1 H), 7.57

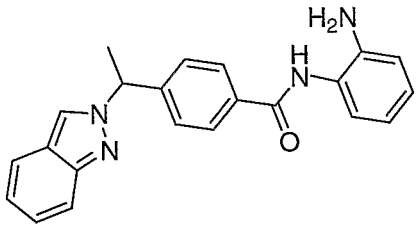
(d, *J*=8.84 Hz, 1 H), 7.88 (d, *J*=8.34 Hz, 2 H), 8.04 (d, *J*=1.26 Hz, 1 H), 9.57 (s, 1 H), 9.94 (s, 1 H). ESI-MS: *m/z* 414.3 $(M + H)^+$.

Example 108: 4-(1-(1*H*-indazol-1-yl)ethyl)-*N*-(2-aminophenyl)benzamide



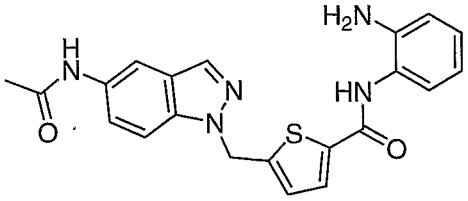
[0430] ^{1}H NMR (400 MHz, DMSO- d_6) δ ppm 1.97 (d, *J*=7.07 Hz, 3 H), 4.86 (s, 2 H), 6.16 (q, *J*=6.99 Hz, 1 H), 6.57 (t, *J*=7.58 Hz, 1 H), 6.75 (d, *J*=6.82 Hz, 1 H), 6.91 - 6.98 (m, 1 H), 7.13 (t, *J*=7.20 Hz, 2 H), 7.34 (t, *J*=7.58 Hz, 1 H), 7.39 (d, *J*=8.34 Hz, 2 H), 7.66 (d, *J*=8.34 Hz, 1 H), 7.77 (d, *J*=8.08 Hz, 1 H), 7.87 (d, *J*=8.08 Hz, 2 H), 8.17 (s, 1 H), 9.55 (s, 1 H). ESI-MS: *m/z* 357.4 $(M + H)^+$.

Example 109: 4-(1-(2*H*-indazol-2-yl)ethyl)-*N*-(2-aminophenyl)benzamide



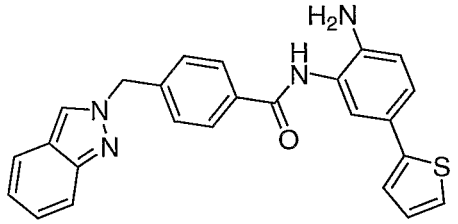
[0431] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 1.99 (d, *J*=7.07 Hz, 3 H), 4.88 (s, 2 H), 6.04 (q, *J*=6.99 Hz, 1 H), 6.57 (t, *J*=7.58 Hz, 1 H), 6.76 (d, *J*=8.08 Hz, 1 H), 6.91 - 6.99 (m, 1 H), 7.01 - 7.06 (m, 1 H), 7.14 (d, *J*=7.58 Hz, 1 H), 7.20 - 7.26 (m, 1 H), 7.44 (d, *J*=8.34 Hz, 2 H), 7.61 (d, *J*=8.84 Hz, 1 H), 7.71 (d, *J*=8.34 Hz, 1 H), 7.92 (d, *J*=8.34 Hz, 2 H), 8.56 (s, 1 H), 9.60 (s, 1 H). ESI-MS: *m/z* 357.4 $(M + H)^+$.

Example 110: 5-((5-acetamido-1*H*-indazol-1-yl)methyl)-*N*-(2-aminophenyl)thiophene-2-carboxamide



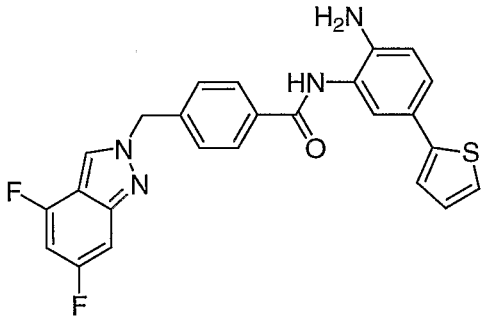
[0432] ^{1}H NMR (400 MHz, DMSO- d_6) δ ppm 2.05 (s, 3 H), 4.86 (s, 2 H), 5.85 (s, 2 H), 6.52 - 6.58 (m, 1 H), 6.74 (d, *J*=6.82 Hz, 1 H), 6.92 - 6.97 (m, 1 H), 7.02 - 7.07 (m, 1 H), 7.16 (d, *J*=3.54 Hz, 1 H), 7.44 (dd, *J*=9.09, 1.77 Hz, 1 H), 7.71 (d, *J*=9.09 Hz, 1 H), 7.78 (d, *J*=3.03 Hz, 1 H), 8.08 (s, 1 H), 8.13 (d, *J*=1.26 Hz, 1 H), 9.62 (s, 1 H), 9.97 (s, 1 H). ESI-MS: *m/z* 406.3 $(M + H)^+$.

Example 111: 4-((2*H*-indazol-2-yl)methyl)-*N*-(2-amino-5-(thiophen-2-yl)phenyl)benzamide



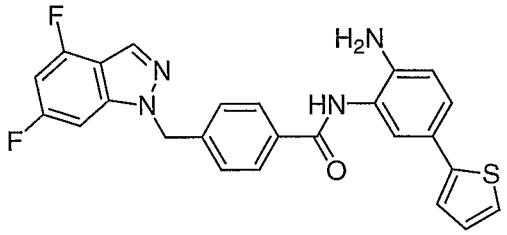
[0433] ^{1}H NMR (400 MHz, DMSO-d_6) of the trifluoroacetic acid salt: δ ppm 5.75 (s, 2 H), 6.98 - 7.09 (m, 3 H), 7.24 (ddd, *J*=8.46, 6.95, 1.26 Hz, 1 H), 7.31 - 7.35 (m, 1 H), 7.39 - 7.47 (m, 4 H), 7.54 (d, *J*=2.02 Hz, 1 H), 7.60 (dd, *J*=8.84, 1.01 Hz, 1 H), 7.73 (d, *J*=8.34 Hz, 1 H), 7.98 (d, *J*=8.34 Hz, 2 H), 8.54 (d, *J*=1.01 Hz, 1 H), 9.96 (s, 1 H). ESI-MS: *m/z* 425.5 $(M + H)^+$.

Example 112: *N*-(2-amino-5-(thiophen-2-yl)phenyl)-4-((4,6-difluoro-2*H*-indazol-2-yl)methyl)benzamide



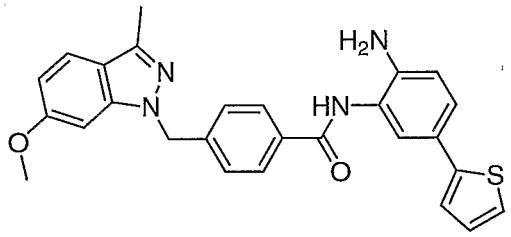
[0434] ^{1}H NMR (400 MHz, DMSO-d_6) of the trifluoroacetic acid salt: δ ppm 5.76 (s, 2 H), 6.93 (s, 1 H), 7.07 (d, *J*=8.59 Hz, 2 H), 7.30 (d, *J*=3.28 Hz, 1 H), 7.35 - 7.42 (m, 4 H), 7.50 (d, *J*=1.77 Hz, 1 H), 7.62 (d, *J*=9.35 Hz, 1 H), 7.95 (d, *J*=8.08 Hz, 2 H), 8.30 (s, 1 H), 9.86 (s, 1 H). ESI-MS: *m/z* 461.3 $(M + H)^+$.

Example 113: *N*-(2-amino-5-(thiophen-2-yl)phenyl)-4-((4,6-difluoro-1*H*-indazol-1-yl)methyl)benzamide



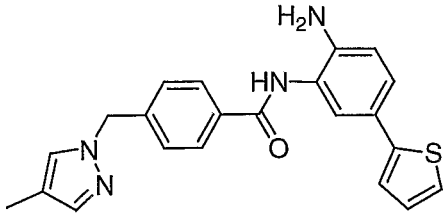
[0435] ^{1}H NMR (400 MHz, DMSO- d_6) of the trifluoroacetic acid salt: δ ppm 5.74 (s, 2 H), 6.85 - 6.97 (m, 2 H), 7.04 - 7.07 (m, 1 H), 7.24 - 7.29 (m, 2 H), 7.34 (dd, *J*=8.34, 1.77 Hz, 1 H), 7.38 (d, *J*=5.05 Hz, 1 H), 7.45 - 7.50 (m, 3 H), 7.98 (d, *J*=8.08 Hz, 2 H), 8.84 (s, 1 H), 9.81 (s, 1 H). ESI-MS: *m/z* 461.3 $(M + H)^+$.

Example 114: *N*-(2-amino-5-(thiophen-2-yl)phenyl)-4-((6-methoxy-3-methyl-1*H*-indazol-1-yl)methyl)benzamide



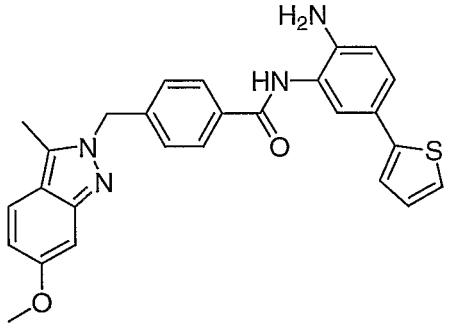
[0436] ^{1}H NMR (400 MHz, DMSO- d_6) of the trifluoroacetic acid salt: δ ppm 2.54 (s, 3 H), 3.78 (s, 3 H), 5.64 (s, 2 H), 6.65 (d, *J*=9.09 Hz, 1 H), 6.86 (s, 2 H), 7.05 (s, 1 H), 7.27 (s, 4 H), 7.37 (s, 1 H), 7.48 (s, 1 H), 7.56 (s, 1 H), 7.96 (d, *J*=7.83 Hz, 2 H), 9.78 (s, 1 H). ESI-MS: *m/z* 469.3 $(M + H)^+$.

Example 115: *N*-(2-amino-5-(thiophen-2-yl)phenyl)-4-((4-methyl-1*H*-pyrazol-1-yl)methyl)benzamide



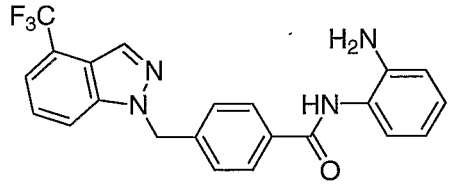
[0437] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 2.02 (s, 3 H), 5.15 (s, 2 H), 5.34 (s, 2 H), 6.80 (d, *J*=8.34 Hz, 1 H), 7.03 - 7.07 (m, 1 H), 7.24 (d, *J*=3.28 Hz, 1 H), 7.27 - 7.33 (m, 4 H), 7.35 (d, *J*=5.05 Hz, 1 H), 7.46 (s, 1 H), 7.60 (s, 1 H), 7.95 (d, *J*=7.83 Hz, 2 H), 9.71 (s, 1 H). ESI-MS: *m/z* 389.3(M + H)$^+$.

Example 116: *N*-(2-amino-5-(thiophen-2-yl)phenyl)-4-((6-methoxy-3-methyl-2*H*-indazol-2-yl)methyl)benzamide



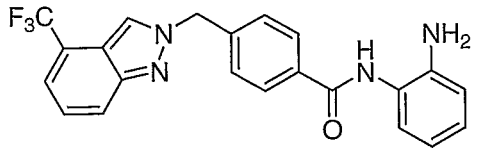
[0438] ^{1}H NMR (400 MHz, DMSO-d_6) of the trifluoroacetic acid salt: δ ppm 2.43 (s, 3 H), 3.81 (s, 3 H), 5.61 (s, 2 H), 6.74 (dd, *J*=8.84, 2.02 Hz, 1 H), 7.00 (d, *J*=8.34 Hz, 1 H), 7.08 (dd, *J*=5.05, 3.79 Hz, 1 H), 7.15 (d, *J*=2.02 Hz, 1 H), 7.35 (d, *J*=8.08 Hz, 3 H), 7.40 - 7.45 (m, 2 H), 7.52 - 7.60 (m, 2 H), 7.93 (d, *J*=8.08 Hz, 2 H), 9.94 (s, 1 H). ESI-MS: *m/z* 469.3 (M + H)$^+$.

Example 117: *N*-(2-aminophenyl)-4-((4-(trifluoromethyl)-1*H*-indazol-1-yl)methyl)benzamide



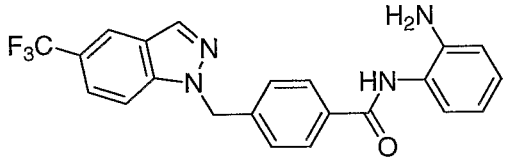
[0439] ^{1}H NMR (400 MHz, DMSO- d_6) of the trifluoroacetic acid salt: δ ppm 5.88 (s, 2 H), 6.95 (t, *J*=7.33 Hz, 1 H), 7.05 (d, *J*=7.33 Hz, 1 H), 7.11 - 7.18 (m, 1 H), 7.27 (d, *J*=7.33 Hz, 1 H), 7.39 (d, *J*=8.34 Hz, 2 H), 7.59 (s, 1 H), 7.60 (d, *J*=2.27 Hz, 1 H), 7.93 (d, *J*=8.08 Hz, 2 H), 8.10 - 8.17 (m, 1 H), 8.27 (s, 1 H), 9.97 (s, 1 H). ESI-MS: *m/z* 411.3 (M + H)$^+$.

Example 118: *N*-(2-aminophenyl)-4-((4-(trifluoromethyl)-2*H*-indazol-2-yl)methyl)benzamide



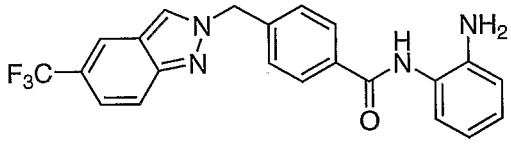
[0440] ^{1}H NMR (400 MHz, DMSO-d_6) of the trifluoroacetic acid salt: δ ppm 5.83 (s, 2 H), 7.11 (t, *J*=7.33 Hz, 1 H), 7.16 - 7.25 (m, 2 H), 7.34 (d, *J*=7.33 Hz, 1 H), 7.38 - 7.44 (m, 1 H), 7.52 (d, *J*=8.08 Hz, 3 H), 7.95 (d, *J*=8.59 Hz, 1 H), 7.99 (d, *J*=8.08 Hz, 2 H), 8.80 (s, 1 H), 10.16 (s, 1 H). ESI-MS: *m/z* 411.3 $(M + H)^+$.

Example 119: *N*-(2-aminophenyl)-4-((5-(trifluoromethyl)-1*H*-indazol-1-yl)methyl)benzamide



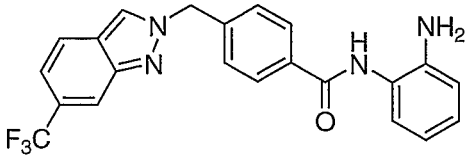
[0441] ^{1}H NMR (400 MHz, DMSO- d_6) of the trifluoroacetic acid salt: δ ppm 5.85 (s, 2 H), 6.93 (t, *J*=7.20 Hz, 1 H), 7.03 (d, *J*=7.83 Hz, 1 H), 7.13 (t, *J*=7.07 Hz, 1 H), 7.25 (d, *J*=7.33 Hz, 1 H), 7.36 (d, *J*=8.08 Hz, 2 H), 7.70 (dd, *J*=8.84, 1.52 Hz, 1 H), 7.91 - 7.99 (m, 3 H), 8.28 (s, 1 H), 8.34 (s, 1 H), 9.95 (s, 1 H). ESI-MS: *m/z* 411.3 $(M + H)^+$.

Example 120: *N*-(2-aminophenyl)-4-((5-(trifluoromethyl)-2*H*-indazol-2-yl)methyl)benzamide



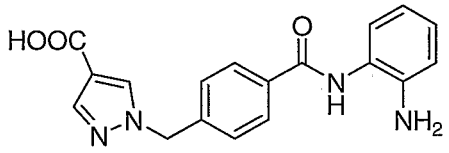
[0442] ^{1}H NMR (400 MHz, DMSO-d_6) of the trifluoroacetic acid salt: δ ppm 5.83 (s, 2 H), 6.98 (t, *J*=7.45 Hz, 1 H), 7.07 (d, *J*=7.83 Hz, 1 H), 7.16 (t, *J*=7.20 Hz, 1 H), 7.29 (d, *J*=7.58 Hz, 1 H), 7.44 - 7.50 (m, 3 H), 7.81 (d, *J*=9.09 Hz, 1 H), 7.98 (d, *J*=8.08 Hz, 2 H), 8.28 (s, 1 H), 8.80 (s, 1 H), 10.03 (s, 1 H). ESI-MS: *m/z* 411.3 $(M + H)^+$.

Example 121: *N*-(2-aminophenyl)-4-((6-(trifluoromethyl)-2*H*-indazol-2-yl)methyl)benzamide



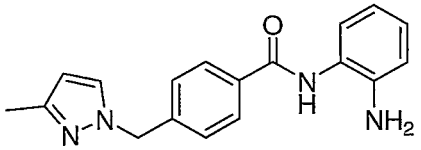
[0443] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 4.90 (s, 2 H), 5.82 (s, 2 H), 6.59 (t, *J*=7.45 Hz, 1 H), 6.77 (d, *J*=7.07 Hz, 1 H), 6.94 - 6.99 (m, 1 H), 7.16 (d, *J*=7.58 Hz, 1 H), 7.45 (d, *J*=8.59 Hz, 3 H), 7.97 (d, *J*=8.34 Hz, 2 H), 8.27 (s, 1 H), 8.74 (s, 1 H), 8.79 (s, 1 H), 9.65 (s, 1 H). ESI-MS: *m/z* 411.3 $(M + H)^+$.

Example 122: 1-(4-(2-aminophenylcarbamoyl)benzyl)-1H-pyrazole-4-carboxylic acid



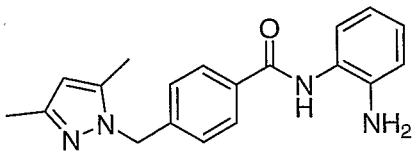
[0444] ^{1}H NMR (400 MHz, DMSO-d_6) of the trifluoroacetic acid salt: δ ppm 5.47 (s, 2 H), 6.93 - 6.99 (m, 1 H), 7.05 (d, *J*=7.33 Hz, 1 H), 7.15 (t, *J*=8.34 Hz, 1 H), 7.28 (d, *J*=7.83 Hz, 1 H), 7.41 (d, *J*=8.34 Hz, 2 H), 7.85 (s, 1 H), 7.97 (d, *J*=8.34 Hz, 2 H), 8.44 (s, 1 H), 10.01 (s, 1 H). ESI-MS: *m/z* 337.3 $(M + H)^+$.

Example 123: N-(2-aminophenyl)-4-((3-methyl-1H-pyrazol-1-yl)methyl)benzamide



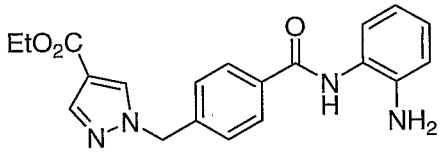
[0445] ^{1}H NMR (400 MHz, DMSO-d_6) of the trifluoroacetic acid salt: δ ppm 2.15 (s, 3 H), 5.33 (s, 2 H), 6.07 (d, *J*=2.27 Hz, 1 H), 7.11 - 7.16 (m, 1 H), 7.18 - 7.26 (m, 2 H), 7.34 (d, *J*=8.34 Hz, 2 H), 7.37 (dd, *J*=7.96, 0.88 Hz, 1 H), 7.74 (d, *J*=2.02 Hz, 1 H), 7.98 (d, *J*=8.34 Hz, 2 H), 10.18 (s, 1 H). ESI-MS: *m/z* 307.4 $(M + H)^+$.

Example 124: N-(2-aminophenyl)-4-((3,5-dimethyl-1H-pyrazol-1-yl)methyl)benzamide



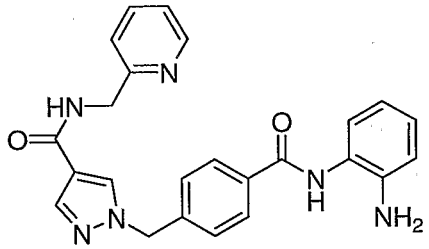
[0446] ^{1}H NMR (400 MHz, DMSO-d_6) of the trifluoroacetic acid salt: δ ppm 2.12 (s, 3 H), 2.17 (s, 3 H), 5.30 (s, 2 H), 5.90 (s, 1 H), 7.10 - 7.15 (m, 1 H), 7.16 - 7.20 (m, 1 H), 7.21 - 7.25 (m, 3 H), 7.35 (dd, *J*=7.83, 1.26 Hz, 1 H), 7.96 (d, *J*=8.34 Hz, 2 H), 10.15 (s, 1 H). ESI-MS: *m/z* 321.4 $(M + H)^+$.

Example 125: Ethyl 1-(4-(2-aminophenylcarbamoyl)benzyl)-1H-pyrazole-4-carboxylate



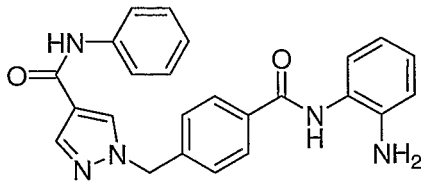
[0447] ^{1}H NMR (400 MHz, DMSO-d_6) of the trifluoroacetic acid salt: δ ppm 1.27 (t, *J*=7.07 Hz, 3 H), 4.22 (q, *J*=7.07 Hz, 2 H), 5.48 (s, 2 H), 6.99 (t, *J*=7.33 Hz, 1 H), 7.05 - 7.11 (m, 1 H), 7.14 - 7.20 (m, 1 H), 7.30 (d, *J*=7.83 Hz, 1 H), 7.41 (d, *J*=8.34 Hz, 2 H), 7.90 (s, 1 H), 7.97 (d, *J*=8.08 Hz, 2 H), 8.53 (s, 1 H), 10.04 (s, 1 H). ESI-MS: *m/z* 365.4 $(M + H)^+$.

Example 126: 1-(4-(2-aminophenylcarbamoyl)benzyl)-N-(pyridin-2-ylmethyl)-1H-pyrazole-4-carboxamide



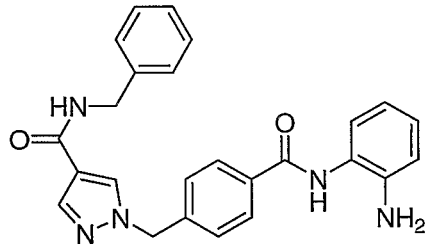
[0448] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 4.49 (d, *J*=6.06 Hz, 2 H), 4.90 (s, 2 H), 5.45 (s, 2 H), 6.59 (td, *J*=7.45, 1.26 Hz, 1 H), 6.77 (dd, *J*=8.08, 1.26 Hz, 1 H), 6.97 (td, *J*=7.58, 1.52 Hz, 1 H), 7.16 (d, *J*=7.07 Hz, 1 H), 7.25 (ddd, *J*=7.58, 4.80, 1.01 Hz, 1 H), 7.30 (d, *J*=7.83 Hz, 1 H), 7.39 (d, *J*=8.08 Hz, 2 H), 7.75 (td, *J*=7.64, 1.89 Hz, 1 H), 7.94 - 7.98 (m, 3 H), 8.34 (s, 1 H), 8.50 (ddd, *J*=4.93, 1.89, 1.01 Hz, 1 H), 8.75 (t, *J*=5.94 Hz, 1 H), 9.65 (s, 1 H). ESI-MS: *m/z* 427.4 $(M + H)^+$.

Example 127: 1-(4-(2-aminophenylcarbamoyl)benzyl)-N-phenyl-1H-pyrazole-4-carboxamide



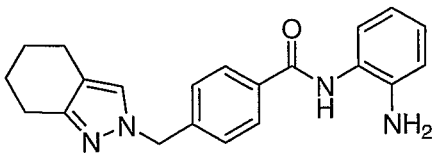
[0449] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 4.90 (s, 2 H), 5.49 (s, 2 H), 6.59 (td, *J*=7.52, 1.39 Hz, 1 H), 6.77 (dd, *J*=7.96, 1.39 Hz, 1 H), 6.97 (td, *J*=7.71, 1.52 Hz, 1 H), 7.04 - 7.09 (m, 1 H), 7.16 (d, *J*=7.33 Hz, 1 H), 7.30 - 7.35 (m, 2 H), 7.40 (d, *J*=8.34 Hz, 2 H), 7.70 (dt, *J*=8.65, 1.61 Hz, 2 H), 7.97 (d, *J*=8.08 Hz, 2 H), 8.09 (d, *J*=0.76 Hz, 1 H), 8.49 (s, 1 H), 9.66 (s, 1 H), 9.86 (s, 1 H). ESI-MS: *m/z* 412.4 $(M + H)^+$.

Example 128: 1-(4-(2-aminophenylcarbamoyl)benzyl)-N-benzyl-1H-pyrazole-4-carboxamide



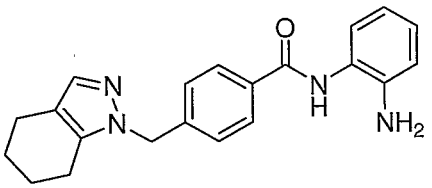
[0450] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 4.41 (d, *J*=6.06 Hz, 2 H), 4.90 (s, 2 H), 5.44 (s, 2 H), 6.59 (td, *J*=7.52, 1.39 Hz, 1 H), 6.77 (dd, *J*=7.96, 1.39 Hz, 1 H), 6.97 (td, *J*=7.58, 1.52 Hz, 1 H), 7.15 (d, *J*=7.07 Hz, 1 H), 7.21 - 7.25 (m, 1 H), 7.27 - 7.34 (m, 4 H), 7.38 (d, *J*=8.34 Hz, 2 H), 7.95 (s, 2 H), 7.97 (s, 1 H), 8.32 (s, 1 H), 8.65 (t, *J*=6.06 Hz, 1 H), 9.65 (s, 1 H). ESI-MS: *m/z* 426.4 $(M + H)^+$.

Example 129: N-(2-aminophenyl)-4-((4,5,6,7-tetrahydro-2H-indazol-2-yl)methyl)benzamide



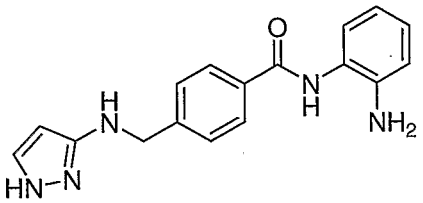
[0451] ^{1}H NMR (400 MHz, DMSO-d_6) of the trifluoroacetic acid salt: δ ppm 1.63 - 1.74 (m, 4 H), 2.45 - 2.49 (m, 4 H), 5.27 (s, 2 H), 6.90 - 6.98 (m, 1 H), 7.04 (d, *J*=8.59 Hz, 1 H), 7.14 (t, *J*=7.83 Hz, 1 H), 7.28 (d, *J*=7.58 Hz, 1 H), 7.36 (d, *J*=8.34 Hz, 2 H), 7.50 (s, 1 H), 7.94 (d, *J*=8.34 Hz, 2 H), 9.96 (s, 1 H). ESI-MS: *m/z* 347.4 $(M + H)^+$.

Example 130: N-(2-aminophenyl)-4-((4,5,6,7-tetrahydro-1H-indazol-1-yl)methyl)benzamide



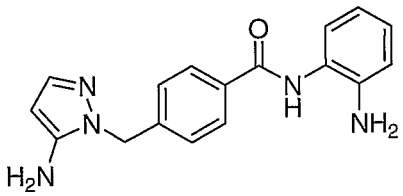
[0452] ^{1}H NMR (400 MHz, DMSO-d_6) of the trifluoroacetic acid salt: δ ppm 1.59 - 1.66 (m, 2 H), 1.68 - 1.76 (m, 2 H), 2.44 (t, *J*=5.94 Hz, 2 H), 2.47 - 2.50 (m, 2 H), 5.31 (s, 2 H), 7.04 (t, *J*=7.33 Hz, 1 H), 7.10 - 7.13 (m, 1 H), 7.16 - 7.21 (m, 1 H), 7.23 - 7.27 (m, 3 H), 7.31 (dd, *J*=7.96, 1.14 Hz, 1 H), 7.95 (d, *J*=8.34 Hz, 2 H), 10.07 (s, 1 H). ESI-MS: *m/z* 347.4 $(M + H)^+$.

Example 131: 4-((1H-pyrazol-3-ylamino)methyl)-N-(2-aminophenyl)benzamide



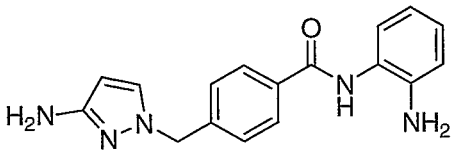
[0453] ^{1}H NMR (400 MHz, DMSO-d_6) of the trifluoroacetic acid salt: δ ppm 4.42 (s, 2 H), 5.74 (d, *J*=2.53 Hz, 1 H), 6.85 (t, *J*=7.45 Hz, 1 H), 6.96 - 7.00 (m, 1 H), 7.10 (td, *J*=7.64, 1.39 Hz, 1 H), 7.23 - 7.27 (m, 1 H), 7.48 (d, *J*=8.34 Hz, 2 H), 7.80 (d, *J*=2.78 Hz, 1 H), 7.97 (d, *J*=8.34 Hz, 2 H), 9.89 (s, 1 H). ESI-MS: *m/z* 308.4 $(M + H)^+$.

Example 132: 4-((5-amino-1H-pyrazol-1-yl)methyl)-N-(2-aminophenyl)benzamide



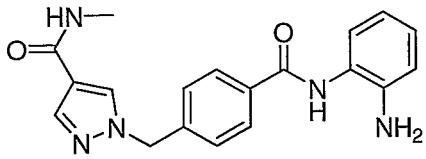
[0454] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 4.89 (s, 2 H), 5.19 (s, 2 H), 5.29 (s, 2 H), 5.31 (d, *J*=2.02 Hz, 1 H), 6.59 (td, *J*=7.52, 1.39 Hz, 1 H), 6.77 (dd, *J*=8.08, 1.52 Hz, 1 H), 6.96 (td, *J*=7.58, 1.52 Hz, 1 H), 7.10 (d, *J*=2.02 Hz, 1 H), 7.15 (d, *J*=6.82 Hz, 1 H), 7.22 (d, *J*=8.34 Hz, 2 H), 7.90 (d, *J*=8.08 Hz, 2 H), 9.60 (s, 1 H). ESI-MS: *m/z* 308.4 (M + H)$^+$.

Example 133: 4-((3-amino-1H-pyrazol-1-yl)methyl)-N-(2-aminophenyl)benzamide



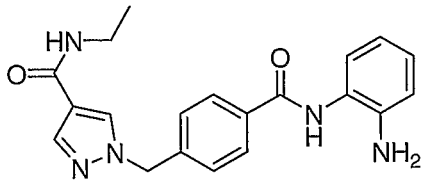
[0455] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 4.59 (s, 2 H), 4.89 (s, 2 H), 5.11 (s, 2 H), 5.44 (d, *J*=2.27 Hz, 1 H), 6.59 (td, *J*=7.58, 1.26 Hz, 1 H), 6.77 (dd, *J*=8.08, 1.52 Hz, 1 H), 6.96 (td, *J*=7.58, 1.52 Hz, 1 H), 7.16 (d, *J*=7.83 Hz, 1 H), 7.28 (d, *J*=8.08 Hz, 2 H), 7.48 (d, *J*=2.02 Hz, 1 H), 7.91 (d, *J*=8.08 Hz, 2 H), 9.61 (s, 1 H). ESI-MS: *m/z* 308.4 (M + H)$^+$.

Example 134: 1-(4-(2-aminophenylcarbamoyl)benzyl)-N-methyl-1H-pyrazole-4-carboxamide



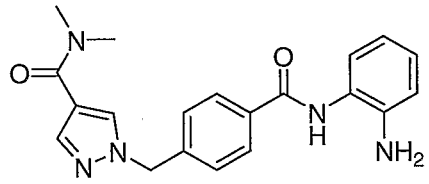
[0456] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 2.70 (d, *J*=4.55 Hz, 3 H), 4.89 (s, 2 H), 5.43 (s, 2 H), 6.59 (td, *J*=7.52, 1.14 Hz, 1 H), 6.77 (dd, *J*=8.08, 1.26 Hz, 1 H), 6.94 - 6.99 (m, 1 H), 7.15 (d, *J*=7.33 Hz, 1 H), 7.35 (d, *J*=8.34 Hz, 2 H), 7.86 (s, 1 H), 7.95 (d, *J*=8.08 Hz, 2 H), 8.05 (q, *J*=4.55 Hz, 1 H), 8.25 (s, 1 H), 9.64 (s, 1 H). ESI-MS: *m/z* 350.3 (M + H)$^+$.

Example 135: 1-(4-(2-aminophenylcarbamoyl)benzyl)-N-ethyl-1H-pyrazole-4-carboxamide



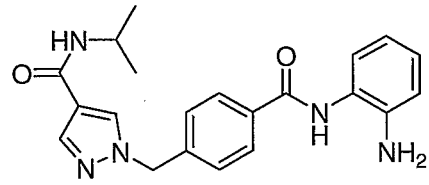
[0457] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 1.07 (t, *J*=7.20 Hz, 3 H), 3.16 - 3.24 (m, 2 H), 4.89 (s, 2 H), 5.43 (s, 2 H), 6.59 (td, *J*=7.58, 1.26 Hz, 1 H), 6.77 (dd, *J*=7.96, 1.39 Hz, 1 H), 6.96 (td, *J*=7.71, 1.52 Hz, 1 H), 7.15 (d, *J*=8.34 Hz, 1 H), 7.35 (d, *J*=8.34 Hz, 2 H), 7.87 (d, *J*=0.76 Hz, 1 H), 7.95 (d, *J*=8.34 Hz, 2 H), 8.07 (t, *J*=5.43 Hz, 1 H), 8.25 (s, 1 H), 9.64 (s, 1 H). ESI-MS: *m/z* 364.4 $(M + H)^+$.

Example 136: 1-(4-(2-aminophenylcarbamoyl)benzyl)-N,N-dimethyl-1H-pyrazole-4-carboxamide



[0458] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 2.97 (m, 3 H), 3.14 (m, 3 H), 4.90 (s, 2 H), 5.44 (s, 2 H), 6.59 (t, *J*=7.71 Hz, 1 H), 6.77 (dd, *J*=7.83, 1.01 Hz, 1 H), 6.94 - 6.99 (m, 1 H), 7.15 (d, *J*=7.83 Hz, 1 H), 7.37 (d, *J*=8.34 Hz, 2 H), 7.77 (s, 1 H), 7.95 (d, *J*=8.34 Hz, 2 H), 8.31 (s, 1 H), 9.63 (s, 1 H). ESI-MS: *m/z* 364.3 $(M + H)^+$.

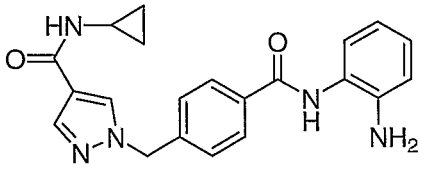
Example 137: 1-(4-(2-aminophenylcarbamoyl)benzyl)-N-isopropyl-1H-pyrazole-4-carboxamide



[0459] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 1.11 (d, *J*=6.82 Hz, 6 H), 4.02 (dq, *J*=13.80, 6.77 Hz, 1 H), 4.89 (s, 2 H), 5.43 (s, 2 H), 6.56 - 6.61 (m, 1 H), 6.77 (dd, *J*=8.08, 1.26 Hz, 1 H), 6.97 (td, *J*=7.58, 1.26 Hz, 1 H), 7.15 (d, *J*=7.58 Hz, 1 H), 7.36 (d, *J*=8.08

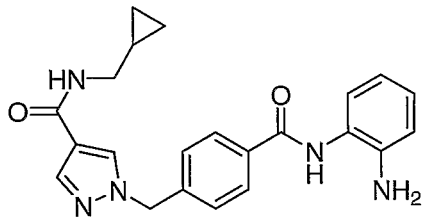
Hz, 2 H), 7.83 (d, *J*=7.83 Hz, 1 H), 7.89 (s, 1 H), 7.96 (d, *J*=8.08 Hz, 2 H), 8.26 (s, 1 H), 9.64 (s, 1 H). ESI-MS: *m/z* 378.4 $(M + H)^+$.

Example 138: 1-(4-(2-aminophenylcarbamoyl)benzyl)-N-cyclopropyl-1H-pyrazole-4-carboxamide



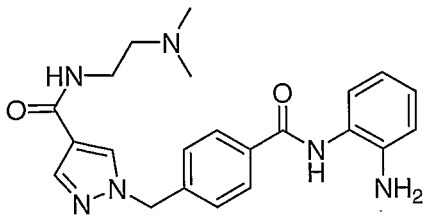
[0460] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 0.48 (m, 2 H), 0.65 (m, 2 H), 2.70 - 2.77 (m, *J*=7.31, 7.31, 3.92, 3.74, 3.74 Hz, 1 H), 4.90 (s, 2 H), 5.42 (s, 2 H), 6.56 - 6.62 (m, 1 H), 6.77 (dd, *J*=8.08, 1.26 Hz, 1 H), 6.94 - 6.99 (m, 1 H), 7.15 (d, *J*=7.33 Hz, 1 H), 7.35 (d, *J*=8.08 Hz, 2 H), 7.87 (s, 1 H), 7.95 (d, *J*=8.08 Hz, 2 H), 8.08 (d, *J*=3.79 Hz, 1 H), 8.25 (s, 1 H), 9.64 (s, 1 H). ESI-MS: *m/z* 376.3 $(M + H)^+$.

Example 139: 1-(4-(2-aminophenylcarbamoyl)benzyl)-N-(cyclopropylmethyl)-1H-pyrazole-4-carboxamide



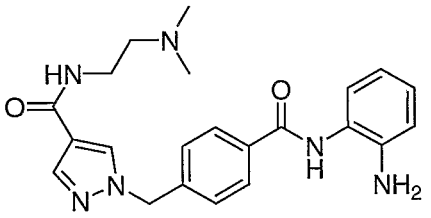
[0461] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 0.17 - 0.21 (m, 2 H), 0.39 - 0.44 (m, 2 H), 0.91 - 1.01 (m, 1 H), 3.07 (t, *J*=6.32 Hz, 2 H), 4.90 (s, 2 H), 5.44 (s, 2 H), 6.59 (t, *J*=7.45 Hz, 1 H), 6.77 (dd, *J*=8.08, 1.01 Hz, 1 H), 6.94 - 6.99 (m, 1 H), 7.15 (d, *J*=7.58 Hz, 1 H), 7.37 (d, *J*=8.08 Hz, 2 H), 7.90 (s, 1 H), 7.96 (d, *J*=8.08 Hz, 2 H), 8.17 (t, *J*=5.68 Hz, 1 H), 8.28 (s, 1 H), 9.65 (s, 1 H). ESI-MS: *m/z* 390.4 $(M + H)^+$.

Example 140: 1-(4-(2-aminophenylcarbamoyl)benzyl)-N-(2-(dimethylamino)ethyl)-1H-pyrazole-4-carboxamide



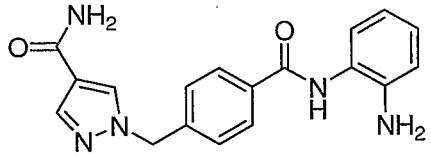
[0462] ^{1}H NMR (400 MHz, DMSO-d_6) of the *bis*-trifluoroacetic acid salt: δ ppm 2.52 - 2.55 (m, 2 H), 2.83 (d, *J*=4.80 Hz, 6 H), 3.17 - 3.23 (m, 2 H), 5.46 (s, 2 H), 6.61 - 6.68 (m, 1 H), 6.82 (d, *J*=7.33 Hz, 1 H), 6.97 - 7.03 (m, 1 H), 7.16 (d, *J*=8.59 Hz, 1 H), 7.38 (d, *J*=7.83 Hz, 2 H), 7.90 (s, 1 H), 7.96 (d, *J*=8.34 Hz, 2 H), 8.30 (s, 1 H), 8.34 (t, *J*=6.06 Hz, 1 H), 9.70 (s, 1 H). ESI-MS: *m/z* 407.4 $(M + H)^+$.

Example 141: 1-(4-(2-aminophenylcarbamoyl)benzyl)-N-(2-(dimethylamino)ethyl)-1H-pyrazole-4-carboxamide



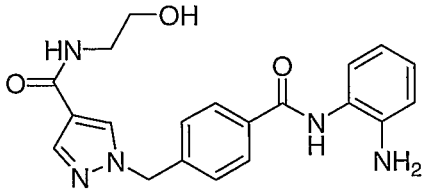
[0463] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 2.23 (s, 6 H), 2.47 - 2.49 (m, 2 H), 3.27 - 3.33 (m, 2 H), 4.89 (s, 2 H), 5.44 (s, 2 H), 6.59 (td, *J*=7.52, 1.39 Hz, 1 H), 6.77 (dd, *J*=8.08, 1.52 Hz, 1 H), 6.94 - 6.99 (m, 1 H), 7.15 (d, *J*=8.34 Hz, 1 H), 7.36 (d, *J*=8.34 Hz, 2 H), 7.88 (s, 1 H), 7.95 (d, *J*=8.34 Hz, 2 H), 8.04 (t, *J*=5.81 Hz, 1 H), 8.27 (s, 1 H), 9.64 (s, 1 H). ESI-MS: *m/z* 407.4 $(M + H)^+$.

Example 142: 1-(4-(2-aminophenylcarbamoyl)benzyl)-1H-pyrazole-4-carboxamide



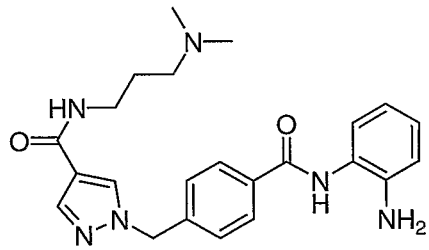
[0464] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 4.90 (s, 2 H), 5.43 (s, 2 H), 6.56 - 6.62 (m, 1 H), 6.77 (dd, *J*=8.08, 1.26 Hz, 1 H), 6.94 - 6.99 (m, 1 H), 7.03 (s, 1 H), 7.15 (d, *J*=7.33 Hz, 1 H), 7.36 (d, *J*=8.08 Hz, 2 H), 7.58 (s, 1 H), 7.88 (s, 1 H), 7.96 (d, *J*=8.34 Hz, 2 H), 8.26 (s, 1 H), 9.64 (s, 1 H). ESI-MS: *m/z* 336.3 $(M + H)^+$.

Example 143: 1-(4-(2-aminophenylcarbamoyl)benzyl)-N-(2-hydroxyethyl)-1H-pyrazole-4-carboxamide



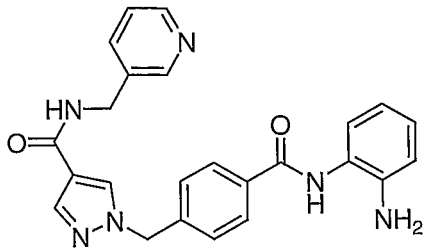
[0465] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 3.24 (q, *J*=5.98 Hz, 2 H), 3.45 (q, *J*=6.15 Hz, 2 H), 4.69 - 4.72 (m, 1 H), 4.89 (s, 2 H), 5.43 (s, 2 H), 6.59 (td, *J*=7.52, 1.39 Hz, 1 H), 6.77 (dd, *J*=8.08, 1.52 Hz, 1 H), 6.97 (td, *J*=7.71, 1.52 Hz, 1 H), 7.15 (d, *J*=7.58 Hz, 1 H), 7.36 (d, *J*=8.34 Hz, 2 H), 7.90 (d, *J*=0.51 Hz, 1 H), 7.95 (d, *J*=8.34 Hz, 2 H), 8.09 (t, *J*=5.68 Hz, 1 H), 8.28 (d, *J*=0.76 Hz, 1 H), 9.64 (s, 1 H). ESI-MS: *m/z* 380.3 $(M + H)^+$.

Example 144: 1-(4-(2-aminophenylcarbamoyl)benzyl)-N-(3-(dimethylamino)propyl)-1H-pyrazole-4-carboxamide



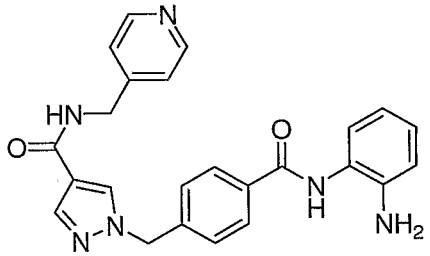
[0466] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 1.59 (qd, *J*=7.07, 6.82 Hz, 2 H), 2.12 (s, 6 H), 2.23 (t, *J*=7.20 Hz, 2 H), 3.16 - 3.22 (m, 2 H), 4.89 (s, 2 H), 5.43 (s, 2 H), 6.59 (td, *J*=7.52, 1.39 Hz, 1 H), 6.77 (dd, *J*=8.08, 1.52 Hz, 1 H), 6.97 (td, *J*=7.58, 1.52 Hz, 1 H), 7.15 (d, *J*=7.33 Hz, 1 H), 7.36 (d, *J*=8.08 Hz, 2 H), 7.87 (d, *J*=0.76 Hz, 1 H), 7.95 (d, *J*=8.34 Hz, 2 H), 8.10 (t, *J*=5.68 Hz, 1 H), 8.25 (d, *J*=0.51 Hz, 1 H), 9.64 (s, 1 H). ESI-MS: *m/z* 421.4 $(M + H)^+$.

Example 145: 1-(4-(2-aminophenylcarbamoyl)benzyl)-N-(pyridin-3-ylmethyl)-1H-pyrazole-4-carboxamide



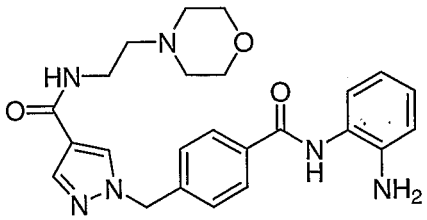
[0467] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 4.42 (d, *J*=5.81 Hz, 2 H), 4.89 (s, 2 H), 5.44 (s, 2 H), 6.59 (td, *J*=7.52, 1.39 Hz, 1 H), 6.77 (dd, *J*=7.96, 1.39 Hz, 1 H), 6.97 (td, *J*=7.58, 1.52 Hz, 1 H), 7.15 (d, *J*=7.33 Hz, 1 H), 7.33 - 7.36 (m, 1 H), 7.36 - 7.39 (m, 2 H), 7.69 (dt, *J*=7.83, 2.02 Hz, 1 H), 7.93 (d, *J*=0.51 Hz, 1 H), 7.95 (d, *J*=8.08 Hz, 2 H), 8.32 (d, *J*=0.51 Hz, 1 H), 8.45 (dd, *J*=4.80, 1.77 Hz, 1 H), 8.52 (d, *J*=1.52 Hz, 1 H), 8.70 (t, *J*=5.94 Hz, 1 H), 9.64 (s, 1 H). ESI-MS: *m/z* 427.3 $(M + H)^+$.

Example 146: 1-(4-(2-aminophenylcarbamoyl)benzyl)-N-(pyridin-4-ylmethyl)-1H-pyrazole-4-carboxamide



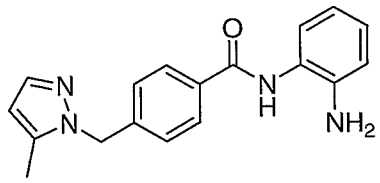
[0468] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 4.43 (d, *J*=6.06 Hz, 2 H), 4.90 (s, 2 H), 5.46 (s, 2 H), 6.59 (td, *J*=7.52, 1.39 Hz, 1 H), 6.77 (dd, *J*=7.96, 1.39 Hz, 1 H), 6.94 - 6.99 (m, 1 H), 7.15 (d, *J*=7.33 Hz, 1 H), 7.26 - 7.29 (m, 2 H), 7.39 (d, *J*=8.34 Hz, 2 H), 7.93 - 7.98 (m, 3 H), 8.34 (s, 1 H), 8.48 - 8.50 (m, 2 H), 8.75 (t, *J*=6.06 Hz, 1 H), 9.65 (s, 1 H). ESI-MS: *m/z* 427.3 $(M + H)^+$.

Example 147: 1-(4-(2-aminophenylcarbamoyl)benzyl)-N-(2-morpholinoethyl)-1H-pyrazole-4-carboxamide



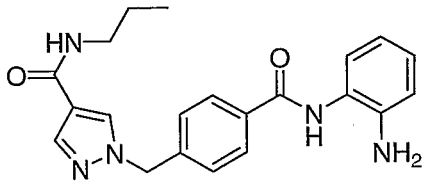
[0469] ^{1}H NMR (400 MHz, DMSO-d_6) of the *bis*-trifluoroacetic acid salt: δ ppm 3.07 - 3.19 (m, 2 H), 3.26 (t, *J*=6.19 Hz, 2 H), 3.49 - 3.59 (m, 4 H), 3.59 - 3.71 (m, 2 H), 4.00 (d, *J*=13.64 Hz, 2 H), 5.46 (s, 2 H), 6.79 (t, *J*=7.20 Hz, 1 H), 6.93 (d, *J*=7.07 Hz, 1 H), 7.05 - 7.10 (m, 1 H), 7.22 (d, *J*=7.07 Hz, 1 H), 7.39 (d, *J*=8.34 Hz, 2 H), 7.91 (d, *J*=0.51 Hz, 1 H), 7.97 (d, *J*=8.34 Hz, 2 H), 8.32 (d, *J*=0.51 Hz, 1 H), 8.42 (t, *J*=5.68 Hz, 1 H), 9.85 (s, 1 H). ESI-MS: *m/z* 449.4 $(M + H)^+$.

Example 148: N-(2-aminophenyl)-4-((5-methyl-1H-pyrazol-1-yl)methyl)benzamide



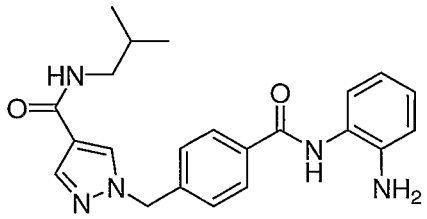
[0470] ^{1}H NMR (400 MHz, DMSO-d_6) of the trifluoroacetic acid salt: δ ppm 2.22 (s, 3 H), 5.40 (s, 2 H), 6.11 (dd, *J*=2.15, 1.14 Hz, 1 H), 7.05 (t, *J*=7.58 Hz, 1 H), 7.11 - 7.15 (m, 1 H), 7.19 (d, *J*=7.33 Hz, 1 H), 7.22 (d, *J*=8.08 Hz, 2 H), 7.32 (d, *J*=7.83 Hz, 1 H), 7.39 (d, *J*=1.77 Hz, 1 H), 7.96 (d, *J*=8.08 Hz, 2 H), 10.09 (s, 1 H). ESI-MS: *m/z* 307.3 $(M + H)^+$.

Example 149: 1-(4-(2-aminophenylcarbamoyl)benzyl)-N-propyl-1H-pyrazole-4-carboxamide



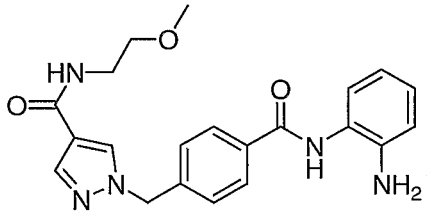
[0471] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 0.86 (t, *J*=7.33 Hz, 3 H), 1.43 - 1.52 (m, *J*=7.23, 7.23, 7.23, 7.23, 7.23 Hz, 2 H), 3.11 - 3.17 (m, 2 H), 4.90 (s, 2 H), 5.43 (s, 2 H), 6.59 (td, *J*=7.45, 1.26 Hz, 1 H), 6.77 (dd, *J*=7.96, 1.39 Hz, 1 H), 6.97 (td, *J*=7.71, 1.52 Hz, 1 H), 7.15 (d, *J*=7.83 Hz, 1 H), 7.36 (d, *J*=8.34 Hz, 2 H), 7.89 (d, *J*=0.51 Hz, 1 H), 7.96 (d, *J*=8.08 Hz, 2 H), 8.06 (t, *J*=5.68 Hz, 1 H), 8.26 (s, 1 H), 9.64 (s, 1 H). ESI-MS: *m/z* 378.3 $(M + H)^+$.

Example 150: 1-(4-(2-aminophenylcarbamoyl)benzyl)-N-isobutyl-1H-pyrazole-4-carboxamide



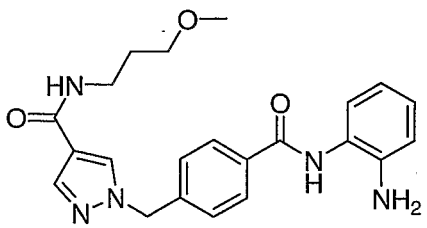
[0472] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 0.86 (d, *J*=6.57 Hz, 6 H), 1.76 (tt, *J*=13.52, 6.82 Hz, 1 H), 2.98 - 3.02 (m, 2 H), 4.90 (s, 2 H), 5.43 (s, 2 H), 6.59 (td, *J*=7.58, 1.26 Hz, 1 H), 6.77 (dd, *J*=8.08, 1.26 Hz, 1 H), 6.97 (td, *J*=7.58, 1.52 Hz, 1 H), 7.15 (d, *J*=7.58 Hz, 1 H), 7.37 (d, *J*=8.34 Hz, 2 H), 7.91 (d, *J*=0.51 Hz, 1 H), 7.96 (d, *J*=8.08 Hz, 2 H), 8.06 (t, *J*=5.94 Hz, 1 H), 8.27 (s, 1 H), 9.64 (s, 1 H). ESI-MS: *m/z* 392.4 $(M + H)^+$.

Example 151: 1-(4-(2-aminophenylcarbamoyl)benzyl)-N-(2-methoxyethyl)-1H-pyrazole-4-carboxamide



[0473] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 3.25 (s, 3 H), 3.33 - 3.36 (m, 2 H), 3.38 - 3.42 (m, 2 H), 4.89 (s, 2 H), 5.43 (s, 2 H), 6.59 (td, *J*=7.52, 1.39 Hz, 1 H), 6.77 (dd, *J*=8.08, 1.26 Hz, 1 H), 6.97 (td, *J*=7.64, 1.39 Hz, 1 H), 7.15 (d, *J*=7.07 Hz, 1 H), 7.36 (d, *J*=8.34 Hz, 2 H), 7.90 (d, *J*=0.51 Hz, 1 H), 7.95 (d, *J*=8.08 Hz, 2 H), 8.16 (t, *J*=5.43 Hz, 1 H), 8.28 (d, *J*=0.51 Hz, 1 H), 9.64 (s, 1 H). ESI-MS: *m/z* 394.3 $(M + H)^+$.

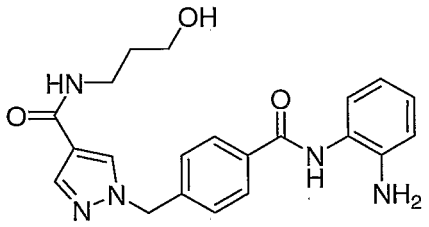
Example 152: 1-(4-(2-aminophenylcarbamoyl)benzyl)-N-(3-methoxypropyl)-1H-pyrazole-4-carboxamide



[0474] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 1.66 - 1.73 (m, 2 H), 3.18 - 3.22 (m, 1 H), 3.22 (s, 4 H), 3.33 (t, *J*=3.16 Hz, 2 H), 4.89 (s, 2 H), 5.43 (s, 2 H), 6.59 (td, *J*=7.58,

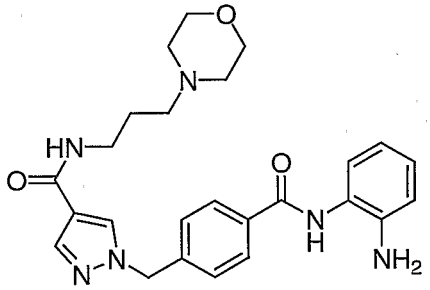
1.26 Hz, 1 H), 6.77 (dd, *J*=7.96, 1.39 Hz, 1 H), 6.97 (td, *J*=7.58, 1.52 Hz, 1 H), 7.15 (d, *J*=7.33 Hz, 1 H), 7.36 (d, *J*=8.34 Hz, 2 H), 7.88 (d, *J*=0.76 Hz, 1 H), 7.95 (d, *J*=8.08 Hz, 2 H), 8.08 (t, *J*=5.68 Hz, 1 H), 8.26 (d, *J*=0.76 Hz, 1 H), 9.64 (s, 1 H). ESI-MS: *m/z* 408.4 $(M + H)^+$.

Example 153: 1-(4-(2-aminophenylcarbamoyl)benzyl)-N-(3-hydroxypropyl)-1H-pyrazole-4-carboxamide



[0475] ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 1.62 (qd, *J*=6.74, 6.57 Hz, 2 H), 3.23 (q, *J*=6.65 Hz, 2 H), 3.40 - 3.46 (m, 2 H), 4.46 (t, *J*=5.31 Hz, 1 H), 4.90 (s, 2 H), 5.43 (s, 2 H), 6.59 (td, *J*=7.52, 1.39 Hz, 1 H), 6.77 (dd, *J*=8.08, 1.26 Hz, 1 H), 6.97 (td, *J*=7.58, 1.52 Hz, 1 H), 7.15 (d, *J*=7.07 Hz, 1 H), 7.36 (d, *J*=8.08 Hz, 2 H), 7.89 (d, *J*=0.51 Hz, 1 H), 7.96 (d, *J*=8.08 Hz, 2 H), 8.07 (t, *J*=5.68 Hz, 1 H), 8.26 (d, *J*=0.51 Hz, 1 H), 9.64 (s, 1 H). ESI-MS: *m/z* 394.3 $(M + H)^+$.

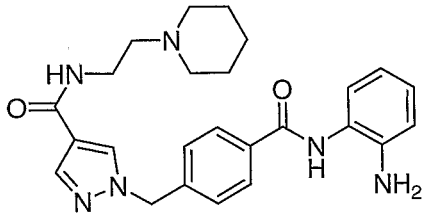
Example 154: 1-(4-(2-aminophenylcarbamoyl)benzyl)-N-(3-morpholinopropyl)-1H-pyrazole-4-carboxamide



[0476] ^{1}H NMR (400 MHz, DMSO-d_6) of the *bis*-trifluoroacetic acid salt: δ ppm 1.83 - 1.91 (m, 2 H), 3.01 - 3.10 (m, 2 H), 3.10 - 3.17 (m, 2 H), 3.26 (q, *J*=6.32 Hz, 2 H), 3.43 (d, *J*=11.87 Hz, 2 H), 3.64 (t, *J*=11.87 Hz, 2 H), 3.97 (d, *J*=11.87 Hz, 2 H), 5.46 (s, 2 H), 6.93 (t, *J*=7.07 Hz, 1 H), 7.04 (dd, *J*=8.08, 1.26 Hz, 1 H), 7.11 - 7.17 (m, 1 H), 7.28 (d, *J*=8.84

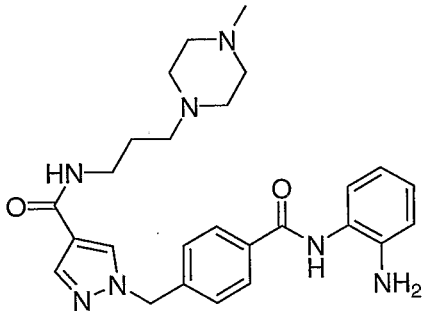
Hz, 1 H), 7.39 (d, *J*=8.34 Hz, 2 H), 7.91 (s, 1 H), 7.98 (d, *J*=8.08 Hz, 2 H), 8.29 - 8.35 (m, 2 H), 10.00 (s, 1 H). ESI-MS: *m/z* 463.4 $(M + H)^+$.

Example 155: 1-(4-(2-aminophenylcarbamoyl)benzyl)-N-(2-(piperidin-1-yl)ethyl)-1H-pyrazole-4-carboxamide



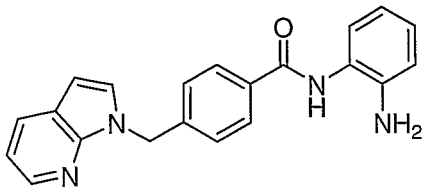
[0477] 1H NMR (400 MHz, DMSO-d_6) of the *bis*-trifluoroacetic acid salt: δ ppm 1.32 - 1.43 (m, 1 H), 1.60 - 1.71 (m, 3 H), 1.81 (d, *J*=14.40 Hz, 2 H), 2.87 - 2.97 (m, 2 H), 3.18 (d, *J*=5.31 Hz, 2 H), 3.49 - 3.59 (m, 4 H), 5.47 (s, 2 H), 6.94 (t, *J*=6.95 Hz, 1 H), 7.05 - 7.08 (m, 1 H), 7.15 (td, *J*=7.64, 1.39 Hz, 1 H), 7.30 (d, *J*=6.82 Hz, 1 H), 7.40 (d, *J*=8.34 Hz, 2 H), 7.92 (d, *J*=0.76 Hz, 1 H), 7.99 (d, *J*=8.08 Hz, 2 H), 10.02 (s, 1 H). ESI-MS: *m/z* 447.4 $(M + H)^+$.

Example 156: 1-(4-(2-aminophenylcarbamoyl)benzyl)-N-(3-(4-methylpiperazin-1-yl)propyl)-1H-pyrazole-4-carboxamide



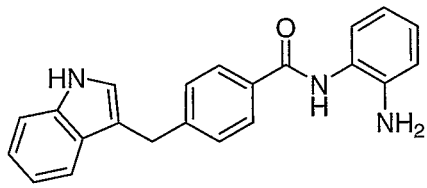
[0478] ^{1}H NMR (400 MHz, DMSO-d_6) of the *bis*-trifluoroacetic acid salt: δ ppm 1.80 - 1.88 (m, 2 H), 2.84 (s, 3 H), 3.06 - 3.13 (m, 2 H), 3.26-3.60 (m, 10 H), 5.45 (s, 2 H), 6.91 (t, *J*=6.95 Hz, 1 H), 7.03 (dd, *J*=8.08, 1.26 Hz, 1 H), 7.13 (td, *J*=7.58, 1.52 Hz, 1 H), 7.27 (d, *J*=8.84 Hz, 1 H), 7.39 (d, *J*=8.34 Hz, 2 H), 7.91 (d, *J*=0.76 Hz, 1 H), 7.98 (d, *J*=8.34 Hz, 2 H), 8.30 (d, *J*=0.76 Hz, 1 H), 9.98 (s, 1 H). ESI-MS: *m/z* 476.4 $(M + H)^+$.

Example 157: 4-((1*H*-Pyrrolo[2,3-b]pyridin-1-yl)methyl)-N-(2-aminophenyl)benzamide



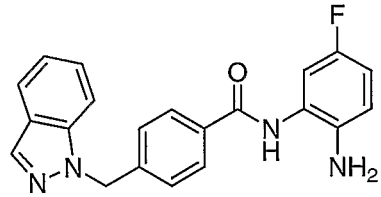
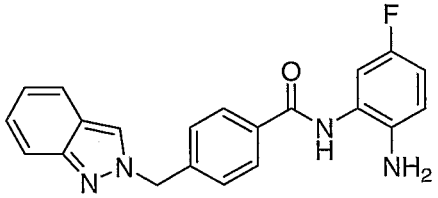
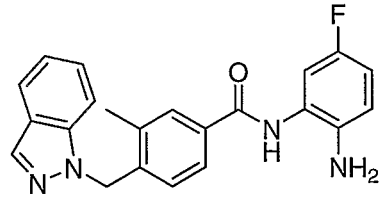
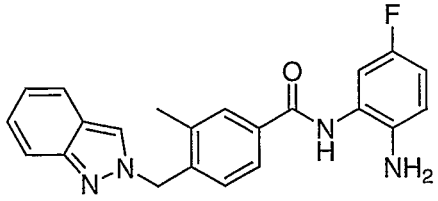
[0479] ^{1}H NMR (400 MHz, DMSO-D6) of the trifluoroacetic acid salt: δ ppm 6.03 (s, 2 H) 6.67 (s, 1 H) 6.83 (s, 1 H) 6.91 - 7.02 (m, 2 H) 7.12 (d, *J*=7.33 Hz, 1 H) 7.31 - 7.40 (m, 2 H) 7.45 (d, *J*=8.34 Hz, 1 H) 7.58 - 7.70 (m, 1 H) 7.87 - 7.99 (m, 2 H) 8.65 - 8.80 (m, 2 H) 9.76 (s, 1 H). ESI-MS: *m/z* 343.4 $(M + H)^+$.

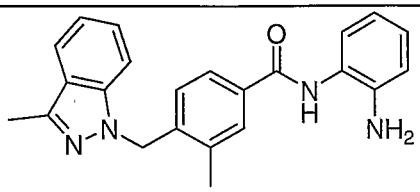
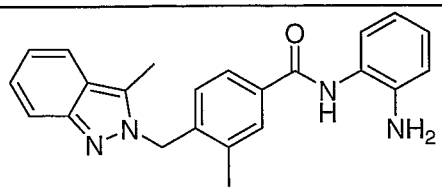
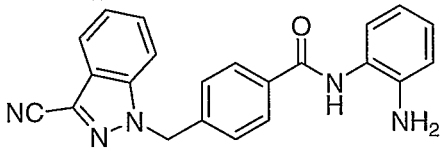
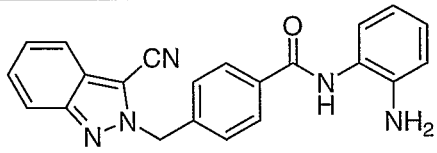
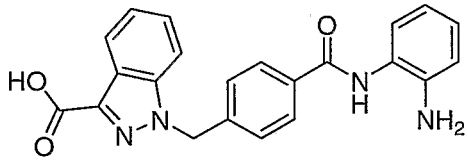
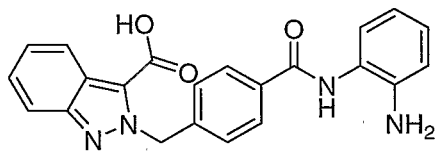
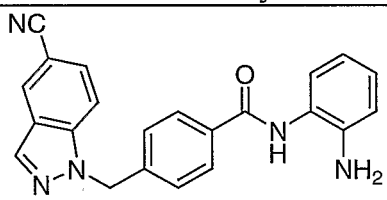
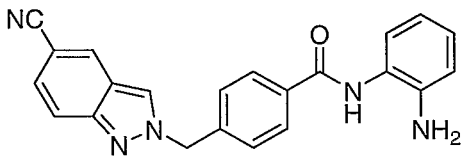
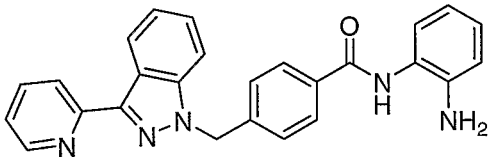
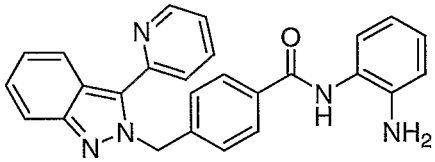
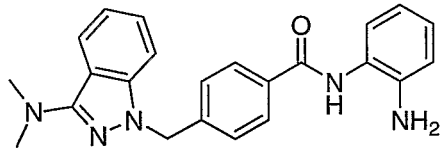
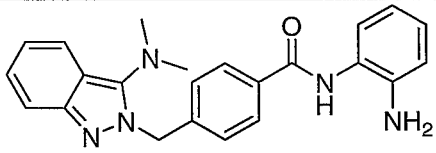
Example 158: 4-((1*H*-Indol-3-yl)methyl)-N-(2-aminophenyl)benzamide

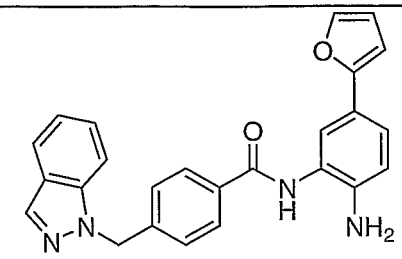
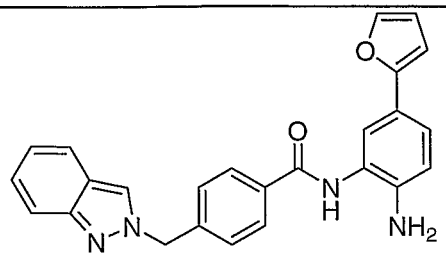
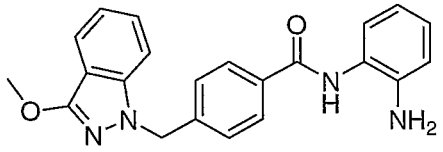
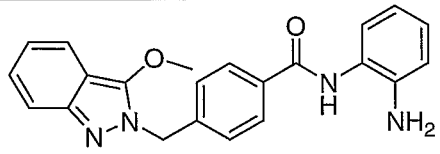
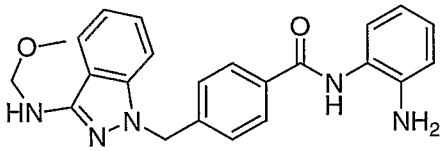
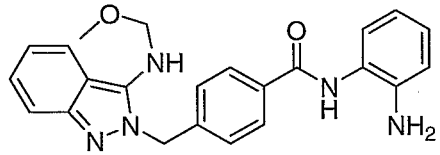
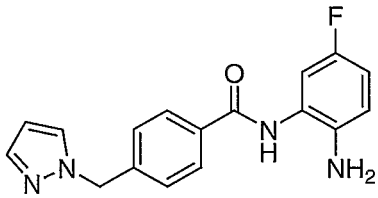
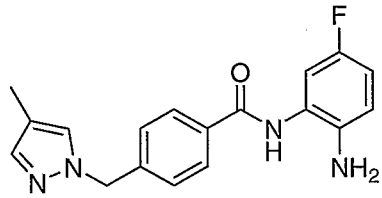
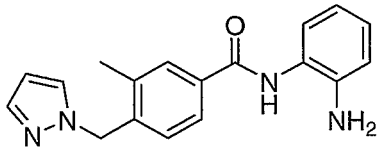
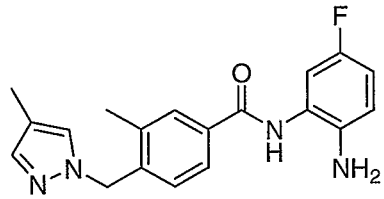
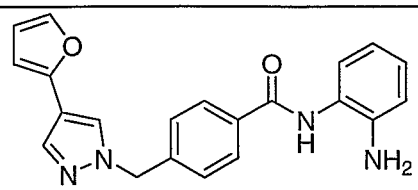
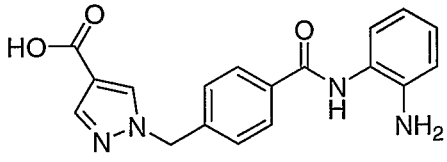


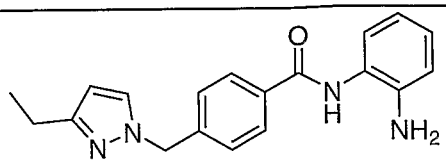
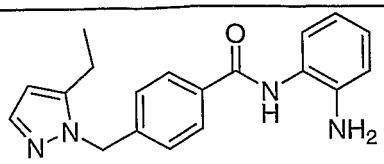
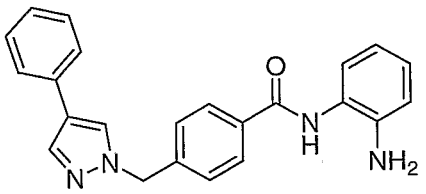
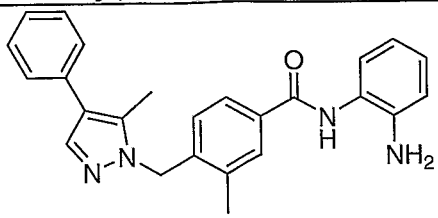
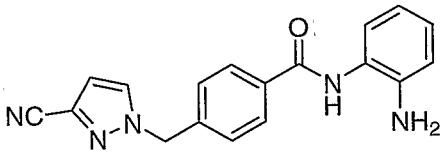
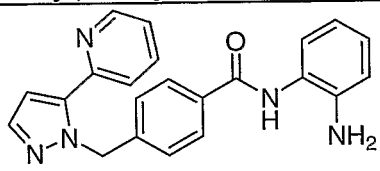
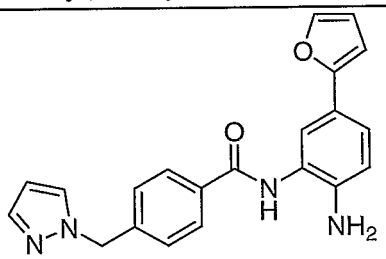
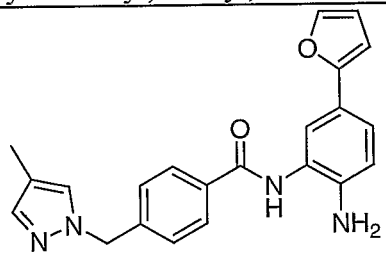
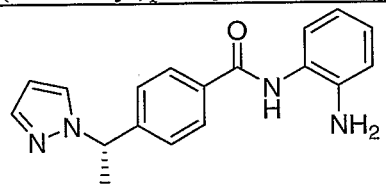
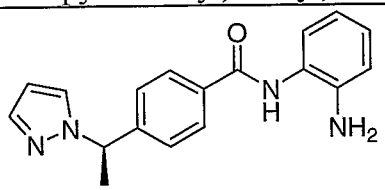
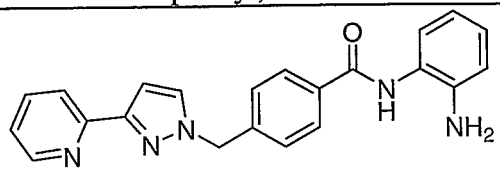
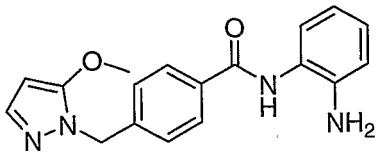
[0480] ^{1}H NMR (400 MHz, DMSO-D6) δ ppm 4.10 (s, 2 H) 4.84 (s, 2 H) 6.53 - 6.60 (m, 1 H) 6.74 (d, *J*=7.83 Hz, 1 H) 6.88 - 6.97 (m, 2 H) 7.00 - 7.07 (m, 2 H) 7.11 (s, 1 H) 7.19 (d, *J*=2.27 Hz, 1 H) 7.32 (d, *J*=8.08 Hz, 1 H) 7.36 - 7.42 (m, 2 H) 7.85 (d, *J*=8.08 Hz, 2 H) 9.54 (s, 1 H) 10.87 (s, 1 H). ESI-MS: *m/z* 342.4 $(M + H)^+$.

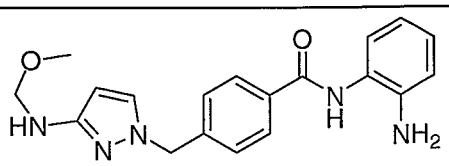
[0481] In addition to the examples described above, the following non-limiting group of compounds can be prepared utilizing the above reaction schemes, and variations thereof, with the appropriate selection of substituents:

 4-((1H-indazol-1-yl)methyl)-N-(2-amino-5-fluorophenyl)benzamide	 4-((2H-indazol-2-yl)methyl)-N-(2-amino-5-fluorophenyl)benzamide
 4-((1H-indazol-1-yl)methyl)-N-(2-amino-5-fluorophenyl)-3-methylbenzamide	 4-((2H-indazol-2-yl)methyl)-N-(2-amino-5-fluorophenyl)-3-methylbenzamide

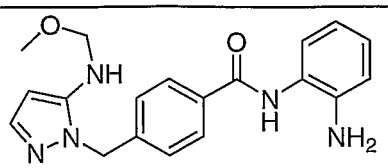
 N-(2-aminophenyl)-3-methyl-4-((3-methyl-1H-indazol-1-yl)methyl)benzamide	 N-(2-aminophenyl)-3-methyl-4-((3-methyl-2H-indazol-2-yl)methyl)benzamide
 N-(2-aminophenyl)-4-((3-cyano-1H-indazol-1-yl)methyl)benzamide	 N-(2-aminophenyl)-4-((3-cyano-2H-indazol-2-yl)methyl)benzamide
 1-(4-((2-aminophenyl)carbamoyl)benzyl)-1H-indazole-3-carboxylic acid	 2-(4-((2-aminophenyl)carbamoyl)benzyl)-2H-indazole-3-carboxylic acid
 N-(2-aminophenyl)-4-((5-cyano-1H-indazol-1-yl)methyl)benzamide	 N-(2-aminophenyl)-4-((5-cyano-2H-indazol-2-yl)methyl)benzamide
 N-(2-aminophenyl)-4-((3-(pyridin-2-yl)-1H-indazol-1-yl)methyl)benzamide	 N-(2-aminophenyl)-4-((3-(pyridin-2-yl)-2H-indazol-2-yl)methyl)benzamide
 N-(2-aminophenyl)-4-((3-(dimethylamino)-1H-indazol-1-yl)methyl)benzamide	 N-(2-aminophenyl)-4-((3-(dimethylamino)-2H-indazol-2-yl)methyl)benzamide

 4-((1H-indazol-1-yl)methyl)-N-(2-amino-5-(furan-2-yl)phenyl)benzamide	 4-((2H-indazol-2-yl)methyl)-N-(2-amino-5-(furan-2-yl)phenyl)benzamide
 N-(2-aminophenyl)-4-((3-methoxy-1H-indazol-1-yl)methyl)benzamide	 N-(2-aminophenyl)-4-((3-methoxy-2H-indazol-2-yl)methyl)benzamide
 N-(2-aminophenyl)-4-((3-(methoxymethylamino)-1H-indazol-1-yl)methyl)benzamide	 N-(2-aminophenyl)-4-((3-(methoxymethylamino)-2H-indazol-2-yl)methyl)benzamide
 4-((1H-pyrazol-1-yl)methyl)-N-(2-amino-5-fluorophenyl)benzamide	 N-(2-amino-5-fluorophenyl)-4-((4-methyl-1H-pyrazol-1-yl)methyl)benzamide
 4-((1H-pyrazol-1-yl)methyl)-N-(2-aminophenyl)-3-methylbenzamide	 N-(2-amino-5-fluorophenyl)-3-methyl-4-((4-methyl-1H-pyrazol-1-yl)methyl)benzamide
 N-(2-aminophenyl)-4-((4-(furan-2-yl)-1H-pyrazol-1-yl)methyl)benzamide	 1-(4-((2-aminophenyl)carbamoyl)benzyl)-1H-pyrazole-4-carboxylic acid

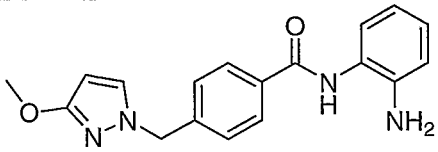
 N-(2-aminophenyl)-4-((3-ethyl-1H-pyrazol-1-yl)methyl)benzamide	 N-(2-aminophenyl)-4-((5-ethyl-1H-pyrazol-1-yl)methyl)benzamide
 N-(2-aminophenyl)-4-((4-phenyl-1H-pyrazol-1-yl)methyl)benzamide	 N-(2-aminophenyl)-3-methyl-4-((5-methyl-4-phenyl-1H-pyrazol-1-yl)methyl)benzamide
 N-(2-aminophenyl)-4-((3-cyano-1H-pyrazol-1-yl)methyl)benzamide	 N-(2-aminophenyl)-4-((5-(pyridin-2-yl)-1H-pyrazol-1-yl)methyl)benzamide
 4-((1H-pyrazol-1-yl)methyl)-N-(2-amino-5-(furan-2-yl)phenyl)benzamide	 N-(2-amino-5-(furan-2-yl)phenyl)-4-((4-methyl-1H-pyrazol-1-yl)methyl)benzamide
 (S)-4-(1-(1H-pyrazol-1-yl)ethyl)-N-(2-aminophenyl)benzamide	 (R)-4-(1-(1H-pyrazol-1-yl)ethyl)-N-(2-aminophenyl)benzamide
 N-(2-aminophenyl)-4-((3-(pyridin-2-yl)-1H-pyrazol-1-yl)methyl)benzamide	 N-(2-aminophenyl)-4-((5-methoxy-1H-pyrazol-1-yl)methyl)benzamide



N-(2-aminophenyl)-4-((3-(methoxymethylamino)-1H-pyrazol-1-yl)methyl)benzamide



N-(2-aminophenyl)-4-((5-(methoxymethylamino)-1H-pyrazol-1-yl)methyl)benzamide



N-(2-aminophenyl)-4-((3-methoxy-1H-pyrazol-1-yl)methyl)benzamide

Biological Testing

[0482] The activity of compounds as HDAC inhibitors may be assayed in vitro, in vivo or in a cell line. Further, compounds according to the present invention may be screened for activity against one or more HDACs. Provided below are assays for activity against HDAC1, HDAC2, HDAC6 and HDAC8.

[0483] Purified HDAC1, HDAC2, HDAC6, and HDAC8 may be obtained as follows.

[0484] For HDAC1, DNA encoding residues 1-482 of the full-length sequence of the human enzyme may be amplified by PCR and cloned into the BamHI/XbaI sites of pFastbac (Invitrogen), which incorporates a Flag tag at both the N- and C-terminus. SEQ ID NO: 1 corresponds to residues 1-482 with the N-and C-terminal Flag tag and SEQ ID NO: 2 is the DNA sequence that was used to encode SEQ ID NO: 1.

[0485] For HDAC2, DNA encoding residues 1-488 of the full-length sequence of the human enzyme may be amplified by PCR and cloned into the BamHI/SmaI sites of pFastbac (Invitrogen), which incorporates a 6-histidine tag at the C-terminus. SEQ ID NO: 3 corresponds to residues 1-488 with the C-terminal 6-histidine tag and SEQ ID NO: 4 is the DNA sequence that was used to encode SEQ ID NO: 3.

[0486] For HDAC6, DNA encoding residues 73-845 of the human enzyme may be amplified by PCR and cloned into the SmaI site of pFastbac (Invitrogen), which incorporates a 6xHistidine tag at the C-terminus. SEQ ID NO: 5 corresponds to residues 73-845 with the C-terminal 6-histidine tag and SEQ ID NO: 6 is the DNA sequence that was used to encode SEQ ID NO: 5.

[0487] For HDAC8, DNA encoding residues 1-377 corresponding to the entire sequence of the human enzyme may be amplified by PCR and cloned into the BamHI/SmaI sites of pFastbac (Invitrogen), which incorporates a 6-histidine tag at the N-terminus. SEQ ID NO: 7 corresponds to residues 1-377 with the N-terminal 6-histidine tag and SEQ ID NO: 8 is the DNA sequence that was used to encode SEQ ID NO: 7.

[0488] Recombinant baculovirus incorporating the HDAC constructs may be generated by transposition using the Bac-to-Bac system (Invitrogen). High-titer viral stocks may be generated by infection of Spodoptera frugiperda Sf9 cells; the expression of recombinant protein may be carried out by infection of Spodoptera frugiperda Sf9 or Trichoplusia ni Hi5 cells (Invitrogen) in 10L Wave Bioreactors (Wave Biotech).

[0489] Recombinant protein may be isolated from cellular extracts by passage over ProBond resin (Invitrogen), or Anti-Flag M2 Affinity Gel (Sigma) for HDAC1. Partially purified HDAC1 may then be further purified by high pressure liquid chromatography over a Mono Q column. Partially purified extracts of HDACs other than HDAC1 and HDAC6 may then be further purified by high pressure liquid chromatography over a BioSep S3000 gel filtration resin. The purity of HDAC proteins may be determined on denaturing SDS-PAGE gel. Purified HDACs may then be concentrated to a final concentration of 0.6 mg/ml for HDAC1, 10 mg/ml for HDAC2, 0.3 mg/ml for HDAC6, and 3 mg/ml for HDAC8. The proteins may be either stored at –78 °C in a buffer containing 25mM TRIS-HCl pH 7.6, 150mM NaCl, 0.1mM EDTA and 0.25 mM TCEP or at –20 °C in the presence of glycerol (final concentration of glycerol at 50%). Alternatively, HDAC6 protein can be stored at –78 °C in a buffer containing 25mM TRIS-HCl pH 7.2, 250mM NaCl, and 5% glycerol.

[0490] It should be noted that a variety of other expression systems and hosts are also suitable for the expression of HDAC, as would be readily appreciated by one of skill in the art.

[0491] The inhibitory properties of compounds relative to HDAC1, HDAC2, HDAC6 and HDAC8 may be determined using a white or black 384-well-plate format under the following reaction conditions: 25 mM Tris pH 8.0, 100 mM NaCl, 50 mM KCl, 0.1 mM EDTA, 0.01% Brij35, 0.1 mM TCEP. 50 μM tBoc-Lys(Ac)-AMC, 2% DMSO. Reaction product may be determined quantitatively by fluorescence intensity using a Fluorescence

plate reader (Molecular Devices Gemini) with an excitation wavelength at 370 nm and emission at 480 nm (for white plates) or 465 nm (for black plates).

[0492] The assay reaction may be initiated as follows: 5 µl of 150 µM tBoc-Lys(Ac)AMC was added to each well of the plate, followed by the addition of 5 µl of inhibitor (2 fold serial dilutions for 11 data points for each inhibitor) containing 6% DMSO. 5 µl of either HDAC1, HDAC2, HDAC6 or HDAC8 solution may be added to initiate the reaction (final enzyme concentrations were 2.5 nM for HDAC1, 1 nM for HDAC2, 2.5 nM for HDAC6 and 10 nM for HDAC8). The reaction mixture may then be incubated at room temperature for 60 minutes, and quenched and developed by addition of 5 µl of 10 mM phenanthroline and 4 mg/ml trypsin (final concentration of phenanthroline is 2.5 mM, and trypsin is 1 mg/ml). Fluorescence intensities of the resulting reaction mixtures may be measured after a 30 minute incubation at room temperature.

[0493] IC50 values may be calculated by non-linear curve fitting of the compound concentrations and fluorescence intensities to the standard IC50 equation. As a reference point for this assay, suberanilohydroxamic acid (SAHA) showed an IC_{50} of 63 nM for HDAC1, 69 nM for HDAC2, 108 nM for HDAC6 and 242 nM for HDAC8. IC_{50} values for selected compounds of the present invention are given in Table 4.

TABLE 4: IC_{50} of SELECTED EXEMPLIFIED COMPOUNDS AGAINST HDAC2

EXAMPLE	IC_{50}
1.	≤50 NM
2.	50-100 NM
3.	≤50 NM
4.	≤50 NM
5.	≤50 NM
6.	≤50 NM
7.	≤50 NM
8.	≤50 NM
9.	50-100 NM
10.	≤50 NM
11.	≤50 NM
12.	≤50 NM
13.	≤50 NM
14.	≤50 NM
15.	≤50 NM

EXAMPLE	IC_{50}
16.	≤50 NM
17.	≤50 NM
18.	≤50 NM
19.	100-500 NM
20.	≤50 NM
21.	≤50 NM
22.	≤50 NM
23.	≤50 NM
24.	100-500 NM
25.	100-500 NM
26.	≤50 NM
27.	≤50 NM
28.	50-100 NM
29.	50-100 NM
30.	50-100 NM
31.	≥500 NM
32.	≤50 NM
33.	≥500 NM
34.	100-500 NM
35.	50-100 NM
36.	50-100 NM
37.	50-100 NM
38.	≤50 NM
39.	≥500 NM
40.	100-500 NM
41.	50-100 NM
42.	≤50 NM
43.	≤50 NM
44.	50-100 NM
45.	50-100 NM
46.	50-100 NM
47.	50-100 NM
48.	50-100 NM
49.	≤50 NM
50.	50-100 NM
51.	50-100 NM
52.	50-100 NM
53.	50-100 NM
54.	100-500 NM
55.	50-100 NM
56.	50-100 NM
57.	50-100 NM
58.	50-100 NM
59.	≤50 NM

EXAMPLE	IC_{50}
60.	50-100 NM
61.	≤50 NM
62.	≤50 NM
63.	50-100 NM
64.	50-100 NM
65.	100-500 NM
66.	≤50 NM
67.	≤50 NM
68.	50-100 NM
69.	50-100 NM
70.	100-500 NM
71.	50-100 NM
72.	50-100 NM
73.	100-500 NM
74.	≤50 NM
75.	100-500 NM
76.	50-100 NM
77.	50-100 NM
78.	≤50 NM
79.	≤50 NM
80.	50-100 NM
81.	50-100 NM
82.	50-100 NM
83.	≤50 NM
84.	100-500 NM
85.	≤50 NM
86.	≤50 NM
87.	50-100 NM
88.	50-100 NM
89.	≤50 NM
90.	≤50 NM
91.	50-100 NM
92.	50-100 NM
93.	50-100 NM
94.	50-100 NM
95.	≤50 NM
96.	50-100 NM
97.	50-100 NM
98.	≤50 NM
99.	≤50 NM
100.	50-100 NM
101.	50-100 NM
102.	≥500 NM
103.	≤50 NM

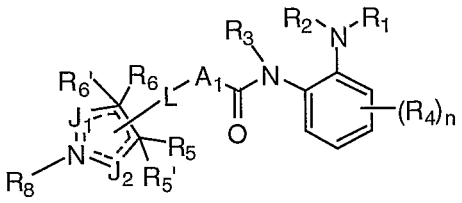
EXAMPLE	IC_{50}
104.	≥500 NM
105.	50-100 NM
106.	≤50 NM
107.	50-100 NM
108.	50-100 NM
109.	50-100 NM
110.	50-100 NM
111.	≤50 NM
112.	100-500 NM
113.	100-500 NM
114.	50-100 NM
115.	≤50 NM
116.	50-100 NM
117.	50-100 NM
118.	50-100 NM
119.	50-100 NM
120.	50-100 NM
121.	≤50 NM
122.	≥500 NM
123.	100-500 NM
124.	100-500 NM
125.	50-100 NM
126.	≤50 NM
127.	≤50 NM
128.	≤50 NM
129.	50-100 NM
130.	100-500 NM
131.	≥500 NM
132.	≥500 NM
133.	100-500 NM
134.	50-100 NM
135.	50-100 NM
136.	100-500 NM
137.	≤50 NM
138.	50-100 NM
139.	50-100 NM
140.	50-100 NM
141.	50-100 NM
142.	50-100 NM
143.	50-100 NM
144.	≤50 NM
145.	≤50 NM
146.	≤50 NM
147.	50-100 NM

EXAMPLE	IC_{50}
148.	100-500 NM
149.	≤50 NM
150.	≤50 NM
151.	50-100 NM
152.	≤50 NM
153.	≤50 NM
154.	≤50 NM
155.	≤50 NM
156.	50-100 NM
157.	100-500 NM
158.	50-100 NM

[0494] It will be apparent to those skilled in the art that various modifications and variations can be made in the compounds, compositions, kits, and methods of the present invention without departing from the spirit or scope of the invention. Thus, it is intended that the present invention cover the modifications and variations of this invention provided they come within the scope of the appended claims and their equivalents.

What is claimed is:

1. A compound comprising:



wherein:

n is selected from the group consisting of 0, 1, 2, 3 and 4;

A_1 is selected from the group consisting of (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl, and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

L is a linker providing a 0-6 atom separation between the two ring atoms to which L is attached;

J_1 is selected from the group consisting of $-CR_7R_7'$- and $-NR_{19}$-;

J_2 is selected from the group consisting of $-CR_{20}R_{20}'$ and $-NR_{10}$-;

R_1 and R_2 are each independently selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_1 and R_2 may be taken together to form a substituted or unsubstituted ring;

R_3 is selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl,

imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

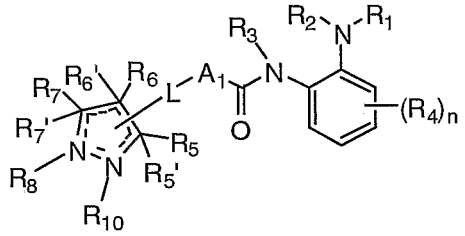
each R_4 is selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

R_5, R_5', R_6, R_6', R_7, R_7', R_{20} and R_{20}' are each independently selected from the group consisting of hydrogen, halo, nitro, cyano, oxo, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or any two of R_5, R_5', R_6, R_6', R_7, R_7', R_{20} and R_{20}' may be taken together to form a substituted or unsubstituted ring, provided that R_5, R_6, R_7 and R_{20}, are each independently absent when the C to which they are bound is bound to L, and R_5', R_6', R_7' and R_{20}', are each independently absent when the C to which they are bound form part of a double bond; and

R_8, R_{10} and R_{19} are each individually selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino,

(C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_8 and any one of R_5, R_5', R_6, R_6', R_7, R_7', R_{20}, R_{20}', R_{10} and R_{19} may be taken together to form a substituted or unsubstituted ring, or R_{10} and any one of R_5, R_5', R_6, R_6', R_7, R_7', R_{20}, R_{20}', and R_{19}, may be taken together to form a substituted or unsubstituted ring, or R_{19} and any one of R_5, R_5', R_6, R_6', R_{20}, and R_{20}', may be taken together to form a substituted or unsubstituted ring, provided that R_8, R_{10} and R_{19} are each independently absent when the N to which they are bound is bound to L, and R_8, R_{10} and R_{19} are each independently absent when the N to which they are bound form part of a double bond.

2. The compound according to claim 1 comprising



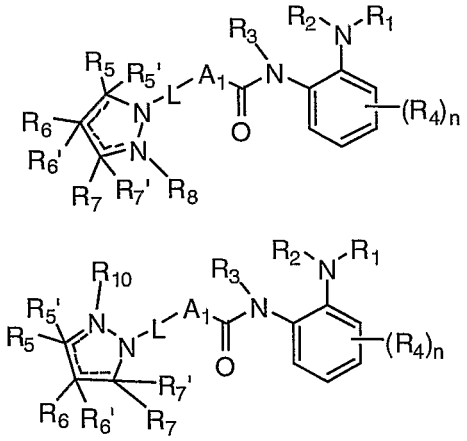
wherein:

R_5, R_5', R_6, R_6', R_7 and R_7' are each independently selected from the group consisting of hydrogen, halo, nitro, cyano, oxo, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and

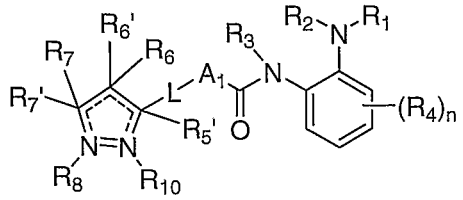
hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or any two of R_5, R_5', R_6, R_6', R_7 and R_7' may be taken together to form a substituted or unsubstituted ring, provided that R_5, R_6 and R_7 are each independently absent when the C to which they are bound is bound to L, and R_5', R_6' and R_7' are each independently absent when the C to which they are bound form part of a double bond; and

R_8 and R_{10} are each individually selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_8 and any one of R_5, R_5', R_6, R_6', R_7, R_7' and R_{10} may be taken together to form a substituted or unsubstituted ring, or R_{10} and any one of R_5, R_5', R_6, R_6', R_7 and R_7' may be taken together to form a substituted or unsubstituted ring, provided that R_8 and R_{10} are each independently absent when the N to which they are bound is bound to L, and R_8 and R_{10} are each independently absent when the N to which they are bound form part of a double bond.

3. The compound according to claim 2, wherein the compound is selected from the group consisting of:



and



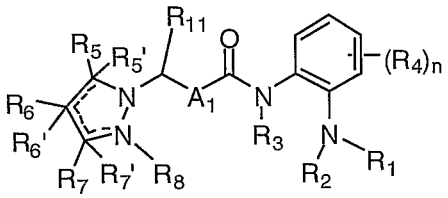
wherein:

R_5, R_5', R_6, R_6', R_7 and R_7' are each independently selected from the group consisting of hydrogen, halo, nitro, cyano, oxo, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or any two of R_5, R_5', R_6, R_6', R_7 and R_7' may be taken together to form a substituted or unsubstituted ring, provided that R_5', R_6' and R_7' are each independently absent when the C to which they are bound form part of a double bond; and

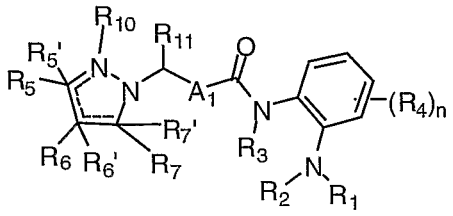
R_8 and R_{10} are each individually selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_8 and any one of R_5, R_5', R_6, R_6', R_7, R_7' and R_{10} may be taken together to form a substituted or unsubstituted ring, or R_{10} and any one of R_5, R_5', R_6, R_6', R_7 and R_7' may be taken together to form a substituted or unsubstituted ring, provided that R_8 and R_{10}

are each independently absent when the N to which they are bound form part of a double bond.

4. The compound according to claim 3, wherein the compound is selected from the group consisting of:



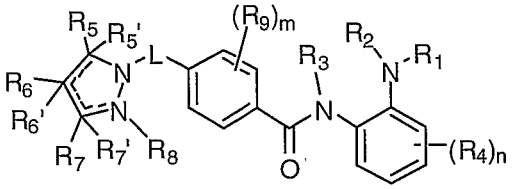
and



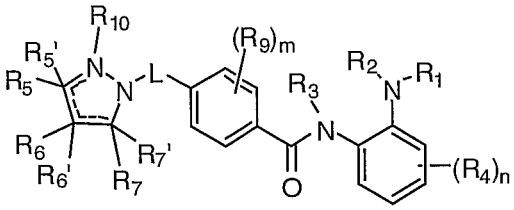
wherein:

R_{11} is selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted.

5. The compound according to claim 3, wherein the compound is selected from the group consisting of:



and

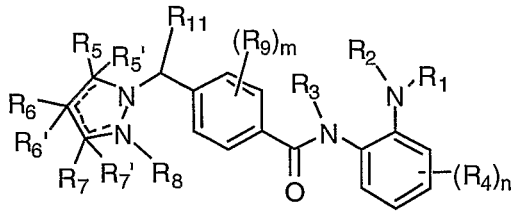


wherein:

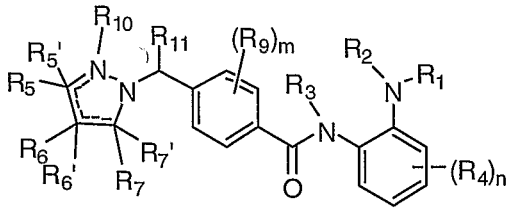
m is selected from the group consisting of 0, 1, 2, 3 and 4;

each R_9 is independently selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or any two R_9 or one R_9 and any one of R_3, R_5, R_5', R_7, R_7', R_8 and R_{10} may be taken together to form a substituted or unsubstituted ring.

6. The compound according to claim 3, wherein the compound is selected from the group consisting of:



and



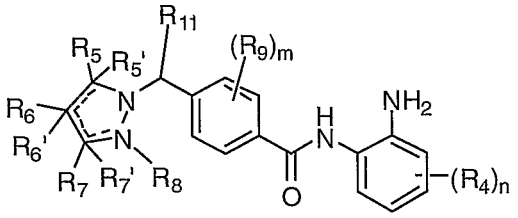
wherein:

m is selected from the group consisting of 0, 1, 2, 3 and 4;

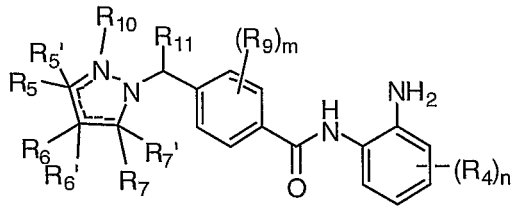
each R_9 is independently selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or any two R_9 or one R_9 and any one of R_3, R_5, R_5', R_7, R_7', R_8 and R_{10} may be taken together to form a substituted or unsubstituted ring; and

R_{11} is selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_{11} and R_9 may be taken together to form a substituted or unsubstituted ring.

7. The compound according to claim 3, wherein the compound is selected from the group consisting of:



and



wherein:

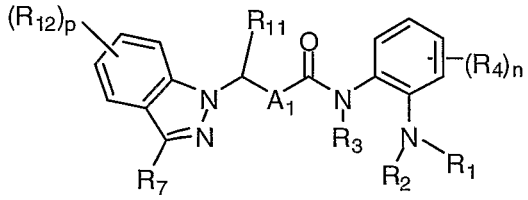
m is selected from the group consisting of 0, 1, 2, 3 and 4;

each R_9 is independently selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or any two R_9 or one R_9 and any one of R_5, R_5', R_7, R_7', R_8 and R_{10} may be taken together to form a substituted or unsubstituted ring; and

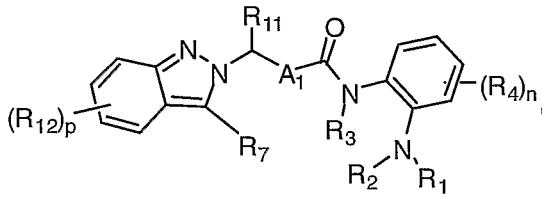
R_{11} is selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl,

hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_{11} and R_9 may be taken together to form a substituted or unsubstituted ring.

8. The compound according to claim 3, wherein the compound is selected from the group consisting of:



and



wherein:

p is selected from the group consisting of 0, 1, 2, 3 and 4;

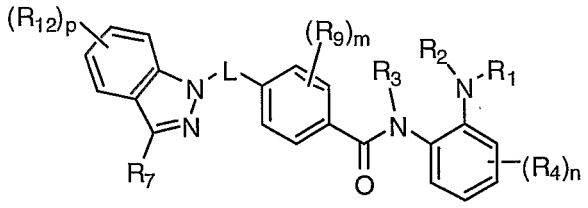
R_7 is selected from the group consisting of hydrogen, halo, nitro, cyano, oxo, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

R_{11} is selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino,

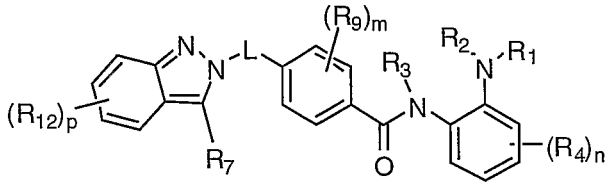
sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_{11} and R_7 may be taken together to form a substituted or unsubstituted ring; and

each R_{12} is independently selected from the group consisting of hydrogen, halo, nitro, cyano, oxo, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_{12} and R_7 or R_{11} may be taken together to form a substituted or unsubstituted ring.

9. The compound according to claim 3, wherein the compound is selected from the group consisting of:



and



wherein:

m is selected from the group consisting of 0, 1, 2, 3 and 4;

p is selected from the group consisting of 0, 1, 2, 3 and 4;

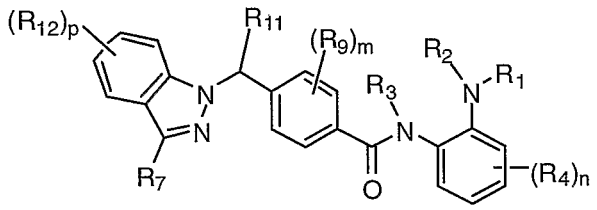
R_7 is selected from the group consisting of hydrogen, halo, nitro, cyano, oxo, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

each R_9 is independently selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or any two R_9, or one R_9 and R_3 may be taken together to form a substituted or unsubstituted ring; and

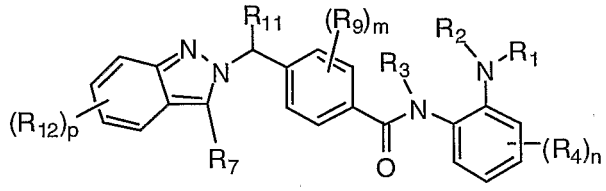
each R_{12} is independently selected from the group consisting of hydrogen, halo, nitro, cyano, oxo, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl,

amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_{12} and R_7 may be taken together to form a substituted or unsubstituted ring.

10. The compound according to claim 3, wherein the compound is selected from the group consisting of:



and



wherein:

m is selected from the group consisting of 0, 1, 2, 3 and 4;

p is selected from the group consisting of 0, 1, 2, 3 and 4;

R_7 is selected from the group consisting of hydrogen, halo, nitro, cyano, oxo, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl,

(C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

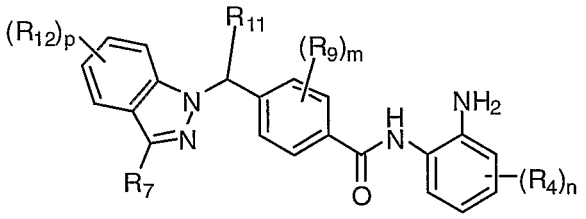
each R_9 is independently selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or any two R_9 or one R_9 and R_3 may be taken together to form a substituted or unsubstituted ring;

R_{11} is selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_{11} and R_9 may be taken together to form a substituted or unsubstituted ring; and

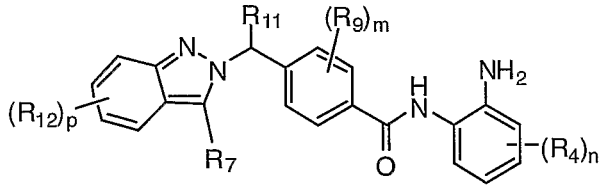
each R_{12} is independently selected from the group consisting of hydrogen, halo, nitro, cyano, oxo, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl,

(C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_{12} and R_7 or R_{11} may be taken together to form a substituted or unsubstituted ring.

11. The compound according to claim 3, wherein the compound is selected from the group consisting of:



and



wherein:

m is selected from the group consisting of 0, 1, 2, 3 and 4;

p is selected from the group consisting of 0, 1, 2, 3 and 4;

R_7 is selected from the group consisting of hydrogen, halo, nitro, cyano, oxo, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl,

hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

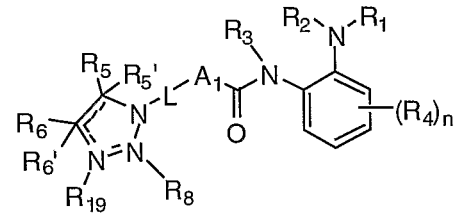
each R_9 is independently selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or any two R_9 may be taken together to form a substituted or unsubstituted ring;

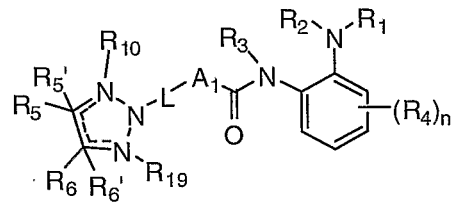
R_{11} is selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_{11} and R_7 or R_9 may be taken together to form a substituted or unsubstituted ring; and

each R_{12} is independently selected from the group consisting of hydrogen, halo, nitro, cyano, oxo, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and

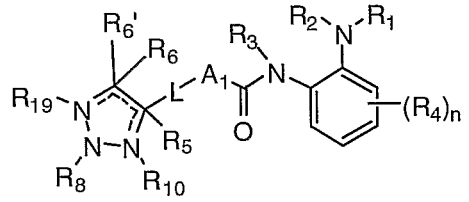
hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_{12} and R_7 or R_{11} may be taken together to form a substituted or unsubstituted ring.

12. The compound according to claim 1, wherein the compound is selected from the group consisting of:





and



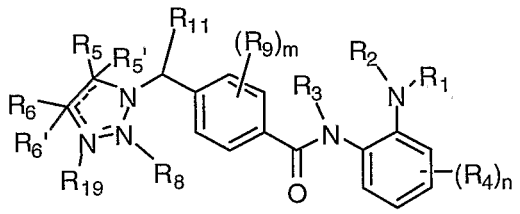
wherein:

R_5, R_5', R_6 and R_6' are each independently selected from the group consisting of hydrogen, halo, nitro, cyano, oxo, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or any two of R_5, R_5', R_6 and R_6' may be taken together to form a substituted or unsubstituted ring, provided that

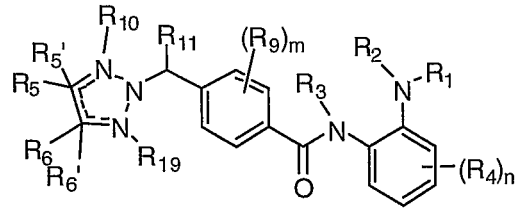
R_5' and R_6' are each independently absent when the C to which they are bound form part of a double bond; and

R_8, R_{10} and R_{19}, are each individually selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_8 and any one of R_5, R_5', R_6, R_6', R_{10} and R_{19} may be taken together to form a substituted or unsubstituted ring, or R_{10} and any one of R_5, R_5', R_6, R_6' and R_{19} may be taken together to form a substituted or unsubstituted ring, or R_{19} and any one of R_5, R_5', R_6 and R_6' may be taken together to form a substituted or unsubstituted ring, provided that R_8, R_{10} and R_{19} are each independently absent when the N to which they are bound form part of a double bond.

13. The compound according to claim 12, wherein the compound is selected from the group consisting of:



and



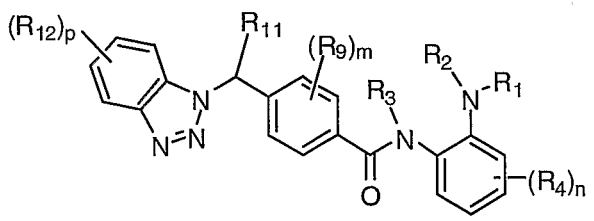
wherein:

m is selected from the group consisting of 0, 1, 2, 3 and 4;

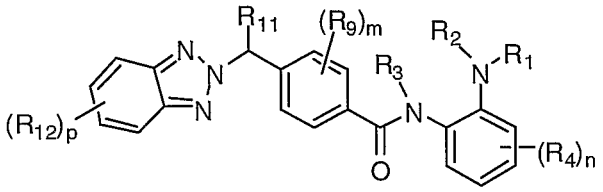
each R_9 is independently selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or any two R_9 or one R_9 and any one of R_3, R_5, R_5', R_8, R_{10} and R_{19} may be taken together to form a substituted or unsubstituted ring; and

R_{11} is selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_{11} and R_9 may be taken together to form a substituted or unsubstituted ring.

14. The compound according to claim 12, wherein the compound is selected from the group consisting of:



and



wherein:

m is selected from the group consisting of 0, 1, 2, 3 and 4;

p is selected from the group consisting of 0, 1, 2, 3 and 4;

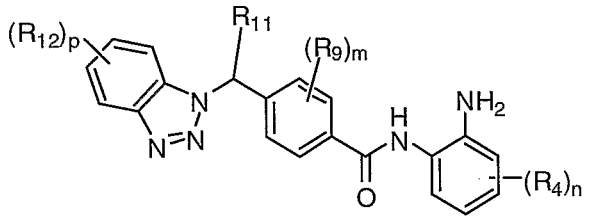
each R_9 is independently selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or any two R_9 or one R_9 and R_3 may be taken together to form a substituted or unsubstituted ring;

R_{11} is selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_{11} and R_9 may be taken together to form a substituted or unsubstituted ring; and

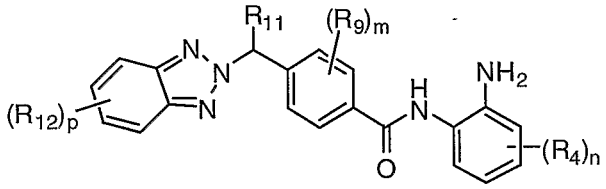
each R_{12} is independently selected from the group consisting of hydrogen, halo, nitro, cyano, oxo, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamido, imino, sulfonyl, sulfinyl,

(C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_{12} and R_{11} may be taken together to form a substituted or unsubstituted.

15. The compound according to claim 12, wherein the compound is selected from the group consisting of:



and



wherein:

m is selected from the group consisting of 0, 1, 2, 3 and 4;

p is selected from the group consisting of 0, 1, 2, 3 and 4;

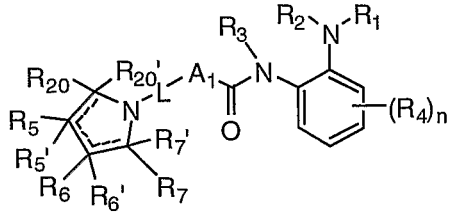
each R_9 is independently selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl,

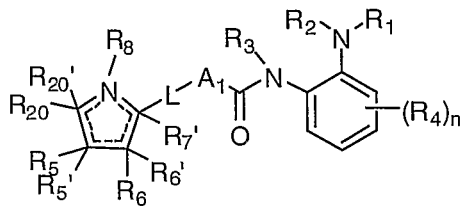
hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or any two R_9 may be taken together to form a substituted or unsubstituted ring;

R_{11} is selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxyl, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_{11} and R_9 may be taken together to form a substituted or unsubstituted ring; and

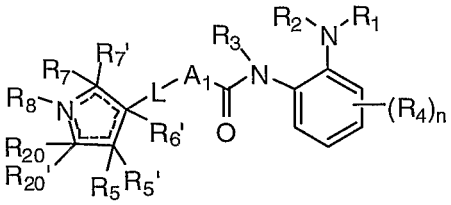
each R_{12} is independently selected from the group consisting of hydrogen, halo, nitro, cyano, oxo, thio, hydroxyl, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamide, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_{12} and R_{11} may be taken together to form a substituted or unsubstituted ring.

16. The compound according to claim 1, wherein the compound is selected from the group consisting of:





and



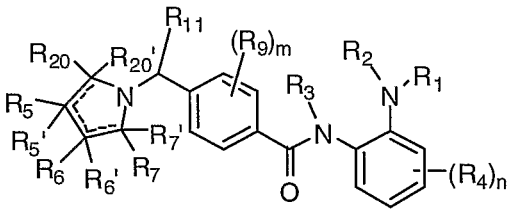
wherein:

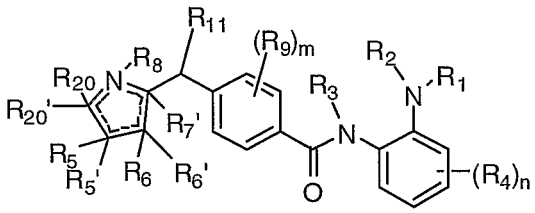
R_5, R_5', R_6, R_6', R_7, R_7', R_{20} and R_{20}' are each independently selected from the group consisting of hydrogen, halo, nitro, cyano, oxo, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or any two of R_5, R_5', R_6, R_6', R_7, R_7', R_{20} and R_{20}' may be taken together to form a substituted or unsubstituted ring, provided that R_5', R_6', R_7' and R_{20}' are each independently absent when the C to which they are bound form part of a double bond; and

R_8 is selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl,

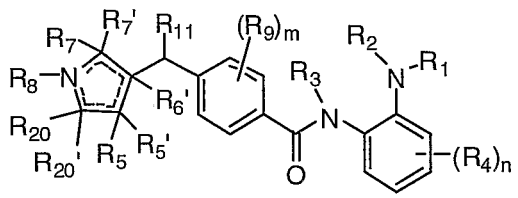
(C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_8 and any one of R_5, R_5', R_6, R_6', R_7, R_7', R_{20} and R_{20}' may be taken together to form a substituted or unsubstituted ring, provided that R_8 is absent when the N to which it is bound forms part of a double bond.

17. The compound according to claim 16, wherein the compound is selected from the group consisting of:





and



wherein:

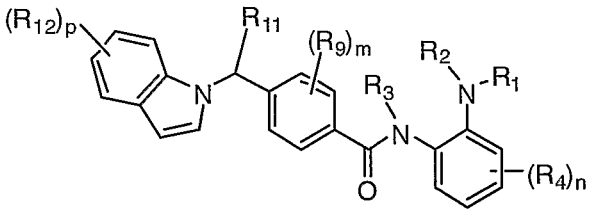
m is selected from the group consisting of 0, 1, 2, 3 and 4;

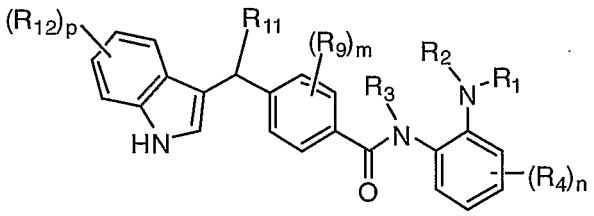
each R_9 is independently selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl,

(C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or any two R_9 or one R_9 and any one of R_3, R_5, R_5', R_6, R_6', R_7, R_7', R_{20}, R_{20}' and R_8 may be taken together to form a substituted or unsubstituted ring; and

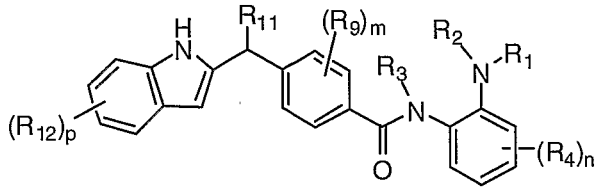
R_{11} is selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_{11} and R_9 may be taken together to form a substituted or unsubstituted ring.

18. The compound according to claim 16, wherein the compound is selected from the group consisting of:





and



wherein:

m is selected from the group consisting of 0, 1, 2, 3 and 4;

p is selected from the group consisting of 0, 1, 2, 3 and 4;

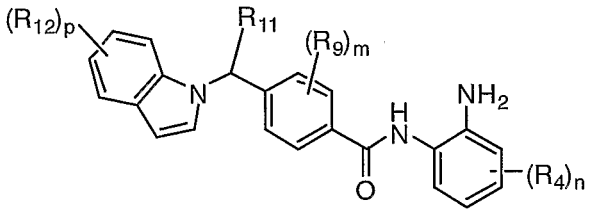
each R_9 is independently selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or any two R_9 or one R_9 and R_3 may be taken together to form a substituted or unsubstituted ring;

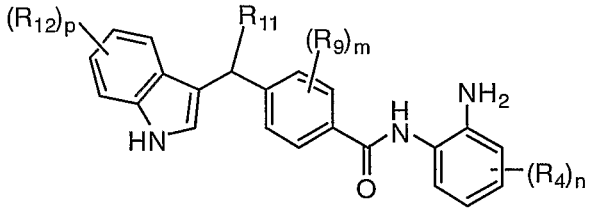
R_{11} is selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_{11} and R_9 may be taken together to form a substituted or unsubstituted ring; and

each R_{12} is independently selected from the group consisting of hydrogen, halo, nitro, cyano, oxo, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamido, imino, sulfonyl, sulfinyl,

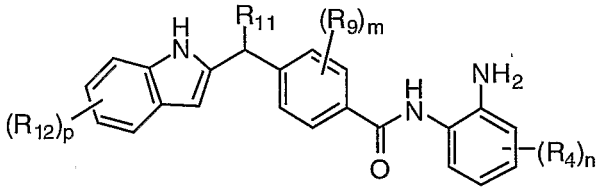
(C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_{12} and R_{11} may be taken together to form a substituted or unsubstituted ring.

19. The compound according to claim 16, wherein the compound is selected from the group consisting of:





and



wherein:

m is selected from the group consisting of 0, 1, 2, 3 and 4;

p is selected from the group consisting of 0, 1, 2, 3 and 4;

each R_9 is independently selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino,

(C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or any two R_9 may be taken together to form a substituted or unsubstituted ring;

R_{11} is selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_{11} and R_9 may be taken together to form a substituted or unsubstituted ring; and

each R_{12} is independently selected from the group consisting of hydrogen, halo, nitro, cyano, oxo, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_{12} and R_{11} may be taken together to form a substituted or unsubstituted ring.

20. The compound according to any one of claims 1-6, 8-10, 12-14 and 16-18, wherein R_1 and R_2 are each independently selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl and imino(C_{1-3})alkyl, each substituted or unsubstituted.

21. The compound according to any one of claims 1-6, 8-10, 12-14 and 16-18, wherein R_1 is hydrogen or a substituent convertible *in vivo* to hydrogen.

22. The compound according to any one of claims 1-6, 8-10, 12-14 and 16-18, wherein R_2 is hydrogen or a substituent convertible *in vivo* to hydrogen.

23. The compound according to any one of claims 1-6, 8-10, 12-14 and 16-18, wherein R_3 is hydrogen or a substituent convertible *in vivo* to hydrogen.

24. The compound according to any one of claims 1-19, wherein R_4 is selected from the group consisting of hydrogen, halo, aryl and heteroaryl, each substituted or unsubstituted.

25. The compound according to any one of claims 1-19, wherein R_4 is selected from the group consisting of phenyl, oxazolyl, thiazolyl, morpholinyl and thiomorpholinyl, each substituted or unsubstituted.

26. The compound according to any one of claims 1-13 and 16-17, wherein R_5, R_6, R_7 and R_{20} are each independently selected from the group consisting of carbonyl, oxo, amino, (C_{1-10})alkylamino, amido, carboxamido, cyano, alkoxy, (C_{1-10})alkyl, aryl, and heteroaryl, each substituted or unsubstituted.

27. The compound according to any one of claims 1-7, 12-13 and 16-17, wherein R_5 and R_6 are taken together to form a substituted or unsubstituted ring.

28. The compound according to any one of claims 1-7, 12-13 and 16-17, wherein R_5 and R_6 are taken together to form a ring selected from the group consisting of aryl and heteroaryl, each substituted or unsubstituted.

29. The compound according to any one of claims 1-7, 12-13 and 16-17, wherein the ring formed by R_5 and R_6 is substituted with a substituent selected from the group consisting of halo, alkoxy, amino(C_{1-10})alkoxy, amino(C_{1-10})alkylamino, amino(C_{1-10})alkylsulfanyl, amido, carboxamido, halo(C_{1-10})alkyl, aryl and heteroaryl, each substituted or unsubstituted.

30. The compound according to any one of claims 1-7, 12-13 and 16-17, wherein the ring formed by R_5 and R_6 is substituted with a substituent selected from the group consisting of thiopheneyl, pyridinyl, furanyl and pyrimidinyl, each substituted or unsubstituted.

31. The compound according to any one of claims 1-7, 12-13 and 16-17, wherein the ring formed by R_5 and R_6 is substituted with –O-CH_2CH_2-$NR_{13}R_{14}$, wherein R_{13} and R_{14} are each independently selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero (C_{8-12})bicycloaryl (C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_{13} and R_{14} may be taken together to form a substituted or unsubstituted ring.

32. The compound according any one of claims 1-7, 12-13 and 16-17, wherein the ring formed by R_5 and R_6 is substituted with –NH-CH_2CH_2-$NR_{13}R_{14}$, wherein R_{13} and R_{14} are

each independently selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero (C_{8-12})bicycloaryl (C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_{13} and R_{14} may be taken together to form a substituted or unsubstituted ring.

33. The compound according to any one of claims 1-7, 12-13 and 16-17, wherein the ring formed by R_5 and R_6 is substituted with $-S-CH_2CH_2-NR_{13}R_{14}$, wherein R_{13} and R_{14} are each independently selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero (C_{8-12})bicycloaryl (C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_{13} and R_{14} may be taken together to form a substituted or unsubstituted ring.

34. The compound according to any one of claims 31-33, wherein R_{13} and R_{14} are each independently selected from the group consisting of hydrogen, (C_{1-10})alkyl, (C_{3-12})cycloalkyl, and heteroaryl, each substituted or unsubstituted.

35. The compound according to any one of claims 31-33, wherein R_{13} and R_{14} are taken together to form a ring selected from the group consisting of morpholinyl, pyrrolidinyl, piperazinyl and thiomorpholinyl, each substituted or unsubstituted.

36. The compound according to any one of claims 1-7, 12-13, and 16-17, wherein R_8, R_{10} and R_{19} are each independently selected from the group consisting of hydrogen and substituted or unsubstituted (C_{1-10})alkyl.

37. The compound according to any one of claims 1-3, 5, 9, 12 and 16 wherein L is a linker providing a 1-5 atom separation between the two ring atoms to which L is attached.

38. The compound according to any one of claims 1-3, 5, 9, 12 and 16, wherein L is a linker providing a 1-3 atom separation between the two ring atoms to which L is attached.

39. The compound according to any one of claims 1-3, 5, 9, 12 and 16, wherein L is a substituted or unsubstituted alkylene.

40. The compound according to any one of claims 1-3, 5, 9, 12 and 16, wherein L is $-CH_2-$.

41. The compound according to any one of claims 1-3, 5, 9, 12 and 16, wherein L is selected from the group consisting of $-NR_{15}-$; $-NR_{15}-CH_2-$; $-O-CH_2-$; $-S-CH_2-$; $-CH_2-NR_{15}-$; $-CH_2-O-$ and $-CH_2-S-$, wherein R_{15} is selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted.

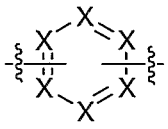
42. The compound according to any one of claims 1-4, 8, 12 and 16, wherein A_1 is selected from the group consisting of aryl and heteroaryl, each substituted or unsubstituted.

43. The compound according to any one of claims 1-4, 8, 12 and 16, wherein A_1 is a substituted or unsubstituted phenylene.

44. The compound according to any one of claims 1-4, 8, 12 and 16, wherein A_1 is a substituted or unsubstituted 1,4-phenylene.

45. The compound according to any one of claims 1-4, 8, 12 and 16, wherein A_1 is selected from the group consisting of a thiophenediyl, furandiyl, pyrrolediyl, thiazolediyl, oxazolediyl, imidazolediyl and pyridinediyl, each substituted or unsubstituted.

46. The compound according to any one of claims 1-4, 8, 12 and 16, wherein A_1 comprises:



wherein:

each X is independently selected from the group consisting of CR_{16} and N; and

each R_{16} is independently selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_{16} is absent

when the C to which it is bound is further bound to L or the carbonyl adjacent to A_1.

47. The compound according to claim 11, wherein m is 0, R_{11} is hydrogen, and R_{12} is selected from the group consisting of hydroxyl, alkoxy, halo, amido, carboxamido, and (C_{1-10})alkylamido, each substituted or unsubstituted.

48. The compound according to claim 47, wherein n is 0, p is 2, and R_{12} is selected from the group consisting of hydroxyl, alkoxy, and halo.

49. The compound according to claim 48, wherein R_7 is hydrogen, and R_{12} is alkoxy.

50. A compound selected from the group consisting of:

4-((1*H*-indazol-1-yl)methyl)-N-(2-aminophenyl)benzamide;

4-((2*H*-indazol-2-yl)methyl)-N-(2-aminophenyl)benzamide;

4-((5-acetamido-1*H*-indazol-1-yl)methyl)-N-(2-aminophenyl)benzamide;

4-((5-acetamido-2*H*-indazol-2-yl)methyl)-N-(2-aminophenyl)benzamide;

N-(2-aminophenyl)-4-((5-nitro-1H-indazol-1-yl)methyl)benzamide;

4-((5-benzamido-1*H*-indazol-1-yl)methyl)-N-(2-aminophenyl)benzamide;

4-((5-amino-1*H*-indazol-1-yl)methyl)-N-(2-aminophenyl)benzamide;

N-(2-aminophenyl)-4-((5-nitro-2*H*-indazol-2-yl)methyl)benzamide;

4-((5-amino-2*H*-indazol-2-yl)methyl)-N-(2-aminophenyl)benzamide;

4-((5-benzamido-2*H*-indazol-1-yl)methyl)-N-(2-aminophenyl)benzamide;

2-Methoxyethyl 2-(4-((2-aminophenyl)carbamoyl)benzyl)-2*H*-indazol-5-ylcarbamate;

Methyl 2-(4-((2-aminophenyl)carbamoyl)benzyl)-2*H*-indazol-5-ylcarbamate;

2-Methoxyethyl 1-(4-((2-aminophenyl)carbamoyl)benzyl)-1*H*-indazol-5-ylcarbamate;

Methyl 1-(4-((2-aminophenyl)carbamoyl)benzyl)-1*H*-indazol-5-ylcarbamate;

Benzyl 1-(4-((2-aminophenyl)carbamoyl)benzyl)-1*H*-indazol-5-ylcarbamate;

Benzyl 2-(4-((2-aminophenyl)carbamoyl)benzyl)-2*H*-indazol-5-ylcarbamate;

N-(4-Amino-biphenyl-3-yl)-4-(5-nitro-indazol-2-ylmethyl)-benzamide;

N-(2-(4-((2-Aminophenyl)carbamoyl)benzyl)-2*H*-indazol-5-yl)morpholine-4-carboxamide;

5-((2*H*-Indazol-2-yl)methyl)-N-(2-aminophenyl)thiophene-2-carboxamide;

N-(2-Aminophenyl)-5-((5-nitro-2*H*-indazol-2-yl)methyl)thiophene-2-carboxamide;

N-(1-(4-((2-Aminophenyl)carbamoyl)benzyl)-1*H*-indazol-5-yl)morpholine-4-carboxamide;

2-Morpholinoethyl 1-(4-((2-aminophenyl)carbamoyl)benzyl)-1*H*-indazol-5-ylcarbamate;

Pyridin-3-ylmethyl 1-(4-((2-aminophenyl)carbamoyl)benzyl)-1*H*-indazol-5-ylcarbamate;

5-((1*H*-Indazol-1-yl)methyl)-N-(2-aminophenyl)thiophene-2-carboxamide;

4-((2*H*-Pyrazolo[3,4-b]pyridine-2-yl)methyl)-N-(2-aminophenyl)benzamide;

N-(4-Amino-biphenyl-3-yl)-4-pyrazolo[3,4-*b*]□yridine-2-ylmethyl-benzamide;

N-(4-Amino-biphenyl-3-yl)-4-indazol-2-ylmethyl-benzamide;

N-(2-Aminophenyl)-4-((3-methyl-1*H*-indazol-1-yl)methyl)benzamide;

N-(2-Aminophenyl)-4-((3-methyl-2*H*-indazol-2-yl)methyl)benzamide;

4-((1H-indazol-3-ylamino)methyl)-N-(2-aminophenyl)benzamide;

4-((1H-pyrazol-1-yl)methyl)-N-(2-aminophenyl)benzamide;

N-(2-(4-((2-Aminophenyl)carbamoyl)benzyl)-2*H*-indazol-5-yl)morpholine-4-carboxamide;

Methyl 3-(4-((2H-indazol-2-yl)methyl)benzamido)-4-aminobenzoate;

N-(2-aminophenyl)-4-((4-methyl-1H-pyrazol-1-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((6-fluoro-2H-indazol-2-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((6-fluoro-1H-indazol-1-yl)methyl)benzamide;
N-(2-aminophenyl)-4-((5-fluoro-1H-indazol-1-yl)methyl)benzamide;
N-(2-aminophenyl)-4-((5-fluoro-2H-indazol-2-yl)methyl)benzamide;
4-(1-(1H-indazol-1-yl)propan-2-yl)-N-(2-aminophenyl)benzamide;
4-(2-(1H-indazol-1-yl)ethyl)-N-(2-aminophenyl)benzamide;
4-(2-(2H-indazol-2-yl)ethyl)-N-(2-aminophenyl)benzamide;
N-(2-aminophenyl)-4-((4-chloro-1H-indazol-1-yl)methyl)benzamide;
N-(2-aminophenyl)-4-((4-chloro-2H-indazol-2-yl)methyl)benzamide;
N-(2-aminophenyl)-4-((4,6-difluoro-1H-indazol-1-yl)methyl)benzamide;
N-(2-aminophenyl)-4-((4,6-difluoro-2H-indazol-2-yl)methyl)benzamide;
N-(2-aminophenyl)-4-((7-fluoro-1H-indazol-1-yl)methyl)benzamide;
N-(2-aminophenyl)-4-((7-fluoro-2H-indazol-2-yl)methyl)benzamide;
N-(2-aminophenyl)-4-((4-fluoro-1H-indazol-1-yl)methyl)benzamide;
N-(2-aminophenyl)-4-((4-fluoro-2H-indazol-2-yl)methyl)benzamide;
(R)-4-(1-(2H-indazol-2-yl)ethyl)-N-(2-aminophenyl)benzamide;
(S)-4-(1-(2H-indazol-2-yl)ethyl)-N-(2-aminophenyl)benzamide;
N-(2-aminophenyl)-4-((7-fluoro-3-methyl-1H-indazol-1-yl)methyl)benzamide;
N-(2-aminophenyl)-4-((7-fluoro-3-methyl-2H-indazol-2-yl)methyl)benzamide;
N-(2-aminophenyl)-4-((4-fluoro-3-methyl-1H-indazol-1-yl)methyl)benzamide;
N-(2-aminophenyl)-4-((4-fluoro-3-methyl-2H-indazol-2-yl)methyl)benzamide;
N-(2-aminophenyl)-4-((5,6-difluoro-3-methyl-1H-indazol-1-yl)methyl)benzamide;
N-(2-aminophenyl)-4-((5,6-difluoro-3-methyl-2H-indazol-2-yl)methyl)benzamide;
N-(2-aminophenyl)-4-((6-methoxy-1H-indazol-1-yl)methyl)benzamide;
N-(2-aminophenyl)-4-((6-methoxy-2H-indazol-2-yl)methyl)benzamide;
N-(2-aminophenyl)-4-((3-chloro-1H-indazol-1-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((3-chloro-2H-indazol-2-yl)methyl)benzamide;

4-((3-amino-5-(trifluoromethyl)-2H-indazol-2-yl)methyl)-N-(2-aminophenyl)benzamide;

4-((3-amino-5-(trifluoromethyl)-1H-indazol-1-yl)methyl)-N-(2-aminophenyl)benzamide;

N-(2-aminophenyl)-4-((3-oxo-2,3-dihydro-1H-indazol-1-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((3-oxo-1H-indazol-2(3H)-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((6-methoxy-3-methyl-1H-indazol-1-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((6-methoxy-3-methyl-2H-indazol-2-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((6-fluoro-3-methyl-1H-indazol-1-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((6-fluoro-3-methyl-2H-indazol-2-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((5-fluoro-3-methyl-1H-indazol-1-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((5-fluoro-3-methyl-2H-indazol-2-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((3-ethyl-1H-indazol-1-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((3-ethyl-2H-indazol-2-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((6-hydroxy-3-methyl-1H-indazol-1-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((6-hydroxy-3-methyl-2H-indazol-2-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((3-phenyl-1H-indazol-1-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((3-phenyl-2H-indazol-2-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((5-methoxy-1H-indazol-1-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((5-methoxy-2H-indazol-2-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((3,5-dimethyl-1H-indazol-1-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((3,5-dimethyl-2H-indazol-2-yl)methyl)benzamide;
N-(2-aminophenyl)-4-((7-methoxy-2H-indazol-2-yl)methyl)benzamide;
N-(2-aminophenyl)-4-((4-methoxy-2H-indazol-2-yl)methyl)benzamide;
N-(2-aminophenyl)-4-((7-methoxy-1H-indazol-1-yl)methyl)benzamide;
N-(2-aminophenyl)-4-((4-methoxy-1H-indazol-1-yl)methyl)benzamide;
4-((6-acetamido-3-methyl-2H-indazol-2-yl)methyl)-N-(2-aminophenyl)benzamide;
4-((6-acetamido-3-methyl-1H-indazol-1-yl)methyl)-N-(2-aminophenyl)benzamide;
4-((3-amino-2H-indazol-2-yl)methyl)-N-(2-aminophenyl)benzamide;
4-((6-acetamido-1H-indazol-1-yl)methyl)-N-(2-aminophenyl)benzamide;
4-((6-acetamido-2H-indazol-2-yl)methyl)-N-(2-aminophenyl)benzamide;
N-(2-aminophenyl)-4-((3-methyl-7-(trifluoromethyl)-2H-indazol-2-yl)methyl)benzamide;
N-(2-aminophenyl)-4-((3-methyl-6-(trifluoromethyl)-2H-indazol-2-yl)methyl)benzamide;
N-(2-aminophenyl)-4-((3-methyl-6-(trifluoromethyl)-1H-indazol-1-yl)methyl)benzamide;
N-(2-aminophenyl)-4-((3-methyl-5-(trifluoromethyl)-1H-indazol-1-yl)methyl)benzamide;
N-(2-aminophenyl)-4-((3-methyl-5-(trifluoromethyl)-2H-indazol-2-yl)methyl)benzamide;
4-((3-amino-1*H*-indazol-1-yl)methyl)-*N*-(2-aminophenyl)benzamide;
N-(2-aminophenyl)-4-((5-hydroxy-6-methoxy-2H-indazol-2-yl)methyl)benzamide;
N-(2-aminophenyl)-4-((5,6-dimethoxy-2H-indazol-2-yl)methyl)benzamide;
N-(2-aminophenyl)-4-((5,6-dimethoxy-1H-indazol-1-yl)methyl)benzamide;
4-((1*H*-benzo[*d*][1,2,3]triazol-1-yl)methyl)-*N*-(2-aminophenyl)benzamide;
4-((2*H*-benzo[*d*][1,2,3]triazol-2-yl)methyl)-*N*-(2-aminophenyl)benzamide;
4-((5-acetamido-1*H*-indazol-1-yl)methyl)-*N*-(2-aminophenyl)benzamide;

1-(4-(2-aminophenylcarbamoyl)benzyl)-N-(2-(piperazin-1-yl)ethyl)-1H-pyrazole-4-carboxamide;

4-((2*H*-indazol-2-yl)methyl)-*N*-(4-aminopyrimidin-5-yl)benzamide;

4-((5-acetamido-3-amino-1*H*-indazol-1-yl)methyl)-*N*-(2-aminophenyl)benzamide;

4-((5-acetamido-3-methyl-2*H*-indazol-2-yl)methyl)-*N*-(2-aminophenyl)benzamide;

4-((5-acetamido-3-methyl-1*H*-indazol-1-yl)methyl)-*N*-(2-aminophenyl)benzamide;

4-(1-(1*H*-indazol-1-yl)ethyl)-*N*-(2-aminophenyl)benzamide;

4-(1-(2*H*-indazol-2-yl)ethyl)-*N*-(2-aminophenyl)benzamide;

5-((5-acetamido-1*H*-indazol-1-yl)methyl)-*N*-(2-aminophenyl)thiophene-2-carboxamide;

4-((2*H*-indazol-2-yl)methyl)-*N*-(2-amino-5-(thiophen-2-yl)phenyl)benzamide;

N-(2-amino-5-(thiophen-2-yl)phenyl)-4-((4,6-difluoro-2*H*-indazol-2-yl)methyl)benzamide;

N-(2-amino-5-(thiophen-2-yl)phenyl)-4-((4,6-difluoro-1*H*-indazol-1-yl)methyl)benzamide;

N-(2-amino-5-(thiophen-2-yl)phenyl)-4-((6-methoxy-3-methyl-1*H*-indazol-1-yl)methyl)benzamide;

N-(2-amino-5-(thiophen-2-yl)phenyl)-4-((4-methyl-1*H*-pyrazol-1-yl)methyl)benzamide;

N-(2-amino-5-(thiophen-2-yl)phenyl)-4-((6-methoxy-3-methyl-2*H*-indazol-2-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((4-(trifluoromethyl)-1*H*-indazol-1-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((4-(trifluoromethyl)-2*H*-indazol-2-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((5-(trifluoromethyl)-1*H*-indazol-1-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((5-(trifluoromethyl)-2*H*-indazol-2-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((6-(trifluoromethyl)-2*H*-indazol-2-yl)methyl)benzamide;

1-(4-(2-aminophenylcarbamoyl)benzyl)-1H-pyrazole-4-carboxylic acid;

N-(2-aminophenyl)-4-((3-methyl-1H-pyrazol-1-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((3,5-dimethyl-1H-pyrazol-1-yl)methyl)benzamide;

Ethyl 1-(4-(2-aminophenylcarbamoyl)benzyl)-1H-pyrazole-4-carboxylate;

1-(4-(2-aminophenylcarbamoyl)benzyl)-N-(pyridine-2-ylmethyl)-1H-pyrazole-4-carboxamide;

1-(4-(2-aminophenylcarbamoyl)benzyl)-N-phenyl-1H-pyrazole-4-carboxamide;

1-(4-(2-aminophenylcarbamoyl)benzyl)-N-benzyl-1H-pyrazole-4-carboxamide;

N-(2-aminophenyl)-4-((4,5,6,7-tetrahydro-2H-indazol-2-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((4,5,6,7-tetrahydro-1H-indazol-1-yl)methyl)benzamide;

4-((1H-pyrazol-3-ylamino)methyl)-N-(2-aminophenyl)benzamide;

4-((5-amino-1H-pyrazol-1-yl)methyl)-N-(2-aminophenyl)benzamide;

4-((3-amino-1H-pyrazol-1-yl)methyl)-N-(2-aminophenyl)benzamide;

1-(4-(2-aminophenylcarbamoyl)benzyl)-N-methyl-1H-pyrazole-4-carboxamide;

1-(4-(2-aminophenylcarbamoyl)benzyl)-N-ethyl-1H-pyrazole-4-carboxamide;

1-(4-(2-aminophenylcarbamoyl)benzyl)-N,N-dimethyl-1H-pyrazole-4-carboxamide;

1-(4-(2-aminophenylcarbamoyl)benzyl)-N-isopropyl-1H-pyrazole-4-carboxamide;

1-(4-(2-aminophenylcarbamoyl)benzyl)-N-cyclopropyl-1H-pyrazole-4-carboxamide;

1-(4-(2-aminophenylcarbamoyl)benzyl)-N-(cyclopropylmethyl)-1H-pyrazole-4-carboxamide;

1-(4-(2-aminophenylcarbamoyl)benzyl)-N-(2-(dimethylamino)ethyl)-1H-pyrazole-4-carboxamide;

1-(4-(2-aminophenylcarbamoyl)benzyl)-1H-pyrazole-4-carboxamide;

1-(4-(2-aminophenylcarbamoyl)benzyl)-N-(2-hydroxyethyl)-1H-pyrazole-4-carboxamide;

1-(4-(2-aminophenylcarbamoyl)benzyl)-N-(3-(dimethylamino)propyl)-1H-pyrazole-4-carboxamide;

1-(4-(2-aminophenylcarbamoyl)benzyl)-N-(pyridine-3-ylmethyl)-1H-pyrazole-4-carboxamide;

1-(4-(2-aminophenylcarbamoyl)benzyl)-N-(pyridine-4-ylmethyl)-1H-pyrazole-4-carboxamide.;

1-(4-(2-aminophenylcarbamoyl)benzyl)-N-(2-morpholinoethyl)-1H-pyrazole-4-carboxamide;

N-(2-aminophenyl)-4-((5-methyl-1H-pyrazol-1-yl)methyl)benzamide;

1-(4-(2-aminophenylcarbamoyl)benzyl)-N-propyl-1H-pyrazole-4-carboxamide;

1-(4-(2-aminophenylcarbamoyl)benzyl)-N-isobutyl-1H-pyrazole-4-carboxamide;

1-(4-(2-aminophenylcarbamoyl)benzyl)-N-(2-methoxyethyl)-1H-pyrazole-4-carboxamide;

1-(4-(2-aminophenylcarbamoyl)benzyl)-N-(3-methoxypropyl)-1H-pyrazole-4-carboxamide;

1-(4-(2-aminophenylcarbamoyl)benzyl)-N-(3-hydroxypropyl)-1H-pyrazole-4-carboxamide;

1-(4-(2-aminophenylcarbamoyl)benzyl)-N-(3-morpholinopropyl)-1H-pyrazole-4-carboxamide;

1-(4-(2-aminophenylcarbamoyl)benzyl)-N-(2-(piperidin-1-yl)ethyl)-1H-pyrazole-4-carboxamide;

1-(4-(2-aminophenylcarbamoyl)benzyl)-N-(3-(4-methylpiperazin-1-yl)propyl)-1H-pyrazole-4-carboxamide;

4-((1*H*-Pyrrolo[2,3-b]pyridine-1-yl)methyl)-N-(2-aminophenyl)benzamide;

4-((1*H*-Indol-3-yl)methyl)-N-(2-aminophenyl)benzamide;

4-((1H-indazol-1-yl)methyl)-N-(2-amino-5-fluorophenyl)benzamide;

4-((2H-indazol-2-yl)methyl)-N-(2-amino-5-fluorophenyl)benzamide;

4-((1H-indazol-1-yl)methyl)-N-(2-amino-5-fluorophenyl)-3-methylbenzamide;

4-((2H-indazol-2-yl)methyl)-N-(2-amino-5-fluorophenyl)-3-methylbenzamide;

N-(2-aminophenyl)-3-methyl-4-((3-methyl-1H-indazol-1-yl)methyl)benzamide;

N-(2-aminophenyl)-3-methyl-4-((3-methyl-2H-indazol-2-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((3-cyano-1H-indazol-1-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((3-cyano-2H-indazol-2-yl)methyl)benzamide;

1-(4-((2-aminophenyl)carbamoyl)benzyl)-1H-indazole-3-carboxylic acid;

2-(4-((2-aminophenyl)carbamoyl)benzyl)-2H-indazole-3-carboxylic acid;

N-(2-aminophenyl)-4-((5-cyano-1H-indazol-1-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((5-cyano-2H-indazol-2-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((3-(pyridine-2-yl)-1H-indazol-1-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((3-(pyridine-2-yl)-2H-indazol-2-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((3-(dimethylamino)-1H-indazol-1-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((3-(dimethylamino)-2H-indazol-2-yl)methyl)benzamide;

4-((1H-indazol-1-yl)methyl)-N-(2-amino-5-(furan-2-yl)phenyl)benzamide;

4-((2H-indazol-2-yl)methyl)-N-(2-amino-5-(furan-2-yl)phenyl)benzamide;

N-(2-aminophenyl)-4-((3-methoxy-1H-indazol-1-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((3-methoxy-2H-indazol-2-yl)methyl)benzamide;
N-(2-aminophenyl)-4-((3-(methoxymethylamino)-1H-indazol-1-yl)methyl)benzamide;
N-(2-aminophenyl)-4-((3-(methoxymethylamino)-2H-indazol-2-yl)methyl)benzamide;
4-((1H-pyrazol-1-yl)methyl)-N-(2-amino-5-fluorophenyl)benzamide;
N-(2-amino-5-fluorophenyl)-4-((4-methyl-1H-pyrazol-1-yl)methyl)benzamide;
4-((1H-pyrazol-1-yl)methyl)-N-(2-aminophenyl)-3-methylbenzamide;
N-(2-amino-5-fluorophenyl)-3-methyl-4-((4-methyl-1H-pyrazol-1-yl)methyl)benzamide;
N-(2-aminophenyl)-4-((4-(furan-2-yl)-1H-pyrazol-1-yl)methyl)benzamide;
1-(4-((2-aminophenyl)carbamoyl)benzyl)-1H-pyrazole-4-carboxylic acid;
N-(2-aminophenyl)-4-((3-ethyl-1H-pyrazol-1-yl)methyl)benzamide;
N-(2-aminophenyl)-4-((5-ethyl-1H-pyrazol-1-yl)methyl)benzamide;
N-(2-aminophenyl)-4-((4-phenyl-1H-pyrazol-1-yl)methyl)benzamide;
N-(2-aminophenyl)-3-methyl-4-((5-methyl-4-phenyl-1H-pyrazol-1-yl)methyl)benzamide;
N-(2-aminophenyl)-4-((3-cyano-1H-pyrazol-1-yl)methyl)benzamide;
N-(2-aminophenyl)-4-((5-(pyridine-2-yl)-1H-pyrazol-1-yl)methyl)benzamide;
4-((1H-pyrazol-1-yl)methyl)-N-(2-amino-5-(furan-2-yl)phenyl)benzamide;
N-(2-amino-5-(furan-2-yl)phenyl)-4-((4-methyl-1H-pyrazol-1-yl)methyl)benzamide;
(S)-4-(1-(1H-pyrazol-1-yl)ethyl)-N-(2-aminophenyl)benzamide;
(R)-4-(1-(1H-pyrazol-1-yl)ethyl)-N-(2-aminophenyl)benzamide;
N-(2-aminophenyl)-4-((3-(pyridine-2-yl)-1H-pyrazol-1-yl)methyl)benzamide;
N-(2-aminophenyl)-4-((5-methoxy-1H-pyrazol-1-yl)methyl)benzamide;
N-(2-aminophenyl)-4-((3-(methoxymethylamino)-1H-pyrazol-1-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((5-(methoxymethylamino)-1H-pyrazol-1-yl)methyl)benzamide; and

N-(2-aminophenyl)-4-((3-methoxy-1H-pyrazol-1-yl)methyl)benzamide.

51. A compound selected from the group consisting of:

4-((1*H*-indazol-1-yl)methyl)-N-(2-aminophenyl)benzamide;

4-((5-acetamido-1*H*-indazol-1-yl)methyl)-N-(2-aminophenyl)benzamide;

4-((5-acetamido-2*H*-indazol-2-yl)methyl)-N-(2-aminophenyl)benzamide;

N-(2-aminophenyl)-4-((5-nitro-1H-indazol-1-yl)methyl)benzamide;

4-((5-benzamido-1*H*-indazol-1-yl)methyl)-N-(2-aminophenyl)benzamide;

4-((5-amino-1*H*-indazol-1-yl)methyl)-N-(2-aminophenyl)benzamide;

N-(2-aminophenyl)-4-((5-nitro-2*H*-indazol-2-yl)methyl)benzamide;

4-((5-benzamido-2*H*-indazol-1-yl)methyl)-N-(2-aminophenyl)benzamide;

2-Methoxyethyl 2-(4-((2-aminophenyl)carbamoyl)benzyl)-2H-indazol-5-ylcarbamate;

Methyl 2-(4-((2-aminophenyl)carbamoyl)benzyl)-2*H*-indazol-5-ylcarbamate;

2-Methoxyethyl 1-(4-((2-aminophenyl)carbamoyl)benzyl)-1*H*-indazol-5-ylcarbamate;

Methyl 1-(4-((2-aminophenyl)carbamoyl)benzyl)-1H-indazol-5-ylcarbamate;

Benzyl 1-(4-((2-aminophenyl)carbamoyl)benzyl)-1*H*-indazol-5-ylcarbamate;

Benzyl 2-(4-((2-aminophenyl)carbamoyl)benzyl)-2*H*-indazol-5-ylcarbamate;

N-(4-Amino-biphenyl-3-yl)-4-(5-nitro-indazol-2-ylmethyl)-benzamide;

N-(2-(4-((2-Aminophenyl)carbamoyl)benzyl)-2*H*-indazol-5-yl)morpholine-4-carboxamide;

N-(2-Aminophenyl)-5-((5-nitro-2*H*-indazol-2-yl)methyl)thiophene-2-carboxamide;

N-(1-(4-((2-Aminophenyl)carbamoyl)benzyl)-1H-indazol-5-yl)morpholine-4-carboxamide;

2-Morpholinoethyl 1-(4-((2-aminophenyl)carbamoyl)benzyl)-1*H*-indazol-5-ylcarbamate;

Pyridin-3-ylmethyl 1-(4-((2-aminophenyl)carbamoyl)benzyl)-1*H*-indazol-5-ylcarbamate;

N-(4-Amino-biphenyl-3-yl)-4-pyrazolo[3,4-*b*]pyridin-2-ylmethyl-benzamide;

N-(4-Amino-biphenyl-3-yl)-4-indazol-2-ylmethyl-benzamide;

N-(2-aminophenyl)-4-((5-fluoro-2H-indazol-2-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((4-chloro-1H-indazol-1-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((4-chloro-2H-indazol-2-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((4-fluoro-2H-indazol-2-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((6-methoxy-2H-indazol-2-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((3-chloro-2H-indazol-2-yl)methyl)benzamide;

4-((3-amino-5-(trifluoromethyl)-2H-indazol-2-yl)methyl)-N-(2-aminophenyl)benzamide;

N-(2-aminophenyl)-4-((6-methoxy-3-methyl-1H-indazol-1-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((6-methoxy-3-methyl-2H-indazol-2-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((6-hydroxy-3-methyl-1H-indazol-1-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((5-methoxy-1H-indazol-1-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((5-methoxy-2H-indazol-2-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((4-methoxy-2H-indazol-2-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((4-methoxy-1H-indazol-1-yl)methyl)benzamide;

4-((6-acetamido-3-methyl-2H-indazol-2-yl)methyl)-N-(2-aminophenyl)benzamide;

4-((6-acetamido-1H-indazol-1-yl)methyl)-N-(2-aminophenyl)benzamide;

4-((6-acetamido-2H-indazol-2-yl)methyl)-N-(2-aminophenyl)benzamide;

N-(2-aminophenyl)-4-((3-methyl-5-(trifluoromethyl)-2H-indazol-2-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((5,6-dimethoxy-2H-indazol-2-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((5,6-dimethoxy-1H-indazol-1-yl)methyl)benzamide;

1-(4-(2-aminophenylcarbamoyl)benzyl)-N-(2-(piperazin-1-yl)ethyl)-1H-pyrazole-4-carboxamide;

4-((2*H*-indazol-2-yl)methyl)-*N*-(2-amino-5-(thiophen-2-yl)phenyl)benzamide;

N-(2-amino-5-(thiophen-2-yl)phenyl)-4-((4-methyl-1*H*-pyrazol-1-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((6-(trifluoromethyl)-2*H*-indazol-2-yl)methyl)benzamide;

1-(4-(2-aminophenylcarbamoyl)benzyl)-N-(pyridin-2-ylmethyl)-1H-pyrazole-4-carboxamide;

1-(4-(2-aminophenylcarbamoyl)benzyl)-N-phenyl-1H-pyrazole-4-carboxamide;

1-(4-(2-aminophenylcarbamoyl)benzyl)-N-benzyl-1H-pyrazole-4-carboxamide;

1-(4-(2-aminophenylcarbamoyl)benzyl)-N-isopropyl-1H-pyrazole-4-carboxamide;

1-(4-(2-aminophenylcarbamoyl)benzyl)-N-(3-(dimethylamino)propyl)-1H-pyrazole-4-carboxamide;

1-(4-(2-aminophenylcarbamoyl)benzyl)-N-(pyridin-3-ylmethyl)-1H-pyrazole-4-carboxamide;

1-(4-(2-aminophenylcarbamoyl)benzyl)-N-(pyridin-4-ylmethyl)-1H-pyrazole-4-carboxamide.;

1-(4-(2-aminophenylcarbamoyl)benzyl)-N-propyl-1H-pyrazole-4-carboxamide;

1-(4-(2-aminophenylcarbamoyl)benzyl)-N-isobutyl-1H-pyrazole-4-carboxamide;

1-(4-(2-aminophenylcarbamoyl)benzyl)-N-(3-methoxypropyl)-1H-pyrazole-4-carboxamide;

1-(4-(2-aminophenylcarbamoyl)benzyl)-N-(3-hydroxypropyl)-1H-pyrazole-4-carboxamide;

1-(4-(2-aminophenylcarbamoyl)benzyl)-N-(3-morpholinopropyl)-1H-pyrazole-4-carboxamide;

1-(4-(2-aminophenylcarbamoyl)benzyl)-N-(2-(piperidin-1-yl)ethyl)-1H-pyrazole-4-carboxamide;

52. A compound selected from the group consisting of:

N-(2-aminophenyl)-4-((4,6-difluoro-1H-indazol-1-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((4,6-difluoro-2H-indazol-2-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((5,6-difluoro-3-methyl-1H-indazol-1-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((5,6-difluoro-3-methyl-2H-indazol-2-yl)methyl)benzamide;

4-((3-amino-2H-indazol-2-yl)methyl)-N-(2-aminophenyl)benzamide;

4-((6-acetamido-1H-indazol-1-yl)methyl)-N-(2-aminophenyl)benzamide;

4-((6-acetamido-2H-indazol-2-yl)methyl)-N-(2-aminophenyl)benzamide;

N-(2-amino-5-(thiophen-2-yl)phenyl)-4-((4,6-difluoro-2*H*-indazol-2-yl)methyl)benzamide;

N-(2-amino-5-(thiophen-2-yl)phenyl)-4-((4,6-difluoro-1*H*-indazol-1-yl)methyl)benzamide;

1-(4-(2-aminophenylcarbamoyl)benzyl)-N-ethyl-1H-pyrazole-4-carboxamide;

N-(2-aminophenyl)-4-((5,6-dimethoxy-1H-indazol-1-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((5,6-dimethoxy-2H-indazol-2-yl)methyl)benzamide; and

N-(2-aminophenyl)-4-((5-hydroxy-6-methoxy-2H-indazol-2-yl)methyl)benzamide.

53. A compound selected from the group consisting of:

1-(4-(2-aminophenylcarbamoyl)benzyl)-N-ethyl-1H-pyrazole-4-carboxamide;

N-(2-aminophenyl)-4-((5,6-dimethoxy-2H-indazol-2-yl)methyl)benzamide;

4-((6-acetamido-2H-indazol-2-yl)methyl)-N-(2-aminophenyl)benzamide; and

4-((3-amino-2H-indazol-2-yl)methyl)-N-(2-aminophenyl)benzamide.

54. A compound selected from the group consisting of:

N-(2-aminophenyl)-4-((5-hydroxy-6-methoxy-2H-indazol-2-yl)methyl)benzamide.

N-(2-aminophenyl)-4-((5,6-dimethoxy-2H-indazol-2-yl)methyl)benzamide;

N-(2-aminophenyl)-4-((5,6-difluoro-3-methyl-2H-indazol-2-yl)methyl)benzamide; and

N-(2-amino-5-(thiophen-2-yl)phenyl)-4-((4,6-difluoro-2*H*-indazol-2-yl)methyl)benzamide.

55. The compound according to any one of claims 1-54, wherein the compound is in the form of a pharmaceutically acceptable salt.

56. The compound according to any one of claims 1-55, wherein the compound is present in a mixture of stereoisomers.

57. The compound according to any one of claims 1-55, wherein the compound comprises a single stereoisomer.

58. A pharmaceutical composition comprising as an active ingredient a compound according to any one of claims 1-57.

59. The pharmaceutical composition according to claim 58, wherein the composition is a solid formulation adapted for oral administration.

60. The pharmaceutical composition according to claim 58, wherein the composition is a liquid formulation adapted for oral administration.

61. The pharmaceutical composition according to claim 58, wherein the composition is a tablet.

62. The pharmaceutical composition according to claim 58, wherein the composition is a liquid formulation adapted for parenteral administration.

63. A pharmaceutical composition comprising a compound according to any one of claims 1-57, wherein the composition is adapted for administration by a route selected from the group consisting of orally, parenterally, intraperitoneally, intravenously, intraarterially, transdermally, sublingually, intramuscularly, rectally, transbuccally, intranasally, liposomally, via inhalation, vaginally, intraoccularly, via local delivery, subcutaneously, intraadiposally, intraarticularly, and intrathecally.

64. A kit comprising:

a compound of any one of claims 1-57; and

instructions which comprise one or more forms of information selected from the group consisting of indicating a disease state for which the compound is to be administered, storage information for the compound, dosing information and instructions regarding how to administer the compound.

65. The kit of claim 64, wherein the kit comprises the compound in a multiple dose form.

66. An article of manufacture comprising:

a compound of any one of claims 1-57; and

packaging materials.

67. The article of manufacture of claim 66, wherein the packaging material comprises a container for housing the compound.

68. The article of manufacture of claim 67, wherein the container comprises a label indicating one or more members of the group consisting of a disease state for which the compound is to be administered, storage information, dosing information and/or instructions regarding how to administer the compound.

69. The article of manufacture of claim 66, wherein the article of manufacture comprises the compound in a multiple dose form.

70. A therapeutic method comprising:
administering a compound according to any one of claims 1-57 to a subject.

71. A method of inhibiting histone deacetylase comprising:
contacting histone deacetylase with a compound according to any one of claims 1-57.

72. A method of inhibiting histone deacetylase comprising:
causing a compound according to any one of claims 1-57 to be present in a subject in order to inhibit histone deacetylase *in vivo*.

73. A method of inhibiting histone deacetylase comprising:
administering a first compound to a subject that is converted *in vivo* to a second compound wherein the second compound inhibits histone deacetylase *in vivo*, the second compound being a compound according to any one of claims 1-57.

74. A method of treating a disease state for which histone deacetylase possesses activity that contributes to the pathology and/or symptomology of the disease state, the method comprising:

causing a compound according to any one of claims 1-57 to be present in a subject in a therapeutically effective amount for the disease state.

75. A method of treating a disease state for which histone deacetylase possesses activity that contributes to the pathology and/or symptomology of the disease state, the method comprising:

administering a first compound to a subject that is converted *in vivo* to a second compound according to any one of claims 1-57 wherein the second compound is present in a subject in a therapeutically effective amount for the disease state.

76. A method of treating a disease state for which histone deacetylase possesses activity that contributes to the pathology and/or symptomology of the disease state, the method comprising:

administering a compound according to any one of claims 1-57, wherein the compound is present in the subject in a therapeutically effective amount for the disease state.

77. The method according to any one of claims 71-76, wherein the histone deacetylase is a HDAC2.

78. The method according to any one of claims 71-76, wherein the histone deacetylase is a HDAC8.

79. A method for treating cancer comprising:

administering a composition according to any one of claims 1-57 to a mammalian species in need thereof.

80. The method of claim 79, wherein the cancer is selected from the group consisting of squamous cell carcinoma, astrocytoma, Kaposi's sarcoma, glioblastoma, non small-cell lung cancer, bladder cancer, head and neck cancer, melanoma, ovarian cancer, prostate

cancer, breast cancer, small-cell lung cancer, glioma, colorectal cancer, genitourinary cancer and gastrointestinal cancer.

81. A method for treating inflammation, inflammatory bowel disease, psoriasis, or transplant rejection, comprising administering a compound according to any one of claims 1-57 to a mammalian species in need thereof.

82. A method for treating arthritis comprising administering a compound according to any one of claims 1-57 to a mammalian species in need thereof.

83. A method for treating degenerative diseases of the eye comprising administering a compound according to any one of claims 1-57 to a mammalian species in need thereof.

84. A method for treating multiple sclerosis, amyotrophic lateral sclerosis, thyroid neoplasm or Alzheimer's disease comprising administering a compound according to any one of claims 1-57 to a mammalian species in need thereof.

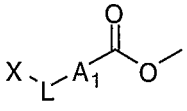
85. A method for treating hyperproliferative skin diseases or inflammatory cutaneous disorders comprising administering a compound according to any one of claims 1-57 to a mammalian species in need thereof.

86. A process comprising:

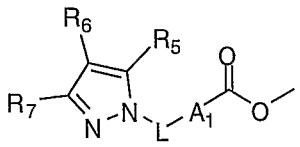
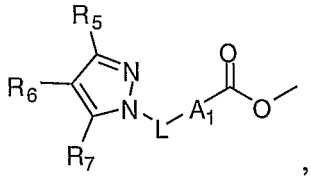
reacting a compound comprising the formula



with a compound comprising the formula



under conditions that form a reaction product comprising a formula selected from the group consisting of

 and ,

wherein

X is a leaving group;

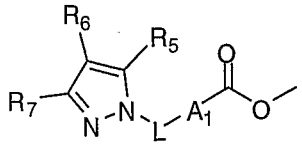
A_1 is selected from the group consisting of (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl, and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

L is a linker providing a 0-6 atom separation between the two ring atoms to which L is attached; and

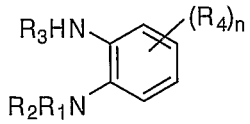
R_5, R_6 and R_7 are each independently selected from the group consisting of hydrogen, halo, nitro, cyano, oxo, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or any two of R_5, R_6 and R_7 may be taken together to form a substituted or unsubstituted ring.

87. A process comprising:

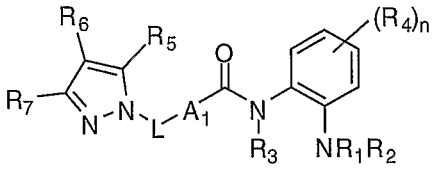
reacting a compound comprising the formula



with a compound comprising the formula



under conditions that form a reaction product comprising a formula



,

wherein

n is selected from the group consisting of 0, 1, 2, 3 and 4;

A_1 is selected from the group consisting of (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl, and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

L is a linker providing a 0-6 atom separation between the two ring atoms to which L is attached;

R_1 and R_2 are each independently selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_1 and R_2 may be taken together to form a substituted or unsubstituted ring;

R_3 is selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl,

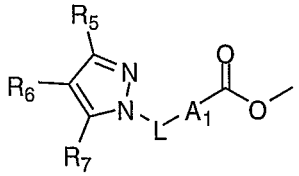
aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

each R_4 is selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted; and

R_5, R_6 and R_7 are each independently selected from the group consisting of hydrogen, halo, nitro, cyano, oxo, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or any two of R_5, R_6 and R_7 may be taken together to form a substituted or unsubstituted ring.

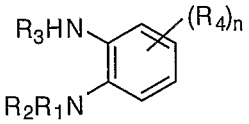
88. A process comprising:

reacting a compound comprising the formula

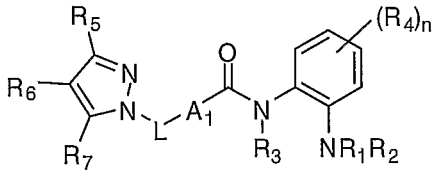


266

with a compound comprising the formula



under conditions that form a reaction product comprising a formula



wherein

n is selected from the group consisting of 0, 1, 2, 3 and 4;

A_1 is selected from the group consisting of (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl, and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

L is a linker providing a 0-6 atom separation between the two ring atoms to which L is attached;

R_1 and R_2 are each independently selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_1 and R_2 may be taken together to form a substituted or unsubstituted ring;

R_3 is selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl,

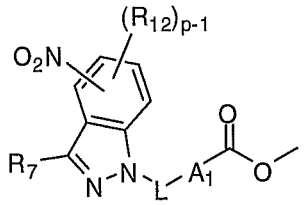
aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

each R_4 is selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted; and

R_5, R_6 and R_7 are each independently selected from the group consisting of hydrogen, halo, nitro, cyano, oxo, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or any two of R_5, R_6 and R_7 may be taken together to form a substituted or unsubstituted ring.

89. A process comprising:

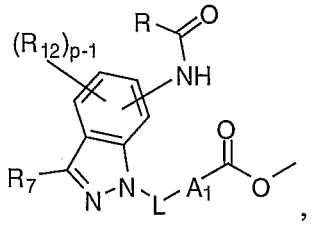
reacting a compound comprising the formula



with a compound comprising the formula

R-C(O)-X

under conditions that form a reaction product comprising a formula



wherein

p is selected from the group consisting of 0, 1, 2, 3 and 4;

A_1 is selected from the group consisting of (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl, and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

L is a linker providing a 0-6 atom separation between the two ring atoms to which L is attached;

R is selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

X is a leaving group;

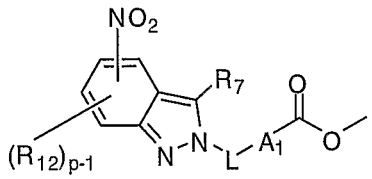
R_7 is selected from the group consisting of hydrogen, halo, nitro, cyano, oxo, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl,

(C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted; and

each R_{12} is independently selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_{12} and R_7 or R_{11} may be taken together to form a substituted or unsubstituted ring.

90. A process comprising:

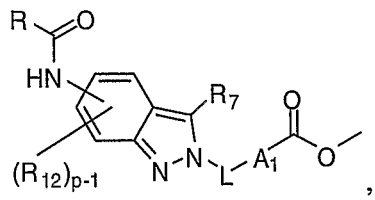
reacting a compound comprising the formula



with a compound comprising the formula

R-C(O)-X

under conditions that form a reaction product comprising a formula



,

wherein

p is selected from the group consisting of 0, 1, 2, 3 and 4;

A_1 is selected from the group consisting of (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl, and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

L is a linker providing a 0-6 atom separation between the two ring atoms to which L is attached;

R is selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

X is a leaving group;

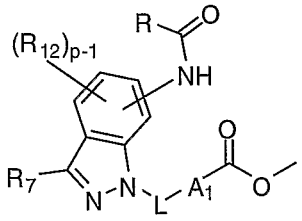
R_7 is selected from the group consisting of hydrogen, halo, nitro, cyano, oxo, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted; and

each R_{12} is independently selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl,

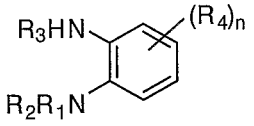
sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_{12} and R_7 or R_{11} may be taken together to form a substituted or unsubstituted ring.

91. A process comprising:

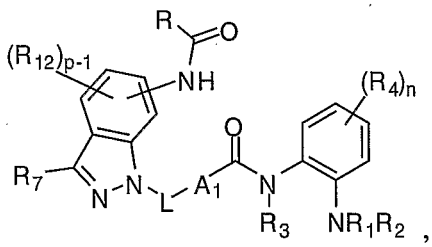
reacting a compound comprising the formula



with a compound comprising the formula



under conditions that form a reaction product comprising a formula



wherein

n is selected from the group consisting of 0, 1, 2, 3 and 4;

p is selected from the group consisting of 0, 1, 2, 3 and 4;

A_1 is selected from the group consisting of (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl, and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

L is a linker providing a 0-6 atom separation between the two ring atoms to which L is attached;

R is selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

R_1 and R_2 are each independently selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_1 and R_2 may be taken together to form a substituted or unsubstituted ring;

R_3 is selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl,

(C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

each R_4 is selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

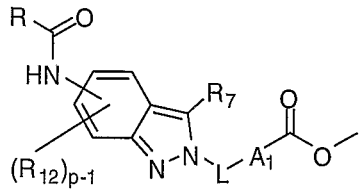
R_7 is selected from the group consisting of hydrogen, halo, nitro, cyano, oxo, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted; and

each R_{12} is independently selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and

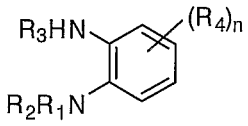
hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_{12} and R_7 or R_{11} may be taken together to form a substituted or unsubstituted ring.

92. A process comprising:

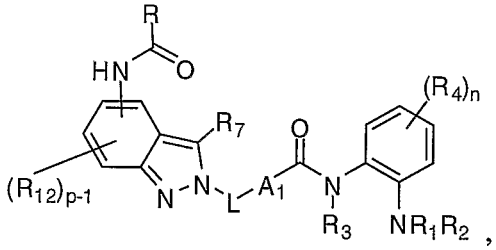
reacting a compound comprising the formula



with a compound comprising the formula



under conditions that form a reaction product comprising a formula



wherein

n is selected from the group consisting of 0, 1, 2, 3 and 4;

p is selected from the group consisting of 0, 1, 2, 3 and 4;

A_1 is selected from the group consisting of (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl, and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

L is a linker providing a 0-6 atom separation between the two ring atoms to which L is attached;

R is selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl,

thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

R_1 and R_2 are each independently selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_1 and R_2 may be taken together to form a substituted or unsubstituted ring;

R_3 is selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

each R_4 is selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl,

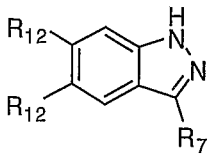
(C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

R_7 is selected from the group consisting of hydrogen, halo, nitro, cyano, oxo, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted; and

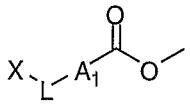
each R_{12} is independently selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_{12} and R_7 or R_{11} may be taken together to form a substituted or unsubstituted ring.

93. A process comprising:

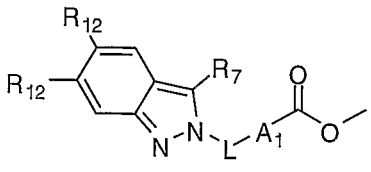
reacting a compound comprising the formula



with a compound comprising the formula

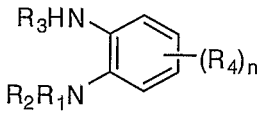


under conditions that form a first reaction product comprising a formula

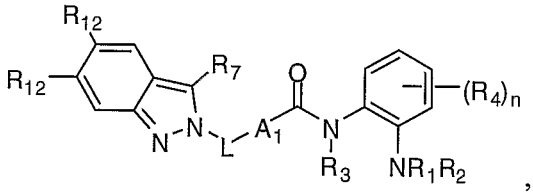


; and

reacting the first reaction product with a compound comprising the formula



under conditions that form a second reaction product comprising a formula



,

wherein

n is selected from the group consisting of 0, 1, 2, 3 and 4;

X is a leaving group;

A_1 is selected from the group consisting of (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl, and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

L is a linker providing a 0-6 atom separation between the two ring atoms to which L is attached;

R_1 and R_2 are each independently selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl,

hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_1 and R_2 may be taken together to form a substituted or unsubstituted ring;

R_3 is selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

each R_4 is selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

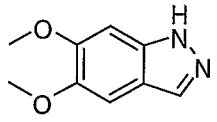
R_7 is selected from the group consisting of hydrogen, halo, nitro, cyano, oxo, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl,

hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted; and

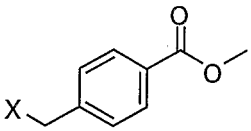
each R_{12} is independently selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_{12} and R_7 or R_{11} may be taken together to form a substituted or unsubstituted ring.

94. The process according to claim 93 comprising:

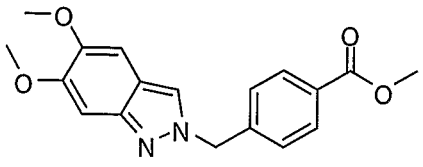
reacting a compound comprising the formula



with a compound comprising the formula

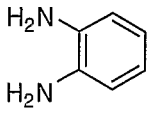


under conditions that form a first reaction product comprising a formula

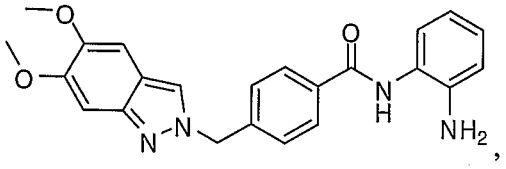


; and

reacting the first reaction product with a compound comprising the formula



under conditions that form a second reaction product comprising a formula



wherein

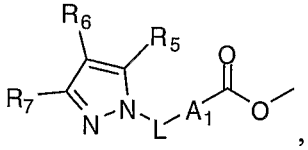
X is a leaving group.

95. The process according to any one of claims 86, 89, 90, 93 and 94 wherein X is halo.

96. The process according to claim 95 wherein X is bromo.

97. The process according to claim 95 wherein X is chloro.

98. A compound comprising:



wherein

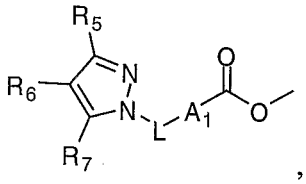
A_1 is selected from the group consisting of (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl, and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

L is a linker providing a 0-6 atom separation between the two ring atoms to which L is attached; and

R_5, R_6 and R_7 are each independently selected from the group consisting of hydrogen, halo, nitro, cyano, oxo, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy,

carbonyl, amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or any two of R_5, R_6 and R_7 may be taken together to form a substituted or unsubstituted ring.

99. A compound comprising:



,

wherein

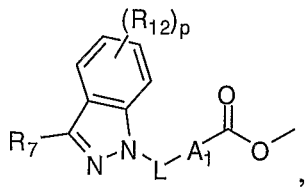
A_1 is selected from the group consisting of (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl, and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

L is a linker providing a 0-6 atom separation between the two ring atoms to which L is attached; and

R_5, R_6 and R_7 are each independently selected from the group consisting of hydrogen, halo, nitro, cyano, oxo, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and

hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or any two of R_5, R_6 and R_7 may be taken together to form a substituted or unsubstituted ring.

100. A compound comprising:



wherein

p is selected from the group consisting of 0, 1, 2, 3 and 4;

A_1 is selected from the group consisting of (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl, and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

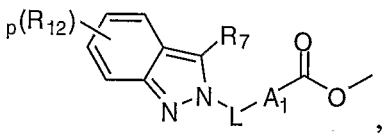
L is a linker providing a 0-6 atom separation between the two ring atoms to which L is attached;

R_7 is selected from the group consisting of hydrogen, halo, nitro, cyano, oxo, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted; and

each R_{12} is independently selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl,

heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_{12} and R_7 or R_{11} may be taken together to form a substituted or unsubstituted ring.

101. A compound comprising:



wherein

p is selected from the group consisting of 0, 1, 2, 3 and 4;

A_1 is selected from the group consisting of (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl, and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

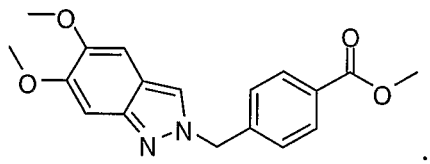
L is a linker providing a 0-6 atom separation between the two ring atoms to which L is attached;

R_7 is selected from the group consisting of hydrogen, halo, nitro, cyano, oxo, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted; and

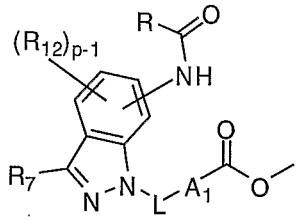
each R_{12} is independently selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl,

sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_{12} and R_7 or R_{11} may be taken together to form a substituted or unsubstituted ring.

102. The compound according to claim 101 comprising:



103. A compound comprising:



wherein

p is selected from the group consisting of 0, 1, 2, 3 and 4;

A_1 is selected from the group consisting of (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl, and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

L is a linker providing a 0-6 atom separation between the two ring atoms to which L is attached;

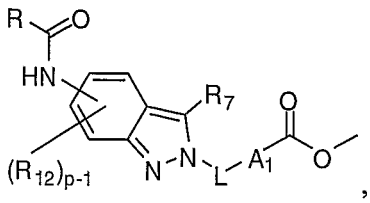
R is selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl,

thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

R_7 is selected from the group consisting of hydrogen, halo, nitro, cyano, oxo, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted; and

each R_{12} is independently selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_{12} and R_7 or R_{11} may be taken together to form a substituted or unsubstituted ring.

104. A compound comprising:



wherein

p is selected from the group consisting of 0, 1, 2, 3 and 4;

A_1 is selected from the group consisting of (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl, and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

L is a linker providing a 0-6 atom separation between the two ring atoms to which L is attached;

R is selected from the group consisting of hydrogen, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted;

R_7 is selected from the group consisting of hydrogen, halo, nitro, cyano, oxo, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted; and

each R_{12} is independently selected from the group consisting of hydrogen, halo, nitro, cyano, thio, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl, amino, (C_{1-10})alkylamino, amido, carboxamido, sulfonamido, imino, sulfonyl, sulfinyl, (C_{1-10})alkyl, halo(C_{1-10})alkyl, carbonyl(C_{1-3})alkyl, thiocarbonyl(C_{1-3})alkyl, sulfonyl(C_{1-3})alkyl, sulfinyl(C_{1-3})alkyl, amino (C_{1-10})alkyl, imino(C_{1-3})alkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl(C_{1-5})alkyl, hetero(C_{8-12})bicycloaryl(C_{1-5})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, (C_{9-12})bicycloalkyl, hetero(C_{3-12})bicycloalkyl, aryl, heteroaryl, (C_{9-12})bicycloaryl and hetero(C_{4-12})bicycloaryl, each substituted or unsubstituted, or R_{12} and R_7 or R_{11} may be taken together to form a substituted or unsubstituted ring.