Certain Substituted Amides, Method of Making, and Method of Use Thereof

[0001] This application claims priority to U.S. Application No. 60/660,746, filed March 10, 2005; Application No. 60/724,860, filed October 6, 2005, Application No. 60/677,763, filed May 3, 2005; and Application No. 60/682,111, filed May 17, 2005, each of which is incorporated herein by reference.

[0002] Provided herein are certain substituted amides and related compounds, compositions comprising such compounds, and methods of their use.

[0003] Protein kinases, the largest family of human enzymes, encompass well over 500 proteins. Bruton's Tyrosine Kinase (Btk) is a member of the Tec family of tyrosine kinases, and is a regulator of early B-cell development as well as mature B-cell activation, signaling, and survival.

[0004] B-cell signaling through the B-cell receptor (BCR) can lead to a wide range of biological outputs, which in turn depend on the developmental stage of the B-cell. The magnitude and duration of BCR signals must be precisely regulated. Aberrant BCR-mediated signaling can cause disregulated B-cell activation and/or the formation of pathogenic auto-antibodies leading to multiple autoimmune and/or inflammatory diseases. Mutation of Btk in humans results in X-linked agammaglobulinaemia (XLA). This disease is associated with the impaired maturation of B-cells, diminished immunoglobulin production, compromised T-cell-independent immune responses and marked attenuation of the sustained calcium sign upon BCR stimulation.

[0005] Evidence for the role of Btk in allergic disorders and/or autoimmune disease and/or inflammatory disease has been established in Btk-deficient mouse models. For example, in standard murine preclinical models of systemic lupus erythematosus (SLE), Btk deficiency has been shown to result in a marked amelioration of disease progression. Moreover, Btk deficient mice can also be resistant to developing collagen-induced arthritis and can be less susceptible to Staphylococcus-induced arthritis.

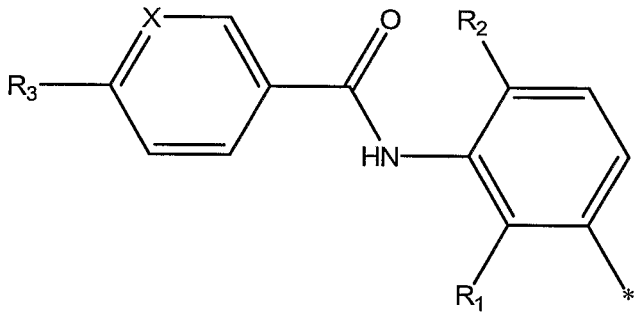
[0006] A large body of evidence supports the role of B-cells and the humoral immune system in the pathogenesis of autoimmune and/or inflammatory diseases.

Protein-based therapeutics (such as Rituxan) developed to deplete B-cells, represent an approach to the treatment of a number of autoimmune and/or inflammatory diseases. Because of Btk's role in B-cell activation, inhibitors of Btk can be useful as inhibitors of B-cell mediated pathogenic activity (such as autoantibody production).

[0007] Btk is also expressed in mast cells and monocytes and has been shown to be important for the function of these cells. For example, Btk deficiency in mice is associated with impaired IgE-mediated mast cell activation (marked diminution of TNF-alpha and other inflammatory cytokine release), and Btk deficiency in humans is associated with greatly reduced TNF-alpha production by activated monocytes.

[0008] Thus, inhibition of Btk activity can be useful for the treatment of allergic disorders and/or autoimmune and/or inflammatory diseases such as: SLE, rheumatoid arthritis, multiple vasculitides, idiopathic thrombocytopenic purpura (ITP), myasthenia gravis, allergic rhinitis, and asthma. In addition, Btk has been reported to play a role in apoptosis; thus, inhibition of Btk activity can be useful for cancer, as well as the treatment of B-cell lymphoma and leukemia.

[0009] Provided is at least one chemical entity comprising a pharmacophore chosen from radicals of Formula 1



(Formula 1)

and pharmaceutically acceptable salts, solvates, chelates, non-covalent complexes, prodrugs, and mixtures thereof, wherein

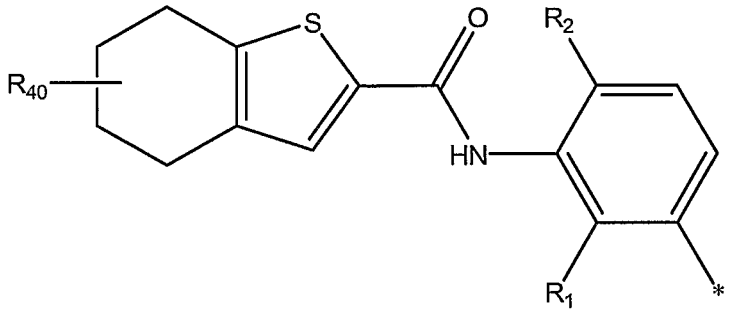
* represents a point of attachment;

R_3 is chosen from optionally substituted piperidinyl, tert-butyl and isopropyl;

X is chosen from CH and N; and

R_1 and R_2 are independently chosen from hydrogen, lower alkyl, and halo, provided that at least one of R_1 and R_2 is not hydrogen.

[0010] Also provided is at least one chemical entity comprising a pharmacophore chosen from radicals of Formula 1A



(Formula 1A)

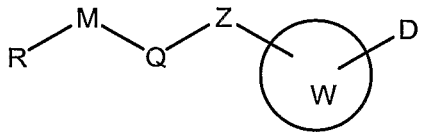
and pharmaceutically acceptable salts, solvates, chelates, non-covalent complexes, prodrugs, and mixtures thereof, wherein

* represents a point of attachment;

R_{40} is chosen from hydrogen, hydroxy, lower alkyl, sulfonyl, halo, lower alkoxy, and heteroaryl; and

R_1 and R_2 are independently chosen from hydrogen, lower alkyl, and halo, provided that at least one of R_1 and R_2 is not hydrogen.

[0011] Also provided is at least one chemical entity chosen from compounds of Formula 2:



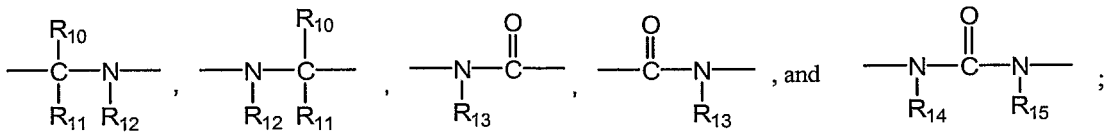
(Formula 2)

and pharmaceutically acceptable salts, solvates, chelates, non-covalent complexes, prodrugs, and mixtures thereof, wherein

R is chosen from optionally substituted cycloalkyl, optionally substituted aryl and optionally substituted heteroaryl;

M is chosen from a covalent bond and –CH=CH–.

Q is chosen from



wherein

R_{10} and R_{11} are independently chosen from hydrogen, C_1-C_6 alkyl, and C_1-C_6 haloalkyl; and

R_{12}, R_{13}, R_{14}, and R_{15} are each independently chosen from hydrogen,

C_1-C_6 alkyl,

C_1-C_6 haloalkyl,

phenyl,

substituted phenyl chosen from mono-, di-, and tri-substituted phenyl wherein the substituents are independently chosen from hydroxy, nitro, cyano, amino, halo, C_1-C_6 alkyl, C_1-C_6 alkoxy, (C_1-C_6 alkyloxy)C_1-C_6 alkoxy, C_1-C_6 perfluoroalkyl, C_1-C_6 perfluoroalkoxy, mono-(C_1-C_6 alkyl)amino, di(C_1-C_6 alkyl)amino, and amino(C_1-C_6 alkyl),

heteroaryl, and

substituted heteroaryl chosen from mono-, di-, and tri-substituted heteroaryl wherein the substituents are independently chosen from hydroxy, nitro, cyano, amino, halo, C_1-C_6 alkyl, C_1-C_6 alkoxy, (C_1-C_6 alkyloxy)C_1-C_6 alkoxy, C_1-C_6 perfluoroalkyl, C_1-C_6 perfluoroalkoxy, mono-(C_1-C_6 alkyl)amino, di(C_1-C_6 alkyl)amino, and amino(C_1-C_6 alkyl); and

Z is chosen from optionally substituted phenylene and optionally substituted pyridylidene;

W is an optionally substituted heteroaryl group other than imidazo[1,2-A]pyrazine group;

and

D is a hydrogen bond donor other than hydrogen, provided that

the compound of Formula 2 is not (4-{6-[(4-chloro-benzyl)-methyl-amino]-pyrazin-2-yl}-phenyl)-piperidin-1-yl-methanone.

[0012] Provided is a pharmaceutical composition, comprising at least one chemical entity described herein, together with at least one pharmaceutically acceptable vehicle chosen from carriers, adjuvants, and excipients.

[0013] Also provided is a packaged pharmaceutical composition, comprising

a pharmaceutical composition described herein; and

instructions for using the composition to treat a patient suffering from a disease responsive to inhibition of Btk activity.

[0014] Also provided is a method for treating a patient having a disease responsive to inhibition of Btk activity, comprising administering to the patient an effective amount of at least one chemical entity described herein.

[0015] Also provided is a method for treating a patient having a disease chosen from cancer, autoimmune diseases, inflammatory diseases, acute inflammatory reactions, and allergic disorders comprising administering to the patient an effective amount of at least one chemical entity described herein.

[0016] Also provided is a method for increasing sensitivity of cancer cells to chemotherapy, comprising administering to a patient undergoing chemotherapy with a chemotherapeutic agent an amount of at least one chemical entity described herein, sufficient to increase the sensitivity of cancer cells to the chemotherapeutic agent.

[0017] Also provided is a method of reducing medication error and enhancing therapeutic compliance of a patient being treated for a disease responsive to inhibition of Btk activity, the method comprising providing a packaged pharmaceutical preparation described herein wherein the instructions additionally include contraindication and adverse reaction information pertaining to the packaged pharmaceutical composition.

[0018] Also provided is a method for inhibiting ATP hydrolysis, the method comprising contacting cells expressing Btk with at least one chemical entity described herein in an amount sufficient to detectably decrease the level of ATP hydrolysis *in vitro*.

[0019] Also provided is a method for determining the presence of Btk in a sample, comprising contacting the sample with at least one chemical entity described herein under conditions that permit detection of Btk activity, detecting a level of Btk

activity in the sample, and therefrom determining the presence or absence of Btk in the sample.

[0020] Also provided is a method for inhibiting B-cell activity comprising contacting cells expressing Btk with at least one chemical entity described herein in an amount sufficient to detectably decrease B-cell activity *in vitro*.

[0021] As used in the present specification, the following words and phrases are generally intended to have the meanings as set forth below, except to the extent that the context in which they are used indicates otherwise. The following abbreviations and terms have the indicated meanings throughout:

[0022] As used herein, when any variable occurs more than one time in a chemical formula, its definition on each occurrence is independent of its definition at every other occurrence. In accordance with the usual meaning of "a" and "the" in patents, reference, for example, to "a" kinase or "the" kinase is inclusive of one or more kinases.

[0023] A dash ("-") that is not between two letters or symbols is used to indicate a point of attachment for a substituent. For example, $-CONH_2$ is attached through the carbon atom.

[0024] By "optional" or "optionally" is meant that the subsequently described event or circumstance may or may not occur, and that the description includes instances where the event or circumstance occurs and instances in which it does not. For example, "optionally substituted alkyl" encompasses both "alkyl" and "substituted alkyl" as defined below. It will be understood by those skilled in the art, with respect to any group containing one or more substituents, that such groups are not intended to introduce any substitution or substitution patterns that are sterically impractical, synthetically non-feasible and/or inherently unstable.

[0025] "Alkyl" encompasses straight chain and branched chain having the indicated number of carbon atoms, usually from 1 to 20 carbon atoms, for example 1 to 8 carbon atoms, such as 1 to 6 carbon atoms. For example C_1-C_6alkyl encompasses both straight and branched chain alkyl of from 1 to 6 carbon atoms. Examples of alkyl groups include methyl, ethyl, propyl, isopropyl, n-butyl, sec-butyl, tert-butyl, pentyl, 2-pentyl, isopentyl, neopentyl, hexyl, 2-hexyl, 3-hexyl, 3-methylpentyl, and the like. Alkylene is another subset of alkyl, referring to the same residues as alkyl,

but having two points of attachment. Alkylene groups will usually have from 2 to 20 carbon atoms, for example 2 to 8 carbon atoms, such as from 2 to 6 carbon atoms. For example, C_0 alkylene indicates a covalent bond and C_1 alkylene is a methylene group. When an alkyl residue having a specific number of carbons is named, all geometric isomers having that number of carbons are intended to be encompassed; thus, for example, "butyl" is meant to include n-butyl, sec-butyl, isobutyl and t-butyl; "propyl" includes n-propyl and isopropyl. "Lower alkyl" refers to alkyl groups having one to four carbons.

[0026] "Cycloalkyl" indicates a saturated hydrocarbon ring group, having the specified number of carbon atoms, usually from 3 to 7 ring carbon atoms. Examples of cycloalkyl groups include cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl as well as bridged and caged saturated ring groups such as norbornane.

[0027] By "alkoxy" is meant an alkyl group of the indicated number of carbon atoms attached through an oxygen bridge such as, for example, methoxy, ethoxy, propoxy, isopropoxy, n-butoxy, sec-butoxy, tert-butoxy, pentoxy, 2-pentyloxy, isopentoxy, neopentoxy, hexoxy, 2-hexoxy, 3-hexoxy, 3-methylpentoxy, and the like. Alkoxy groups will usually have from 1 to 6 carbon atoms attached through the oxygen bridge. "Lower alkoxy" refers to alkoxy groups having one to four carbons.

[0028] "Mono- and di-alkylcarboxamide" encompasses a group of the formula $-(C{=}O)NR_aR_b$ where R_a and R_b are independently chosen from hydrogen and alkyl groups of the indicated number of carbon atoms, provided that R_a and R_b are not both hydrogen.

[0029] By "alkylthio" is meant an alkyl group of the indicated number of carbon atoms attached through a sulfur bridge.

[0030] "Acyl" refers to the groups (alkyl)-C(O)-; (cycloalkyl)-C(O)-; (aryl)-C(O)-; (heteroaryl)-C(O)-; and (heterocycloalkyl)-C(O)-, wherein the group is attached to the parent structure through the carbonyl functionality and wherein alkyl, cycloalkyl, aryl, heteroaryl, and heterocycloalkyl are as described herein. Acyl groups have the indicated number of carbon atoms, with the carbon of the keto group being included in the numbered carbon atoms. For example a C_2 acyl group is an acetyl group having the formula $CH_3(C{=}O)$-.

[0031] By "alkoxycarbonyl" is meant an ester group of the formula (alkoxy)(C=O)- attached through the carbonyl carbon wherein the alkoxy group has the indicated number of carbon atoms. Thus a C_1-C_6alkoxycarbonyl group is an alkoxy group having from 1 to 6 carbon atoms attached through its oxygen to a carbonyl linker.

[0032] By "amino" is meant the group -NH_2.

[0033] "Mono- and di-(alkyl)amino" encompasses secondary and tertiary alkyl amino groups, wherein the alkyl groups are as defined above and have the indicated number of carbon atoms. The point of attachment of the alkylamino group is on the nitrogen. Examples of mono- and di-alkylamino groups include ethylamino, dimethylamino, and methyl-propyl-amino.

[0034] "Mono- and di-(alkyl)aminoalkyl" encompasses mono- and di-(alkyl)amino as defined above linked to an alkyl group.

[0035] By "amino(alkyl)" is meant an amino group linked to an alkyl group having the indicated number of carbons. Similarly "hydroxyalkyl" is a hydroxy group linked to an alkyl group.

[0036] The term "aminocarbonyl" refers to the group -$CONR^bR^c$, where

R^b is chosen from H, optionally substituted C_1-C_6 alkyl, optionally substituted aryl, and optionally substituted heteroaryl; and

R^c is chosen from hydrogen and optionally substituted C_1-C_4 alkyl; or

R^b and R^c taken together with the nitrogen to which they are bound, form an optionally substituted 5- to 7-membered nitrogen-containing heterocycloalkyl which optionally includes 1 or 2 additional heteroatoms selected from O, N, and S in the heterocycloalkyl ring;

where each substituted group is independently substituted with one or more substituents independently selected from C_1-C_4 alkyl, aryl, heteroaryl, aryl-C_1-C_4 alkyl-, heteroaryl-C_1-C_4 alkyl-, C_1-C_4 haloalkyl-, -OC_1-C_4 alkyl, -OC_1-C_4 alkylphenyl, -C_1-C_4 alkyl-OH, -OC_1-C_4 haloalkyl, halo, -OH, -NH_2, -C_1-C_4 alkyl-NH_2, -N(C_1-C_4 alkyl)(C_1-C_4 alkyl), -NH(C_1-C_4 alkyl), -N(C_1-C_4 alkyl)(C_1-C_4 alkylphenyl), -NH(C_1-C_4 alkylphenyl), cyano, nitro, oxo (as a substitutent for heteroaryl), -CO_2H, -C(O)OC_1-C_4 alkyl, -CON(C_1-C_4 alkyl)(C_1-C_4 alkyl), -CONH(C_1-C_4 alkyl), -$CONH_2$,

-NHC(O)(C_1-C_4 alkyl), -NHC(O)(phenyl), -N(C_1-C_4 alkyl)C(O)(C_1-C_4 alkyl), -N(C_1-C_4 alkyl)C(O)(phenyl), -C(O)C_1-C_4 alkyl, -C(O)C_1-C_4 phenyl, -C(O)C_1-C_4 haloalkyl, -OC(O)C_1-C_4 alkyl, -SO_2(C_1-C_4 alkyl), -SO_2(phenyl), -SO_2(C_1-C_4 haloalkyl), -SO_2NH_2, -SO_2NH(C_1-C_4 alkyl), -SO_2NH(phenyl), -NHSO_2(C_1-C_4 alkyl), -NHSO_2(phenyl), and -NHSO_2(C_1-C_4 haloalkyl).

[0037] "Aryl" encompasses:

5- and 6-membered carbocyclic aromatic rings, for example, benzene;

bicyclic ring systems wherein at least one ring is carbocyclic and aromatic, for example, naphthalene, indane, and tetralin; and

tricyclic ring systems wherein at least one ring is carbocyclic and aromatic, for example, fluorene.

For example, aryl includes 5- and 6-membered carbocyclic aromatic rings fused to a 5- to 7-membered heterocycloalkyl ring containing 1 or more heteroatoms chosen from N, O, and S. For such fused, bicyclic ring systems wherein only one of the rings is a carbocyclic aromatic ring, the point of attachment may be at the carbocyclic aromatic ring or the heterocycloalkyl ring. Bivalent radicals formed from substituted benzene derivatives and having the free valences at ring atoms are named as substituted phenylene radicals. Bivalent radicals derived from univalent polycyclic hydrocarbon radicals whose names end in "-yl" by removal of one hydrogen atom from the carbon atom with the free valence are named by adding "-idene" to the name of the corresponding univalent radical, e.g., a naphthyl group with two points of attachment is termed naphthylidene. Aryl, however, does not encompass or overlap in any way with heteroaryl, separately defined below. Hence, if one or more carbocyclic aromatic rings is fused with a heterocycloalkyl aromatic ring, the resulting ring system is heteroaryl, not aryl, as defined herein.

[0038] The term "aryloxy" refers to the group -O-aryl.

[0039] The term "halo" includes fluoro, chloro, bromo, and iodo, and the term "halogen" includes fluorine, chlorine, bromine, and iodine.

[0040] "Haloalkyl" indicates alkyl as defined above having the specified number of carbon atoms, substituted with 1 or more halogen atoms, up to the maximum allowable number of halogen atoms. Examples of haloalkyl include, but are not limited to, trifluoromethyl, difluoromethyl, 2-fluoroethyl, and penta-

fluoroethyl.

[0041] "Heteroaryl" encompasses:

5- to 7-membered aromatic, monocyclic rings containing one or more, for example, from 1 to 4, or in certain embodiments, from 1 to 3, heteroatoms chosen from N, O, and S, with the remaining ring atoms being carbon; and

bicyclic heterocycloalkyl rings containing one or more, for example, from 1 to 4, or in certain embodiments, from 1 to 3, heteroatoms chosen from N, O, and S, with the remaining ring atoms being carbon and wherein at least one heteroatom is present in an aromatic ring.

For example, heteroaryl includes a 5- to 7-membered heterocycloalkyl, aromatic ring fused to a 5- to 7-membered cycloalkyl ring. For such fused, bicyclic heteroaryl ring systems wherein only one of the rings contains one or more heteroatoms, the point of attachment may be at the heteroaromatic ring or the cycloalkyl ring. When the total number of S and O atoms in the heteroaryl group exceeds 1, those heteroatoms are not adjacent to one another. In certain embodiments, the total number of S and O atoms in the heteroaryl group is not more than 2. In certain embodiments, the total number of S and O atoms in the aromatic heterocycle is not more than 1. Examples of heteroaryl groups include, but are not limited to, (as numbered from the linkage position assigned priority 1), 2-pyridyl, 3-pyridyl, 4-pyridyl, 2,3-pyrazinyl, 3,4-pyrazinyl, 2,4-pyrimidinyl, 3,5-pyrimidinyl, 2,3-pyrazolinyl, 2,4-imidazolinyl, isoxazolinyl, oxazolinyl, thiazolinyl, thiadiazolinyl, tetrazolyl, thienyl, benzothiophenyl, furanyl, benzofuranyl, benzoimidazolinyl, indolinyl, pyridizinyl, triazolyl, quinolinyl, pyrazolyl, and 5,6,7,8-tetrahydroisoquinoline. Bivalent radicals derived from univalent heteroaryl radicals whose names end in "-yl" by removal of one hydrogen atom from the atom with the free valence are named by adding "-idene" to the name of the corresponding univalent radical, e.g., a pyridyl group with two points of attachment is a pyridylidene. Heteroaryl does not encompass or overlap with aryl as defined above.

[0042] Substituted heteroaryl also includes ring systems substituted with one or more oxide ($-O^-$) substituents, such as pyridinyl N-oxides.

[0043] In the term "heteroarylalkyl," heteroaryl and alkyl are as defined

herein, and the point of attachment is on the alkyl group. This term encompasses, but is not limited to, pyridylmethyl, thiophenylmethyl, and (pyrrolyl)1-ethyl.

[0044] By "heterocycloalkyl" is meant a single aliphatic ring, usually with 3 to 7 ring atoms, containing at least 2 carbon atoms in addition to 1-3 heteroatoms independently selected from oxygen, sulfur, and nitrogen, as well as combinations comprising at least one of the foregoing heteroatoms. Suitable heterocycloalkyl groups include, for example (as numbered from the linkage position assigned priority 1), 2-pyrrolinyl, 2,4-imidazolidinyl, 2,3-pyrazolidinyl, 2-piperidyl, 3-piperidyl, 4-piperdyl, and 2,5-piperzinyl. Morpholinyl groups are also contemplated, including 2-morpholinyl and 3-morpholinyl (numbered wherein the oxygen is assigned priority 1). Substituted heterocycloalkyl also includes ring systems substituted with one or more oxo moieties, such as piperidinyl N-oxide, morpholinyl-N-oxide, 1-oxo-1-thiomorpholinyl and 1,1-dioxo-1-thiomorpholinyl.

[0045] "Carbamimidoyl" refers to the group $-C(=NH)-NH_2$.

[0046] "Substituted carbamimidoyl" refers to the group $-C(=NR^e)-NR^fR^g$ where R^e, R^f, and R^g is independently chosen from: hydrogen optionally substituted alkyl, optionally substituted cycloalkyl, optionally substituted aryl, optionally substituted heteroaryl, and optionally substituted heterocycloalkyl, provided that at least one of R^e, R^f, and R^g is not hydrogen and wherein substituted alkyl, cycloalkyl, aryl, heterocycloalkyl, and heteroaryl refer respectively to alkyl, cycloalkyl, aryl, heterocycloalkyl, and heteroaryl wherein one or more (such as up to 5, for example, up to 3) hydrogen atoms are replaced by a substituent independently chosen from:

$-R^a$, $-OR^b$, $-O(C_1-C_2$ alkyl$)O-$ (e.g., methylenedioxy-), $-SR^b$, guanidine, guanidine wherein one or more of the guanidine hydrogens are replaced with a lower-alkyl group, $-NR^bR^c$, halo, cyano, nitro, $-COR^b$, $-CO_2R^b$, $-CONR^bR^c$, $-OCOR^b$, $-OCO_2R^a$, $-OCONR^bR^c$, $-NR^cCOR^b$, $-NR^cCO_2R^a$, $-NR^cCONR^bR^c$, $-CO_2R^b$, $-CONR^bR^c$, $-NR^cCOR^b$, $-SOR^a$, $-SO_2R^a$, $-SO_2NR^bR^c$, and $-NR^cSO_2R^a$,

where R^a is chosen from optionally substituted C_1-C_6 alkyl, optionally substituted aryl, and optionally substituted heteroaryl;

R^b is chosen from H, optionally substituted C_1-C_6 alkyl, optionally substituted aryl, and optionally substituted heteroaryl; and

R^c is independently chosen from hydrogen and optionally substituted C_1-C_4 alkyl; or

R^b and R^c, and the nitrogen to which they are attached, form an optionally substituted heterocycloalkyl group; and

where each optionally substituted group is unsubstituted or independently substituted with one or more, such as one, two, or three, substituents independently selected from C_1-C_4 alkyl, aryl, heteroaryl, aryl-C_1-C_4 alkyl-, heteroaryl-C_1-C_4 alkyl-, C_1-C_4 haloalkyl-, -OC_1-C_4 alkyl, -OC_1-C_4 alkylphenyl, -C_1-C_4 alkyl-OH, -OC_1-C_4 haloalkyl, halo, -OH, -NH_2, -C_1-C_4 alkyl-NH_2, -N(C_1-C_4 alkyl)(C_1-C_4 alkyl), -NH(C_1-C_4 alkyl), -N(C_1-C_4 alkyl)(C_1-C_4 alkylphenyl), -NH(C_1-C_4 alkylphenyl), cyano, nitro, oxo (as a substitutent for cycloalkyl, heterocycloalkyl, or heteroaryl), -CO_2H, -C(O)OC_1-C_4 alkyl, -CON(C_1-C_4 alkyl)(C_1-C_4 alkyl), -CONH(C_1-C_4 alkyl), -$CONH_2$, -NHC(O)(C_1-C_4 alkyl), -NHC(O)(phenyl), -N(C_1-C_4 alkyl)C(O)(C_1-C_4 alkyl), -N(C_1-C_4 alkyl)C(O)(phenyl), -C(O)C_1-C_4 alkyl, -C(O)C_1-C_4 phenyl, -C(O)C_1-C_4 haloalkyl, -OC(O)C_1-C_4 alkyl, -SO_2(C_1-C_4 alkyl), -SO_2(phenyl), -SO_2(C_1-C_4 haloalkyl), -SO_2NH_2, -SO_2NH(C_1-C_4 alkyl), -SO_2NH(phenyl), -NHSO_2(C_1-C_4 alkyl), -NHSO_2(phenyl), and -NHSO_2(C_1-C_4 haloalkyl).

[0047] As used herein, "modulation" refers to a change in kinase activity as a direct or indirect response to the presence of compounds of Formula 1, relative to the activity of the kinase in the absence of the compound. The change may be an increase in activity or a decrease in activity, and may be due to the direct interaction of the compound with the kinase, or due to the interaction of the compound with one or more other factors that in turn affect kinase activity. For example, the presence of the compound may, for example, increase or decrease kinase activity by directly binding to the kinase, by causing (directly or indirectly) another factor to increase or decrease the kinase activity, or by (directly or indirectly) increasing or decreasing the amount of kinase present in the cell or organism.

[0048] The term "sulfanyl" includes the groups: -S-(optionally substituted (C_1-C_6)alkyl), -S-(optionally substituted aryl), -S-(optionally substituted heteroaryl), and -S-(optionally substituted heterocycloalkyl). Hence, sulfanyl includes the group C_1-C_6 alkylsulfanyl.

[0049] The term "sulfinyl" includes the groups: -S(O)-H, -S(O)-(optionally substituted (C_1-C_6)alkyl), -S(O)-optionally substituted aryl), -S(O)-optionally substituted heteroaryl), -S(O)-(optionally substituted heterocycloalkyl); and -S(O)-(optionally substituted amino).

[0050] The term "sulfonyl" includes the groups: -S(O_2)-H, -S(O_2)-(optionally substituted (C_1-C_6)alkyl), -S(O_2)-optionally substituted aryl), -S(O_2)-optionally substituted heteroaryl), -S(O_2)-(optionally substituted heterocycloalkyl) ,-S(O_2)-(optionally substituted alkoxy), -S(O_2)-optionally substituted aryloxy), -S(O_2)-optionally substituted heteroaryloxy), -S(O_2)-(optionally substituted heterocyclyloxy); and -S(O_2)-(optionally substituted amino).

[0051] The term "substituted", as used herein, means that any one or more hydrogens on the designated atom or group is replaced with a selection from the indicated group, provided that the designated atom's normal valence is not exceeded. When a substituent is oxo (i.e., =O) then 2 hydrogens on the atom are replaced. Combinations of substituents and/or variables are permissible only if such combinations result in stable compounds or useful synthetic intermediates. A stable compound or stable structure is meant to imply a compound that is sufficiently robust to survive isolation from a reaction mixture, and subsequent formulation as an agent having at least practical utility. Unless otherwise specified, substituents are named into the core structure. For example, it is to be understood that when (cycloalkyl)alkyl is listed as a possible substituent, the point of attachment of this substituent to the core structure is in the alkyl portion.

[0052] The terms "substituted" alkyl, cycloalkyl, aryl, heterocycloalkyl, and heteroaryl, unless otherwise expressly defined, refer respectively to alkyl, cycloalkyl, aryl, heterocycloalkyl, and heteroaryl wherein one or more (such as up to 5, for example, up to 3) hydrogen atoms are replaced by a substituent independently chosen from:

$-R^a$, $-OR^b$, -O(C_1-C_2 alkyl)O- (e.g., methylenedioxy-), $-SR^b$, guanidine, guanidine wherein one or more of the guanidine hydrogens are replaced with a lower-alkyl group, $-NR^bR^c$, halo, cyano, nitro, $-COR^b$, $-CO_2R^b$, $-CONR^bR^c$, $-OCOR^b$, $-OCO_2R^a$, $-OCONR^bR^c$, $-NR^cCOR^b$, $-NR^cCO_2R^a$, $-NR^cCONR^bR^c$, $-CO_2R^b$, $-CONR^bR^c$, $-NR^cCOR^b$, $-SOR^a$, $-SO_2R^a$, $-SO_2NR^bR^c$, and $-NR^cSO_2R^a$,

where R^a is chosen from optionally substituted C_1-C_6 alkyl, optionally substituted aryl, and optionally substituted heteroaryl;

R^b is chosen from H, optionally substituted C_1-C_6 alkyl, optionally substituted aryl, and optionally substituted heteroaryl; and

R^c is chosen from hydrogen and optionally substituted C_1-C_4 alkyl; or

R^b and R^c, and the nitrogen to which they are attached, form an optionally substituted heterocycloalkyl group; and

where each optionally substituted group is unsubstituted or independently substituted with one or more, such as one, two, or three, substituents independently selected from C_1-C_4 alkyl, aryl, heteroaryl, aryl-C_1-C_4 alkyl-, heteroaryl-C_1-C_4 alkyl-, C_1-C_4 haloalkyl-, -OC_1-C_4 alkyl, -OC_1-C_4 alkylphenyl, -C_1-C_4 alkyl-OH, -OC_1-C_4 haloalkyl, halo, -OH, -NH_2, -C_1-C_4 alkyl-NH_2, -N(C_1-C_4 alkyl)(C_1-C_4 alkyl), -NH(C_1-C_4 alkyl), -N(C_1-C_4 alkyl)(C_1-C_4 alkylphenyl), -NH(C_1-C_4 alkylphenyl), cyano, nitro, oxo (as a substitutent for heteroaryl), -CO_2H, -C(O)OC_1-C_4 alkyl, -CON(C_1-C_4 alkyl)(C_1-C_4 alkyl), -CONH(C_1-C_4 alkyl), -$CONH_2$, -NHC(O)(C_1-C_4 alkyl), -NHC(O)(phenyl), -N(C_1-C_4 alkyl)C(O)(C_1-C_4 alkyl), -N(C_1-C_4 alkyl)C(O)(phenyl), -C(O)C_1-C_4 alkyl, -C(O)C_1-C_4 phenyl, -C(O)C_1-C_4 haloalkyl, -OC(O)C_1-C_4 alkyl, -SO_2(C_1-C_4 alkyl), -SO_2(phenyl), -SO_2(C_1-C_4 haloalkyl), -SO_2NH_2, -SO_2NH(C_1-C_4 alkyl), -SO_2NH(phenyl), -NHSO_2(C_1-C_4 alkyl), -NHSO_2(phenyl), and -NHSO_2(C_1-C_4 haloalkyl).

[0053] The term "substituted acyl" refers to the groups (substituted alkyl)-C(O)-; (substituted cycloalkyl)-C(O)-; (substituted aryl)-C(O)-; (substituted heteroaryl)-C(O)-; and (substituted heterocycloalkyl)-C(O)-, wherein the group is attached to the parent structure through the carbonyl functionality and wherein substituted alkyl, cycloalkyl, aryl, heteroaryl, and heterocycloalkyl, refer respectively to alkyl, cycloalkyl, aryl, heteroaryl, and heterocycloalkyl wherein one or more (such as up to 5, for example, up to 3) hydrogen atoms are replaced by a substituent independently chosen from:

-R^a, -OR^b, -O(C_1-C_2 alkyl)O- (e.g., methylenedioxy-), -SR^b, guanidine, guanidine wherein one or more of the guanidine hydrogens are replaced with a lower-alkyl group, -NR^bR^c, halo, cyano, nitro, -COR^b, -CO_2R^b, -$CONR^bR^c$, -$OCOR^b$,

$-OCO_2R^a$, $-OCONR^bR^c$, $-NR^cCOR^b$, $-NR^cCO_2R^a$, $-NR^cCONR^bR^c$, $-CO_2R^b$, $-CONR^bR^c$, $-NR^cCOR^b$, $-SOR^a$, $-SO_2R^a$, $-SO_2NR^bR^c$, and $-NR^cSO_2R^a$,

where R^a is chosen from optionally substituted C_1-C_6 alkyl, optionally substituted aryl, and optionally substituted heteroaryl;

R^b is chosen from H, optionally substituted C_1-C_6 alkyl, optionally substituted aryl, and optionally substituted heteroaryl; and

R^c is chosen from hydrogen and optionally substituted C_1-C_4 alkyl; or

R^b and R^c, and the nitrogen to which they are attached, form an optionally substituted heterocycloalkyl group; and

where each optionally substituted group is unsubstituted or independently substituted with one or more, such as one, two, or three, substituents independently selected from C_1-C_4 alkyl, aryl, heteroaryl, aryl-C_1-C_4 alkyl-, heteroaryl-C_1-C_4 alkyl-, C_1-C_4 haloalkyl-, -OC_1-C_4 alkyl, -OC_1-C_4 alkylphenyl, -C_1-C_4 alkyl-OH, -OC_1-C_4 haloalkyl, halo, -OH, $-NH_2$, -C_1-C_4 alkyl-NH_2, -N(C_1-C_4 alkyl)(C_1-C_4 alkyl), -NH(C_1-C_4 alkyl), -N(C_1-C_4 alkyl)(C_1-C_4 alkylphenyl), -NH(C_1-C_4 alkylphenyl), cyano, nitro, oxo (as a substitutent for heteroaryl), $-CO_2H$, -C(O)OC_1-C_4 alkyl, -CON(C_1-C_4 alkyl)(C_1-C_4 alkyl), -CONH(C_1-C_4 alkyl), $-CONH_2$, -NHC(O)(C_1-C_4 alkyl), -NHC(O)(phenyl), -N(C_1-C_4 alkyl)C(O)(C_1-C_4 alkyl), -N(C_1-C_4 alkyl)C(O)(phenyl), -C(O)C_1-C_4 alkyl, -C(O)C_1-C_4 phenyl, -C(O)C_1-C_4 haloalkyl, -OC(O)C_1-C_4 alkyl, $-SO_2$(C_1-C_4 alkyl), $-SO_2$(phenyl), $-SO_2$(C_1-C_4 haloalkyl), $-SO_2NH_2$, $-SO_2NH$(C_1-C_4 alkyl), $-SO_2NH$(phenyl), $-NHSO_2$(C_1-C_4 alkyl), $-NHSO_2$(phenyl), and $-NHSO_2$(C_1-C_4 haloalkyl).

[0054] The term "substituted alkoxy" refers to alkoxy wherein the alkyl constituent is substituted (i.e., -O-(substituted alkyl)) wherein "substituted alkyl" refers to alkyl wherein one or more (such as up to 5, for example, up to 3) hydrogen atoms are replaced by a substituent independently chosen from:

$-R^a$, $-OR^b$, -O(C_1-C_2 alkyl)O- (e.g., methylenedioxy-), $-SR^b$, guanidine, guanidine wherein one or more of the guanidine hydrogens are replaced with a lower-alkyl group, $-NR^bR^c$, halo, cyano, nitro, $-COR^b$, $-CO_2R^b$, $-CONR^bR^c$, $-OCOR^b$, $-OCO_2R^a$, $-OCONR^bR^c$, $-NR^cCOR^b$, $-NR^cCO_2R^a$, $-NR^cCONR^bR^c$, $-CO_2R^b$, $-CONR^bR^c$, $-NR^cCOR^b$, $-SOR^a$, $-SO_2R^a$, $-SO_2NR^bR^c$, and $-NR^cSO_2R^a$,

where R^a is chosen from optionally substituted C_1-C_6 alkyl, optionally substituted aryl, and optionally substituted heteroaryl;

R^b is chosen from H, optionally substituted C_1-C_6 alkyl, optionally substituted aryl, and optionally substituted heteroaryl; and

R^c is chosen from hydrogen and optionally substituted C_1-C_4 alkyl; or

R^b and R^c, and the nitrogen to which they are attached, form an optionally substituted heterocycloalkyl group; and

where each optionally substituted group is unsubstituted or independently substituted with one or more, such as one, two, or three, substituents independently selected from C_1-C_4 alkyl, aryl, heteroaryl, aryl-C_1-C_4 alkyl-, heteroaryl-C_1-C_4 alkyl-, C_1-C_4 haloalkyl-, -OC_1-C_4 alkyl, -OC_1-C_4 alkylphenyl, -C_1-C_4 alkyl-OH, -OC_1-C_4 haloalkyl, halo, -OH, $-NH_2$, -C_1-C_4 alkyl-NH_2, -N(C_1-C_4 alkyl)(C_1-C_4 alkyl), -NH(C_1-C_4 alkyl), -N(C_1-C_4 alkyl)(C_1-C_4 alkylphenyl), -NH(C_1-C_4 alkylphenyl), cyano, nitro, oxo (as a substitutent for heteroaryl), $-CO_2H$, -C(O)OC_1-C_4 alkyl, -CON(C_1-C_4 alkyl)(C_1-C_4 alkyl), -CONH(C_1-C_4 alkyl), $-CONH_2$, -NHC(O)(C_1-C_4 alkyl), -NHC(O)(phenyl), -N(C_1-C_4 alkyl)C(O)(C_1-C_4 alkyl), -N(C_1-C_4 alkyl)C(O)(phenyl), -C(O)C_1-C_4 alkyl, -C(O)C_1-C_4 phenyl, -C(O)C_1-C_4 haloalkyl, -OC(O)C_1-C_4 alkyl, $-SO_2$(C_1-C_4 alkyl), $-SO_2$(phenyl), $-SO_2$(C_1-C_4 haloalkyl), $-SO_2NH_2$, $-SO_2$NH(C_1-C_4 alkyl), $-SO_2$NH(phenyl), $-NHSO_2$(C_1-C_4 alkyl), $-NHSO_2$(phenyl), and $-NHSO_2$(C_1-C_4 haloalkyl). In some embodiments, a substituted alkoxy group is "polyalkoxy" or -O-(optionally substituted alkylene)-(optionally substituted alkoxy), and includes groups such as $-OCH_2CH_2OCH_3$, and residues of glycol ethers such as polyethyleneglycol, and $-O(CH_2CH_2O)_xCH_3$, where x is an integer of 2-20, such as 2-10, and for example, 2-5. Another substituted alkoxy group is hydroxyalkoxy or $-OCH_2(CH_2)_yOH$, where y is an integer of 1-10, such as 1-4.

[0055] The term "substituted alkoxycarbonyl" refers to the group (substituted alkyl)-O-C(O)- wherein the group is attached to the parent structure through the carbonyl functionality and wherein substituted refers to alkyl wherein one or more (such as up to 5, for example, up to 3) hydrogen atoms are replaced by a substituent independently chosen from:

-R^a, -OR^b, -O(C_1-C_2 alkyl)O- (e.g., methylenedioxy-), -SR^b, guanidine, guanidine wherein one or more of the guanidine hydrogens are replaced with a lower-alkyl group, -NR^bR^c, halo, cyano, nitro, -COR^b, -CO_2R^b, -$CONR^bR^c$, -$OCOR^b$, -OCO_2R^a, -$OCONR^bR^c$, -NR^cCOR^b, -$NR^cCO_2R^a$, -$NR^cCONR^bR^c$, -CO_2R^b, -$CONR^bR^c$, -NR^cCOR^b, -SOR^a, -SO_2R^a, -$SO_2NR^bR^c$, and -$NR^cSO_2R^a$,

where R^a is chosen from optionally substituted C_1-C_6 alkyl, optionally substituted aryl, and optionally substituted heteroaryl;

R^b is chosen from H, optionally substituted C_1-C_6 alkyl, optionally substituted aryl, and optionally substituted heteroaryl; and

R^c is chosen from hydrogen and optionally substituted C_1-C_4 alkyl; or

R^b and R^c, and the nitrogen to which they are attached, form an optionally substituted heterocycloalkyl group; and

where each optionally substituted group is unsubstituted or independently substituted with one or more, such as one, two, or three, substituents independently selected from C_1-C_4 alkyl, aryl, heteroaryl, aryl-C_1-C_4 alkyl-, heteroaryl-C_1-C_4 alkyl-, C_1-C_4 haloalkyl-, -OC_1-C_4 alkyl, -OC_1-C_4 alkylphenyl, -C_1-C_4 alkyl-OH, -OC_1-C_4 haloalkyl, halo, -OH, -NH_2, -C_1-C_4 alkyl-NH_2, -N(C_1-C_4 alkyl)(C_1-C_4 alkyl), -NH(C_1-C_4 alkyl), -N(C_1-C_4 alkyl)(C_1-C_4 alkylphenyl), -NH(C_1-C_4 alkylphenyl), cyano, nitro, oxo (as a substitutent for heteroaryl), -CO_2H, -C(O)OC_1-C_4 alkyl, -CON(C_1-C_4 alkyl)(C_1-C_4 alkyl), -CONH(C_1-C_4 alkyl), -$CONH_2$, -NHC(O)(C_1-C_4 alkyl), -NHC(O)(phenyl), -N(C_1-C_4 alkyl)C(O)(C_1-C_4 alkyl), -N(C_1-C_4 alkyl)C(O)(phenyl), -C(O)C_1-C_4 alkyl, -C(O)C_1-C_4 phenyl, -C(O)C_1-C_4 haloalkyl, -OC(O)C_1-C_4 alkyl, -SO_2(C_1-C_4 alkyl), -SO_2(phenyl), -SO_2(C_1-C_4 haloalkyl), -SO_2NH_2, -SO_2NH(C_1-C_4 alkyl), -SO_2NH(phenyl), -$NHSO_2$(C_1-C_4 alkyl), -$NHSO_2$(phenyl), and -$NHSO_2$(C_1-C_4 haloalkyl).

[0056] The term "substituted amino" refers to the group –NHR^d or –NR^dR^d where each R^d is independently chosen from: hydroxy, optionally substituted alkyl, optionally substituted cycloalkyl, optionally substituted acyl, aminocarbonyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted heterocycloalkyl, alkoxycarbonyl, sulfinyl and sulfonyl, provided that only one R^d may be hydroxyl, and wherein substituted alkyl, cycloalkyl, aryl, heterocycloalkyl, and heteroaryl refer respectively to alkyl, cycloalkyl, aryl, heterocycloalkyl, and

heteroaryl wherein one or more (such as up to 5, for example, up to 3) hydrogen atoms are replaced by a substituent independently chosen from:

$-R^a$, $-OR^b$, $-O(C_1-C_2$ alkyl$)O-$ (e.g., methylenedioxy-), $-SR^b$, guanidine, guanidine wherein one or more of the guanidine hydrogens are replaced with a lower-alkyl group, $-NR^bR^c$, halo, cyano, nitro, $-COR^b$, $-CO_2R^b$, $-CONR^bR^c$, $-OCOR^b$, $-OCO_2R^a$, $-OCONR^bR^c$, $-NR^cCOR^b$, $-NR^cCO_2R^a$, $-NR^cCONR^bR^c$, $-CO_2R^b$, $-CONR^bR^c$, $-NR^cCOR^b$, $-SOR^a$, $-SO_2R^a$, $-SO_2NR^bR^c$, and $-NR^cSO_2R^a$,

where R^a is chosen from optionally substituted C_1-C_6 alkyl, optionally substituted aryl, and optionally substituted heteroaryl;

R^b is chosen from H, optionally substituted C_1-C_6 alkyl, optionally substituted aryl, and optionally substituted heteroaryl; and

R^c is chosen from hydrogen and optionally substituted C_1-C_4 alkyl; or

R^b and R^c, and the nitrogen to which they are attached, form an optionally substituted heterocycloalkyl group; and

where each optionally substituted group is unsubstituted or independently substituted with one or more, such as one, two, or three, substituents independently selected from C_1-C_4 alkyl, aryl, heteroaryl, aryl-C_1-C_4 alkyl-, heteroaryl-C_1-C_4 alkyl-, C_1-C_4 haloalkyl-, $-OC_1-C_4$ alkyl, $-OC_1-C_4$ alkylphenyl, $-C_1-C_4$ alkyl-OH, $-OC_1-C_4$ haloalkyl, halo, -OH, $-NH_2$, $-C_1-C_4$ alkyl-NH_2, $-N(C_1-C_4$ alkyl$)(C_1-C_4$ alkyl$)$, $-NH(C_1-C_4$ alkyl$)$, $-N(C_1-C_4$ alkyl$)(C_1-C_4$ alkylphenyl$)$, $-NH(C_1-C_4$ alkylphenyl$)$, cyano, nitro, oxo (as a substitutent for heteroaryl), $-CO_2H$, $-C(O)OC_1-C_4$ alkyl, $-CON(C_1-C_4$ alkyl$)(C_1-C_4$ alkyl$)$, $-CONH(C_1-C_4$ alkyl$)$, $-CONH_2$, $-NHC(O)(C_1-C_4$ alkyl$)$, -NHC(O)(phenyl), $-N(C_1-C_4$ alkyl$)C(O)(C_1-C_4$ alkyl$)$, $-N(C_1-C_4$ alkyl$)C(O)$(phenyl), $-C(O)C_1-C_4$ alkyl, $-C(O)C_1-C_4$ phenyl, $-C(O)C_1-C_4$ haloalkyl, $-OC(O)C_1-C_4$ alkyl, $-SO_2(C_1-C_4$ alkyl$)$, $-SO_2$(phenyl), $-SO_2(C_1-C_4$ haloalkyl$)$, $-SO_2NH_2$, $-SO_2NH(C_1-C_4$ alkyl$)$, $-SO_2NH$(phenyl), $-NHSO_2(C_1-C_4$ alkyl$)$, $-NHSO_2$(phenyl), and $-NHSO_2(C_1-C_4$ haloalkyl$)$; and

wherein optionally substituted acyl, aminocarbonyl, alkoxycarbonyl, sulfinyl and sulfonyl are as defined herein.

[0057] The term "substituted amino" also refers to N-oxides of the groups $-NHR^d$, and NR^dR^d each as described above. N-oxides can be prepared by treatment of the corresponding amino group with, for example, hydrogen peroxide or m-

chloroperoxybenzoic acid. The person skilled in the art is familiar with reaction conditions for carrying out the N-oxidation.

[0058] Compounds of Formula 1 include, but are not limited to, optical isomers of compounds of Formula 1, racemates, and other mixtures thereof. In those situations, the single enantiomers or diastereomers, i.e., optically active forms, can be obtained by asymmetric synthesis or by resolution of the racemates. Resolution of the racemates can be accomplished, for example, by conventional methods such as crystallization in the presence of a resolving agent, or chromatography, using, for example a chiral high-pressure liquid chromatography (HPLC) column. In addition, compounds of Formula 1 include Z- and E- forms (or *cis*- and *trans*- forms) of compounds with carbon-carbon double bonds. Where compounds of Formula 1 exists in various tautomeric forms, chemical entities of the present invention include all tautomeric forms of the compound. Compounds of Formula 1 also include crystal forms including polymorphs and clathrates.

[0059] Chemical entities of the present invention include, but are not limited to compounds of Formula 1 and all pharmaceutically acceptable forms thereof. Pharmaceutically acceptable forms of the compounds recited herein include pharmaceutically acceptable salts, solvates, chelates, non-covalent complexes, prodrugs, and mixtures thereof. In certain embodiments, the compounds described herein are in the form of pharmaceutically acceptable salts. Hence, the terms "chemical entity" and "chemical entities" also encompass pharmaceutically acceptable salts, solvates, chelates, non-covalent complexes, prodrugs, and mixtures.

[0060] "Pharmaceutically acceptable salts" include, but are not limited to salts with inorganic acids, such as hydrochlorate, phosphate, diphosphate, hydrobromate, sulfate, sulfinate, nitrate, and like salts; as well as salts with an organic acid, such as malate, maleate, fumarate, tartrate, succinate, citrate, acetate, lactate, methanesulfonate, p-toluenesulfonate, 2-hydroxyethylsulfonate, benzoate, salicylate, stearate, and alkanoate such as acetate, $HOOC-(CH_2)_n-COOH$ where n is 0-4, and like salts. Similarly, pharmaceutically acceptable cations include, but are not limited to sodium, potassium, calcium, aluminum, lithium, and ammonium.

[0061] In addition, if the compound of Formula 1 is obtained as an acid addition salt, the free base can be obtained by basifying a solution of the acid salt.

Conversely, if the product is a free base, an addition salt, particularly a pharmaceutically acceptable addition salt, may be produced by dissolving the free base in a suitable organic solvent and treating the solution with an acid, in accordance with conventional procedures for preparing acid addition salts from base compounds. Those skilled in the art will recognize various synthetic methodologies that may be used to prepare non-toxic pharmaceutically acceptable addition salts.

[0062] As noted above, prodrugs also fall within the scope of chemical entities, for example ester or amide derivatives of the compounds of Formula 1. The term "prodrugs" includes any compounds that become compounds of Formula 1 when administered to a patient, e.g., upon metabolic processing of the prodrug. Examples of prodrugs include, but are not limited to, acetate, formate, and benzoate and like derivatives of functional groups (such as alcohol or amine groups) in the compounds of Formula 1.

[0063] The term "solvate" refers to the chemical entity formed by the interaction of a solvent and a compound. Suitable solvates are pharmaceutically acceptable solvates, such as hydrates, including monohydrates and hemi-hydrates.

[0064] The term "chelate" refers to the chemical entity formed by the coordination of a compound to a metal ion at two (or more) points.

[0065] The term "non-covalent complex" refers to the chemical entity formed by the interaction of a compound and another molecule wherein a covalent bond is not formed between the compound and the molecule. For example, complexation can occur through van der Waals interactions, hydrogen bonding, and electrostatic interactions (also called ionic bonding).

[0066] The term "hydrogen bond" refers to a form of association between an electronegative atom (also known as a hydrogen bond acceptor) and a hydrogen atom attached to a second, relatively electronegative atom (also known as a hydrogen bond donor). Suitable hydrogen bond donor and acceptors are well understood in medicinal chemistry (G. C. Pimentel and A. L. McClellan, The Hydrogen Bond, Freeman, San Francisco, 1960; R. Taylor and O. Kennard, "Hydrogen Bond Geometry in Organic Crystals", Accounts of Chemical Research, 17, pp. 320-326 (1984)).

[0067] "Hydrogen bond acceptor" refers to a group comprising an oxygen or nitrogen, especially an oxygen or nitrogen that is sp^2 –hybridized, an ether oxygen, or the oxygen of a sulfoxide or N-oxide.

[0068] The term "hydrogen bond donor" refers to an oxygen, nitrogen, or heteroaromatic carbon that bears a hydrogen.group containing a ring nitrogen or a heteroaryl group containing a ring nitrogen.

[0069] The term "pharmacophore" is known in the art, and, as used herein, refers to a molecular moiety capable of exerting a selected biochemical effect, e.g., inhibition of an enzyme, such as inhibition of Btk. A selected pharmacophore can have more than one biochemical effect, e.g., can be an inhibitor of one receptor (or enzyme) and an antagonist, agonist or partial agonist of a second receptor (or enzyme). A therapeutic agent can include one or more pharmacophores, which can have the same or different biochemical activities.

[0070] As used herein the terms "group", "radical" or "fragment" are synonymous and are intended to indicate functional groups or fragments of molecules attachable to a bond or other fragments of molecules.

[0071] The term "active agent" is used to indicate a chemical entity which has biological activity. In certain embodiments, an "active agent" is a compound having pharmaceutical utility. For example an active agent may be an anti-cancer therapeutic.

[0072] The term "therapeutically effective amount" of a chemical entity of this invention means an amount effective, when administered to a human or non-human patient, to provide a therapeutic benefit such as amelioration of symptoms, slowing of disease progression, or prevention of disease e.g., a therapeutically effective amount may be an amount sufficient to decrease the symptoms of a disease responsive to inhibition of Btk activity. In some embodiments, a therapeutically effective amount is an amount sufficient to reduce cancer symptoms, the symptoms of an allergic disorder, the symptoms of an autoimmune and/or inflammatory disease, or the symptoms of an acute inflammatory reaction. In some embodiments a therapeutically effective amount is an amount sufficient to decrease the number of detectable cancerous cells in an organism, detectably slow, or stop the growth of a cancerous tumor. In some embodiments, a therapeutically effective amount is an amount

sufficient to shrink a cancerous tumor. In certain circumstances a patient suffering from cancer may not present symptoms of being affected. In some embodiments, a therapeutically effective amount of a chemical entity is an amount sufficient to prevent a significant increase or significantly reduce the detectable level of cancerous cells or cancer markers in the patient's blood, serum, or tissues. In methods described herein for treating allergic disorders and/or autoimmune and/or inflammatory diseases and/or acute inflammatory reactions, a therapeutically effective amount may also be an amount sufficient, when administered to a patient, to detectably slow progression of the disease, or prevent the patient to whom the chemical entity is given from presenting symptoms of the allergic disorders and/or autoimmune and/or inflammatory disease, and/or acute inflammatory response. In certain methods described herein for treating allergic disorders and/or autoimmune and/or inflammatory diseases and/or acute inflammatory reactions, a therapeutically effective amount may also be an amount sufficient to produce a detectable decrease in the amount of a marker protein or cell type in the patient's blood or serum. For example, in some embodiments a therapeutically effective amount is an amount of a chemical entity described herein sufficient to significantly decrease the activity of B-cells. In another example, in some embodiments a therapeutically effective amount is an amount of a chemical entity described herein sufficient to significantly decrease the number of B-cells. In another example, in some embodiments a therapeutically effective amount is an amount of a chemical entity described herein sufficient to decrease the level of anti- acetylcholine receptor antibody in a patient's blood with the disease myasthenia gravis.

[0073] The term "inhibition" indicates a significant decrease in the baseline activity of a biological activity or process. "Inhibition of Btk activity" refers to a decrease in Btk activity as a direct or indirect response to the presence of at least one chemical entity described herein, relative to the activity of Btk in the absence of the at least one chemical entity. The decrease in activity may be due to the direct interaction of the compound with Btk, or due to the interaction of the chemical entity(ies) described herein with one or more other factors that in turn affect Btk activity. For example, the presence of the chemical entity(ies) may decrease Btk activity by directly binding to the Btk, by causing (directly or indirectly) another factor to

decrease Btk activity, or by (directly or indirectly) decreasing the amount of Btk present in the cell or organism.

[0074] Inhibition of Btk activity also refers to observable inhibition of Btk activity in a standard biochemical assay for Btk activity, such as the ATP hydrolysis assay described below. In some embodiments, the chemical entity described herein has an IC_{50} value less than or equal to 1 micromolar. In some embodiments, the chemical entity has an IC_{50} value less than or equal to less than 100 nanomolar. In some embodiments, the chemical entity has an IC_{50} value less than or equal to 10 nanomolar.

[0075] "Inhibition of B-cell activity" refers to a decrease in B-cell activity as a direct or indirect response to the presence of at least one chemical entity described herein, relative to the activity of B-cells in the absence of the at least one chemical entity. The decrease in activity may be due to the direct interaction of the compound with Btk or with one or more other factors that in turn affect B-cell activity.

[0076] Inhibition of B-cell activity also refers to observable inhibition of CD86 expression in a standard assay such as the assay described below. In some embodiments, the chemical entity described herein has an IC_{50} value less than or equal to 10 micromolar. In some embodiments, the chemical entity has an IC_{50} value less than or equal to less than 1 micromolar. In some embodiments, the chemical entity has an IC_{50} value less than or equal to 500 nanomolar.

[0077] "B cell activity" also includes activation, redistribution, reorganization, or capping of one or more various B cell membrane receptors, or membrane-bound immunoglobulins, e.g, IgM, IgG, and IgD. Most B cells also have membrane receptors for Fc portion of IgG in the form of either antigen-antibody complexes or aggregated IgG. B cells also carry membrane receptors for the activated components of complement, e.g., C3b, C3d, C4, and Clq. These various membrane receptors and membrane-bound immunoglobulins have membrane mobility and can undergo redistribution and capping that can initiate signal transduction.

[0078] B cell activity also includes the synthesis or production of antibodies or immunoglobulins. Immunoglobulins are synthesized by the B cell series and have common structural features and structural units. Five immunoglobulin classes, i.e., IgG, IgA, IgM, IgD, and IgE, are recognized on the basis of structural differences of

their heavy chains including the amino acid sequence and length of the polypeptide chain. Antibodies to a given antigen may be detected in all or several classes of immunoglobulins or may be restricted to a single class or subclass of immunoglobulin. Autoantibodies or autoimmune antibodies may likewise belong to one or several classes of immunoglobulins. For example, rheumatoid factors (antibodies to IgG) are most often recognized as an IgM imnnunoglobulin, but can also consist of IgG or IgA.

[0079] In addition, B cell activity also is intended to include a series of events leading to B cell clonal expansion (proliferation) from precursor B lymphocytes and differentiation into antibody-synthesizing plasma cells which takes place in conjunction with antigen-binding and with cytokine signals from other cells.

[0080] "Inhibition of B-cell proliferation" refers to inhibition of proliferation of abnormal B-cells, such as cancerous B-cells, e.g. lymphoma B-cells and/ or inhibition of normal, non-diseased B-cells. The term "inhibition of B-cell proliferation" indicates any significant decrease in the number of B-cells, either *in vitro* or *in vivo*. Thus an inhibition of B-cell proliferation *in vitro* would be any significant decrease in the number of B-cells in an *in vitro* sample contacted with at least one chemical entity described herein as compared to a matched sample not contacted with the chemical entity(ies).

[0081] Inhibition of B-cell proliferation also refers to observable inhibition of B-cell proliferation in a standard thymidine incorporation assay for B-cell proliferation, such as the assay described herein. In some embodiments, the chemical entity has an IC_{50} value less than or equal to 10 micromolar. In some embodiments, the chemical entity has an IC_{50} value less than or equal to less than 1 micromolar. In some embodiments, the chemical entity has an IC_{50} value less than or equal to 500 nanomolar.

[0082] An "allergy" or "allergic disorder" refers to acquired hypersensitivity to a substance (allergen). Allergic conditions include eczema, allergic rhinitis or coryza, hay fever, bronchial asthma, urticaria (hives) and food allergies, and other atopic conditions.

[0083] "Asthma" refers to a disorder of the respiratory system characterized by inflammation, narrowing of the airways and increased reactivity of the airways to

inhaled agents. Asthma is frequently, although not exclusively associated with atopic or allergic symptoms.

[0084] By "significant" is meant any detectable change that is statistically significant in a standard parametric test of statistical significance such as Student's T-test, where $p < 0.05$.

[0085] A "disease responsive to inhibition of Btk activity" is a disease in which inhibiting Btk kinase provides a therapeutic benefit such as an amelioration of symptoms, decrease in disease progression, prevention or delay of disease onset, or inhibition of aberrant activity of certain cell-types (monocytes, B-cells, and mast cells).

[0086] "Treatment or treating means any treatment of a disease in a patient, including:

a) preventing the disease, that is, causing the clinical symptoms of the disease not to develop;

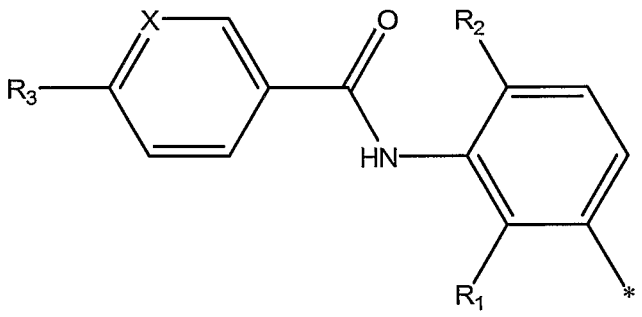
b) inhibiting the disease;

c) slowing or arresting the development of clinical symptoms; and/or

d) relieving the disease, that is, causing the regression of clinical symptoms.

[0087] "Patient" refers to an animal, such as a mammal, that has been or will be the object of treatment, observation or experiment. The methods of the invention can be useful in both human therapy and veterinary applications. In some embodiments, the patient is a mammal; in some embodiments the patient is human; and in some embodiments the patient is chosen from cats and dogs.

[0088] Provided is at least one chemical entity comprising a pharmacophore chosen from radicals of Formula 1



(Formula 1)

and pharmaceutically acceptable salts, solvates, chelates, non-covalent complexes, prodrugs, and mixtures thereof, wherein

* represents a point of attachment;

R_3 is chosen from optionally substituted piperidinyl, tert-butyl and isopropyl;

X is chosen from CH and N; and

R_1 and R_2 are independently chosen from hydrogen, lower alkyl, and halo, provided that at least one of R_1 and R_2 is not hydrogen.

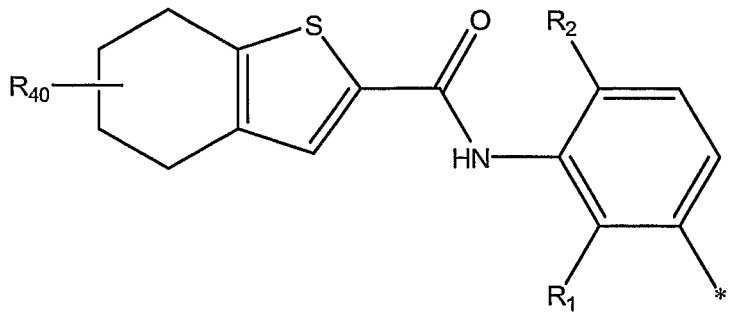
[0089] In some embodiments, R_1 and R_2 are independently chosen from hydrogen, methyl, and fluoro. In some embodiments, R_1 is chosen from methyl and fluoro and R_2 is hydrogen. In some embodiments, R_2 is chosen from methyl and fluoro and R_1 is hydrogen. In some embodiments, R_1 and R_2 are independently chosen from methyl and fluoro.

[0090] In some embodiments, R_3 is chosen from *tert*-butyl and *iso*-propyl. In some embodiments, R_3 is *tert*-butyl. In some embodiments, R_3 is *iso*-propyl. In some embodiments, R_3 is piperidinyl substituted with one or two groups independently chosen from amino, hydroxy, optionally substituted lower alkyl, optionally substituted lower alkoxy, and carbamoyl. In some embodiments, R_3 is piperidinyl optionally substituted with one or two groups independently chosen from amino, hydroxy, methyl, ethyl, methoxy, hydroxymethyl, methoxymethoxy, and carbamoyl. In some embodiments, R_3 is piperidin-1-yl optionally substituted with one or two groups independently chosen from amino, hydroxy, methyl, ethyl, methoxy, hydroxymethyl, methoxymethoxy, and carbamoyl. In some embodiments, R_3 is piperidin-1-yl.

In some embodiments, X is CH. In some embodiments, X is N.

[0091] In certain embodiments, the pharmacophore is coupled to another radical to form a chemical entity capable of inhibition of Btk. The structure of that other radical may vary so long as the chemical entity inhibits Btk as described further below.

[0092] Also provided is least one chemical entity comprising a pharmacophore chosen from radicals of Formula 1A

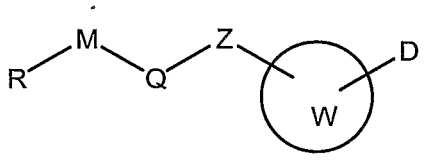


(Formula 1A)

and pharmaceutically acceptable salts, solvates, chelates, non-covalent complexes, prodrugs, and mixtures thereof, wherein R_1 and R_2 are as described above and wherein R_{40} is chosen from hydrogen, hydroxy, lower alkyl, sulfonyl, halo, lower alkoxy, and heteroaryl.

[0093] In certain embodiments, R_{40} is chosen from hydrogen and lower alkyl.

[0094] Provided is at least one chemical entity chosen from compounds of Formula 2:



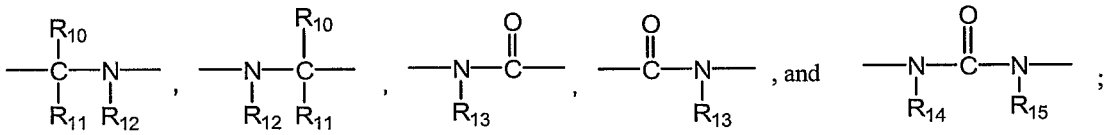
(Formula 2)

and pharmaceutically acceptable salts, solvates, chelates, non-covalent complexes, prodrugs, and mixtures thereof, wherein

R is chosen from optionally substituted cycloalkyl, optionally substituted aryl and optionally substituted heteroaryl;

M is chosen from a covalent bond and –CH=CH–.

Q is chosen from



wherein

R_{10} and R_{11} are independently chosen from hydrogen, C_1-C_6 alkyl, and C_1-C_6 haloalkyl; and

R_{12}, R_{13}, R_{14}, and R_{15} are each independently chosen from hydrogen,

C_1-C_6 alkyl,

C_1-C_6 haloalkyl,

phenyl,

substituted phenyl chosen from mono-, di-, and tri-substituted phenyl wherein the substituents are independently chosen from hydroxy, nitro, cyano, amino, halo, C_1-C_6 alkyl, C_1-C_6 alkoxy, (C_1-C_6 alkyloxy)C_1-C_6 alkoxy, C_1-C_6 perfluoroalkyl, C_1-C_6 perfluoroalkoxy, mono-(C_1-C_6 alkyl)amino, di(C_1-C_6 alkyl)amino, and amino(C_1-C_6 alkyl),

heteroaryl, and

substituted heteroaryl chosen from mono-, di-, and tri-substituted heteroaryl wherein the substituents are independently chosen from hydroxy, nitro, cyano, amino, halo, C_1-C_6 alkyl, C_1-C_6 alkoxy, (C_1-C_6 alkyloxy)C_1-C_6 alkoxy, C_1-C_6 perfluoroalkyl, C_1-C_6 perfluoroalkoxy, mono-(C_1-C_6 alkyl)amino, di(C_1-C_6 alkyl)amino, and amino(C_1-C_6 alkyl); and

Z is chosen from optionally substituted phenylene and optionally substituted pyridylidene;

W is an optionally substituted heteroaryl group;

and

D is a hydrogen bond donor, provided that

W is not an imidazo[1,2-A]pyrazine group;

D is not hydrogen; and

the compound of Formula 2 is not (4-{6-[(4-chloro-benzyl)-methyl-amino]-pyrazin-2-yl}-phenyl)-piperidin-1-yl-methanone.

[0095] In certain embodiments, R is chosen from optionally substituted aryl and optionally substituted heteroaryl.

[0096] In certain embodiments, R is chosen from

phenyl,

substituted phenyl chosen from mono-, di-, and tri-substituted phenyl wherein the substituents are independently chosen from hydroxy, lower alkyl, sulfanyl, sulfonyl, optionally substituted amino, lower alkoxy, lower alkyl substituted with one or more halo, lower alkoxy substituted with one or more halo, lower alkyl substituted with hydroxy, lower alkyl substituted with lower alkoxy, optionally substituted piperidinyl, and heteroaryl,

pyridyl,

substituted pyridyl chosen from mono-, di-, and tri-substituted pyridyl wherein the substituents are independently chosen from hydroxy, lower alkyl, sulfonyl, halo, lower alkoxy, optionally substituted piperidinyl, and heteroaryl,

pyrimidinyl,

substituted pyrimidinyl chosen from mono-, di-, and tri-substituted pyridyl wherein the substituents are independently chosen from hydroxy, lower alkyl, sulfonyl, halo, lower alkoxy, optionally substituted piperidinyl, and heteroaryl,

pyrazinyl,

substituted pyrazinyl chosen from mono-, di-, and tri-substituted pyridyl wherein the substituents are independently chosen from hydroxy, lower alkyl, sulfonyl, halo, lower alkoxy, optionally substituted piperidinyl, and heteroaryl,

pyridazinyl,

substituted pyridazinyl chosen from mono-, di-, and tri-substituted pyridyl wherein the substituents are independently chosen from hydroxy, lower alkyl, sulfonyl, halo, lower alkoxy, optionally substituted piperidinyl, and heteroaryl,

oxazol-2-yl,

substituted oxazol-2-yl l chosen from mono-, di-, and tri-substituted oxazol-2-yl wherein the substituents are independently chosen from hydroxy,

lower alkyl, sulfonyl, halo, lower alkoxy, optionally substituted piperidinyl, and heteroaryl,

2H-pyrazol-3-yl,

substituted 2H-pyrazol-3-yl chosen from mono-, di-, and tri-substituted 2H-pyrazol-3-yl wherein the substituents are independently chosen from hydroxy, lower alkyl, sulfonyl, halo, lower alkoxy, optionally substituted piperidinyl, and heteroaryl,

[1,2,3]thiadiazol-4-yl,

substituted [1,2,3]thiadiazol-4-yl chosen from mono-, di-, and tri-substituted [1,2,3]thiadiazol-4-yl wherein the substituents are independently chosen from hydroxy, lower alkyl, sulfonyl, halo, lower alkoxy, optionally substituted piperidinyl, and heteroaryl,

isoxazol-5-yl,

substituted isoxazol-5-yl chosen from mono-, di-, and tri-substituted isoxazol-5-yl wherein the substituents are independently chosen from hydroxy, lower alkyl, sulfonyl, halo, lower alkoxy, optionally substituted piperidinyl, and heteroaryl,

4,5,6,7-tetrahydrobenzo[b]thiophen-2-yl,

substituted 4,5,6,7-tetrahydrobenzo[b]thiophen-2-yl chosen from mono-, di-, and tri-substituted 4,5,6,7-tetrahydrobenzo[b]thiophen-2-yl wherein the substituents are independently chosen from hydroxy, lower alkyl, sulfonyl, halo, lower alkoxy, optionally substituted piperidinyl, and heteroaryl,

4,5,6,7-tetrahydrobenzofuran-2-yl,

substituted 4,5,6,7-tetrahydrobenzofuran-2-yl chosen from mono-, di-, and tri-substituted 4,5,6,7-tetrahydrobenzofuran-2-yl wherein the substituents are independently chosen from hydroxy, lower alkyl, sulfonyl, halo, lower alkoxy, optionally substituted piperidinyl, and heteroaryl,

4,5,6,7-tetrahydro-1H-indol-2-yl,

substituted 4,5,6,7-tetrahydro-1H-indol-2-yl chosen from mono-, di-, and tri-substituted 4,5,6,7-tetrahydro-1H-indol-2-yl wherein the substituents are independently chosen from hydroxy, lower alkyl, sulfonyl, halo,

lower alkoxy, optionally substituted piperidinyl, and heteroaryl and wherein the amine nitrogen of the indole ring is optionally substituted with an optionally substituted lower alkyl group,

1H-indol-2-yl,

substituted 1H-indol-2-yl chosen from mono-, di-, and tri-substituted 1H-indol-2-yl wherein the substituents are independently chosen from hydroxy, lower alkyl, sulfonyl, halo, lower alkoxy, optionally substituted piperidinyl, and heteroaryl and wherein the amine nitrogen of the indole ring is optionally substituted with an optionally substituted lower alkyl group,

benzofuran-2-yl,

substituted benzofuran-2-yl chosen from mono-, di-, and tri-substituted benzofuran-2-yl wherein the substituents are independently chosen from hydroxy, lower alkyl, sulfonyl, halo, lower alkoxy, optionally substituted piperidinyl, and heteroaryl,

benzo[b]thiophen-2-yl, and

substituted benzo[b]thiophen-2-yl chosen from mono-, di-, and tri-substituted benzo[b]thiophen-2-yl wherein the substituents are independently chosen from hydroxy, lower alkyl, sulfonyl, halo, lower alkoxy, optionally substituted piperidinyl, and heteroaryl.

[0097] In certain embodiments, R is chosen from

phenyl,

substituted phenyl chosen from mono-, di-, and tri-substituted phenyl wherein the substituents are independently chosen from hydroxy, lower alkyl, sulfonyl, halo, lower alkoxy, optionally substituted piperidinyl, and heteroaryl,

pyridyl,

substituted pyridyl chosen from mono-, di-, and tri-substituted pyridyl wherein the substituents are independently chosen from hydroxy, lower alkyl, sulfonyl, halo, lower alkoxy, optionally substituted piperidinyl, and heteroaryl,

oxazol-2-yl,

substituted oxazol-2-yl l chosen from mono-, di-, and tri-substituted oxazol-2-yl wherein the substituents are independently chosen from hydroxy, lower alkyl, sulfonyl, halo, lower alkoxy, optionally substituted piperidinyl, and heteroaryl,

2H-pyrazol-3-yl,

substituted 2H-pyrazol-3-yl chosen from mono-, di-, and tri-substituted 2H-pyrazol-3-yl wherein the substituents are independently chosen from hydroxy, lower alkyl, sulfonyl, halo, lower alkoxy, optionally substituted piperidinyl, and heteroaryl,

[1,2,3]thiadiazol-4-yl,

substituted [1,2,3]thiadiazol-4-yl chosen from mono-, di-, and tri-substituted [1,2,3]thiadiazol-4-yl wherein the substituents are independently chosen from hydroxy, lower alkyl, sulfonyl, halo, lower alkoxy, optionally substituted piperidinyl, and heteroaryl,

4,5,6,7-tetrahydrobenzo[b]thiophen-2-yl,

substituted 4,5,6,7-tetrahydrobenzo[b]thiophen-2-yl chosen from mono-, di-, and tri-substituted 4,5,6,7-tetrahydrobenzo[b]thiophen-2-yl wherein the substituents are independently chosen from hydroxy, lower alkyl, sulfonyl, halo, lower alkoxy, optionally substituted piperidinyl, and heteroaryl,

isoxazol-5-yl, and

substituted isoxazol-5-yl chosen from mono-, di-, and tri-substituted isoxazol-5-yl wherein the substituents are independently chosen from hydroxy, lower alkyl, sulfonyl, halo, lower alkoxy, optionally substituted piperidinyl, and heteroaryl.

[0098] In certain embodiments, R is chosen from

phenyl,

substituted phenyl chosen from mono-, di-, and tri-substituted phenyl wherein the substituents are independently chosen from hydroxy, lower alkyl, sulfanyl, sulfonyl, optionally substituted amino, lower alkoxy, lower alkyl substituted with one or more halo, lower alkoxy substituted with

one or more halo, lower alkyl substituted with hydroxy, lower alkyl substituted with lower alkoxy, and heteroaryl,

pyridyl,

substituted pyridyl chosen from mono-, di-, and tri-substituted pyridyl wherein the substituents are independently chosen from hydroxy, lower alkyl, sulfonyl, halo, lower alkoxy, and heteroaryl,

pyrimidinyl,

substituted pyrimidinyl chosen from mono-, di-, and tri-substituted pyridyl wherein the substituents are independently chosen from hydroxy, lower alkyl, sulfonyl, halo, lower alkoxy, and heteroaryl,

pyrazinyl,

substituted pyrazinyl chosen from mono-, di-, and tri-substituted pyridyl wherein the substituents are independently chosen from hydroxy, lower alkyl, sulfonyl, halo, lower alkoxy, and heteroaryl,

pyridazinyl,

substituted pyridazinyl chosen from mono-, di-, and tri-substituted pyridyl wherein the substituents are independently chosen from hydroxy, lower alkyl, sulfonyl, halo, lower alkoxy, and heteroaryl,

oxazol-2-yl,

substituted oxazol-2-yl l chosen from mono-, di-, and tri-substituted oxazol-2-yl wherein the substituents are independently chosen from hydroxy, lower alkyl, sulfonyl, halo, lower alkoxy, and heteroaryl,

2H-pyrazol-3-yl,

substituted 2H-pyrazol-3-yl chosen from mono-, di-, and tri-substituted 2H-pyrazol-3-yl wherein the substituents are independently chosen from hydroxy, lower alkyl, sulfonyl, halo, lower alkoxy, and heteroaryl,

[1,2,3]thiadiazol-4-yl,

substituted [1,2,3]thiadiazol-4-yl chosen from mono-, di-, and tri-substituted [1,2,3]thiadiazol-4-yl wherein the substituents are independently chosen from hydroxy, lower alkyl, sulfonyl, halo, lower alkoxy, and heteroaryl,

isoxazol-5-yl,

substituted isoxazol-5-yl chosen from mono-, di-, and tri-substituted isoxazol-5-yl wherein the substituents are independently chosen from hydroxy, lower alkyl, sulfonyl, halo, lower alkoxy, and heteroaryl,

4,5,6,7-tetrahydrobenzo[b]thiophen-2-yl,

substituted 4,5,6,7-tetrahydrobenzo[b]thiophen-2-yl chosen from mono-, di-, and tri-substituted 4,5,6,7-tetrahydrobenzo[b]thiophen-2-yl wherein the substituents are independently chosen from hydroxy, lower alkyl, sulfonyl, halo, lower alkoxy, and heteroaryl,

4,5,6,7-tetrahydrobenzofuran-2-yl,

substituted 4,5,6,7-tetrahydrobenzofuran-2-yl chosen from mono-, di-, and tri-substituted 4,5,6,7-tetrahydrobenzofuran-2-yl wherein the substituents are independently chosen from hydroxy, lower alkyl, sulfonyl, halo, lower alkoxy, and heteroaryl,

4,5,6,7-tetrahydro-1H-indol-2-yl,

substituted 4,5,6,7-tetrahydro-1H-indol-2-yl chosen from mono-, di-, and tri-substituted 4,5,6,7-tetrahydro-1H-indol-2-yl wherein the substituents are independently chosen from hydroxy, lower alkyl, sulfonyl, halo, lower alkoxy, and heteroaryl and wherein the amine nitrogen of the indole ring is optionally substituted with an optionally substituted lower alkyl group,

1H-indol-2-yl,

substituted 1H-indol-2-yl chosen from mono-, di-, and tri-substituted 1H-indol-2-yl wherein the substituents are independently chosen from hydroxy, lower alkyl, sulfonyl, halo, lower alkoxy, and heteroaryl and wherein the amine nitrogen of the indole ring is optionally substituted with an optionally substituted lower alkyl group,

benzofuran-2-yl,

substituted benzofuran-2-yl chosen from mono-, di-, and tri-substituted benzofuran-2-yl wherein the substituents are independently chosen from hydroxy, lower alkyl, sulfonyl, halo, lower alkoxy, and heteroaryl,

benzo[b]thiophen-2-yl, and

substituted benzo[b]thiophen-2-yl chosen from mono-, di-, and tri-substituted benzo[b]thiophen-2-yl wherein the substituents are independently chosen from hydroxy, lower alkyl, sulfonyl, halo, lower alkoxy, and heteroaryl.

[0099] In certain embodiments, R is chosen from

phenyl,

substituted phenyl chosen from mono-, di-, and tri-substituted phenyl wherein the substituents are independently chosen from hydroxy, lower alkyl, sulfonyl, halo, lower alkoxy, and heteroaryl,

pyridyl,

substituted pyridyl chosen from mono-, di-, and tri-substituted pyridyl wherein the substituents are independently chosen from hydroxy, lower alkyl, sulfonyl, halo, lower alkoxy, and heteroaryl,

oxazol-2-yl,

substituted oxazol-2-yl 1 chosen from mono-, di-, and tri-substituted oxazol-2-yl wherein the substituents are independently chosen from hydroxy, lower alkyl, sulfonyl, halo, lower alkoxy, and heteroaryl,

2H-pyrazol-3-yl,

substituted 2H-pyrazol-3-yl chosen from mono-, di-, and tri-substituted 2H-pyrazol-3-yl wherein the substituents are independently chosen from hydroxy, lower alkyl, sulfonyl, halo, lower alkoxy, and heteroaryl,

[1,2,3]thiadiazol-4-yl,

substituted [1,2,3]thiadiazol-4-yl chosen from mono-, di-, and tri-substituted [1,2,3]thiadiazol-4-yl wherein the substituents are independently chosen from hydroxy, lower alkyl, sulfonyl, halo, lower alkoxy, and heteroaryl,

4,5,6,7-tetrahydrobenzo[b]thiophen-2-yl,

substituted 4,5,6,7-tetrahydrobenzo[b]thiophen-2-yl chosen from mono-, di-, and tri-substituted 4,5,6,7-tetrahydrobenzo[b]thiophen-2-yl wherein the substituents are independently chosen from hydroxy, lower alkyl, sulfonyl, halo, lower alkoxy, and heteroaryl,

isoxazol-5-yl, and

substituted isoxazol-5-yl chosen from mono-, di-, and tri-substituted isoxazol-5-yl wherein the substituents are independently chosen from hydroxy, lower alkyl, sulfonyl, halo, lower alkoxy, and heteroaryl.

[00100] In certain embodiments, R is chosen from 4,5,6,7-tetrahydrobenzo[b]thiophen-2-yl and substituted 4,5,6,7-tetrahydrobenzo[b]thiophen-2-yl chosen from mono-, di-, and tri-substituted 4,5,6,7-tetrahydrobenzo[b]thiophen-2-yl wherein the substituents are independently chosen from hydroxy, lower alkyl, sulfonyl, halo, lower alkoxy, and heteroaryl.

[00101] In certain embodiments, R is chosen from 4,5,6,7-tetrahydrobenzo[b]thiophen-2-yl and substituted 4,5,6,7-tetrahydrobenzo[b]thiophen-2-yl chosen from mono-, di-, and tri-substituted 4,5,6,7-tetrahydrobenzo[b]thiophen-2-yl wherein the substituents is lower alkyl.

[00102] In certain embodiments, R is substituted phenyl chosen from mono-, di-, and tri-substituted phenyl wherein the substituents are independently chosen from hydroxy, lower alkyl, sulfanyl, sulfonyl, optionally substituted amino, lower alkoxy, lower alkyl substituted with one or more halo, lower alkoxy substituted with one or more halo, lower alkyl substituted with hydroxy, lower alkyl substituted with lower alkoxy, and heteroaryl.

[00103] In certain embodiments, R is substituted phenyl chosen from mono-, di-, and tri-substituted phenyl wherein the substituents are independently chosen from hydroxy, lower alkyl, sulfonyl, halo, lower alkoxy, and heteroaryl. In certain embodiments, R is 4-lower alkyl-phenyl-. In certain embodiments, R is 4-*tert*-butyl-phenyl.

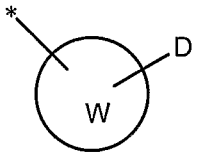
[00104] In certain embodiments, M is a covalent bond. In certain embodiments, M is –CH=CH–.

[00105] In certain embodiments, R_{12}, R_{13}, R_{14}, and R_{15} are each independently chosen from hydrogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl, and phenyl. In some embodiments, R_{13}, R_{14}, and R_{15} are independently chosen from hydrogen and C_1-C_6 alkyl. In certain embodiments, R_{13} is chosen from hydrogen and C_1-C_6 alkyl.

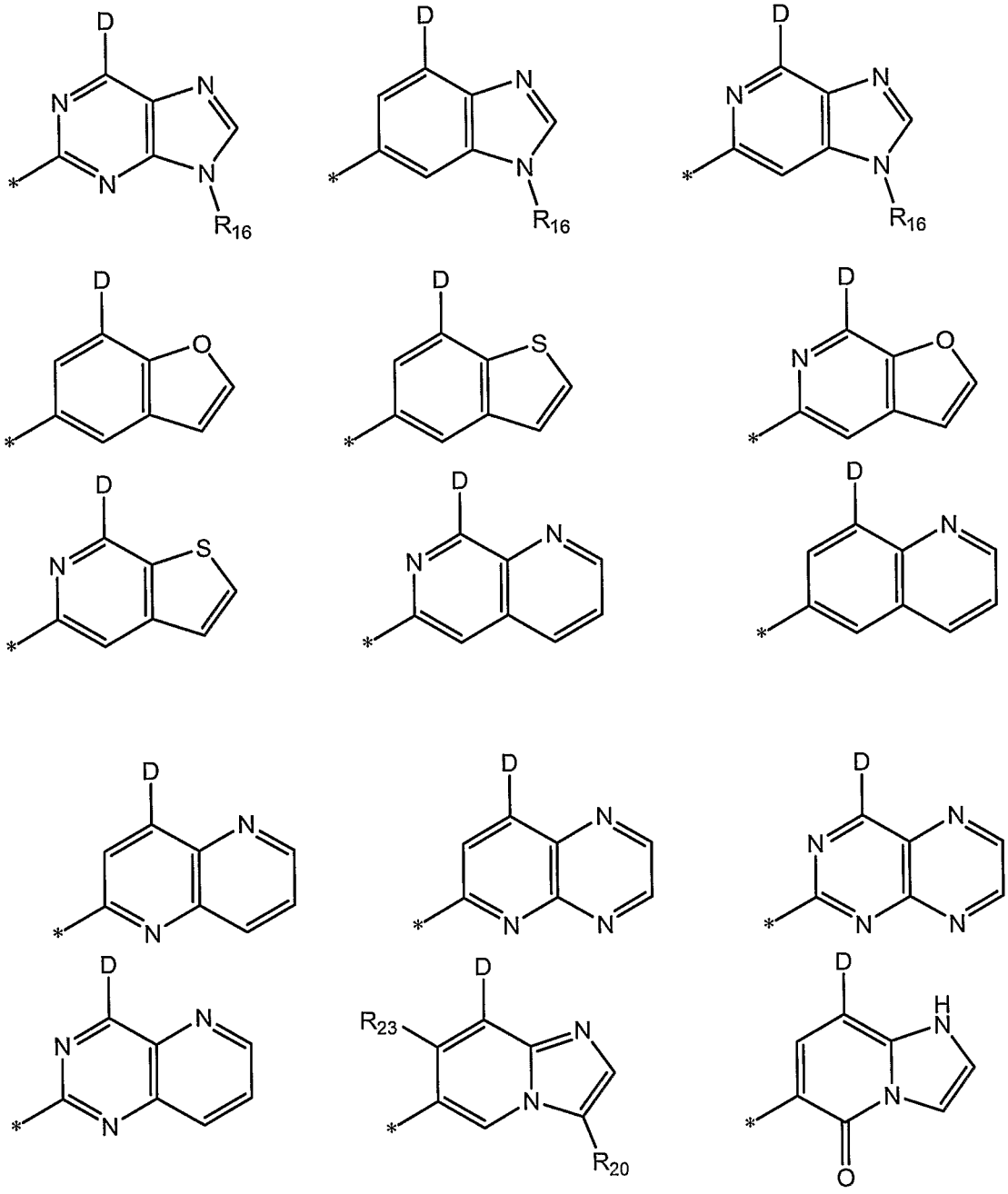
[00106] In certain embodiments, Z is chosen from ortho-phenylene, meta-phenylene, para-phenylene, ortho-pyridylidene, meta-pyridylidene, and para-pyridylidene, each of which is optionally substituted with a group chosen from

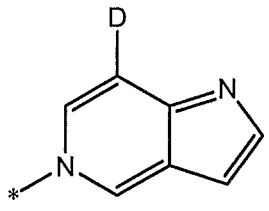
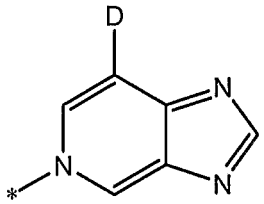
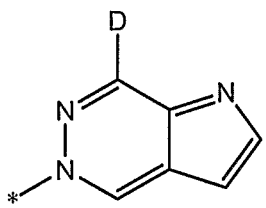
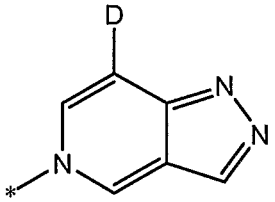
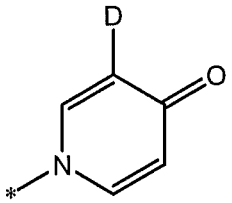
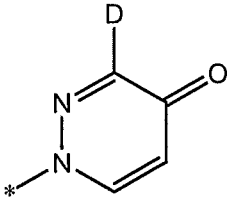
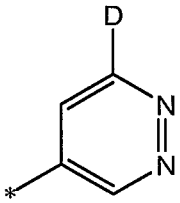
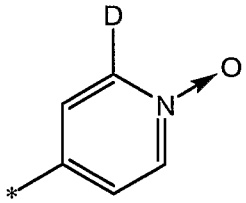
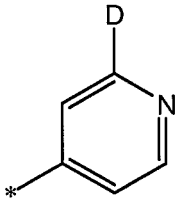
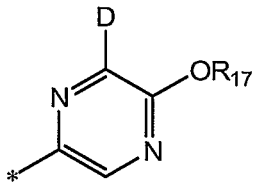
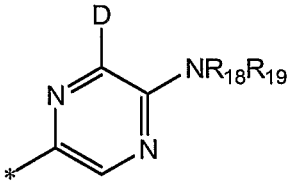
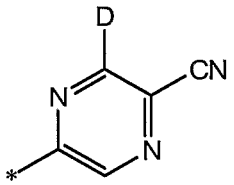
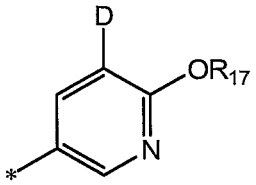
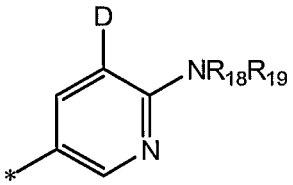
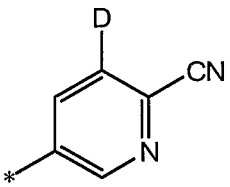
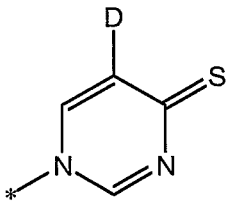
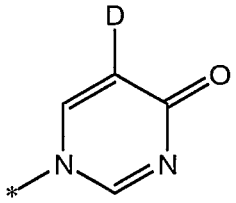
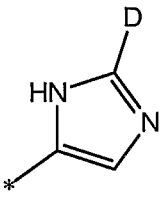
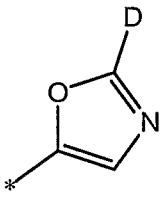
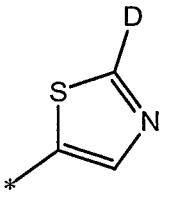
optionally substituted lower alkyl, optionally substituted lower alkoxy, halo, and hydroxy. In certain embodiments, Z is chosen from meta-phenylene and meta-phenylene substituted with a group chosen from optionally substituted lower alkyl, optionally substituted lower alkoxy, halo, and hydroxy. In certain embodiments, Z is chosen from meta-phenylene and meta-phenylene substituted with a group chosen from lower alkyl and halo. In certain embodiments, Z is chosen from meta-phenylene and meta-phenylene substituted with a group chosen from methyl and halo.

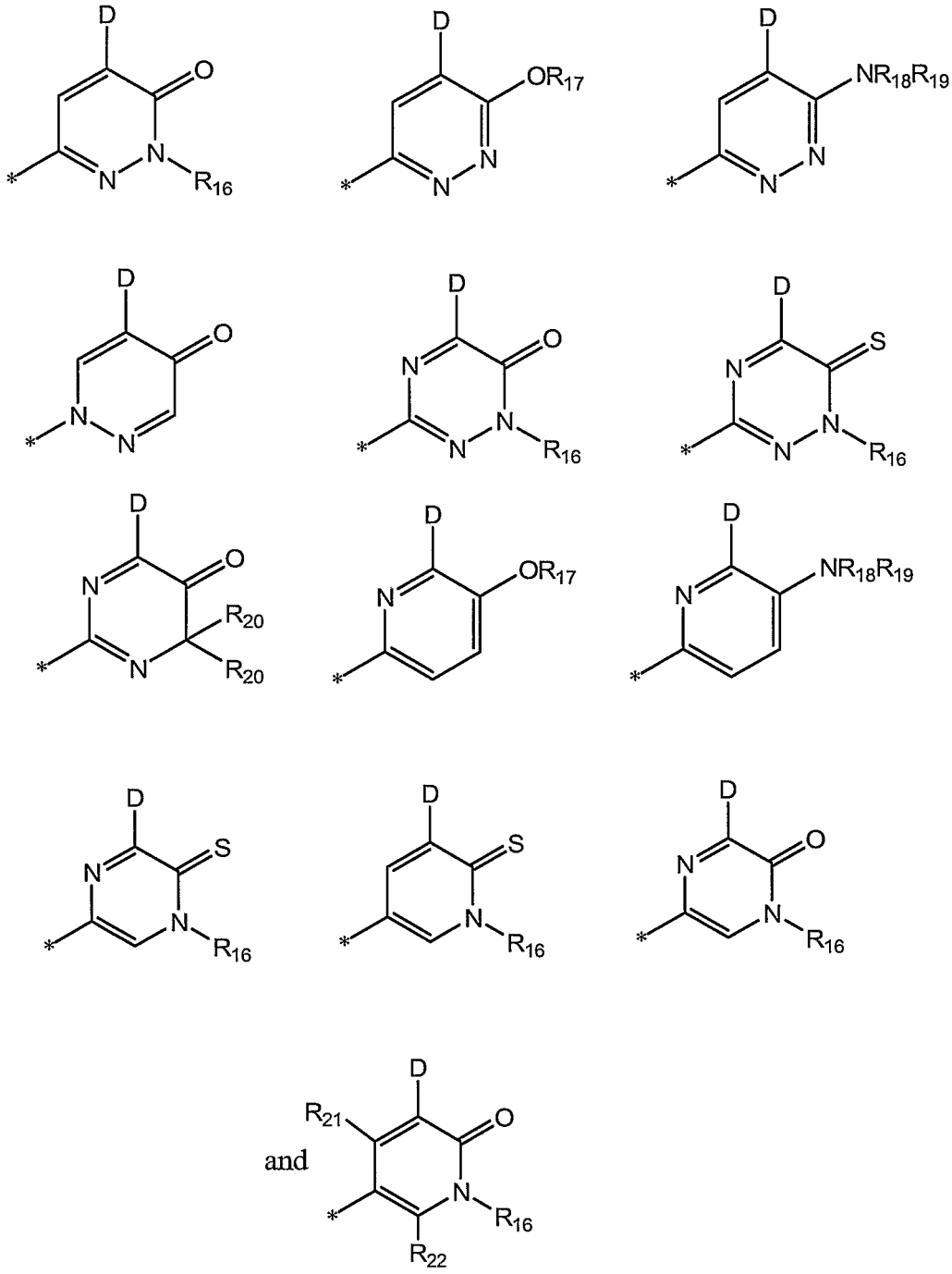
[00107] In certain embodiments, W is an optionally substituted heteroaryl group that further comprises a hydrogen bond acceptor.

[00108] In certain embodiments, 

is chosen from





each of which is optionally substituted with one or two groups chosen from hydroxy, cyano, halo, optionally substituted lower alkyl, and optionally substituted lower alkoxy and wherein

R_{16} is chosen from is chosen from hydrogen, cyano, optionally substituted cycloalkyl, and optionally substituted lower alkyl;

R_{17}, R_{18}, R_{19}, R_{21}, R_{22}, and R_{23} are independently chosen from hydrogen and optionally substituted lower alkyl; and

R_{20} is chosen from hydrogen, hydroxy, cyano, halo, optionally substituted lower alkyl, and optionally substituted lower alkoxy.

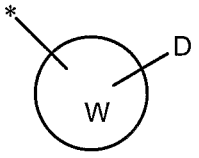
[00109] In certain embodiments, R_{17}, R_{18}, R_{19}, R_{21}, and R_{22} are independently chosen from hydrogen and lower alkyl.

[00110] In some embodiments, R_{16} is chosen from hydrogen, lower alkyl, and lower alkyl substituted with a group chosen from optionally substituted alkoxy, optionally substituted amino, and optionally substituted acyl. In some embodiments, R_{16} is chosen from hydrogen and lower alkyl. In some embodiments, R_{16} is chosen from hydrogen, methyl, and ethyl. In some embodiments, R_{16} is chosen from methyl and ethyl.

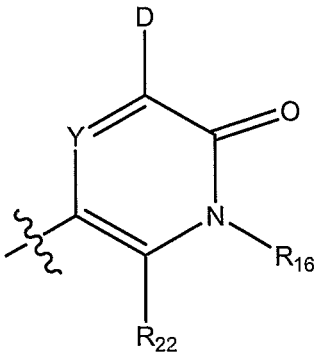
[00111] In certain embodiments, R_{21} is chosen from hydrogen and lower alkyl. In certain embodiments, R_{21} is chosen from hydrogen and methyl. In certain embodiments, R_{21} is hydrogen.

[00112] In certain embodiments, R_{22} is chosen from hydrogen and lower alkyl. In certain embodiments, R_{22} is chosen from hydrogen and methyl. In certain embodiments, R_{22} is hydrogen.

[00113] In certain embodiments, R_{20} is hydrogen.

[00114] In certain embodiments, 

comprises



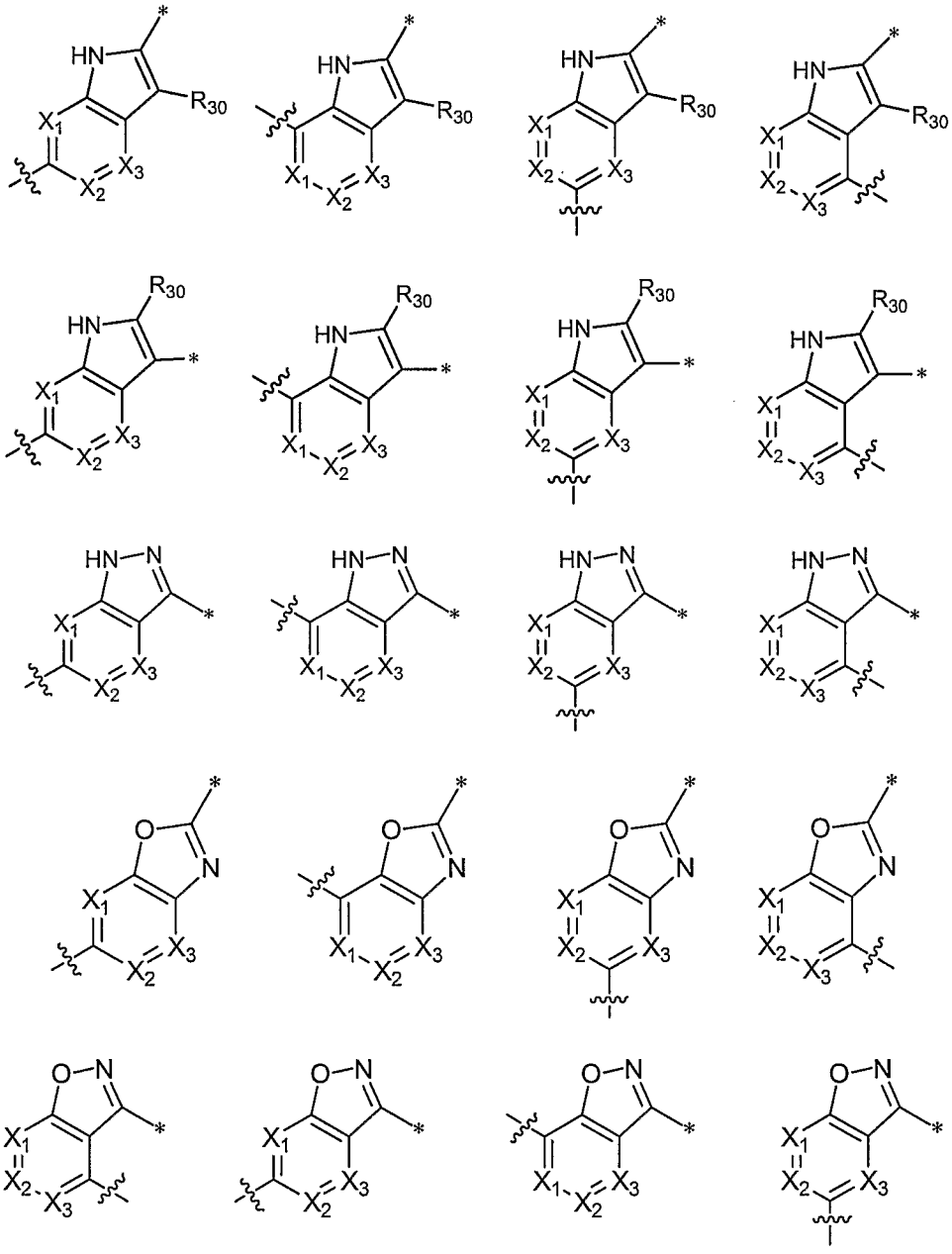
wherein Y is chosen from N and CR_{21}; and

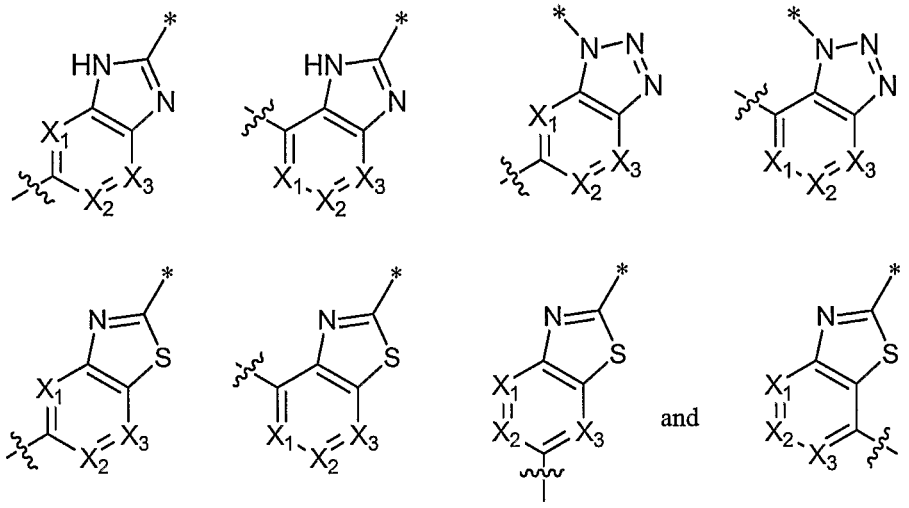
R_{16}, R_{21}, and R_{22} are independently chosen from hydrogen and optionally substituted lower alkyl.

[00115] In certain embodiments, D is $-NHR_9$ wherein R_9 is chosen from optionally substituted aryl and optionally substituted heteroaryl.

[00116] In certain embodiments, D is –N(H)-B-L-G wherein

B is chosen from optionally substituted phenylene, optionally substituted pyridylidene, optionally substituted 2-oxo-1,2-dihydropyridinyl,





wherein

* indicates the point of attachment to the group –L-G and the broken bond  indicates the point of attachment to the amino group;

X_1 is chosen from N and CR_{31};

X_2 is chosen from N and CR_{31}; and

X_3 is chosen from N and CR_{31}; and wherein no more than one of X_1, X_2, and X_3 is N,

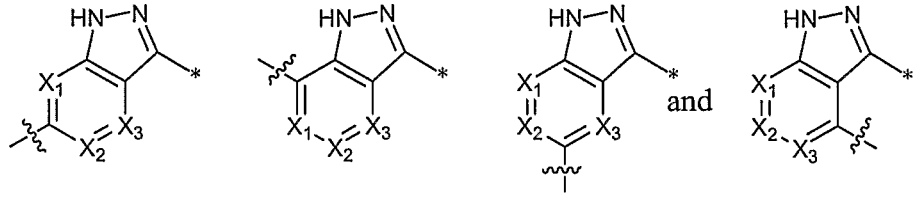
R_{30} is chosen from hydrogen, hydroxy, cyano, halo, optionally substituted lower alkyl, and optionally substituted lower alkoxy;

R_{31} is chosen from hydrogen, hydroxy, cyano, halo, optionally substituted lower alkyl, and optionally substituted lower alkoxy;

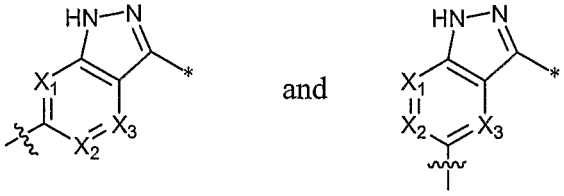
L is chosen from optionally substituted C_0-C_4alkylene, -O-optionally substituted C_0-C_4alkylene, -(C_0-C_4alkylene)(SO)-, -(C_0-C_4alkylene)(SO_2)-; and -(C_0-C_4alkylene)(C=O)-; and

G is chosen from hydrogen, halo, hydroxy, alkoxy, nitro, optionally substituted alkyl, optionally substituted amino, optionally substituted carbamimidoyl, optionally substituted heterocycloalkyl, optionally substituted cycloalkyl, optionally substituted aryl, and optionally substituted heteroaryl.

[00117] In certain embodiments, B is chosen from ortho-phenylene, meta-phenylene, para-phenylene, ortho-pyridylidene, meta-pyridylidene, para-pyridylidene,



[00118] In certain embodiments, B is chosen from para-phenylene and meta-phenylene. In certain embodiments, B is meta-phenylene.

[00119] In certain embodiments, B is chosen from .

[00120] In certain embodiments, L is chosen from optionally substituted C_0-C_4alkylene, -O-optionally substituted C_0-C_4alkylene, -(C_0-C_4alkylene)(SO_2)-; and -(C_0-C_4alkylene)(C=O)-. In certain embodiments, L is chosen from a covalent bond, -(C=O)-, -CH_2-, -CH_2(C=O)-, -SO_2- and -$CH(CH_3)$(C=O)-. In some embodiments, L is chosen from -(C=O)-, -CH_2-, -CH_2(C=O)-, -SO_2- and -$CH(CH_3)$(C=O)-.

[00121] In certain embodiments, G is chosen from hydrogen, hydroxy, C_1-C_6alkoxy, optionally substituted amino, optionally substituted C_3-C_7heterocycloalkyl, optionally substituted C_3-C_7cycloalkyl, optionally substituted aryl, and optionally substituted heteroaryl.

[00122] In certain embodiments, G is chosen from

hydrogen,

hydroxy,

-NR_7R_8 wherein R_7 and R_8 are independently chosen from hydrogen, optionally substituted acyl, and optionally substituted (C_1-C_6)alkyl; or wherein R_7 and R_8, together with the nitrogen to which they are bound, form an optionally substituted 5- to 7-membered nitrogen containing heterocycloalkyl which optionally further includes one or two additional heteroatoms chosen from N, O, and S;

optionally substituted 5,6-dihydro-8H-imidazo[1,2-a]pyrazin-7-yl,

lower alkoxy, and

1H-tetrazol-5-yl.

[00123] In certain embodiments, G is chosen from

hydrogen,

hydroxy,

N-methylethanolamino,

optionally substituted morpholin-4-yl,

optionally substituted piperazin-1-yl, and

optionally substituted homopiperazin-1-yl.

[00124] In certain embodiments, G is chosen from

hydrogen,

morpholin-4-yl,

4-acyl-piperazin-1-yl,

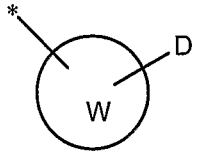
4-lower alkyl-piperazin-1-yl,

3-oxo-piperazin-1-yl,

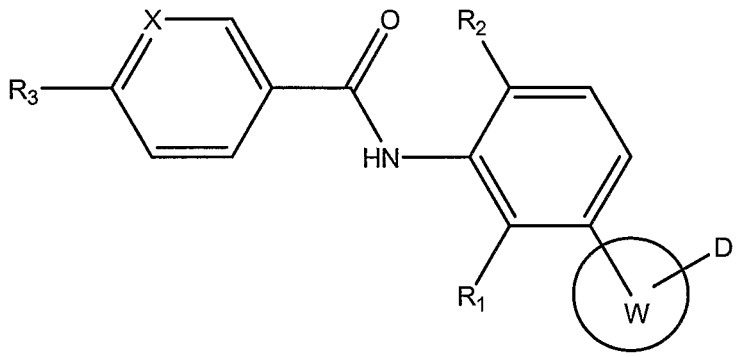
homopiperazin-1-yl, and

4-lower alkyl-homopiperazin-1-yl.

[00125] In certain embodiments, L is a covalent bond and G is hydrogen.

[00126] Also provided is at least one chemical entity wherein the radical of Formula I is attached to the 

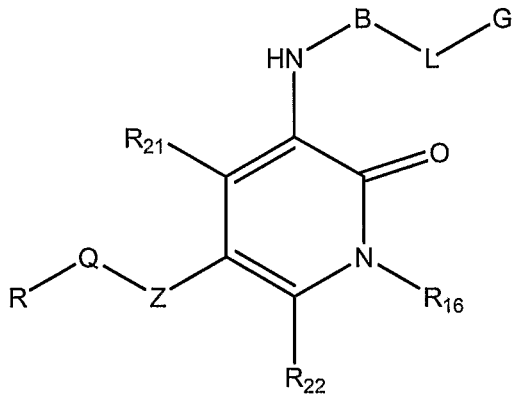
radical found in Formula 2. Accordingly, also provided is at least one chemical entity chosen from compounds of Formula 3:



(Formula 3)

and pharmaceutically acceptable salts, solvates, chelates, non-covalent complexes, prodrugs, and mixtures thereof, wherein W and D are as described for compounds of Formula 2 and wherein R_1, R_2, R_3, and X are as described for radicals of Formula 1.

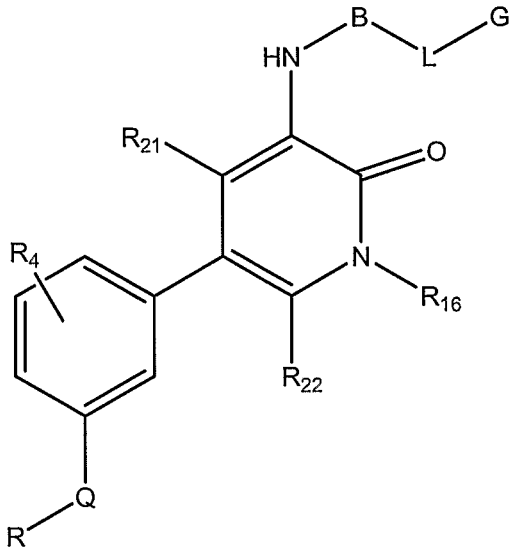
[00127] Also provided is at least one chemical entity chosen from compounds of Formula 4:



(Formula 4)

and pharmaceutically acceptable salts, solvates, chelates, non-covalent complexes, prodrugs, and mixtures thereof, wherein R, Q, Z, B, L, G, R_{16}, R_{21}, and R_{22} are as described above.

[00128] Also provided is at least one chemical entity chosen from compounds of Formula 6:



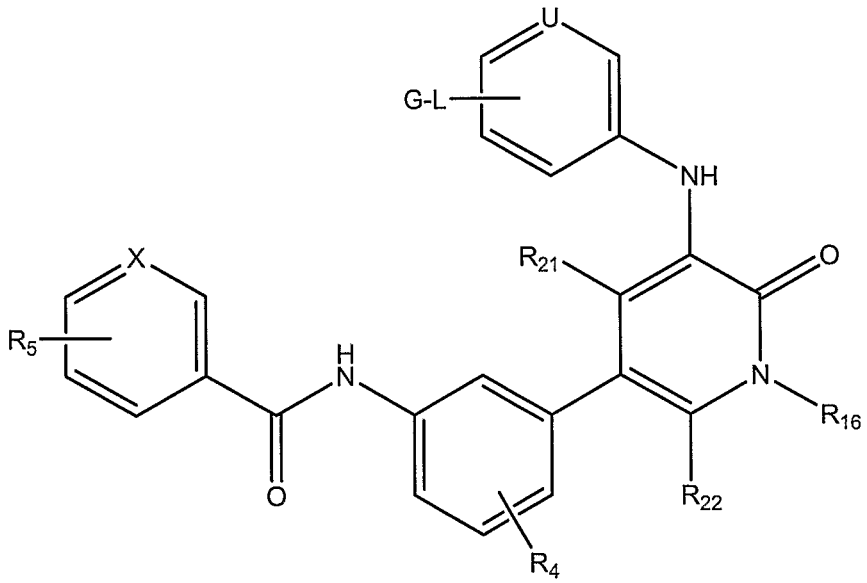
(Formula 6)

and pharmaceutically acceptable salts, solvates, chelates, non-covalent complexes, prodrugs, and mixtures thereof, wherein R, Q, R_{21}, R_{22}, R_{16}, B, L, and G are as described above, and wherein

R_4 is chosen from hydrogen, optionally substituted lower alkyl, optionally substituted lower alkoxy, cyano, halo, and hydroxy.

[00129] In certain embodiments, R_4 is chosen from hydrogen, optionally substituted lower alkyl, optionally substituted lower alkoxy, cyano, halo, and hydroxy. In somer embodiments, R_4 is chosen from hydrogen, optionally substituted lower alkyl (such as lower alkyl substituted with one or more halo), optionally substituted lower alkoxy (such as lower alkoxy substituted with one or more halo), halo, and hydroxy. In some embodiments, R_4 is chosen from methyl, trifluoromethyl, difluoromethyl, methoxy, trifluoromethoxy, difluoromethoxy, and fluoro. In some embodiments, R_4 is methyl.

[00130] Also provided is at least one chemical entity chosen from compounds of Formula 8:



(Formula 8)

and pharmaceutically acceptable salts, solvates, chelates, non-covalent complexes, prodrugs, and mixtures thereof, wherein R_4, R_{16}, R_{21}, R_{22}, L, and G are as described above; and wherein

X is chosen from N and CH;

U is chosen from N and CR_{41};

R_{41} is chosen from hydrogen, halo, optionally substituted lower alkyl, optionally substituted lower alkoxy, hydroxy, nitro, cyano, sulfhydryl, sulfanyl, sulfinyl, sulfonyl, carboxy, aminocarbonyl, and optionally substituted amino; and

R_5 is chosen from hydrogen, halo, hydroxy, lower alkyl, sulfonyl, optionally substituted amino, lower alkoxy, lower alkyl substituted with one or more halo, cycloalkyl, lower alkoxy substituted with one or more halo, lower alkyl substituted with hydroxy, optionally substituted heterocycloalkyl, and optionally substituted heteroaryl.

[00131] In certain embodiments X is N. In certain embodiments, X is CH.

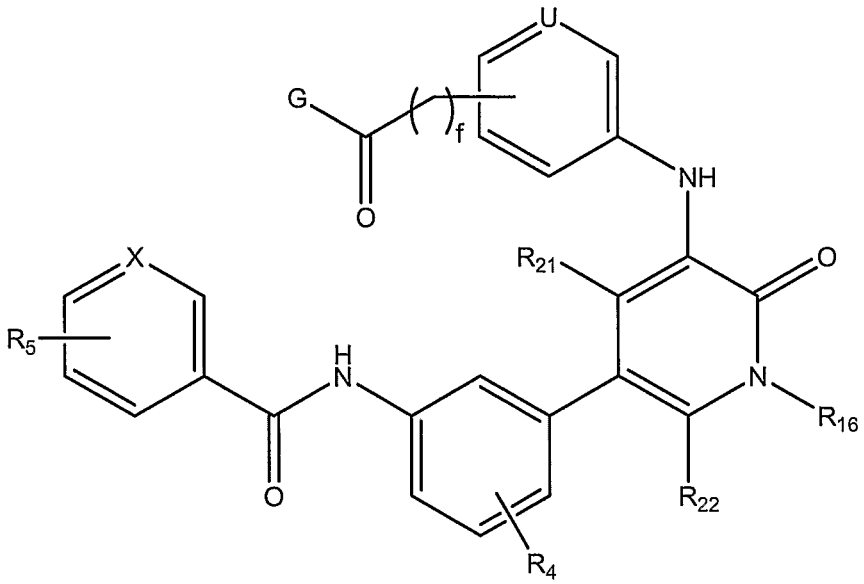
[00132] In certain embodiments, U is N. In certain embodiments, U is CR_{41}.

[00133] In certain embodiments, R_{41} is chosen from hydrogen, halo, lower alkyl, lower alkoxy, hydroxy, nitro, and amino. In certain embodiments, R_{41} is hydrogen.

[00134] In some embodiments, R_5 is chosen from hydrogen, hydroxy, lower alkyl, sulfonyl, optionally substituted amino, lower alkoxy, lower alkyl substituted with one or more halo, lower alkoxy substituted with one or more halo, lower alkyl substituted with hydroxy, optionally substituted heterocycloalkyl, and optionally substituted heteroaryl. In some embodiments, R_5 is chosen from hydrogen, optionally substituted piperidinyl, and lower alkyl. In some embodiments, R_5 is chosen from hydrogen, optionally substituted piperidinyl, *iso*-propyl, and *tert*-butyl. In some embodiments, R_5 is *tert*-butyl. In some embodiments, R_5 is *iso*-propyl. In some embodiments, R_5 is piperidinyl substituted with one or two groups independently chosen from amino, hydroxy, optionally substituted lower alkyl, optionally substituted lower alkoxy, and carbamoyl. In some embodiments, R_5 is piperidinyl substituted with one or two groups independently chosen from amino, hydroxy, methyl, ethyl, methoxy, hydroxymethyl, methoxymethoxy, and carbamoyl. In some embodiments, R_5 is piperidin-1-yl substituted with one or two groups independently chosen from amino, hydroxy, methyl, ethyl, methoxy, hydroxymethyl, methoxymethoxy, and carbamoyl. .

[00135] Also provided is at least one chemical entity chosen from compounds

of Formula 10:



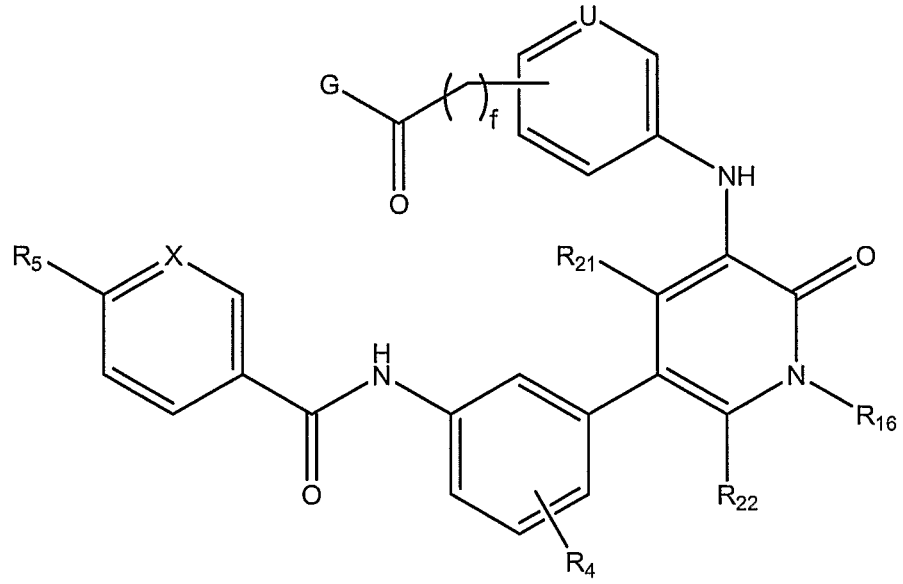
(Formula 10)

and pharmaceutically acceptable salts, solvates, chelates, non-covalent complexes, prodrugs, and mixtures thereof, wherein R_5, X, R_4, R_{22}, R_{16}, R_{21}, U, and G are as described above; and wherein

f is chosen from 0, 1 and 2.

[00136] In certain embodiments, f is 0. In certain embodiments, f is 1. In certain embodiments, f is 2. In certain embodiments, the group G-C(O)-$(CH_2)_f$- is attached to the 3 position of the ring. In certain embodiments, the group G-C(O)-$(CH_2)_f$- is attached to the 4 position of the ring.

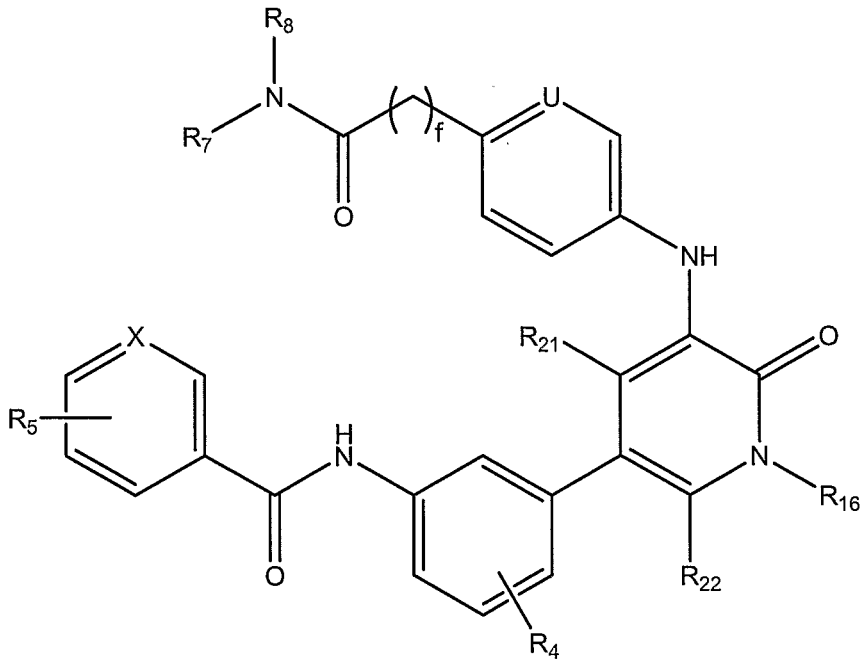
[00137] Also provided is at least one chemical entity chosen from compounds of Formula 11:



(Formula 11)

and pharmaceutically acceptable salts, solvates, chelates, non-covalent complexes, prodrugs, and mixtures thereof, wherein R_5, X, R_4, R_{16}, R_{21}, R_{22}, Y, f, U, and G are as described above.

[00138] Also provided is at least one chemical entity chosen from compounds of Formula 14:



(Formula 14)

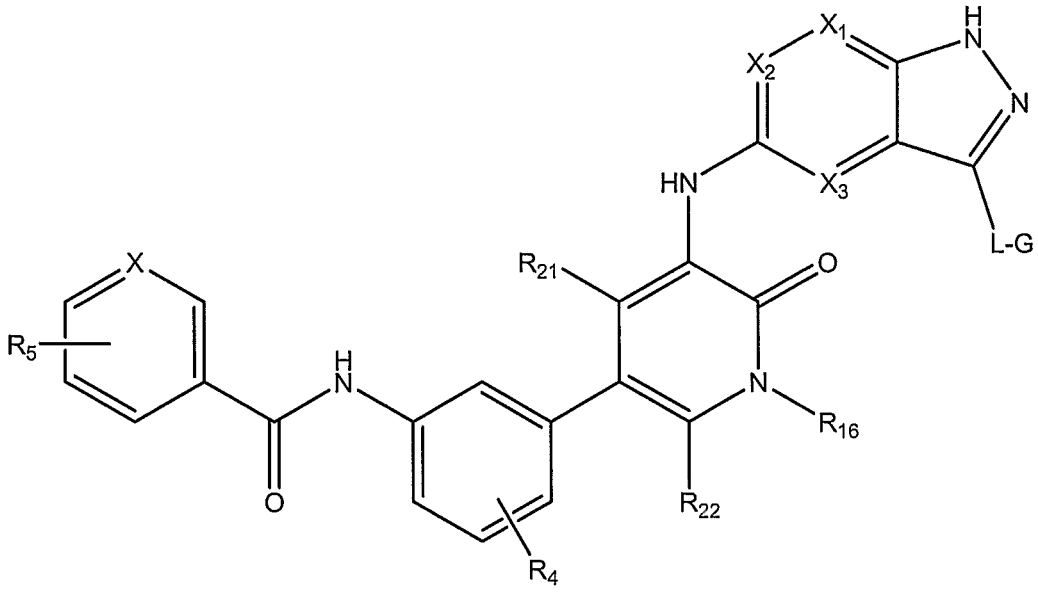
and pharmaceutically acceptable salts, solvates, chelates, non-covalent complexes, prodrugs, and mixtures thereof, wherein R_5, X, R_4, R_{16}, R_{21}, R_{22}, U, f, and G are as described above, and wherein

R_7 and R_8 are independently chosen from hydrogen and optionally substituted (C_1-C_6)alkyl; or R_7 and R_8, together with the nitrogen to which they are bound, form an optionally substituted 5- to 7-membered nitrogen-containing heterocycloalkyl which optionally further includes one or two additional heteroatoms chosen from N, O, and S.

[00139] In certain embodiments, R_7 and R_8, together with the nitrogen to which they are bound, form a 5- to 7-membered nitrogen-containing heterocycloalkyl chosen from optionally substituted morpholin-4-yl and optionally substituted piperazin-1-yl ring.

[00140] In certain embodiments, R_7 and R_8, together with the nitrogen to which they are bound, form a 5- to 7-membered nitrogen-containing heterocycloalkyl chosen from morpholin-4-yl, 4-acyl-piperazin-1-yl, and 4-lower alkyl-piperazin-1-yl.

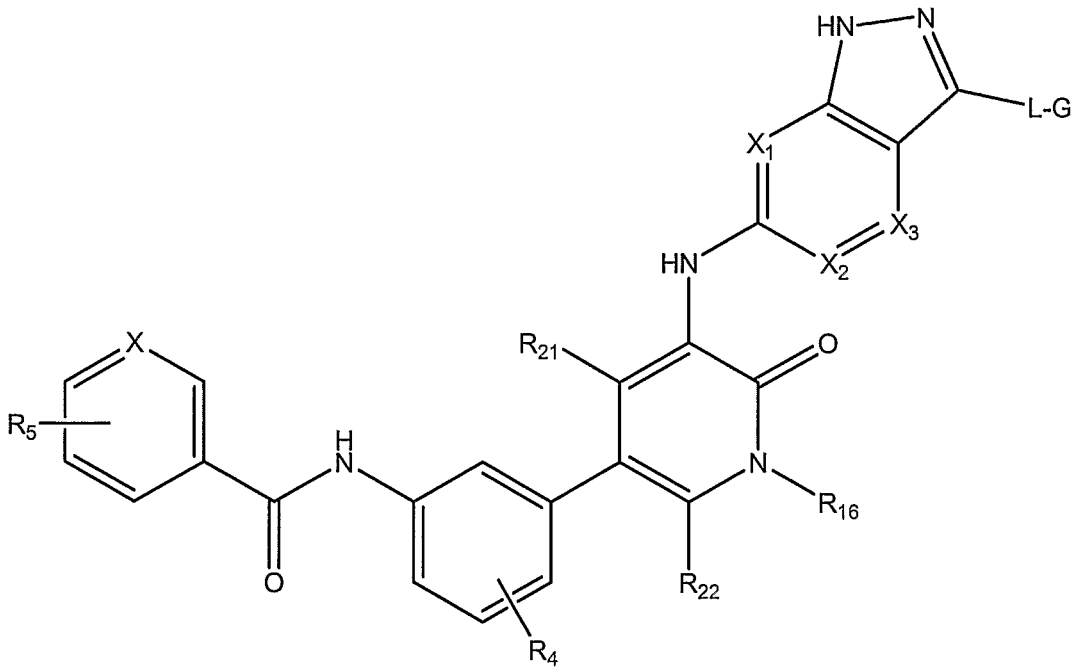
[00141] Also provided is at least one chemical entity chosen from compounds of Formula 16:



(Formula 16)

and pharmaceutically acceptable salts, solvates, chelates, non-covalent complexes, prodrugs, and mixtures thereof, wherein R_5, X, R_4, R_{16}, R_{21}, R_{22}, X_1, X_2, X_3, L, and G are as described above.

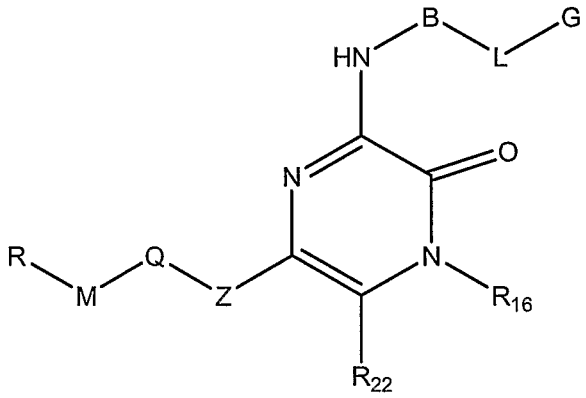
[00142] Also provided is at least one chemical entity chosen from compounds of Formula 18:



(Formula 18)

and pharmaceutically acceptable salts, solvates, chelates, non-covalent complexes, prodrugs, and mixtures thereof, wherein R_5, X, R_4, R_{16}, R_{21}, R_{22}, X_1, X_2, X_3, L, and G are as described above.

[00143] Also provided is at least one chemical entity chosen from compounds of Formula 5:

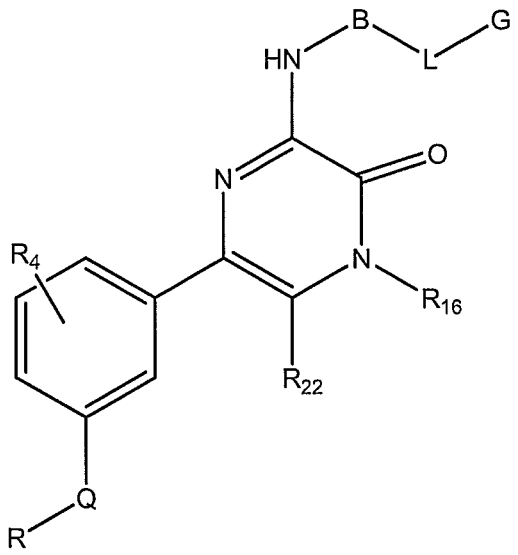


(Formula 5)

and pharmaceutically acceptable salts, solvates, chelates, non-covalent complexes, prodrugs, and mixtures thereof, wherein M, R, Q, Z, R_{16}, R_{22}, B, L, and G are as

described above.

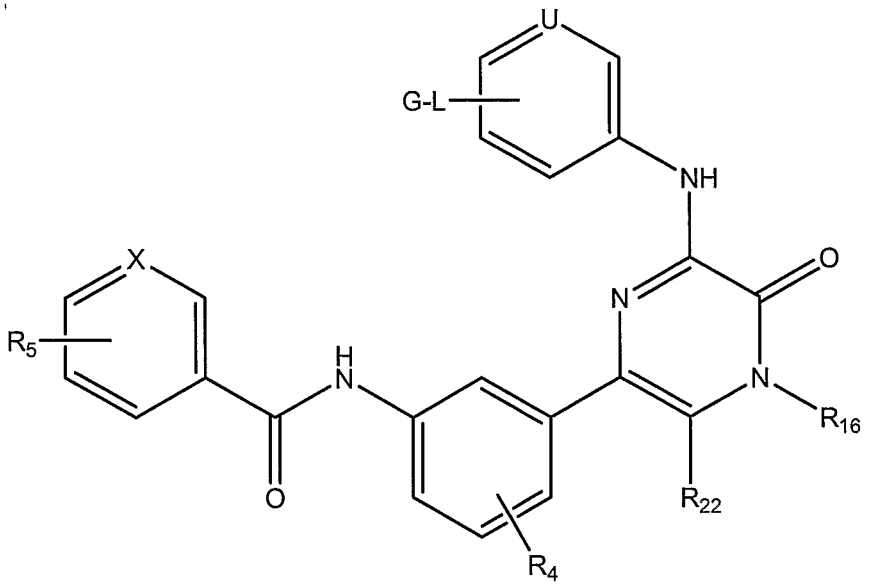
[00144] Also provided is at least one chemical entity chosen from compounds of Formula 7:



(Formula 7)

and pharmaceutically acceptable salts, solvates, chelates, non-covalent complexes, prodrugs, and mixtures thereof, wherein R, Q, R_4, R_{16}, R_{22}, B, L, and G are as described above.

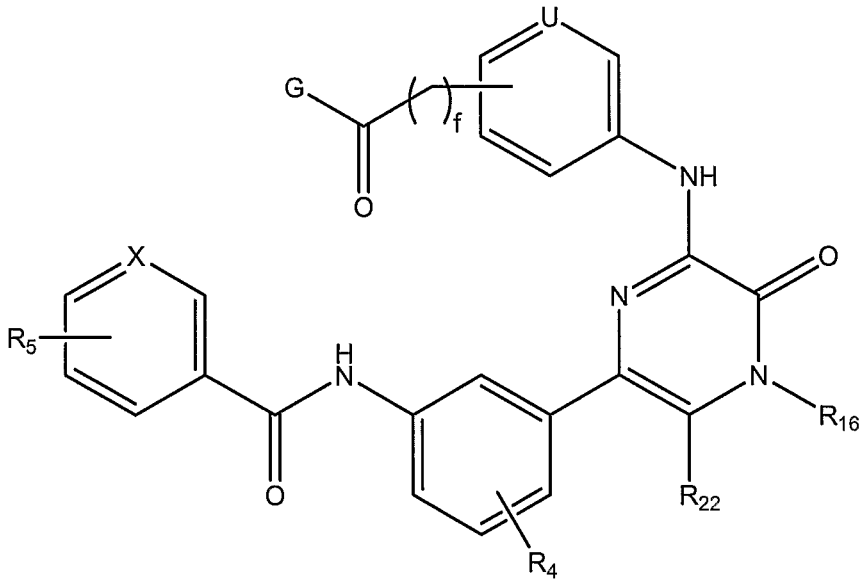
[00145] Also provided is at least one chemical entity chosen from compounds of Formula 9:



(Formula 9)

and pharmaceutically acceptable salts, solvates, chelates, non-covalent complexes, prodrugs, and mixtures thereof, wherein R_5, X, R_4, R_{16}, R_{22}, U, L, and G are as described above.

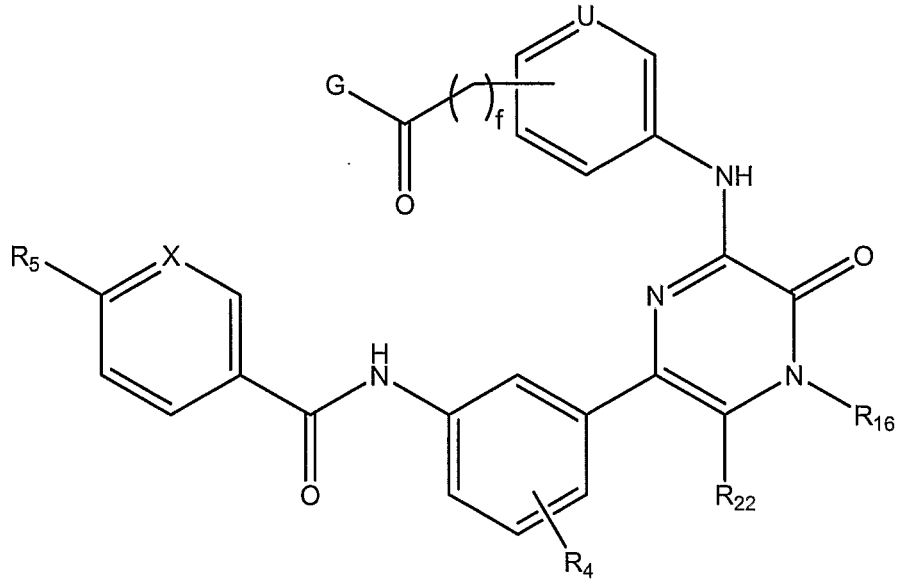
[00146] Also provided is at least one chemical entity chosen from compounds of Formula 12:



(Formula 12)

and pharmaceutically acceptable salts, solvates, chelates, non-covalent complexes, prodrugs, and mixtures thereof, wherein R_5, X, R_4, R_{16}, R_{22}, U, f, and G are as described above.

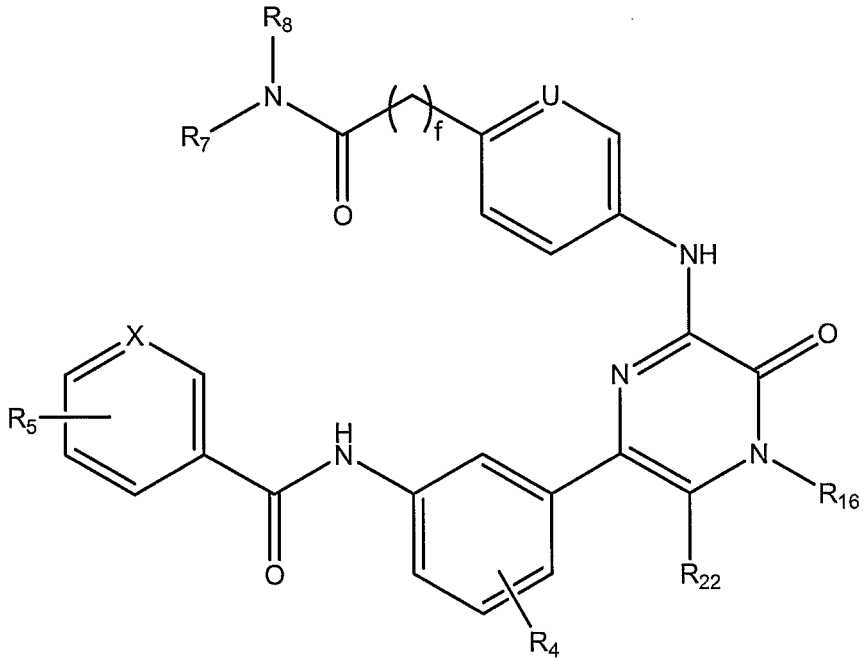
[00147] Also provided is at least one chemical entity chosen from compounds of Formula 13:



(Formula 13)

and pharmaceutically acceptable salts, solvates, chelates, non-covalent complexes, prodrugs, and mixtures thereof, wherein R_5, X, R_4, R_{16}, R_{22}, U, f, R_7, and R_8 are as described above.

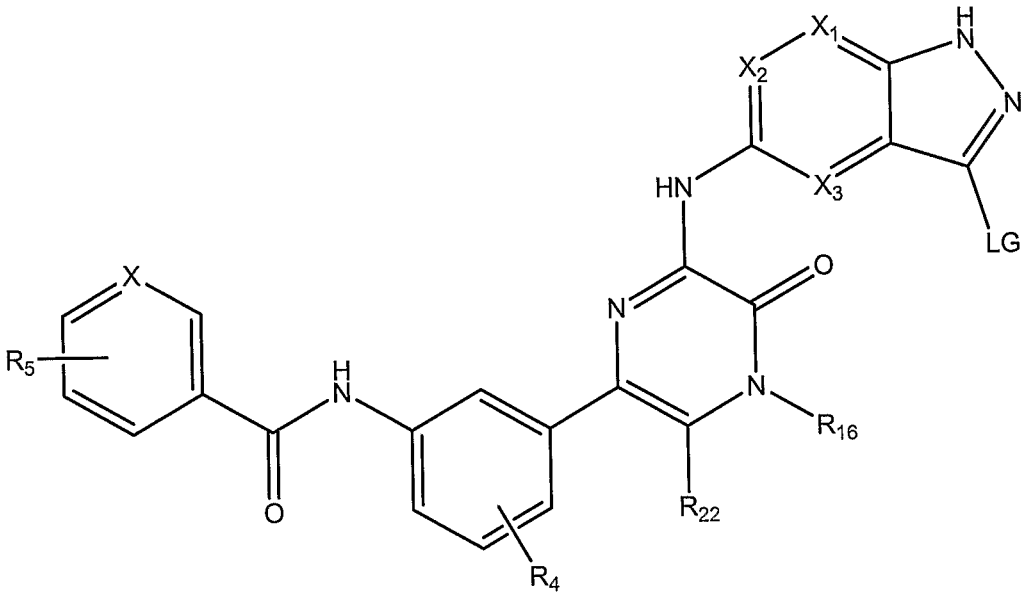
[00148] Also provided is at least one chemical entity chosen from compounds of Formula 15:



(Formula 15)

and pharmaceutically acceptable salts, solvates, chelates, non-covalent complexes, prodrugs, and mixtures thereof, wherein R_5, X, R_4, R_{16}, R_{22}, f, U, and G are as described above.

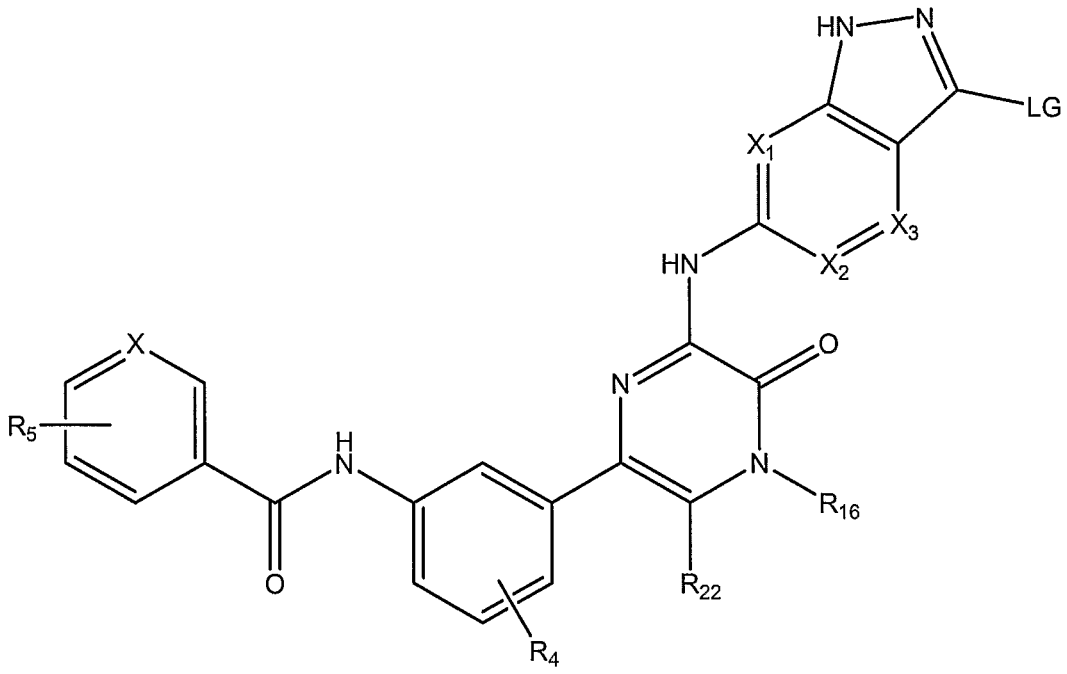
[00149] Also provided is at least one chemical entity chosen from compounds of Formula 17:



(Formula 17)

and pharmaceutically acceptable salts, solvates, chelates, non-covalent complexes, prodrugs, and mixtures thereof, wherein R_5, X, R_4, R_{16}, R_{22}, X_1, X_2, X_3, L, and G are as described above.

[00150] Also provided is at least one chemical entity chosen from compounds of Formula 19:



(Formula 19)

and pharmaceutically acceptable salts, solvates, chelates, non-covalent complexes, prodrugs, and mixtures thereof, wherein R_5, X, R_4, R_{16}, R_{22}, X_1, X_2, X_3, L, and G are as described above.

[00151] Also provided is at least one chemical entity chosen from

4-tert-Butyl-N-(2-methyl-3-{1-methyl-5-[4-(morpholine-4-carbonyl)-phenylamino]-6-oxo-1,6-dihydro-pyridin-3-yl}-phenyl)-benzamide;

4-{5-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-1-methyl-2-oxo-1,2-dihydro-pyridin-3-ylamino}-benzoic acid;

4-tert-Butyl-N-(2-methyl-3-{1-methyl-5-[4-(4-methyl-piperazine-1-carbonyl)-phenylamino]-6-oxo-1,6-dihydro-pyridin-3-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(2-methyl-3-{1-methyl-5-[4-(N-methylethanolamine-2-carbonyl)-phenylamino]-6-oxo-1,6-dihydro-pyrazin-3-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(2-methyl-3-{1-methyl-5-[4-([1,4]oxazepane-4-carbonyl)-phenylamino]-6-oxo-1,6-dihydro-pyridin-3-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(3-{5-[4-(4-hydroxy-piperidine-1-carbonyl)-phenylamino]-1-methyl-6-oxo-1,6-dihydro-pyridin-3-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-(2-methyl-3-{1-methyl-5-[4-(morpholine-4-carbonyl)-phenylamino]-6-oxo-1,6-dihydro-pyridin-3-yl}-phenyl)-benzamide;

4-{5-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-1-methyl-2-oxo-1,2-dihydro-pyridin-3-ylamino}-benzoic acid;

4-tert-Butyl-N-(2-methyl-3-{1-methyl-5-[4-(4-methyl-piperazine-1-carbonyl)-phenylamino]-6-oxo-1,6-dihydro-pyridin-3-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(2-methyl-3-{1-methyl-5-[4-(N-methylethanolamine-2-carbonyl)-phenylamino]-6-oxo-1,6-dihydro-pyrazin-3-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(2-methyl-3-{1-methyl-5-[4-([1,4]oxazepane-4-carbonyl)-phenylamino]-6-oxo-1,6-dihydro-pyridin-3-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(3-{5-[4-(4-hydroxy-piperidine-1-carbonyl)-phenylamino]-1-methyl-6-oxo-1,6-dihydro-pyridin-3-yl}-2-methyl-phenyl)-benzamide;

4-{6-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-benzoic acid;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-{6-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-benzoic acid ethyl ester;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[4-(4-methyl-piperazine-1-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[4-(4-methyl-[1,4]diazepane-1-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(3-{4-methyl-6-[4-(2-hydroxyethyl-methyl-carbamoyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-{6-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-benzamide;

4-{6-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-4-ethyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-benzoic acid;

4-tert-Butyl-N-(3-{4-ethyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-(3-{4-ethyl-6-[4-(4-methyl-piperazine-1-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-(2-methyl-3-{4-ethyl-6-[4-(N-methylethanolamine-2-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(3-{4-ethyl-6-[4-(methyl-carbamoyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-{3-[6-(4-fluoro-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide;

4-{6-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-4,5-dimethyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-benzoic acid;

4-{6-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-2-fluoro-benzoic acid;

4-tert-Butyl-N-(3-{3,4-dimethyl-6-[4-(methyl-carbamoyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-(3-{3,4-dimethyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-(3-{3,4-dimethyl-6-[4-(4-methyl-piperazine-1-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-(3-{3,4-dimethyl-6-[4-(2-hydroxyethyl-methyl-carbamoyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-{3-[6-(1H-indazol-6-ylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide;

4-tert-Butyl-N-{3-[6-(1H-indazol-5-ylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide;

4-tert-Butyl-N-(2-fluoro-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(2-fluoro-3-{4-methyl-6-[4-(4-methyl-piperazine-1-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(3-{6-[3-fluoro-4-(morpholine-4-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-(2-fluoro-3-{6-[4-(1H-imidazol-2-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-{3-[6-(4-methanesulfonylaminocarbonyl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide;

4-tert-Butyl-N-(3-{4-methyl-6-[4-(3-aminopropyl-carbamoyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-(3-{6-[4-(1H-imidazol-2-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-5-oxo-6-[4-(thiomorpholine-4-carbonyl)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-5-oxo-6-[4-(1-oxo-1l4-thiomorpholine-4-carbonyl)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(3-{6-[4-(1,1-dioxo-1l6-thiomorpholine-4-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-{2-methyl-3-[4-methyl-5-oxo-6-(4-sulfamoyl-phenylamino)-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide;

4-tert-Butyl-N-{2-fluoro-3-[4-methyl-5-oxo-6-(4-sulfamoyl-phenylamino)-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide;

4-tert-Butyl-N-(2-fluoro-3-{4-methyl-5-oxo-6-[4-(1H-tetrazol-5-yl)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-{6-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-benzoic acid;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-{6-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-benzoic acid ethyl ester;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[4-(4-methyl-piperazine-1-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[4-(4-methyl-[1,4]diazepane-1-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(3-{4-methyl-6-[4-(2-hydroxyethyl-methyl-carbamoyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-{6-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-benzamide;

4-{6-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-4-ethyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-benzoic acid;

4-tert-Butyl-N-(3-{4-ethyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-(3-{4-ethyl-6-[4-(4-methyl-piperazine-1-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-(2-methyl-3-{4-ethyl-6-[4-(N-methylethanolamine-2-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(3-{4-ethyl-6-[4-(methyl-carbamoyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-{3-[6-(4-fluoro-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide;

4-{6-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-4,5-dimethyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-benzoic acid;

4-{6-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-2-fluoro-benzoic acid;

4-tert-Butyl-N-(3-{3,4-dimethyl-6-[4-(methyl-carbamoyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-(3-{3,4-dimethyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-(3-{3,4-dimethyl-6-[4-(4-methyl-piperazine-1-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-(3-{3,4-dimethyl-6-[4-(2-hydroxyethyl-methyl-carbamoyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-{3-[6-(1H-indazol-6-ylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide;

4-tert-Butyl-N-{3-[6-(1H-indazol-5-ylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide;

4-tert-Butyl-N-(2-fluoro-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(2-fluoro-3-{4-methyl-6-[4-(4-methyl-piperazine-1-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(3-{6-[3-fluoro-4-(morpholine-4-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-(2-fluoro-3-{6-[4-(1H-imidazol-2-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(5-{6-[4-(1H-imidazol-2-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-{3-[6-(4-methanesulfonylaminocarbonyl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide;

4-tert-Butyl-N-(3-{4-methyl-6-[4-(3-aminopropyl-carbamoyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-(3-{6-[4-(1H-imidazol-2-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-5-oxo-6-[4-(thiomorpholine-4-carbonyl)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-5-oxo-6-[4-(1-oxo-1λ^4-thiomorpholine-4-carbonyl)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(3-{6-[4-(1,1-dioxo-1λ6-thiomorpholine-4-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-{2-methyl-3-[4-methyl-5-oxo-6-(4-sulfamoyl-phenylamino)-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide;

4-tert-Butyl-N-{2-fluoro-3-[4-methyl-5-oxo-6-(4-sulfamoyl-phenylamino)-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide;

4-tert-Butyl-N-{2-methyl-5-[4-methyl-5-oxo-6-(4-sulfamoyl-phenylamino)-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide;

4-tert-Butyl-N-(2-fluoro-3-{4-methyl-5-oxo-6-[4-(1H-tetrazol-5-yl)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-{6-[3-(4-tert-Butyl-benzoylamino)-phenyl]-4,5-dimethyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-benzoic acid;

3-{6-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-benzoic acid;

4-tert-Butyl-N-(3-{3,4-dimethyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[3-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(2-fluoro-3-{4-methyl-6-[4-(N,N-bis-(2-hydroxyethyl)aminocarbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[4-(N,N-bis-(2-hydroxyethyl)aminocarbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-5-oxo-6-[4-(1H-tetrazol-5-yl)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-{6-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-benzenesulfinic acid morpholin-4-yl ester;

N-{3-[6-(1H-Benzoimidazol-5-ylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-4-tert-butyl-benzamide;

4-tert-Butyl-N-{2-methyl-3-[4-methyl-6-(4-morpholin-4-ylmethyl-phenylamino)-5-oxo-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide;

4-tert-Butyl-N-(2-cyano-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-{3-[6-(6-hydroxy-pyridin-3-ylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide;

4-tert-Butyl-N-(3-{6-[4-(4-ethyl-piperazine-1-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-5-oxo-6-[4-(3-oxo-piperazine-1-carbonyl)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[4-(N-methyl –N-(cyanomethyl)amino carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(6-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-pyridin-2-yl)-benzamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[4-(N-(2-methoxyethyl)amino carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[4-(N-(2-dimethylaminoethyl)amino carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-{2-fluoro-3-[4-methyl-6-(4-morpholin-4-ylmethyl-phenylamino)-5-oxo-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide;

4-tert-Butyl-N-{2-methyl-3-[4-methyl-6-(4-oxazol-2-yl-phenylamino)-5-oxo-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide;

4-tert-Butyl-N-{2-fluoro-3-[4-methyl-6-(4-oxazol-2-yl-phenylamino)-5-oxo-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide;

4-tert-Butyl-N-{3-[6-(4-imidazol-1-yl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide;

4-tert-Butyl-N-{2-fluoro-3-[6-(4-imidazol-1-yl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide;

4-tert-Butyl-N-(2-fluoro-3-{4-methyl-6-[4-(N,N-bis-(2-methoxyethyl)aminocarbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

N-(3-{6-[4-(4-Acetyl-piperazine-1-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide;

N-(3-{6-[4-(4-Acetyl-piperazine-1-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-fluoro-phenyl)-4-tert-butyl-benzamide;

4-tert-Butyl-N-(2-fluoro-3-{4-methyl-5-oxo-6-[4-(thiomorpholine-4-carbonyl)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(2-fluoro-3-{6-[4-(4-hydroxy-piperidine-1-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-Bromo-N-(2-fluoro-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(2-fluoro-3-{4-methyl-5-oxo-6-[4-(1-oxo-1λ^4-thiomorpholine-4-carbonyl)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-(1-Hydroxy-1-methyl-ethyl)-N-(2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-{2-methyl-3-[4-methyl-5-oxo-6-(4-thiomorpholin-4-yl-phenylamino)-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide;

4-tert-Butyl-N-{3-[6-(4-imidazol-1-ylmethyl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide;

4-Bromo-N-(2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(2-fluoro-3-{4-methyl-6-[4-([1,4]oxazepane-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-{6-[3-(4-tert-Butyl-benzoylamino)-2-fluoro-phenyl]-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-benzoic acid;

4-tert-Butyl-N-(2-fluoro-3-{4-methyl-5-oxo-6-[4-(4-oxo-piperidine-1-carbonyl)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(2-fluoro-3-{6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(2-fluoro-3-{6-[4-(4-hydroxymethyl-piperidine-1-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(2-fluoro-3-{6-[4-(2-hydroxymethyl-morpholine-4-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-5-oxo-6-[4-(1-oxo-1λ^4-thiomorpholin-4-yl)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(2-fluoro-3-{4-methyl-6-[4-(N-(2,2-Dimethyl-[1,3]dioxolan-4-ylmethyl)aminocarbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

5-tert-Butyl-thiophene-2-carboxylic acid (2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-amide;

4-tert-Butyl-N-{2-fluoro-3-[4-methyl-6-(4-morpholin-4-yl-phenylamino)-5-oxo-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide;

4-tert-Butyl-N-(2-fluoro-3-{4-methyl-6-[4-(N-(2-(2-hydroxy-ethoxy)-ethyl)aminocarbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-{2-fluoro-3-[6-(4-imidazol-1-ylmethyl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide;

4-tert-Butyl-N-(3-{6-[4-(4-hydroxy-piperidine-1-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[4-([1,4]oxazepane-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(2-fluoro-3-{4-methyl-6-[4-(N-(2,3-dihydroxy-propyl)aminocarbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-{2-fluoro-3-[4-methyl-5-oxo-6-(4-thiomorpholin-4-ylmethyl-phenylamino)-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide;

4-tert-Butyl-N-(3-{6-[4-(4-hydroxymethyl-piperidine-1-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-(3-{6-[4-(2-hydroxymethyl-morpholine-4-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-(3-{6-[4-(1,1-dioxo-1λ6-thiomorpholin-4-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-{2-fluoro-3-[4-methyl-5-oxo-6-(4-thiomorpholin-4-yl-phenylamino)-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide;

4-tert-Butyl-cyclohexanecarboxylic acid (2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-amide;

4-tert-Butyl-N-(3-{4-ethyl-5-oxo-6-[4-(1-oxo-1λ^4-thiomorpholin-4-yl)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-Dimethylamino-N-(2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(2-fluoro-3-{4-methyl-5-oxo-6-[4-(1-oxo-1λ^4-thiomorpholin-4-yl)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-5-oxo-6-[4-(4-oxo-4H-pyridin-1-yl)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-Isopropyl-N-(2-methyl-3-{4-methyl-5-oxo-6-[4-(1-oxo-1λ^4-thiomorpholin-4-yl)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-(1-Hydroxy-1-methyl-ethyl)-N-(2-methyl-3-{4-methyl-5-oxo-6-[4-(1-oxo-1λ^4-thiomorpholin-4-yl)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-{2-fluoro-3-[4-methyl-5-oxo-6-(4-pyrrolidin-1-ylmethyl-phenylamino)-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide;

4-tert-Butyl-N-(3-{6-[4-(2-hydroxymethyl-morpholin-4-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-(2-fluoro-3-{4-methyl-5-oxo-6-[4-(1-oxo-1λ^4-thiomorpholin-4-ylmethyl)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(3-{6-[4-(1,1-dioxo-1λ6-thiomorpholin-4-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-(2-fluoro-3-{4-methyl-6-[4-N-(2-Methoxy-ethyl)-N-methylaminocarbonyl-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(2-fluoro-3-{6-[4-(4-methyl-piperazine-1-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(2-fluoro-3-{6-[4-(4-hydroxy-piperidine-1-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

6-tert-Butyl-N-(2-methyl-3-{4-methyl-5-oxo-6-[4-(1-oxo-1λ^4-thiomorpholin-4-yl)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-nicotinamide;

4-{6-[3-(4-tert-Butyl-benzoylamino)-2,4-difluoro-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-benzoic acid;

4-tert-Butyl-N-(2-fluoro-3-{6-[4-(4-methoxy-piperidin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[4-(N-methyl-N-ethylaminocarbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-5-oxo-6-[4-(pyrrolidine-1-carbonyl)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

N-(2-Methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-3-phenyl-acrylamide;

N-(2-Fluoro-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-3-(3-fluoro-phenyl)-acrylamide;

Benzo[b]thiophene-2-carboxylic acid (2-fluoro-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-amide;

Benzo[b]thiophene-2-carboxylic acid (2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-amide;

5-Bromo-thiophene-2-carboxylic acid (2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-amide;

5-Bromo-thiophene-2-carboxylic acid (2-fluoro-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-amide;

N-(2-Fluoro-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-4-methylsulfanyl-benzamide;

N-(2-Methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-4-methylsulfanyl-benzamide;

4-Ethylsulfanyl-N-(2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

Benzofuran-2-carboxylic acid (2-fluoro-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-amide;

4,5-Dibromo-thiophene-2-carboxylic acid (2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-amide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-5-oxo-6-[6-(1-oxo-1λ^4-thiomorpholin-4-yl)-pyridin-3-ylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(2,6-difluoro-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-Cyclopropyl-N-(2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(2-fluoro-3-{4-methyl-5-oxo-6-[4-(1-oxo-1λ^4-thiomorpholin-4-yl)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-{3-[6-(3-fluoro-4-thiomorpholin-4-yl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide;

4-tert-Butyl-N-(3-{6-[3-fluoro-4-(1-oxo-1λ^4-thiomorpholin-4-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

6-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-nicotinamide;

4-tert-Butyl-N-(3-{6-[4-(4-methoxy-piperidin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-(3-{6-[4-(4-methanesulfonyl-piperazin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-(2-fluoro-3-{6-[4-(4-methanesulfonyl-piperazin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-cyclohexanecarboxylic acid (2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-amide;

4-tert-Butyl-N-{2-methyl-3-[4-methyl-6-(4-morpholin-4-yl-phenylamino)-5-oxo-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide;

4-tert-Butyl-N-(3-{6-[4-(ethyl-methyl-amino)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-(3-{6-[4-(ethyl-methyl-amino)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-fluoro-phenyl)-benzamide;

4-tert-Butyl-N-{2-methyl-3-[4-methyl-6-(2-morpholin-4-yl-pyridin-4-ylamino)-5-oxo-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide;

Benzo[b]thiophene-2-carboxylic acid (2-methyl-3-{4-methyl-5-oxo-6-[4-(1-oxo-1λ^4-thiomorpholin-4-yl)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-amide;

N-(3-{6-[4-(4-Acetyl-piperazin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-fluoro-phenyl)-4-tert-butyl-benzamide;

N-(3-{6-[4-(4-Acetyl-piperazin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide;

4-tert-Butyl-N-{3-[6-(4-hydroxymethyl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide;

4-tert-Butyl-N-(3-{6-[4-(4-hydroxy-piperidin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-{2-methyl-3-[4-methyl-5-oxo-6-(4-piperidin-1-yl-phenylamino)-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide;

4-tert-Butyl-N-{2-methyl-3-[4-methyl-5-oxo-6-(4-pyridin-4-yl-phenylamino)-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide;

4-tert-Butyl-N-{2-fluoro-3-[4-methyl-6-(4-methylaminomethyl-phenylamino)-5-oxo-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide;

4-tert-Butyl-N-(3-{6-[4-(3-ethyl-1-methyl-ureidomethyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-fluoro-phenyl)-benzamide;

4-tert-Butyl-N-{3-[6-(3-hydroxymethyl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide;

4-tert-Butyl-N-(3-{6-[4-(3-hydroxy-pyrrolidin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-{2-methyl-3-[4-methyl-5-oxo-6-(4-pyridin-3-yl-phenylamino)-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide;

4-tert-Butyl-N-[2-fluoro-3-(6-{4-[(methanesulfonyl-methyl-amino)-methyl]-phenylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-phenyl]-benzamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-5-oxo-6-[4-(1-oxy-pyridin-3-yl)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

1-(4-{6-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-phenyl)-piperidine-4-carboxylic acid amide;

4-tert-Butyl-N-(2-fluoro-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-N-methyl-benzamide;

N-(3-{6-[4-(4-Acetyl-[1,4]diazepan-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide;

4-tert-Butyl-N-(3-{6-[4-(4-methanesulfonyl-[1,4]diazepan-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-(2-ethyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

1-(4-{6-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-phenyl)-piperidine-3-carboxylic acid amide;

1-(4-{6-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-phenyl)-pyrrolidine-2-carboxylic acid amide;

4-tert-Butyl-N-{2-methyl-3-[4-methyl-5-oxo-6-(pyridin-4-ylamino)-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide;

4-tert-Butyl-N-(3-{6-[4-(1,1-dioxo-1λ6-thiomorpholin-4-yl)-phenylamino]-4-ethyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-{2-methyl-3-[4-methyl-5-oxo-6-(1-oxy-pyridin-3-ylamino)-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide;

4-tert-Butyl-N-{2-methyl-3-[4-methyl-5-oxo-6-(1-oxy-pyridin-4-ylamino)-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide

4-tert-Butyl-N-(3-{6-[4-(1,4-dioxa-8-aza-spiro[4.5]dec-8-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-{3-[6-(4-carbamimidoylmethyl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide;

4-tert-Butyl-N-(3-{4-cyclopropyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-{3-[6-(3-dimethylaminomethyl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[4-(N-(pyridin-4-ylmethyl)aminocarbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[4-(N-(pyridin-3-ylmethyl)aminocarbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

6-tert-Butyl-N-(3-{6-[4-(1,1-dioxo-1λ6-thiomorpholin-4-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-nicotinamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-5-oxo-6-[4-(1-oxy-pyridin-4-yl)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-{3-[6-(1-ethyl-2-oxo-1,2-dihydro-pyridin-4-ylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide;

4-tert-Butyl-N-(3-{4-cyano-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[4-(N-(piperidin-4-yl)aminocarbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-{2-methyl-3-[4-methyl-6-(3-morpholin-4-ylmethyl-phenylamino)-5-oxo-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide;

5,6,7,8-Tetrahydro-naphthalene-2-carboxylic acid (2-methyl-3-{4-methyl-5-oxo-6-[4-(1-oxo-1λ4-thiomorpholin-4-yl)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-amide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[4-(N-(1-ethyl-piperidin-4-yl)aminocarbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-{3-[6-(4-hydroxy-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide;

4-tert-Butyl-N-{2-methyl-3-[4-methyl-6-(3-nitro-phenylamino)-5-oxo-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide;

4-tert-Butyl-N-{3-[6-(4-methanesulfonyl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide;

N-{3-[6-(3-Amino-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-4-tert-butyl-benzamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-5-oxo-6-[4-(piperidin-4-yloxy)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-{3-[6-(3-hydroxy-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[4-(N-(2-pyridin-4-yl-ethyl)aminocarbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[4-(2-methyl-thiazol-4-yl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[4-(2-morpholin-4-yl-ethoxy)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4,5,6,7-Tetrahydro-benzo[b]thiophene-2-carboxylic acid (2-methyl-3-{4-methyl-5-oxo-6-[4-(1-oxo-1λ4-thiomorpholin-4-yl)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-amide;

6-Methyl-4,5,6,7-tetrahydro-benzo[b]thiophene-2-carboxylic acid (2-methyl-3-{4-methyl-5-oxo-6-[4-(1-oxo-1λ4-thiomorpholin-4-yl)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-amide;

N-(2-Methyl-3-{4-methyl-5-oxo-6-[4-(1-oxo-1λ4-thiomorpholin-4-yl)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-4-piperidin-1-yl-benzamide;

6-tert-Butyl-N-{2-methyl-3-[4-methyl-6-(4-morpholin-4-ylmethyl-phenylamino)-5-oxo-4,5-dihydro-pyrazin-2-yl]-phenyl}-nicotinamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[4-(N-(3-amino-phenyl)aminocarbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

N-(3-{6-[4-(4-Amino-piperidine-1-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide;

4-tert-Butyl-N-(3-{6-[4-(1-ethyl-piperidin-4-yloxy)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

N-{3-[6-(Benzothiazol-6-ylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-4-tert-butyl-benzamide;

N-(3-{6-[4-(2-Amino-pyridin-4-ylmethoxy)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide;

4-tert-Butyl-N-[3-(6-{4-[4-(2-hydroxy-ethyl)-piperazine-1-carbonyl]-phenylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-benzamide;

4-tert-Butyl-N-{3-[6-(2,3-dihydro-benzo[1,4]dioxin-6-ylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide;

4,5,6,7-Tetrahydro-benzo[b]thiophene-2-carboxylic acid (2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-amide;

4,5,6,7-Tetrahydro-benzo[b]thiophene-2-carboxylic acid (2-fluoro-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-amide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[4-(2-morpholin-4-yl-acetyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

5-tert-Butyl-pyridine-2-carboxylic acid (2-methyl-3-{4-methyl-5-oxo-6-[4-(1-oxo-1λ4-thiomorpholin-4-yl)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-amide;

N-(2-Methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-4-piperidin-1-yl-benzamide;

N-(2-Fluoro-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-4-piperidin-1-yl-benzamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-5-oxo-6-[4-(pyridin-4-yloxy)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

6-tert-Butyl-N-(2-methyl-3-{4-methyl-5-oxo-6-[4-(pyridin-4-yloxy)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-nicotinamide;

4-tert-Butyl-N-[3-(6-{4-[4-(2-hydroxy-ethyl)-piperazin-1-yl]-phenylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-benzamide;

6-tert-Butyl-N-[3-(6-{4-[4-(2-hydroxy-ethyl)-piperazin-1-yl]-phenylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-nicotinamide;

N-{3-[6-(3-Amino-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-6-tert-butyl-nicotinamide;

3,4,5,6-Tetrahydro-2H-[1,2']bipyridinyl-5'-carboxylic acid (2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-amide;

N-{3-[6-(2-Amino-pyridin-4-ylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-4-tert-butyl-benzamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[4-(N,N-bis-(2-methoxy-ethyl)aminocarbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

5-tert-Butyl-pyridine-2-carboxylic acid (2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-amide;

5-tert-Butyl-pyridine-2-carboxylic acid (2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-amide;

4-Iodo-N-(2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

N-{3-[6-(3-Benzylamino-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-4-tert-butyl-benzamide;

6-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[4-(2-morpholin-4-yl-ethoxy)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-nicotinamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[4-(N-(tetrahydro-pyran-4-yl)aminocarbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-[2-methyl-3-(4-methyl-5-oxo-6-{4-[(tetrahydro-pyran-4-ylamino)-methyl]-phenylamino}-4,5-dihydro-pyrazin-2-yl)-phenyl]-benzamide;

N-(2-Methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-4-pyrrolidin-1-yl-benzamide;

Tetrahydro-furan-2-carboxylic acid (3-{6-[3-(4-tert-butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-phenyl)-amide;

4-tert-Butyl-N-(3-{6-[3-(cyclohexanecarbonyl-amino)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

N-{3-[6-(3-Amino-4-fluoro-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-4-tert-butyl-benzamide;

5,6-Dihydro-4H-cyclopenta[b]thiophene-2-carboxylic acid (2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-amide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[1-(2-morpholin-4-yl-ethyl)-2-oxo-1,2-dihydro-pyridin-4-ylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

N-(2-Methyl-3-{4-methyl-6-[4-(1-methyl-piperidin-4-yloxy)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-4-piperidin-1-yl-benzamide;

6-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[4-(4-methyl-piperazine-1-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-nicotinamide;

6-tert-Butyl-N-(3-{6-[4-(4-ethyl-piperazine-1-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-nicotinamide;

6-tert-Butyl-N-[3-(6-{4-[4-(2-hydroxy-ethyl)-piperazine-1-carbonyl]-phenylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-nicotinamide;

4-(6-{3-[(6-tert-Butyl-pyridine-3-carbonyl)-amino]-2-methyl-phenyl}-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino)-benzoic acid;

Benzo[b]thiophene-5-carboxylic acid (2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-amide;

6-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[4-(4-methyl-[1,4]diazepane-1-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-nicotinamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-5-oxo-6-[3-(pyridin-3-yloxy)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

6-tert-Butyl-N-(2-methyl-3-{4-methyl-5-oxo-6-[3-(pyridin-3-yloxy)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-nicotinamide;

4,4-Dimethyl-chroman-7-carboxylic acid (2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-amide;

6-tert-Butyl-N-(3-{6-[4-(2-hydroxymethyl-morpholin-4-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-nicotinamide;

6-tert-Butyl-N-(2-fluoro-3-{6-[4-(2-hydroxymethyl-morpholin-4-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-nicotinamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-5-oxo-6-[3-(pyridin-4-yloxy)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

6-tert-Butyl-N-(2-methyl-3-{4-methyl-5-oxo-6-[3-(pyridin-4-yloxy)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-nicotinamide;

6-tert-Butyl-N-(3-{6-[4-(2-hydroxymethyl-morpholine-4-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-nicotinamide;

6-tert-Butyl-N-(2-fluoro-3-{6-[4-(2-hydroxymethyl-morpholine-4-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-nicotinamide;

6-tert-Butyl-N-(2-fluoro-3-{4-methyl-6-[4-(4-methyl-[1,4]diazepane-1-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-nicotinamide;

6-tert-Butyl-N-(3-{6-[4-(4-hydroxy-piperidine-1-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-nicotinamide;

6-tert-Butyl-N-(2-fluoro-3-{6-[4-(4-hydroxy-piperidine-1-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-nicotinamide;

4-tert-Butyl-N-{2-methyl-3-[4-methyl-6-(4-nitro-phenylamino)-5-oxo-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide;

N-{3-[6-(4-Amino-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-4-tert-butyl-benzamide;

N-(3-{6-[4-(4-Amino-piperidine-1-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-6-tert-butyl-nicotinamide;;

4-(6-{3-[(6-tert-Butyl-pyridine-3-carbonyl)-amino]-2-fluoro-phenyl}-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino)-benzoic acid;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-5-oxo-6-[4-(pyridin-3-ylmethoxy)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-5-oxo-6-[4-(pyridin-3-yloxy)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

6-tert-Butyl-N-(2-methyl-3-{4-methyl-5-oxo-6-[4-(pyridin-3-yloxy)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-nicotinamide;

6-tert-Butyl-N-(2-methyl-3-{4-methyl-5-oxo-6-[4-(piperazine-1-carbonyl)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-nicotinamide;

6-tert-Butyl-N-[2-fluoro-3-(6-{4-[4-(2-hydroxy-ethyl)-piperazin-1-yl]-phenylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-phenyl]-nicotinamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[4-(4-methyl-piperazin-1-yl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(3-{6-[4-(4-ethyl-piperazin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[4-(N-(hydroxy)aminocarbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

N-{3-[6-(3-Amino-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-4-piperidin-1-yl-benzamide;

6-tert-Butyl-N-[3-(6-{4-[(2-hydroxy-ethyl)-methyl-carbamoyl]-phenylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-nicotinamide;

6-tert-Butyl-N-(3-{6-[4-(cyanomethyl-methyl-carbamoyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-nicotinamide;

6-tert-Butyl-N-(2-methyl-3-{4-methyl-5-oxo-6-[4-(3-oxo-piperazine-1-carbonyl)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-nicotinamide;

N-(3-{6-[4-(4-Ethyl-piperazine-1-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-piperidin-1-yl-benzamide;

6-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[4-(4-methyl-piperazin-1-yl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-nicotinamide;

6-tert-Butyl-N-(3-{6-[4-(4-ethyl-piperazin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-nicotinamide;

N-{2-Methyl-3-[4-methyl-6-(4-morpholin-4-ylmethyl-phenylamino)-5-oxo-4,5-dihydro-pyrazin-2-yl]-phenyl}-4-piperidin-1-yl-benzamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-5-oxo-6-[4-(N-(1-amino-ethylidene))-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-{3-[6-(3-cyclopropylaminomethyl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide;

4-tert-Butyl-N-{2-methyl-3-[4-methyl-5-oxo-6-(3-piperidin-1-ylmethyl-phenylamino)-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide;

4-tert-Butyl-N-[3-(6-{3-[(cyanomethyl-methyl-amino)-methyl]-phenylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-benzamide;

1-(3-{6-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-benzyl)-piperidine-4-carboxylic acid amide;

4-tert-Butyl-N-{3-[6-(3-{[(2-hydroxy-ethyl)-methyl-amino]-methyl}-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide;

4-tert-Butyl-N-[3-(6-{3-[(2-hydroxy-ethylamino)-methyl]-phenylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-benzamide;

4-tert-Butyl-N-(3-{6-[3-(4-hydroxy-piperidin-1-ylmethyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-(3-{6-[3-(2-hydroxymethyl-morpholin-4-ylmethyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

Tetrahydro-furan-2-carboxylic acid (4-{6-[3-(4-tert-butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-phenyl)-amide;

Tetrahydro-furan-3-carboxylic acid (4-{6-[3-(4-tert-butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-phenyl)-amide;

3,4,5,6-Tetrahydro-2H-[1,3']bipyridinyl-6'-carboxylic acid (2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-amide;

6-tert-Butyl-N-(2-fluoro-3-{4-methyl-5-oxo-6-[4-(piperazine-1-carbonyl)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-nicotinamide;

N-(3-{6-[4-(1,1-Dioxo-116-thiomorpholin-4-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-piperidin-1-yl-benzamide;

6-tert-Butyl-N-(3-{6-[4-(1,1-dioxo-116-thiomorpholin-4-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-fluoro-phenyl)-nicotinamide;

2-tert-Butyl-pyrimidine-5-carboxylic acid (2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-amide;

6-tert-Butyl-N-(2-methyl-3-{4-methyl-5-oxo-6-[4-(pyridin-3-ylmethoxy)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-nicotinamide;

N-(3-{6-[4-(4-Amino-piperidine-1-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-fluoro-phenyl)-6-tert-butyl-nicotinamide;

6-tert-Butyl-N-(2-fluoro-3-{4-methyl-6-[4-(4-methyl-piperazine-1-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-nicotinamide;

5-tert-Butyl-pyrazine-2-carboxylic acid (2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-amide;

6-tert-Butyl-N-(2-fluoro-3-{6-[4-(4-hydroxy-piperidin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-nicotinamide;

N-(2-Methyl-3-{4-methyl-6-[4-(4-methyl-piperazin-1-yl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-4-piperidin-1-yl-benzamide;

N-(3-{6-[4-(4-Ethyl-piperazin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-piperidin-1-yl-benzamide;

6-tert-Butyl-N-(2-fluoro-3-{4-methyl-6-[4-(4-methyl-piperazin-1-yl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-nicotinamide;

6-tert-Butyl-N-(3-{6-[4-(4-ethyl-piperazin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-fluoro-phenyl)-nicotinamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-5-oxo-6-[4-(4-oxo-piperidin-1-yl)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

N-(3-{6-[4-(3-Amino-propylcarbamoyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-fluoro-phenyl)-6-tert-butyl-nicotinamide;

N-(3-{6-[4-(4-Hydroxy-piperidin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-piperidin-1-yl-benzamide

6-tert-Butyl-N-(3-{6-[4-(4-hydroxy-piperidin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-nicotinamide;

4-Azepan-1-yl-N-(2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

5-tert-Butyl-pyridine-2-carboxylic acid (2-fluoro-3-{6-[4-(4-hydroxy-piperidine-1-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-amide;

N-{3-[5-(3-Amino-phenylamino)-1-methyl-6-oxo-1,6-dihydro-pyridin-3-yl]-2-methyl-phenyl}-4-tert-butyl-benzamide;

Tetrahydro-furan-2-carboxylic acid (3-{5-[3-(4-tert-butyl-benzoylamino)-2-methyl-phenyl]-1-methyl-2-oxo-1,2-dihydro-pyridin-3-ylamino}-phenyl)-amide;

4-tert-Butyl-N-{3-[1,4-dimethyl-5-(4-morpholin-4-yl-phenylamino)-6-oxo-1,6-dihydro-pyridin-3-yl]-2-methyl-phenyl}-benzamide;

4-tert-Butyl-N-(3-{5-[4-(1,1-dioxo-1l6-thiomorpholin-4-yl)-phenylamino]-1-methyl-6-oxo-1,6-dihydro-pyridin-3-yl}-2-methyl-phenyl)-benzamide;

6-tert-Butyl-N-(3-{6-[4-(carbamoylmethyl-methyl-carbamoyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-nicotinamide;

6-tert-Butyl-N-{3-[6-(4-hydroxycarbamoyl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-nicotinamide;

5-tert-Butyl-pyridine-2-carboxylic acid (3-{6-[4-(4-ethyl-piperazin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-amide;

N-(3-{6-[4-(4-Amino-piperidin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide;

4-{6-[3-(4-(1-piperidinyl)-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-benzohydroxamic acid;

5-tert-Butyl-pyridine-2-carboxylic acid (3-{6-[4-(1,1-dioxo-1λ^6-thiomorpholin-4-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-amide;

5-tert-Butyl-pyrazine-2-carboxylic acid (2-methyl-3-{4-methyl-6-[4-(4-methyl-piperazine-1-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-amide;

5-tert-Butyl-pyridine-2-carboxylic acid (3-{6-[4-(4-hydroxy-piperidine-1-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-amide;

N-(2-Methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-4-(4-methyl-piperidin-1-yl)-benzamide;

4-tert-Butyl-N-{2-methyl-3-[4-methyl-6-(5-methyl-1H-pyrazol-3-ylamino)-5-oxo-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide;

5-tert-Butyl-pyridine-2-carboxylic acid (3-{6-[4-(2-hydroxymethyl-morpholin-4-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-amide;

N-(2-Methyl-3-{4-methyl-5-oxo-6-[4-(3-oxo-piperazine-1-carbonyl)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-4-piperidin-1-yl-benzamide;

4-(1-Piperidinyl)-N-(3-{4-methyl-6-[4-(2-hydroxyethyl-methyl-carbamoyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-{2-methyl-3-[4-methyl-5-oxo-6-(1H-pyrazol-3-ylamino)-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide;

N-(3-{6-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-phenyl)-isonicotinamide;

5-tert-Butyl-pyrazine-2-carboxylic acid (3-{6-[4-(1,1-dioxo-1λ^6-thiomorpholin-4-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-amide;

Tetrahydro-furan-2-carboxylic acid (3-{6-[3-(4-tert-butyl-benzoylamino)-2-fluoro-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-phenyl)-amide;

5-tert-Butyl-pyridine-2-carboxylic acid (3-{6-[4-(carbamoylmethyl-methyl-carbamoyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-amide;

4,5,6,7-Tetrahydro-benzo[b]thiophene-2-carboxylic acid (3-{6-[4-(carbamoylmethyl-methyl-carbamoyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-amide;

N-(2-Methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-4-(3-methyl-piperidin-1-yl)-benzamide;

N-{3-[6-(3-Acetylamino-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-4-tert-butyl-benzamide;

Tetrahydro-furan-3-carboxylic acid (3-{6-[3-(4-tert-butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-phenyl)-amide;

Thiazole-4-carboxylic acid (3-{6-[3-(4-tert-butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-phenyl)-amide;

(3-{6-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-phenyl)-carbamic acid ethyl ester;

4-tert-Butyl-N-(3-{6-[3-(2-methoxy-acetylamino)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

5-tert-Butyl-pyrimidine-2-carboxylic acid (2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-amide;

4-(Isopropyl-methyl-amino)-N-(2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(2-methyl-3-{6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(3-{6-[4-(1,1-dioxo-1λ^6-thiomorpholin-4-ylmethyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

N-[2-Methyl-3-(4-methyl-5-oxo-6-{4-[(tetrahydro-pyran-4-ylamino)-methyl]-phenylamino}-4,5-dihydro-pyrazin-2-yl)-phenyl]-4-piperidin-1-yl-benzamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[4-(4-methyl-piperazin-1-ylmethyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(3-{6-[4-(4-ethyl-piperazin-1-ylmethyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-{3-[6-(4-{[(2-hydroxy-ethyl)-methyl-amino]-methyl}-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide;

N-[3-(6-{4-[4-(2-Hydroxy-ethyl)-piperazine-1-carbonyl]-phenylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-4-piperidin-1-yl-benzamide;

1-(4-{4-Methyl-6-[2-methyl-3-(4-piperidin-1-yl-benzoylamino)-phenyl]-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-phenyl)-piperidine-4-carboxylic acid amide;

5-tert-Butyl-pyrazine-2-carboxylic acid (3-{6-[4-(4-amino-piperidin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-amide;

N-(2-Methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-4-(4-methyl-piperazin-1-ylmethyl)-benzamide;

4-tert-Butyl-N-[2-fluoro-3-(4-methyl-6-{3-[2-(4-methyl-piperazin-1-yl)-acetylamino]-phenylamino}-5-oxo-4,5-dihydro-pyrazin-2-yl)-phenyl]-benzamide;

N-{3-[6-(3-Amino-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-fluoro-phenyl}-4-tert-butyl-benzamide;

N-{3-[6-(3-Amino-phenylamino)-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-4-tert-butyl-benzamide;

5-tert-Butyl-pyridine-2-carboxylic acid (2-methyl-3-{4-methyl-5-oxo-6-[4-(piperazine-1-carbonyl)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-amide;

Tetrahydro-furan-2-carboxylic acid (3-{6-[3-(4-tert-butyl-benzoylamino)-2-methyl-phenyl]-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-phenyl)-amide;

Tetrahydro-furan-2-carboxylic acid [3-(6-{2-methyl-3-[(4,5,6,7-tetrahydro-benzo[b]thiophene-2-carbonyl)-amino]-phenyl}-3-oxo-3,4-dihydro-pyrazin-2-ylamino)-phenyl]-amide;

Tetrahydro-furan-2-carboxylic acid (5-{6-[3-(4-tert-butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-2-fluoro-phenyl)-amide;

Acetic acid 3-{6-[3-(4-tert-butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-phenyl ester;

N-(2-Methyl-3-{6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-4-piperidin-1-yl-benzamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[4-(morpholin-2-ylmethoxy)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

6-tert-Butyl-pyridazine-3-carboxylic acid (2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-amide;

4-tert-Butyl-N-{2-methyl-3-[4-methyl-5-oxo-6-(3-oxo-3,4-dihydro-2H-benzo[1,4]oxazin-6-ylamino)-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide;

4-Imidazol-1-yl-N-(2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(3-{6-[3-(3-methoxy-propionylamino)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

Furan-2-carboxylic acid (3-{6-[3-(4-tert-butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-phenyl)-amide;

6-tert-Butyl-N-(3-{6-[4-(1,1-dioxo-1λ^6-thiomorpholin-4-yl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-nicotinamide;

4-tert-Butyl-N-[3-(6-{4-[2-(4-ethyl-piperazin-1-yl)-ethoxy]-phenylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-benzamide;

(3-{6-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-phenyl)-carbamic acid tetrahydro-furan-3-yl ester;

Tetrahydro-furan-2-carboxylic acid (3-{6-[3-(4-tert-butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-phenyl)-amide;

Tetrahydro-furan-2-carboxylic acid (3-{6-[3-(4-tert-butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-phenyl)-amide;

N-{3-[6-(5-Amino-pyridin-3-ylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-4-tert-butyl-benzamide;

4-tert-Butyl-N-{3-[6-(1H-indol-5-ylamino)-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide;

Pyrrolidine-2-carboxylic acid (3-{6-[3-(4-tert-butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-phenyl)-amide;

4-tert-Butyl-N-(3-{6-[3-(2-hydroxy-acetylamino)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-[3-(6-cyclopropylamino-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-benzamide;

4-tert-Butyl-N-[3-(6-hydroxy-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-benzamide;

4-tert-Butyl-N-(3-{6-[3-(2-ethoxy-acetylamino)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

N-{3-[6-(3-Amino-4-methyl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-4-tert-butyl-benzamide;

4-tert-Butyl-N-(3-{6-[4-(4-hydroxymethyl-piperidin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-(3-{6-[3-(2-hydroxy-2-methyl-propionylamino)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

Tetrahydro-pyran-4-carboxylic acid (3-{6-[3-(4-tert-butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-phenyl)-amide;

4-tert-Butyl-N-{2-methyl-3-[4-methyl-5-oxo-6-(4-thiomorpholin-4-ylmethyl-phenylamino)-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide;

4-(4-Hydroxy-piperidin-1-yl)-N-(2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

N-{3-[6-(3-Amino-4-chloro-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-4-tert-butyl-benzamide;

N-(3-{6-[3-Amino-4-(morpholine-4-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide;

N-(2-Methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-4-(2-methyl-piperidin-1-yl)-benzamide;

4,5,6,7-Tetrahydro-benzo[b]thiophene-2-carboxylic acid (3-{6-[4-(1,1-dioxo-1λ^6-thiomorpholin-4-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-amide;

4-tert-Butyl-N-{3-[6-(3-dimethylamino-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-5-oxo-6-[4-(piperidin-4-ylmethoxy)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-[3-(6-{4-[(2-hydroxy-ethylamino)-methyl]-phenylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-benzamide;

(3-{6-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-phenyl)-carbamic acid phenyl ester;

4-tert-Butyl-N-{3-[6-(4-cyclopropylaminomethyl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide;

4-tert-Butyl-N-[3-(6-{4-[(carbamoylmethyl-amino)-methyl]-phenylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-benzamide;

4-(4-Methoxymethoxy-piperidin-1-yl)-N-(2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

N-(3-{6-[3-(2-Amino-acetylamino)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide;

Azetidine-2-carboxylic acid (3-{6-[3-(4-tert-butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-phenyl)-amide;

Tetrahydro-furan-2-carboxylic acid (5-{6-[3-(4-tert-butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-2-methyl-phenyl)-amide;

4-tert-Butyl-N-(3-{6-[4-(4-hydroxy-4-methyl-piperidin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

1-Methyl-3-[4-(morpholine-4-carbonyl)-phenylamino]-5-(2-phenyl-benzooxazol-7-yl)-1H-pyrazin-2-one;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[4-(1-methyl-piperidin-2-ylmethoxy)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

5-[2-(4-Methoxy-phenyl)-benzooxazol-7-yl]-1-methyl-3-[4-(morpholine-4-carbonyl)-phenylamino]-1H-pyrazin-2-one;

4-tert-Butyl-N-{3-[6-(1H-indol-5-ylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide;

N-{3-[6-(3-Aminomethyl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-4-tert-butyl-benzamide;

4-tert-Butyl-N-(3-{6-[4-(1-ethyl-piperidin-4-ylmethoxy)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-{2-methyl-3-[4-methyl-5-oxo-6-(1-pyridin-4-ylmethyl-1H-indol-6-ylamino)-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide;

4-Furan-2-yl-N-(2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-(2-Methoxy-1,1-dimethyl-ethyl)-N-(2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(3-{6-[4-(4-hydroxy-4-methyl-piperidine-1-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-(3-{6-[4-(4-hydroxy-4-methyl-piperidin-1-ylmethyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

6-Methyl-4,5,6,7-tetrahydro-benzo[b]thiophene-2-carboxylic acid {3-[6-(3-amino-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-amide;

4-{6-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-2-hydroxy-benzoic acid;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-3-nitro-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

5-Ethyl-4,5,6,7-tetrahydro-benzo[b]thiophene-2-carboxylic acid (2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-amide;

4-Azetidin-1-yl-N-(2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-3-methoxy-N-(2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-{6-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-2-methoxy-benzoic acid;

1,4,4-Trimethyl-1,2,3,4-tetrahydro-quinoline-7-carboxylic acid (2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-amide;

4-(1-Methoxy-1-methyl-ethyl)-N-(2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-(2,2-Dimethyl-propionyl)-N-(2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(3-{6-[3-methoxy-4-(morpholine-4-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-{6-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-2-methoxy-N-(3-methoxy-propyl)-benzamide;

N-{3-[6-(3-Acryloylamino-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-4-tert-butyl-benzamide;

4-tert-Butyl-N-{3-[6-(1H-indol-4-ylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide;

4-tert-Butyl-N-[3-(6-{4-[(2-methoxy-ethylamino)-methyl]-phenylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-benzamide;

4-tert-Butyl-N-{3-[6-(4-ethylaminomethyl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide;

4-tert-Butyl-N-{3-[6-(4-diethylaminomethyl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide;

4-tert-Butyl-N-[3-(6-{4-[(isopropyl-methyl-amino)-methyl]-phenylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-benzamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[4-(2-methyl-piperidin-1-ylmethyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-[2-methyl-3-(4-methyl-5-oxo-6-{4-[2-(tetrahydro-pyran-4-ylamino)-ethyl]-phenylamino}-4,5-dihydro-pyrazin-2-yl)-phenyl]-benzamide;

5-Amino-2-{6-[3-(4-tert-butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-N-cyclopropyl-benzamide;

5-Amino-benzo[b]thiophene-2-carboxylic acid (2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-amide;

2-Amino-N-{3-[6-(benzothiazol-6-ylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-4-piperidin-1-yl-benzamide;

4-tert-Butyl-N-[3-(6-{2-[(2-hydroxy-ethyl)-methyl-amino]-pyridin-4-ylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-benzamide;

4-tert-Butyl-N-(3-{6-[3-methoxy-4-(4-methyl-piperazine-1-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-{6-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-N-(2-hydroxy-ethyl)-2-methoxy-N-methyl-benzamide;

4-tert-Butyl-N-(3-{6-[3-methoxy-4-(piperidine-1-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

N-{3-[6-(3-Amino-4-morpholin-4-yl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-4-tert-butyl-benzamide;

N-{3-[6-(4-Amino-2-piperidin-1-ylmethyl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-4-tert-butyl-benzamide;

(4-{6-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-benzylamino)-acetic acid;

4-tert-Butyl-N-[3-(6-{4-[(cyclopropylmethyl-amino)-methyl]-phenylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-benzamide;

N-{3-[6-(3-Amino-4-thiomorpholin-4-yl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-4-tert-butyl-benzamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-5-oxo-6-[4-(piperidin-3-ylmethoxy)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

N-(3-{6-[3-Amino-4-(1,1-dioxo-1λ^6-thiomorpholin-4-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide;

N-(3-{6-[3-Amino-4-(piperidine-1-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide;

4-tert-Butyl-N-{2-methyl-3-[4-methyl-5-oxo-6-(1,2,3,4-tetrahydro-isoquinolin-6-ylamino)-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide;

4-tert-Butyl-N-[3-(6-{4-[2-(4-ethyl-piperazin-1-yl)-ethyl]-phenylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-benzamide;

4-tert-Butyl-N-[3-(6-{4-[2-(2-hydroxy-ethylamino)-ethyl]-phenylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-benzamide;

4-tert-Butyl-N-{3-[6-(4-{2-[(2-hydroxy-ethyl)-methyl-amino]-ethyl}-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide;

4-tert-Butyl-N-(3-{6-[4-(2-diethylamino-ethyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

2-Amino-4-{6-[3-(4-tert-butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-N-(2-hydroxy-ethyl)-N-methyl-benzamide;

4-[2-(2-Methoxy-ethoxy)-1,1-dimethyl-ethyl]-N-(2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-(3-Methoxymethoxy-piperidin-1-yl)-N-(2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-{3-[6-(4-hydroxymethyl-3-methoxy-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide;

4-tert-Butyl-N-{3-[6-(1H-indol-6-ylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide;

N-(3-{6-[3-Amino-4-(4-methyl-piperazine-1-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide;

N-(3-{6-[3-Amino-4-(4-ethyl-piperazine-1-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide;

2-Amino-4-{6-[3-(4-tert-butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-N-(2-dimethylamino-ethyl)-benzamide;

4-tert-Butyl-N-{2-methyl-3-[6-(4-morpholin-4-yl-3-nitro-phenylamino)-5-oxo-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide;

4-tert-Butyl-N-{2-methyl-3-[4-methyl-6-(4-morpholin-4-yl-3-nitro-phenylamino)-5-oxo-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide;

N-{3-[6-(3-Amino-4-morpholin-4-yl-phenylamino)-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-4-tert-butyl-benzamide;

2-Amino-4-{6-[3-(4-tert-butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-N-(2-diethylamino-ethyl)-benzamide;

4-tert-Butyl-N-(3-{4-ethyl-6-[4-(phenyl-carbamoyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-(3-{4-ethyl-6-[4-(2-methyl-phenyl-carbamoyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-{3-[6-(4-cyclopropylaminomethyl-3-methoxy-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide;

4-tert-Butyl-N-{3-[6-(4-cyclopropylaminomethyl-3-methoxy-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide;

4-tert-Butyl-N-{3-[6-(3-{2-[(2-hydroxy-ethyl)-methyl-amino]-ethyl}-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide;

N-(3-{6-[3-Amino-4-(1-oxo-1λ^4-thiomorpholine-4-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide;

4-(1-Methyl-cyclobutyl)-N-(2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

N-{3-[6-(4-{[Bis-(2-hydroxy-ethyl)-amino]-methyl}-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-4-tert-butyl-benzamide;

4-tert-Butyl-N-[3-(6-{3-[2-(2-hydroxy-ethylamino)-ethyl]-phenylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-benzamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[3-(2-morpholin-4-yl-ethyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-[3-(6-{3-[2-(1,1-dioxo-1λ^6-thiomorpholin-4-yl)-ethyl]-phenylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-benzamide;

4-tert-Butyl-N-[3-(6-{3-[2-(4-ethyl-piperazin-1-yl)-ethyl]-phenylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-benzamide;

N-{3-[6-(3-{2-[Bis-(2-hydroxy-ethyl)-amino]-ethyl}-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-4-tert-butyl-benzamide;

4-tert-Butyl-N-{3-[6-(3,4-dihydro-2H-benzo[1,4]oxazin-6-ylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide;

N-(3-{6-[4-(4-Aminomethyl-4-hydroxy-piperidin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide;

2-Amino-4-{6-[3-(4-tert-butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-benzoic acid;

5-(3-Amino-2-methyl-phenyl)-1-methyl-3-(4-morpholin-4-yl-3-nitro-phenylamino)-1H-pyrazin-2-one;

5-tert-Butyl-pyridine-2-carboxylic acid {3-[6-(3-amino-4-morpholin-4-yl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-amide;

4,5,6,7-Tetrahydro-benzo[b]thiophene-2-carboxylic acid {3-[6-(3-amino-4-morpholin-4-yl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-amide;

N-{3-[6-(3-Amino-4-morpholin-4-yl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-4-piperidin-1-yl-benzamide;

N-(2-Methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-4-methylsulfanyl-benzamide;

N-{3-[6-(3-Amino-4-cyclopropylaminomethyl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-4-tert-butyl-benzamide;

5-Methyl-4,5,6,7-tetrahydro-benzo[b]thiophene-2-carboxylic acid (3-{6-[3-amino-4-(morpholine-4-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-amide;

N-(3-{6-[3-Amino-4-(thiomorpholine-4-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide;

2-Amino-4-{6-[3-(4-tert-butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-N-pyridin-3-yl-benzamide;

N-(5-{6-[3-Amino-4-(morpholine-4-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide;

2-Amino-4-{6-[3-(4-tert-butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-N-(2-methoxy-ethyl)-N-methyl-benzamide;

Octahydro-isoquinoline-2-carboxylic acid (2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-amide;

N-(3-{6-[3-Amino-4-(morpholine-4-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-6-tert-butyl-nicotinamide;

N-{3-[6-(2-Amino-indan-5-ylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-4-tert-butyl-benzamide;

N-(3-{6-[3-Amino-4-(morpholine-4-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-fluoro-phenyl)-4-tert-butyl-benzamide;

N-{3-[6-(3-Amino-4-methoxy-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-4-tert-butyl-benzamide;

N-(3-{6-[3-Amino-4-(1-oxo-1λ^4-thiomorpholin-4-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide;

N-(3-{6-[3-Amino-4-(4-hydroxy-piperidin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide;

N-(3-{6-[3-Amino-4-(4-ethyl-piperazin-1-ylmethyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide;

1-(2-Amino-4-{6-[3-(4-tert-butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-phenyl)-piperidine-4-carboxylic acid amide;

N-{3-[6-(3-Amino-4-morpholin-4-yl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-fluoro-phenyl}-4-tert-butyl-benzamide;

N-(3-{6-[3-Amino-4-(4-ethyl-piperazin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide;

N-(3-{6-[4-(4-Aminomethyl-4-hydroxy-piperidine-1-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide;

N-(3-{6-[4-(1,1-Dioxo-1λ^6-thiomorpholin-4-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-pentafluoroethyl-benzamide;

5-Methyl-4,5,6,7-tetrahydro-benzo[b]thiophene-2-carboxylic acid {2-methyl-3-[4-methyl-6-(4-morpholin-4-ylmethyl-phenylamino)-5-oxo-4,5-dihydro-pyrazin-2-yl]-phenyl}-amide;

5-Methyl-4,5,6,7-tetrahydro-benzo[b]thiophene-2-carboxylic acid (3-{6-[3-amino-4-(morpholine-4-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-fluoro-phenyl)-amide;

N-{3-[6-(3-Amino-4-[1,4]oxazepan-4-yl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-4-tert-butyl-benzamide;

5-Methyl-4,5,6,7-tetrahydro-benzo[b]thiophene-2-carboxylic acid (3-{6-[3-amino-4-(4-hydroxy-piperidin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-amide;

N-[3-(6-{3-Amino-4-[4-(2-hydroxy-ethyl)-piperazin-1-yl]-phenylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-4-tert-butyl-benzamide;

4-tert-Butyl-N-{3-[6-(3-methoxy-4-morpholin-4-ylmethyl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide;

N-(3-{6-[3-Amino-4-(4-hydroxy-4-methyl-piperidin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide;

N-(3-{6-[3-Amino-4-(2-morpholin-4-yl-ethoxy)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide;

4,5,6,7-Tetrahydro-benzo[b]thiophene-2-carboxylic acid (3-{6-[3-amino-4-(morpholine-4-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-amide;

N-[3-(6-{3-Amino-4-[(2-methoxy-ethyl)-methyl-amino]-phenylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-4-tert-butyl-benzamide;

4-{6-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-2-methyl-benzoic acid methyl ester;

4-{6-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-2-methyl-benzoic acid;

4,5,6,7-Tetrahydro-benzo[b]thiophene-2-carboxylic acid (3-{6-[3-amino-4-(morpholine-4-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-fluoro-phenyl)-amide;

4-tert-Butyl-N-{2-methyl-3-[4-methyl-6-(3-methyl-4-morpholin-4-yl-phenylamino)-5-oxo-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide;

4,5,6,7-Tetrahydro-benzo[b]thiophene-2-carboxylic acid (2-methyl-3-{4-methyl-6-[4-(4-methyl-piperazine-1-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-amide;

5-Methyl-4,5,6,7-tetrahydro-benzo[b]thiophene-2-carboxylic acid [2-methyl-3-(4-methyl-5-oxo-6-{4-[(tetrahydro-pyran-4-ylamino)-methyl]-phenylamino}-4,5-dihydro-pyrazin-2-yl)-phenyl]-amide;

4-tert-Butyl-N-{2-methyl-3-[4-methyl-6-(4-[1,4]oxazepan-4-ylmethyl-phenylamino)-5-oxo-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide;

5-Methyl-4,5,6,7-tetrahydro-benzo[b]thiophene-2-carboxylic acid {3-[6-(4-hydroxymethyl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-amide;

5-Methyl-4,5,6,7-tetrahydro-benzo[b]thiophene-2-carboxylic acid [3-(6-{4-[(carbamoylmethyl-amino)-methyl]-phenylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-amide;

5-Methyl-4,5,6,7-tetrahydro-benzo[b]thiophene-2-carboxylic acid (3-{6-[3-amino-4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-amide;

4,5,6,7-Tetrahydro-benzo[b]thiophene-2-carboxylic acid (3-{6-[3-amino-4-(4-hydroxy-piperidin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-amide;

1-(2-Amino-4-{6-[3-(4-tert-butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-phenyl)-4-hydroxy-pyridinium;

N-[3-(6-{3-Amino-4-[(2-hydroxy-ethyl)-methyl-amino]-phenylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-4-tert-butyl-benzamide;

N-(3-{6-[3-Amino-4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-piperidin-1-yl-benzamide;

N-(3-{6-[3-Amino-4-(4-methyl-piperazin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide; and

5,6,7,8-Tetrahydro-naphthalene-2-carboxylic acid (2-methyl-3-{4-methyl-5-oxo-6-[4-(1-oxo-1λ^4-thiomorpholin-4-yl)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-amide,

4,5,6,7-Tetrahydro-benzo[b]thiophene-2-carboxylic acid (2-methyl-3-{4-methyl-6-[4-(4-methyl-piperazine-1-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-amide;

5-Methyl-4,5,6,7-tetrahydro-benzo[b]thiophene-2-carboxylic acid [2-methyl-3-(4-methyl-5-oxo-6-{4-[(tetrahydro-pyran-4-ylamino)-methyl]-phenylamino}-4,5-dihydro-pyrazin-2-yl)-phenyl]-amide;

4-tert-Butyl-N-{2-methyl-3-[4-methyl-6-(4-[1,4]oxazepan-4-ylmethyl-phenylamino)-5-oxo-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide;

5-Methyl-4,5,6,7-tetrahydro-benzo[b]thiophene-2-carboxylic acid {3-[6-(4-hydroxymethyl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-amide;

5-Methyl-4,5,6,7-tetrahydro-benzo[b]thiophene-2-carboxylic acid [3-(6-{4-[(carbamoylmethyl-amino)-methyl]-phenylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-amide;

5-Methyl-4,5,6,7-tetrahydro-benzo[b]thiophene-2-carboxylic acid (3-{6-[3-amino-4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-amide;

4,5,6,7-Tetrahydro-benzo[b]thiophene-2-carboxylic acid (3-{6-[3-amino-4-(4-hydroxy-piperidin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-amide;

1-(2-Amino-4-{6-[3-(4-tert-butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-phenyl)-4-hydroxy-pyridinium;

N-[3-(6-{3-Amino-4-[(2-hydroxy-ethyl)-methyl-amino]-phenylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-4-tert-butyl-benzamide;

N-(3-{6-[3-Amino-4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-piperidin-1-yl-benzamide;

N-(3-{6-[3-Amino-4-(4-methyl-piperazin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide;

4,5,6,7-Tetrahydro-benzo[b]thiophene-2-carboxylic acid (3-{6-[3-amino-4-(4-hydroxy-piperidine-1-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-amide;

N-(3-{6-[3-Amino-4-(3-hydroxy-piperidin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide;

N-(3-{6-[3-Amino-4-(3-hydroxy-pyrrolidin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide;

N-{3-[6-(3-Amino-4-piperidin-1-yl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-4-tert-butyl-benzamide;

4-(2-Hydroxy-1,1-dimethyl-ethyl)-N-(2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

1-[2-Amino-4-(4-methyl-6-{2-methyl-3-[(4,5,6,7-tetrahydro-benzo[b]thiophene-2-carbonyl)-amino]-phenyl}-3-oxo-3,4-dihydro-pyrazin-2-ylamino)-benzoyl]-piperidine-4-carboxylic acid amide;

4,5,6,7-Tetrahydro-benzo[b]thiophene-2-carboxylic acid (3-{6-[3-amino-4-(3-hydroxy-pyrrolidine-1-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-amide;

4,5,6,7-Tetrahydro-benzo[b]thiophene-2-carboxylic acid (3-{6-[3-amino-4-(4-ethyl-piperazine-1-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-amide;

4,5,6,7-Tetrahydro-benzo[b]thiophene-2-carboxylic acid (3-{6-[3-amino-4-(3-hydroxy-piperidine-1-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-amide;

N-(3-{6-[3-Amino-4-(4-methyl-[1,4]diazepan-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide;

N-(3-{6-[3-Amino-4-(2-hydroxymethyl-morpholin-4-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide;

N-(3-{6-[3-Amino-4-(4-hydroxymethyl-piperidin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide;

1-[2-Amino-4-(4-methyl-6-{2-methyl-3-[(4,5,6,7-tetrahydro-benzo[b]thiophene-2-carbonyl)-amino]-phenyl}-3-oxo-3,4-dihydro-pyrazin-2-ylamino)-phenyl]-piperidine-4-carboxylic acid amide;

4,5,6,7-Tetrahydro-benzo[b]thiophene-2-carboxylic acid (3-{6-[3-amino-4-(2-hydroxymethyl-morpholin-4-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-amide;

4,5,6,7-Tetrahydro-benzo[b]thiophene-2-carboxylic acid [3-(6-{3-amino-4-[(2-hydroxy-ethyl)-methyl-carbamoyl]-phenylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-amide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[3-nitro-4-(pyridin-3-yloxy)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

N-[3-(6-{3-Amino-4-[4-(2-hydroxy-ethyl)-piperidin-1-yl]-phenylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-4-tert-butyl-benzamide;

4,5,6,7-Tetrahydro-benzo[b]thiophene-2-carboxylic acid {2-methyl-3-[4-methyl-5-oxo-6-(pyridin-3-ylamino)-4,5-dihydro-pyrazin-2-yl]-phenyl}-amide;

4-tert-Butyl-N-{3-[6-(3-fluoro-4-morpholin-4-ylmethyl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide;

N-(3-{6-[3-Amino-4-(4-methoxy-piperidin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide;

N-(3-{6-[3-Amino-4-(4-cyano-piperidin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide;

1-[2-Amino-4-(4-methyl-6-{2-methyl-3-[(4,5,6,7-tetrahydro-benzo[b]thiophene-2-carbonyl)-amino]-phenyl}-3-oxo-3,4-dihydro-pyrazin-2-ylamino)-phenyl]-piperidine-3-carboxylic acid amide;

N-(3-{6-[3-Amino-4-(3-hydroxymethyl-piperidin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide;

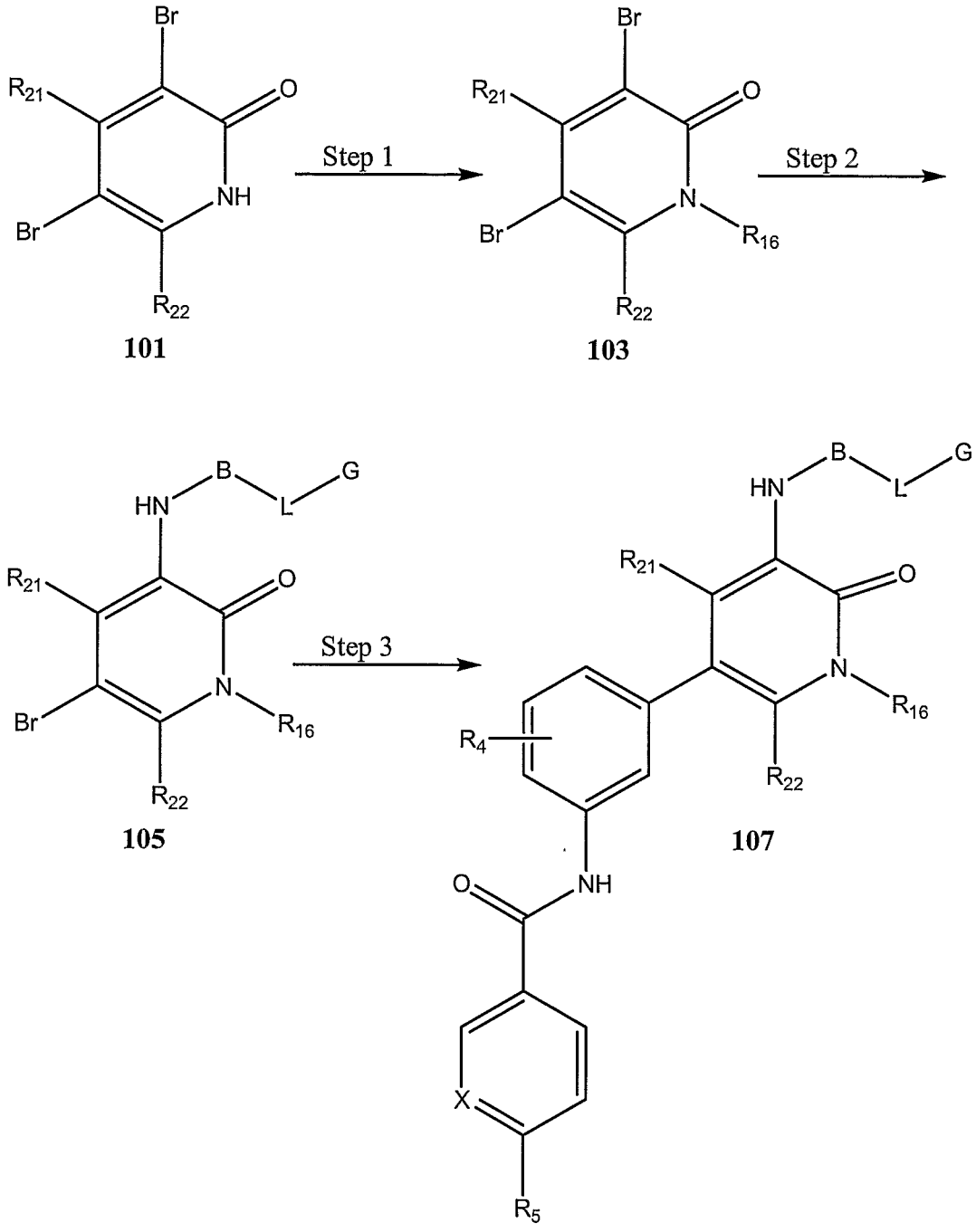
N-(3-{6-[3-Amino-4-(3-methyl-piperazin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide; and

4,5,6,7-Tetrahydro-benzo[b]thiophene-2-carboxylic acid {2-methyl-3-[4-methyl-5-oxo-6-(pyridin-4-ylamino)-4,5-dihydro-pyrazin-2-yl]-phenyl}-amide, and

pharmaceutically acceptable salts, solvates, chelates, non-covalent complexes, prodrugs, and mixtures thereof.

[00152] Methods for obtaining the novel compounds described herein will be apparent to those of ordinary skill in the art, suitable procedures being described, for example, in the reaction scheme and examples below, and in the references cited herein.

Reaction Scheme 1



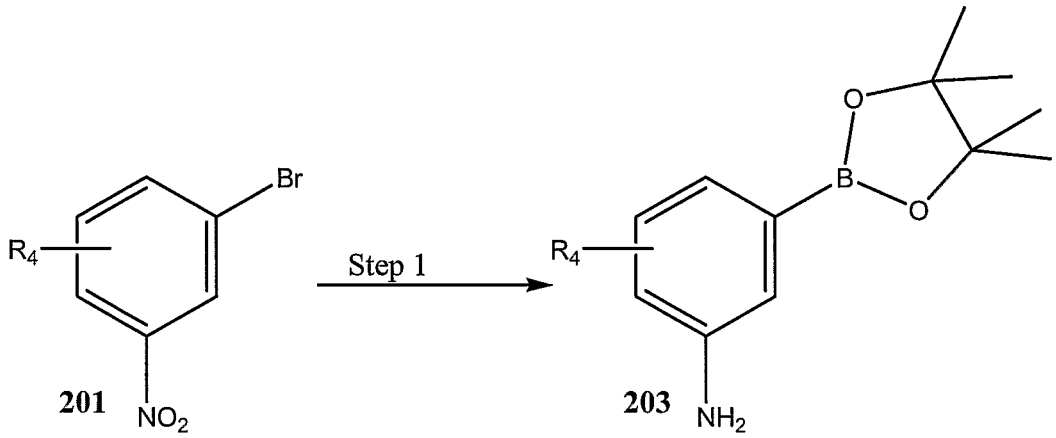
[00153] Referring to Reaction Scheme 1, Step 1, to a suspension of 3,5-dibromo-1H-pyridin-2-one and powdered potassium carbonate in an inert solvent such as DMF is added an excess (such as about 1.1 equivalents) of a compound of Formula R_{16} -Q wherein Q is a leaving group, such as halo. The mixture is stirred at room temperature under nitrogen for about 18 h. The product, a compound of

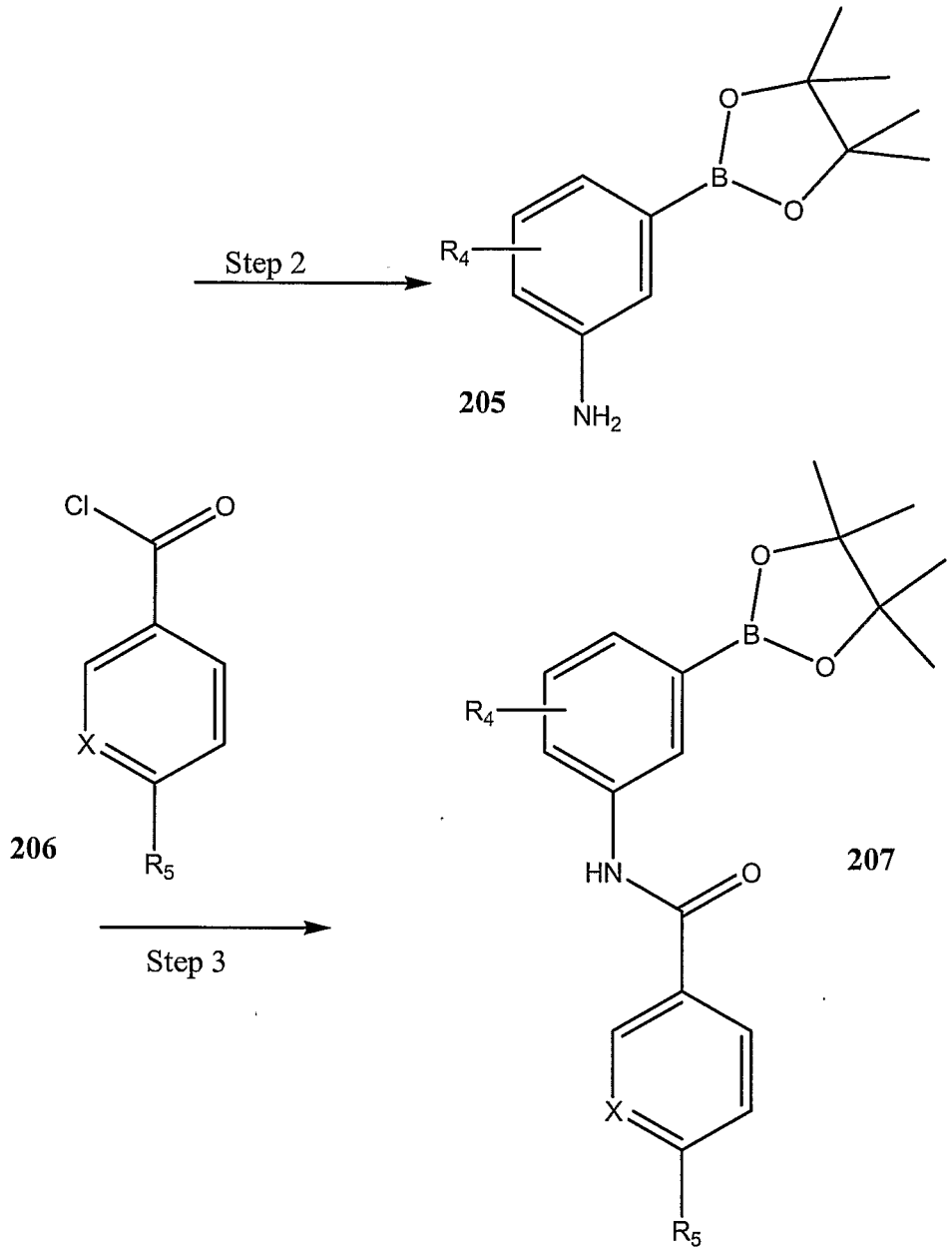
Formula 103, is isolated and optionally purified.

[00154] Referring to Reaction Scheme 1, Step 2, to a solution of a compound of Formula 103 in an inert solvent such as toluene is added an excess (such as about 1.2 equivalents) of a compound of formula NH_2-B-L-G, about 0.07 equivalent of racemic-2,2'-bis(diphenylphosphino)-1,1'-binaphthyl, about 0.05 equivalent of tris(dibenzylideneacetone)dipalladium(0), and an excess (such as about 1.4 equivalents) of cesium carbonate. The reaction tube is sealed and heated at about 120 °C for about 2 d. The product, a compound of Formula 105, is isolated and optionally purified.

[00155] Referring to Reaction Scheme 1, Step 3, a mixture of a compound of Formula 105 and an excess (such as about 1.1 equivalents) of a compound of Formula 207, shown below in Reaction Scheme 2; 0.1 equivalent of tetrakis(triphenylphosphine)palladium; and a base such as 1N sodium carbonate in an inert solvent such as 1,2-dimethoxyethane is heated at about 100 °C in a sealed pressure vessel for about 16h. The product, a compound of Formula 107, is isolated and optionally purified.

Reaction Scheme 2





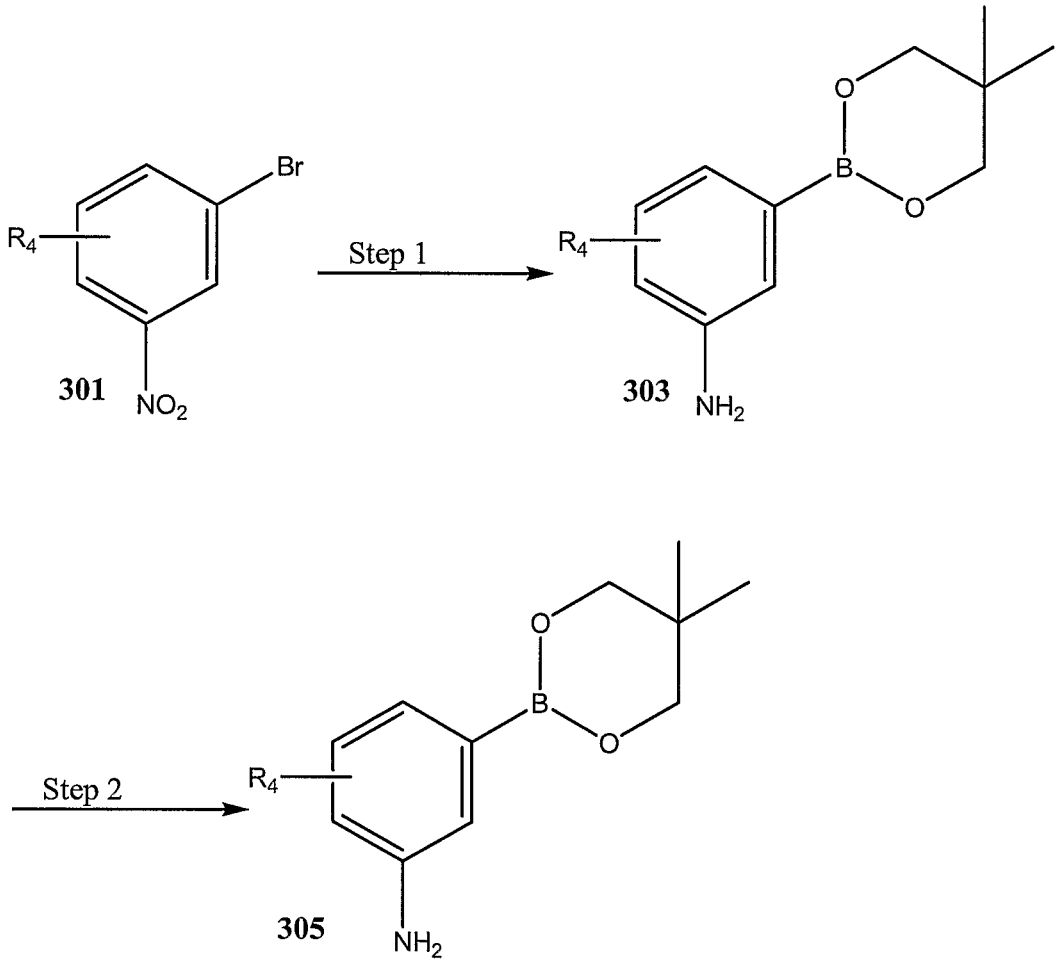
[00156] Referring to Reaction Scheme 2, Step 1, to a suspension of a compound of Formula 201, bis(pinacolato)diboron, and a base such as potassium acetate is added about 0.03 equivalent of [1,1' bis(diphenylphosphino)-ferrocene]dichloropalladium (II) complex with dichloromethane (1:1). The reaction is heated at about 85 °C for for about 20 h. The product, a compound of Formula 203, is isolated and optionally purified.

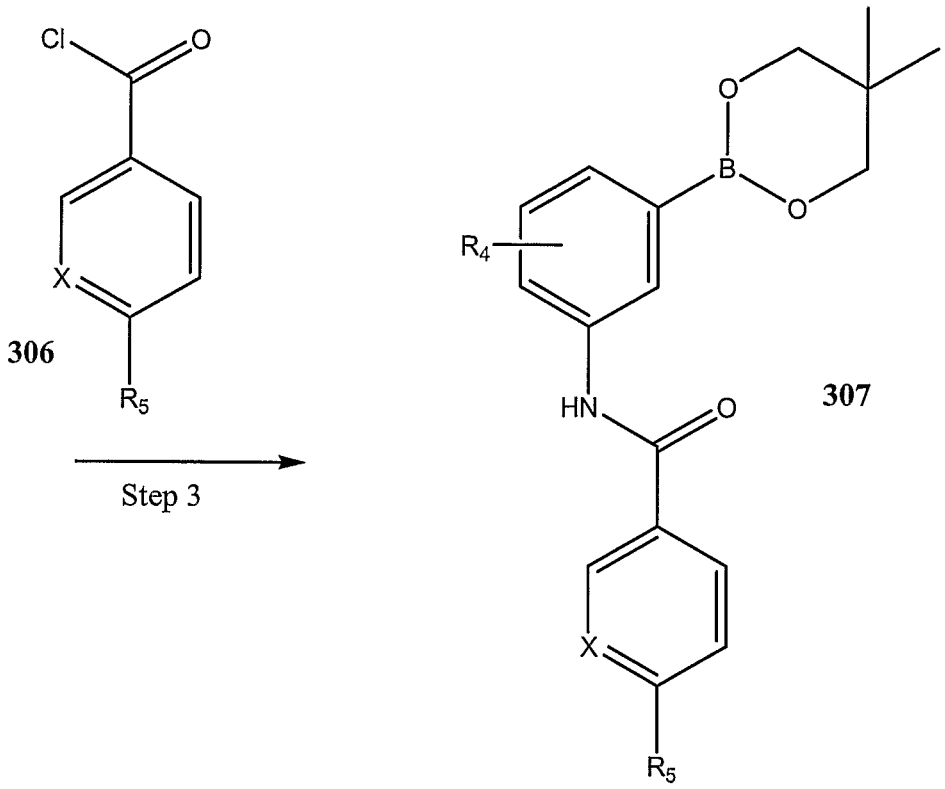
[00157] Referring to Reaction Scheme 2, Step 2, 10% palladium on charcoal is added to a mixture of a compound of Formula 203 in a polar, protic solvent such as

methanol. To the mixture is added hydrogen gas. The reaction is stirred under balloon pressure of hydrogen at room temperature for about 13 h. The product, a compound of Formula 205, is isolated and optionally purified.

[00158] Referring to Reaction Scheme 2, Step 3, a solution of about an equivalent of a compound of formula 206 in an inert solvent such as dichloromethane is added portionwise to a solution of a compound of Formula 205 and a base such as triethylamine in an inert solvent such as dichloromethane. The mixture is stirred at room temperature for about 16 h. The product, a compound of Formula 207, is isolated and optionally purified.

Reaction Scheme 3



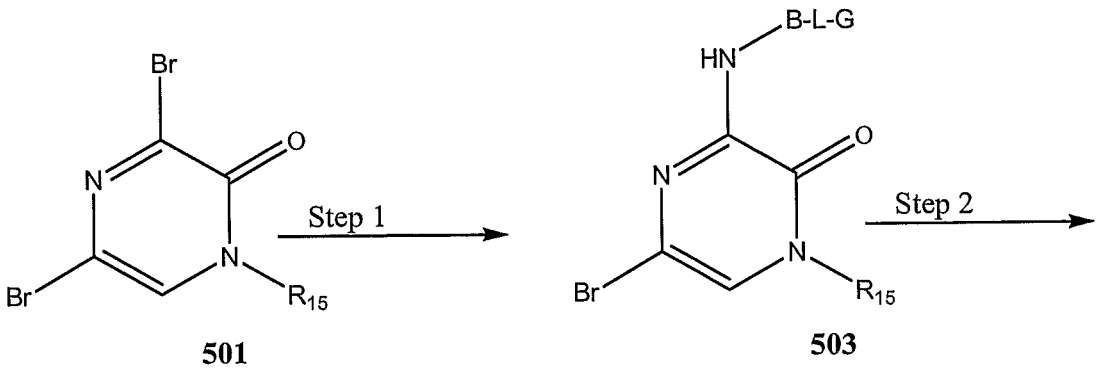


[00159] Referring to Reaction Scheme 3, Step 1, a mixture of a compound of Formula 301; an excess (such as about 1.2 equivalents) of bis(neopentyl glycolato)diboron; and about 0.3 equivalent of [1,1'-bis(diphenylphosphino)-ferrocene]dichloropalladium, 1:1 complex with dichloromethane; and a base such as potassium acetate in an inert solvent such as dioxane is heated at reflux for about 3h. The product, a compound of Formula 303, is isolated and optionally purified.

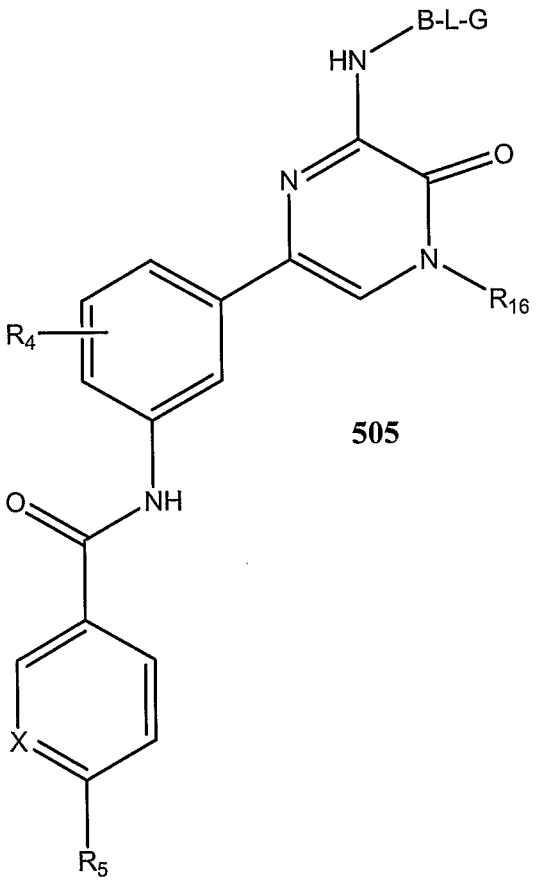
[00160] Referring to Reaction Scheme 3, Step 2, a mixture of a compound of Formula 303 and 10% palladium-on-carbon in an inert solvent such as ethyl acetate methanol is treated with 40psi of hydrogen for about 2h at room temperature. The product, a compound of Formula 305, is isolated and optionally purified.

[00161] Referring to Reaction Scheme 3, Step 3, a solution of a compound of Formula 305 and a base, such as triethylamine in an inert solvent such as THF is treated dropwise with about an equivalent of an acid chloride of the formula 306 and the mixture is stirred at room temperature for about 15 min. The product, a compound of Formula 307, is isolated and optionally purified.

Reaction Scheme 4



501 **503**



505

[00162] Referring to Reaction Scheme 4, Step 1, a mixture of a compound of Formula 501, about an equivalent of a compound of NH_2-B-L-G, and an inert base such as 1-methyl-2-pyrollidinone is heated at about 130°C for about 1 hr. The

product, a compound of Formula 503, is isolated and optionally purified.

[00163] Referring to Reaction Scheme 4, Step 2, a mixture of a compound of Formula 503, an excess (such as about 1.2 equivalents) of a compound of Formula 107, about 0.05 equivalent of tetrakis(triphenylphosphine)palladium and a base such as 1N sodium carbonate in an inert solvent such as 1,2-dimethoxyethane is heated at about 100 °C in a sealed pressure vessel for about 16 hr. The product, a compound of Formula 505, is isolated and optionally purified.

[00164] In some embodiments, the chemical entities described herein are administered as a pharmaceutical composition or formulation. Accordingly, the invention provides pharmaceutical formulations comprising at least one chemical entity chosen from compounds of Formula 1 and pharmaceutically acceptable salts, solvates, chelates, non-covalent complexes, prodrugs, and mixtures thereof, together with at least one pharmaceutically acceptable vehicle chosen from carriers, adjuvants, and excipients.

[00165] Pharmaceutically acceptable vehicles must be of sufficiently high purity and sufficiently low toxicity to render them suitable for administration to the animal being treated. The vehicle can be inert or it can possess pharmaceutical benefits. The amount of vehicle employed in conjunction with the chemical entity is sufficient to provide a practical quantity of material for administration per unit dose of the chemical entity.

[00166] Exemplary pharmaceutically acceptable carriers or components thereof are sugars, such as lactose, glucose and sucrose; starches, such as corn starch and potato starch; cellulose and its derivatives, such as sodium carboxymethyl cellulose, ethyl cellulose, and methyl cellulose; powdered tragacanth; malt; gelatin; talc; solid lubricants, such as stearic acid and magnesium stearate; calcium sulfate; synthetic oils; vegetable oils, such as peanut oil, cottonseed oil, sesame oil, olive oil, and corn oil; polyols such as propylene glycol, glycerine, sorbitol, mannitol, and polyethylene glycol; alginic acid; phosphate buffer solutions; emulsifiers, such as the TWEENS; wetting agents, such as sodium lauryl sulfate; coloring agents; flavoring agents; tableting agents; stabilizers; antioxidants; preservatives; pyrogen-free water; isotonic saline; and phosphate buffer solutions.

[00167] Optional active agents may be included in a pharmaceutical

composition, which do not substantially interfere with the activity of the chemical entity of the present invention.

[00168] Effective concentrations of at least one chemical entity chosen from compounds of Formula 1 and pharmaceutically acceptable salts, solvates, chelates, non-covalent complexes, prodrugs, and mixtures thereof, are mixed with a suitable pharmaceutical acceptable vehicle. In instances in which the chemical entity exhibits insufficient solubility, methods for solubilizing 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.

[00169] Upon mixing or addition of the chemical entity described herein, the resulting mixture may be a solution, suspension, emulsion or the like. The form of the resulting mixture depends upon a number of factors, including the intended mode of administration and the solubility of the chemical entity in the chosen vehicle. The effective concentration sufficient for ameliorating the symptoms of the disease treated may be empirically determined.

[00170] Chemical entities described herein may be administered orally, topically, parenterally, intravenously, by intramuscular injection, by inhalation or spray, sublingually, transdermally, via buccal administration, rectally, as an ophthalmic solution, or by other means, in dosage unit formulations.

[00171] Dosage formulations suitable for oral use, include, for example, tablets, troches, lozenges, aqueous or oily suspensions, dispersible powders or granules, emulsions, hard or soft capsules, or syrups or elixirs. Compositions intended for oral use may be prepared according to any method known to the art for the manufacture of pharmaceutical compositions and such compositions may contain one or more agents, such as sweetening agents, flavoring agents, coloring agents and preserving agents, in order to provide pharmaceutically elegant and palatable preparations. In some embodiments, oral formulations contain from 0.1 to 99% of at least one chemical entity described herein. In some embodiments, oral formulations contain at least 5% (weight %) of at least one chemical entity described herein. Some embodiments contain from 25% to 50% or from 5% to 75 % of at least one chemical entity described herein.

[00172] Orally administered compositions also include liquid solutions, emulsions, suspensions, powders, granules, elixirs, tinctures, syrups, and the like. The pharmaceutically acceptable carriers suitable for preparation of such compositions are well known in the art. Oral formulations may contain preservatives, flavoring agents, sweetening agents, such as sucrose or saccharin, taste-masking agents, and coloring agents.

[00173] Typical components of carriers for syrups, elixirs, emulsions and suspensions include ethanol, glycerol, propylene glycol, polyethylene glycol, liquid sucrose, sorbitol and water. Syrups and elixirs may be formulated with sweetening agents, for example glycerol, propylene glycol, sorbitol, or sucrose. Such formulations may also contain a demulcent.

[00174] Chemical entities described herein can be incorporated into oral liquid preparations such as aqueous or oily suspensions, solutions, emulsions, syrups, or elixirs, for example. Moreover, formulations containing these chemical entities can be presented as a dry product for constitution with water or other suitable vehicle before use. Such liquid preparations can contain conventional additives, such as suspending agents (e.g., sorbitol syrup, methyl cellulose, glucose/sugar, syrup, gelatin, hydroxyethyl cellulose, carboxymethyl cellulose, aluminum stearate gel, and hydrogenated edible fats), emulsifying agents (e.g., lecithin, sorbitan monsoleate, or acacia), non-aqueous vehicles, which can include edible oils (e.g., almond oil, fractionated coconut oil, silyl esters, propylene glycol and ethyl alcohol), and preservatives (e.g., methyl or propyl p-hydroxybenzoate and sorbic acid).

[00175] For a suspension, typical suspending agents include methylcellulose, sodium carboxymethyl cellulose, AVICEL RC-591, tragacanth and sodium alginate; typical wetting agents include lecithin and polysorbate 80; and typical preservatives include methyl paraben and sodium benzoate.

[00176] Aqueous suspensions contain the active material(s) in admixture with excipients suitable for the manufacture of aqueous suspensions. Such excipients include suspending agents, for example sodium carboxymethylcellulose, methylcellulose, hydropropylmethylcellulose, sodium alginate, polyvinylpyrrolidone, gum tragacanth and gum acacia; dispersing or wetting agents; naturally-occurring phosphatides, for example, lecithin, or condensation products of an alkylene oxide

with fatty acids, for example polyoxyethylene stearate, or condensation products of ethylene oxide with long chain aliphatic alcohols, for example heptadecaethyleneoxycetanol, or condensation products of ethylene oxide with partial esters derived from fatty acids and a hexitol such as polyoxyethylene sorbitol substitute, or condensation products of ethylene oxide with partial esters derived from fatty acids and hexitol anhydrides, for example polyethylene sorbitan substitute. The aqueous suspensions may also contain one or more preservatives, for example ethyl, or n- propyl p-hydroxybenzoate.

[00177] Oily suspensions may be formulated by suspending the active ingredients in a vegetable oil, for example peanut oil, olive oil, sesame oil or coconut oil, or in a mineral oil such as liquid paraffin. The oily suspensions may contain a thickening agent, for example beeswax, hard paraffin or cetyl alcohol. Sweetening agents such as those set forth above, and flavoring agents may be added to provide palatable oral preparations. These compositions may be preserved by the addition of an anti-oxidant such as ascorbic acid.

[00178] Pharmaceutical compositions of the invention may also be in the form of oil-in-water emulsions. The oily phase may be a vegetable oil, for example olive oil or peanut oil, or a mineral oil, for example liquid paraffin or mixtures of these. Suitable emulsifying agents may be naturally-occurring gums, for example gum acacia or gum tragacanth, naturally-occurring phosphatides, for example soy bean, lecithin, and esters or partial esters derived from fatty acids and hexitol, anhydrides, for example sorbitan monoleate, and condensation products of the said partial esters with ethylene oxide, for example polyoxyethylene sorbitan monoleate.

[00179] Dispersible powders and granules suitable for preparation of an aqueous suspension by the addition of water provide the active ingredient in admixture with a dispersing or wetting agent, suspending agent and one or more preservatives. Suitable dispersing or wetting agents and suspending agents are exemplified by those already mentioned above.

[00180] Tablets typically comprise conventional pharmaceutically acceptable adjuvants as inert diluents, such as calcium carbonate, sodium carbonate, mannitol, lactose and cellulose; binders such as starch, gelatin and sucrose; disintegrants such as starch, alginic acid and croscarmelose; lubricants such as magnesium stearate, stearic

acid and talc. Glidants such as silicon dioxide can be used to improve flow characteristics of the powder mixture. Coloring agents, such as the FD&C dyes, can be added for appearance. Sweeteners and flavoring agents, such as aspartame, saccharin, menthol, peppermint, and fruit flavors, can be useful adjuvants for chewable tablets. Capsules (including time release and sustained release formulations) typically comprise one or more solid diluents disclosed above. The selection of carrier components often depends on secondary considerations like taste, cost, and shelf stability.

[00181] Such compositions may also be coated by conventional methods, typically with pH or time-dependent coatings, such that the chemical entity is released in the gastrointestinal tract in the vicinity of the desired topical application, or at various times to extend the desired action. Such dosage forms typically include, but are not limited to, one or more of cellulose acetate phthalate, polyvinylacetate phthalate, hydroxypropyl methylcellulose phthalate, ethyl cellulose, Eudragit coatings, waxes and shellac.

[00182] Formulations for oral use may also be presented as hard gelatin capsules wherein the active ingredient is mixed with an inert solid diluent, for example, calcium carbonate, calcium phosphate or kaolin, or as soft gelatin capsules wherein the active ingredient is mixed with water or an oil medium, for example peanut oil, liquid paraffin or olive oil.

[00183] Pharmaceutical compositions may be in the form of a sterile injectable aqueous or oleaginous suspension. This suspension may be formulated according to the known art using those suitable dispersing or wetting agents and suspending agents that have been mentioned above. The sterile injectable preparation may also be sterile injectable solution or suspension in a non-toxic parentally acceptable vehicle, for example as a solution in 1,3-butanediol. Among the acceptable vehicles that may be employed are water, Ringer's solution, and isotonic sodium chloride solution. In addition, sterile, fixed oils are conventionally employed as a solvent or suspending medium. For this purpose any bland fixed oil may be employed including synthetic mono- or diglycerides. In addition, fatty acids such as oleic acid can be useful in the preparation of injectables.

[00184] Chemical entities described herein may be administered parenterally in

a sterile medium. Parenteral administration includes subcutaneous injections, intravenous, intramuscular, intrathecal injection or infusion techniques. Chemical entities described herein, depending on the vehicle and concentration used, can either be suspended or dissolved in the vehicle. Advantageously, adjuvants such as local anesthetics, preservatives and buffering agents can be dissolved in the vehicle. In many compositions for parenteral administration the carrier comprises at least 90% by weight of the total composition. In some embodiments, the carrier for parenteral administration is chosen from propylene glycol, ethyl oleate, pyrrolidone, ethanol, and sesame oil.

[00185] Chemical entites described herein may also be administered in the form of suppositories for rectal administration of the drug. These compositions can be prepared by mixing the drug with a suitable non-irritating excipient that is solid at ordinary temperatures but liquid at rectal temperature and will therefore melt in the rectum to release the drug. Such materials include cocoa butter and polyethylene glycols.

[00186] Chemical entities described herein may 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. Topical compositions may be in any form including, for example, solutions, creams, ointments, gels, lotions, milks, cleansers, moisturizers, sprays, skin patches, and the like.

[00187] Such solutions may be formulated as 0.01% -10% isotonic solutions, pH 5-7, with appropriate salts. Chemical entities described herein may also be formulated for transdermal administration as a transdermal patch.

[00188] Topical compositions comprising at least one chemical entity described herein can be admixed with a variety of carrier materials well known in the art, such as, for example, water, alcohols, aloe vera gel, allantoin, glycerine, vitamin A and E oils, mineral oil, propylene glycol, PPG-2 myristyl propionate, and the like.

[00189] Other materials suitable for use in topical carriers include, for example, emollients, solvents, humectants, thickeners and powders. Examples of each of these types of materials, which can be used singly or as mixtures of one or more materials, are as follows:

[00190] Representative emollients include stearyl alcohol, glyceryl monoricinoleate, glyceryl monostearate, propane-1,2-diol, butane-1,3-diol, mink oil, cetyl alcohol, iso-propyl isostearate, stearic acid, iso-butyl palmitate, isocetyl stearate, oleyl alcohol, isopropyl laurate, hexyl laurate, decyl oleate, octadecan-2-ol, isocetyl alcohol, cetyl palmitate, dimethylpolysiloxane, di-n-butyl sebacate, iso-propyl myristate, iso-propyl palmitate, iso-propyl stearate, butyl stearate, polyethylene glycol, triethylene glycol, lanolin, sesame oil, coconut oil, arachis oil, castor oil, acetylated lanolin alcohols, petroleum, mineral oil, butyl myristate, isostearic acid, palmitic acid, isopropyl linoleate, lauryl lactate, myristyl lactate, decyl oleate, and myristyl myristate; propellants, such as propane, butane, iso-butane, dimethyl ether, carbon dioxide, and nitrous oxide; solvents, such as ethyl alcohol, methylene chloride, iso-propanol, castor oil, ethylene glycol monoethyl ether, diethylene glycol monobutyl ether, diethylene glycol monoethyl ether, dimethyl sulphoxide, dimethyl formamide, tetrahydrofuran; humectants, such as glycerin, sorbitol, sodium 2-pyrrolidone-5-carboxylate, soluble collagen, dibutyl phthalate, and gelatin; and powders, such as chalk, talc, fullers earth, kaolin, starch, gums, colloidal silicon dioxide, sodium polyacrylate, tetra alkyl ammonium smectites, trialkyl aryl ammonium smectites, chemically modified magnesium aluminium silicate, organically modified montmorillonite clay, hydrated aluminium silicate, fumed silica, carboxyvinyl polymer, sodium carboxymethyl cellulose, and ethylene glycol monostearate.

[00191] Chemical entities described herein may also be topically administered in the form of liposome delivery systems, such as small unilamellar vesicles, large unilamellar vesicles, and multilamellar vesicles. Liposomes can be formed from a variety of phospholipids, such as cholesterol, stearylamine and phosphatidylcholines.

[00192] Other compositions useful for attaining systemic delivery of the chemical entity include sublingual, buccal and nasal dosage forms. Such compositions typically comprise one or more of soluble filler substances such as sucrose, sorbitol and mannitol, and binders such as acacia, microcrystalline cellulose, carboxymethyl cellulose, and hydroxypropyl methylcellulose. Glidants, lubricants, sweeteners, colorants, antioxidants and flavoring agents disclosed above may also be included.

[00193] Compositions for inhalation typically can be provided in the form of a solution, suspension or emulsion that can be administered as a dry powder or in the form of an aerosol using a conventional propellant (e.g., dichlorodifluoromethane or trichlorofluoromethane).

[00194] The compositions of the present invention may also optionally comprise an activity enhancer. The activity enhancer can be chosen from a wide variety of molecules that function in different ways to enhance or be independent of therapeutic effects of the chemical entities described herein. Particular classes of activity enhancers include skin penetration enhancers and absorption enhancers.

[00195] Pharmaceutical compositions of the invention may also contain additional active agents that can be chosen from a wide variety of molecules, which can function in different ways to enhance the therapeutic effects of at least one chemical entity described herein. These optional other active agents, when present, are typically employed in the compositions of the invention at a level ranging from 0.01% to 15%. Some embodiments contain from 0.1% to 10% by weight of the composition. Other embodiments contain from 0.5% to 5% by weight of the composition.

[00196] The invention includes packaged pharmaceutical formulations. Such packaged formulations include a pharmaceutical composition comprising at least one chemical entity chosen from compounds of Formula 1 and pharmaceutically acceptable salts, solvates, chelates, non-covalent complexes, prodrugs, and mixtures thereof, and instructions for using the composition to treat a mammal (typically a human patient). In some embodiments, the instructions are for using the pharmaceutical composition to treat a patient suffering from a disease responsive to inhibition of Btk activity and/ or inhibition of B-cell activity. The invention can include providing prescribing information; for example, to a patient or health care provider, or as a label in a packaged pharmaceutical formulation. Prescribing information may include for example efficacy, dosage and administration, contraindication and adverse reaction information pertaining to the pharmaceutical formulation.

[00197] In all of the foregoing the chemical entities can be administered alone, as mixtures, or in combination with other active agents.

[00198] Accordingly, the invention includes a method of treating a patient, for example, a mammal, such as a human, having a disease responsive to inhibition of Btk activity, comprising administrating to the patient having such a disease, an effective amount of at least one chemical entity chosen from compounds of Formula 1 and pharmaceutically acceptable salts, solvates, chelates, non-covalent complexes, prodrugs, and mixtures thereof.

[00199] To the extent that Btk is implicated in disease, alleviation of the disease, disease symptoms, preventative, and prophylactic treatment is within the scope of this invention. In some embodiments, the chemical entities described herein may also inhibit other kinases, such that alleviation of disease, disease symptoms, preventative, and prophylactic treatment of conditions associated with these kinases is also within the scope of this invention.

[00200] Methods of treatment also include inhibiting Btk activity and/ or inhibiting B-cell activity, by inhibiting ATP binding or hydrolysis by Btk or by some other mechanism, *in vivo*, in a patient suffering from a disease responsive to inhibition of Btk activity, by administering an effective concentration of at least one chemical entity chosen from compounds of Formula 1 and pharmaceutically acceptable salts, solvates, chelates, non-covalent complexes, prodrugs, and mixtures thereof. An example of an effective concentration would be that concentration sufficient to inhibit Btk activity *in vitro*. An effective concentration may be ascertained experimentally, for example by assaying blood concentration of the chemical entity, or theoretically, by calculating bioavailability.

[00201] In some embodiments, the condition responsive to inhibition of Btk activity and/ or B-cell activity is cancer, an allergic disorder and/or an autoimmune and/or inflammatory disease, and/or an acute inflammatory reaction.

[00202] The invention includes a method of treating a patient having cancer, an allergic disorder and/or an autoimmune and/or inflammatory disease, and/or an acute inflammatory reaction, by administering an effective amount of at least one chemical entity chosen from compounds of Formula 1 and pharmaceutically acceptable salts, solvates, chelates, non-covalent complexes, prodrugs, and mixtures thereof.

[00203] In some embodiments, the conditions and diseases that can be affected using chemical entities described herein, include, but are not limited to:

allergic disorders, including but not limited to eczema, allergic rhinitis or coryza, hay fever, bronchial asthma, urticaria (hives) and food allergies, and other atopic conditions;

autoimmune and/or inflammatory diseases, including but not limited to psoriasis, Crohn's disease, irritable bowel syndrome, Sjogren's disease, tissue graft rejection, and hyperacute rejection of transplanted organs, asthma, systemic lupus erythematosus (and associated glomerulonephritis), dermatomyositis, multiple sclerosis, scleroderma , vasculitis (ANCA-associated and other vasculitides), autoimmune hemolytic and thrombocytopenic states, Goodpasture's syndrome (and associated glomerulonephritis and pulmonary hemorrhage), atherosclerosis, rheumatoid arthritis, chronic Idiopathic thrombocytopenic purpura (ITP), Addison's disease, Parkinson's disease, Alzheimer's disease, diabetes, septic shock, myasthenia gravis, and the like,

acute inflammatory reactions, including but not limited to skin sunburn, inflammatory pelvic disease, inflammatory bowel disease, urethritis, uvitis, sinusitis, pneumonitis, encephalitis, meningitis, myocarditis, nephritis, osteomyelitis, myositis, hepatitis, gastritis, enteritis, dermatitis, gingivitis, appendicitis, pancreatitis, and cholocystitis, and

cancer, including but not limited to, B-cell lymphoma, lymphoma (including Hodgkin's and non-Hodgkins lymphoma), hairy cell leukemia, multiple myeloma, chronic and acute myelogenous leukemia, and chronic and acute lymphocytic leukemia.

[00204] Btk is a known inhibitor of apoptosis in lymphoma B-cells. Defective apoptosis contributes to the pathogenesis and drug resistance of human leukemias and lymphomas. Thus, further provided is a method of promoting or inducing apoptosis in cells expressing Btk comprising contacting the cell with at least one chemical entity chosen from compounds of Formula 1 pharmaceutically acceptable salts, solvates, chelates, non-covalent complexes, prodrugs, and mixtures thereof.

[00205] The invention provides methods of treatment in which at least one chemical entity chosen from compounds of Formula 1 pharmaceutically acceptable salts, solvates, chelates, non-covalent complexes, prodrugs, and mixtures thereof, is the only active agent given to a patient and also includes methods of treatment in

which at least one chemical entity chosen from compounds of Formula 1 and pharmaceutically acceptable salts, solvates, chelates, non-covalent complexes, prodrugs, and mixtures thereof, is given to a patient in combination with one or more additional active agents.

[00206] Thus in one embodiment the invention provides a method of treating cancer, an allergic disorder and/or an autoimmune and/or inflammatory disease, and/or an acute inflammatory reaction, which comprises administering to a patient in need thereof an effective amount of at least one chemical entity chosen from compounds of Formula 1 and pharmaceutically acceptable salts, solvates, chelates, non-covalent complexes, prodrugs, and mixtures thereof, together with a second active agent, which can be useful for treating a cancer, an allergic disorder and/or an autoimmune and/or inflammatory disease, and/or an acute inflammatory reaction. For example the second agent may be an anti-inflammatory agent. Treatment with the second active agent may be prior to, concomitant with, or following treatment with at least one chemical entity chosen from compounds of Formula 1 and pharmaceutically acceptable salts, solvates, chelates, non-covalent complexes, prodrugs, and mixtures thereof. In certain embodiments, at least one chemical entity chosen from compounds of Formula 1 and pharmaceutically acceptable salts, solvates, chelates, non-covalent complexes, prodrugs, and mixtures thereof, is combined with another active agent in a single dosage form. Suitable antitumor therapeutics that may be used in combination with at least one chemical entity described herein include, but are not limited to, chemotherapeutic agents, for example mitomycin C, carboplatin, taxol, cisplatin, paclitaxel, etoposide, doxorubicin, or a combination comprising at least one of the foregoing chemotherapeutic agents. Radiotherapeutic antitumor agents may also be used, alone or in combination with chemotherapeutic agents.

[00207] Chemical entities described herein can be useful as chemosensitizing agents, and, thus, can be useful in combination with other chemotherapeutic drugs, in particular, drugs that induce apoptosis.

[00208] A method for increasing sensitivity of cancer cells to chemotherapy, comprising administering to a patient undergoing chemotherapy a chemotherapeutic agent together with at least one chemical entity chosen from compounds of Formula 1 and pharmaceutically acceptable salts, solvates, chelates, non-covalent complexes,

prodrugs, and mixtures thereof, in an amount sufficient to increase the sensitivity of cancer cells to the chemotherapeutic agent is also provided herein.

[00209] Examples of other chemotherapeutic drugs that can be used in combination with chemical entities described herein include topoisomerase I inhibitors (camptothesin or topotecan), topoisomerase II inhibitors (e.g. daunomycin and etoposide), alkylating agents (e.g. cyclophosphamide, melphalan and BCNU), tubulin directed agents (e.g. taxol and vinblastine), and biological agents (e.g. antibodies such as anti CD20 antibody, IDEC 8, immunotoxins, and cytokines).

[00210] Included herein are methods of treatment in which at least one chemical entity chosen from compounds of Formula 1 and pharmaceutically acceptable salts, solvates, chelates, non-covalent complexes, prodrugs, and mixtures thereof, is administered in combination with an anti-inflammatory agent. Anti-inflammatory agents include but are not limited to NSAIDs, non-specific and COX- 2 specific cyclooxgenase enzyme inhibitors, gold compounds, corticosteroids, methotrexate, tumor necrosis factor receptor (TNF) receptors antagonists, immunosuppressants and methotrexate.

[00211] Examples of NSAIDs include, but are not limited to ibuprofen, flurbiprofen, naproxen and naproxen sodium, diclofenac, combinations of diclofenac sodium and misoprostol, sulindac, oxaprozin, diflunisal, piroxicam, indomethacin, etodolac, fenoprofen calcium, ketoprofen, sodium nabumetone, sulfasalazine, tolmetin sodium, and hydroxychloroquine. Examples of NSAIDs also include COX-2 specific inhibitors (i.e., a compound that inhibits COX-2 with an IC_{50} that is at least 50-fold lower than the IC_{50} for COX-1) such as celecoxib, valdecoxib, lumiracoxib, etoricoxib and/or rofecoxib.

[00212] In a further embodiment, the anti-inflammatory agent is a salicylate. Salicylates include but are not limited to acetylsalicylic acid or aspirin, sodium salicylate, and choline and magnesium salicylates.

[00213] The anti-inflammatory agent may also be a corticosteroid. For example, the corticosteroid may be chosen from cortisone, dexamethasone, methylprednisolone, prednisolone, prednisolone sodium phosphate, and prednisone.

[00214] In additional embodiments the anti-inflammatory therapeutic agent is a gold compound such as gold sodium thiomalate or auranofin.

[00215] The invention also includes embodiments in which the anti-inflammatory agent is a metabolic inhibitor such as a dihydrofolate reductase inhibitor, such as methotrexate or a dihydroorotate dehydrogenase inhibitor, such as leflunomide.

[00216] Other embodiments of the invention pertain to combinations in which at least one anti-inflammatory compound is an anti-C5 monoclonal antibody (such as eculizumab or pexelizumab), a TNF antagonist, such as entanercept, or infliximab, which is an anti-TNF alpha monoclonal antibody.

[00217] Still other embodiments of the invention pertain to combinations in which at least one active agent is an immunosuppressant compound such as methotrexate, leflunomide, cyclosporine, tacrolimus, azathioprine, or mycophenolate mofetil.

[00218] Dosage levels of the order, for example, of from 0.1 mg to 140 mg per kilogram of body weight per day can be useful in the treatment of the above-indicated conditions (0.5 mg to 7 g per patient per day). The amount of active ingredient that may be combined with the vehicle to produce a single dosage form will vary depending upon the host treated and the particular mode of administration. Dosage unit forms will generally contain from 1 mg to 500 mg of an active ingredient.

[00219] Frequency of dosage may also vary depending on the compound used and the particular disease treated. In some embodiments, for example, for the treatment of an allergic disorder and/or autoimmune and/or inflammatory disease, a dosage regimen of 4 times daily or less is used. In some embodiments, a dosage regimen of 1 or 2 times daily is used. It will be understood, however, that the specific dose level for any particular patient will depend upon a variety of factors including the activity of the specific compound employed, the age, body weight, general health, sex, diet, time of administration, route of administration, and rate of excretion, drug combination and the severity of the particular disease in the patient undergoing therapy.

[00220] A labeled form of a compound of the invention can be used as a diagnostic for identifying and/or obtaining compounds that have the function of modulating an activity of a kinase as described herein. The compounds of the invention may additionally be used for validating, optimizing, and standardizing

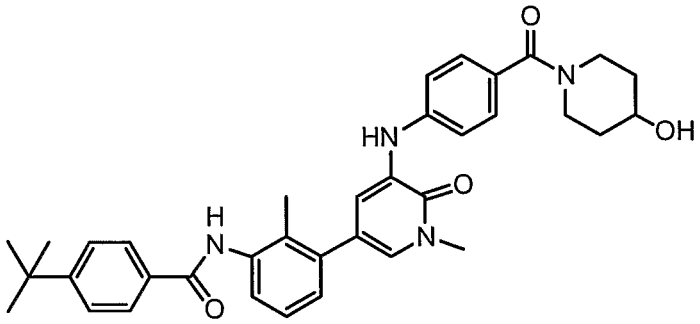
bioassays.

[00221] By "labeled" herein is meant that the compound is either directly or indirectly labeled with a label which provides a detectable signal, e.g., radioisotope, fluorescent tag, enzyme, antibodies, particles such as magnetic particles, chemiluminescent tag, or specific binding molecules, etc. Specific binding molecules include pairs, such as biotin and streptavidin, digoxin and antidigoxin etc. For the specific binding members, the complementary member would normally be labeled with a molecule which provides for detection, in accordance with known procedures, as outlined above. The label can directly or indirectly provide a detectable signal.

[00222] The invention is further illustrated by the following non-limiting examples.

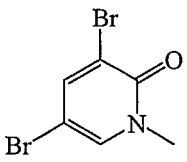
Example 1

4-tert-Butyl-N-(3-{5-[4-(4-hydroxy-piperidine-1-carbonyl)-phenylamino]-1-methyl-6-oxo-1,6-dihydro-pyridin-3-yl}-2-methyl-phenyl)-benzamide



(8)

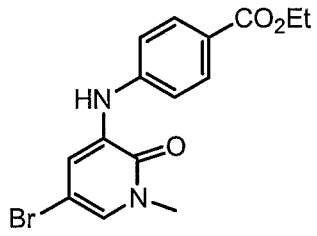
3,5-Dibromo-1-methyl-1H-pyridin-2-one (1)



(1)

[00223] A 1-L round-bottomed flask equipped with a magnetic stirrer was charged with 3,5-dibromo-1H-pyridin-2-one (7.0 g, 27.7 mmol), anhydrous DMF (280 mL) and powdered potassium carbonate (-350 mesh, 8.4 g, 61.1 mmol), and the suspension stirred for 15 min at ambient temperature. After this time, methyl iodide (4.3 g, 30.5 mmol) was added, and the mixture was stirred at room temperature under nitrogen for a further 18 h. The reaction mixture was then diluted with water (200 mL), extracted with ethyl acetate (3 × 250 mL), dried over sodium sulfate and concentrated in vacuo. The resulting residue was purified by flash chromatography on silica to give an 84% yield (6.2 g) of 3,5-dibromo-1-methyl-1H-pyridin-2-one **(1)** as an off-white solid: mp 87-88 °C; MS (ESI+) *m/z* 266 (M+H).

4-(5-Bromo-1-methyl-2-oxo-1,2-dihydropyridin-3-ylamino)-benzoic acid ethyl ester (2)

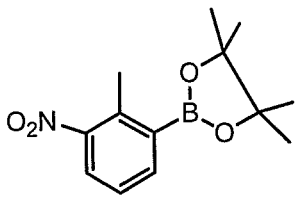


(2)

[00224] A solution of 3,5-dibromo-1-methyl-1*H*pyridin-2-one **(1)** (990 g; 3.7 mmol) in toluene (12 mL) was sparged with argon for 15 minutes. Ethyl 4-aminobenzoate (740 mg; 4.5 mmol), racemic-2,2'-bis(diphenylphosphino)-1,1'-binaphthyl (170 mg, 0.28 mmol), tris(dibenzylideneacetone)dipalladium(0) (170 mg, 0.19 mmol) and cesium carbonate (1.7 g, 5.2 mmol) were then added. The reaction tube was then sealed and heated at 120 °C for 2 d. The mixture was cooled to room temperature, diluted with water (50 mL) and extracted with EtOAc (3x50 mL). The combined organic layers were washed with and brine (1x100mL), dried over sodium sulfate and concentrated *in vacuo*. The crude residue was purified by flash chromatography (9:1 – 1:1, hexanes/EtOAc, gradient) to give 4-(5-bromo-1-methyl-2-

oxo-1,2-dihydropyridin-3-ylamino)-benzoic acid ethyl ester **(2)** as a light brown solid (380 mg).

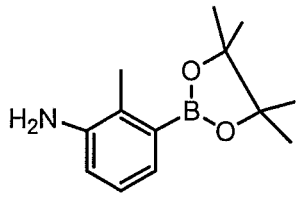
4,4,5,5-Tetramethyl-2-(2-methyl-3-nitro-phenyl)-[1,3,2]dioxaborolane (3)



(3)

[00226] A 1-L three-neck round-bottomed flask equipped with a mechanical stirrer and thermoregulator was purged with nitrogen and charged with 2-bromo-6-nitrotoluene (60.2 g; 278mmol), bis(pinacolato)diboron (85.2 g; 336mmol), potassium acetate (82.4 g; 840mmol) and DMSO (320mL). A stream of nitrogen was passed through the resulting suspension for 30 min, [1,1' bis(diphenylphosphino)-ferrocene]dichloropalladium (II), complex with dichloromethane (1:1) (7.60 g; 9.30mmol) was then added and the reaction heated at 85 °C for 20 h. After this time the mixture was cooled to ambient temperature, poured into a mixture of water (1300mL) and M*t*BE (500mL) and treated with Cellpure P65 (150 cc). The resulting suspension was filtered through a pad of Cellpure P65 (200 cc) packed onto a fritted funnel (ID 185 mm). The filter cake was washed with M*t*BE (3 × 180mL) and the organic layer of the filtrate separated, washed with water (3 × 1L) and dried over sodium sulfate. After filtering off sodium sulfate, the filtrate was concentrated and purified by flash chromatography to afford 4,4,5,5-tetramethyl-2-(2-methyl-3-nitro-phenyl)-[1,3,2]dioxaborolane **(3)** as a light yellow solid: mp 52-53 °C; MS (APCI+) *m/z* 264 (M+H).

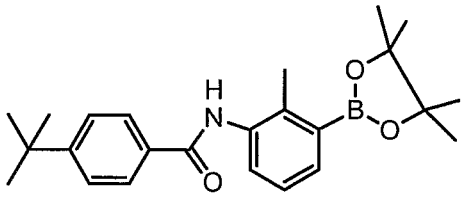
2-Methyl-3-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenylamine (4)



(4)

[00227] A 500-mL round-bottomed flask equipped with a magnetic stirrer was charged with 4,4,5,5-Tetramethyl-2-(2-methyl-3-nitro-phenyl)-[1,3,2]dioxaborolane **(3)** (8.44 g; 32.1mmol) and methanol (150mL). The reaction flask was twice evacuated and back-filled with argon. 10% Palladium on charcoal (50% wet, 425 mg dry weight) was then added to the solution, and the reaction flask evacuated and back-filled with hydrogen three times. The reaction was then stirred under balloon pressure of hydrogen at room temperature for 13 h. After this time, the flask was twice evacuated and back-filled with argon, then filtered through a pad of Celite 521 and the filtrate concentrated in vacuo. The resulting residue was dried under high vacuum for 1 d to afford a quantitative yield (8.16 g) of 2-methyl-3-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenylamine **(4)** as a white solid: mp 110-112 °C; MS (ESI+) *m/z* 234 (M+H).

4-tert-Butyl-N-[2-methyl-3-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-benzamide (5)

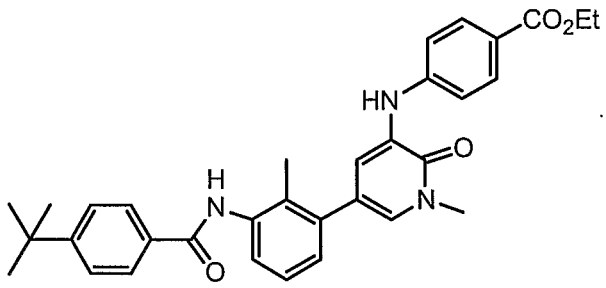


(5)

[00228] A solution of 4-tert-butylbenzoyl chloride (5.24g; 26.7mmol) in dichloromethane (40mL) was added portionwise to a solution of 2-methyl-3-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenylamine **(4)** (6.22g; 26.7mmol) and

triethylamine (5.6mL; 40.1mmol) in dichloromethane (60mL) and the mixture was stirred at room temperature for 16hr. Water (100mL) was added and the mixture extracted with dichloromethane (3x70mL). The combined organic layers were washed with water (2x100mL) and brine (1x100mL), dried over magnesium sulfate and evaporated under reduced pressure to give 4-tert-butyl-N-[2-methyl-3-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-benzamide **(5)** as a white solid (9.7g).

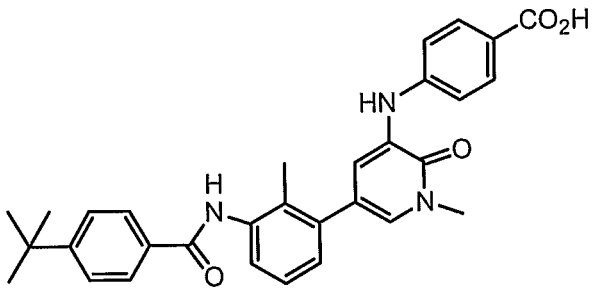
4-{5-[3-(4-tert-Butyl-benzoylamino)-2-methylphenyl]-1-methyl-2-oxo-1,2-dihydro-pyridin-3-ylamino}-benzoic acid ethyl ester (6)



(6)

[00229] A mixture of 4-(5-bromo-1-methyl-2-oxo-1,2-dihydropyridin-3-ylamino)-benzoic acid ethyl ester **(2)** (380 mg; 1.1 mmol), 4-tert-butyl-N-[2-methyl-3-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-benzamide **(5)** (510 mg; 1.3 mmol), tetrakis(triphenylphosphine)palladium (130 mg; 0.1 mmol), 1N sodium carbonate (1.6 mL; 3.2 mmol), and 1,2-dimethoxyethane (8 mL) was heated at 100 °C in a sealed pressure vessel for 16h. The mixture was cooled to room temperature, treated with water (70 mL) and extracted with ethyl acetate (3x60 mL). The combined organic extracts were washed with water (1x40 mL) and brine (1x40 mL), dried over sodium sulfate and concentrated *in vacuo*. The crude residue was purified by flash chromatography (3:1-1:3, hexane/EtOAc, gradient) to give 4-{5-[3-(4-tert-butyl-benzoylamino)-2-methylphenyl]-1-methyl-2-oxo-1,2-dihydropyridin-3-ylamino}-benzoic acid ethyl ester **(6)** as a brown solid (460 mg).

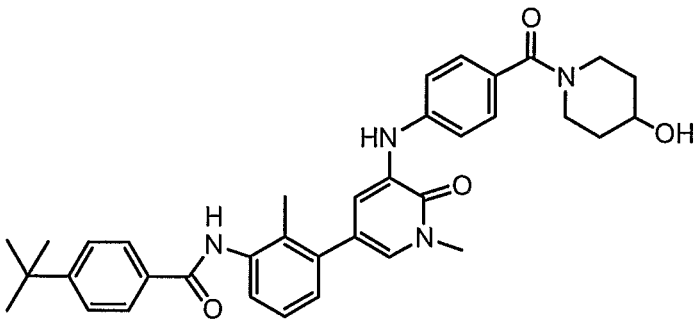
4-{5-[3-(4-tert-Butyl-benzoylamino)-2-methylphenyl]-1-methyl-2-oxo-1,2-dihydropyridin-3-ylamino}-benzoic acid (7)



(7)

[00230] A mixture of 4-{5-[3-(4-tert-butyl-benzoylamino)-2-methylphenyl]-1-methyl-2-oxo-1,2-dihydropyridin-3-ylamino}-benzoic acid ethyl ester **(6)** (460 mg; 0.86 mmol), 1N NaOH (10 mL), and ethanol (10 mL) was heated at reflux for 1.5h. The mixture was cooled to room temperature, the resulting slurry was washed with ethyl acetate (2x40 mL), and the ethyl acetate was decanted off. The aqueous slurry was taken to pH 5 with 1N HCl, filtered, washed with water and then diethyl ether to yield 4-{5-[3-(4-tert-butyl-benzoylamino)-2-methyl-phenyl]-1-methyl-2-oxo-1,2-dihydropyridin-3-ylamino}-benzoic acid **(7)** as a light brown solid (248 mg), MS 510.34 (M+H).

4-tert-Butyl-N-(3-{5-[4-(4-hydroxy-piperidine-1-carbonyl)-phenylamino]-1-methyl-6-oxo-1,6-dihydro-pyridin-3-yl}-2-methyl-phenyl)-benzamide (8)

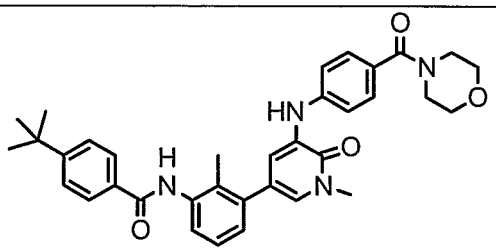


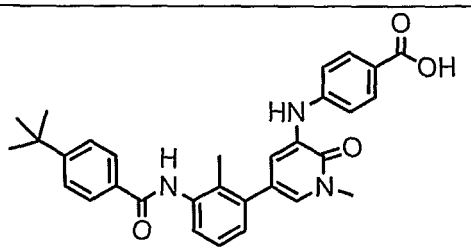
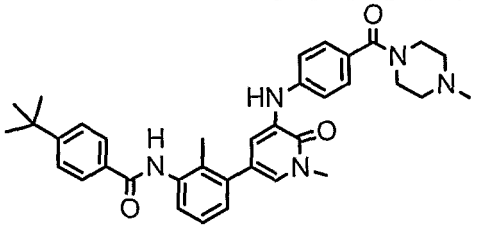
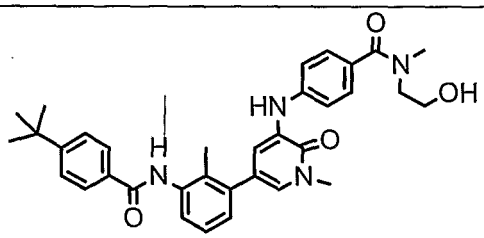
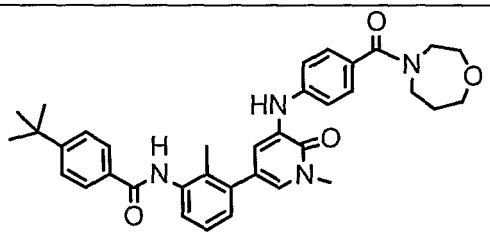
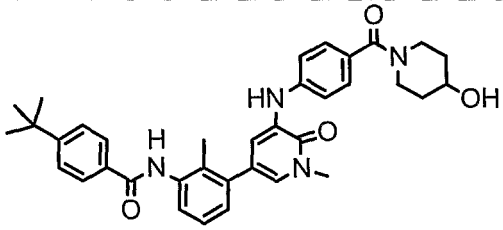
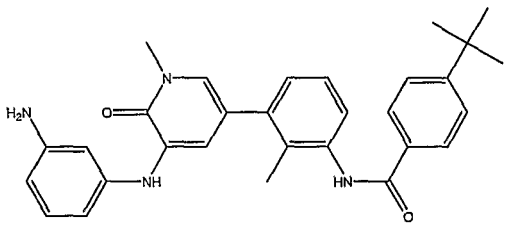
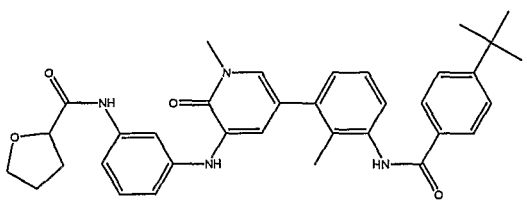
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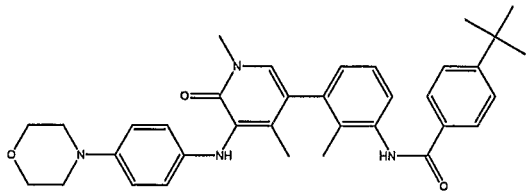
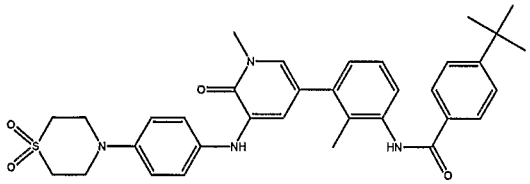
[00231] A solution of 4-{5-[3-(4-tert-butyl-benzoylamino)-2-methyl-phenyl]-1-methyl-2-oxo-1,2-dihydropyridin-3-ylamino}-benzoic acid **(7)** (56 mg; 0.11 mmol), benzotriazol-1-yloxytris(dimethylamino)phosphonium hexafluorophosphate (58 mg; 0.13 mmol) and N,N-dimethylformamide (2 mL) was stirred at room temperature for 0.5h. 4-Hydroxypiperidine (56 mg; 0.55 mmol) was added and the mixture was stirred at room temperature for 16h. Water (15 mL) was added and the mixture was extracted with ethyl acetate (3x30 mL). The combined organic extracts were washed with water (2x30 mL) and brine (1x30 mL), dried over sodium sulfate, and concentrated in vacuo. The residue was slurried with diethyl ether and filtered to give 4-tert-butyl-N-(3-{5-[4-(4-hydroxy-piperidine-1-carbonyl)-phenylamino]-1-methyl-6-oxo-1,6-dihydro-pyridin-3-yl}-2-methyl-phenyl)-benzamide **(8)** as a light brown solid (40 mg), MS 593.41 (M+H)

Example 2

The following compounds were prepared using procedures similar to those described in Example 1.

Structure	Name MW	MS m/z
	4-tert-Butyl-N-(2-methyl-3-{1-methyl-5-[4-(morpholine-4-carbonyl)-phenylamino]-6-oxo-1,6-dihydro-pyridin-3-yl}-phenyl)-benzamide 578.70	579.51

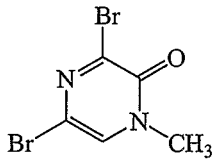
	4-{5-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-1-methyl-2-oxo-1,2-dihydro-pyridin-3-ylamino}-benzoic acid 509.60	510.34
	4-tert-Butyl-N-(2-methyl-3-{1-methyl-5-[4-(4-methyl-piperazine-1-carbonyl)-phenylamino]-6-oxo-1,6-dihydro-pyridin-3-yl}-phenyl)-benzamide 591.7	592.37
	4-tert-Butyl-N-(2-methyl-3-{1-methyl-5-[4-(N-methylethanolamine-2-carbonyl)-phenylamino]-6-oxo-1,6-dihydro-pyrazin-3-yl}-phenyl)-benzamide 566.69	567.32
	4-tert-Butyl-N-(2-methyl-3-{1-methyl-5-[4-([1,4]oxazepane-4-carbonyl)-phenylamino]-6-oxo-1,6-dihydro-pyridin-3-yl}-phenyl)-benzamide 592.73	593.36
	4-tert-Butyl-N-(3-{5-[4-(4-hydroxy-piperidine-1-carbonyl)-phenylamino]-1-methyl-6-oxo-1,6-dihydro-pyridin-3-yl}-2-methyl-phenyl)-benzamide 592.73	593.41
	N-{3-[5-(3-Amino-phenylamino)-1-methyl-6-oxo-1,6-dihydro-pyridin-3-yl]-2-methyl-phenyl}-4-tert-butyl-benzamide 480.25	481.17
	Tetrahydro-furan-2-carboxylic acid (3-{5-[3-(4-tert-butyl-benzoylamino)-2-methyl-phenyl]-1-methyl-2-oxo-1,2-dihydro-pyridin-3-ylamino}-phenyl)-amide	578.37

	578.29	
	4-tert-Butyl-N-{3-[1,4-dimethyl-5-(4-morpholin-4-yl-phenylamino)-6-oxo-1,6-dihydro-pyridin-3-yl]-2-methyl-phenyl}-benzamide 564.31	565.37
	4-tert-Butyl-N-(3-{5-[4-(1,1-dioxo-116-thiomorpholin-4-yl)-phenylamino]-1-methyl-6-oxo-1,6-dihydro-pyridin-3-yl}-2-methyl-phenyl)-benzamide 598.26	599.30

Example 3A

4-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[4-(4-methyl-piperazine-1-carbonyl)-phenylamino]-5-oxo-4, 5-dihydro-pyrazin-2-yl}-phenyl)-benzamide

3,5-dibromo-1-methyl-2(1*H*)pyrazinone (1)



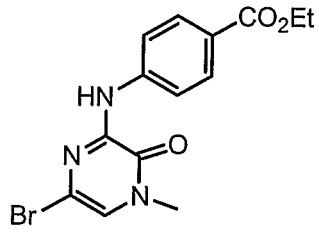
(1)

(J. Heterocycl. Chem. **1983**, *20*, 919)

[00232] A 250-mL three-neck round-bottomed flask equipped with a magnetic stirrer and reflux condenser was charged with 1,2-dichlorobenzene (100mL) and oxalyl bromide (60.6 g; 281mmol). To the solution was added methylaminoacetonitrile (7.01 g; 65.8mmol) and the reaction heated under nitrogen to

80 °C. After 18 h the resulting mixture was cooled to room temperature, evaporated under reduced pressure and the resulting residue purified by flash chromatography to afford 3,5-dibromo-1-methyl-2(1*H*)pyrazinone **(1)** (2.87 g, 16%) as an off-white solid: mp 94–95 °C; MS (ESI+) *m/z* 267 (M+H).

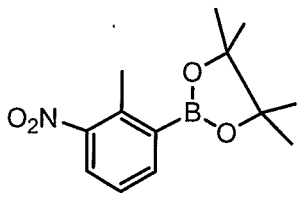
4-(6-Bromo-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino)-benzoic acid ethyl ester (2)



(2)

[00233] A mixture of 3,5-dibromo-1-methyl-2(1*H*)pyrazinone **(1)** (21.3g; 79.5mmol), ethyl 4-aminobenzoate (13.1g; 79.5mmol), and 1-methyl-2-pyrollidinone (10mL) was heated at 130 degrees for 1hr. The mixture was cooled to room temperature, diluted with dichloromethane and filtered to give a dull brown solid. This was slurried with 0.5N NaOH, filtered, washed with water and diethyl ether to give 4-(6-bromo-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino)-benzoic acid ethyl ester **(2)** as a light brown solid (21.3g)

4,4,5,5-Tetramethyl-2-(2-methyl-3-nitro-phenyl)-[1,3,2]dioxaborolane (3)

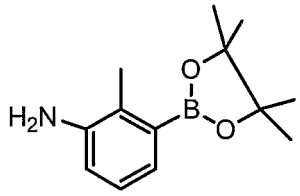


(3)

[00234] A 1-L three-neck round-bottomed flask equipped with a mechanical

stirrer and thermoregulator was purged with nitrogen and charged with 2-bromo-6-nitrotoluene (60.2 g; 278mmol), bis(pinacolato)diboron (85.2 g; 336mmol), potassium acetate (82.4 g; 840mmol) and DMSO (320mL). A stream of nitrogen was passed through the resulting suspension for 30 min, [1,1' bis(diphenylphosphino)-ferrocene]dichloropalladium (II), complex with dichloromethane (1:1) (7.60 g; 9.30mmol) was then added and the reaction heated at 85 °C for 20 h. After this time the mixture was cooled to ambient temperature, poured into a mixture of water (1300mL) and M*t*BE (500mL) and treated with Cellpure P65 (150 cc). The resulting suspension was filtered through a pad of Cellpure P65 (200 cc) packed onto a fritted funnel (ID 185 mm). The filter cake was washed with M*t*BE (3 × 180mL) and the organic layer of the filtrate separated, washed with water (3 × 1L) and dried over sodium sulfate. After filtering off sodium sulfate, the filtrate was concentrated and purified by flash chromatography to afford 4,4,5,5-tetramethyl-2-(2-methyl-3-nitro-phenyl)-[1,3,2]dioxaborolane **(3)** as a light yellow solid: mp 52-53 °C; MS (APCI+) *m/z* 264 (M+H).

2-Methyl-3-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenylamine (4)

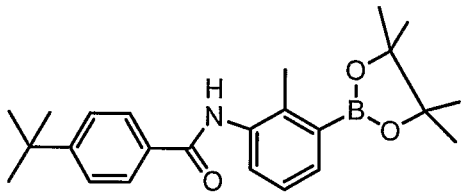


(4)

[00235] A 500-mL round-bottomed flask equipped with a magnetic stirrer was charged with 4,4,5,5-Tetramethyl-2-(2-methyl-3-nitro-phenyl)-[1,3,2]dioxaborolane **(3)** (8.44 g; 32.1mmol) and methanol (150mL). The reaction flask was twice evacuated and back-filled with argon. 10% Palladium on charcoal (50% wet, 425 mg dry weight) was then added to the solution, and the reaction flask evacuated and back-filled with hydrogen three times. The reaction was then stirred under balloon pressure of hydrogen at room temperature for 13 h. After this time, the flask was twice evacuated and back-filled with argon, then filtered through a pad of Celite 521 and the

filtrate concentrated in vacuo. The resulting residue was dried under high vacuum for 1 d to afford a quantitative yield (8.16 g) of 2-methyl-3-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenylamine **(4)** as a white solid: mp 110-112 °C; MS (ESI+) *m/z* 234 (M+H).

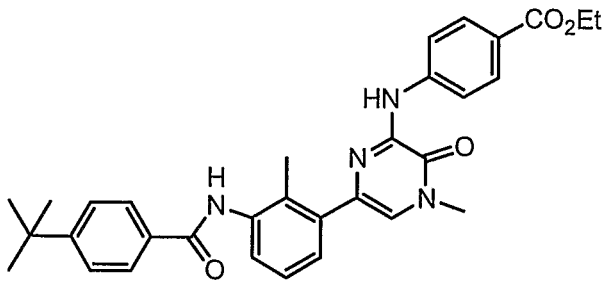
4-tert-Butyl-N-[2-methyl-3-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-benzamide (5)



(5)

[00236] A solution of 4-tert-butylbenzoyl chloride (5.24g; 26.7mmol) in dichloromethane (40mL) was added portionwise to a solution of 2-methyl-3-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenylamine **(4)** (6.22g; 26.7mmol) and triethylamine (5.6mL; 40.1mmol) in dichloromethane (60mL) and the mixture was stirred at room temperature for 16hr. Water (100mL) was added and the mixture extracted with dichloromethane (3x70mL). The combined organic layers were washed with water (2x100mL) and brine (1x100mL), dried over magnesium sulfate and evaporated under reduced pressure to give 4-tert-butyl-N-[2-methyl-3-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-benzamide **(5)** as a white solid, 9.7g.

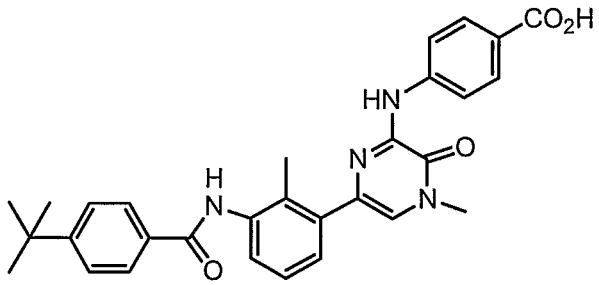
4-{6-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-benzoic acid ethyl ester (6)



(6)

[00237] A mixture of 4-(6-bromo-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino)-benzoic acid ethyl ester **(2)** (340mg; 0.97mmol), 4-tert-butyl-N-[2-methyl-3-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-benzamide **(5)** (457mg; 1.16mmol), tetrakis(triphenylphosphine)palladium (56mg; 0.05mmol), 1N sodium carbonate (2.9mL; 2.9mmol), and 1,2-dimethoxyethane (30mL) was heated at 100 degrees in a sealed pressure vessel for 16hr. The mixture was cooled to room temperature, treated with water (70mL) and extracted with ethyl acetate (3x60mL). The combined organic extracts were washed with water (2x40mL) and brine (1x40mL), dried over magnesium sulfate, and evaporated under reduced pressure. The resulting residue was triturated with diethyl ether/dichloromethane to give 4-{6-[3-(4-tert-butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-benzoic acid ethyl ester **(6)** as a gray solid (330mg), MS 539.49 (M+H).

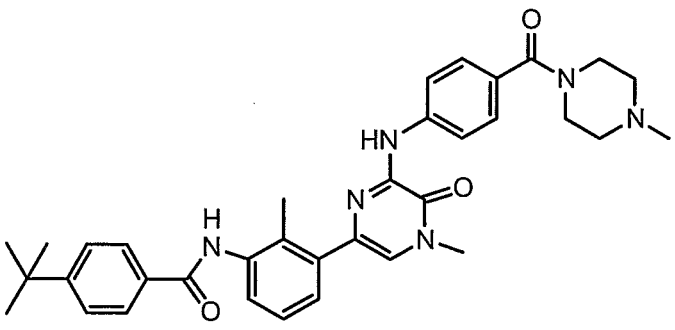
4-{6-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-benzoic acid (7)



(7)

[00238] A mixture of give 4-{6-[3-(4-tert-butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-benzoic acid ethyl ester **(6)** (300mg; 0.56mmol), 1N NaOH (5mL), and ethanol (5mL) was heated at reflux for 1hr. The mixture was cooled to room temperature and the resulting slurry was washed with ethyl acetate (2x40mL) and the ethyl acetate was decanted off. The aqueous slurry was taken to pH 5 with 1N HCl, filtered, washed with water and then diethyl ether to give 4-{6-[3-(4-tert-butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-benzoic acid **(7)** as a gray solid (110mg), MS 511.46 (M+H).

4-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[4-(4-methyl-piperazine-1-carbonyl)-phenylamino]-5-oxo-4, 5-dihydro-pyrazin-2-yl}-phenyl)-benzamide (8)



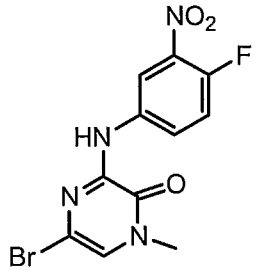
(8)

[00239] A solution of 4-{6-[3-(4-tert-butyl-benzoylamino)-2-methyl-phenyl]-

4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-benzoic acid (7) (80mg; 0.16mmol), benzotriazol-1-yloxytris(dimethylamino)phosphonium hexafluorophosphate (69mg; 0.16mmol), N,N-diisopropylethylamine (0.09mL; 0.48mmol), and N,N-dimethylformamide (1mL) was stirred at room temperature for 0.5hr. N-Methylpiperazine (80mg; 0.8mmol) was added and the mixture was stirred at room temperature for 16hr. Water (30mL) was added and the mixture was extracted with ethyl acetate (3x60mL). The combined organic extracts were washed with water (2x30mL) and brine (1x30mL), dried over magnesium sulfate, and evaporated under reduced pressure. The residue was slurried with diethyl ether and filtered to give 4-tert-butyl-N-(2-methyl-3-{4-methyl-6-[4-(4-methyl-piperazine-1-carbonyl)-phenylamino]-5-oxo-4, 5-dihydro-pyrazin-2-yl}-phenyl)-benzamide (8) as a cream solid (50mg), MS 593.35 (M+H)

Example 3B

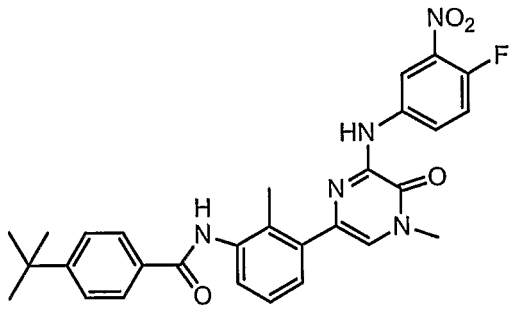
5-Bromo-3-(4-fluoro-3-nitro-phenylamino)-1-methyl-1H-pyrazin-2-one (1)



(1)

[00240] A mixture of 3,5-dibromo-1-methyl-2(1*H*)pyrazinone (10g; 37.5mmol), 4-fluoro-3-nitroaniline (5.9g; 37.5mmol), and 1-methyl-2-pyrollidinone (30mL) was heated at 140 degrees for 1hr. The mixture was cooled to room temperature, diluted with ethyl acetate (100mL) and filtered to give 5-bromo-3-(4-fluoro-3-nitro-phenylamino)-1-methyl-1H-pyrazin-2-one **(1)** as a yellow solid (8.9g).

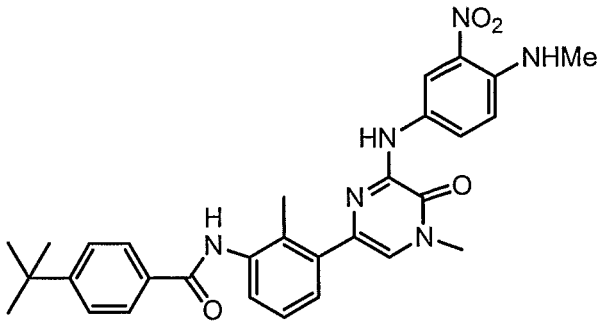
4-tert-Butyl-N-{3-[6-(4-fluoro-3-nitro-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide (2)



(2)

[00241] A mixture of 5-bromo-3-(4-fluoro-3-nitro-phenylamino)-1-methyl-1H-pyrazin-2-one (1) (8.8g; 25.7mmol), 4-tert-butyl-N-[2-methyl-3-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-benzamide (11.1g; 28.3mmol), tetrakis(triphenylphosphine)palladium (1.48g; 1.28mmol), 1N sodium carbonate (77mL; 77mmol), and 1,2-dimethoxyethane (100mL) was heated at 100 degrees in a sealed pressure vessel for 16hr. The mixture was cooled to room temperature, filtered, and the residue washed with water (3 x 60mL). The solid was slurried with ethyl acetate for 1hr, filtered, and washed with diethyl ether to give 4-tert-butyl-N-{3-[6-(4-fluoro-3-nitro-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide (2) as a dull yellow solid (13g).

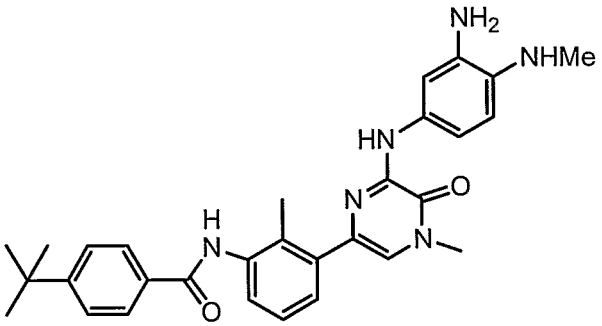
4-tert-Butyl-N-{2-methyl-3-[4-methyl-6-(4-methylamino-3-nitro-phenylamino)-5-oxo-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide (3)



(3)

[00242] A mixture of give 4-tert-butyl-N-{3-[6-(4-fluoro-3-nitro-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide (2) (600mg; 1.13mmol), methylamine (5mL of a 2M solution in THF), and 1-methyl-2-pyrollidinone (10mL) was heated at 60 degrees in a sealed pressure vessel for 16hr. The mixture was cooled to room temperature, treated with water (30mL) and filtered to give 4-tert-butyl-N-{2-methyl-3-[4-methyl-6-(4-methylamino-3-nitro-phenylamino)-5-oxo-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide (3) as a red solid (501mg).

N-{3-[6-(3-Amino-4-methylamino-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-4-tert-butyl-benzamide (4)

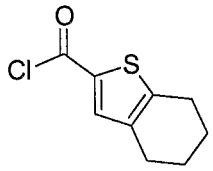


(4)

[00243] A mixture of 4-tert-butyl-N-{2-methyl-3-[4-methyl-6-(4-methylamino-3-nitro-phenylamino)-5-oxo-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide (3) (500mg), 10% palladium-on-carbon (100mg), ethanol (50mL), and ethyl acetate (100mL) was hydrogenated at room temperature and 40psi hydrogen for 16hr. The mixture was filtered through a celite pad, washing with ethyl acetate (2 x 100mL). The combined filtrates were evaporated to give N-{3-[6-(3-amino-4-methylamino-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-4-tert-butyl-benzamide (4) as a yellow solid (402mg), m/z 512.08 (MH+).

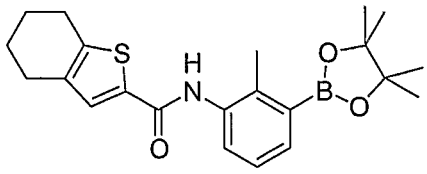
Example 3C

4,5,6,7-Tetrahydro-benzo[b]thiophene-2-carbonyl chloride (1):



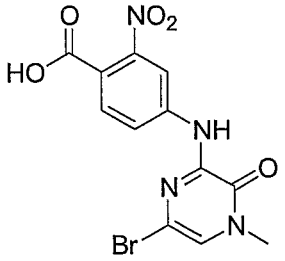
[00244] 4,5,6,7-Tetrahydro-benzo[b]thiophene-2-carboxylic acid (1.0g, 5.50 mmol) is dissolved in dichloromethane [DCM] (25 mL) that contains 5 drops of N,N-dimethylformamide [DMF] under nitrogen and cooled to 0°C. Oxalyl chloride (13.7 mL of a 2.0M solution in DCM) is added via syringe and allowed to warm to RT over 1 hour. All solvent is then removed under reduced pressure, and the resultant oil is reduced from toluene (3 x 20 mL) to remove residual oxalyl chloride. The residue is then dissolved in ethyl acetate and washed with saturated sodium bicarbonate (1 x 100mL), then washed with saturated sodium chloride (1 x 100mL) and dried over sodium sulfate. The solution is then filtered and concentrated under reduced pressure to give 4,5,6,7-tetrahydro-benzo[b]thiophene-2-carbonyl chloride **(1)** as an off-white solid (1.03g).

4,5,6,7-Tetrahydro-benzo[b]thiophene-2-carboxylic acid [2-methyl-3-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-amide (2):



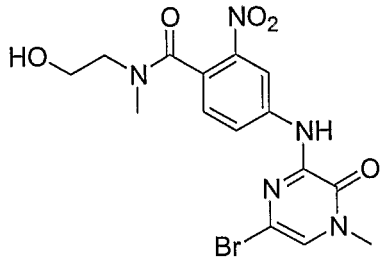
[00245] 2-Methyl-3-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenylamine (1.20g, 5.16 mmol, 1.0 equiv) and pyridine (0.42mL, 25.8 mmol) are dissolved in DCM (40 mL) at 0°C under a nitrogen atmosphere. 4,5,6,7-Tetrahydro-benzo[b]thiophene-2-carbonyl chloride **(1)** (1.03g, 5.16 mmol) is then added in portions over 5 min and allowed to react warming to RT over 60 min. All solvent is then removed under reduced pressure, and the resultant oil is reduced from toluene (3 x 20 mL) to remove residual pyridine. The residue is then dissolved in ethyl acetate and washed with sodium hydroxide (1N, 1 x 100 mL), then washed with saturated sodium chloride (1 x 100mL) and dried over sodium sulfate. The solution is then filtered and concentrated under reduced pressure to give 4,5,6,7-tetrahydro-benzo[b]thiophene-2-carboxylic acid [2-methyl-3-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-amide **(2)** as an off-white solid (1.87g).

4-(6-Bromo-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino)-2-nitro-benzoic acid (3):



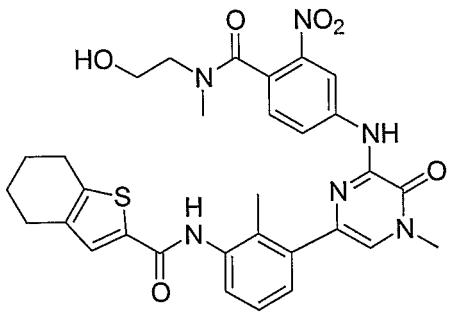
[00246] 3,5-Dibromo-1-methyl-1H-pyrazin-2-one (1.0g, 3.73 mmol) and 4-amino-2-nitrobenzoic acid (0.68g, 3.73 mmol) are dissolved in isopropanol (20 mL) and heated at 90°C for 4 hours. The reaction is cooled to room temperature and the resulting suspension is filtered. The filter cake is then washed with ethyl ether (3 x 100mL) and air dried to give 4-(6-bromo-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino)-2-nitro-benzoic acid **(3)** as a tan solid (1.17g).

4-(6-Bromo-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino)-N-(2-hydroxy-ethyl)-
N-methyl-2-nitro-benzamide (4):



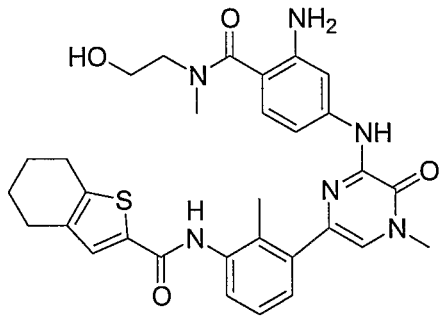
[00247] 4-(6-Bromo-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino)-2-nitro-benzoic acid **(3)** (1.0g, 2.72 mmol), (benzotriazol-1-yloxy)tris(dimethylamino)phosphonium hexafluorophosphate [BOP] (120 mg, 2.72 mmol,), diisopropylethylamine (1.42 mL, 8.15 mmol) and 2-methylaminoethanol (0.33 mL, 4.07 mmol) are dissolved in DMF (25mL) at room temperature and allowed to react for 60 min. The reaction is quenched by the addition of water (120 mL) and the resulting suspension was allowed to stir for 15 min. The suspension is then filtered, washed with water (3 x 50mL) and then air-dried to give 4-(6-bromo-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino)-N-(2-hydroxy-ethyl)-
N-methyl-2-nitro-benzamide **(4)** as a yellow solid (1.05g).

4,5,6,7-Tetrahydro-benzo[b]thiophene-2-carboxylic acid [3-(6-{4-[(2-hydroxy-ethyl)-methyl-carbamoyl]-3-nitro-phenylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-amide (5):



[00248] 4-(6-Bromo-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino)-N-(2-hydroxy-ethyl)-N-methyl-2-nitro-benzamide **(4)** (250 mg, 0.59 mmol, 1.0 equiv), 4,5,6,7-Tetrahydro-benzo[b]thiophene-2-carboxylicacid[2-methyl-3-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-amide (257 mg, 0.65 mmol) and tetrakis (triphenylphosphine)palladium (68mg, 0.06mmol) are dissolved in 1,4-dioxane (2.0mL) and sodium carbonate (1N, 1.0mL) and heated in a microwave glass reactor for 6 minutes at 140°C. Once completed the reaction is transferred to a seperatory funnel with ethyl acetate (50mL) and washed with saturated sodium bicarbonate (1 x 100mL), then washed with saturated sodium chloride (1 x 100mL) and dried over sodium sulfate. The solution is then filtered and concentrated under reduced pressure. The resulting residue is then triturated with DCM and hexane to give 4,5,6,7-tetrahydro-benzo[b]thiophene-2-carboxylic acid [3-(6-{4-[(2-hydroxy-ethyl)-methyl-carbamoyl]-3-nitro-phenylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-amide **(5)** as a light yellow solid (225mg).

4,5,6,7-Tetrahydro-benzo[b]thiophene-2-carboxylic acid [3-(6-{3-amino-4-[(2-hydroxy-ethyl)-methyl-carbamoyl]-phenylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-amide (6):

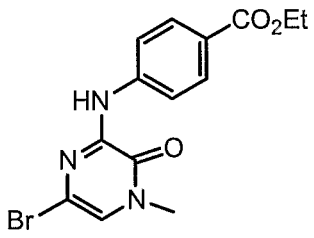


[00249] 4,5,6,7-Tetrahydro-benzo[b]thiophene-2-carboxylic acid [3-(6-{4-[(2-hydroxy-ethyl)-methyl-carbamoyl]-3-nitro-phenylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-amide **(5)** (200mg, 0.32 mmol) is dissolved in a mixture of ethanol (25mL) and water (5.0mL). Ammonium chloride (200mg, 3.81 mmol) and iron powder (200mg, 3.58 mmol) are then added and the reaction is

allowed to proceed at 95°C for 30min. The reaction contents are then hot-filtered through celite and then transferred to a seperatory funnel with ethyl acetate (100 mL). The crude solution is then washed with saturated sodium bicarbonate (1 x 100mL), then washed with saturated sodium chloride (1 x 100mL) and dried over sodium sulfate. The solution is then filtered and concentrated under reduced pressure. The resulting residue is then triturated with DCM and ethyl ether to give 4,5,6,7-tetrahydro-benzo[b]thiophene-2-carboxylic acid [3-(6-{3-amino-4-[(2-hydroxy-ethyl)-methyl-carbamoyl]-phenylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-amide **(6)** as an off-white solid (135mg), m/z 587.20 (MH+).

Example 3D

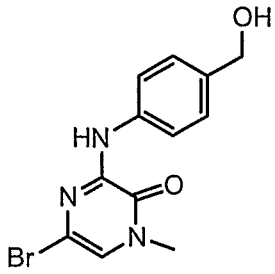
4-(6-Bromo-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino)-benzoic acid ethyl ester (1)



(1)

[00250] A mixture of 3,5-dibromo-1-methyl-2(1*H*)pyrazinone (21.3g; 79.5mmol), ethyl 4-aminobenzoate (13.1g; 79.5mmol), and 1-methyl-2-pyrrolidinone (10mL) was heated at 130 degrees for 1hr. The mixture was cooled to room temperature, diluted with dichloromethane and filtered to give a dull brown solid. This was slurried with 0.5N NaOH, filtered, washed with water and diethyl ether to give 4-(6-bromo-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino)-benzoic acid ethyl ester **(1)** as a light brown solid (21.3g)

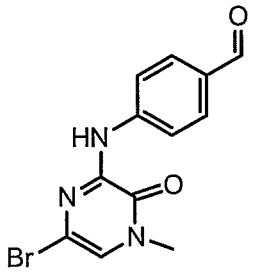
5-Bromo-3-(4-hydroxymethyl-phenylamino)-1-methyl-1H-pyrazin-2-one (2)



(2)

[00251] A slurry of 4-(6-bromo-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino)-benzoic acid ethyl ester **(1)** (7.75g; 22.02mmol) in CH_2Cl_2 (200mL) was cooled to -78 °C under N_2. A solution of DIBAL-H (100mL; 1.0 M in CH_2Cl_2) was added dropwise over 30 min. to the stirring slurry, and the reaction allowed to warm gradually to rt over 30 min. The reaction stirred for 1 hr at rt, and was monitored by LC-MS until only product was observed. The reaction was cooled to 0 °C in an ice bath and was quenched by slow addition of 1.0 N NaOH (75mL). The reaction bilayer was extracted with EtOAc (5x100mL) and the EtOAc layers were pooled, washed with brine and dried over solid Na_2SO_4. After filtering off the solids, the filtrate was evaporated down to an orange-red oil, which was then redissolved in 3mL CH_2Cl_2 and triturated slowly with diethyl ether (20mL) to provide 5-bromo-3-(4-hydroxymethyl-phenylamino)-1-methyl-1H-pyrazin-2-one **(2)** as a light orange solid (3.1g). MS 311.25 & 313.20 (M+H)

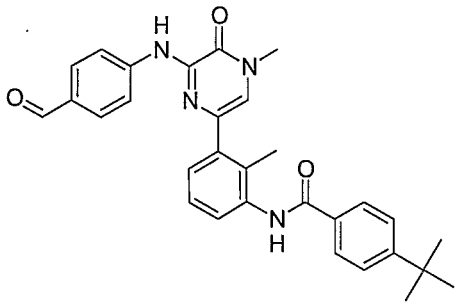
4-(6-Bromo-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino)-benzaldehyde (3)



(3)

[00252] Compound **(2)** (3.1g; 10mmol) was dissolved in 150mL CH_2Cl_2 at rt under N_2. Solid I_2 (5.1g; 20mmol) was added portion-wise to the stirring reaction, followed by catalytic 2,2,6,6-tetramethyl-1-piperdinyloxy, free radical (TEMPO; 0.23g; 1.50mmol). Saturated sodium bicarbonate solution was then added (20 mL) and the reaction allowed to stir overnight at rt under N_2. The resulting light orange solid was filtered off and washed repeatedly with CH_2Cl_2 and diethyl ether until the extractions ran clear and colorless. After drying, 4-(6-bromo-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino)-benzaldehyde **(3)** was obtained in nearly quantitative yields (3.1g) and was carried directly on to the next reaction. MS 308.01 & 310.01 (M+H)

4-tert-Butyl-N-{3-[6-(4-formyl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide (4)

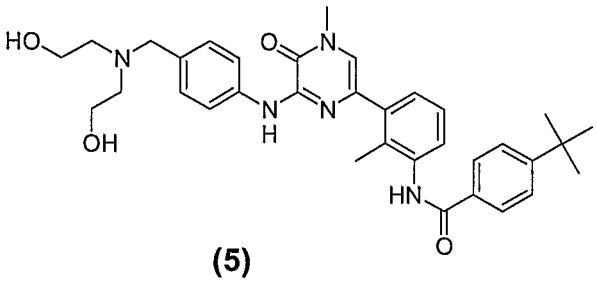


(4)

[00253] A mixture of 4-(6-Bromo-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino)-benzaldehyde **(3)** (2.0g; 6.51mmol), 4-tert-butyl-N-[2-methyl-3-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-benzamide (3.28g; 7.8mmol), tetrakis(triphenylphosphine)palladium (0.75g; 0.65mmol), 1N sodium carbonate (16.0mL), and 1,2-dimethoxyethane (50mL) was heated at 95 °C in a sealed pressure vessel for 12hr. The mixture was cooled to room temperature, treated with water (70mL) and extracted with ethyl acetate (3x100mL). The combined organic extracts were washed with water (2x75mL) and brine (1x75mL), dried over solid sodium sulfate, and evaporated under reduced pressure. The resulting residue was triturated with diethyl ether/dichloromethane to give 4-tert-butyl-N-{3-[6-(4-formyl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-

benzamide **(4)** as a light gray solid (3.6g), MS 495.35 (M+H).

N-{3-[6-(4-{[Bis-(2-hydroxy-ethyl)-amino]-methyl}-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-4-tert-butyl-benzamide (5)

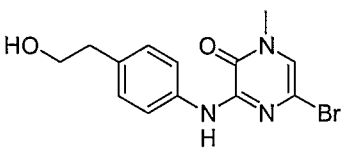


(5)

[00254] 4-tert-butyl-N-{3-[6-(4-formyl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide (4) (110mg; 0.22mmol) was dissolved in methanol (10mL) and 1 mL 2-(2-hydroxy-ethylamino)-ethanol was added. To the stirring reaction solution was then added 0.25mL glacial acetic acid, followed by 0.25g powdered molecular sieves (4Å; activated) and the resulting slurry allowed to stir at rt for 4 hr under N_2, then heated to 50 °C. After 3 hr at 50 °C, the reaction was cooled to rt and excess $NaBH_4$ powder (0.5g) was added portionwise to the stirring slurry. After gas evolution ceased, the reaction slurry was then adsorbed directly onto silica gel and was chromatographed using methanol/CH_2Cl_2 (1:9) as eluent to provide N-{3-[6-(4-{[bis-(2-hydroxy-ethyl)-amino]-methyl}-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-4-tert-butyl-benzamide (5) (75mg) as an off-white solid. MS 584.24 (M+H).

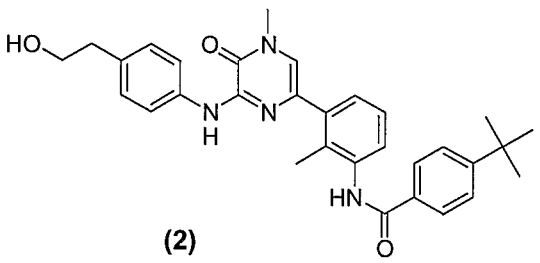
Example 3E

5-Bromo-3-[4-(2-hydroxy-ethyl)-phenylamino]-1-methyl-1H-pyrazin-2-one (1)



[00255] A mixture of 3,5-dibromo-1-methyl-2(1*H*)pyrazinone (2.0g; 7.5mmol), 2-(4-Amino-phenyl)-ethanol (1.0g; 7.3mmol), and 1-methyl-2-pyrrolidinone (1mL) was heated at 120 °C for 1hr. The mixture was cooled to room temperature, diluted with dichloromethane and filtered to give a dull brown oil. This was dissolved in CH_2Cl_2 and washed with 0.01N NaOH, and dried over solid sodium sulfate. After filtration and evaporation of the CH_2Cl_2 layer, the resulting brown solid was chromatographed on silica using methanol/CH_2Cl_2 (1:9) as eluent to provide 2.0g of 5-bromo-3-[4-(2-hydroxy-ethyl)-phenylamino]-1-methyl-1H-pyrazin-2-one **(1)** as a light tan solid. MS 324.23 (M+H).

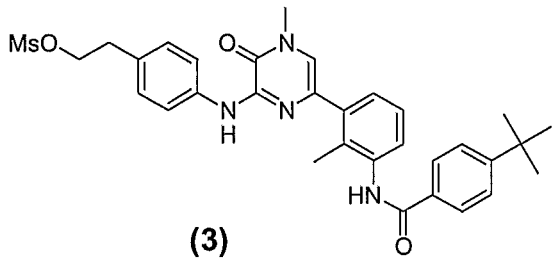
4-tert-Butyl-N-(3-{6-[4-(2-hydroxy-ethyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide (2)



(2)

[00256] A mixture of 5-bromo-3-[4-(2-hydroxy-ethyl)-phenylamino]-1-methyl-1H-pyrazin-2-one **(1)** (1.0g; 3.11mmol), 4-tert-butyl-N-[2-methyl-3-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-benzamide (1.5g; 3.57mmol), tetrakis(triphenylphosphine)palladium (560mg; 0.5mmol), 1N sodium carbonate (8mL), and 1,2-dimethoxyethane (40mL) was heated at 95 °C in a sealed pressure vessel for 16hr. The mixture was cooled to room temperature, treated with water (70mL) and extracted with ethyl acetate (3x60mL). The combined organic extracts were washed with water (2x40mL) and brine (1x40mL), dried over solid sodium sulfate, and evaporated under reduced pressure. The resulting residue was chromatographed on silica using methanol/CH_2Cl_2 (1:9) as eluent to provide 1.2g of 5-bromo-3-[4-(2-hydroxy-ethyl)-phenylamino]-1-methyl-1H-pyrazin-2-one **(2)** as a light tan solid. MS 511.23 (M+H).

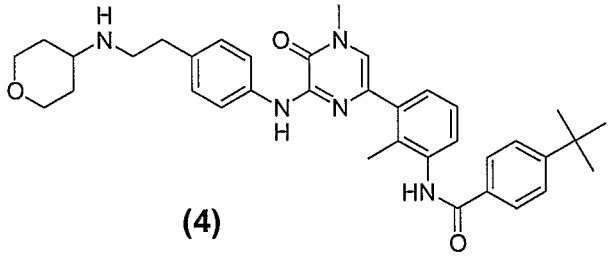
Methanesulfonic acid 2-(4-{6-[3-(4-tert-butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-phenyl)-ethyl ester (3)



(3)

[00257] A solution of 5-bromo-3-[4-(2-hydroxy-ethyl)-phenylamino]-1-methyl-1H-pyrazin-2-one (2) (1.2g; 2.35mmol) in CH_2Cl_2 (30mL) was cooled to 0 °C and 1.5 mL of diisopropylethyl amine was added. A second solution containing 0.75mL mesyl chloride in 3mL CH_2Cl_2 was added dropwise to the stirring reaction solution under N_2 and the reaction allowed to warm to rt for 1hr. 0.1N Sodium hydroxide was then added carefully to the reaction, and the layers separated. The CH_2Cl_2 layer was washed with brine and dried over solid sodium sulfate, then filtered and evaporated to a light red-brown oil (1.5g). The crude methanesulfonic acid 2-(4-{6-[3-(4-tert-butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-phenyl)-ethyl ester (3) was used directly in subsequent reactions.

4-tert-Butyl-N-[2-methyl-3-(4-methyl-5-oxo-6-{4-[2-(tetrahydro-pyran-4-ylamino)-ethyl]-phenylamino}-4,5-dihydro-pyrazin-2-yl)-phenyl]-benzamide (4)



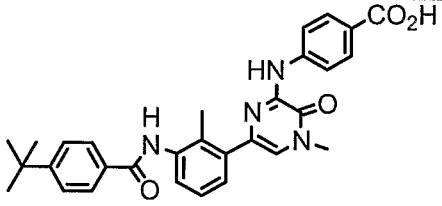
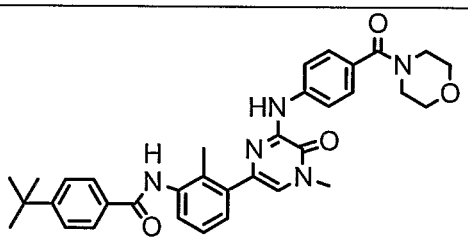
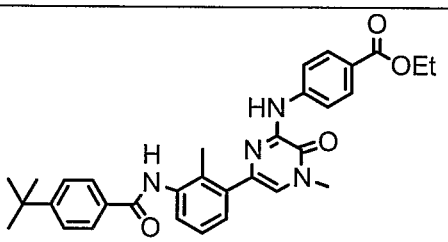
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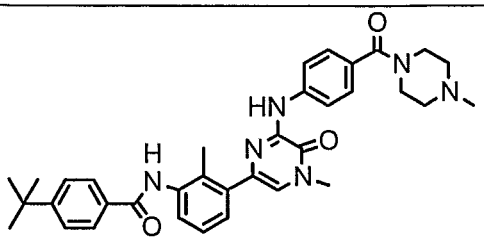
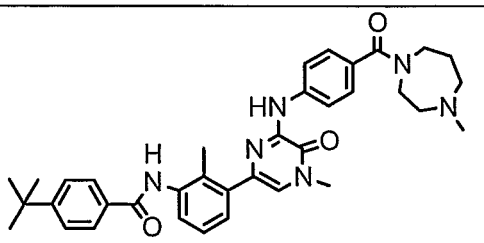
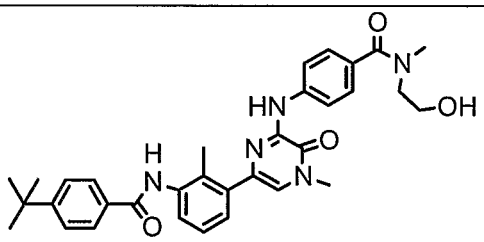
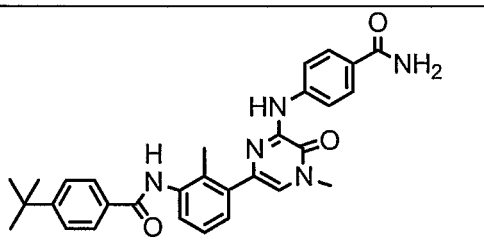
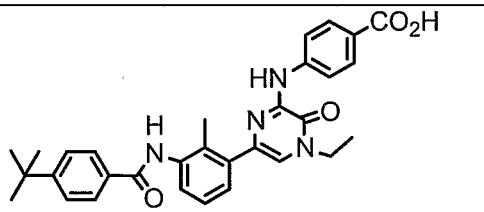
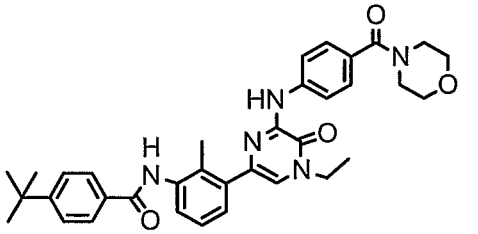
[00258] Methanesulfonic acid 2-(4-{6-[3-(4-tert-butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-phenyl)-ethyl ester

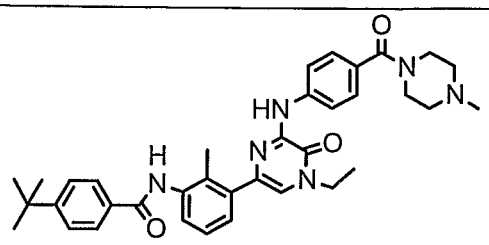
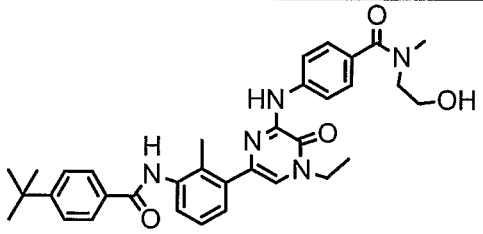
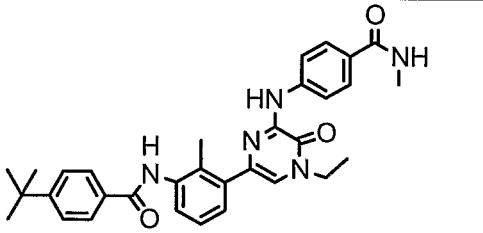
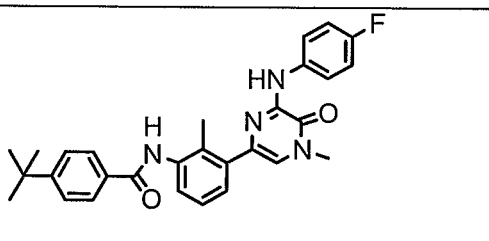
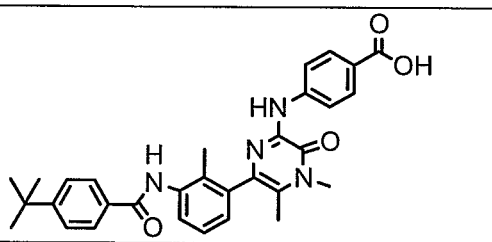
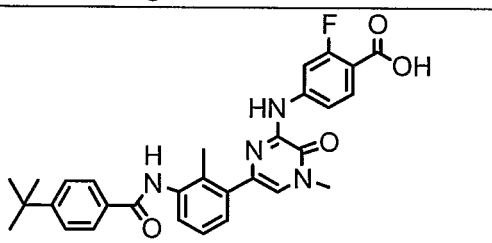
(3) (0.2g; 0.34mmol) was dissolved in acetonitrile (2mL) and excess 4-aminotetrahydropyran (0.25mL) was added. The reaction vessel was sealed and heated to 90 °C for 4hr. Water (10mL) was added to the reaction vessel and the reaction was extracted with EtOAc (3x25mL). The EtOAc layers were pooled, washed with brine, dried over solid sodium sulfate and filtered. The filtrate was then adsorbed directly onto silica and chromatographed using methanol/CH_2Cl_2 (1:9) as eluent to provide 75mg of 4-tert-butyl-N-[2-methyl-3-(4-methyl-5-oxo-6-{4-[2-(tetrahydro-pyran-4-ylamino)-ethyl]-phenylamino}-4,5-dihydro-pyrazin-2-yl)-phenyl]-benzamide (4) as a light tan solid. MS 594.33 (M+H).

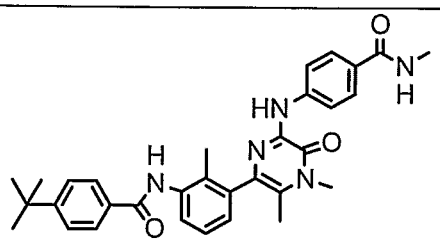
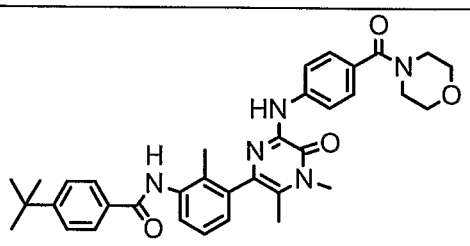
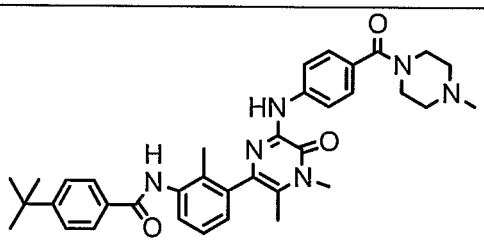
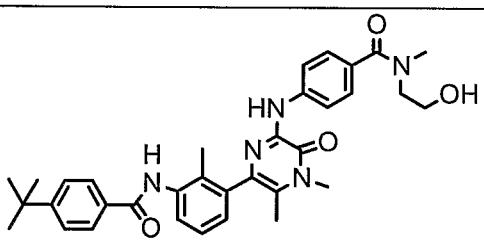
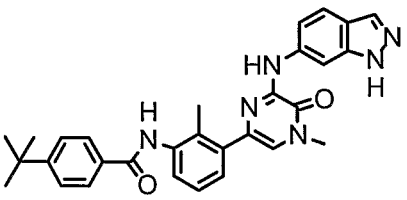
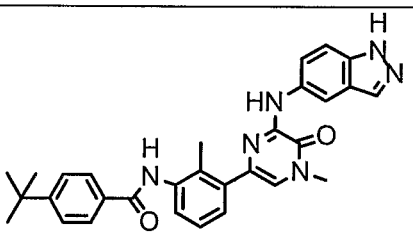
Example 4

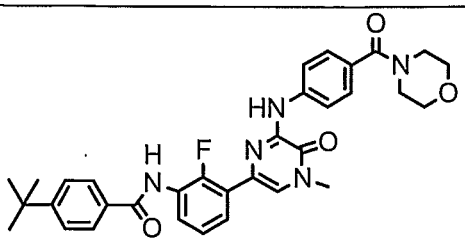
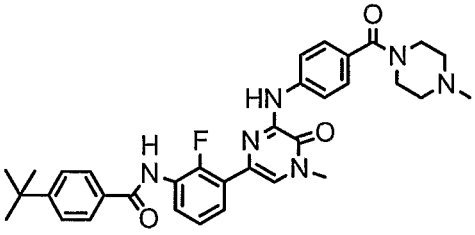
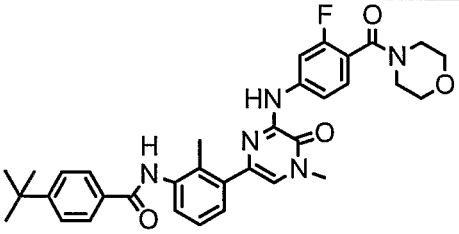
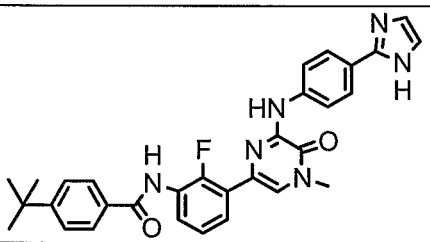
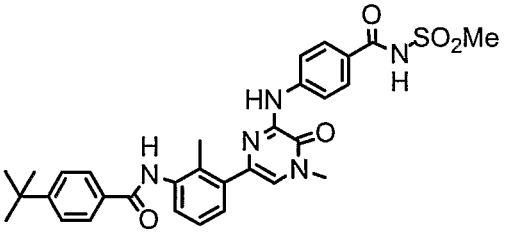
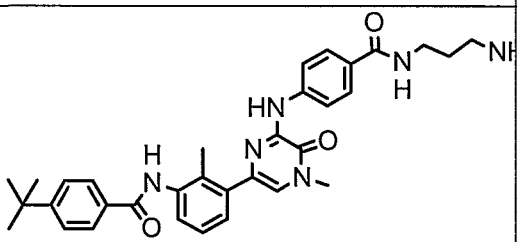
[00259] The following compounds were prepared using procedures similar to those described in Examples 3A-E.

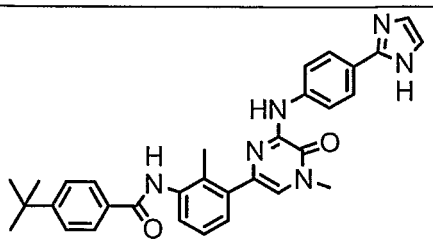
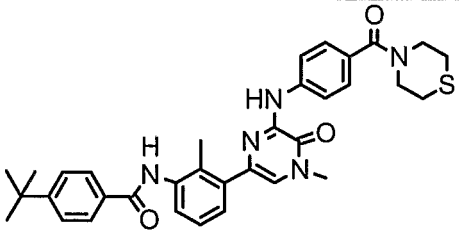
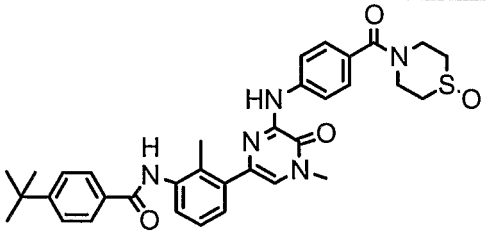
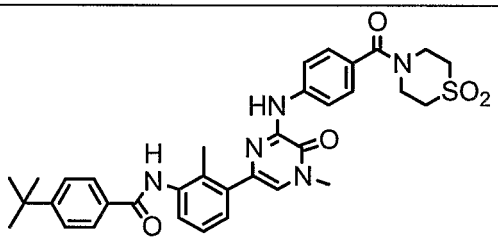
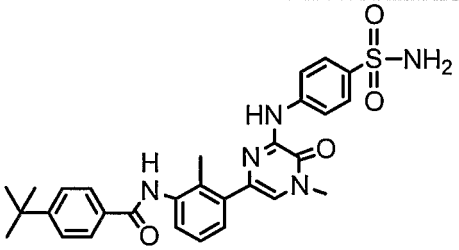
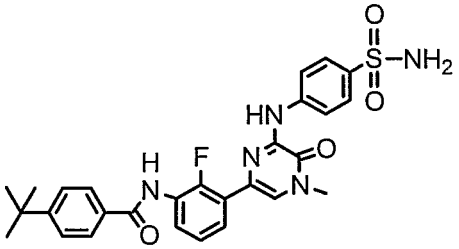
Structure	Name MW	MS m/z
	4-{6-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-benzoic acid 510.23	511.46
	4-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide 579.28	590.52
	4-{6-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-benzoic acid ethyl ester 538.26	539.46

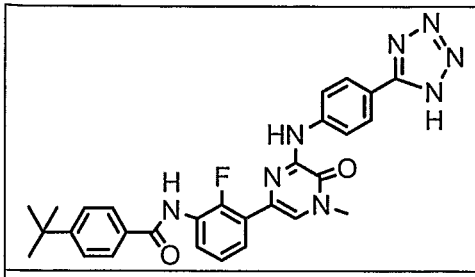
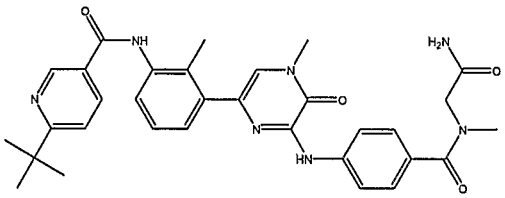
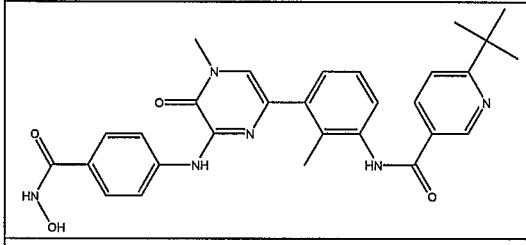
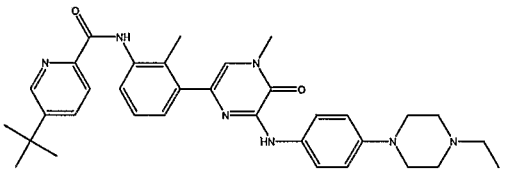
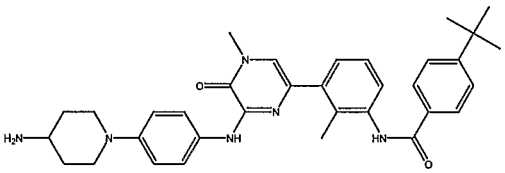
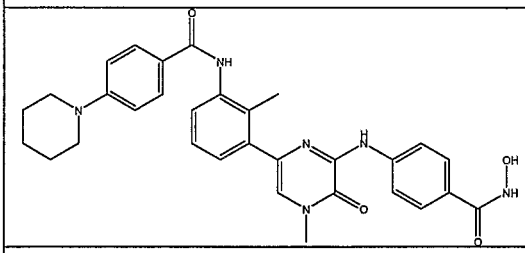
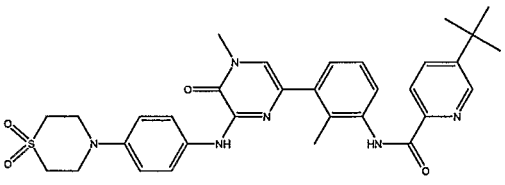
	4-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[4-(4-methyl-piperazine-1-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide 592.3	593.35
	4-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[4-(4-methyl-[1,4]diazepane-1-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide 606.33	607.35
	4-tert-Butyl-N-(3-{4-methyl-6-[4-(2-hydroxyethyl-methyl-carbamoyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide 567.28	568.48
	4-{6-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-benzamide 509.24	510.38
	4-{6-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-4-ethyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-benzoic acid 524.24	525.44
	4-tert-Butyl-N-(3-{4-ethyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide 593.30	594.51

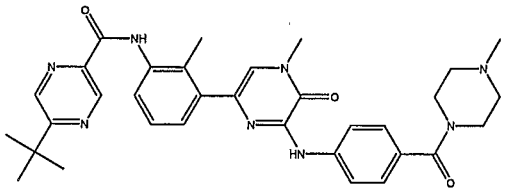
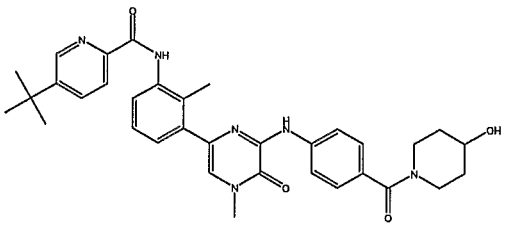
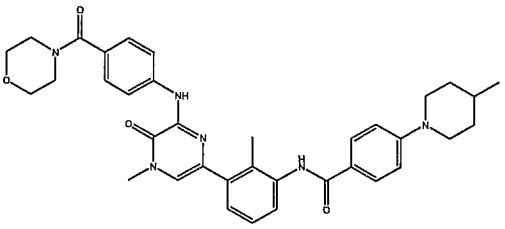
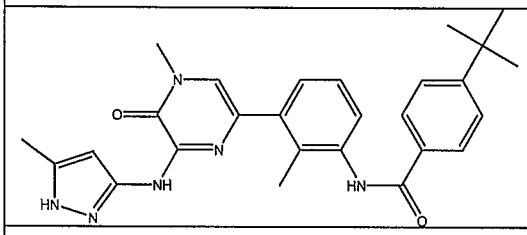
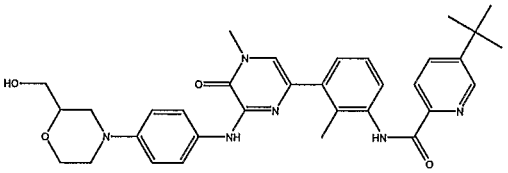
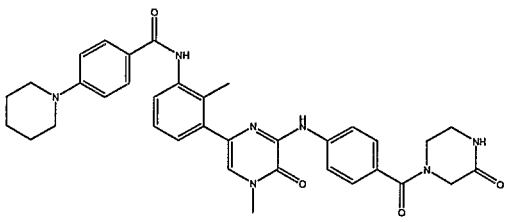
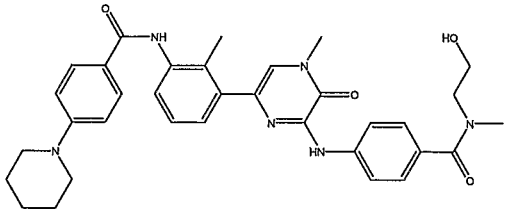
	4-tert-Butyl-N-(3-{4-ethyl-6-[4-(4-methyl-piperazine-1-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide 606.33	607.36
	4-tert-Butyl-N-(2-methyl-3-{4-ethyl-6-[4-(N-methylethanolamine-2-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide 581.30	582.46
	4-tert-Butyl-N-(3-{4-ethyl-6-[4-(methyl-carbamoyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide 537.27	538.48
	4-tert-Butyl-N-{3-[6-(4-fluoro-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide 484.23	485.42
	4-{6-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-4,5-dimethyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-benzoic acid 524.61	525.42
	4-{6-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-2-fluoro-benzoic acid 528.57	529.44

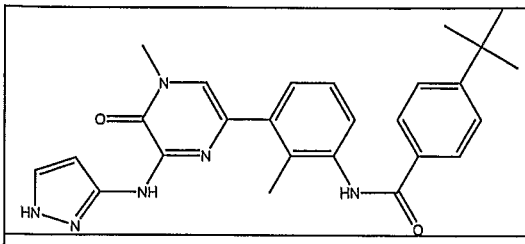
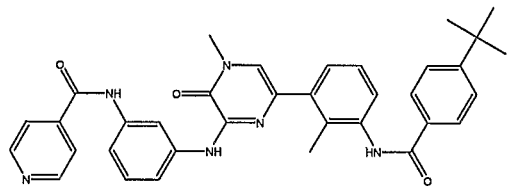
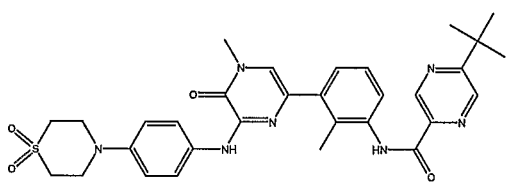
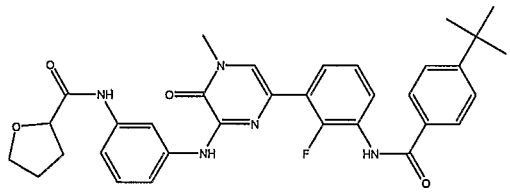
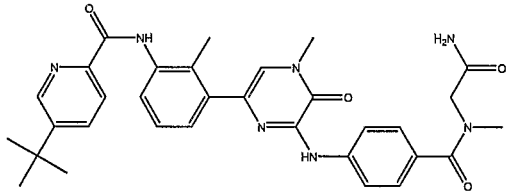
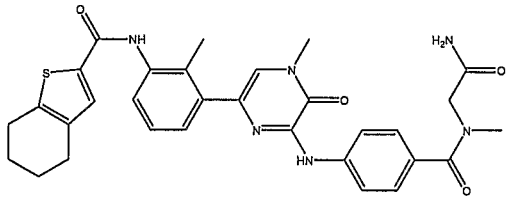
	4-tert-Butyl-N-(3-{3,4-dimethyl-6-[4-(methyl-carbamoyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide 537.65	538.45
	4-tert-Butyl-N-(3-{3,4-dimethyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide 593.72	594.47
	4-tert-Butyl-N-(3-{3,4-dimethyl-6-[4-(4-methyl-piperazine-1-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide 606.76	607.41
	4-tert-Butyl-N-(3-{3,4-dimethyl-6-[4-(2-hydroxyethyl-methyl-carbamoyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide 581.70	582.45
	4-tert-Butyl-N-{3-[6-(1H-indazol-6-ylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide 506.60	507.47
	4-tert-Butyl-N-{3-[6-(1H-indazol-5-ylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide 506.60	507.43

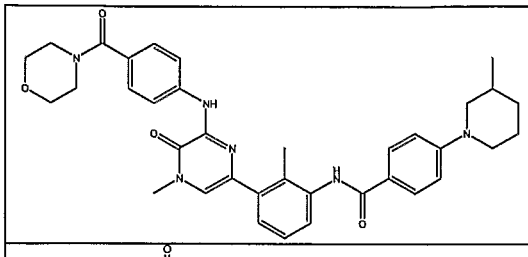
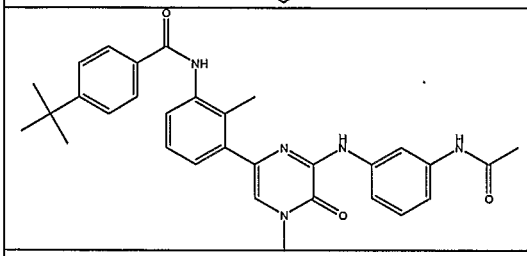
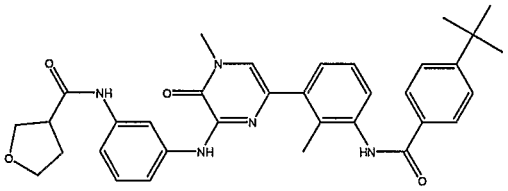
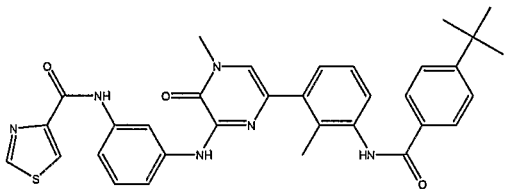
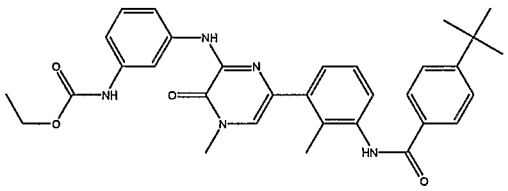
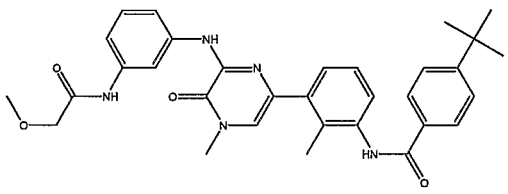
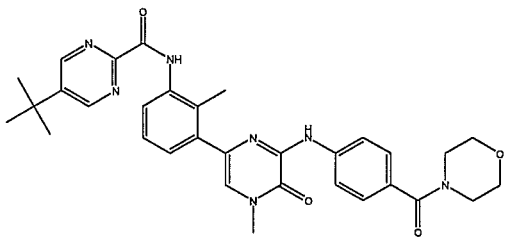
	4-tert-Butyl-N-(2-fluoro-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide 583.65	584.47
	4-tert-Butyl-N-(2-fluoro-3-{4-methyl-6-[4-(4-methyl-piperazine-1-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide 596.69	597.29
	4-tert-Butyl-N-(3-{6-[3-fluoro-4-(morpholine-4-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide 597.68	598.45
	4-tert-Butyl-N-(2-fluoro-3-{6-[4-(1H-imidazol-2-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide 536.60	537.35
	4-tert-Butyl-N-{3-[6-(4-methanesulfonylaminocarbonyl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide 587.69	588.52
	4-tert-Butyl-N-(3-{4-methyl-6-[4-(3-aminopropyl-carbamoyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide 566.69	567.40

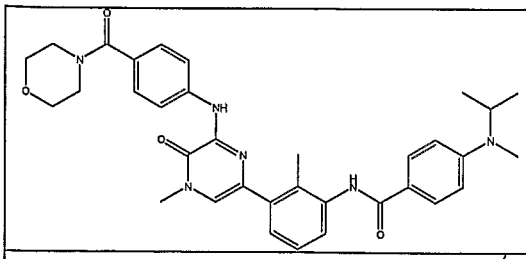
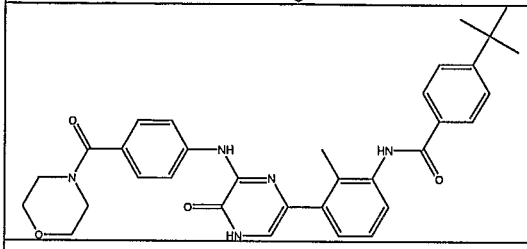
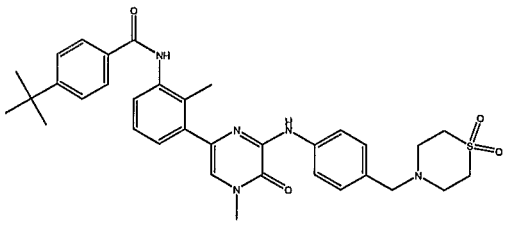
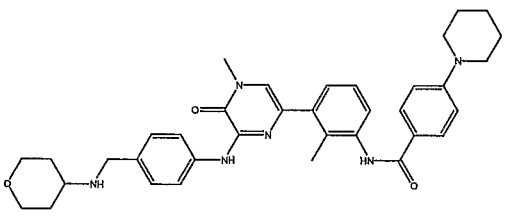
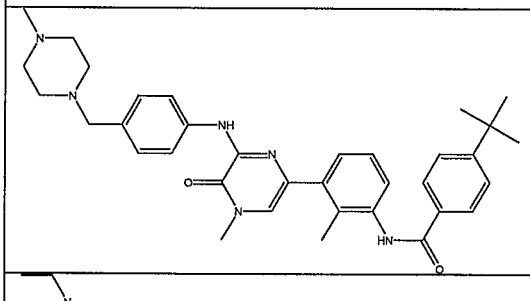
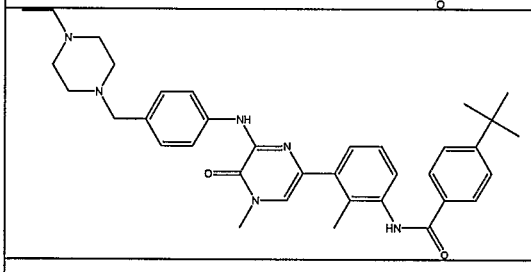
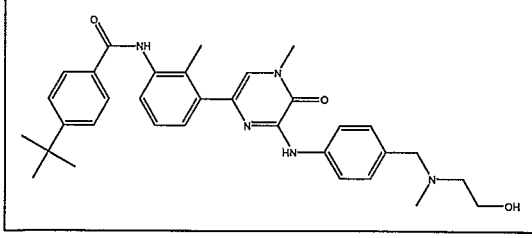
	4-tert-Butyl-N-(3-{6-[4-(1H-imidazol-2-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide 532.64	533.36
	4-tert-Butyl-N-(2-methyl-3-{4-methyl-5-oxo-6-[4-(thiomorpholine-4-carbonyl)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide 595.76	596.49
	4-tert-Butyl-N-(2-methyl-3-{4-methyl-5-oxo-6-[4-(1-oxo-1l4-thiomorpholine-4-carbonyl)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide 611.75	612.49
	4-tert-Butyl-N-(3-{6-[4-(1,1-dioxo-1l6-thiomorpholine-4-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide 627.75	628.45
	4-tert-Butyl-N-{2-methyl-3-[4-methyl-5-oxo-6-(4-sulfamoyl-phenylamino)-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide 545.21	546.40
	4-tert-Butyl-N-{2-fluoro-3-[4-methyl-5-oxo-6-(4-sulfamoyl-phenylamino)-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide 549.18	550.39

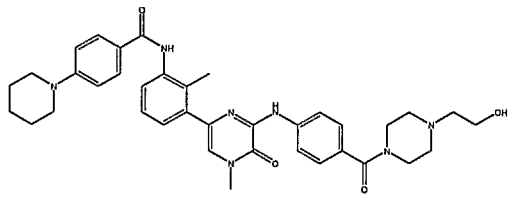
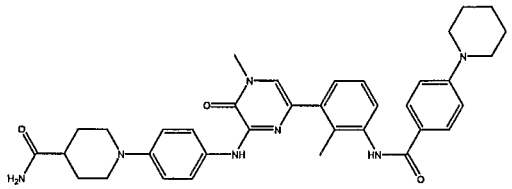
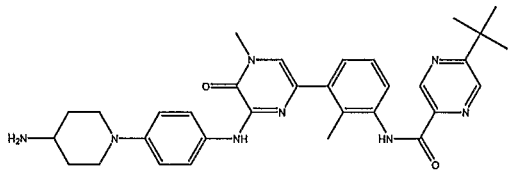
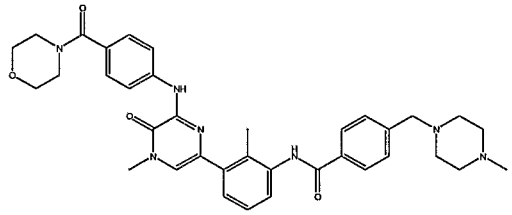
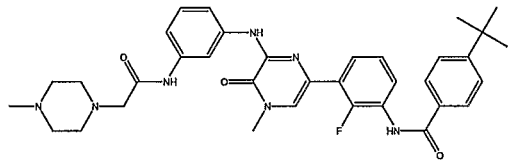
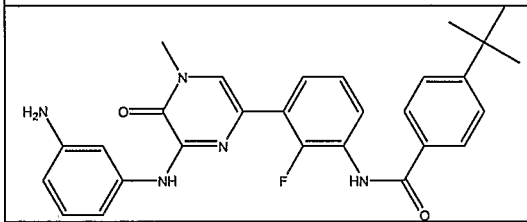
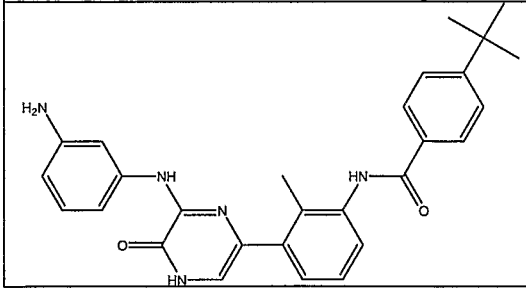
	4-tert-Butyl-N-(2-fluoro-3-{4-methyl-5-oxo-6-[4-(1H-tetrazol-5-yl)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide 538.22	539.38
	6-tert-Butyl-N-(3-{6-[4-(carbamoylmethyl-methyl-carbamoyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-nicotinamide 581.28	582.29
	6-tert-Butyl-N-{3-[6-(4-hydroxycarbamoyl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-nicotinamide 526.23	505.21
	5-tert-Butyl-pyridine-2-carboxylic acid (3-{6-[4-(4-ethyl-piperazin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-amide 579.33	580.32
	N-(3-{6-[4-(4-Amino-piperidin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide 564.32	565.31
	4-{6-[3-(4-(1-piperidinyl)-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-benzohydroxamic acid 552.25	531.26
	5-tert-Butyl-pyridine-2-carboxylic acid (3-{6-[4-(1,1-dioxo-1λ⁶-thiomorpholin-4-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-amide 600.25	601.23

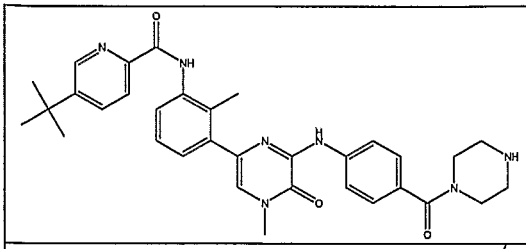
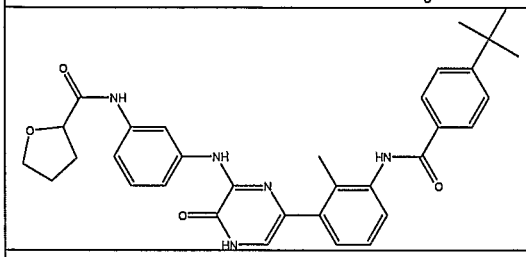
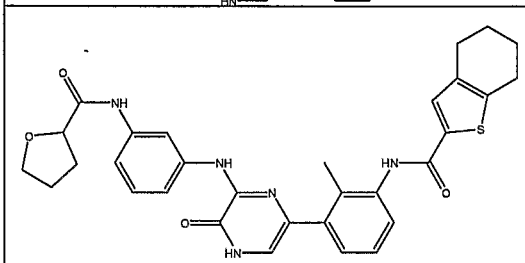
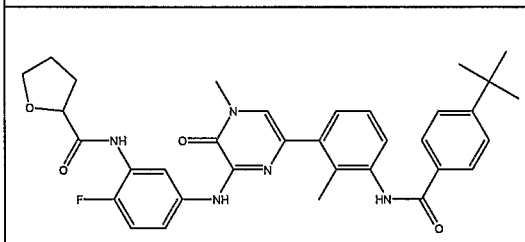
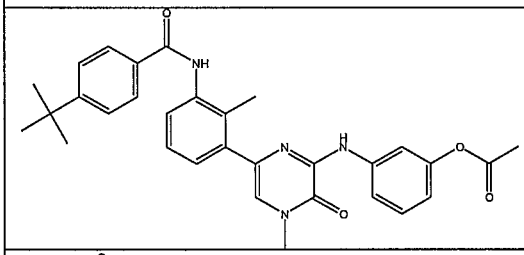
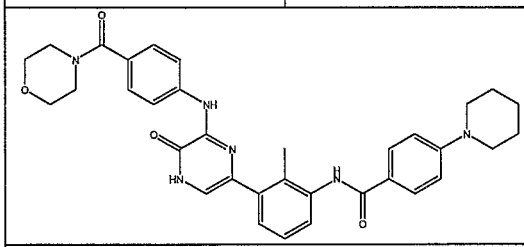
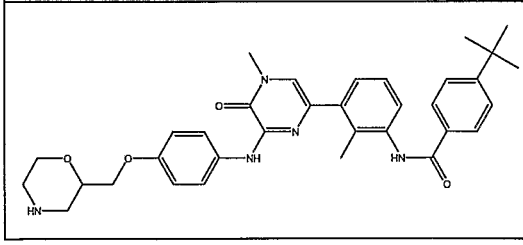
	5-tert-Butyl-pyrazine-2-carboxylic acid (2-methyl-3-{4-methyl-6-[4-(4-methyl-piperazine-1-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-amide 594.31	595.27
	5-tert-Butyl-pyridine-2-carboxylic acid (3-{6-[4-(4-hydroxy-piperidine-1-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-amide 594.30	595.26
	N-(2-Methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-4-(4-methyl-piperidin-1-yl)-benzamide 620.31	621.30
	4-tert-Butyl-N-{2-methyl-3-[4-methyl-6-(5-methyl-1H-pyrazol-3-ylamino)-5-oxo-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide 470.24	471.13
	5-tert-Butyl-pyridine-2-carboxylic acid (3-{6-[4-(2-hydroxymethyl-morpholin-4-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-amide 582.30	583.24
	N-(2-Methyl-3-{4-methyl-5-oxo-6-[4-(3-oxo-piperazine-1-carbonyl)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-4-piperidin-1-yl-benzamide 619.29	620.28
	4-(1-Piperidinyl)-N-(3-{4-methyl-6-[4-(2-hydroxyethyl-methyl-carbamoyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide 594.29	595.26

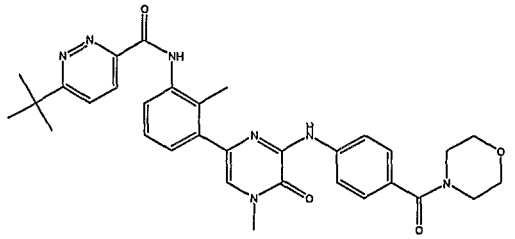
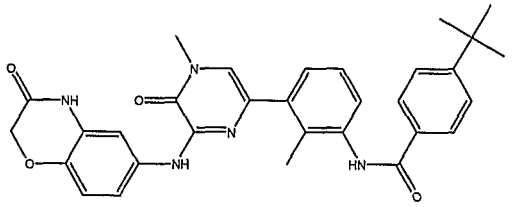
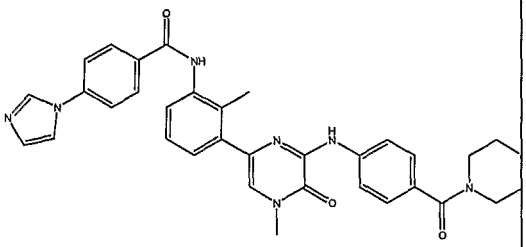
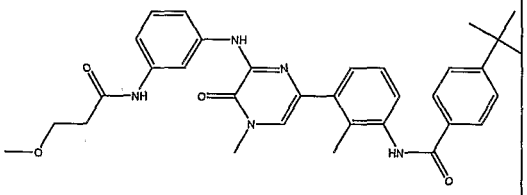
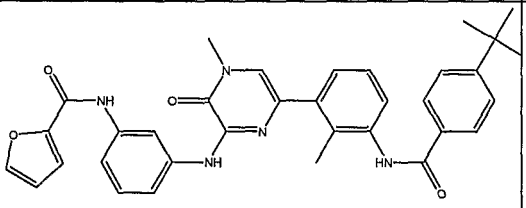
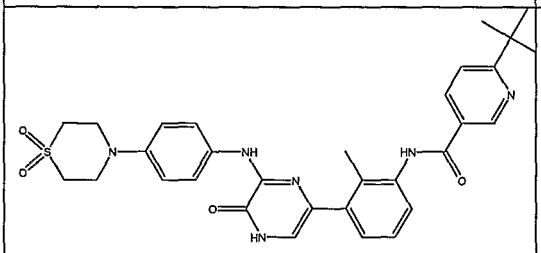
	4-tert-Butyl-N-{2-methyl-3-[4-methyl-5-oxo-6-(1H-pyrazol-3-ylamino)-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide 456.23	457.10
	N-(3-{6-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-phenyl)-isonicotinamide 586.27	587.24
	5-tert-Butyl-pyrazine-2-carboxylic acid (3-{6-[4-(1,1-dioxo-1λ^6-thiomorpholin-4-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-amide 601.25	602.22
	Tetrahydro-furan-2-carboxylic acid (3-{6-[3-(4-tert-butyl-benzoylamino)-2-fluoro-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-phenyl)-amide 583.25	585.12
	5-tert-Butyl-pyridine-2-carboxylic acid (3-{6-[4-(carbamoylmethyl-methyl-carbamoyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-amide 581.27	583.12
	4,5,6,7-Tetrahydro-benzo[b]thiophene-2-carboxylic acid (3-{6-[4-(carbamoylmethyl-methyl-carbamoyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-amide 584.22	585.22

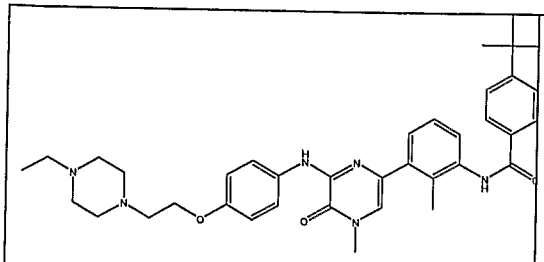
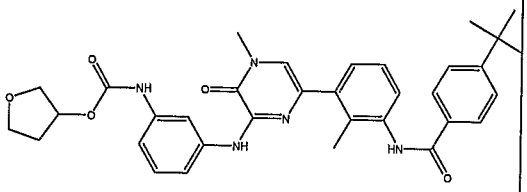
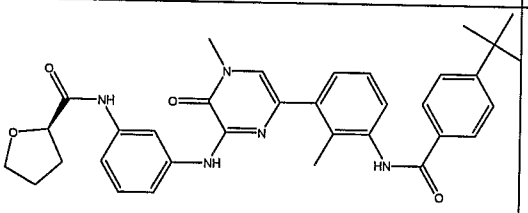
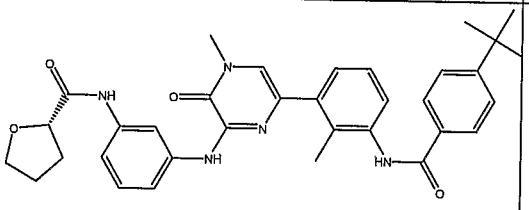
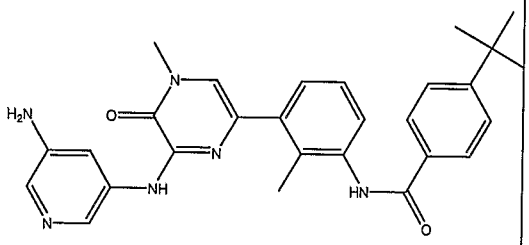
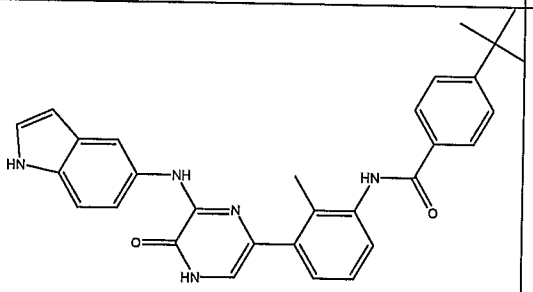
	N-(2-Methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-4-(3-methyl-piperidin-1-yl)-benzamide 620.31	621.30
	N-{3-[6-(3-Acetylamino-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-4-tert-butyl-benzamide 523.26	524.20
	Tetrahydro-furan-3-carboxylic acid (3-{6-[3-(4-tert-butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-phenyl)-amide 579.28	580.30
	Thiazole-4-carboxylic acid (3-{6-[3-(4-tert-butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-phenyl)-amide 592.22	593.26
	(3-{6-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-phenyl)-carbamic acid ethyl ester 553.27	554.25
	4-tert-Butyl-N-(3-{6-[3-(2-methoxy-acetylamino)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide 553.27	554.26
	5-tert-Butyl-pyrimidine-2-carboxylic acid (2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-amide 581.27	582.28

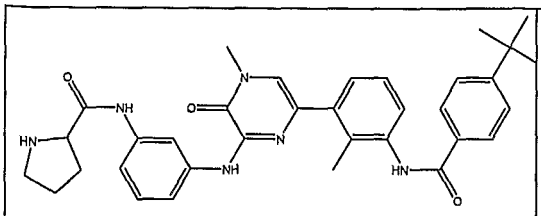
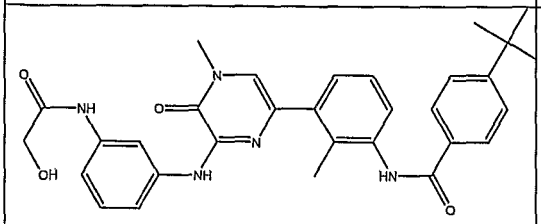
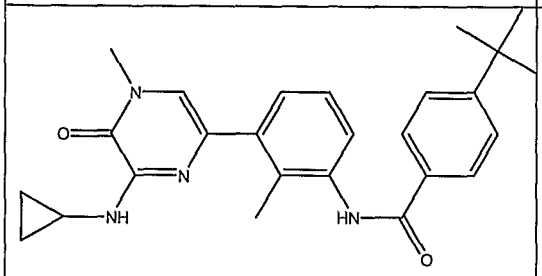
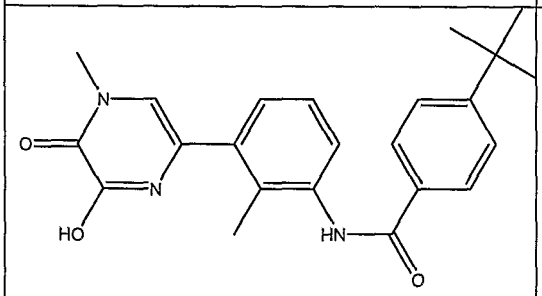
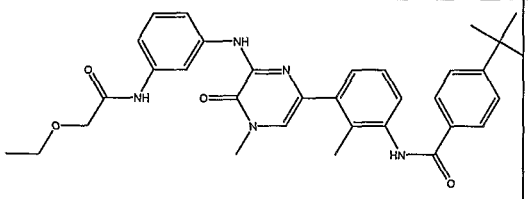
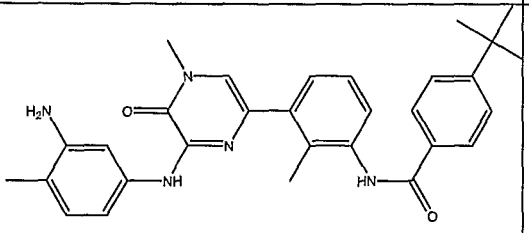
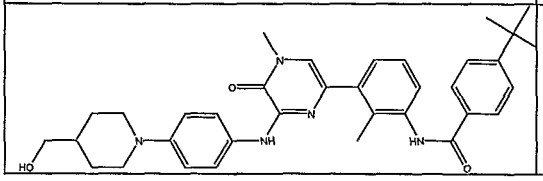
	4-(Isopropyl-methyl-amino)-N-(2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide 594.29	595.30
	4-tert-Butyl-N-(2-methyl-3-{6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide 565.27	566.31
	4-tert-Butyl-N-(3-{6-[4-(1,1-dioxo-1λ^6-thiomorpholin-4-ylmethyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide 613.27	614.33
	N-[2-Methyl-3-(4-methyl-5-oxo-6-{4-[(tetrahydro-pyran-4-ylamino)-methyl]-phenylamino}-4,5-dihydro-pyrazin-2-yl)-phenyl]-4-piperidin-1-yl-benzamide 606.33	607.38
	4-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[4-(4-methyl-piperazin-1-ylmethyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide 578.33	579.33
	4-tert-Butyl-N-(3-{6-[4-(4-ethyl-piperazin-1-ylmethyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide 592.35	593.36
	4-tert-Butyl-N-{3-[6-(4-{[(2-hydroxy-ethyl)-methyl-amino]-methyl}-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide 553.30	554.29

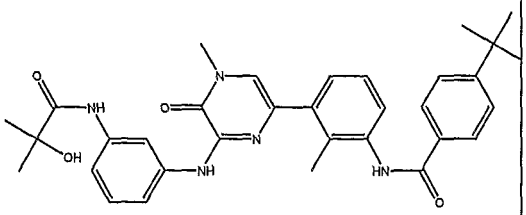
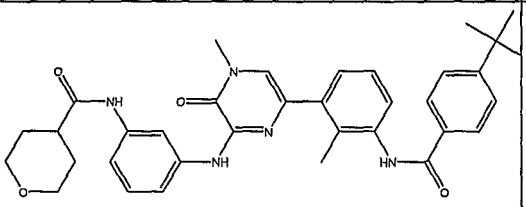
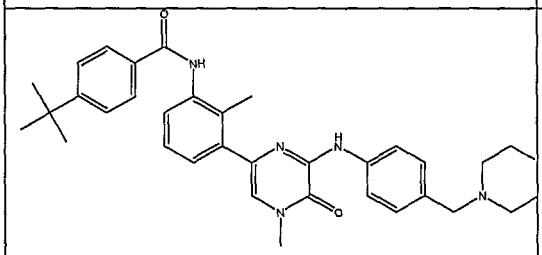
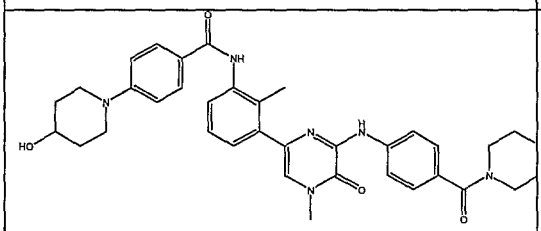
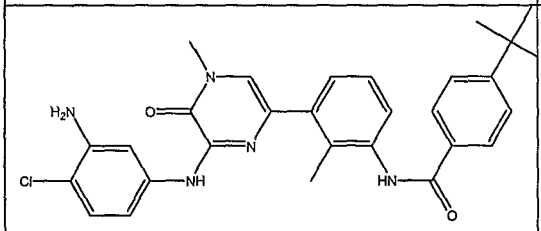
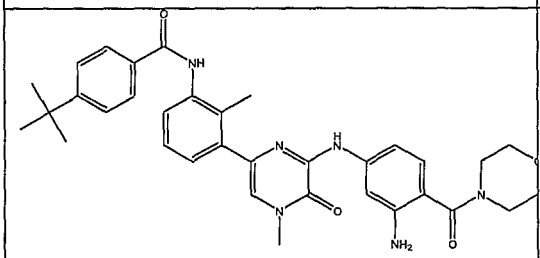
	N-[3-(6-{4-[4-(2-Hydroxy-ethyl)-piperazine-1-carbonyl]-phenylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-4-piperidin-1-yl-benzamide 649.34	650.40
	1-(4-{4-Methyl-6-[2-methyl-3-(4-piperidin-1-yl-benzoylamino)-phenyl]-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-phenyl)-piperidine-4-carboxylic acid amide 619.32	620.36
	5-tert-Butyl-pyrazine-2-carboxylic acid (3-{6-[4-(4-amino-piperidin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-amide 566.31	567.34
	N-(2-Methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-4-(4-methyl-piperazin-1-ylmethyl)-benzamide 635.32	636.36
	4-tert-Butyl-N-[2-fluoro-3-(4-methyl-6-{3-[2-(4-methyl-piperazin-1-yl)-acetylamino]-phenylamino}-5-oxo-4,5-dihydro-pyrazin-2-yl)-phenyl]-benzamide 625.31	626.33
	N-{3-[6-(3-Amino-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-fluoro-phenyl}-4-tert-butyl-benzamide 485.22	486.15
	N-{3-[6-(3-Amino-phenylamino)-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-4-tert-butyl-benzamide 467.23	468.97

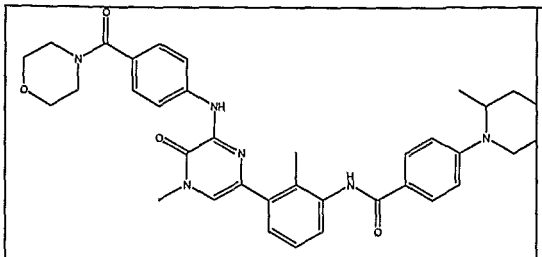
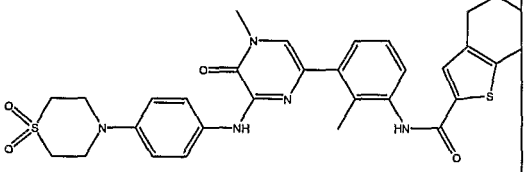
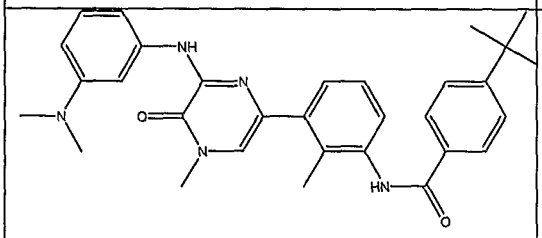
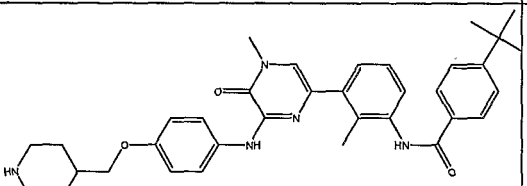
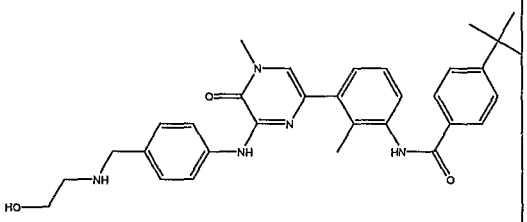
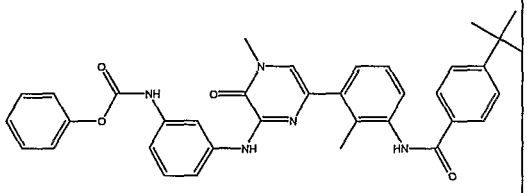
	5-tert-Butyl-pyridine-2-carboxylic acid (2-methyl-3-{4-methyl-5-oxo-6-[4-(piperazine-1-carbonyl)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-amide 579.30	581.18
	Tetrahydro-furan-2-carboxylic acid (3-{6-[3-(4-tert-butyl-benzoylamino)-2-methyl-phenyl]-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-phenyl)-amide 565.27	567.16
	Tetrahydro-furan-2-carboxylic acid [3-(6-{2-methyl-3-[(4,5,6,7-tetrahydro-benzo[b]thiophene-2-carbonyl)-amino]-phenyl}-3-oxo-3,4-dihydro-pyrazin-2-ylamino)-phenyl]-amide 569.21	571.10
	Tetrahydro-furan-2-carboxylic acid (5-{6-[3-(4-tert-butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-2-fluoro-phenyl)-amide 597.27	599.21
	Acetic acid 3-{6-[3-(4-tert-butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-phenyl ester 524.24	525.20
	N-(2-Methyl-3-{6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-4-piperidin-1-yl-benzamide 592.28	593.25
	4-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[4-(morpholin-2-ylmethoxy)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide 581.3	582.33

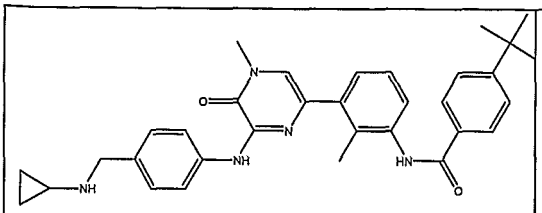
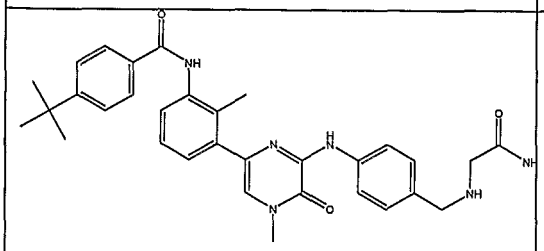
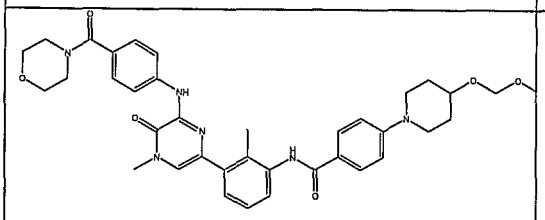
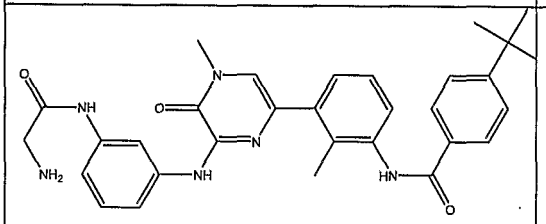
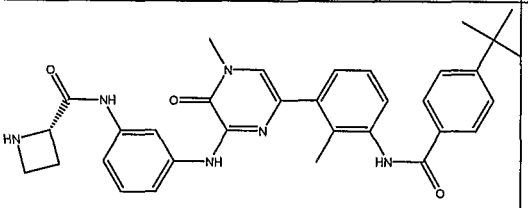
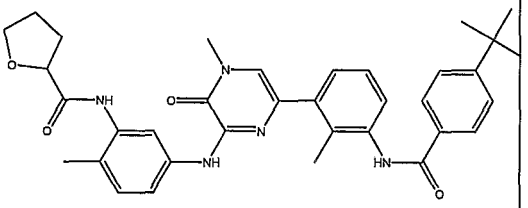
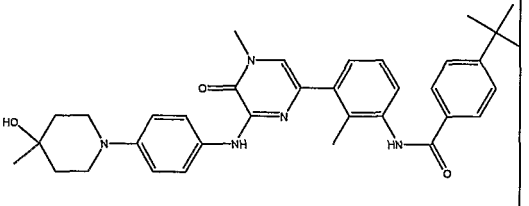
	6-tert-Butyl-pyridazine-3-carboxylic acid (2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-amide 581.27	582.26
	4-tert-Butyl-N-{2-methyl-3-[4-methyl-5-oxo-6-(3-oxo-3,4-dihydro-2H-benzo[1,4]oxazin-6-ylamino)-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide 537.23	538.18
	4-Imidazol-1-yl-N-(2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide 589.24	589.29
	4-tert-Butyl-N-(3-{6-[3-(3-methoxy-propionylamino)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide 567.28	567.34
	Furan-2-carboxylic acid (3-{6-[3-(4-tert-butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-phenyl)-amide 575.25	575.33
	6-tert-Butyl-N-(3-{6-[4-(1,1-dioxo-1λ^6-thiomorpholin-4-yl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-nicotinamide 586.23	587.22

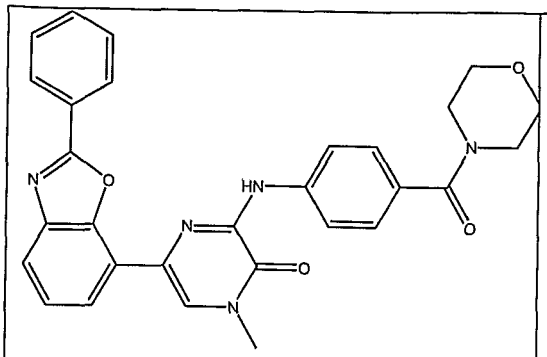
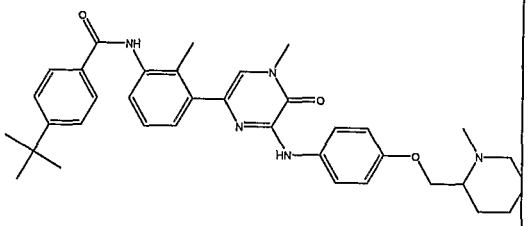
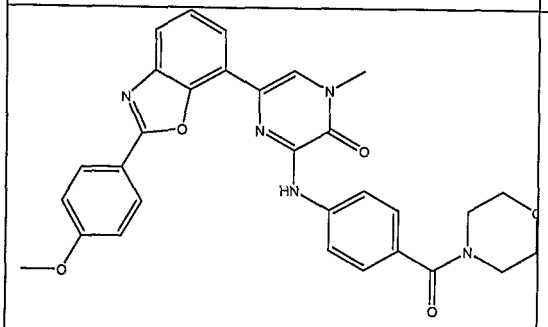
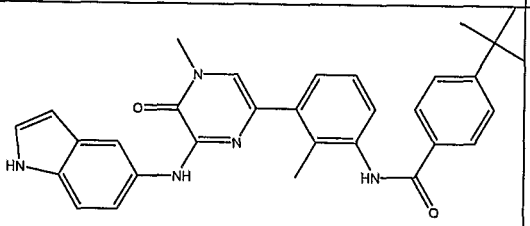
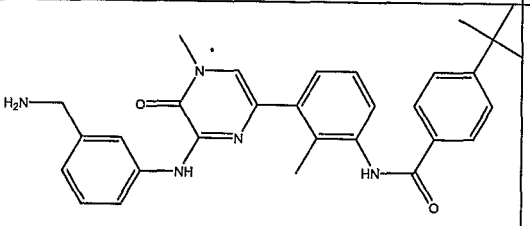
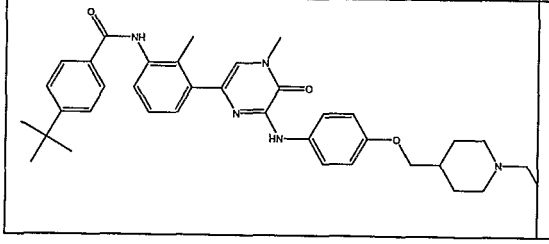
	4-tert-Butyl-N-[3-(6-{4-[2-(4-ethyl-piperazin-1-yl)-ethoxy]-phenylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-benzamide 622.36	622.39
	(3-{6-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-phenyl)-carbamic acid tetrahydro-furan-3-yl ester 595.28	595.34
	Tetrahydro-furan-2-carboxylic acid (3-{6-[3-(4-tert-butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-phenyl)-amide 579.28	579.36
	Tetrahydro-furan-2-carboxylic acid (3-{6-[3-(4-tert-butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-phenyl)-amide 579.28	579.37
	N-{3-[6-(5-Amino-pyridin-3-ylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-4-tert-butyl-benzamide 482.24	483.25
	4-tert-Butyl-N-{3-[6-(1H-indol-5-ylamino)-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide 491.23	492.21

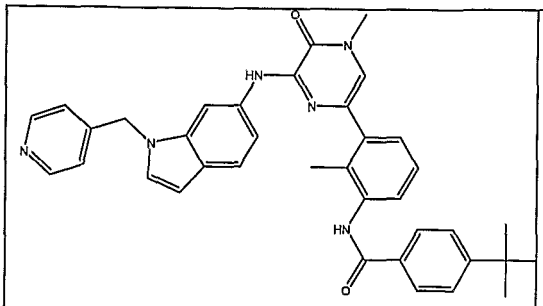
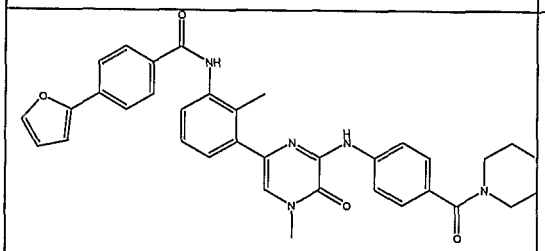
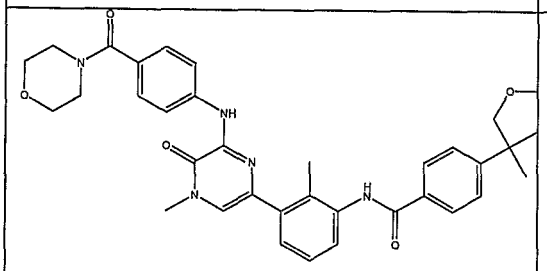
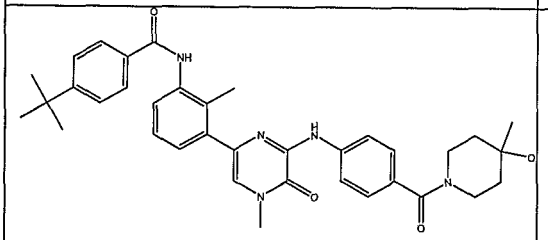
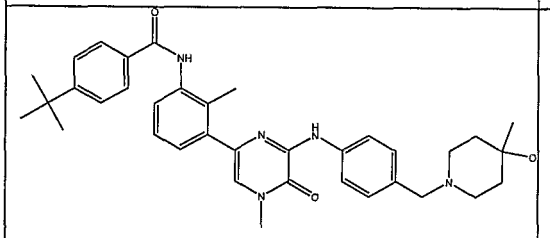
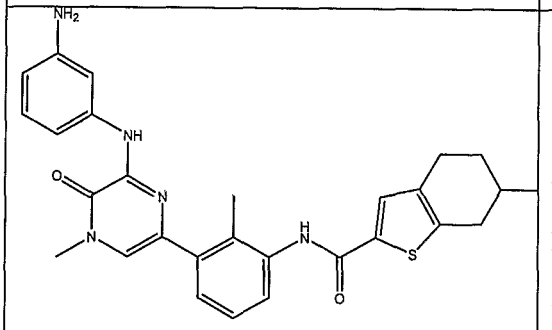
	Pyrrolidine-2-carboxylic acid (3-{6-[3-(4-tert-butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-phenyl)-amide 578.30	579.37
	4-tert-Butyl-N-(3-{6-[3-(2-hydroxy-acetylamino)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide 539.25	539.36
	4-tert-Butyl-N-[3-(6-cyclopropylamino-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-benzamide 430.23	431.21
	4-tert-Butyl-N-[3-(6-hydroxy-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-benzamide 391.19	392.15
	4-tert-Butyl-N-(3-{6-[3-(2-ethoxy-acetylamino)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide 567.28	567.29
	N-{3-[6-(3-Amino-4-methyl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-4-tert-butyl-benzamide 495.26	495.39
	4-tert-Butyl-N-(3-{6-[4-(4-hydroxymethyl-piperidin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide	580.29

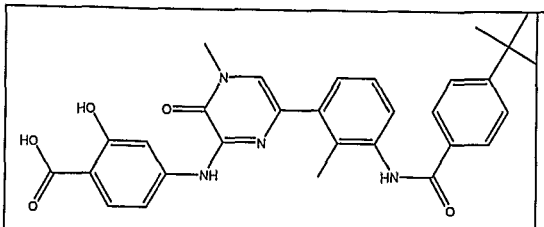
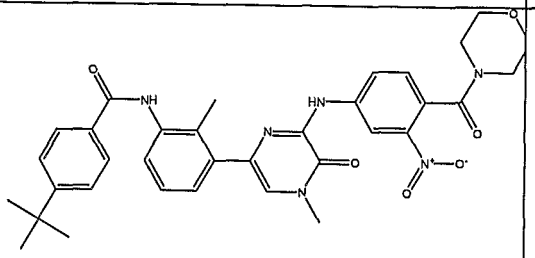
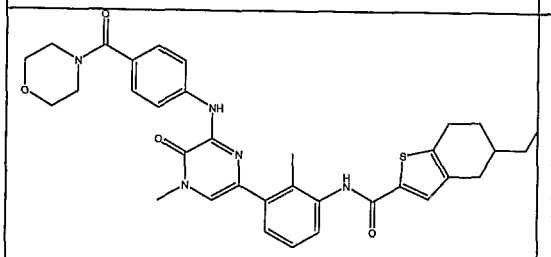
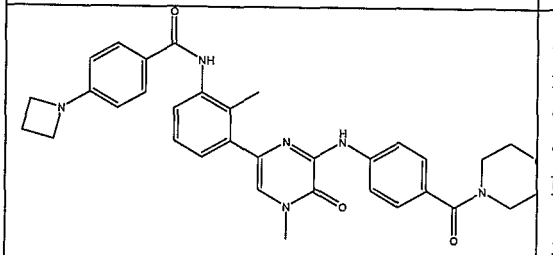
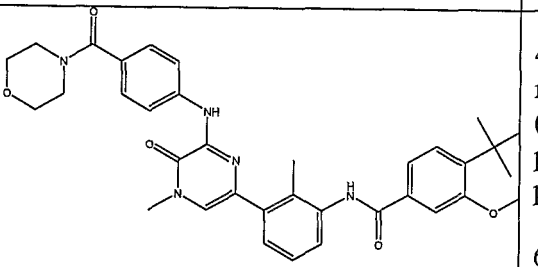
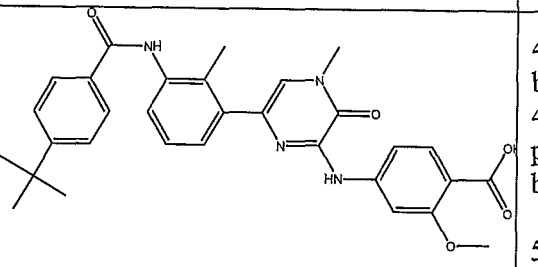
	579.32	
	4-tert-Butyl-N-(3-{6-[3-(2-hydroxy-2-methyl-propionylamino)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide 567.28	568.30
	Tetrahydro-pyran-4-carboxylic acid (3-{6-[3-(4-tert-butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-phenyl)-amide 593.3	594.36
	4-tert-Butyl-N-{2-methyl-3-[4-methyl-5-oxo-6-(4-thiomorpholin-4-ylmethyl-phenylamino)-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide 581.28	582.32
	4-(4-Hydroxy-piperidin-1-yl)-N-(2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide 622.29	623.33
	N-{3-[6-(3-Amino-4-chloro-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-4-tert-butyl-benzamide 515.21	515.32
	N-(3-{6-[3-Amino-4-(morpholine-4-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide 594.29	595.32

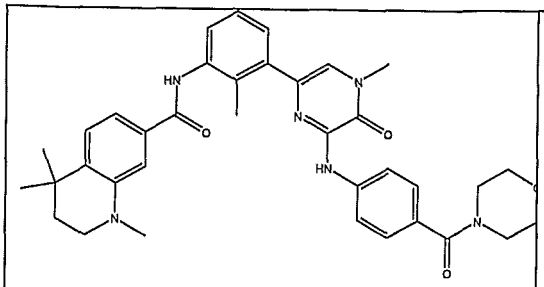
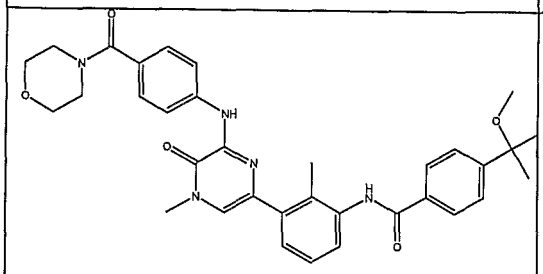
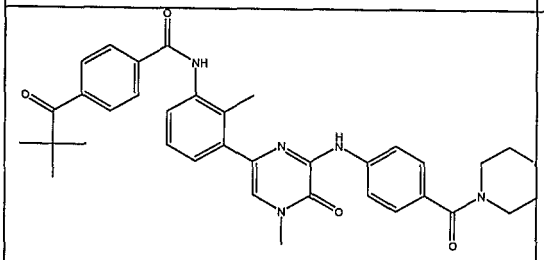
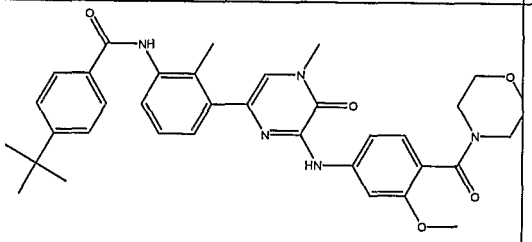
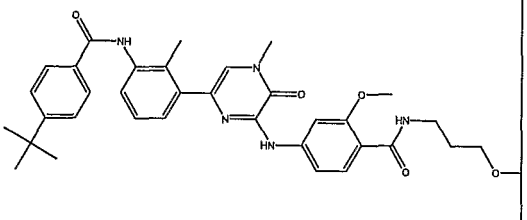
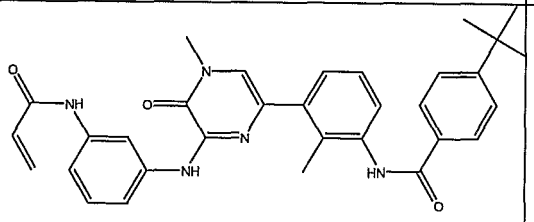
	N-(2-Methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-4-(2-methyl-piperidin-1-yl)-benzamide 620.31	621.41
	4,5,6,7-Tetrahydro-benzo[b]thiophene-2-carboxylic acid (3-{6-[4-(1,1-dioxo-1λ^6-thiomorpholin-4-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-amide 603.19	604.15
	4-tert-Butyl-N-{3-[6-(3-dimethylamino-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide 509.28	510.30
	4-tert-Butyl-N-(2-methyl-3-{4-methyl-5-oxo-6-[4-(piperidin-4-ylmethoxy)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide 579.32	580.32
	4-tert-Butyl-N-[3-(6-{4-[(2-hydroxy-ethylamino)-methyl]-phenylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-benzamide 539.29	540.19
	(3-{6-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-phenyl)-carbamic acid phenyl ester 601.26	602.29

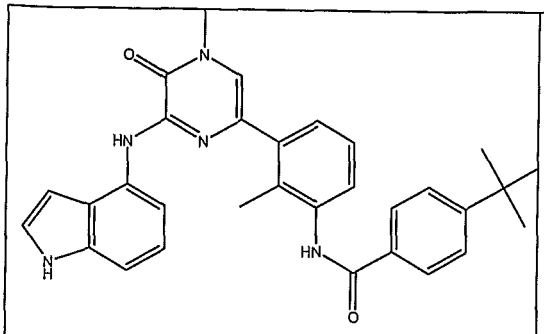
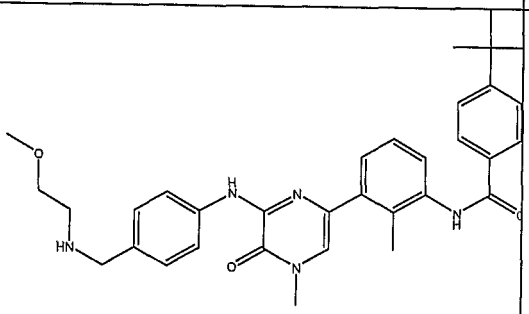
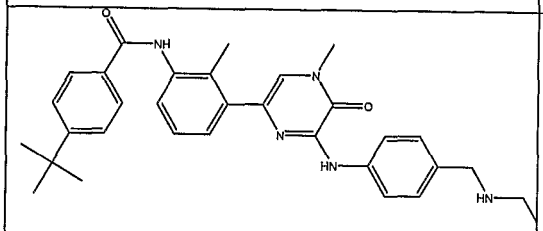
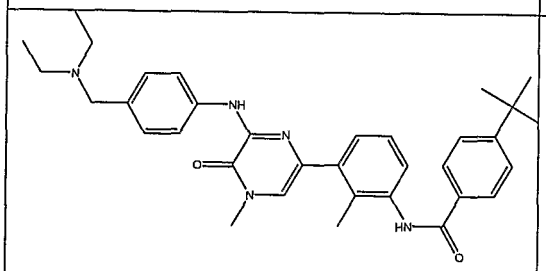
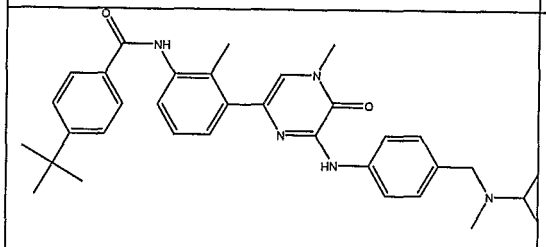
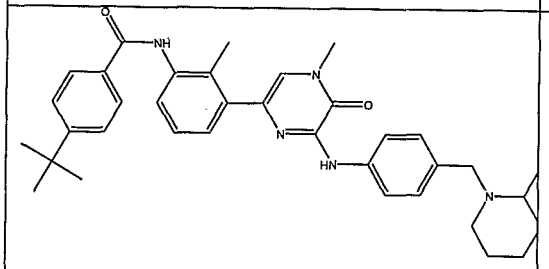
	4-tert-Butyl-N-{3-[6-(4-cyclopropylaminomethyl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide 535.29	536.28
	4-tert-Butyl-N-[3-(6-{4-[(carbamoylmethyl-amino)-methyl]-phenylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-benzamide 552.28	553.31
	4-(4-Methoxymethoxy-piperidin-1-yl)-N-(2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide 666.31	666.29
	N-(3-{6-[3-(2-Amino-acetylamino)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide 538.26	539.38
	Azetidine-2-carboxylic acid (3-{6-[3-(4-tert-butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-phenyl)-amide 564.28	656.37
	Tetrahydro-furan-2-carboxylic acid (5-{6-[3-(4-tert-butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-2-methyl-phenyl)-amide 593.3	594.29
	4-tert-Butyl-N-(3-{6-[4-(4-hydroxy-4-methyl-piperidin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide 579.32	580.31

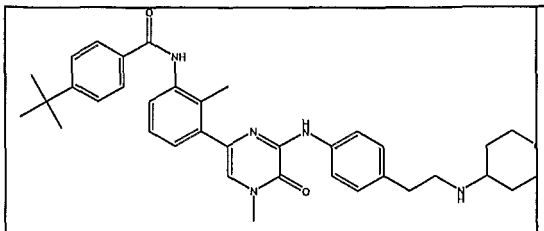
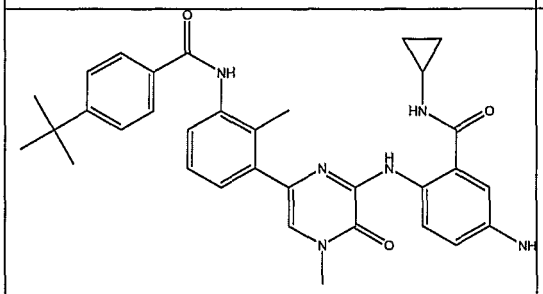
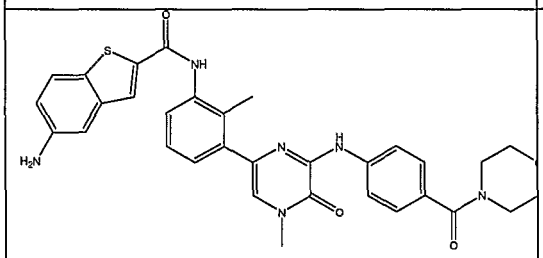
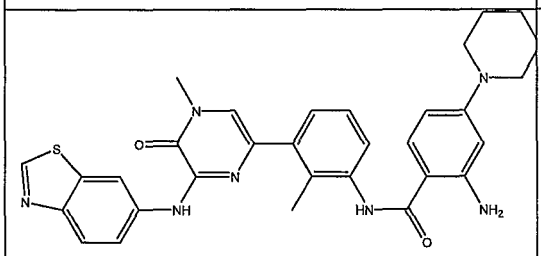
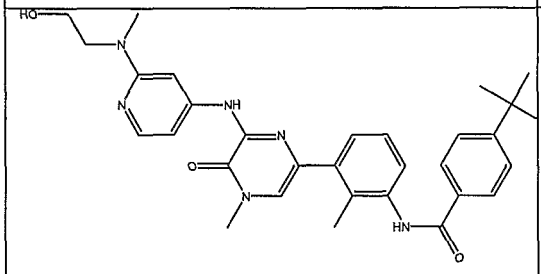
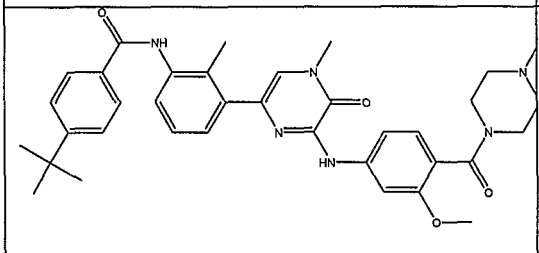
	1-Methyl-3-[4-(morpholine-4-carbonyl)-phenylamino]-5-(2-phenyl-benzooxazol-7-yl)-1H-pyrazin-2-one 507.19	508.15
	4-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[4-(1-methyl-piperidin-2-ylmethoxy)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide 593.33	594.38
	5-[2-(4-Methoxy-phenyl)-benzooxazol-7-yl]-1-methyl-3-[4-(morpholine-4-carbonyl)-phenylamino]-1H-pyrazin-2-one 537.20	538.18
	4-tert-Butyl-N-{3-[6-(1H-indol-5-ylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide 505.24	506.17
	N-{3-[6-(3-Aminomethyl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-4-tert-butyl-benzamide 495.26	496.19
	4-tert-Butyl-N-(3-{6-[4-(1-ethyl-piperidin-4-ylmethoxy)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide 607.35	608.37

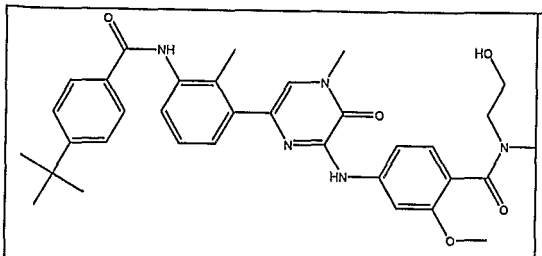
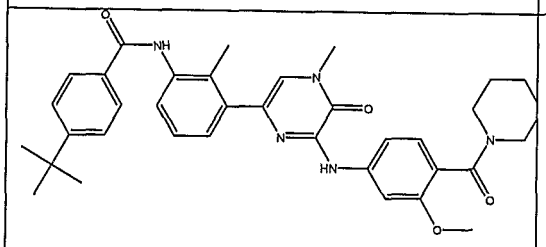
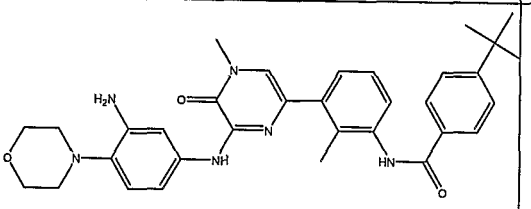
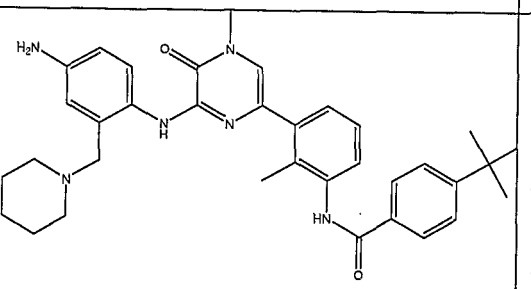
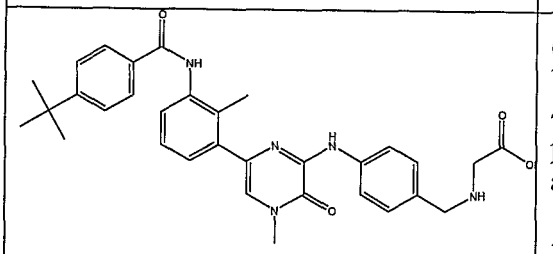
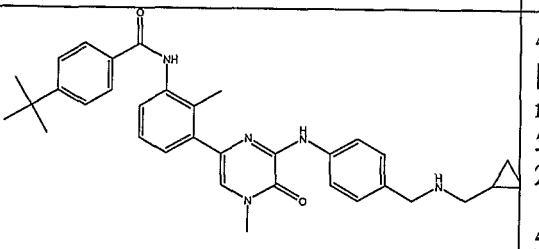
	4-tert-Butyl-N-{2-methyl-3-[4-methyl-5-oxo-6-(1-pyridin-4-ylmethyl-1H-indol-6-ylamino)-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide 596.29	597.28
	4-Furan-2-yl-N-(2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide 589.23	590.25
	4-(2-Methoxy-1,1-dimethyl-ethyl)-N-(2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide 609.29	610.31
	4-tert-Butyl-N-(3-{6-[4-(4-hydroxy-4-methyl-piperidine-1-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide 607.31	608.33
	4-tert-Butyl-N-(3-{6-[4-(4-hydroxy-4-methyl-piperidin-1-ylmethyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide 593.33	594.38
	6-Methyl-4,5,6,7-tetrahydro-benzo[b]thiophene-2-carboxylic acid {3-[6-(3-amino-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-amide 499.20	500.13

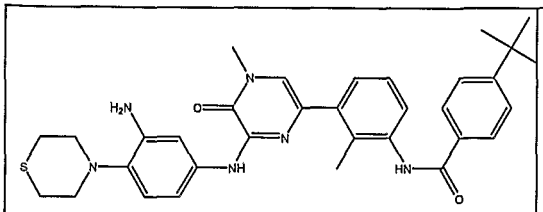
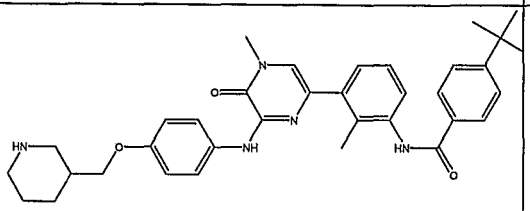
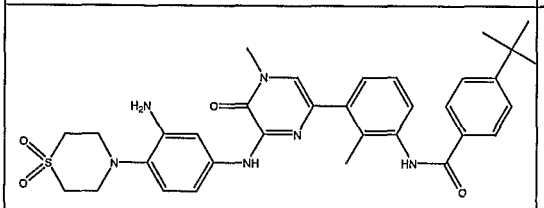
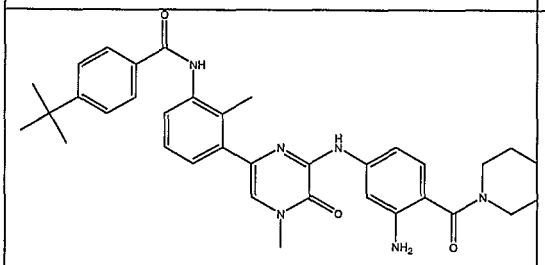
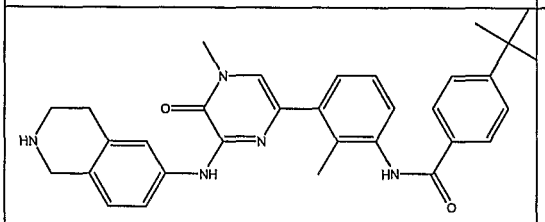
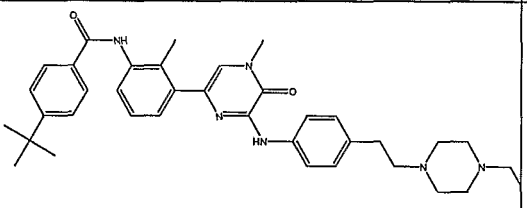
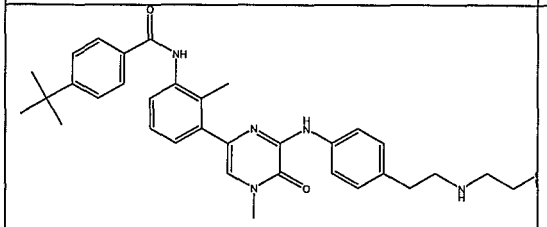
	4-{6-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-2-hydroxy-benzoic acid 526.22	527.19
	4-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-3-nitro-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide 624.26	625.32
	5-Ethyl-4,5,6,7-tetrahydro-benzo[b]thiophene-2-carboxylic acid (2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-amide 611.25	612.28
	4-Azetidin-1-yl-N-(2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide 578.26	579.27
	4-tert-Butyl-3-methoxy-N-(2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide 609.29	610.31
	4-{6-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-2-methoxy-benzoic acid 540.23	541.20

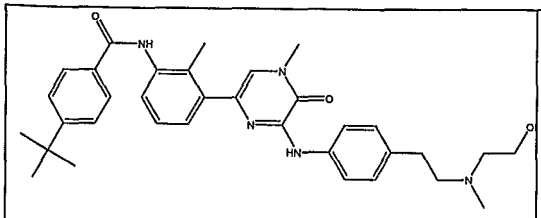
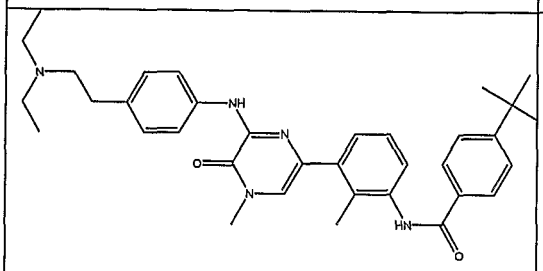
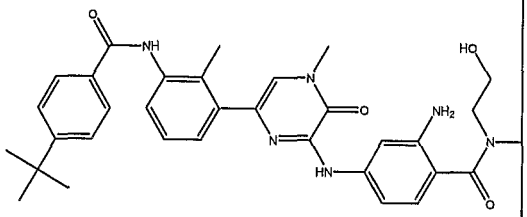
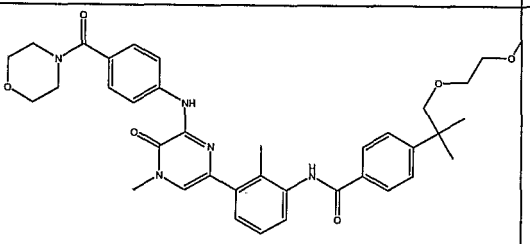
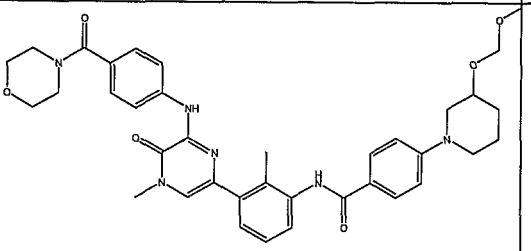
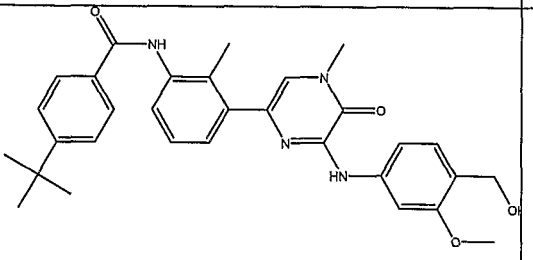
	1,4,4-Trimethyl-1,2,3,4-tetrahydro-quinoline-7-carboxylic acid (2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-amide 620.31	621.32
	4-(1-Methoxy-1-methyl-ethyl)-N-(2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide 595.28	496.19
	4-(2,2-Dimethyl-propionyl)-N-(2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide 607.28	608.30
	4-tert-Butyl-N-(3-{6-[3-methoxy-4-(morpholine-4-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide 609.29	610.33
	4-{6-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-2-methoxy-N-(3-methoxy-propyl)-benzamide 611.31	612.31
	N-{3-[6-(3-Acryloylamino-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-4-tert-butyl-benzamide 535.26	536.20

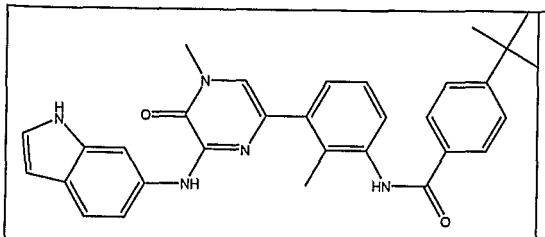
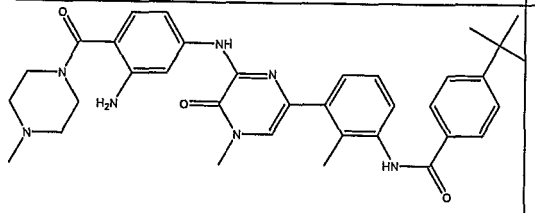
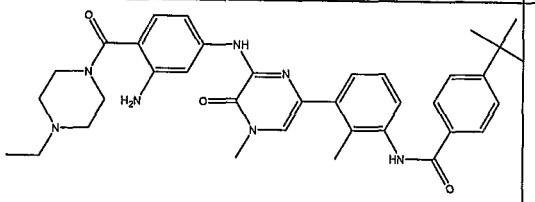
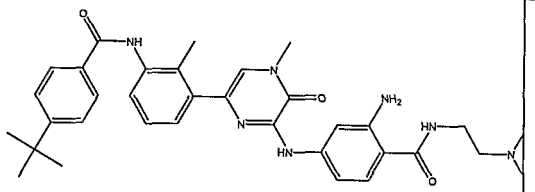
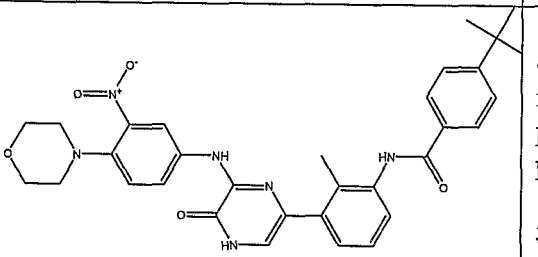
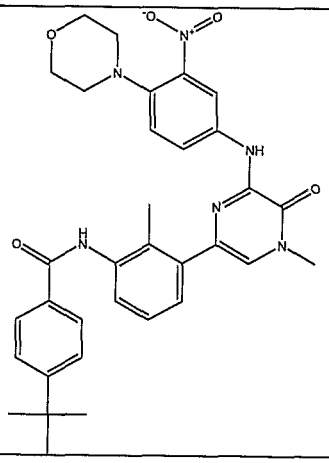
	4-tert-Butyl-N-{3-[6-(1H-indol-4-ylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide 505.24	506.23
	4-tert-Butyl-N-[3-(6-{4-[(2-methoxy-ethylamino)-methyl]-phenylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-benzamide 553.30	554.27
	4-tert-Butyl-N-{3-[6-(4-ethylaminomethyl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide 523.29	524.26
	4-tert-Butyl-N-{3-[6-(4-diethylaminomethyl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide 551.32	552.30
	4-tert-Butyl-N-[3-(6-{4-[(isopropyl-methyl-amino)-methyl]-phenylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-benzamide 551.32	552.26
	4-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[4-(2-methyl-piperidin-1-ylmethyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide 577.34	578.32

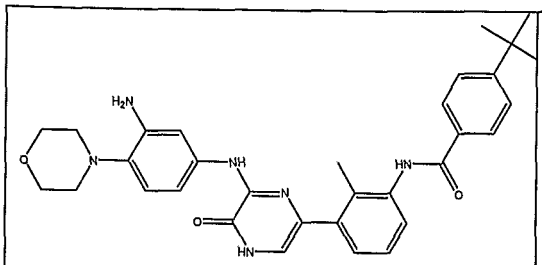
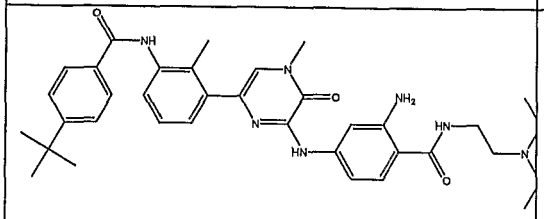
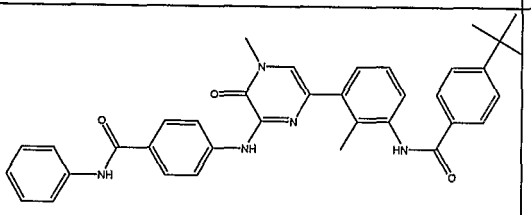
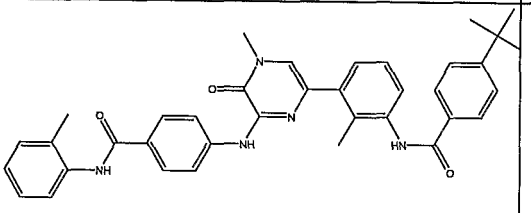
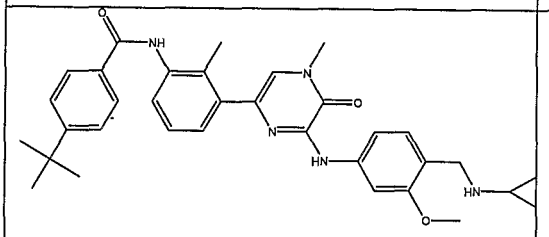
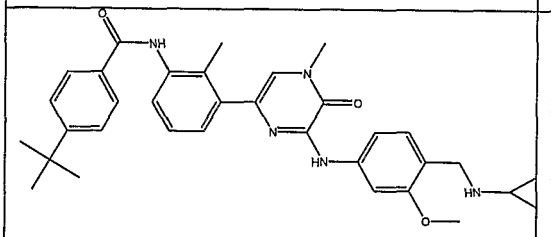
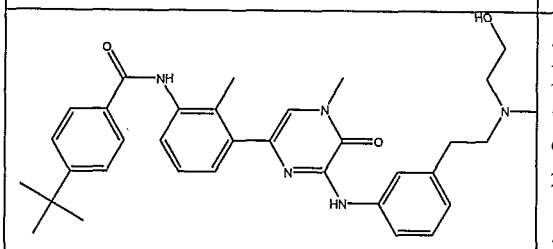
	4-tert-Butyl-N-[2-methyl-3-(4-methyl-5-oxo-6-{4-[2-(tetrahydro-pyran-4-ylamino)-ethyl]-phenylamino}-4,5-dihydro-pyrazin-2-yl)-phenyl]-benzamide 593.33	594.33
	5-Amino-2-{6-[3-(4-tert-butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-N-cyclopropyl-benzamide 564.28	565.27
	5-Amino-benzo[b]thiophene-2-carboxylic acid (2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-amide 594.20	595.19
	2-Amino-N-{3-[6-(benzothiazol-6-ylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-4-piperidin-1-yl-benzamide 565.22	566.21
	4-tert-Butyl-N-[3-(6-{2-[(2-hydroxy-ethyl)-methyl-amino]-pyridin-4-ylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-benzamide 540.28	541.23
	4-tert-Butyl-N-(3-{6-[3-methoxy-4-(4-methyl-piperazine-1-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide 622.32	623.33

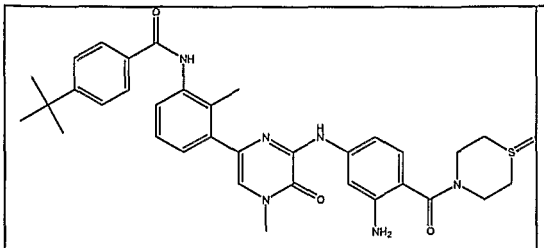
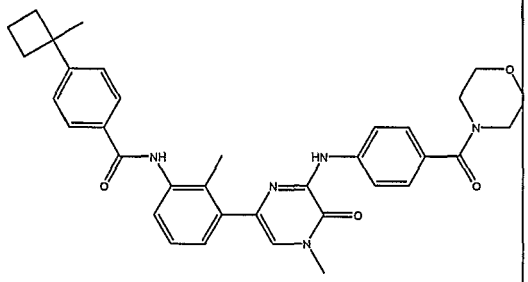
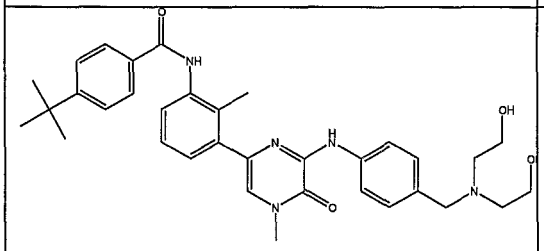
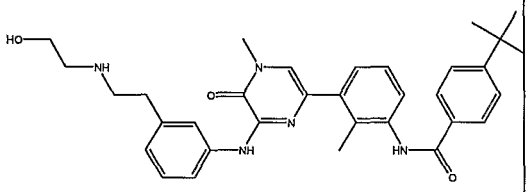
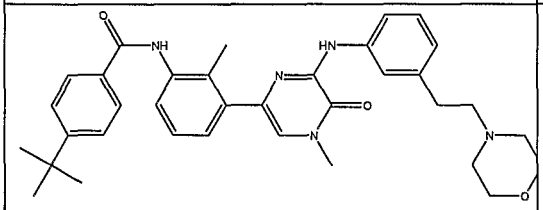
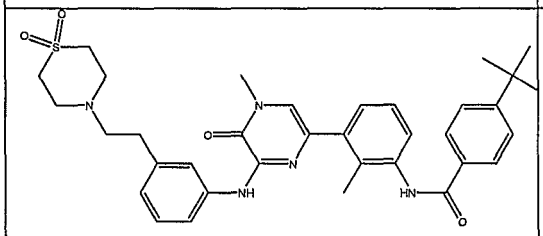
	4-{6-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-N-(2-hydroxy-ethyl)-2-methoxy-N-methyl-benzamide 597.29	598.32
	4-tert-Butyl-N-(3-{6-[3-methoxy-4-(piperidine-1-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide 607.31	608.32
	N-{3-[6-(3-Amino-4-morpholin-4-yl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-4-tert-butyl-benzamide 566.30	567.10
	N-{3-[6-(4-Amino-2-piperidin-1-ylmethyl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-4-tert-butyl-benzamide 578.33	579.38
	(4-{6-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-benzylamino)-acetic acid 553.26	576.28
	4-tert-Butyl-N-[3-(6-{4-[(cyclopropylmethyl-amino)-methyl]-phenylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-benzamide 549.31	550.31

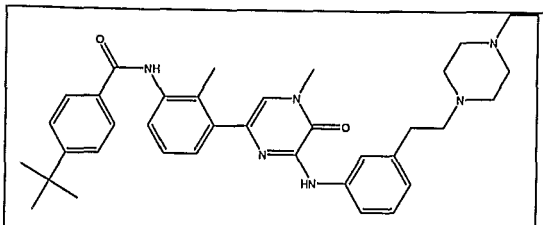
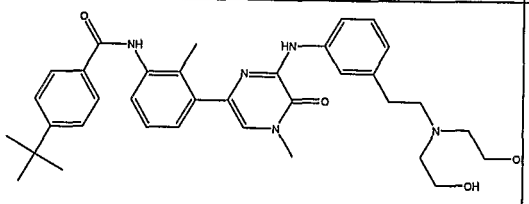
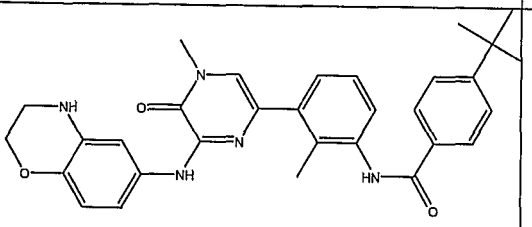
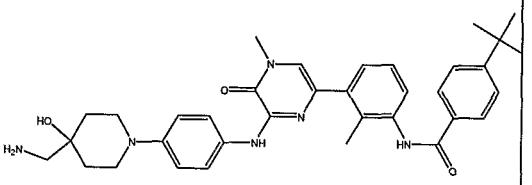
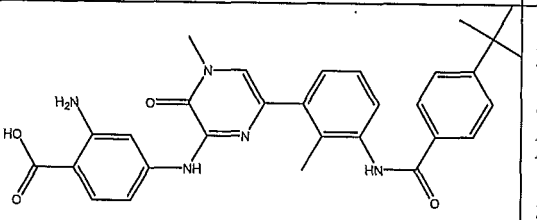
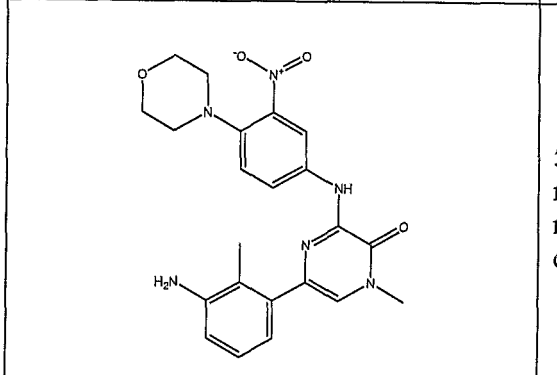
	N-{3-[6-(3-Amino-4-thiomorpholin-4-yl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-4-tert-butyl-benzamide 582.27	583.37
	4-tert-Butyl-N-(2-methyl-3-{4-methyl-5-oxo-6-[4-(piperidin-3-ylmethoxy)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide 579.32	580.45
	N-(3-{6-[3-Amino-4-(1,1-dioxo-1λ^6-thiomorpholin-4-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide 614.26	615.33
	N-(3-{6-[3-Amino-4-(piperidine-1-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide 592.31	593.36
	4-tert-Butyl-N-{2-methyl-3-[4-methyl-5-oxo-6-(1,2,3,4-tetrahydro-isoquinolin-6-ylamino)-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide 521.28	522.25
	4-tert-Butyl-N-[3-(6-{4-[2-(4-ethyl-piperazin-1-yl)-ethyl]-phenylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-benzamide 606.36	607.42
	4-tert-Butyl-N-[3-(6-{4-[2-(2-hydroxy-ethylamino)-ethyl]-phenylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-benzamide 553.30	554.30

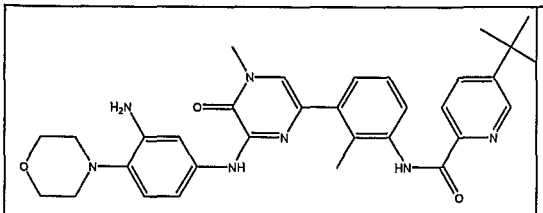
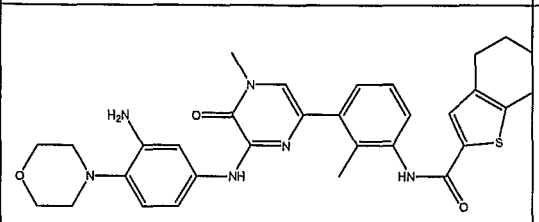
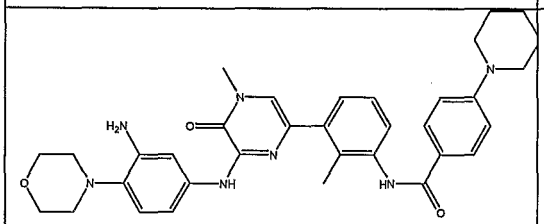
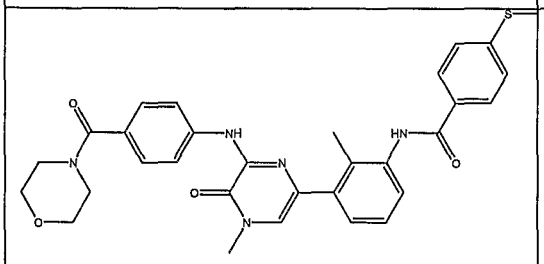
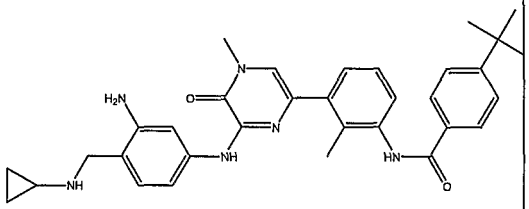
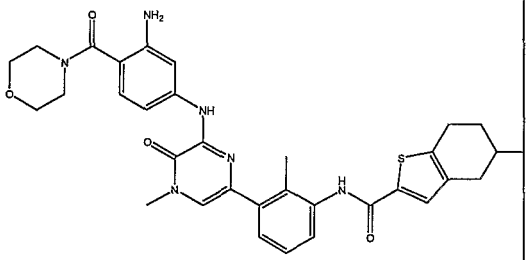
	4-tert-Butyl-N-{3-[6-(4-{2-[(2-hydroxy-ethyl)-methyl-amino]-ethyl}-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide 567.32	568.33
	4-tert-Butyl-N-(3-{6-[4-(2-diethylamino-ethyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide 565.34	566.34
	2-Amino-4-{6-[3-(4-tert-butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-N-(2-hydroxy-ethyl)-N-methyl-benzamide 582.29	583.30
	4-[2-(2-Methoxy-ethoxy)-1,1-dimethyl-ethyl]-N-(2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide 653.32	654.40
	4-(3-Methoxymethoxy-piperidin-1-yl)-N-(2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide 666.31	667.57
	4-tert-Butyl-N-{3-[6-(4-hydroxymethyl-3-methoxy-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide 526.25	527.23

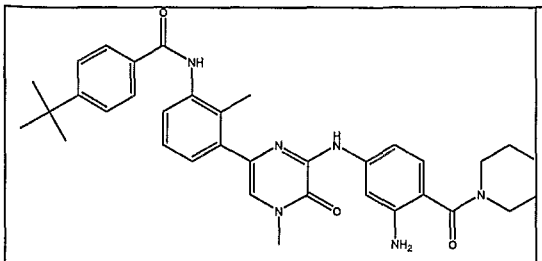
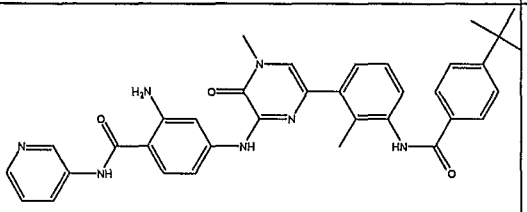
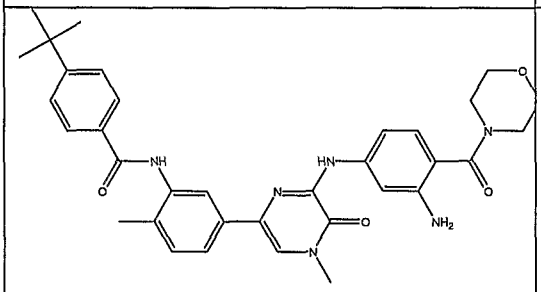
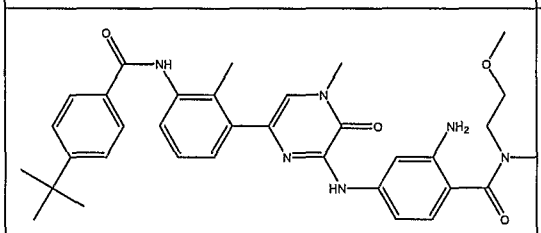
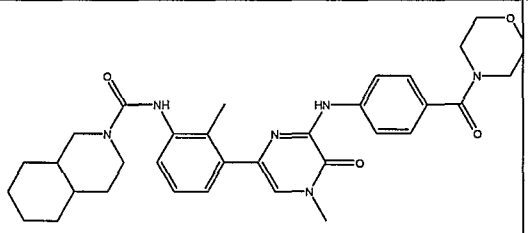
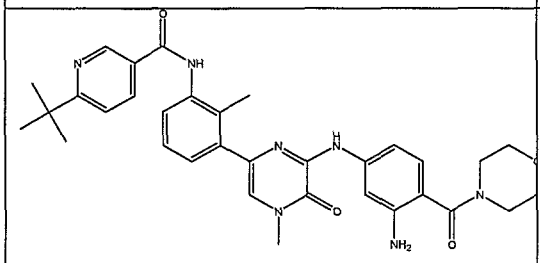
	4-tert-Butyl-N-{3-[6-(1H-indol-6-ylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide 505.24	506.19
	N-(3-{6-[3-Amino-4-(4-methyl-piperazine-1-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide 607.32	608.38
	N-(3-{6-[3-Amino-4-(4-ethyl-piperazine-1-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide 621.34	622.35
	2-Amino-4-{6-[3-(4-tert-butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-N-(2-dimethylamino-ethyl)-benzamide 595.32	596.31
	4-tert-Butyl-N-{2-methyl-3-[6-(4-morpholin-4-yl-3-nitro-phenylamino)-5-oxo-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide 582.26	583.32
	4-tert-Butyl-N-{2-methyl-3-[4-methyl-6-(4-morpholin-4-yl-3-nitro-phenylamino)-5-oxo-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide 596.27	597.28

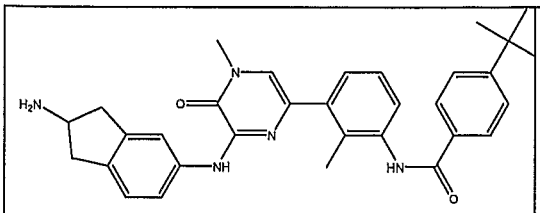
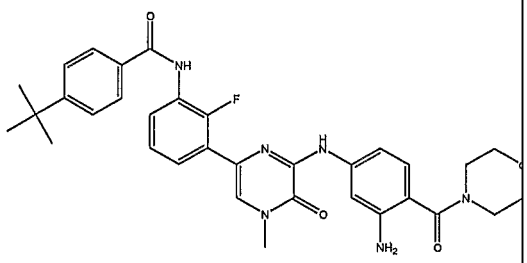
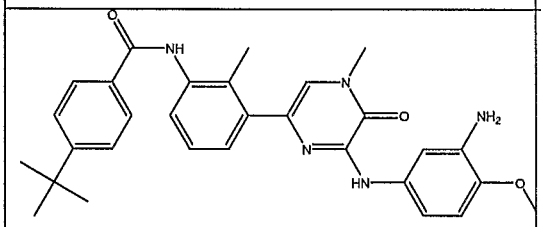
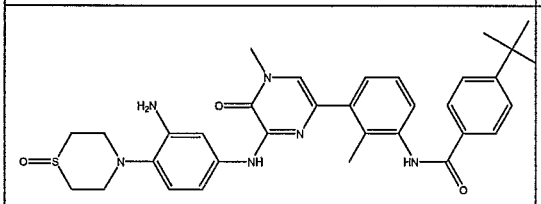
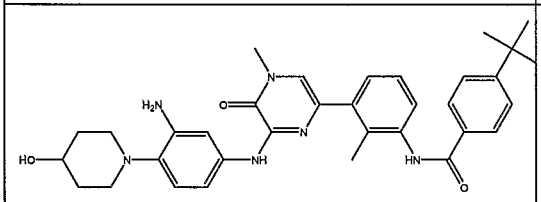
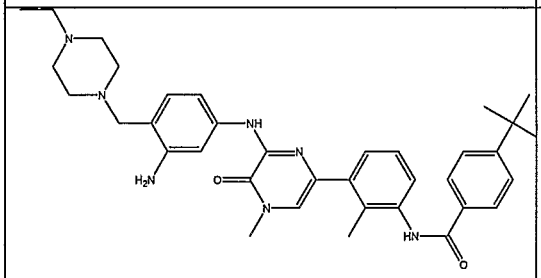
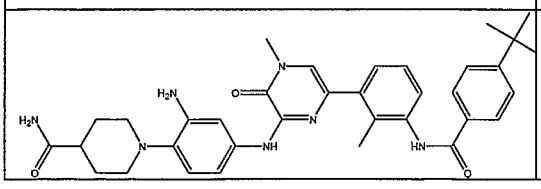
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	2-Amino-4-{6-[3-(4-tert-butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-N-(2-diethylamino-ethyl)-benzamide 623.36	624.34
	4-tert-Butyl-N-(3-{4-ethyl-6-[4-(phenyl-carbamoyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide 585.27	586.29
	4-tert-Butyl-N-(3-{4-ethyl-6-[4-(2-methyl-phenyl-carbamoyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide 599.29	600.33
	4-tert-Butyl-N-{3-[6-(4-cyclopropylaminomethyl-3-methoxy-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide 565.30	566.26
	4-tert-Butyl-N-{3-[6-(4-cyclopropylaminomethyl-3-methoxy-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide 642.26	643.49
	4-tert-Butyl-N-{3-[6-(3-{2-[(2-hydroxy-ethyl)-methyl-amino]-ethyl}-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide 567.32	568.33

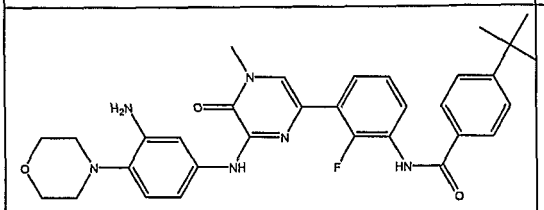
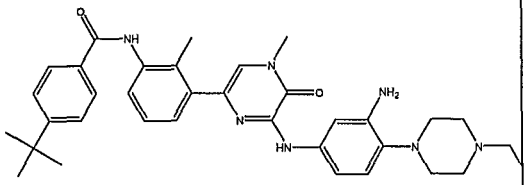
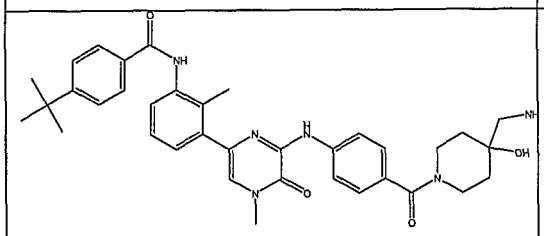
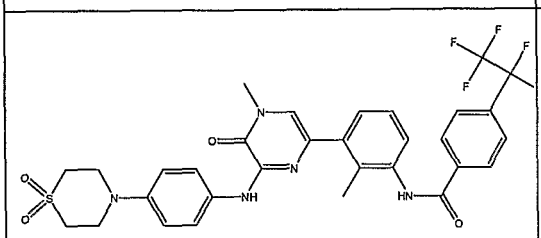
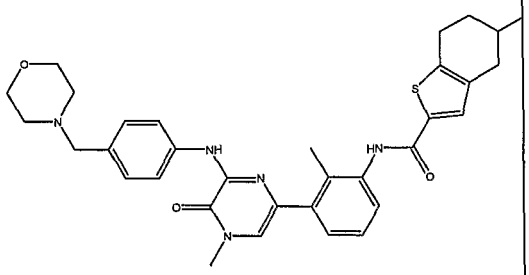
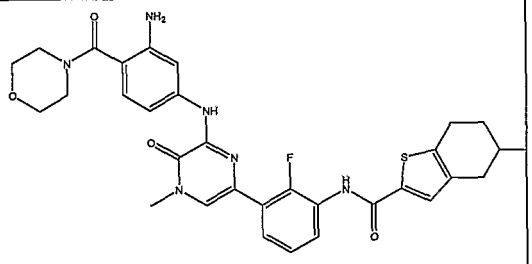
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	4-(1-Methyl-cyclobutyl)-N-(2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide 591.28	592.33
	N-{3-[6-(4-{[Bis-(2-hydroxy-ethyl)-amino]-methyl}-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-4-tert-butyl-benzamide 583.31	584.24
	4-tert-Butyl-N-[3-(6-{3-[2-(2-hydroxy-ethylamino)-ethyl]-phenylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-benzamide 553.30	554.19
	4-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[3-(2-morpholin-4-yl-ethyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide 579.32	580.20
	4-tert-Butyl-N-[3-(6-{3-[2-(1,1-dioxo-1λ^6-thiomorpholin-4-yl)-ethyl]-phenylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-benzamide 627.28	628.25

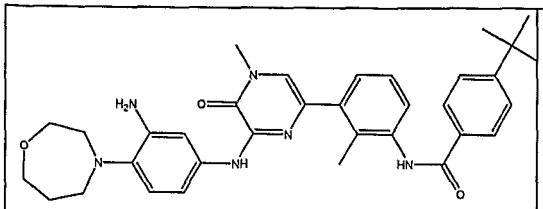
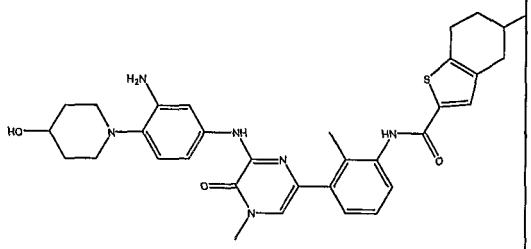
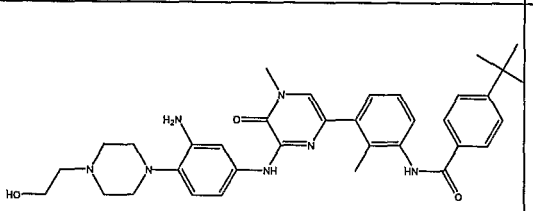
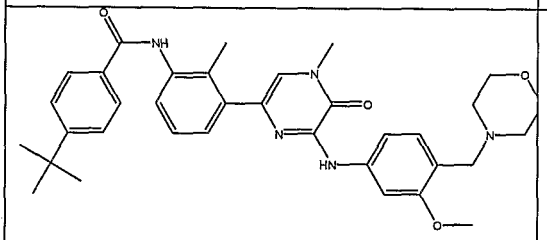
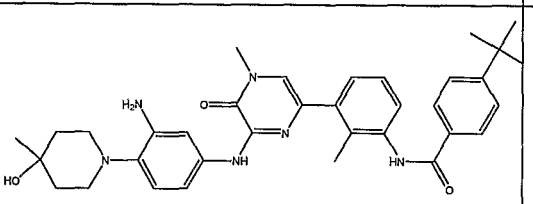
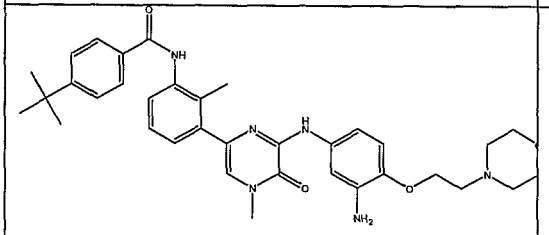
	4-tert-Butyl-N-[3-(6-{3-[2-(4-ethyl-piperazin-1-yl)-ethyl]-phenylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-benzamide 606.36	607.28
	N-{3-[6-(3-{2-[Bis-(2-hydroxy-ethyl)-amino]-ethyl}-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-4-tert-butyl-benzamide 597.33	598.25
	4-tert-Butyl-N-{3-[6-(3,4-dihydro-2H-benzo[1,4]oxazin-6-ylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide 523.25	524.10
	N-(3-{6-[4-(4-Aminomethyl-4-hydroxy-piperidin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide 594.33	595.38
	2-Amino-4-{6-[3-(4-tert-butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-benzoic acid 525.23	526.28
	5-(3-Amino-2-methyl-phenyl)-1-methyl-3-(4-morpholin-4-yl-3-nitro-phenylamino)-1H-pyrazin-2-one 436.18	437.20

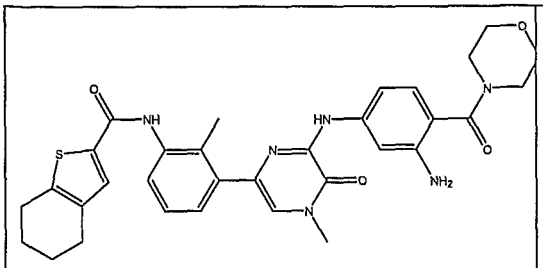
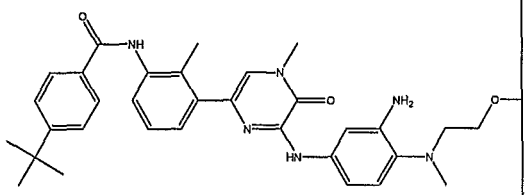
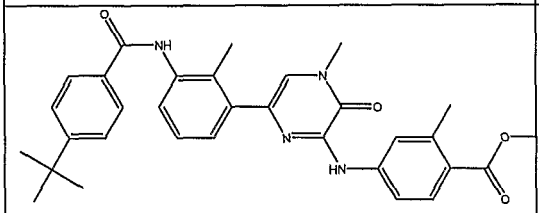
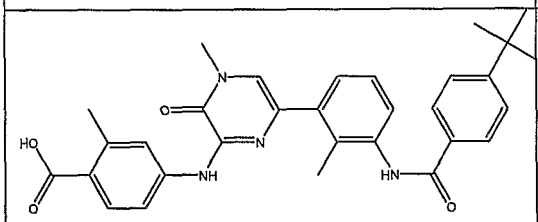
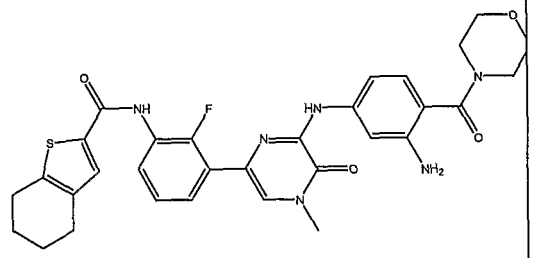
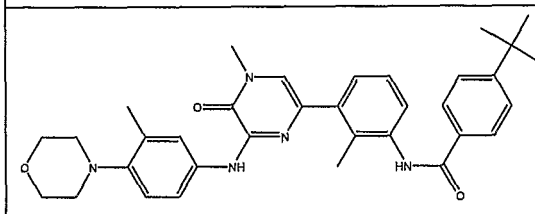
	5-tert-Butyl-pyridine-2-carboxylic acid {3-[6-(3-amino-4-morpholin-4-yl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-amide 567.29	568.21
	4,5,6,7-Tetrahydro-benzo[b]thiophene-2-carboxylic acid {3-[6-(3-amino-4-morpholin-4-yl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-amide 570.24	571.31
	N-{3-[6-(3-Amino-4-morpholin-4-yl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-4-piperidin-1-yl-benzamide 593.31	594.26
	N-(2-Methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-4-methylsulfanyl-benzamide 569.21	570.15
	N-{3-[6-(3-Amino-4-cyclopropylaminomethyl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-4-tert-butyl-benzamide 550.30	551.41
	5-Methyl-4,5,6,7-tetrahydro-benzo[b]thiophene-2-carboxylic acid (3-{6-[3-amino-4-(morpholine-4-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-amide 612.25	613.21

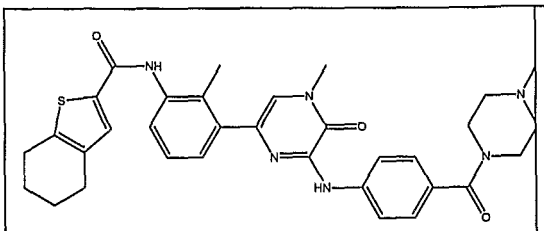
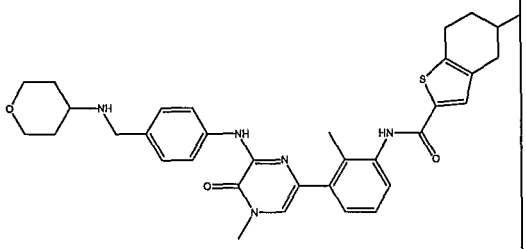
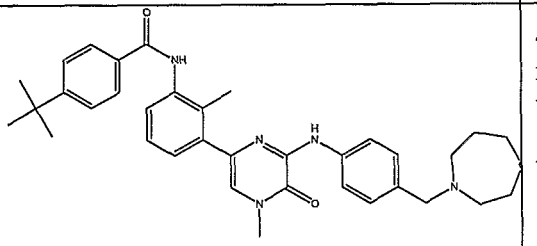
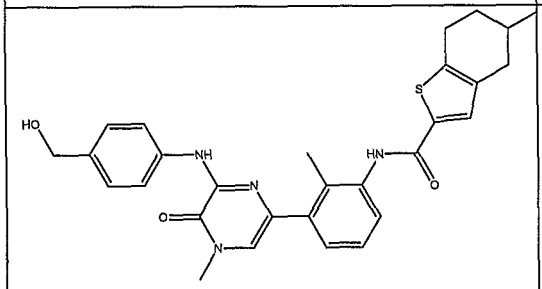
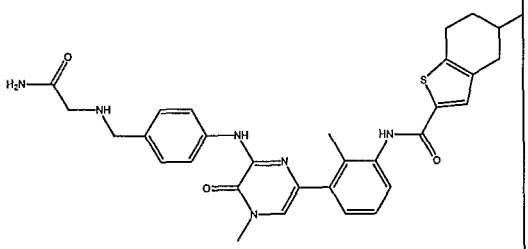
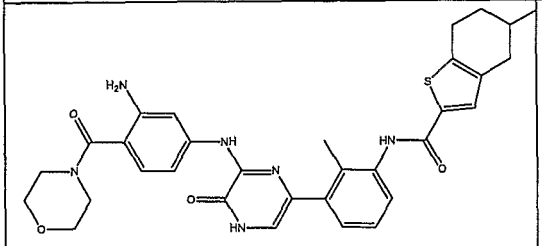
	N-(3-{6-[3-Amino-4-(thiomorpholine-4-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide 610.27	611.44
	2-Amino-4-{6-[3-(4-tert-butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-N-pyridin-3-yl-benzamide 601.28	602.36
	N-(5-{6-[3-Amino-4-(morpholine-4-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide 594.29	595.46
	2-Amino-4-{6-[3-(4-tert-butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-N-(2-methoxy-ethyl)-N-methyl-benzamide 596.31	597.37
	Octahydro-isoquinoline-2-carboxylic acid (2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-amide 584.31	585.29
	N-(3-{6-[3-Amino-4-(morpholine-4-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-6-tert-butyl-nicotinamide 595.29	596.40

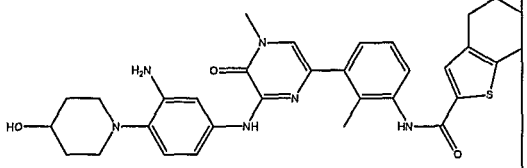
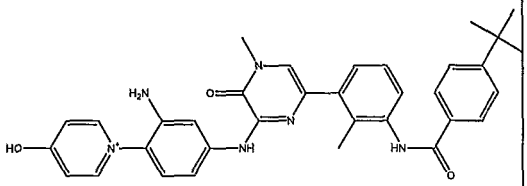
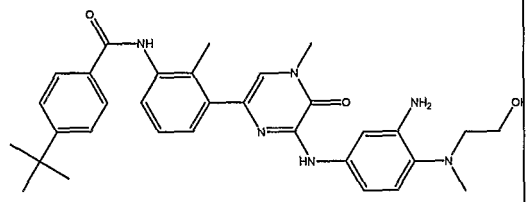
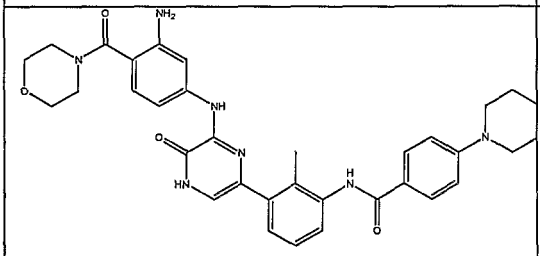
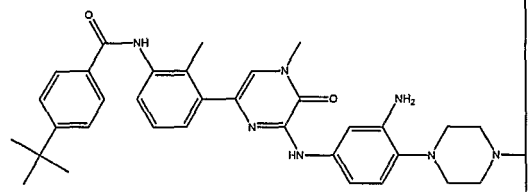
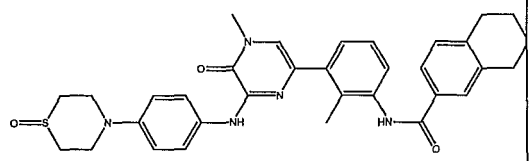
	N-{3-[6-(2-Amino-indan-5-ylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-4-tert-butyl-benzamide 521.28	522.26
	N-(3-{6-[3-Amino-4-(morpholine-4-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-fluoro-phenyl)-4-tert-butyl-benzamide 598.27	599.43
	N-{3-[6-(3-Amino-4-methoxy-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-4-tert-butyl-benzamide 511.25	512.34
	N-(3-{6-[3-Amino-4-(1-oxo-1λ^4-thiomorpholin-4-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide 598.27	599.38
	N-(3-{6-[3-Amino-4-(4-hydroxy-piperidin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide 580.31	581.35
	N-(3-{6-[3-Amino-4-(4-ethyl-piperazin-1-ylmethyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide 607.3632	608.53
	1-(2-Amino-4-{6-[3-(4-tert-butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-phenyl)-piperidine-4-carboxylic acid amide	608.43

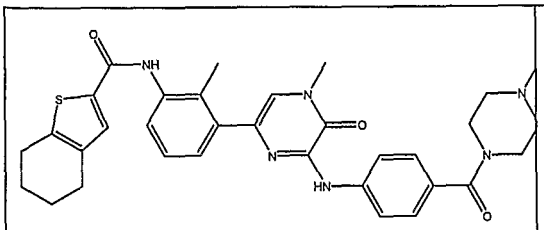
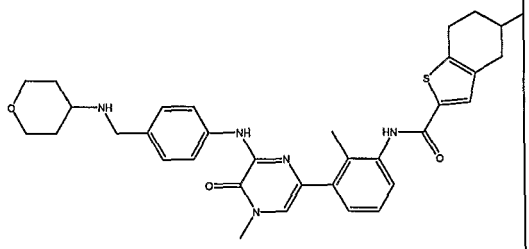
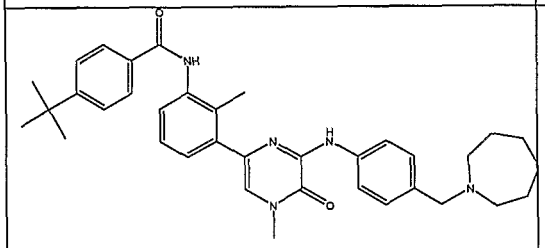
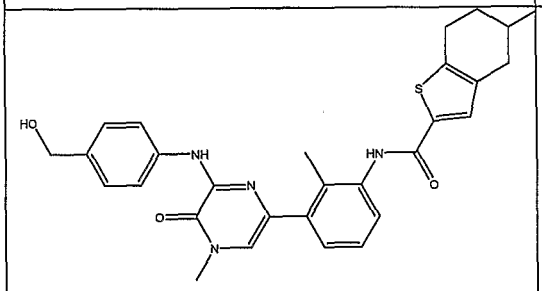
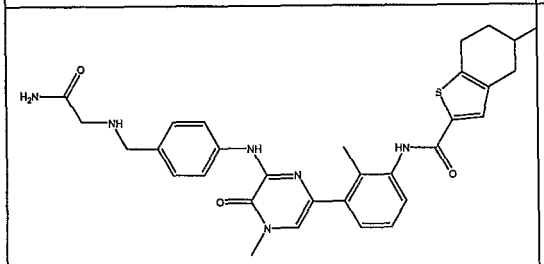
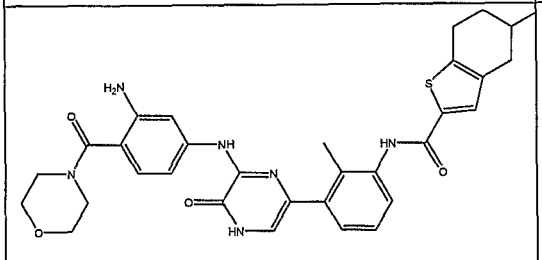
	607.32	
	N-{3-[6-(3-Amino-4-morpholin-4-yl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-fluoro-phenyl}-4-tert-butyl-benzamide 570.27	571.39
	N-(3-{6-[3-Amino-4-(4-ethyl-piperazin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide 593.34	594.39
	N-(3-{6-[4-(4-Aminomethyl-4-hydroxy-piperidine-1-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide 622.32	623.70
	N-(3-{6-[4-(1,1-Dioxo-1λ^6-thiomorpholin-4-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-pentafluoroethyl-benzamide 661.17	662.32
	5-Methyl-4,5,6,7-tetrahydro-benzo[b]thiophene-2-carboxylic acid {2-methyl-3-[4-methyl-6-(4-morpholin-4-ylmethyl-phenylamino)-5-oxo-4,5-dihydro-pyrazin-2-yl]-phenyl}-amide 583.26	584.28
	5-Methyl-4,5,6,7-tetrahydro-benzo[b]thiophene-2-carboxylic acid (3-{6-[3-amino-4-(morpholine-4-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-fluoro-phenyl)-amide 616.22	617.39

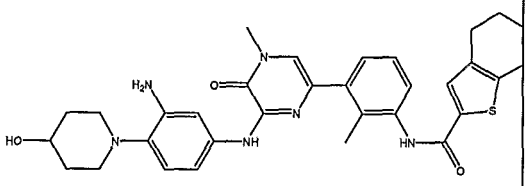
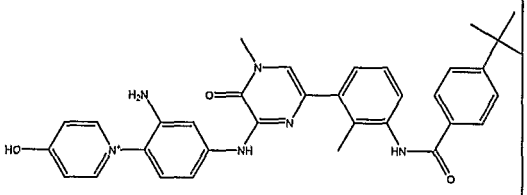
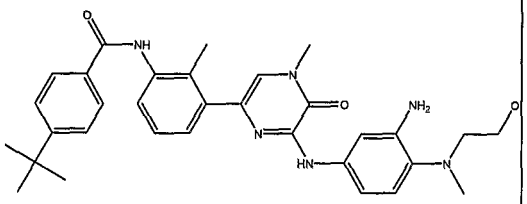
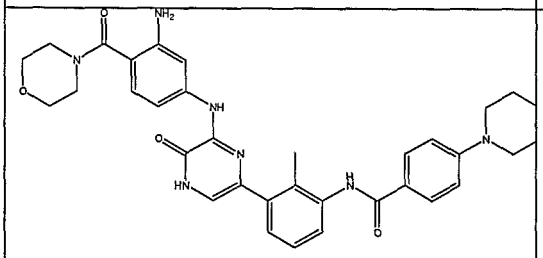
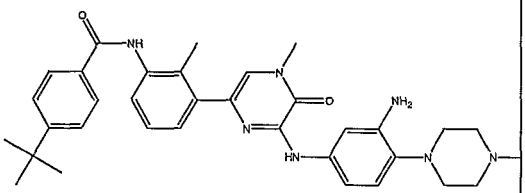
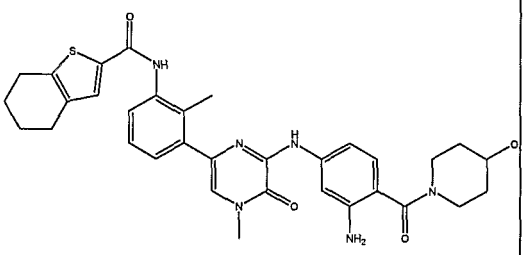
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	5-Methyl-4,5,6,7-tetrahydro-benzo[b]thiophene-2-carboxylic acid (3-{6-[3-amino-4-(4-hydroxy-piperidin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-amide 598.27	600.30
	N-[3-(6-{3-Amino-4-[4-(2-hydroxy-ethyl)-piperazin-1-yl]-phenylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-4-tert-butyl-benzamide 609.34	611.40
	4-tert-Butyl-N-{3-[6-(3-methoxy-4-morpholin-4-ylmethyl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide 595.31	596.21
	N-(3-{6-[3-Amino-4-(4-hydroxy-4-methyl-piperidin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide 594.33	596.31
	N-(3-{6-[3-Amino-4-(2-morpholin-4-yl-ethoxy)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide 610.32	612.40

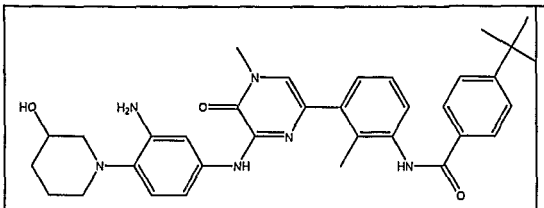
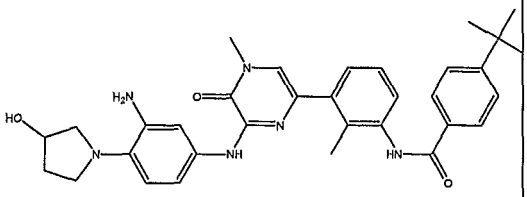
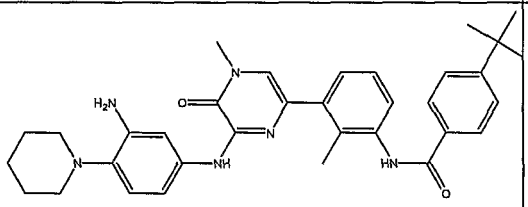
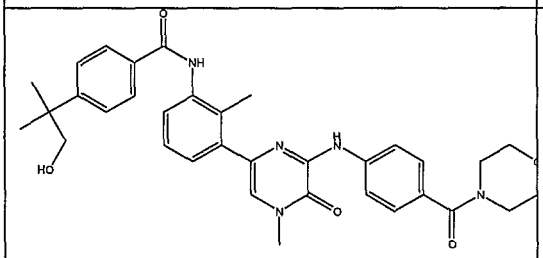
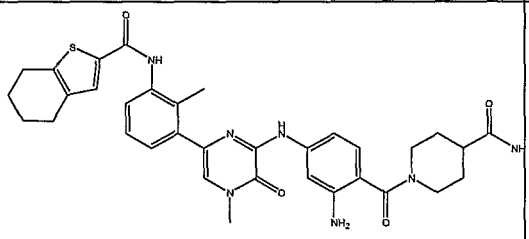
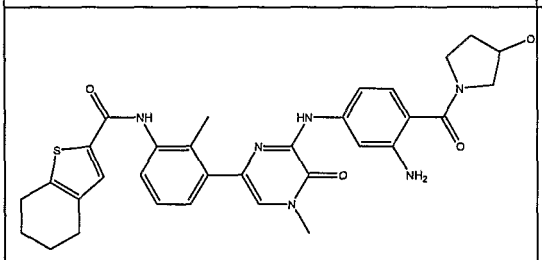
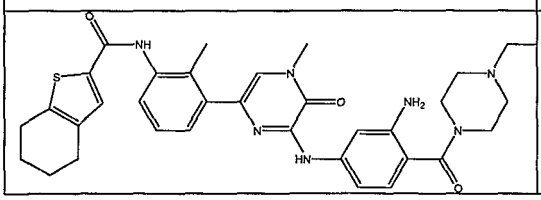
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	N-[3-(6-{3-Amino-4-[(2-methoxy-ethyl)-methyl-amino]-phenylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-4-tert-butyl-benzamide 568.31	569.21
	4-{6-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-2-methyl-benzoic acid methyl ester 538.25	539.36
	4-{6-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-2-methyl-benzoic acid 524.24	525.33
	4,5,6,7-Tetrahydro-benzo[b]thiophene-2-carboxylic acid (3-{6-[3-amino-4-(morpholine-4-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-fluoro-phenyl)-amide 602.21	604.31
	4-tert-Butyl-N-{2-methyl-3-[4-methyl-6-(3-methyl-4-morpholin-4-yl-phenylamino)-5-oxo-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide 565.30	566.33

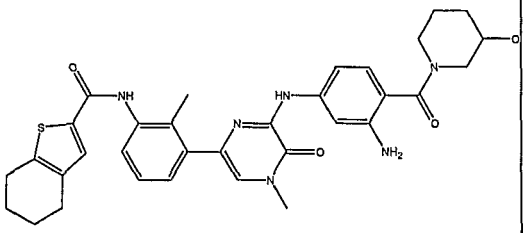
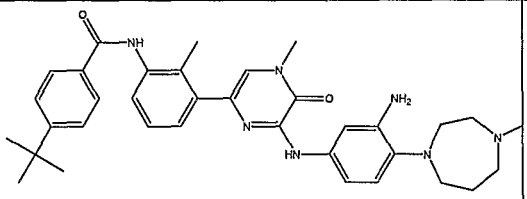
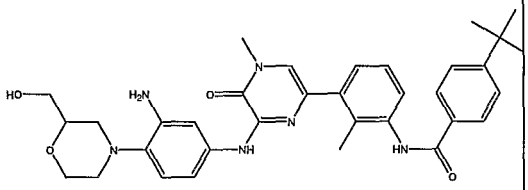
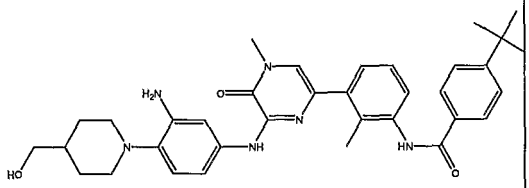
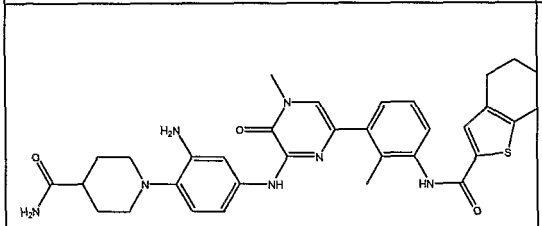
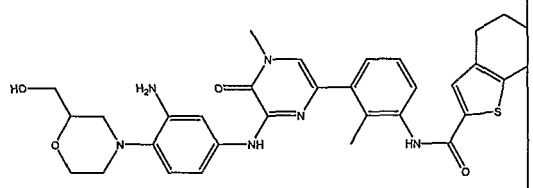
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	5-Methyl-4,5,6,7-tetrahydro-benzo[b]thiophene-2-carboxylic acid [2-methyl-3-(4-methyl-5-oxo-6-{4-[(tetrahydro-pyran-4-ylamino)-methyl]-phenylamino}-4,5-dihydro-pyrazin-2-yl)-phenyl]-amide 597.28	598.17
	4-tert-Butyl-N-{2-methyl-3-[4-methyl-6-(4-[1,4]oxazepan-4-ylmethyl-phenylamino)-5-oxo-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide 579.32	580.17
	5-Methyl-4,5,6,7-tetrahydro-benzo[b]thiophene-2-carboxylic acid {3-[6-(4-hydroxymethyl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-amide 514.20	515.23
	5-Methyl-4,5,6,7-tetrahydro-benzo[b]thiophene-2-carboxylic acid [3-(6-{4-[(carbamoylmethyl-amino)-methyl]-phenylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-amide 570.24	571.20
	5-Methyl-4,5,6,7-tetrahydro-benzo[b]thiophene-2-carboxylic acid (3-{6-[3-amino-4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-	599.24

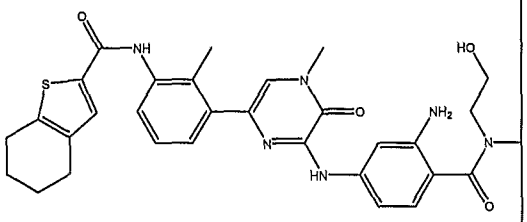
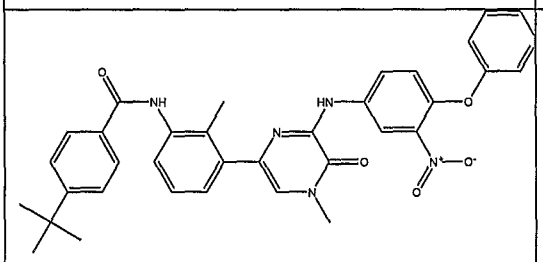
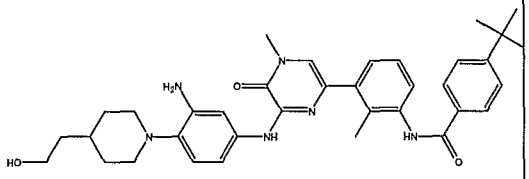
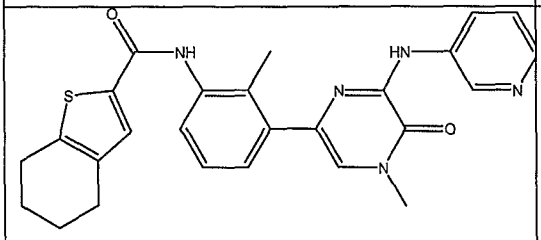
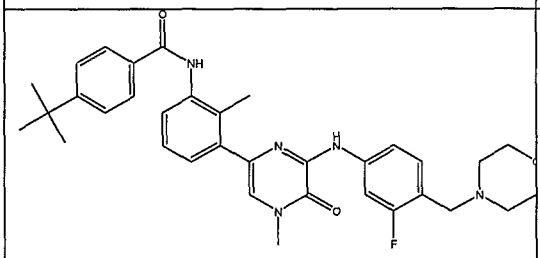
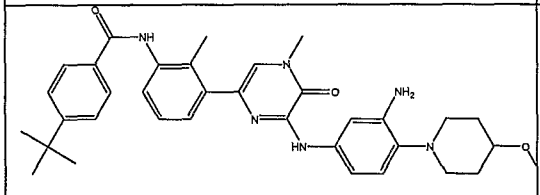
	amide 598.23	
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	1-(2-Amino-4-{6-[3-(4-tert-butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-phenyl)-4-hydroxy-pyridinium 575.28	575.23
	N-[3-(6-{3-Amino-4-[(2-hydroxy-ethyl)-methyl-amino]-phenylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-4-tert-butyl-benzamide 554.30	555.18
	N-(3-{6-[3-Amino-4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-piperidin-1-yl-benzamide 607.29	608.22
	N-(3-{6-[3-Amino-4-(4-methyl-piperazin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide 579.33	580.24
	5,6,7,8-Tetrahydro-naphthalene-2-carboxylic acid (2-methyl-3-{4-methyl-5-oxo-6-[4-(1-oxo-1λ⁴-thiomorpholin-4-yl)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-amide 581.25	582.25

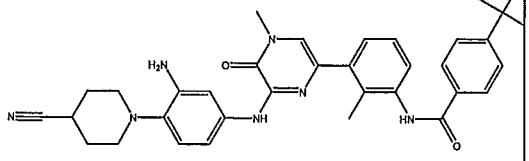
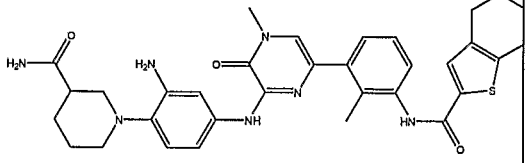
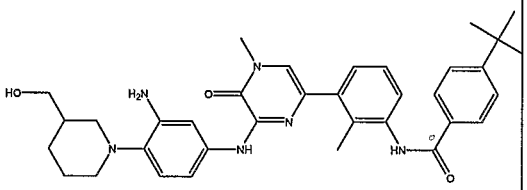
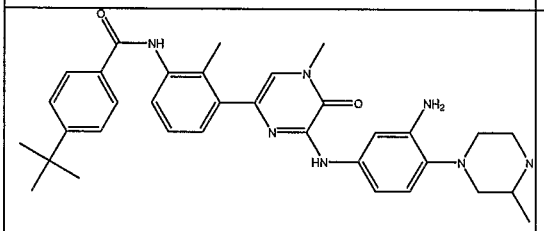
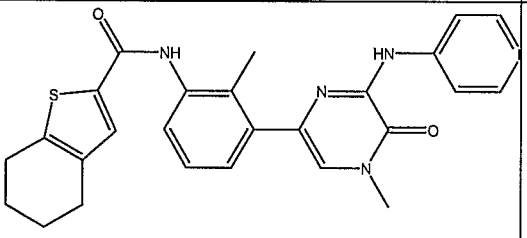
	4,5,6,7-Tetrahydro-benzo[b]thiophene-2-carboxylic acid (2-methyl-3-{4-methyl-6-[4-(4-methyl-piperazine-1-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-amide 596.26	597.21
	5-Methyl-4,5,6,7-tetrahydro-benzo[b]thiophene-2-carboxylic acid [2-methyl-3-(4-methyl-5-oxo-6-{4-[(tetrahydro-pyran-4-ylamino)-methyl]-phenylamino}-4,5-dihydro-pyrazin-2-yl)-phenyl]-amide 597.28	598.17
	4-tert-Butyl-N-{2-methyl-3-[4-methyl-6-(4-[1,4]oxazepan-4-ylmethyl-phenylamino)-5-oxo-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide 579.32	580.17
	5-Methyl-4,5,6,7-tetrahydro-benzo[b]thiophene-2-carboxylic acid {3-[6-(4-hydroxymethyl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-amide 514.20	515.23
	5-Methyl-4,5,6,7-tetrahydro-benzo[b]thiophene-2-carboxylic acid [3-(6-{4-[(carbamoylmethyl-amino)-methyl]-phenylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-amide 570.24	571.20
	5-Methyl-4,5,6,7-tetrahydro-benzo[b]thiophene-2-carboxylic acid (3-{6-[3-amino-4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-amide 598.24	599.23

	4,5,6,7-Tetrahydro-benzo[b]thiophene-2-carboxylic acid (3-{6-[3-amino-4-(4-hydroxy-piperidin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-amide 584.26	585.16
	1-(2-Amino-4-{6-[3-(4-tert-butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-phenyl)-4-hydroxy-pyridinium 575.28	575.23
	N-[3-(6-{3-Amino-4-[(2-hydroxy-ethyl)-methyl-amino]-phenylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-4-tert-butyl-benzamide 554.30	555.25
	N-(3-{6-[3-Amino-4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-piperidin-1-yl-benzamide 607.29	608.13
	N-(3-{6-[3-Amino-4-(4-methyl-piperazin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide 579.33	580.26
	4,5,6,7-Tetrahydro-benzo[b]thiophene-2-carboxylic acid (3-{6-[3-amino-4-(4-hydroxy-piperidine-1-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-amide 612.25	613.18

	N-(3-{6-[3-Amino-4-(3-hydroxy-piperidin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide 580.32	581.23
	N-(3-{6-[3-Amino-4-(3-hydroxy-pyrrolidin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide 566.30	567.23
	N-{3-[6-(3-Amino-4-piperidin-1-yl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-4-tert-butyl-benzamide 564.32	565.23
	4-(2-Hydroxy-1,1-dimethyl-ethyl)-N-(2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide 595.28	596.19
	1-[2-Amino-4-(4-methyl-6-{2-methyl-3-[(4,5,6,7-tetrahydro-benzo[b]thiophene-2-carbonyl)-amino]-phenyl}-3-oxo-3,4-dihydro-pyrazin-2-ylamino)-benzoyl]-piperidine-4-carboxylic acid amide 639.26	640.18
	4,5,6,7-Tetrahydro-benzo[b]thiophene-2-carboxylic acid (3-{6-[3-amino-4-(3-hydroxy-pyrrolidine-1-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-amide 598.24	599.18
	4,5,6,7-Tetrahydro-benzo[b]thiophene-2-carboxylic acid (3-{6-[3-amino-4-(4-ethyl-piperazine-1-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-	626.19

	dihydro-pyrazin-2-yl}-2-methyl-phenyl)-amide 625.28	
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	N-(3-{6-[3-Amino-4-(4-methyl-[1,4]diazepan-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide 593.35	594.25
	N-(3-{6-[3-Amino-4-(2-hydroxymethyl-morpholin-4-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide 596.31	597.22
	N-(3-{6-[3-Amino-4-(4-hydroxymethyl-piperidin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide 594.33	595.30
	1-[2-Amino-4-(4-methyl-6-{2-methyl-3-[(4,5,6,7-tetrahydro-benzo[b]thiophene-2-carbonyl)-amino]-phenyl}-3-oxo-3,4-dihydro-pyrazin-2-ylamino)-phenyl]-piperidine-4-carboxylic acid amide 611.26	612.16
	4,5,6,7-Tetrahydro-benzo[b]thiophene-2-carboxylic acid (3-{6-[3-amino-4-(2-hydroxymethyl-morpholin-4-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-amide	601.15

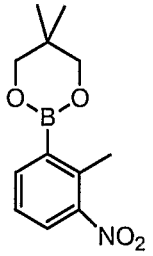
	600.25	
	4,5,6,7-Tetrahydro-benzo[b]thiophene-2-carboxylic acid [3-(6-{3-amino-4-[(2-hydroxy-ethyl)-methyl-carbamoyl]-phenylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-amide 586.24	587.20
	4-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[3-nitro-4-(pyridin-3-yloxy)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide 604.24	605.26
	N-[3-(6-{3-Amino-4-[4-(2-hydroxy-ethyl)-piperidin-1-yl]-phenylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-4-tert-butyl-benzamide 608.35	609.26
	4,5,6,7-Tetrahydro-benzo[b]thiophene-2-carboxylic acid {2-methyl-3-[4-methyl-5-oxo-6-(pyridin-3-ylamino)-4,5-dihydro-pyrazin-2-yl]-phenyl}-amide 471.17	472.13
	4-tert-Butyl-N-{3-[6-(3-fluoro-4-morpholin-4-ylmethyl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide 583.30	584.27
	N-(3-{6-[3-Amino-4-(4-methoxy-piperidin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide 594.33	595.25

	N-(3-{6-[3-Amino-4-(4-cyano-piperidin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide 589.32	590.23
	1-[2-Amino-4-(4-methyl-6-{2-methyl-3-[(4,5,6,7-tetrahydro-benzo[b]thiophene-2-carbonyl)-amino]-phenyl}-3-oxo-3,4-dihydro-pyrazin-2-ylamino)-phenyl]-piperidine-3-carboxylic acid amide 611.27	612.2
	N-(3-{6-[3-Amino-4-(3-hydroxymethyl-piperidin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide 594.33	595.3
	N-(3-{6-[3-Amino-4-(3-methyl-piperazin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide 579.33	580.3
	4,5,6,7-Tetrahydro-benzo[b]thiophene-2-carboxylic acid {2-methyl-3-[4-methyl-5-oxo-6-(pyridin-4-ylamino)-4,5-dihydro-pyrazin-2-yl]-phenyl}-amide 471.17	472.07

Example 5

Synthesis of 4-tert-Butyl-N-(2-methyl-3-{8-[4-(morpholine-4-carbonyl)-phenylamino]-imidazo[1,2-a]pyrazin-6-yl}-phenyl)-benzamide

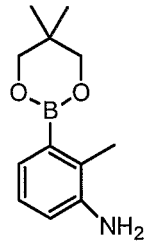
STEP 1: **2-(2-Methyl-3-nitrophenyl)-5,5-dimethyl[1,3,2]dioxaborinane**



[00260] A mixture of 2-bromo-6-nitrotoluene (3.2g; 14.8mmol), bis(neopentyl glycolato)diboron (4g; 17.7mmol), [1,1'-bis(diphenylphosphino)-ferrocene]dichlropalladium, 1:1 complex with dichloromethane (362mg; 0.44mmol), potassium acetate (7.3g; 73.8mmol), and dioxane (75mL) is heated at reflux for 3h.

[00261] The mixture is then cooled to room temperature, treated with water (100mL), and extracted with ethyl acetate (3 x 80mL). The extracts are washed with water (2 x 50mL) and brine (1 x 50mL), dried over anhydrous sodium sulfate and concentrated in vacuo. The residue is purified by flash chromatography over silica gel (elution with hexane/EtOAc 95/5 – 6/1, gradient) to afford 2-(2-methyl-3-nitrophenyl)-5,5-dimethyl[1,3,2]dioxaborinane as a white solid (3.3g)

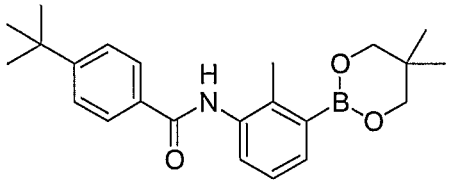
STEP 2: 3-(5,5-Dimethyl[1,3,2]dioxaborinan-2-yl)-2-methylaniline



[00262] A mixture of 2-(2-methyl-3-nitrophenyl)-5,5-dimethyl[1,3,2]dioxaborinan (6.7g; 27.7mmol), 10% palladium-on-carbon (670mg), ethyl acetate (75mL) and methanol (75mL) is treated with 40psi of hydrogen for 2h at room temperature.

[00263] The mixture is filtered through celite, washing with DCM (2 x 100mL), and the filtrate is concentrated in vacuo to afford 3-(5,5-dimethyl[1,3,2]dioxaborinan-2-yl)-2-methylaniline as a white solid (6.0g)

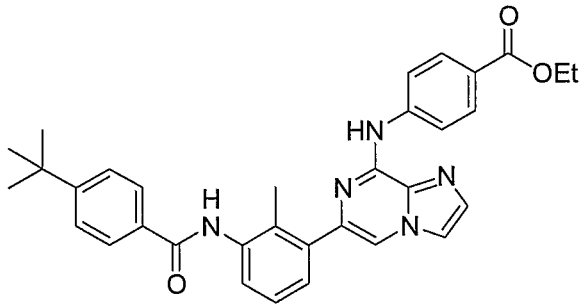
STEP 3: 4-t-Butyl-N-[3-(5,5-dimethyl[1,3,2]dioxaborinan-2-yl)-2-methylphenyl]-benzamide



[00264] A solution of 3-(5,5-dimethyl[1,3,2]dioxaborinan-2-yl)-2-methylaniline (3.1g; 14.2mmol) and triethylamine (3.0mL; 21.2mmol) in THF (110mL) is treated dropwise with 4-(t-butyl)benzoyl chloride (2.6mL; 14.2mmol) and the mixture is stirred at room temperature for 15min.

[00265] The mixture is then filtered through Celite, and washed with EtOAc, the filtrate is concentrated in vacuo to afford 4-t-butyl-N-[3-(5,5-dimethyl[1,3,2]dioxaborinan-2-yl)-2-methylphenyl]-benzamide as a white solid (4.0g).

STEP 4: 4-{6-[3-(4-tert-Butyl-benzoylamino)-2-methylphenyl]-imidazo[1,2-a]pyrazin-8-ylamino}-benzoic acid ethyl ester

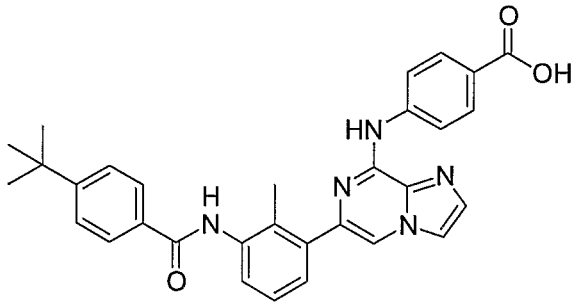


[00266] A mixture of 4-(6-bromo-imidazo[1,2-a]pyrazin-8-ylamino)-benzoic acid ethyl ester (687mg; 1.9mmol), 4-t-butyl-N-[3-(5,5-dimethyl[1,3,2]dioxaborinan-2-yl)-2-methylphenyl]-benzamide (866mg; 2.3mmol), palladium tetrakis(triphenylphosphine) (220mg; 0.19mmol), 1N aqueous sodium carbonate

(3mL), and DME (13mL) is heated at 95 °C in a sealed tube for 16h.

[00267] The mixture is then cooled to room temperature, treated with water (30mL) and extracted with ethyl acetate (3 x 40mL). The extracts are washed with brine (1 x 50mL), dried over anhydrous sodium sulfate, and concentrated in vacuo. The residue is triturated with hexane and filtered to afford 4-{6-[3-(4-tert-butyl-benzoylamino)-2-methylphenyl]-imidazo[1,2-a]pyrazin-8-ylamino}-benzoic acid ethyl ester as a dark yellow solid (600mg).

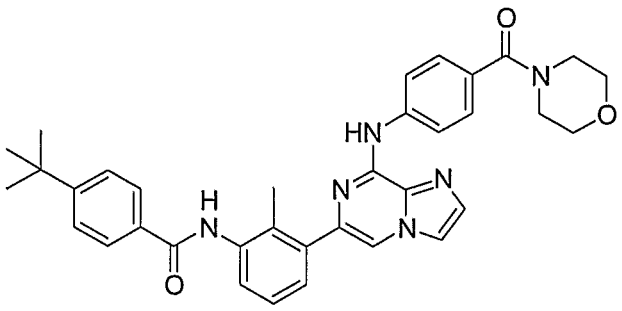
STEP 5: **4-{6-[3-(4-tert-Butyl-benzoylamino)-2-methylphenyl]-imidazo[1,2-a]pyrazin-8-ylamino}-benzoic acid**



[00268] A mixture of 4-{6-[3-(4-tert-butyl-benzoylamino)-2-methylphenyl]-imidazo[1,2-a]pyrazin-8-ylamino}-benzoic acid ethyl ester (600mg; 1.1mmol), ethanol (50mL) and 1N aqueous sodium hydroxide (50mL) is heated at reflux for 1h.

[00269] The mixture is then cooled to room temperature, adjusted to pH 6 with 1N HCl and extracted with ethyl actetate (3 x 100ml). The extracts are washed with brine (1 x 50mL), dried over anhydrous sodium sulfate and concentrated in vacuo. The residue is triturated with ethyl acetate to afford 4-{6-[3-(4-tert-butyl-benzoylamino)-2-methylphenyl]-imidazo[1,2-a]pyrazin-8-ylamino}-benzoic acid as a white solid (300mg).

STEP 6: **4-tert-Butyl-N-(2-methyl-3-{8-[4-(morpholine-4-carbonyl)-phenylamino]-imidazo[1,2-a]pyrazin-6-yl}-phenyl)-benzamide**

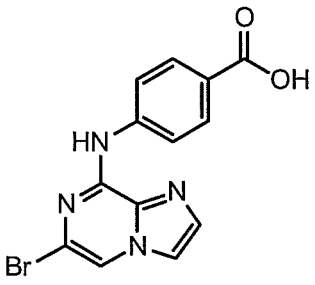


[00270] A mixture of 4-{6-[3-(4-tert-butyl-benzoylamino)-2-methylphenyl]-imidazo[1,2-a]pyrazin-8-ylamino}-benzoic acid (52mg; 0.1mmol), benzotriazol-1-yloxytris(dimethylamino)phosphonium hexafluorophosphate (49mg; 0.11mmol), diisopropylethylamine (0.05mL; 0.3mmol), and DMF (1.7mL) is stirred at room temperature for 20min. Morpholine (0.04mL) is added and the mixture is stirred at room temperature for 2h.

[00271] Water (10mL) is then added and the mixture filtered to afford 4-tert-Butyl-N-(2-methyl-3-{8-[4-(morpholine-4-carbonyl)-phenylamino]-imidazo[1,2-a]pyrazin-6-yl}-phenyl)-benzamide as a white solid (40mg).

Example 6

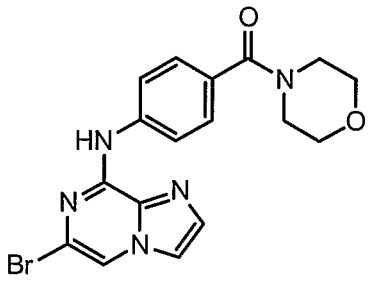
Synthesis of 6-*tert*-Butyl-N-{2-methyl-3-[8-(4-morpholin-4-ylmethyl-phenylamino)-imidazo[1,2-a]pyrazin-6-yl]-phenyl}-nicotinamide



STEP 1: 4-(6-Bromo-imidazo[1,2-a]pyrazin-8-ylamino)-benzoic acid

[00272] 4-(6-Bromo-imidazo[1,2-a]pyrazin-8-ylamino)-benzoic acid ethyl ester

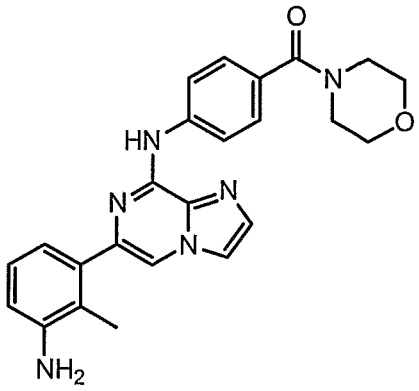
(10.0g; 27.7mmol) is dissolved in 200mL ethanol (200 proof) and 100mL 1 N NaOH is added. The reaction is refluxed for 2 hours and then cooled to rt. The resulting solid is filtered and collected, then slurried up in 0.1 N HCl (75mL) and extracted with CH_2Cl_2 (2 x 75mL). The pooled CH_2Cl_2 layers is washed with brine, then dried over anhydrous sodium sulfate and concentrated *in vacuo* to provide 4-(6-bromo-imidazo[1,2-a]pyrazin-8-ylamino)-benzoic acid as a white solid (8g).



STEP 2: [4-(6-Bromo-imidazo[1,2-a]pyrazin-8-ylamino)-phenyl]-morpholin-4-yl-methanone

[00273] A mixture of 4-(6-bromo-imidazo[1,2-a]pyrazin-8-ylamino)-benzoic acid (4.0g, 12.0mmol), benzotriazol-1-yloxytris(dimethylamino)phosphonium hexafluorophosphate (6.0g; 13.6mmol), and diisopropylethylamine (6mL; 34.4mmol) is dissolved in dimethylacetamide (50mL) and stirred at room temperature for 20min. Morpholine (5mL; 57mmol) is added and the mixture is stirred at room temperature for 16hr.

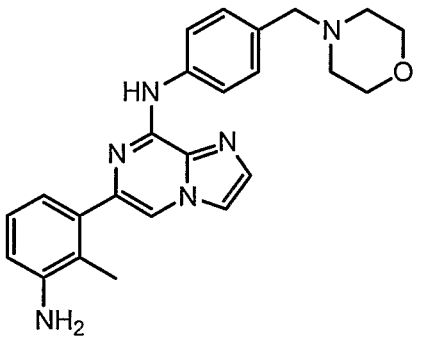
[00274] Water (100mL) is added and the mixture is filtered to give [4-(6-bromo-imidazo[1,2-a]pyrazin-8-ylamino)-phenyl]-morpholin-4-yl-methanone as a cream solid (2.65g)



STEP 3: **{4-[6-(3-Amino-2-methyl-phenyl)-imidazo[1,2-a]pyrazin-8-ylamino]-phenyl}-morpholin-4-yl-methanone**

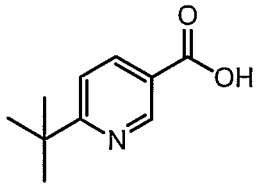
[00275] A mixture of [4-(6-bromo-imidazo[1,2-a]pyrazin-8-ylamino)-phenyl]-morpholin-4-yl-methanone (500mg; 1.24mmol), 3-(5,5-dimethyl-[1,3,2]dioxaborinan-2-yl)-2-methyl-phenylamine (340mg; 1.6mmol), palladium tetrakis(triphenylphosphine) (200mg; 0.17mmol), 1M sodium carbonate (10mL), and DME (25mL) is heated at 95° in a sealed tube for 16hr.

[00276] The mixture is cooled to room temperature, treated with water (75mL) and extracted with ethyl acetate (3 x 80mL). The extracts are washed with water (2 x 100mL) and brine (1 x 100mL), dried over anhydrous sodium sulfate, and concentrated *in vacuo*. The residue is triturated with ether and filtered to give {4-[6-(3-amino-2-methyl-phenyl)-imidazo[1,2-a]pyrazin-8-ylamino]-phenyl}-morpholin-4-yl-methanone as a tan solid (540mg).



STEP 4: [6-(3-Amino-2-methyl-phenyl)-imidazo[1,2-a]pyrazin-8-yl]-(4-morpholin-4-ylmethyl-phenyl)-amine

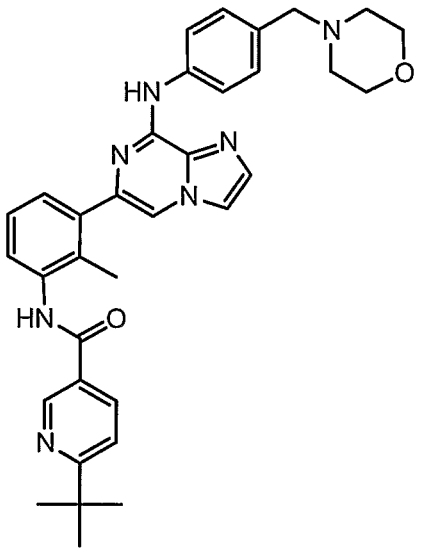
[00277] {4-[6-(3-Amino-2-methyl-phenyl)-imidazo[1,2-a]pyrazin-8-ylamino]-phenyl}-morpholin-4-yl-methanone (350mg; 0.82mmol) is dissolved in anhydrous THF (50mL) under nitrogen at rt. Solid lithium aluminum hydride (0.5g) is added portion-wise to the stirring reaction, and the reaction refluxed under nitrogen for 2 hr. The reaction is cooled to 0°C in an ice bath and quenched carefully by the dropwise addition of water (0.5 mL), then 15% $NaOH_{(aq)}$ (0.5mL), and finally by more water (5mL). The reaction is stirred at 0°C for 15 minutes then the slurry is filtered through celite to remove the aluminum salts. The filtrate is partitioned between water and ethyl acetate, and the ethyl acetate layer is washed with water (1 x 50mL), and brine (1 x 50 mL), then dried over anhydrous sodium sulfate and concentrated *in vacuo* to provide [6-(3-amino-2-methyl-phenyl)-imidazo[1,2-a]pyrazin-8-yl]-(4-morpholin-4-ylmethyl-phenyl)-amine as a tan solid (300mg), which is pure enough to use in further steps.



STEP 5: 6-*tert*-Butyl-nicotinic acid

[00278] Nicotinic acid (1.0g; 7.3mmol) is dissolved in a mixture of water (10mL) and conc. H_2SO_4 (0.5mL) with stirring. *tert*-Butyl carboxylic acid is added, and the resulting crystalline slurry stirred under nitrogen. Catalytic $AgNO_3$ and ammonium persulfate (140mg; 0.61mmol) are then added, the flask wrapped in aluminum foil to shield from light and the reaction heated to 90°C for 3 hr. The reaction is cooled to 0°C, basified to pH 10 and extracted with EtOAc (4 x 50mL). The pooled organic layers are washed with saturated sodium carbonate (2 x 50mL) and brine, dried over anhydrous sodium sulfate and concentrated *in vacuo*. The

resulting oil is purified by flash chromatography over silica gel to provide 6-*tert*-butyl-nicotinic acid (1.1g) as a white solid.



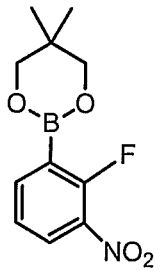
STEP 6: 6-*tert*-Butyl-N-{2-methyl-3-[8-(4-morpholin-4-ylmethyl-phenylamino)-imidazo[1,2-a]pyrazin-6-yl]-phenyl}-nicotinamide

[00279] A mixture of [6-(3-amino-2-methyl-phenyl)-imidazo[1,2-a]pyrazin-8-yl]-(4-morpholin-4-ylmethyl-phenyl)-amine (150mg; 0.36mmol), benzotriazol-1-yloxytris(dimethylamino)phosphonium hexafluorophosphate (450mg; 1.0mmol), and diisopropylethylamine (0.3mL; 1.7mmol) is dissolved in dimethylacetamide (1mL) and stirred at room temperature for 20min. 6-*tert*-butyl-nicotinic acid (200mg; 1.1mmol) is added and the mixture is stirred at room temperature for 16hr.

[00280] Water (10mL) is added and the mixture is filtered to give 6-*tert*-Butyl-N-{2-methyl-3-[8-(4-morpholin-4-ylmethyl-phenylamino)-imidazo[1,2-a]pyrazin-6-yl]-phenyl}-nicotinamide as a crude tan solid (120mg). The crude solid is purified by flash chromatography over silica gel to provide the final compound as a pale cream solid (100mg)

Example 7

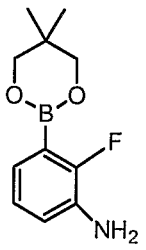
Synthesis of 3-(5,5-Dimethyl-[1,3,2]dioxaborinan-2-yl)-2-fluoro-phenylamine



STEP 1: 2-(2-Fluoro-3-nitro-phenyl)-5,5-dimethyl-[1,3,2]dioxaborinane

[00281] A mixture of 1-bromo-2-fluoro-3-nitrobenzene (800mg; 3.63mmol), bis(neopentyl glycolato)diboron (900mg; 3.98mmol), [1,1'-bis(diphenylphosphino)-ferrocene]dichlropalladium, 1:1 complex with dichloromethane (100mg; 0.12mmol), potassium acetate (1.0 g; 10.2mmol), and dioxane (20mL) was heated at reflux for 16hr.

[00282] The mixture is cooled to room temperature, treated with water (100mL), and extracted with ethyl acetate (3 x 25mL). The extracts are washed with water (2 x 25mL) and brine (1 x 25mL), dried over sodium sulfate, and concentrated *in vacuo*. The residue is purified by flash chromatography over silica gel (elution with ether/hexane 1/2) to give 2-(2-fluoro-3-nitro-phenyl)-5,5-dimethyl-[1,3,2]dioxaborinane as a pale yellow solid (350mg)



STEP 2: 3-(5,5-Dimethyl-[1,3,2]dioxaborinan-2-yl)-2-fluoro-phenylamine

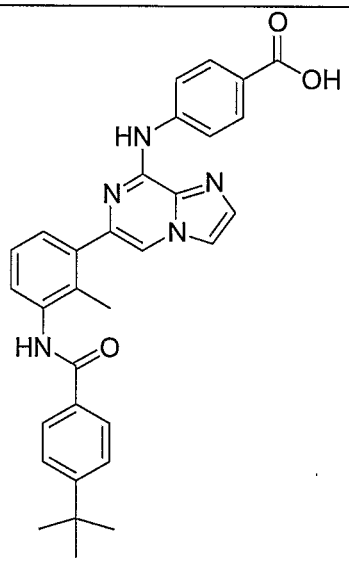
[00283] A mixture of 2-(2-fluoro-3-nitro-phenyl)-5,5-dimethyl-

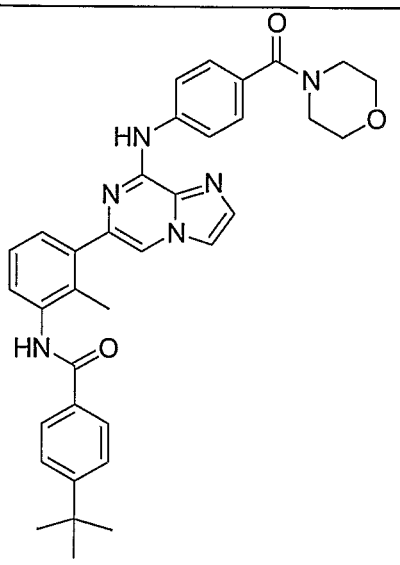
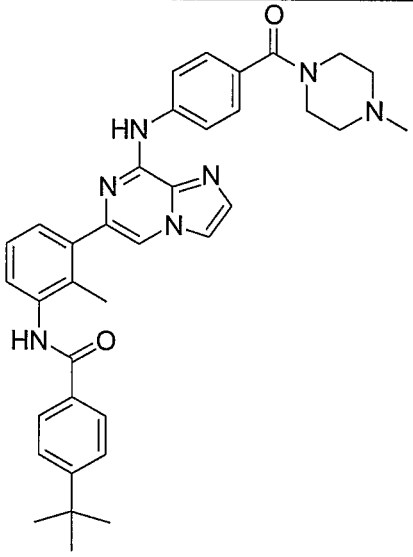
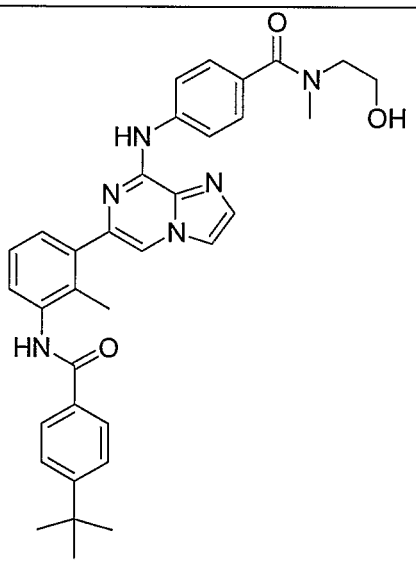
[1,3,2]dioxaborinane (240mg; 1.1mmol), 10% palladium-on-carbon (100mg) and ethyl acetate (75mL) is hydrogenated at room temperature and 40psi hydrogen for 2hr.

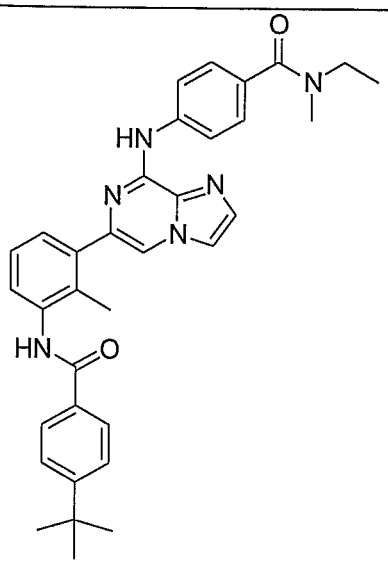
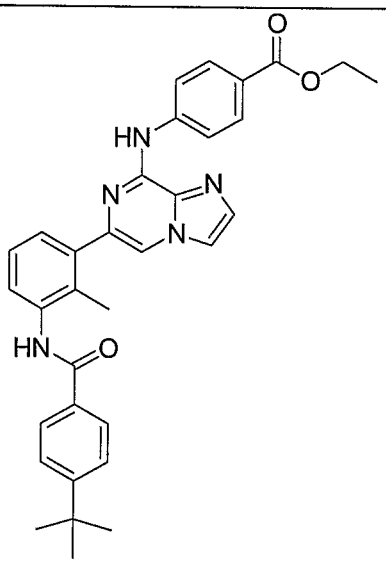
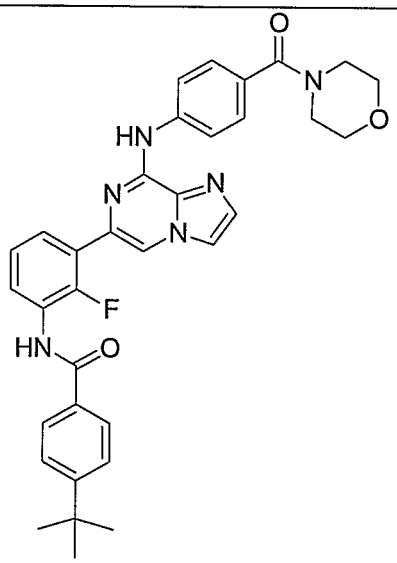
[00284] The mixture is filtered through celite, washed with CH_2Cl_2 (2 x 100mL), and the filtrate is evaporated to give 3-(5,5-dimethyl-[1,3,2]dioxaborinan-2-yl)-2-fluoro-phenylamine as an tan solid (200mg)

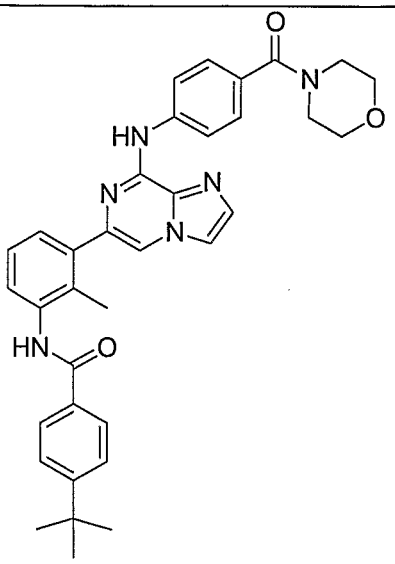
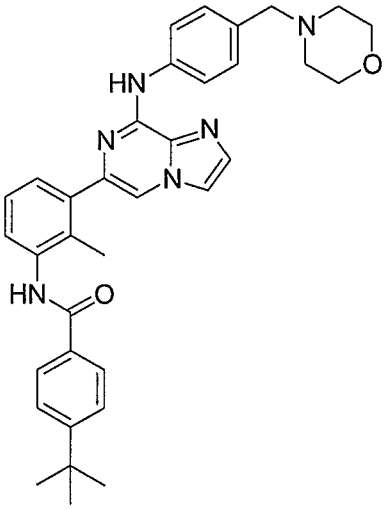
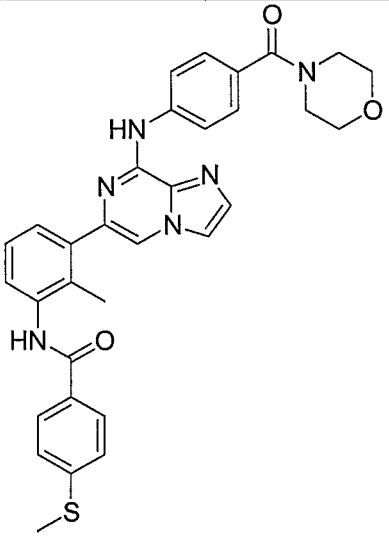
Example 8

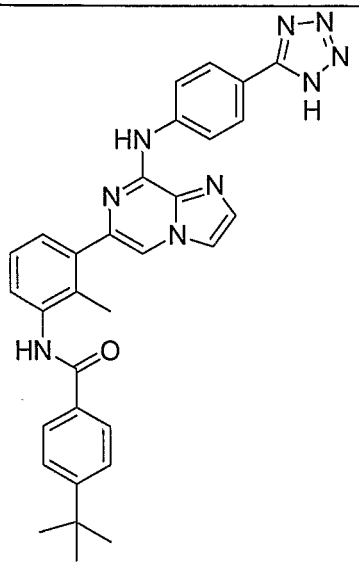
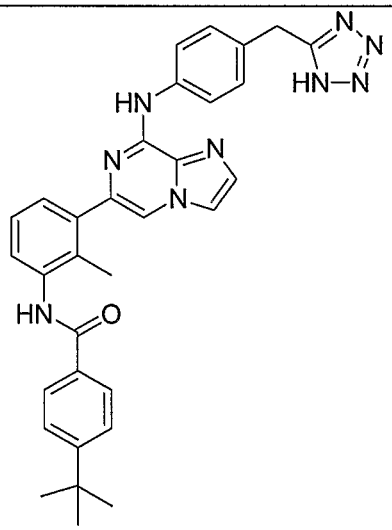
The following compounds were prepared using procedures similar to those described in Examples 5-7.

Structure	Name MW	M+
	4-{6-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-imidazo[1,2-a]pyrazin-8-ylamino}-benzoic acid $C_{31}H_{29}N_5O_3$ Mol. Wt.: 519.59	520.2

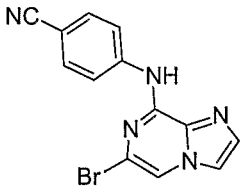
	4-tert-Butyl-N-(2-methyl-3-{8-[4-(morpholine-4-carbonyl)-phenylamino]-imidazo[1,2-a]pyrazin-6-yl}-phenyl)-benzamide $C_{35}H_{36}N_6O_3$ Mol. Wt.: 588.70	589.2
	4-tert-Butyl-N-(2-methyl-3-{8-[4-(4-methyl-piperazine-1-carbonyl)-phenylamino]-imidazo[1,2-a]pyrazin-6-yl}-phenyl)-benzamide $C_{36}H_{39}N_7O_2$ Mol. Wt.: 601.74	602.3
	4-tert-Butyl-N-(2-methyl-3-{8-[4-(N-methylhydroxyethyl-1-carbonyl)-phenylamino]-imidazo[1,2-a]pyrazin-6-yl}-phenyl)-benzamide $C_{34}H_{36}N_6O_3$ Mol. Wt.: 576.69	577.1

	4-tert-Butyl-N-(2-methyl-3-{8-[4-(N-methylethyl-1-carbonyl)-phenylamino]-imidazo[1,2-a]pyrazin-6-yl}-phenyl)-benzamide $C_{34}H_{36}N_6O_2$ Mol. Wt.: 560.69	561.3
	4-{6-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-imidazo[1,2-a]pyrazin-8-ylamino}-benzoic acid ethyl ester $C_{33}H_{33}N_5O_3$ Mol. Wt.: 547.65	548.3
	4-tert-Butyl-N-(2-fluoro-3-{8-[4-(morpholine-4-carbonyl)-phenylamino]-imidazo[1,2-a]pyrazin-6-yl}-phenyl)-benzamide $C_{34}H_{33}FN_6O_3$ Mol. Wt.: 592.66	593.3

	4-tert-Butyl-N-(2-methyl-3-{8-[4-(morpholine-4-carbonyl)-phenylamino]-imidazo[1,2-a]pyrazin-6-yl}-phenyl)-benzamide $C_{35}H_{36}N_6O_3$ Mol. Wt.: 588.70	534.5
	4-tert-Butyl-N-{2-methyl-3-[8-(4-morpholin-4-ylmethyl-phenylamino)-imidazo[1,2-a]pyrazin-6-yl]-phenyl}-benzamide $C_{35}H_{38}N_6O_2$ Mol. Wt.: 574.72	575.3
	N-(2-Methyl-3-{8-[4-(morpholine-4-carbonyl)-phenylamino]-imidazo[1,2-a]pyrazin-6-yl}-phenyl)-4-methylsulfanyl-benzamide $C_{32}H_{30}N_6O_3S$ Mol. Wt.: 578.69	579.5

	4-tert-Butyl-N-(2-methyl-3-{8-[4-(1H-tetrazol-5-yl)-phenylamino]-imidazo[1,2-a]pyrazin-6-yl}-phenyl)-benzamide $C_{31}H_{29}N_9O$ Mol. Wt.: 543.62	544.2
	4-tert-Butyl-N-(2-methyl-3-{8-[4-(1H-tetrazol-5-ylmethyl)-phenylamino]-imidazo[1,2-a]pyrazin-6-yl}-phenyl)-benzamide $C_{32}H_{31}N_9O$ Mol. Wt.: 557.65	558.4

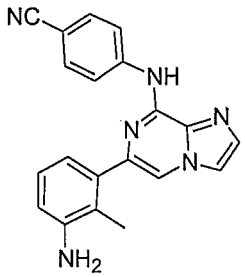
Example 9



4-(6-Bromo-imidazo[1,2-a]pyrazin-8-ylamino)-benzonitrile

[00285] A mixture of 4-aminobenzonitrile (220mg; 1.89mmol) and 6,8-dibromo-imidazo[1,2-a]pyrazine (500mg; 1.81mmol) is slurried in DMF (1mL) and heated to 140°C for 20 minutes. The reaction is allowed to cool, and when the bath reaches 75°C, ethyl acetate (40mL) is added and the slurry is stirred to break up large

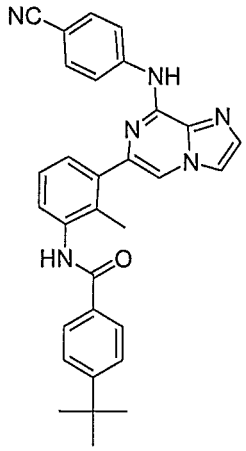
solid lumps into fine powder. The powdered 4-(6-bromo-imidazo[1,2-a]pyrazin-8-ylamino)-benzonitrile is filtered, washed with diethyl ether (2 x 50mL) and dried under vacuum to a fine orange/tan solid (600mg).



4-[6-(3-Amino-2-methyl-phenyl)-imidazo[1,2-a]pyrazin-8-ylamino]-benzonitrile

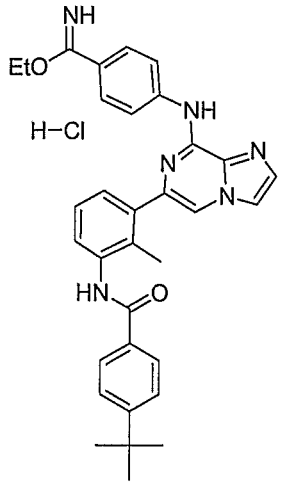
[00286] A solution of 4-(6-bromo-imidazo[1,2-a]pyrazin-8-ylamino)-benzonitrile (1.02g; 3.27mmol) is slurried in ethylene glycol, dimethyl ether (DME; 60mL) and nitrogen gas bubbled through the reaction for 15 minutes with stirring at rt.

[00287] 3-(5,5-Dimethyl-[1,3,2]dioxaborinan-2-yl)-2-methyl-phenylamine (950mg; 3.63mmol) and palladium tetrakis(triphenylphosphine) (500mg; 0.43mmol) are added and nitrogen is bubbled through the reaction slurry for an additional 10 minutes at rt. 20 mL of a 1.0N solution of sodium carbonate is added and the biphasic mixture is heated to 95°C for 16hrs with vigorous stirring under nitrogen. The mixture is partitioned between ethyl acetate (100mL) and water (100mL) and the water layer extracted with ethyl acetate (2 x 50mL). The organic layers are pooled, washed with brine and dried over anhydrous sodium sulfate. The filtrate is then concentrated *in vacuo* and the crude oil dissolved in a minimum volume of CH_2Cl_2. Diethyl ether is added and the resulting precipitate is filtered and washed with diethyl ether to provide 4-[6-(3-amino-2-methyl-phenyl)-imidazo[1,2-a]pyrazin-8-ylamino]-benzonitrile as a pale tan solid (650mg).



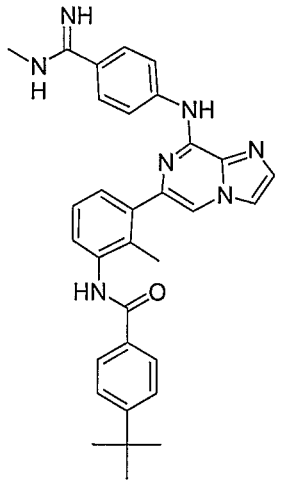
4-*tert*-Butyl-N-{3-[8-(4-cyano-phenylamino)-imidazo[1,2-a]pyrazin-6-yl]-2-methyl-phenyl}-benzamide

[00288] A solution of 4-[6-(3-amino-2-methyl-phenyl)-imidazo[1,2-a]pyrazin-8-ylamino]-benzonitrile (380mg; 1.12 mmol) and diisopropylethylamine (187mg; 1.45mmol) in anhydrous THF (25mL) is stirred under nitrogen at rt. A solution of 4-*tert*-Butyl-benzoyl chloride (230mg; 1.17mmol) in 5mL anhydrous THF is then added dropwise to the stirring reaction solution. After 30 minutes, the mixture is partitioned between ethyl acetate (75mL) and water (75mL) and the water layer extracted with ethyl acetate (2 x 50mL). The organic layers are pooled, washed with brine and dried over anhydrous sodium sulfate. The filtrate is then concentrated *in vacuo* and the crude oil dissolved in a minimum volume of CH_2Cl_2. Diethyl ether is added and the resulting precipitate is filtered and washed with diethyl ether to provide 4-*tert*-butyl-N-{3-[8-(4-cyano-phenylamino)-imidazo[1,2-a]pyrazin-6-yl]-2-methyl-phenyl}-benzamide as a light orange solid (450mg)



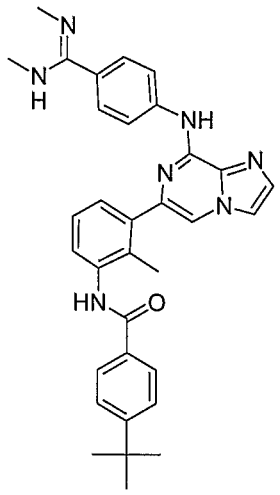
4-{6-[3-(4-*tert*-Butyl-benzoylamino)-2-methyl-phenyl]-imidazo[1,2-a]pyrazin-8-ylamino}-benzimidic acid ethyl ester hydrochloride

[00289] 4-*tert*-Butyl-N-{3-[8-(4-cyano-phenylamino)-imidazo[1,2-a]pyrazin-6-yl]-2-methyl-phenyl}-benzamide is slurried in 200mL ethanol (200 proof) and the reaction cooled to 0°C in an ice bath. The reaction is then saturated with hydrogen chloride gas and allowed to gradually warm to rt over 16hrs with stirring. The solvent is removed *in vacuo* and the resulting tan solid 4-{6-[3-(4-*tert*-butyl-benzoylamino)-2-methyl-phenyl]-imidazo[1,2-a]pyrazin-8-ylamino}-benzimidic acid ethyl ester hydrochloride (500mg) is used without further purification.



4-*tert*-Butyl-N-(2-methyl-3-{8-[4-(N-methylcarbamimidoyl)-phenylamino]-imidazo[1,2-a]pyrazin-6-yl}-phenyl)-benzamide

[00290] 4-{6-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-imidazo[1,2-a]pyrazin-8-ylamino}-benzimidic acid ethyl ester hydrochloride (150mg; 0.26mmol) is dissolved in methanol (1mL) in a glass pressure reaction vessel, and a solution of methylamine in THF added (2.0N; 2mL). The reaction is heated to 50°C for 2hr then concentrated *in vacuo*. The oil is dissolved in 2 mL CH_2Cl_2 and diethyl ether (20mL) is added to precipitate out 4-*tert*-butyl-N-(2-methyl-3-{8-[4-(N-methylcarbamimidoyl)-phenylamino]-imidazo[1,2-a]pyrazin-6-yl}-phenyl)-benzamide as a clean light tan solid (140mg).

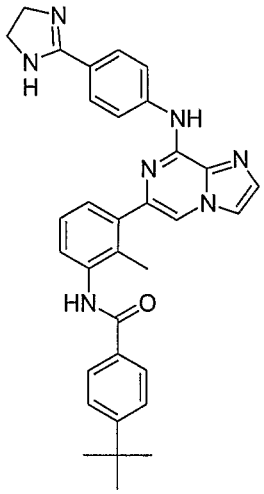


4-*tert*-Butyl-N-(3-{8-[4-(N,N'-dimethyl-carbamimidoyl)-phenylamino]-imidazo[1,2-a]pyrazin-6-yl}-2-methyl-phenyl)-benzamide

[00291] 4-*tert*-Butyl-N-(2-methyl-3-{8-[4-(N-methylcarbamimidoyl)-phenylamino]-imidazo[1,2-a]pyrazin-6-yl}-phenyl)-benzamide (100mg; 0.19mmol) is dissolved in methanol (1mL) in a glass pressure reaction vessel, and a solution of methylamine in THF is added (2.0N; 5mL). The reaction is heated to 60°C for 16hr then concentrated *in vacuo*. The resulting oil is dissolved in 2 mL CH_2Cl_2 and diethyl ether (20mL) is added to precipitate out 4-*tert*-butyl-N-(3-{8-[4-(N,N'-dimethyl-carbamimidoyl)-phenylamino]-imidazo[1,2-a]pyrazin-6-yl}-2-methyl-phenyl)-benzamide (80mg). Gradient silica flash chromatography using (90:9:1) (CH_2Cl_2 : methanol : ammonium hydroxide) as the eluent provides the pure material as a white solid (60mg).

[00292] Alternatively, 4-{6-[3-(4-*tert*-butyl-benzoylamino)-2-methyl-phenyl]-

imidazo[1,2-a]pyrazin-8-ylamino}-benzimidic acid ethyl ester hydrochloride (150mg; 0.26mmol) is dissolved in methanol (1mL) in a glass pressure reaction vessel, and a solution of methylamine in THF added (2.0N; 5mL). The reaction is heated to 60°C for 16hr then concentrated *in vacuo*. The oil is dissolved in 2 mL CH_2Cl_2 and diethyl ether (20mL) is added to precipitate out 4-*tert*-butyl-N-(3-{8-[4-(N,N'-dimethyl-carbamimidoyl)-phenylamino]-imidazo[1,2-a]pyrazin-6-yl}-2-methyl-phenyl)-benzamide as a light tan solid (100mg). Gradient silica flash chromatography using (90:9:1) (CH_2Cl_2 : methanol : ammonium hydroxide) as the eluent provides the pure material as a white solid (50mg).



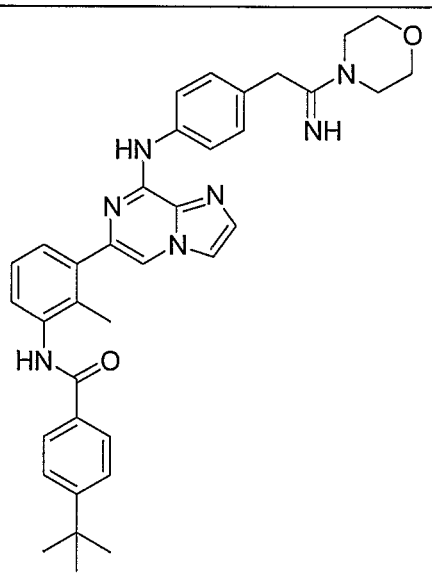
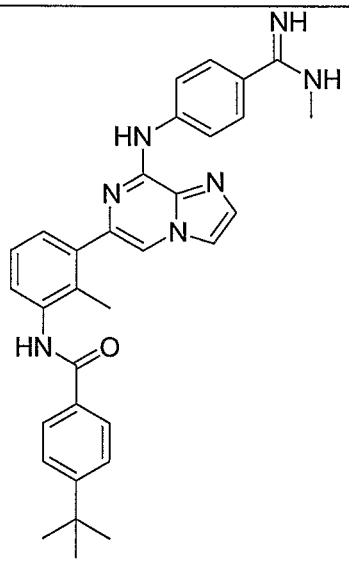
4-*tert*-Butyl-N-(3-{8-[4-(4,5-dihydro-1H-imidazol-2-yl)-phenylamino]-imidazo[1,2-a]pyrazin-6-yl}-2-methyl-phenyl)-benzamide

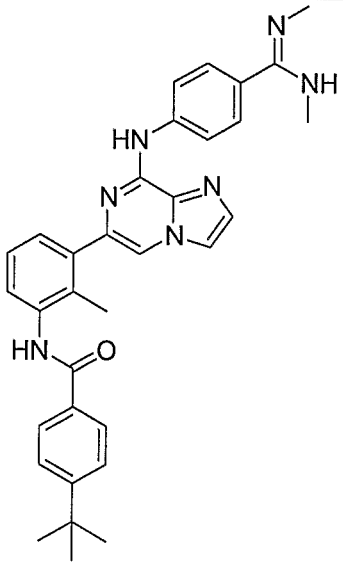
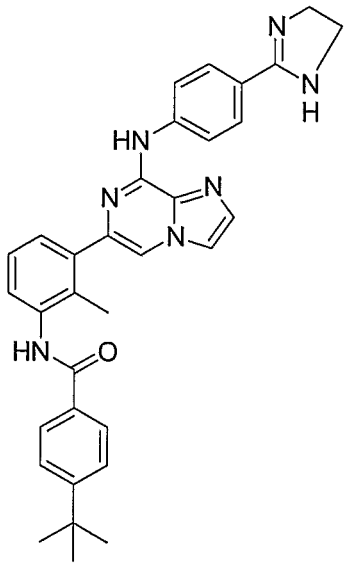
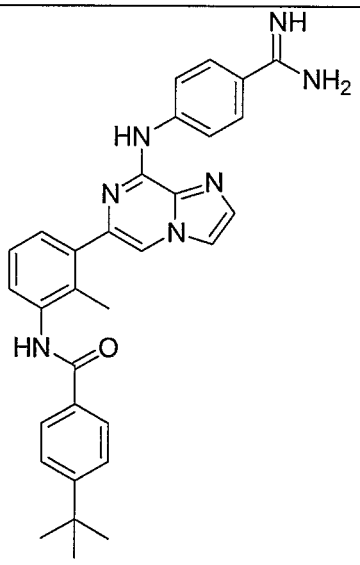
[00293] 4-{6-[3-(4-*tert*-Butyl-benzoylamino)-2-methyl-phenyl]-imidazo[1,2-a]pyrazin-8-ylamino}-benzimidic acid ethyl ester hydrochloride (150mg; 0.26mmol) is dissolved in methanol (5mL) in a glass pressure reaction vessel, and ethylenediamine (100mg; excess) is added. The reaction is heated to 60°C for 16hr then concentrated *in vacuo*. The oil is dissolved in 2 mL CH_2Cl_2 and diethyl ether (20mL) is added to precipitate out 4-*tert*-butyl-N-(3-{8-[4-(4,5-dihydro-1H-imidazol-2-yl)-phenylamino]-imidazo[1,2-a]pyrazin-6-yl}-2-methyl-phenyl)-benzamide as a light tan solid (100mg). Gradient silica flash chromatography using (90:9:1) (CH_2Cl_2 : methanol : ammonium hydroxide) as the eluent provides the pure material as a white

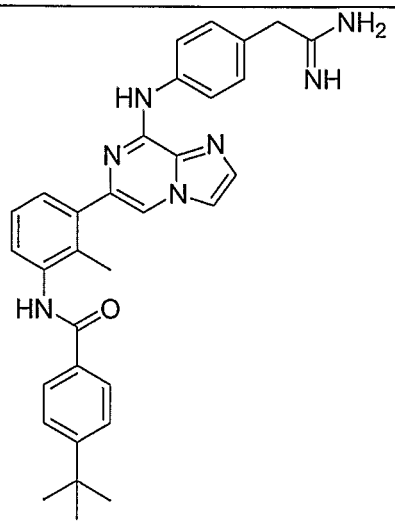
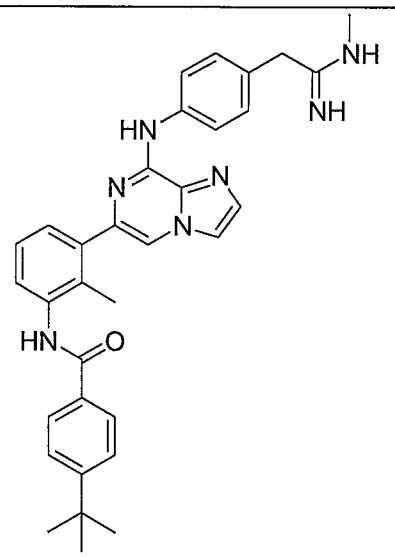
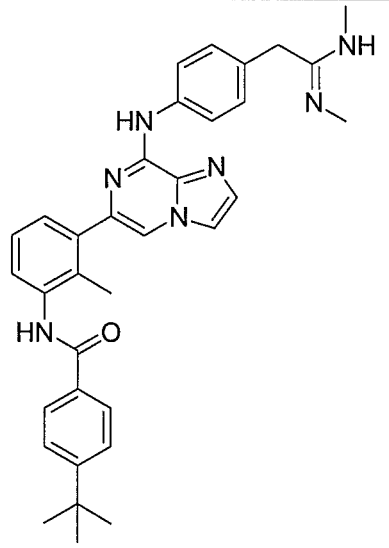
solid (50mg).

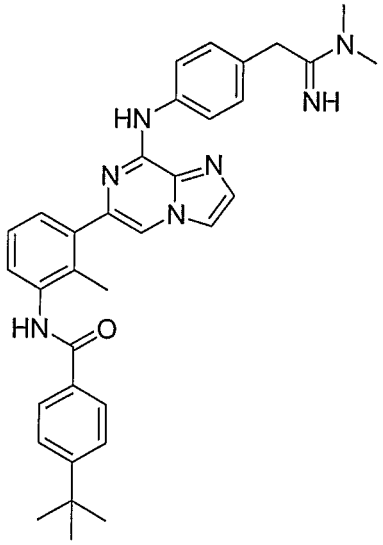
Example 10

The following compounds were prepared using procedures similar to those described in Example 9 above.

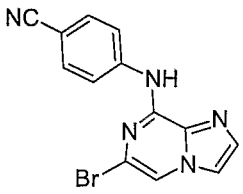
Structure	Name MW	M+
	4-tert-Butyl-N-(3-{8-[4-(2-imino-2-morpholin-4-yl-ethyl)-phenylamino]-imidazo[1,2-a]pyrazin-6-yl}-2-methyl-phenyl)-benzamide $C_{36}H_{39}N_7O_2$ Mol. Wt.: 601.74	602.22
	4-tert-Butyl-N-(2-methyl-3-{8-[4-(N-methylcarbamimidoyl)-phenylamino]-imidazo[1,2-a]pyrazin-6-yl}-phenyl)-benzamide $C_{32}H_{33}N_7O$ Mol. Wt.: 531.65	532.23

	4-tert-Butyl-N-(3-{8-[4-(N,N'-dimethyl-carbamimidoyl)-phenylamino]-imidazo[1,2-a]pyrazin-6-yl}-2-methyl-phenyl)-benzamide $C_{33}H_{35}N_7O$ Mol. Wt.: 545.68	546.19
	4-tert-Butyl-N-(3-{8-[4-(4,5-dihydro-1H-imidazol-2-yl)-phenylamino]-imidazo[1,2-a]pyrazin-6-yl}-2-methyl-phenyl)-benzamide $C_{33}H_{33}N_7O$ Mol. Wt.: 543.66	544.22
	4-tert-Butyl-N-{3-[8-(4-carbamimidoyl-phenylamino)-imidazo[1,2-a]pyrazin-6-yl]-2-methyl-phenyl}-benzamide $C_{31}H_{31}N_7O$ Mol. Wt.: 517.62	518.06

	4-tert-Butyl-N-{3-[8-(4-carbamimidoylmethyl-phenylamino)-imidazo[1,2-a]pyrazin-6-yl]-2-methyl-phenyl}-benzamide $C_{32}H_{33}N_7O$ Mol. Wt.: 531.65	532.1
	4-tert-Butyl-N-(2-methyl-3-{8-[4-(N-methylcarbamimidoylmethyl)-phenylamino]-imidazo[1,2-a]pyrazin-6-yl}-phenyl)-benzamide $C_{33}H_{35}N_7O$ Mol. Wt.: 545.68	546.1
	4-tert-Butyl-N-(3-{8-[4-(N,N'-dimethyl-carbamimidoylmethyl)-phenylamino]-imidazo[1,2-a]pyrazin-6-yl}-2-methyl-phenyl)-benzamide $C_{34}H_{37}N_7O$ Mol. Wt.: 559.70	560.05

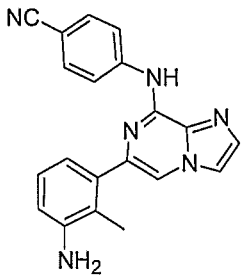
	4-tert-Butyl-N-(3-{8-[4-(N,N-dimethyl-carbamimidoylmethyl)-phenylamino]-imidazo[1,2-a]pyrazin-6-yl}-2-methyl-phenyl)-benzamide $C_{34}H_{37}N_7O$ Mol. Wt.: 559.70	560.05

Example 11



4-(6-Bromo-imidazo[1,2-a]pyrazin-8-ylamino)-benzonitrile

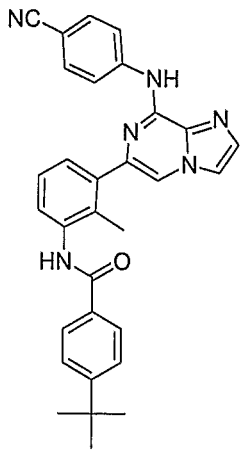
[00294] A mixture of 4-aminobenzonitrile (220mg; 1.89mmol) and 6,8-dibromo-imidazo[1,2-a]pyrazine (500mg; 1.81mmol) is slurried in DMF (1mL) and heated to 140°C for 20 minutes. The reaction is allowed to cool, and when the bath reaches 75°C, ethyl acetate (40mL) is added and the slurry is stirred to break up large solid lumps into fine powder. The powdered 4-(6-bromo-imidazo[1,2-a]pyrazin-8-ylamino)-benzonitrile is filtered, washed with diethyl ether (2 x 50mL) and dried under vacuum to a fine orange/tan solid (600mg).



4-[6-(3-Amino-2-methyl-phenyl)-imidazo[1,2-a]pyrazin-8-ylamino]-benzonitrile

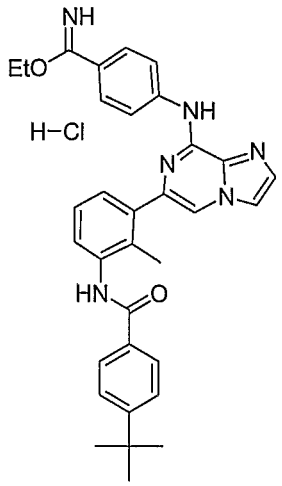
[00295] A solution of 4-(6-bromo-imidazo[1,2-a]pyrazin-8-ylamino)-benzonitrile (1.02g; 3.27mmol) is slurried in ethylene glycol, dimethyl ether (DME; 60mL) and nitrogen gas bubbled through the reaction for 15 minutes with stirring at rt.

[00296] 3-(5,5-Dimethyl-[1,3,2]dioxaborinan-2-yl)-2-methyl-phenylamine (950mg; 3.63mmol) and palladium tetrakis(triphenylphosphine) (500mg; 0.43mmol) are added and nitrogen is bubbled through the reaction slurry for an additional 10 minutes at rt. 20 mL of a 1.0N solution of sodium carbonate is added and the biphasic mixture is heated to 95°C for 16hrs with vigorous stirring under nitrogen. The mixture is partitioned between ethyl acetate (100mL) and water (100mL) and the water layer extracted with ethyl acetate (2 x 50mL). The organic layers are pooled, washed with brine and dried over anhydrous sodium sulfate. The filtrate is then concentrated *in vacuo* and the crude oil dissolved in a minimum volume of CH_2Cl_2. Diethyl ether is added and the resulting precipitate is filtered and washed with diethyl ether to provide 4-[6-(3-amino-2-methyl-phenyl)-imidazo[1,2-a]pyrazin-8-ylamino]-benzonitrile as a pale tan solid (650mg).



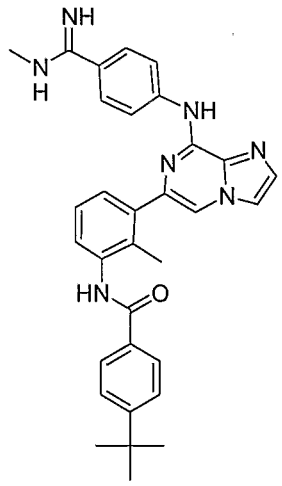
4-*tert*-Butyl-N-{3-[8-(4-cyano-phenylamino)-imidazo[1,2-a]pyrazin-6-yl]-2-methyl-phenyl}-benzamide

[00297] A solution of 4-[6-(3-amino-2-methyl-phenyl)-imidazo[1,2-a]pyrazin-8-ylamino]-benzonitrile (380mg; 1.12 mmol) and diisopropylethylamine (187mg; 1.45mmol) in anhydrous THF (25mL) is stirred under nitrogen at rt. A solution of 4-*tert*-Butyl-benzoyl chloride (230mg; 1.17mmol) in 5mL anhydrous THF is then added dropwise to the stirring reaction solution. After 30 minutes, the mixture is partitioned between ethyl acetate (75mL) and water (75mL) and the water layer extracted with ethyl acetate (2 x 50mL). The organic layers are pooled, washed with brine and dried over anhydrous sodium sulfate. The filtrate is then concentrated *in vacuo* and the crude oil dissolved in a minimum volume of CH_2Cl_2. Diethyl ether is added and the resulting precipitate is filtered and washed with diethyl ether to provide 4-*tert*-butyl-N-{3-[8-(4-cyano-phenylamino)-imidazo[1,2-a]pyrazin-6-yl]-2-methyl-phenyl}-benzamide as a light orange solid (450mg)



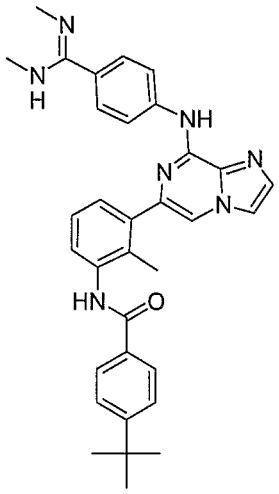
4-{6-[3-(4-*tert*-Butyl-benzoylamino)-2-methyl-phenyl]-imidazo[1,2-a]pyrazin-8-ylamino}-benzimidic acid ethyl ester hydrochloride

[00298] 4-*tert*-Butyl-N-{3-[8-(4-cyano-phenylamino)-imidazo[1,2-a]pyrazin-6-yl]-2-methyl-phenyl}-benzamide is slurried in 200mL ethanol (200 proof) and the reaction cooled to 0°C in an ice bath. The reaction is then saturated with hydrogen chloride gas and allowed to gradually warm to rt over 16hrs with stirring. The solvent is removed *in vacuo* and the resulting tan solid 4-{6-[3-(4-*tert*-butyl-benzoylamino)-2-methyl-phenyl]-imidazo[1,2-a]pyrazin-8-ylamino}-benzimidic acid ethyl ester hydrochloride (500mg) is used without further purification.



4-*tert*-Butyl-N-(2-methyl-3-{8-[4-(N-methylcarbamimidoyl)-phenylamino]-imidazo[1,2-a]pyrazin-6-yl}-phenyl)-benzamide

[00299] 4-{6-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-imidazo[1,2-a]pyrazin-8-ylamino}-benzimidic acid ethyl ester hydrochloride (150mg; 0.26mmol) is dissolved in methanol (1mL) in a glass pressure reaction vessel, and a solution of methylamine in THF added (2.0N; 2mL). The reaction is heated to 50°C for 2hr then concentrated *in vacuo*. The oil is dissolved in 2 mL CH_2Cl_2 and diethyl ether (20mL) is added to precipitate out 4-*tert*-butyl-N-(2-methyl-3-{8-[4-(N-methylcarbamimidoyl)-phenylamino]-imidazo[1,2-a]pyrazin-6-yl}-phenyl)-benzamide as a clean light tan solid (140mg).

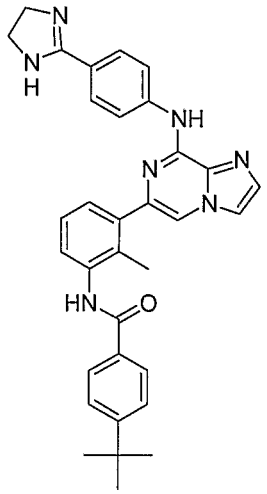


4-*tert*-Butyl-N-(3-{8-[4-(N,N'-dimethyl-carbamimidoyl)-phenylamino]-imidazo[1,2-a]pyrazin-6-yl}-2-methyl-phenyl)-benzamide

[00300] 4-*tert*-Butyl-N-(2-methyl-3-{8-[4-(N-methylcarbamimidoyl)-phenylamino]-imidazo[1,2-a]pyrazin-6-yl}-phenyl)-benzamide (100mg; 0.19mmol) is dissolved in methanol (1mL) in a glass pressure reaction vessel, and a solution of methylamine in THF is added (2.0N; 5mL). The reaction is heated to 60°C for 16hr then concentrated *in vacuo*. The resulting oil is dissolved in 2 mL CH_2Cl_2 and diethyl ether (20mL) is added to precipitate out 4-*tert*-butyl-N-(3-{8-[4-(N,N'-dimethyl-carbamimidoyl)-phenylamino]-imidazo[1,2-a]pyrazin-6-yl}-2-methyl-phenyl)-benzamide (80mg). Gradient silica flash chromatography using (90:9:1) (CH_2Cl_2 : methanol : ammonium hydroxide) as the eluent provides the pure material as a white solid (60mg).

[00301] Alternatively, 4-{6-[3-(4-*tert*-butyl-benzoylamino)-2-methyl-phenyl]-

imidazo[1,2-a]pyrazin-8-ylamino}-benzimidic acid ethyl ester hydrochloride (150mg; 0.26mmol) is dissolved in methanol (1mL) in a glass pressure reaction vessel, and a solution of methylamine in THF added (2.0N; 5mL). The reaction is heated to 60°C for 16hr then concentrated *in vacuo*. The oil is dissolved in 2 mL CH_2Cl_2 and diethyl ether (20mL) is added to precipitate out 4-*tert*-butyl-N-(3-{8-[4-(N,N'-dimethyl-carbamimidoyl)-phenylamino]-imidazo[1,2-a]pyrazin-6-yl}-2-methyl-phenyl)-benzamide as a light tan solid (100mg). Gradient silica flash chromatography using (90:9:1) (CH_2Cl_2 : methanol : ammonium hydroxide) as the eluent provides the pure material as a white solid (50mg).



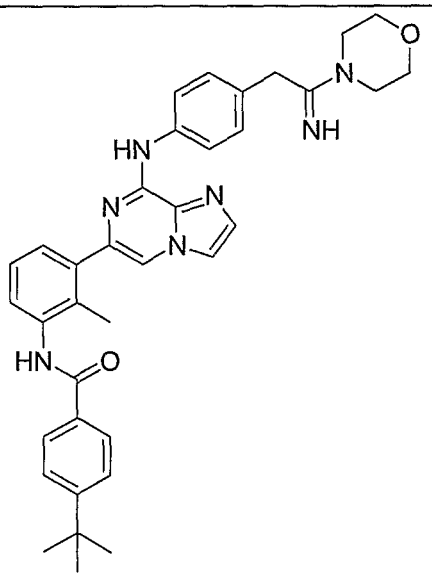
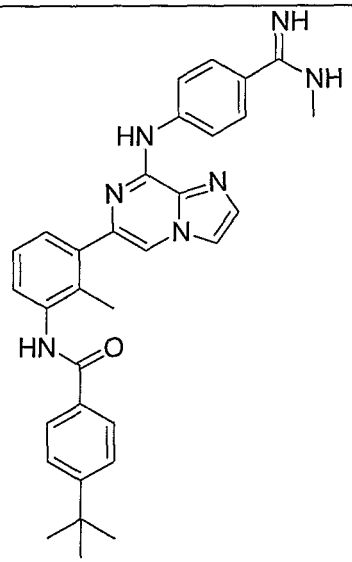
4-*tert*-Butyl-N-(3-{8-[4-(4,5-dihydro-1H-imidazol-2-yl)-phenylamino]-imidazo[1,2-a]pyrazin-6-yl}-2-methyl-phenyl)-benzamide

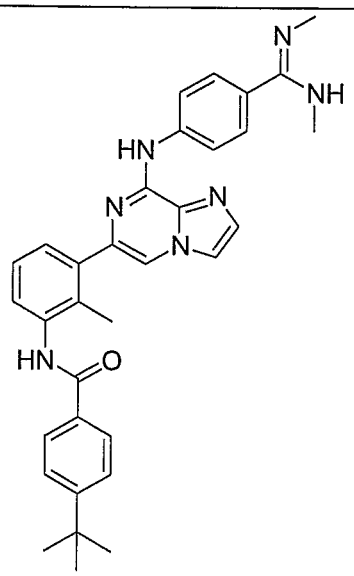
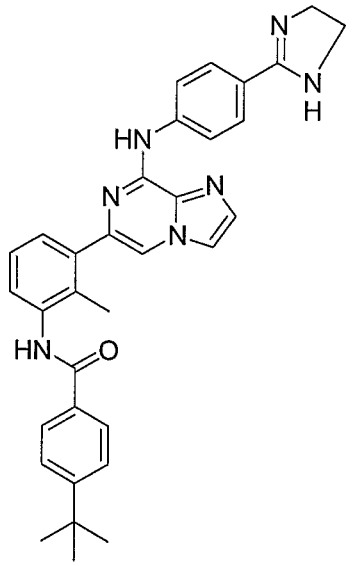
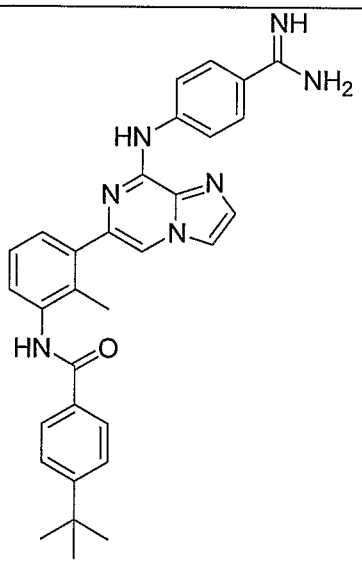
[00302] 4-{6-[3-(4-*tert*-Butyl-benzoylamino)-2-methyl-phenyl]-imidazo[1,2-a]pyrazin-8-ylamino}-benzimidic acid ethyl ester hydrochloride (150mg; 0.26mmol) is dissolved in methanol (5mL) in a glass pressure reaction vessel, and ethylenediamine (100mg; excess) is added. The reaction is heated to 60°C for 16hr then concentrated *in vacuo*. The oil is dissolved in 2 mL CH_2Cl_2 and diethyl ether (20mL) is added to precipitate out 4-*tert*-butyl-N-(3-{8-[4-(4,5-dihydro-1H-imidazol-2-yl)-phenylamino]-imidazo[1,2-a]pyrazin-6-yl}-2-methyl-phenyl)-benzamide as a light tan solid (100mg). Gradient silica flash chromatography using (90:9:1) (CH_2Cl_2 : methanol : ammonium hydroxide) as the eluent provides the pure material as a white

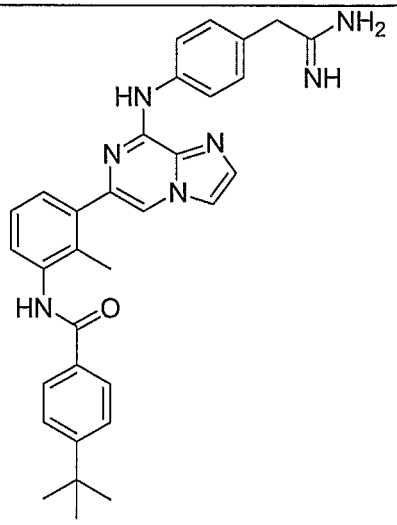
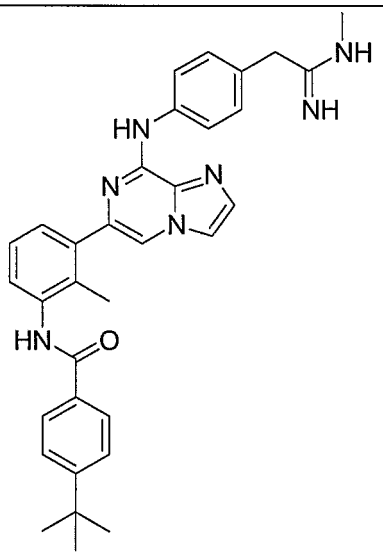
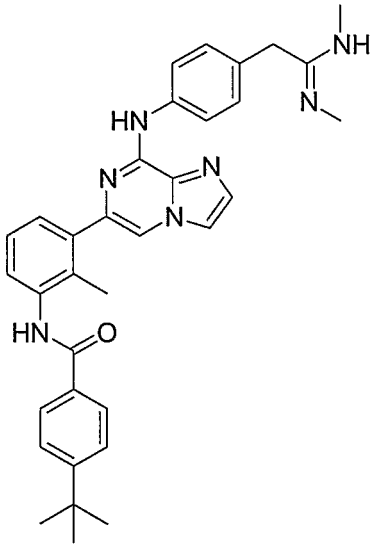
solid (50mg).

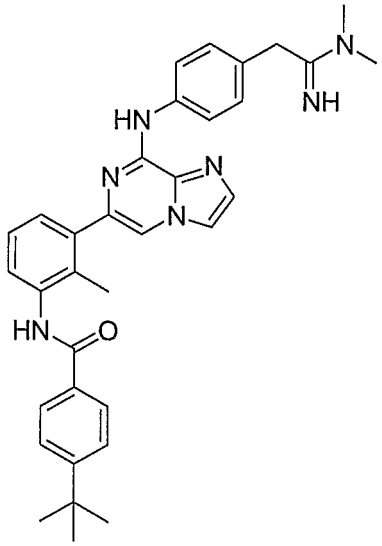
Example 12

The following compounds were prepared using procedures similar to those described in Example 11 above.

Structure	Name MW	M+
	4-tert-Butyl-N-(3-{8-[4-(2-imino-2-morpholin-4-yl-ethyl)-phenylamino]-imidazo[1,2-a]pyrazin-6-yl}-2-methyl-phenyl)-benzamide $C_{36}H_{39}N_7O_2$ Mol. Wt.: 601.74	602.22
	4-tert-Butyl-N-(2-methyl-3-{8-[4-(N-methylcarbamimidoyl)-phenylamino]-imidazo[1,2-a]pyrazin-6-yl}-phenyl)-benzamide $C_{32}H_{33}N_7O$ Mol. Wt.: 531.65	532.23

	4-tert-Butyl-N-(3-{8-[4-(N,N'-dimethyl-carbamimidoyl)-phenylamino]-imidazo[1,2-a]pyrazin-6-yl}-2-methyl-phenyl)-benzamide $C_{33}H_{35}N_7O$ Mol. Wt.: 545.68	546.19
	4-tert-Butyl-N-(3-{8-[4-(4,5-dihydro-1H-imidazol-2-yl)-phenylamino]-imidazo[1,2-a]pyrazin-6-yl}-2-methyl-phenyl)-benzamide $C_{33}H_{33}N_7O$ Mol. Wt.: 543.66	544.22
	4-tert-Butyl-N-{3-[8-(4-carbamimidoyl-phenylamino)-imidazo[1,2-a]pyrazin-6-yl]-2-methyl-phenyl}-benzamide $C_{31}H_{31}N_7O$ Mol. Wt.: 517.62	518.06

	4-tert-Butyl-N-{3-[8-(4-carbamimidoylmethyl-phenylamino)-imidazo[1,2-a]pyrazin-6-yl]-2-methyl-phenyl}-benzamide $C_{32}H_{33}N_7O$ Mol. Wt.: 531.65	532.1
	4-tert-Butyl-N-(2-methyl-3-{8-[4-(N-methylcarbamimidoylmethyl)-phenylamino]-imidazo[1,2-a]pyrazin-6-yl}-phenyl)-benzamide $C_{33}H_{35}N_7O$ Mol. Wt.: 545.68	546.1
	4-tert-Butyl-N-(3-{8-[4-(N,N'-dimethyl-carbamimidoylmethyl)-phenylamino]-imidazo[1,2-a]pyrazin-6-yl}-2-methyl-phenyl)-benzamide $C_{34}H_{37}N_7O$ Mol. Wt.: 559.70	560.05

	4-tert-Butyl-N-(3-{8-[4-(N,N-dimethyl-carbamimidoylmethyl)-phenylamino]-imidazo[1,2-a]pyrazin-6-yl}-2-methyl-phenyl)-benzamide $C_{34}H_{37}N_7O$ Mol. Wt.: 559.70	560.05

Example 13

Biochemical Btk Assay

[00303] A generalized procedure for one standard biochemical Btk Kinase Assay that can be used to test compounds disclosed in this application is as follows.

[00304] A master mix minus Btk enzyme is prepared containing 1X Cell Signaling kinase buffer (25 mM Tris-HCl, pH 7.5, 5 mM beta-glycerophosphate, 2 mM dithiothreitol, 0.1 mM Na_3VO_4, 10 mM $MgCl_2$), 0.5 μM Promega PTK Biotinylated peptide substrate 2, and 0.01% BSA. A master mix plus Btk enzyme is prepared containing 1X Cell Signaling kinase buffer, 0.5 μM PTK Biotinylated peptide substrate 2, 0.01% BSA, and 100 ng/well (0.06 mU/well) Btk enzyme. Btk enzyme is prepared as follows: full length human wildtype Btk (accession number NM-000061) with a C-terminal V5 and 6x His tag was subcloned into pFastBac vector for making baculovirus carrying this epitope-tagged Btk. Generation of baculovirus is done based on Invitrogen's instructions detailed in its published protocol "Bac-toBac Baculovirus Expression Systems" (Cat. Nos. 10359-016 and 10608-016). Passage 3 virus is used to infect Sf9 cells to overexpress the recombinant Btk protein. The Btk protein is then purified to homogeneity using Ni-NTA column. The purity of the final protein preparation is greater than 95% based on the sensitive Sypro-Ruby staining. A solution of 200 μM ATP is prepared in water and adjusted to pH7.4 with 1N NaOH. A quantity of 1.25 μL of compounds in

5%DMSO is transferred to a 96-well ½ area Costar polystyrene plate Compounds are tested singly and with an 11-point dose-responsive curve (starting concentration is 10 μM; 1:2 dilution). A quantity of 18.75 μL of master mix minus enzyme (as a negative control) and master mix plus enzyme is transferred to appropriate wells in 96-well ½ area costar polystyrene plate. 5 μL of 200 μM ATP is added to that mixture in the 96-well ½ area Costar polystyrene plate for final ATP concentration of 40 μM. The reaction is allowed to incubate for 1 hour at room temperature. The reaction is stopped with Perkin Elmer 1X detection buffer containing 30 mM EDTA, 20 nM SA-APC, and 1 nM PT66 Ab. The plate is read using time-resolved fluorescence with a Perkin Elmer Envision using excitation filter 330 nm, emission filter 665 nm, and 2nd emission filter 615 nm. IC_{50} values are subsequently calculated.

Example 14

Ramos Cell Btk Assay

[00305] Another generalized procedure for a standard cellular Btk Kinase Assay that can be used to test compounds disclosed in this application is as follows.

[00306] Ramos cells are incubated at a density of $0.5x10^7$ cells/ml in the presence of test compound for 1 hr at 37 °C. Cells are then stimulated by incubating with 10 μg/ml anti-human IgM $F(ab)_2$ for 5 minutes at 37 °C. Cells are pelleted, lysed, and a protein assay is performed on the cleared lysate. Equal protein amounts of each sample are subject to SDS-PAGE and western blotting with either anti-phosphoBtk(Tyr223) antibody (Cell Signaling Technology #3531) to assess Btk autophosphorylation or an anti-Btk antibody (BD Transduction Labs #611116) to control for total amounts of Btk in each lysate.

Example 15

B-Cell Proliferation Assay

[00307] A generalized procedure for a standard cellular B-cell proliferation assay that can be used to test compounds disclosed in this application is as follows.

[00308] B-cells are purified from spleens of 8-16 week old Balb/c mice using a B-cell isolation kit (Miltenyi Biotech, Cat # 130-090-862). Testing compounds are diluted in 0.25% DMSO and incubated with 2.5×10^5 purified mouse splenic B-cells

for 30 min prior to addition of 10μg/ml of an anti-mouse IgM antibody (Southern Biotechnology Associates Cat # 1022-01) in a final volume of 100 μl. Following 24 hr incubation, 1 μCi ^{3}H-thymidine is added and plates are incubated an additional 36 hr prior to harvest using the manufacturer's protocol for SPA[^{3}H] thymidine uptake assay system (Amersham Biosciences # RPNQ 0130). SPA-bead based fluorescence is counted in a microbeta counter (Wallace Triplex 1450, Perkin Elmer).

Example 16

T Cell Proliferation Assay

[00309] A generalized procedure for a standard T cell proliferation assay that can be used to test compounds disclosed in this application is as follows.

[00310] T cells are purified from spleens of 8-16 week old Balb/c mice using a Pan T cell isolation kit (Miltenyi Biotech, Cat # 130-090-861). Testing compounds are diluted in 0.25% DMSO and incubated with 2.5 x 10^5 purified mouse splenic T cells in a final volume of 100 μl in flat clear bottom plates precoated for 90 min at 37°C with 10 μg/ml each of anti-CD3 (BD # 553057) and anti-CD28 (BD # 553294) antibodies. Following 24 hr incubation, 1 μCi ^{3}H-thymidine is added and plates incubated an additional 36 hr prior to harvest using the manufacturer's protocol for SPA[^{3}H] thymidine uptake assay system (Amersham Biosciences # RPNQ 0130). SPA-bead based fluorescence was counted in a microbeta counter (Wallace Triplex 1450, Perkin Elmer).

Example 17

CD86 Inhibition Assay

[00311] A generalized procedure for a standard assay for the inhibition of B cell activity that can be used to test compounds disclosed in this application is as follows.

[00312] Total mouse splenocytes are purified from spleens of 8-16 week old Balb/c mice by red blood cell lysis (BD Pharmingen #555899). Testing compounds are diluted to 0.5% DMSO and incubated with 1.25 x 10^6 splenocytes in a final volume of 200 μl in flat clear bottom plates (Falcon 353072) for 60 min at 37°C. Cells are then stimulated with the addition of 15 μ[g/ml IgM (Jackson

ImmunoResearch 115-006-020), and incubated for 24 hr at 37°C, 5% CO_2. Following the 24 hr incubation, cells are transferred to conical bottom clear 96-well plates and pelleted by centrifugation at 1200 x g x 5 min. Cells are preblocked by CD16/CD32 (BD Pharmingen #553142), followed by triple staining with CD19-FITC (BD Pharmingen #553785), CD86-PE (BD Pharmingen #553692), and 7AAD (BD Pharmingen #51-68981E). Cells are sorted on a BD FACSCalibur and gated on the $CD19^+/7AAD^-$ population. The levels of CD86 surface expression on the gated population is measured versus test compound concentration.

Example 18

B-ALL Cell Survival Assay

[00313] The following is a procedure for a standard B-ALL cell survival study using an XTT readout to measure the number of viable cells. This assay can be used to test compounds disclosed in this applicationfor their ability to inhibit the survival of B-ALL cells in culture. One human B-cell acute lymphoblastic leukemia line that can be used is SUP-B15, a human Pre-B-cell ALL line that is available from the ATCC.

[00314] SUP-B15 pre-B-ALL cells are plated in multiple 96-well microtiter plates in 100 µl of Iscove's media + 20% FBS at a concentration of 5 x 10^5 cells/ml. Test compounds are then added with a final conc. of 0.4% DMSO. Cells are incubated at 37°C with 5% CO_2 for up to 3 days. After 3 days cells are split 1:3 into fresh 96-well plates containing the test compound and allowed to grow up to an additional 3 days. After each 24h period, 50 ul of an XTT solution (Roche) is added to one of the replicate 96-well plates and absorbance readings are taken at 2, 4 and 20 hours following manufacturer's directions. The reading taken with an OD for DMSO only treated cells within the linear range of the assay (0.5- 1.5) is then taken and the percentage of viable cells in the compound treated wells are measured versus the DMSO only treated cells.

Example 19

[00315] The compounds disclosed in the examples above were tested in the Btk biochemical assay described herein (Example 13) and certain of those compounds

exhibited an IC_{50} value less than or equal to 1 micromolar. Certain of those compounds exhibited an IC_{50} value less than or equal to 100 nM. Certain of those compounds exhibited an IC_{50} value less than or equal to 10 nM.

[00316] Some of the compounds disclosed in synthetic Example 2 were tested in the B-cell proliferation assay (as described in Example 15) and exhibited an IC_{50} value less than or equal to 10 micromolar. Certain of those compounds exhibited an IC_{50} value less than or equal to 1 micromolar. Certain of those compounds exhibited an IC_{50} value less than or equal to 500 nM in this assay.

[00317] Certain of those compounds did not inhibit T-cell proliferation and had IC_{50} values greater than or equal to 5 micromolar when assayed under conditions described herein (as described in Example 16).

[00318] Certain compounds disclosed herein exhibited IC_{50} values for inhibition of T-cell proliferation that were at least 3-fold, and in some instances 5-fold, or even 10-fold greater than the IC_{50} values of those compounds for inhibition of B-cell proliferation.

[00319] Some of the compounds disclosed herein were tested in an assay for inhibition of B cell activity (under the conditions described in example 17), and exhibited an IC_{50} value less than or equal to 10 micromolar. Certain of those compounds exhibited an IC_{50} value less than or equal to 1 micromolar. Certain of those compounds exhibited an IC_{50} value less than or equal to 500 nM in this assay.

[00320] Some of the compounds disclosed herein were tested in a B-cell leukemia cell survival assay (under the conditions described in example 18), and exhibit an IC_{50} value less than or equal to 10 micromolar.

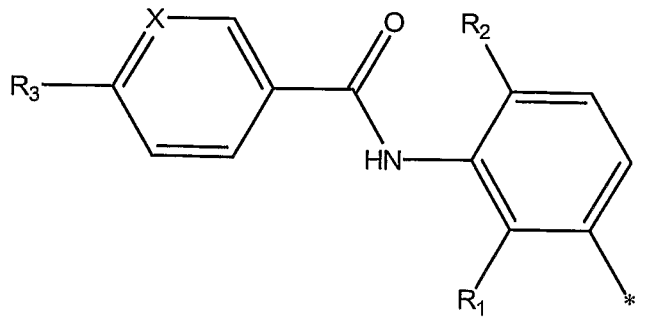
[00321] Some of the compounds disclosed in disclosed herein exhibited both biochemical and cell-based activity. For example, some of the compounds disclosed herein exhibited an IC_{50} value less than or equal to 10 micromolar in the Btk biochemical assay described herein (Example 13) and an IC_{50} value less than or equal to 10 micromolar in at least one of the cell-based assays (other than the T-cell assay) described herein (Examples 14, 15, 17 or 18). Certain of those compounds exhibited an IC_{50} value less than or equal to 1 micromolar in the Btk biochemical assay described herein (Example 13) and an IC_{50} value less than or equal to 10 micromolar in at least one of the cell-based assays (other than the T-cell assay) described herein

(Examples 14, 15, 17 or 18). Certain of those compounds exhibited an IC_{50} value less than or equal to 0.1 micromolar and an IC_{50} value less than or equal to 10 micromolar in at least one of the cell-based assays (other than the T-cell assay) described herein (Examples 14, 15, 17 or 18).

[00322] While some embodiments have been shown and described, various modifications and substitutions may be made thereto without departing from the spirit and scope of the invention. For example, for claim construction purposes, it is not intended that the claims set forth hereinafter be construed in any way narrower than the literal language thereof, and it is thus not intended that exemplary embodiments from the specification be read into the claims. Accordingly, it is to be understood that the present invention has been described by way of illustration and not limitations on the scope of the claims.

What is claimed is:

1. At least one chemical entity comprising a pharmacophore chosen from radicals of Formula 1



(Formula 1)

and pharmaceutically acceptable salts, solvates, chelates, non-covalent complexes, prodrugs, and mixtures thereof, wherein

* represents a point of attachment;

R_3 is chosen from optionally substituted piperidinyl, tert-butyl and isopropyl;

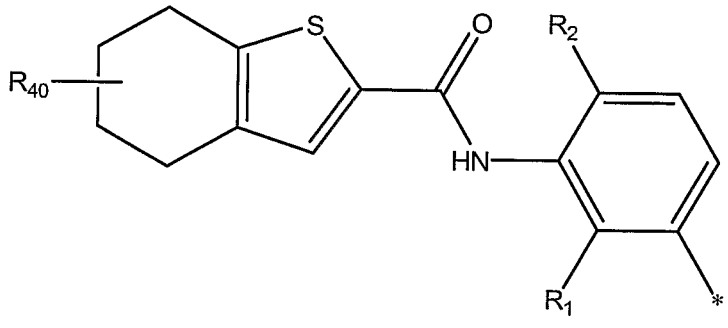
X is chosen from CH and N; and

R_1 and R_2 are independently chosen from hydrogen, lower alkyl, and halo, provided that at least one of R_1 and R_2 is not hydrogen.

2. At least one chemical entity of claim 1 wherein X is CH.

3. At least one chemical entity of claim 1 wherein X is N.

4. At least one chemical entity comprising a pharmacophore chosen from radicals of Formula 1A



(Formula 1A)

and pharmaceutically acceptable salts, solvates, chelates, non-covalent complexes, prodrugs, and mixtures thereof, wherein

* represents a point of attachment;

R_{40} is chosen from hydrogen, hydroxy, lower alkyl, sulfonyl, halo, lower alkoxy, and heteroaryl; and

R_1 and R_2 are independently chosen from hydrogen, lower alkyl, and halo, provided that at least one of R_1 and R_2 is not hydrogen.

5. At least one chemical entity of any one of claims 1 to 4 wherein R_1 and R_2 are independently chosen from hydrogen, methyl, and fluoro.

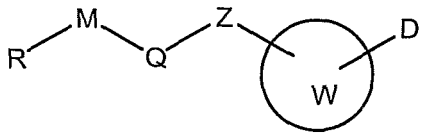
6. At least one chemical entity of claim 5 wherein R_1 is chosen from methyl and fluoro and R_2 is hydrogen.

7. At least one chemical entity of claim 5 wherein R_2 is chosen from methyl and fluoro and R_1 is hydrogen.

8. At least one chemical entity of claim 5 wherein R_1 and R_2 are independently chosen from methyl and fluoro.

9. At least one chemical entity of any one of claims 3 to 8 wherein R_{40} is chosen from hydrogen and lower alkyl.

10. At least one chemical entity chosen from compounds of Formula 2:



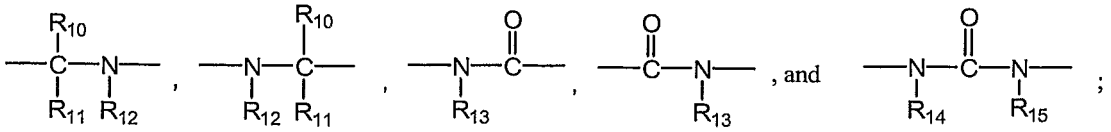
(Formula 2)

and pharmaceutically acceptable salts, solvates, chelates, non-covalent complexes, prodrugs, and mixtures thereof, wherein

R is chosen from optionally substituted cycloalkyl, optionally substituted aryl and optionally substituted heteroaryl;

M is chosen from a covalent bond and –CH=CH–.

Q is chosen from



wherein

R_{10} and R_{11} are independently chosen from hydrogen, C_1-C_6 alkyl, and C_1-C_6 haloalkyl; and

R_{12}, R_{13}, R_{14}, and R_{15} are each independently chosen from hydrogen,

C_1-C_6 alkyl,

C_1-C_6 haloalkyl,

phenyl,

substituted phenyl chosen from mono-, di-, and tri-substituted phenyl wherein the substituents are independently chosen from hydroxy, nitro, cyano, amino, halo, C_1-C_6 alkyl, C_1-C_6 alkoxy, (C_1-C_6 alkyloxy)C_1-C_6 alkoxy, C_1-C_6 perfluoroalkyl, C_1-C_6 perfluoroalkoxy, mono-(C_1-C_6 alkyl)amino, di(C_1-C_6 alkyl)amino, and amino(C_1-C_6 alkyl),

heteroaryl, and

substituted heteroaryl chosen from mono-, di-, and tri-substituted heteroaryl wherein the substituents are independently chosen from hydroxy, nitro, cyano, amino, halo, C_1-C_6 alkyl, C_1-C_6 alkoxy, (C_1-C_6 alkyloxy)C_1-C_6 alkoxy, C_1-C_6 perfluoroalkyl, C_1-C_6 perfluoroalkoxy, mono-(C_1-C_6 alkyl)amino, di(C_1-C_6 alkyl)amino, and amino(C_1-C_6 alkyl); and

Z is chosen from optionally substituted phenylene and optionally substituted pyridylidene;

W is an optionally substituted heteroaryl group other than imidazo[1,2-A]pyrazine group;

and

D is a hydrogen bond donor other than hydrogen, provided that

the compound of Formula 2 is not (4-{6-[(4-chloro-benzyl)-methyl-amino]-pyrazin-2-yl}-phenyl)-piperidin-1-yl-methanone.

11. At least one chemical entity of claim 10 wherein Z is chosen from ortho-phenylene, meta-phenylene, para-phenylene, ortho-pyridylidene, meta-pyridylidene, and para-pyridylidene, each of which is optionally substituted with a group chosen from optionally substituted lower alkyl, optionally substituted lower alkoxy, halo, and hydroxy.

12. At least one chemical entity of claim 11 wherein Z is chosen from meta-phenylene and meta-phenylene substituted with a group chosen from optionally substituted lower alkyl, optionally substituted lower alkoxy, halo, and hydroxy.

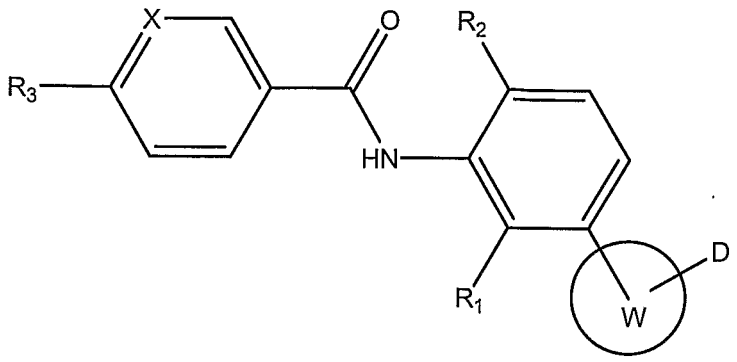
13. At least one chemical entity of claim 12 wherein Z is chosen from meta-phenylene and meta-phenylene substituted with a group chosen from lower alkyl and halo.

14. At least one chemical entity of claim 13 wherein Z is chosen from meta-phenylene and meta-phenylene substituted with a group chosen from methyl and halo.

15. At least one chemical entity of any one of claims 10 to 14 wherein M is a covalent bond.

16. At least one chemical entity of any one of claims 10 to 14 wherein M is –CH=CH–.

17. At least one chemical entity of claim 10 wherein the compound of Formula 2 is chosen from compounds of Formula 3:



(Formula 3)

wherein

R_3 is chosen from optionally substituted piperidinyl, tert-butyl and isopropyl;

X is chosen from CH and N;

R_1 and R_2 are independently chosen from hydrogen, lower alkyl, and halo, provided that at least one of R_1 and R_2 is not hydrogen.

18. At least one chemical entity of claim 17 wherein X is CH.

19. At least one chemical entity of claim 17 wherein X is N.

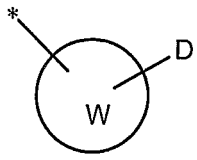
20. At least one chemical entity of any one of claims 17 to 19 wherein R_1 and R_2 are independently chosen from hydrogen, methyl, and fluoro.

21. At least one chemical entity of claim 20 wherein R_1 is chosen from methyl and fluoro and R_2 is hydrogen.

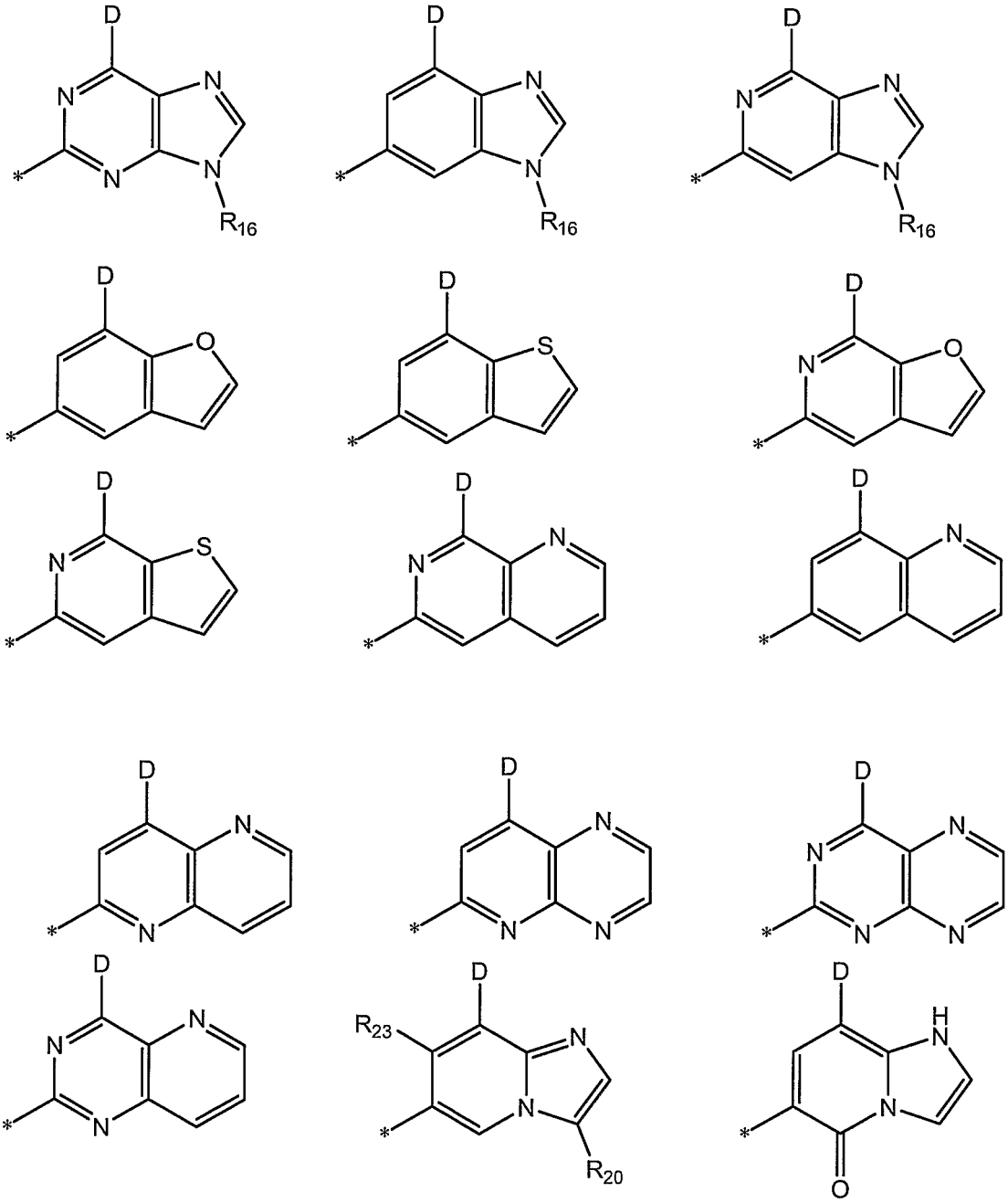
22. At least one chemical entity of claim 20 wherein R_1 and R_2 are independently chosen from methyl and fluoro.

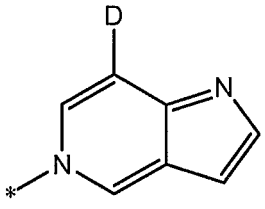
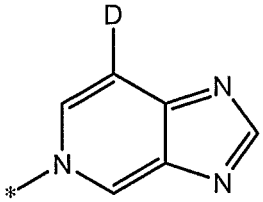
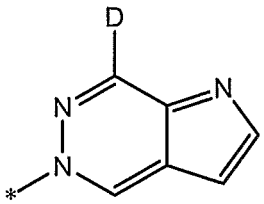
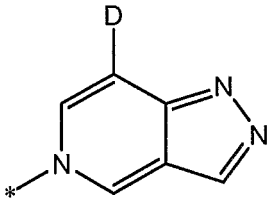
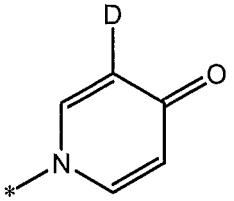
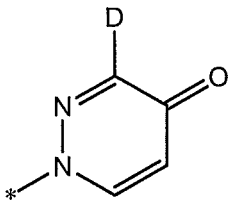
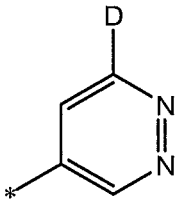
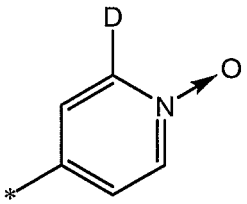
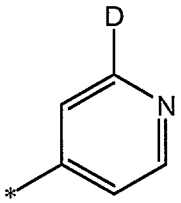
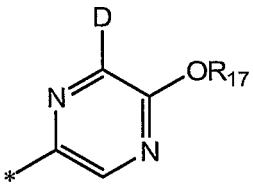
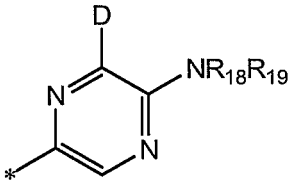
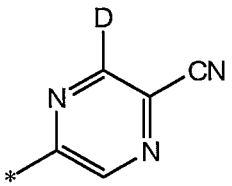
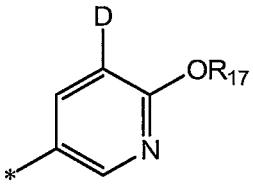
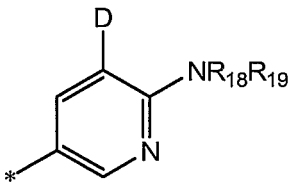
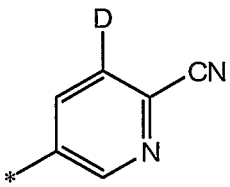
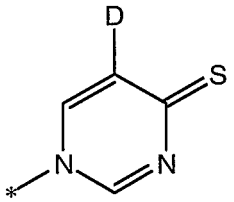
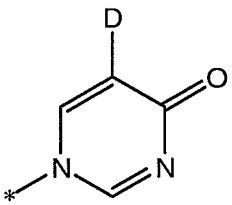
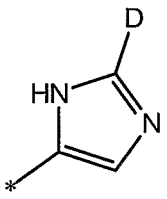
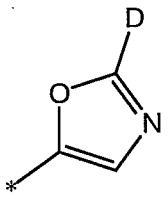
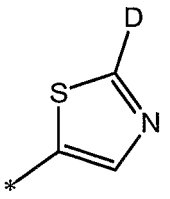
23. At least one chemical entity of any one of claims 10 to 22 wherein W is an optionally substituted heteroaryl group that further comprises a hydrogen bond acceptor.

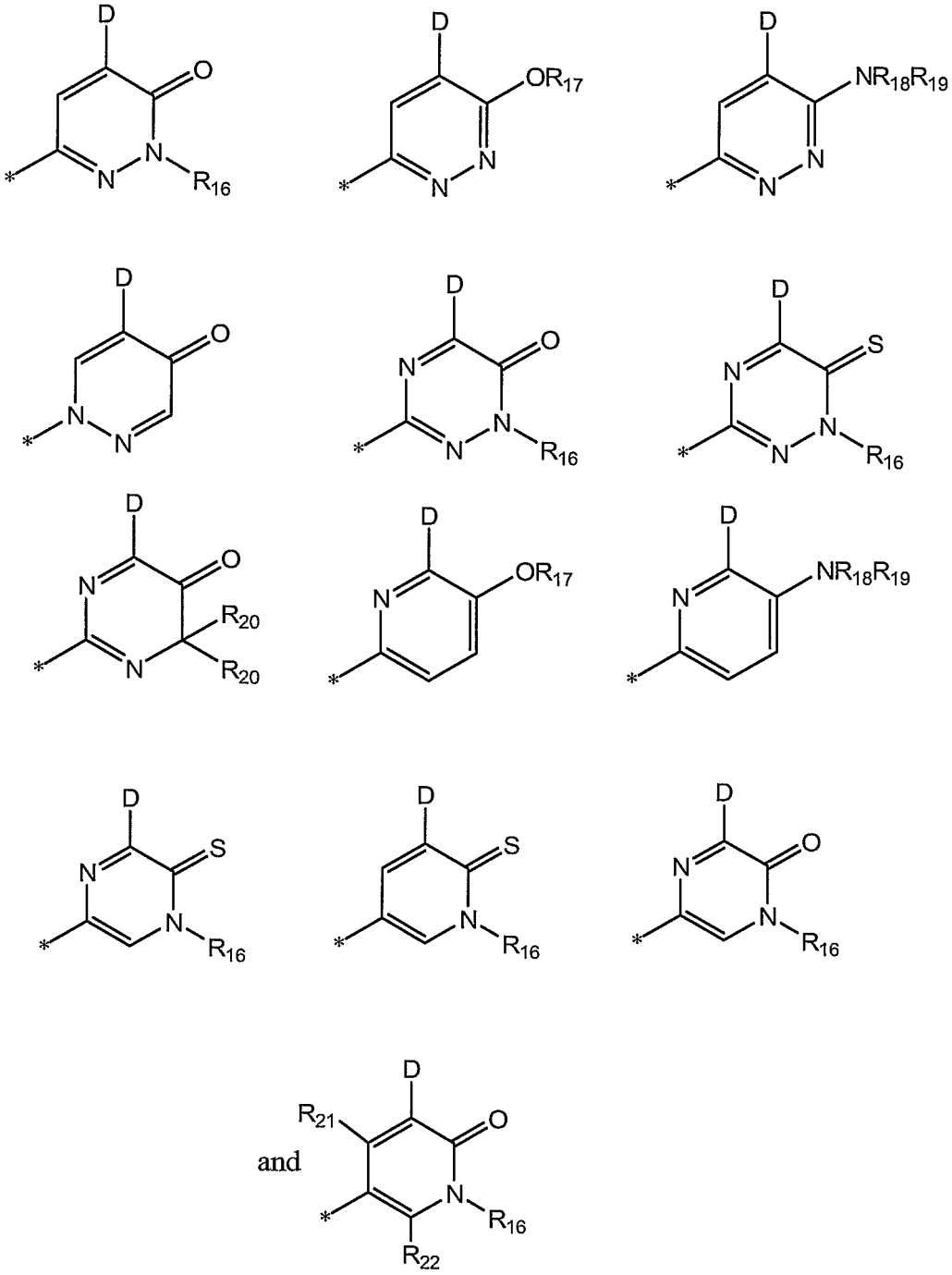
24. At least one chemical entity of any one of claims 10 to 22 wherein



is chosen from





each of which is optionally substituted with one or two groups chosen from hydroxy, cyano, halo, optionally substituted lower alkyl, and optionally substituted lower alkoxy and wherein

R_{16} is chosen from

hydrogen, cyano, optionally substituted cycloalkyl, and optionally substituted lower alkyl;

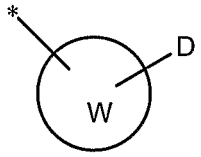
R_{17}, R_{18}, R_{19}, R_{21}, R_{22}, and R_{23} are independently chosen from hydrogen and optionally substituted lower alkyl; and

R_{20} is chosen from hydrogen, hydroxy, cyano, halo, optionally substituted lower alkyl, and optionally substituted lower alkoxy.

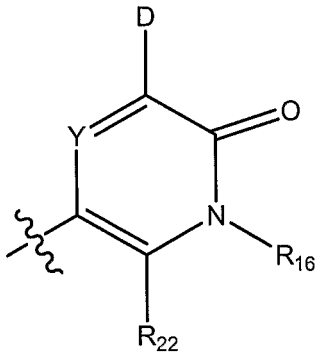
25. At least one chemical entity of claim 24 wherein R_{17}, R_{18}, R_{19}, R_{21}, and R_{22} are independently chosen from hydrogen and lower alkyl.

26. At least one chemical entity of claim 24 or 25 wherein R_{20} is hydrogen.

27. At least one chemical entity of any one of claims 10 to 22 wherein



comprises



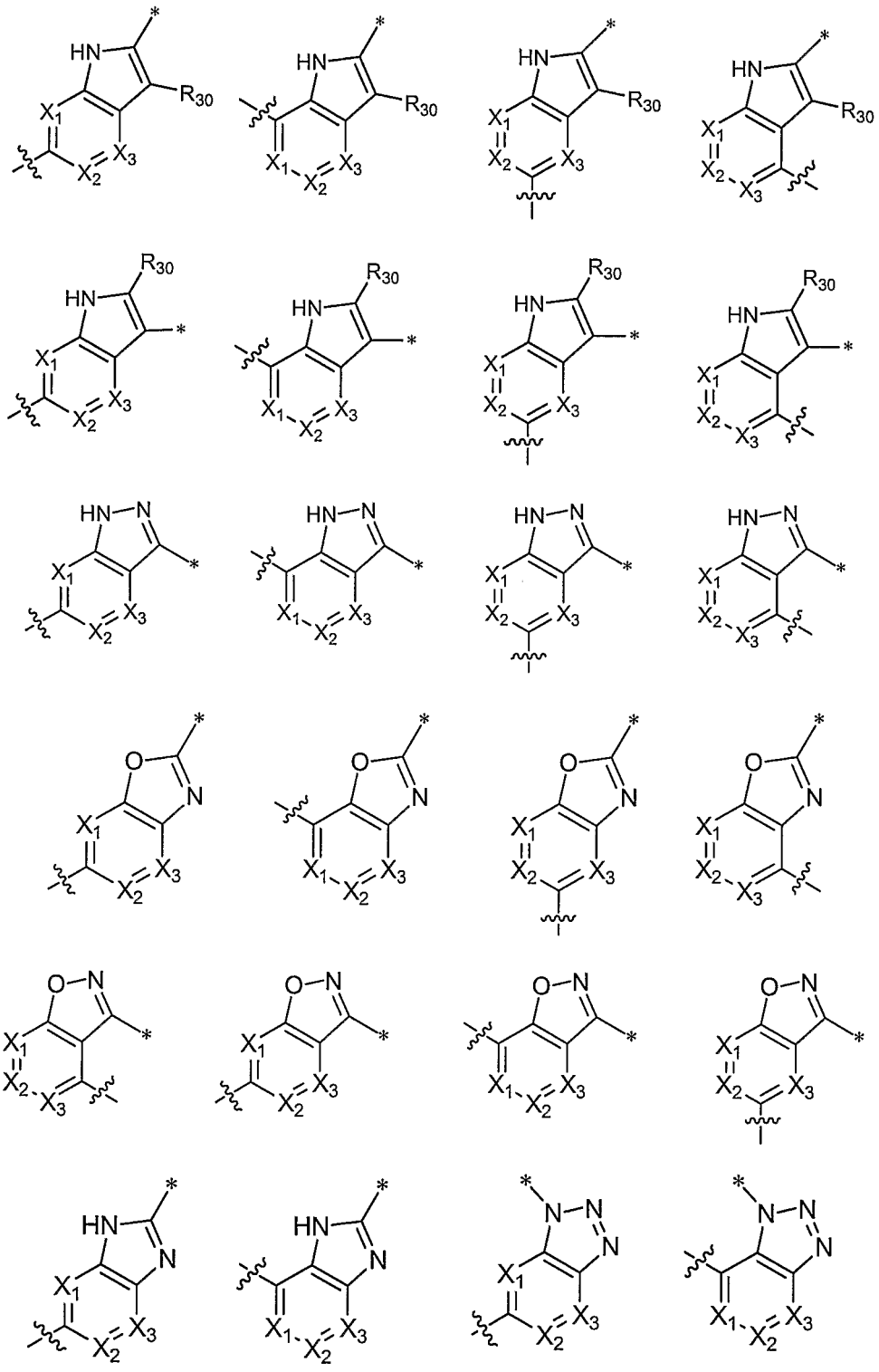
wherein Y is chosen from N and CR_{21}; and

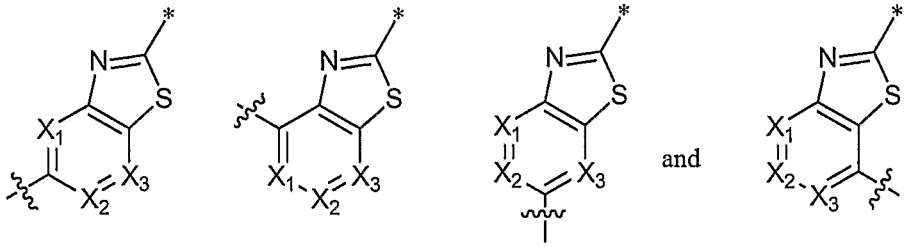
R_{16}, R_{21}, and R_{22} are independently chosen from hydrogen and optionally substituted lower alkyl;

28. At least one chemical entity of any one of claims 10 to 27 wherein D is $-NHR_9$ wherein R_9 is chosen from optionally substituted aryl and optionally substituted heteroaryl.

29. At least one chemical entity of any one of claims 10 to 27 wherein D is –N(H)-B-L-G wherein

B is chosen from optionally substituted phenylene, optionally substituted pyridylidene, optionally substituted 2-oxo-1,2-dihydropyridinyl,





wherein

* indicates the point of attachment to the group –L-G and the broken bond

 indicates the point of attachment to the amino group;

X_1 is chosen from N and CR_{31};

X_2 is chosen from N and CR_{31}; and

X_3 is chosen from N and CR_{31}; and wherein no more than one of X_1, X_2, and X_3 is N,

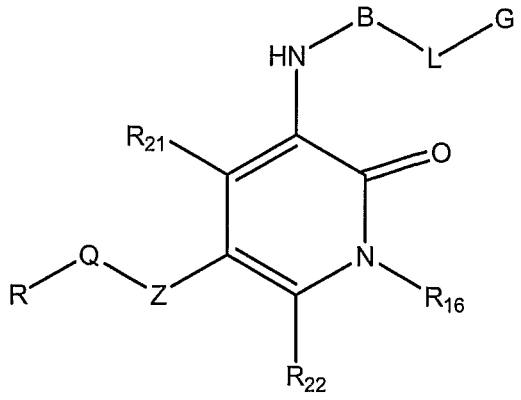
R_{30} is chosen from hydrogen, hydroxy, cyano, halo, optionally substituted lower alkyl, and optionally substituted lower alkoxy;

R_{31} is chosen from hydrogen, hydroxy, cyano, halo, optionally substituted lower alkyl, and optionally substituted lower alkoxy;

L is chosen from optionally substituted C_0-C_4alkylene, -O-optionally substituted C_0-C_4alkylene, -(C_0-C_4alkylene)(SO)-, -(C_0-C_4alkylene)(SO_2)-; and -(C_0-C_4alkylene)(C=O)-; and

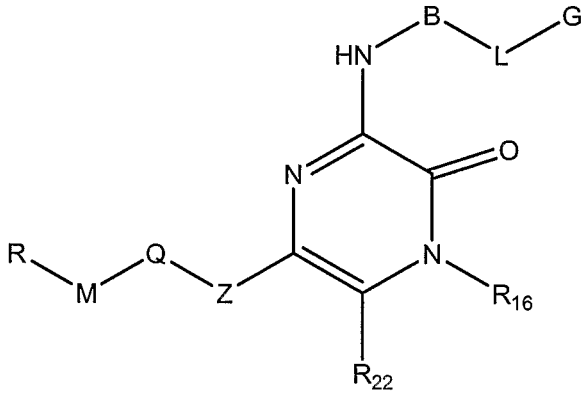
G is chosen from hydrogen, halo, hydroxy, alkoxy, nitro, optionally substituted alkyl, optionally substituted amino, optionally substituted carbamimidoyl, optionally substituted heterocycloalkyl, optionally substituted cycloalkyl, optionally substituted aryl, and optionally substituted heteroaryl.

30. At least one chemical entity of claim 29 comprising a compound of Formula 4:



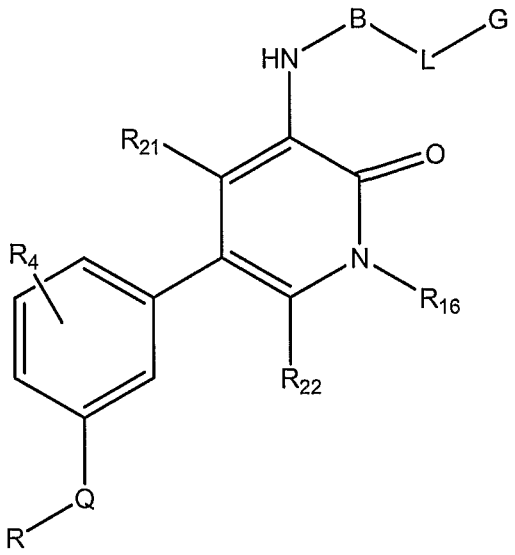
(Formula 4).

31. At least one chemical entity of claim 29 comprising a compound of Formula 5:



(Formula 5).

32. At least one chemical entity of claim 30 comprising a compound of Formula 6:

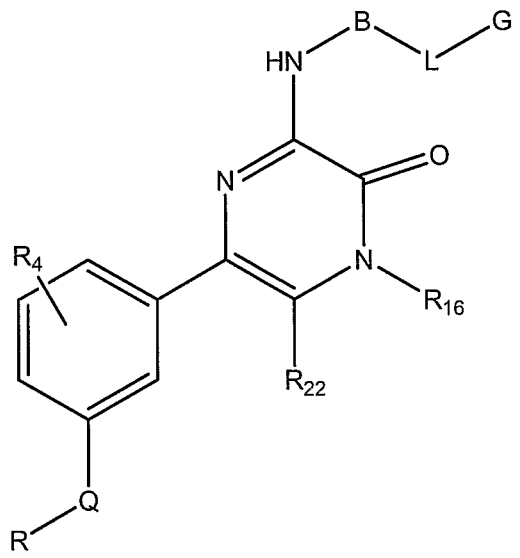


(Formula 6)

wherein

R_4 is chosen from hydrogen, optionally substituted lower alkyl, optionally substituted lower alkoxy, halo, and hydroxy.

33. At least one chemical entity of claim 31 comprising a compound of Formula 7:

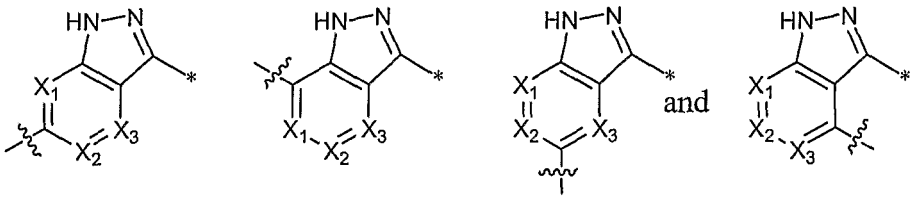


(Formula 7)

wherein

R_4 is chosen from hydrogen, optionally substituted lower alkyl, optionally substituted lower alkoxy, halo, and hydroxy.

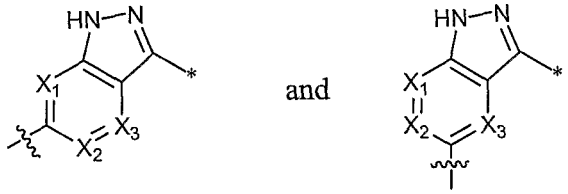
34. At least one chemical entity of any one of claims 29 to 33 wherein B is chosen from ortho-phenylene, meta-phenylene, para-phenylene, ortho-pyridylidene, meta-pyridylidene, para-pyridylidene,



35. At least one chemical entity of claim 34 wherein B is chosen from para-phenylene and meta-phenylene.

36. At least one chemical entity of claim 35 wherein B is meta-phenylene.

37. At least one chemical entity of claim 34 wherein, B is chosen



from

38. At least one chemical entity of any one of claims 10 to 37 wherein R_{12}, R_{13}, R_{14}, and R_{15} are each independently chosen from hydrogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl, and phenyl.

39. At least one chemical entity of claim 38 wherein R_{13} is chosen from hydrogen and C_1-C_6 alkyl.

40. At least one chemical entity of any one of claims 10 to 39 wherein R is chosen from

phenyl,

substituted phenyl chosen from mono-, di-, and tri-substituted phenyl wherein the substituents are independently chosen from hydroxy, lower alkyl, sulfanyl, sulfonyl, optionally substituted amino, lower alkoxy, lower alkyl substituted with one or more halo, lower alkoxy substituted with one or more halo, lower alkyl substituted with hydroxy, lower alkyl substituted with lower alkoxy, optionally substituted piperidinyl, and heteroaryl,

pyridyl,

substituted pyridyl chosen from mono-, di-, and tri-substituted pyridyl wherein the substituents are independently chosen from hydroxy, lower alkyl, sulfonyl, halo, lower alkoxy,optionally substituted piperidinyl, and heteroaryl,

pyrimidinyl,

substituted pyrimidinyl chosen from mono-, di-, and tri-substituted pyridyl wherein the substituents are independently chosen from hydroxy, lower alkyl, sulfonyl, halo, lower alkoxy, optionally substituted piperidinyl, and heteroaryl,

pyrazinyl,

substituted pyrazinyl chosen from mono-, di-, and tri-substituted pyridyl wherein the substituents are independently chosen from hydroxy, lower alkyl, sulfonyl, halo, lower alkoxy, optionally substituted piperidinyl, and heteroaryl,

pyridazinyl,

substituted pyridazinyl chosen from mono-, di-, and tri-substituted pyridyl wherein the substituents are independently chosen from hydroxy, lower alkyl, sulfonyl, halo, lower alkoxy, optionally substituted piperidinyl, and heteroaryl,

oxazol-2-yl,

substituted oxazol-2-yl l chosen from mono-, di-, and tri-substituted oxazol-2-yl wherein the substituents are independently chosen from hydroxy, lower alkyl, sulfonyl, halo, lower alkoxy, optionally substituted piperidinyl, and heteroaryl,

2H-pyrazol-3-yl,

substituted 2H-pyrazol-3-yl chosen from mono-, di-, and tri-substituted 2H-pyrazol-3-yl wherein the substituents are independently chosen from hydroxy, lower alkyl, sulfonyl, halo, lower alkoxy, optionally substituted piperidinyl, and heteroaryl,

[1,2,3]thiadiazol-4-yl,

substituted [1,2,3]thiadiazol-4-yl chosen from mono-, di-, and tri-substituted [1,2,3]thiadiazol-4-yl wherein the substituents are independently chosen from hydroxy, lower alkyl, sulfonyl, halo, lower alkoxy, optionally substituted piperidinyl, and heteroaryl,

isoxazol-5-yl,

substituted isoxazol-5-yl chosen from mono-, di-, and tri-substituted isoxazol-5-yl wherein the substituents are independently chosen from hydroxy, lower alkyl, sulfonyl, halo, lower alkoxy, optionally substituted piperidinyl, and heteroaryl,

4,5,6,7-tetrahydrobenzo[b]thiophen-2-yl,

substituted 4,5,6,7-tetrahydrobenzo[b]thiophen-2-yl chosen from mono-, di-, and tri-substituted 4,5,6,7-tetrahydrobenzo[b]thiophen-2-yl wherein the substituents are independently chosen from hydroxy, lower alkyl, sulfonyl, halo, lower alkoxy, optionally substituted piperidinyl, and heteroaryl,

4,5,6,7-tetrahydrobenzofuran-2-yl,

substituted 4,5,6,7-tetrahydrobenzofuran-2-yl chosen from mono-, di-, and tri-substituted 4,5,6,7-tetrahydrobenzofuran-2-yl wherein the substituents are independently chosen from hydroxy, lower alkyl, sulfonyl, halo, lower alkoxy, optionally substituted piperidinyl, and heteroaryl,

4,5,6,7-tetrahydro-1H-indol-2-yl,

substituted 4,5,6,7-tetrahydro-1H-indol-2-yl chosen from mono-, di-, and tri-substituted 4,5,6,7-tetrahydro-1H-indol-2-yl wherein the substituents are independently chosen from hydroxy, lower alkyl, sulfonyl, halo, lower alkoxy, optionally substituted piperidinyl, and heteroaryl and

wherein the amine nitrogen of the indole ring is optionally substituted with an optionally substituted lower alkyl group,

1H-indol-2-yl,

substituted 1H-indol-2-yl chosen from mono-, di-, and tri-substituted 1H-indol-2-yl wherein the substituents are independently chosen from hydroxy, lower alkyl, sulfonyl, halo, lower alkoxy, optionally substituted piperidinyl, and heteroaryl and wherein the amine nitrogen of the indole ring is optionally substituted with an optionally substituted lower alkyl group,

benzofuran-2-yl,

substituted benzofuran-2-yl chosen from mono-, di-, and tri-substituted benzofuran-2-yl wherein the substituents are independently chosen from hydroxy, lower alkyl, sulfonyl, halo, lower alkoxy, optionally substituted piperidinyl, and heteroaryl,

benzo[b]thiophen-2-yl, and

substituted benzo[b]thiophen-2-yl chosen from mono-, di-, and tri-substituted benzo[b]thiophen-2-yl wherein the substituents are independently chosen from hydroxy, lower alkyl, sulfonyl, halo, lower alkoxy, optionally substituted piperidinyl, and heteroaryl.

41. At least one chemical entity of claim 40 wherein R is chosen from

phenyl,

substituted phenyl chosen from mono-, di-, and tri-substituted phenyl wherein the substituents are independently chosen from hydroxy, lower alkyl, sulfonyl, halo, lower alkoxy, optionally substituted piperidinyl, and heteroaryl,

pyridyl,

substituted pyridyl chosen from mono-, di-, and tri-substituted pyridyl wherein the substituents are independently chosen from hydroxy, lower alkyl, sulfonyl, halo, lower alkoxy, optionally substituted piperidinyl, and heteroaryl,

oxazol-2-yl,

substituted oxazol-2-yl l chosen from mono-, di-, and tri-substituted oxazol-2-yl wherein the substituents are independently chosen from hydroxy, lower alkyl, sulfonyl, halo, lower alkoxy, optionally substituted piperidinyl, and heteroaryl,

2H-pyrazol-3-yl,

substituted 2H-pyrazol-3-yl chosen from mono-, di-, and tri-substituted 2H-pyrazol-3-yl wherein the substituents are independently chosen from hydroxy, lower alkyl, sulfonyl, halo, lower alkoxy, optionally substituted piperidinyl, and heteroaryl,

4,5,6,7-tetrahydrobenzo[b]thiophen-2-yl,

substituted 4,5,6,7-tetrahydrobenzo[b]thiophen-2-yl chosen from mono-, di-, and tri-substituted 4,5,6,7-tetrahydrobenzo[b]thiophen-2-yl wherein the substituents are independently chosen from hydroxy, lower alkyl, sulfonyl, halo, lower alkoxy, optionally substituted piperidinyl, and heteroaryl,

[1,2,3]thiadiazol-4-yl,

substituted [1,2,3]thiadiazol-4-yl chosen from mono-, di-, and tri-substituted [1,2,3]thiadiazol-4-yl wherein the substituents are independently chosen from hydroxy, lower alkyl, sulfonyl, halo, lower alkoxy, optionally substituted piperidinyl, and heteroaryl,

isoxazol-5-yl, and

substituted isoxazol-5-yl chosen from mono-, di-, and tri-substituted isoxazol-5-yl wherein the substituents are independently chosen from hydroxy, lower alkyl, sulfonyl, halo, lower alkoxy, optionally substituted piperidinyl, and heteroaryl.

42. At least one chemical entity of claim 41 wherein R is chosen from 4,5,6,7-tetrahydrobenzo[b]thiophen-2-yl and substituted 4,5,6,7-tetrahydrobenzo[b]thiophen-2-yl chosen from mono-, di-, and tri-substituted 4,5,6,7-tetrahydrobenzo[b]thiophen-2-yl wherein the substituents are independently chosen from hydroxy, lower alkyl, sulfonyl, halo, lower alkoxy, and heteroaryl.

43. At least one chemical entity of claim 42 wherein R is chosen from 4,5,6,7-tetrahydrobenzo[b]thiophen-2-yl and substituted 4,5,6,7-tetrahydrobenzo[b]thiophen-2-yl chosen from mono-, di-, and tri-substituted 4,5,6,7-tetrahydrobenzo[b]thiophen-2-yl wherein the substituents is lower alkyl.

44. At least one chemical entity of claim 43 wherein R is substituted phenyl chosen from mono-, di-, and tri-substituted phenyl wherein the substituents are independently chosen from hydroxy, lower alkyl, sulfanyl, sulfonyl, optionally substituted amino, lower alkoxy, lower alkyl substituted with one or more halo, lower alkoxy substituted with one or more halo, lower alkyl substituted with hydroxy, lower alkyl substituted with lower alkoxy, optionally substituted piperidinyl, and heteroaryl.

45. At least one chemical entity of claim 44 wherein R is substituted phenyl chosen from mono-, di-, and tri-substituted phenyl wherein the substituents are independently chosen from hydroxy, lower alkyl, sulfonyl, halo, lower alkoxy, optionally substituted piperidinyl, and heteroaryl.

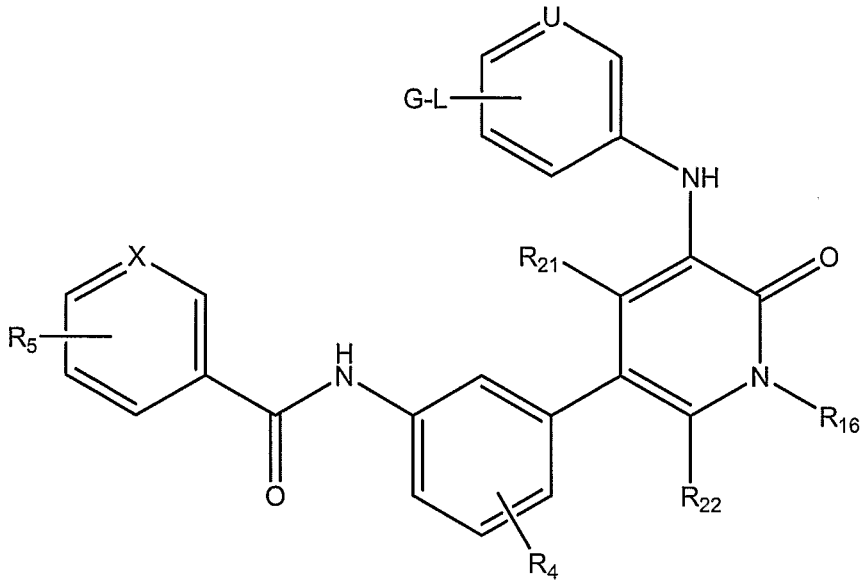
46. At least one chemical entity of claim 45 wherein R is 4-lower alkyl-phenyl-.

47. At least one chemical entity of claim 46 wherein R is 4-*tert*-butyl-phenyl.

48. At least one chemical entity of claim 46 wherein R is 4-*iso*-propyl-phenyl.

49. At least one chemical entity of claim 45 wherein R is phenyl substituted with an optionally substituted piperidinyl.

50. At least one chemical entity of claim 32 comprising a compound of Formula 8:



(Formula 8)

and wherein

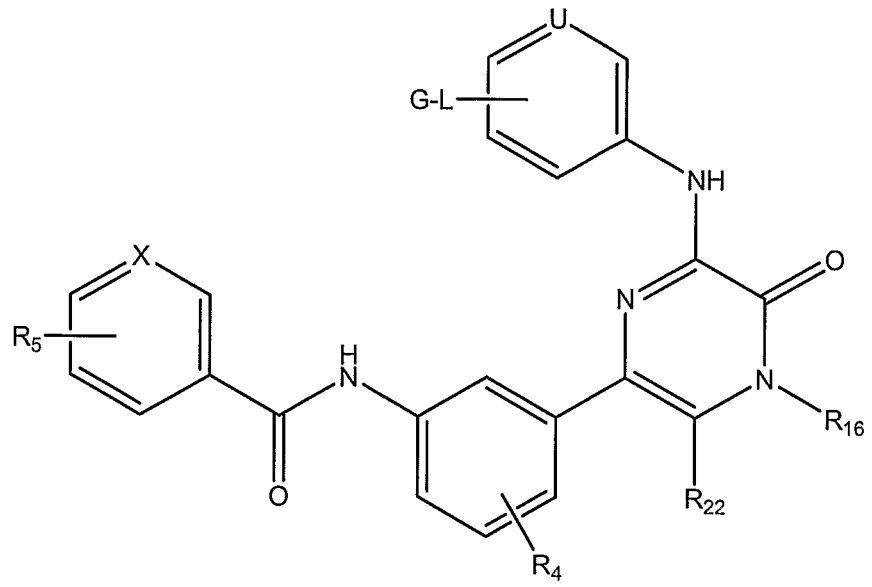
X is chosen from N and CH;

U is chosen from N and CR_{41};

R_{41} is chosen from hydrogen, halo, optionally substituted lower alkyl, optionally substituted lower alkoxy, hydroxy, nitro, cyano, sulfhydryl, sulfanyl, sulfinyl, sulfonyl, carboxy, aminocarbonyl, and optionally substituted amino; and

R_5 is chosen from hydrogen, hydroxy, lower alkyl, sulfonyl, optionally substituted amino, lower alkoxy, lower alkyl substituted with one or more halo, lower alkoxy substituted with one or more halo, lower alkyl substituted with hydroxy, optionally substituted heterocycloalkyl, and optionally substituted heteroaryl.

51. At least one chemical entity of claim 33 comprising a compound of Formula 9:



(Formula 9)

and wherein

X is chosen from N and CH;

U is chosen from N and CR_{41};

R_{41} is chosen from hydrogen, halo, optionally substituted lower alkyl, optionally substituted lower alkoxy, hydroxy, nitro, cyano, sulfhydryl, sulfanyl, sulfinyl, sulfonyl, carboxy, aminocarbonyl, and optionally substituted amino;

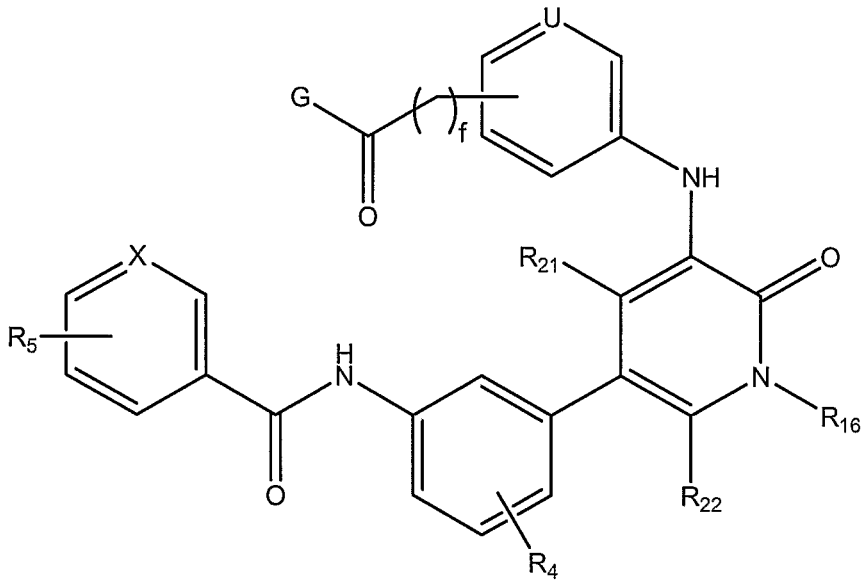
R_5 is chosen from hydrogen, halo, hydroxy, lower alkyl, sulfanyl, sulfonyl, optionally substituted amino, lower alkoxy, cycloalkyl, optionally substituted heterocycloalkyl, lower alkyl substituted with hydroxy, lower alkyl substituted with one or more halo, lower alkoxy substituted with one or more halo, lower alkyl substituted with hydroxy, and optionally substituted heteroaryl.

52. At least one chemical entity of any one of claims 29 to 51 wherein L is chosen from optionally substituted C_0-C_4alkylene, -O-optionally substituted C_0-C_4alkylene, -(C_0-C_4alkylene)(SO_2)-; and -(C_0-C_4alkylene)(C=O)-.

53. At least one chemical entity of claim 52 wherein L is chosen from a covalent bond, -(C=O)-, -CH_2-, -CH_2(C=O)-, -SO_2-, and -$CH(CH_3)$(C=O)-.

54. At least one chemical entity of claim 53 wherein L is chosen from -(C=O)-, -CH_2-, -CH_2(C=O)-, -SO_2- and -CH(CH_3)(C=O)-.

55. At least one chemical entity of claim 50 comprising a compound of Formula 10:

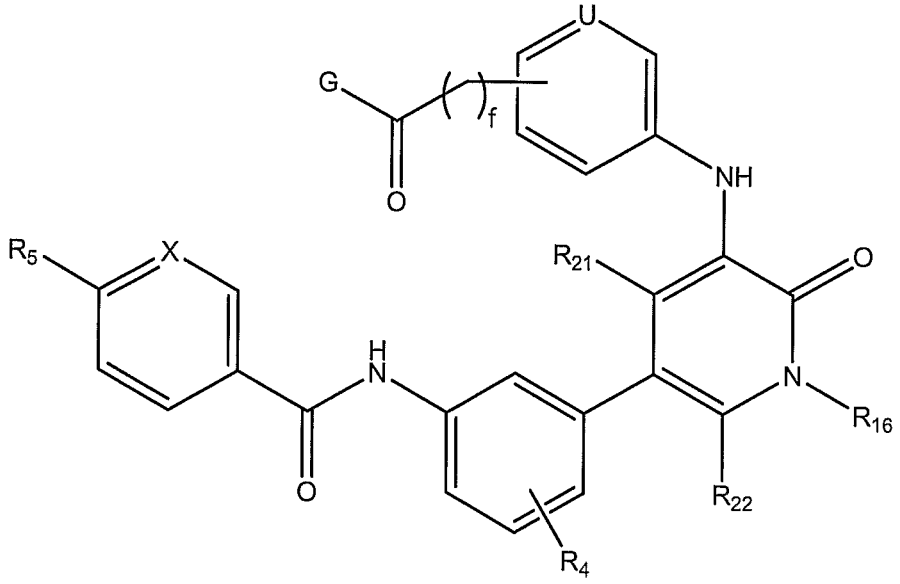


(Formula 10)

wherein

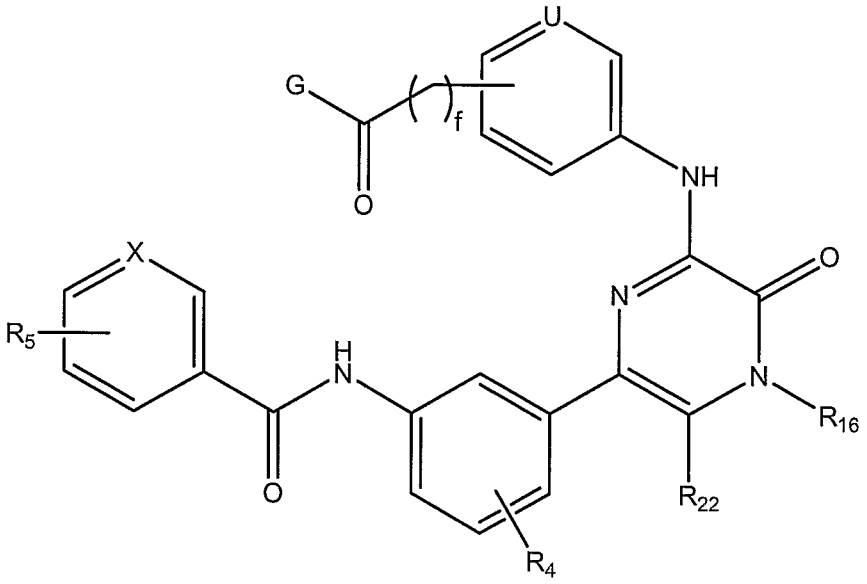
f is chosen from 0, 1 and 2.

56. At least one chemical entity of claim 55 comprising a compound of Formula 11:



(Formula 11).

57. At least one chemical entity of claim 51 comprising a compound of Formula 12:

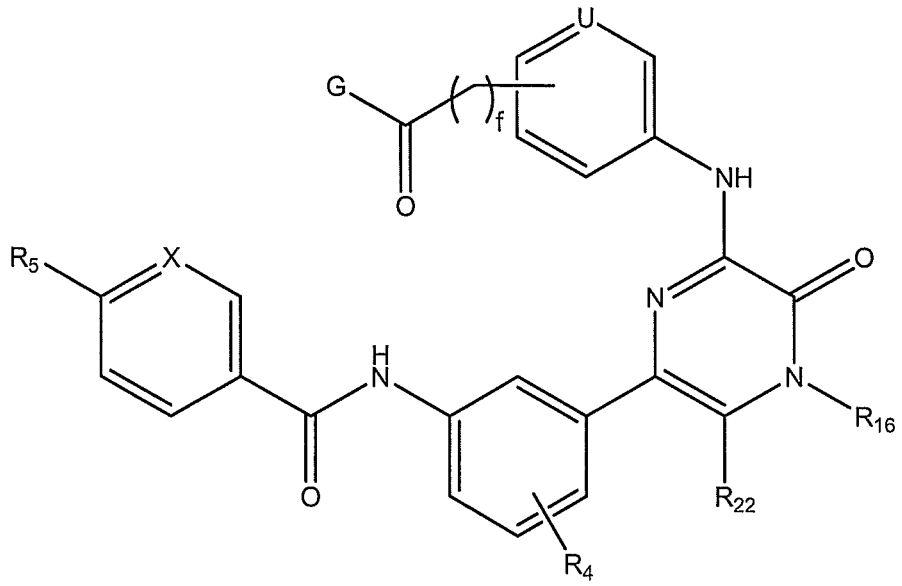


(Formula 12)

wherein

f is chosen from 0, 1 and 2.

58. At least one chemical entity of claim 57 comprising a compound of Formula 13:



(Formula 13).

59. At least one chemical entity of any one of claims 54 to 58 wherein the group G-C(O)-$(CH_2)_f$- is attached to the 3 position of the ring.

60. At least one chemical entity of any one of claims 54 to 58 wherein the group G-C(O)-$(CH_2)_f$- is attached to the 4 position of the ring.

61. At least one chemical entity of any one of claims 29 to 60 wherein G is chosen from

hydrogen,

hydroxy,

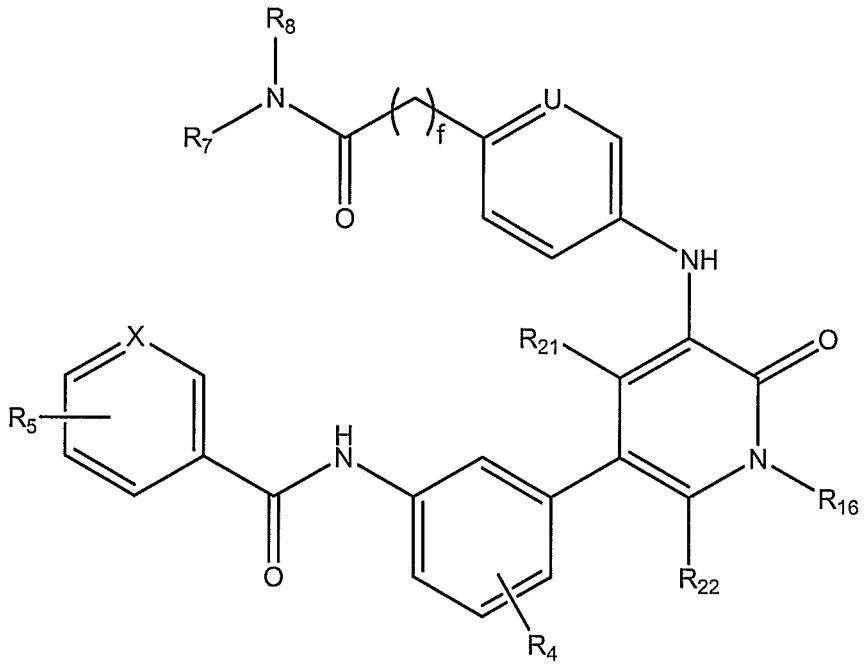
-NR_7R_8 wherein R_7 and R_8 are independently chosen from hydrogen, optionally substituted acyl, and optionally substituted (C_1-C_6)alkyl; or wherein R_7 and R_8, together with the nitrogen to which they are bound, form an optionally substituted 5- to 7-membered nitrogen containing heterocycloalkyl which optionally further includes one or two

additional heteroatoms chosen from N, O, and S;
optionally substituted 5,6-dihydro-8H-imidazo[1,2-a]pyrazin-7-yl,
lower alkoxy, and
1H-tetrazol-5-yl.

62. At least one chemical entity of claim 61 wherein G is chosen from
hydrogen,
hydroxy,
N-methylethanolamino,
optionally substituted morpholin-4-yl,
optionally substituted piperazin-1-yl, and
optionally substituted homopiperazin-1-yl.

63. At least one chemical entity of claim 62 wherein G is chosen from
hydrogen,
morpholin-4-yl,
4-acyl-piperazin-1-yl,
4-lower alkyl-piperazin-1-yl,
3-oxo-piperazin-1-yl,
homopiperazin-1-yl, and
4-lower alkyl-homopiperazin-1-yl.

64. At least one chemical entity of claim 55 comprising a compound of Formula 14:

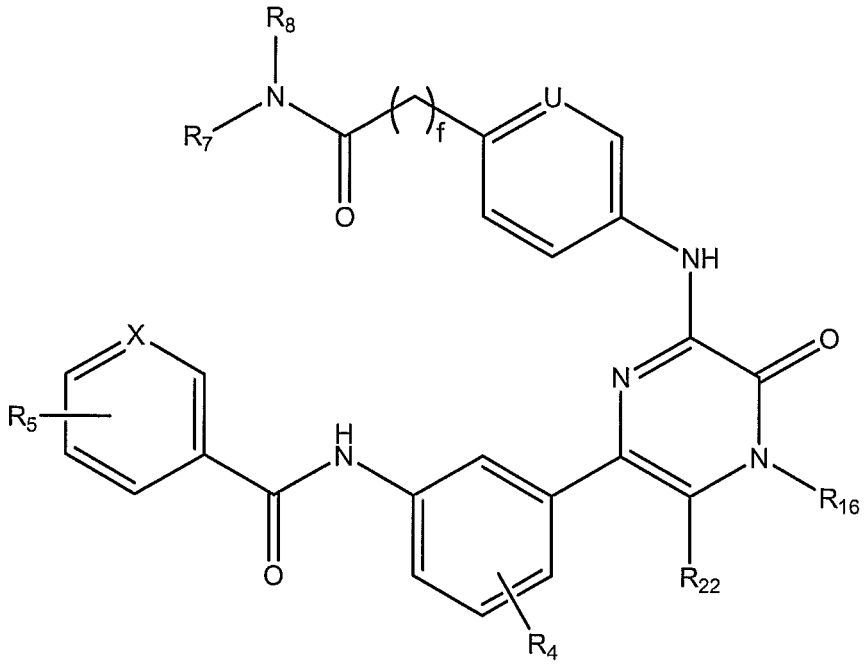


(Formula 14)

wherein

R_7 and R_8 are independently chosen from hydrogen and optionally substituted (C_1-C_6)alkyl; or R_7 and R_8, together with the nitrogen to which they are bound, form an optionally substituted 5- to 7-membered nitrogen-containing heterocycloalkyl which optionally further includes one or two additional heteroatoms chosen from N, O, and S.

65. At least one chemical entity of claim 57 comprising a compound of Formula 15:



(Formula 15)

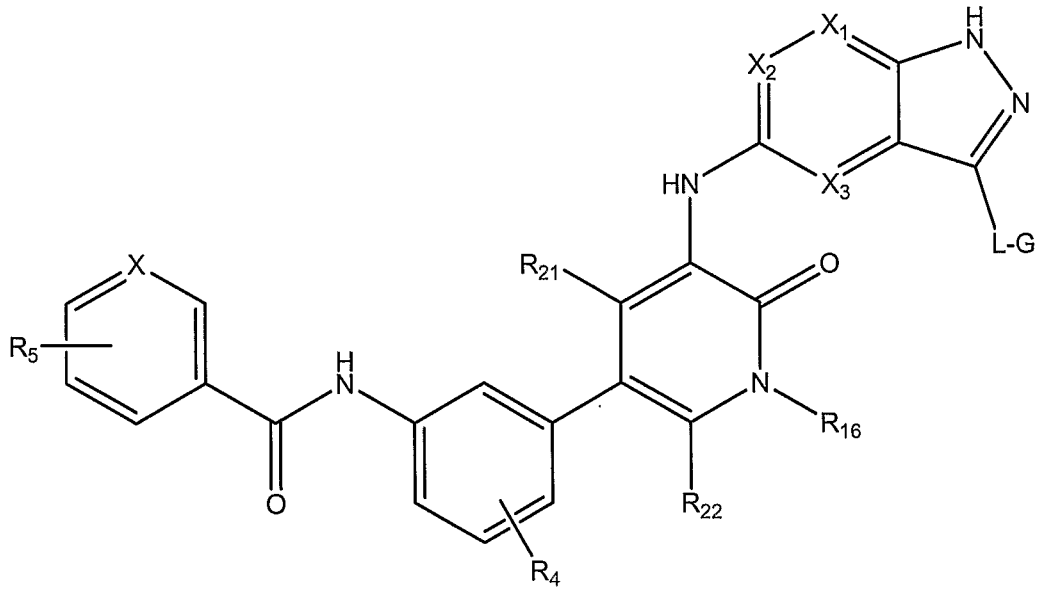
wherein

R_7 and R_8 are independently chosen from hydrogen and optionally substituted (C_1-C_6)alkyl; or R_7 and R_8, together with the nitrogen to which they are bound, form an optionally substituted 5- to 7-membered nitrogen containing heterocycloalkyl which optionally further includes one or two additional heteroatoms chosen from N, O, and S.

66. At least one chemical entity of claim 64 or 65 wherein R_7 and R_8, together with the nitrogen to which they are bound, form a 5- to 7-membered nitrogen-containing heterocycloalkyl chosen from optionally substituted morpholin-4-yl and optionally substituted piperazin-1-yl ring.

67. At least one chemical entity of claim 66 wherein R_7 and R_8, together with the nitrogen to which they are bound, form a 5- to 7-membered nitrogen-containing heterocycloalkyl chosen from morpholin-4-yl, 4-acyl-piperazin-1-yl, and 4-lower alkyl-piperazin-1-yl.

68. At least one chemical entity of claim 29 comprising a compound of Formula 16:



(Formula 16)

wherein

X is chosen from N and CH;

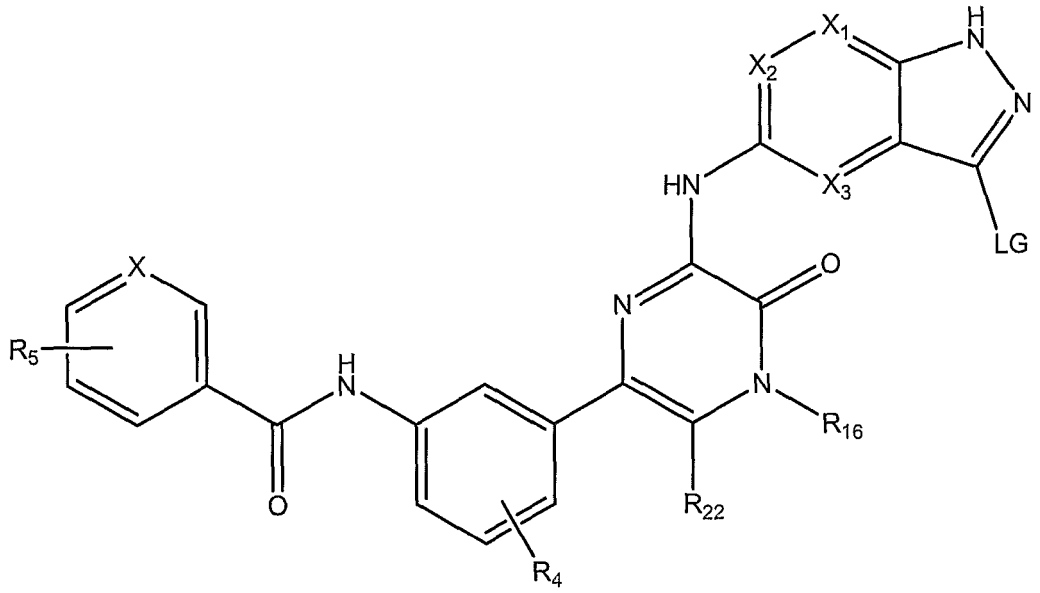
R_5 is chosen from hydrogen, hydroxy, lower alkyl, sulfonyl, optionally substituted amino, lower alkoxy, lower alkyl substituted with one or more halo, lower alkoxy substituted with one or more halo, lower alkyl substituted with hydroxy, optionally substituted heterocycloalkyl, and optionally substituted heteroaryl;

R_4 is chosen from hydrogen, optionally substituted lower alkyl, optionally substituted lower alkoxy, halo, and hydroxy;

R_{16} is chosen from hydrogen, cyano, optionally substituted cycloalkyl, and optionally substituted lower alkyl; and

R_{22} is chosen from hydrogen and optionally substituted lower alkyl.

69. At least one chemical entity of claim 29 comprising a compound of Formula 17:



(Formula 17)

wherein

X is chosen from N and CH;

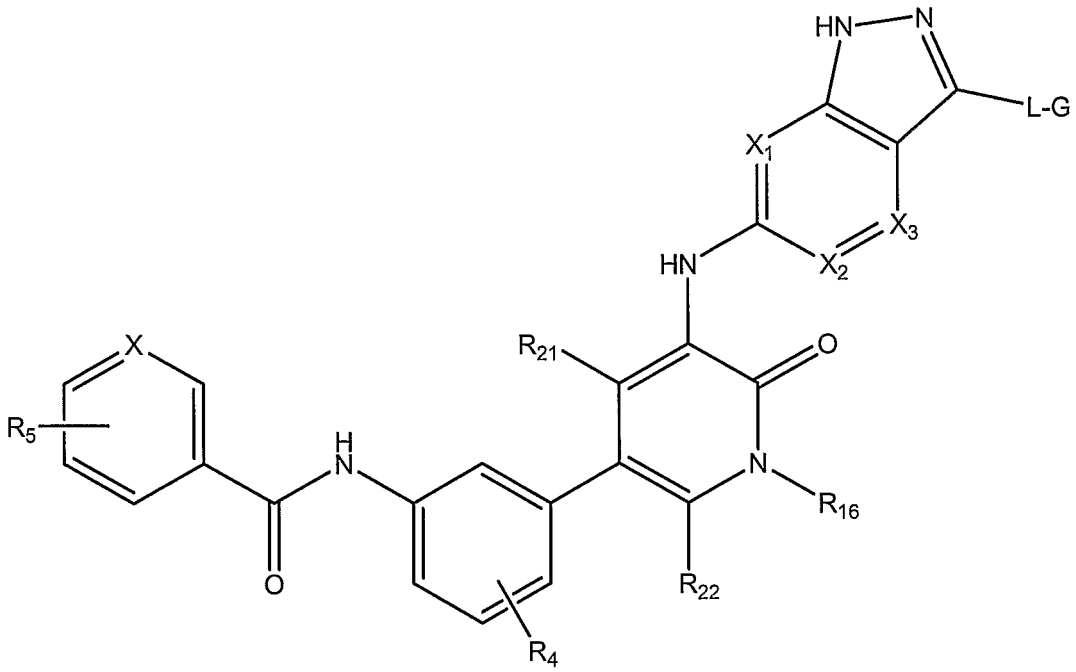
R_5 is chosen from hydrogen, hydroxy, lower alkyl, sulfonyl, optionally substituted amino, lower alkoxy, lower alkyl substituted with one or more halo, lower alkoxy substituted with one or more halo, lower alkyl substituted with hydroxy, optionally substituted heterocycloalkyl, and optionally substituted heteroaryl;

R_4 is chosen from hydrogen, optionally substituted lower alkyl, optionally substituted lower alkoxy, halo, and hydroxy;

R_{16} is chosen from hydrogen, cyano, optionally substituted cycloalkyl, and optionally substituted lower alkyl; and

R_{22} is chosen from hydrogen and optionally substituted lower alkyl.

70. At least one chemical entity of claim 29 comprising a compound of Formula 18:



(Formula 18)

wherein

X is chosen from N and CH;

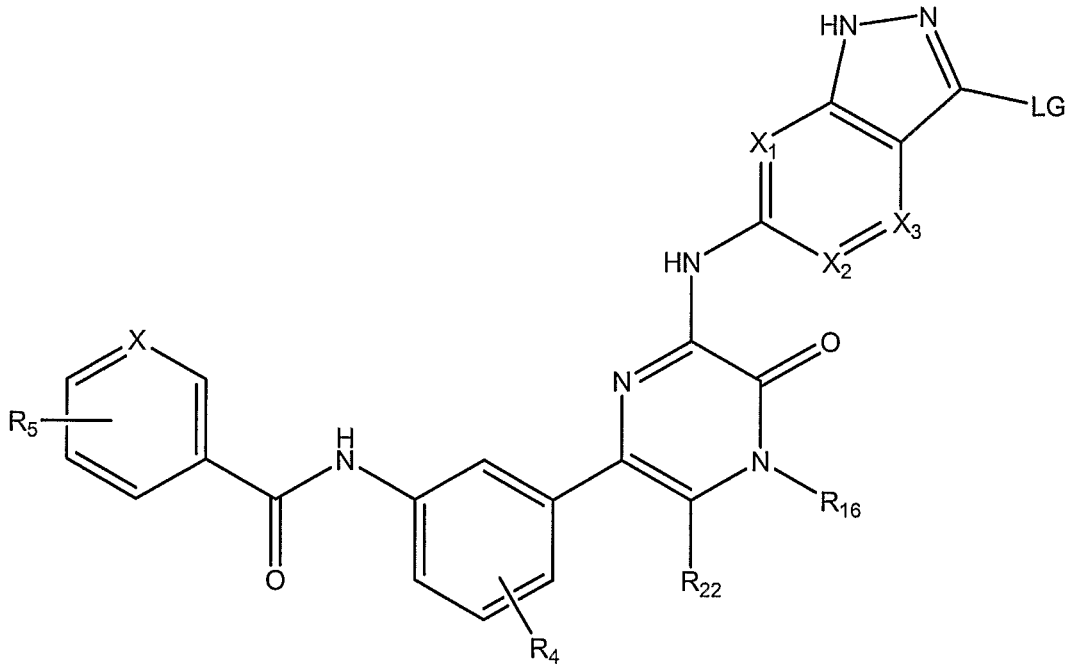
R_5 is chosen from hydrogen, hydroxy, lower alkyl, sulfonyl, optionally substituted amino, lower alkoxy, lower alkyl substituted with one or more halo, lower alkoxy substituted with one or more halo, lower alkyl substituted with hydroxy, optionally substituted heterocycloalkyl, and optionally substituted heteroaryl;

R_4 is chosen from hydrogen, optionally substituted lower alkyl, optionally substituted lower alkoxy, halo, and hydroxy;

R_{16} is chosen from hydrogen, cyano, optionally substituted cycloalkyl, and optionally substituted lower alkyl; and

R_{22} is chosen from hydrogen and optionally substituted lower alkyl.

71. At least one chemical entity of claim 29 comprising a compound of Formula 19:



(Formula 19)

wherein

X is chosen from N and CH;

R_5 is chosen from hydrogen, hydroxy, lower alkyl, sulfonyl, optionally substituted amino, lower alkoxy, lower alkyl substituted with one or more halo, lower alkoxy substituted with one or more halo, lower alkyl substituted with hydroxy, optionally substituted heterocycloalkyl, and optionally substituted heteroaryl;

R_4 is chosen from hydrogen, optionally substituted lower alkyl, optionally substituted lower alkoxy, halo, and hydroxy;

R_{16} is chosen from hydrogen, cyano, optionally substituted cycloalkyl, and optionally substituted lower alkyl; and

R_{22} is chosen from hydrogen and optionally substituted lower alkyl.

72. At least one chemical entity of any one of claims 68 to 71 wherein L is a covalent bond and G is hydrogen.

73. At least one chemical entity of any one of claims 55 to 72 wherein f is 0.

74. At least one chemical entity of any one of claims 50 to 67 wherein U is CR_{41}.

75. At least one chemical entity of any one of claims 50 to 74 wherein R_5 is chosen from hydrogen, optionally substituted piperidinyl, and lower alkyl.

76. At least one chemical entity of claim 75 wherein R_5 is chosen from hydrogen, optionally substituted piperidinyl, *iso*-propyl, and *tert*-butyl.

77. At least one chemical entity of claim 75 wherein R_5 is *tert*-butyl.

78. At least one chemical entity of any one of claims 30 to 77 wherein R_{22} is chosen from hydrogen and methyl.

79. At least one chemical entity of claim 78 wherein R_{22} is hydrogen.

80. At least one chemical entity of any one of claims 10 to 79, wherein the at least one chemical entity exhibits an IC_{50} of 10 micromolar or less in an in vitro biochemical assay of Btk activity.

81. At least one chemical entity of claim 80, wherein the at least one chemical entity exhibits an IC_{50} of 1 micromolar or less in an in vitro biochemical assay of Btk activity.

82. At least one chemical entity of claim 81, wherein the at least one chemical entity exhibits an IC_{50} of 0.1 micromolar or less in an in vitro biochemical assay of Btk activity.

83. At least one chemical entity of any one of claims 10 to 82 wherein the at least one chemical entity exhibits an IC_{50} of 10 micromolar or less in an assay for inhibition of B-cell activity.

84. At least one chemical entity of claim 83 wherein the at least one chemical entity exhibits an IC_{50} of 1 micromolar or less in an assay for inhibition of B-cell activity.

85. At least one chemical entity of claim 84 wherein the at least one chemical entity exhibits an IC_{50} of 500 nanomolar or less in an assay for inhibition of B-cell activity.

86. At least one chemical entity of any one of claims 10 to 85 wherein the at least one chemical entity exhibits an IC_{50} value in an assay for inhibition of T-cell proliferation that is at least 3-fold greater than an IC_{50} value exhibited by the at least one chemical entity exhibits in an assay for inhibition of B-cell proliferation.

87. At least one chemical entity of claim 86, wherein the at least one chemical entity exhibits an IC_{50} value in an assay for inhibition of T-cell proliferation that is at least 5-fold greater than an IC_{50} value that the at least one chemical entity exhibits in an assay for inhibition of B-cell proliferation.

88. At least one chemical entity of claim 87, wherein the at least one chemical entity exhibits an IC_{50} value in an assay for inhibition of T-cell proliferation that is at least 10-fold greater than an IC_{50} value that the at least one chemical entity exhibits in an assay for inhibition of B-cell proliferation.

89. At least one chemical entity of any one of claims 10 to 88 wherein the at least one chemical entity exhibits an IC_{50} of 10 micromolar or less in a B-ALL cell survival assay.

90. At least one chemical entity of claim 10 wherein the compound of Formula 1 is chosen from

4-tert-Butyl-N-(2-methyl-3-{1-methyl-5-[4-(morpholine-4-carbonyl)-phenylamino]-6-oxo-1,6-dihydro-pyridin-3-yl}-phenyl)-benzamide;

4-{5-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-1-methyl-2-oxo-1,2-dihydro-pyridin-3-ylamino}-benzoic acid;

4-tert-Butyl-N-(2-methyl-3-{1-methyl-5-[4-(4-methyl-piperazine-1-carbonyl)-phenylamino]-6-oxo-1,6-dihydro-pyridin-3-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(2-methyl-3-{1-methyl-5-[4-(N-methylethanolamine-2-carbonyl)-phenylamino]-6-oxo-1,6-dihydro-pyrazin-3-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(2-methyl-3-{1-methyl-5-[4-([1,4]oxazepane-4-carbonyl)-phenylamino]-6-oxo-1,6-dihydro-pyridin-3-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(3-{5-[4-(4-hydroxy-piperidine-1-carbonyl)-phenylamino]-1-methyl-6-oxo-1,6-dihydro-pyridin-3-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-(2-methyl-3-{1-methyl-5-[4-(morpholine-4-carbonyl)-phenylamino]-6-oxo-1,6-dihydro-pyridin-3-yl}-phenyl)-benzamide;

4-{5-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-1-methyl-2-oxo-1,2-dihydro-pyridin-3-ylamino}-benzoic acid;

4-tert-Butyl-N-(2-methyl-3-{1-methyl-5-[4-(4-methyl-piperazine-1-carbonyl)-phenylamino]-6-oxo-1,6-dihydro-pyridin-3-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(2-methyl-3-{1-methyl-5-[4-(N-methylethanolamine-2-carbonyl)-phenylamino]-6-oxo-1,6-dihydro-pyrazin-3-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(2-methyl-3-{1-methyl-5-[4-([1,4]oxazepane-4-carbonyl)-phenylamino]-6-oxo-1,6-dihydro-pyridin-3-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(3-{5-[4-(4-hydroxy-piperidine-1-carbonyl)-phenylamino]-1-methyl-6-oxo-1,6-dihydro-pyridin-3-yl}-2-methyl-phenyl)-benzamide;

4-{6-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-benzoic acid;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-{6-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-benzoic acid ethyl ester;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[4-(4-methyl-piperazine-1-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[4-(4-methyl-[1,4]diazepane-1-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(3-{4-methyl-6-[4-(2-hydroxyethyl-methyl-carbamoyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-{6-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-benzamide;

4-{6-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-4-ethyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-benzoic acid;

4-tert-Butyl-N-(3-{4-ethyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-(3-{4-ethyl-6-[4-(4-methyl-piperazine-1-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-(2-methyl-3-{4-ethyl-6-[4-(N-methylethanolamine-2-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(3-{4-ethyl-6-[4-(methyl-carbamoyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-{3-[6-(4-fluoro-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide;

4-{6-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-4,5-dimethyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-benzoic acid;

4-{6-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-2-fluoro-benzoic acid;

4-tert-Butyl-N-(3-{3,4-dimethyl-6-[4-(methyl-carbamoyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-(3-{3,4-dimethyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-(3-{3,4-dimethyl-6-[4-(4-methyl-piperazine-1-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-(3-{3,4-dimethyl-6-[4-(2-hydroxyethyl-methyl-carbamoyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-{3-[6-(1H-indazol-6-ylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide;

4-tert-Butyl-N-{3-[6-(1H-indazol-5-ylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide;

4-tert-Butyl-N-(2-fluoro-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(2-fluoro-3-{4-methyl-6-[4-(4-methyl-piperazine-1-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(3-{6-[3-fluoro-4-(morpholine-4-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-(2-fluoro-3-{6-[4-(1H-imidazol-2-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-{3-[6-(4-methanesulfonylaminocarbonyl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide;

4-tert-Butyl-N-(3-{4-methyl-6-[4-(3-aminopropyl-carbamoyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-(3-{6-[4-(1H-imidazol-2-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-5-oxo-6-[4-(thiomorpholine-4-carbonyl)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-5-oxo-6-[4-(1-oxo-114-thiomorpholine-4-carbonyl)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(3-{6-[4-(1,1-dioxo-116-thiomorpholine-4-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-{2-methyl-3-[4-methyl-5-oxo-6-(4-sulfamoyl-phenylamino)-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide;

4-tert-Butyl-N-{2-fluoro-3-[4-methyl-5-oxo-6-(4-sulfamoyl-phenylamino)-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide;

4-tert-Butyl-N-(2-fluoro-3-{4-methyl-5-oxo-6-[4-(1H-tetrazol-5-yl)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-{6-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-benzoic acid;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-{6-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-benzoic acid ethyl ester;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[4-(4-methyl-piperazine-1-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[4-(4-methyl-[1,4]diazepane-1-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(3-{4-methyl-6-[4-(2-hydroxyethyl-methyl-carbamoyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-{6-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-benzamide;

4-{6-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-4-ethyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-benzoic acid;

4-tert-Butyl-N-(3-{4-ethyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-(3-{4-ethyl-6-[4-(4-methyl-piperazine-1-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-(2-methyl-3-{4-ethyl-6-[4-(N-methylethanolamine-2-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(3-{4-ethyl-6-[4-(methyl-carbamoyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-{3-[6-(4-fluoro-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide;

4-{6-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-4,5-dimethyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-benzoic acid;

4-{6-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-2-fluoro-benzoic acid;

4-tert-Butyl-N-(3-{3,4-dimethyl-6-[4-(methyl-carbamoyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-(3-{3,4-dimethyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-(3-{3,4-dimethyl-6-[4-(4-methyl-piperazine-1-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-(3-{3,4-dimethyl-6-[4-(2-hydroxyethyl-methyl-carbamoyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-{3-[6-(1H-indazol-6-ylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide;

4-tert-Butyl-N-{3-[6-(1H-indazol-5-ylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide;

4-tert-Butyl-N-(2-fluoro-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(2-fluoro-3-{4-methyl-6-[4-(4-methyl-piperazine-1-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(3-{6-[3-fluoro-4-(morpholine-4-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-(2-fluoro-3-{6-[4-(1H-imidazol-2-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(5-{6-[4-(1H-imidazol-2-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-{3-[6-(4-methanesulfonylaminocarbonyl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide;

4-tert-Butyl-N-(3-{4-methyl-6-[4-(3-aminopropyl-carbamoyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-(3-{6-[4-(1H-imidazol-2-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-5-oxo-6-[4-(thiomorpholine-4-carbonyl)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-5-oxo-6-[4-(1-oxo-1λ^4-thiomorpholine-4-carbonyl)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(3-{6-[4-(1,1-dioxo-1λ6-thiomorpholine-4-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-{2-methyl-3-[4-methyl-5-oxo-6-(4-sulfamoyl-phenylamino)-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide;

4-tert-Butyl-N-{2-fluoro-3-[4-methyl-5-oxo-6-(4-sulfamoyl-phenylamino)-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide;

4-tert-Butyl-N-{2-methyl-5-[4-methyl-5-oxo-6-(4-sulfamoyl-phenylamino)-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide;

4-tert-Butyl-N-(2-fluoro-3-{4-methyl-5-oxo-6-[4-(1H-tetrazol-5-yl)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-{6-[3-(4-tert-Butyl-benzoylamino)-phenyl]-4,5-dimethyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-benzoic acid;

3-{6-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-benzoic acid;

4-tert-Butyl-N-(3-{3,4-dimethyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[3-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(2-fluoro-3-{4-methyl-6-[4-(N,N-bis-(2-hydroxyethyl)aminocarbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[4-(N,N-bis-(2-hydroxyethyl)aminocarbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-5-oxo-6-[4-(1H-tetrazol-5-yl)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-{6-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-benzenesulfinic acid morpholin-4-yl ester;

N-{3-[6-(1H-Benzoimidazol-5-ylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-4-tert-butyl-benzamide;

4-tert-Butyl-N-{2-methyl-3-[4-methyl-6-(4-morpholin-4-ylmethyl-phenylamino)-5-oxo-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide;

4-tert-Butyl-N-(2-cyano-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-{3-[6-(6-hydroxy-pyridin-3-ylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide;

4-tert-Butyl-N-(3-{6-[4-(4-ethyl-piperazine-1-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-5-oxo-6-[4-(3-oxo-piperazine-1-carbonyl)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[4-(N-methyl –N-(cyanomethyl)amino carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(6-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-pyridin-2-yl)-benzamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[4-(N-(2-methoxyethyl)amino carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[4-(N-(2-dimethylaminoethyl)amino carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-{2-fluoro-3-[4-methyl-6-(4-morpholin-4-ylmethyl-phenylamino)-5-oxo-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide;

4-tert-Butyl-N-{2-methyl-3-[4-methyl-6-(4-oxazol-2-yl-phenylamino)-5-oxo-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide;

4-tert-Butyl-N-{2-fluoro-3-[4-methyl-6-(4-oxazol-2-yl-phenylamino)-5-oxo-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide;

4-tert-Butyl-N-{3-[6-(4-imidazol-1-yl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide;

4-tert-Butyl-N-{2-fluoro-3-[6-(4-imidazol-1-yl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide;

4-tert-Butyl-N-(2-fluoro-3-{4-methyl-6-[4-(N,N-bis-(2-methoxyethyl)aminocarbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

N-(3-{6-[4-(4-Acetyl-piperazine-1-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide;

N-(3-{6-[4-(4-Acetyl-piperazine-1-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-fluoro-phenyl)-4-tert-butyl-benzamide;

4-tert-Butyl-N-(2-fluoro-3-{4-methyl-5-oxo-6-[4-(thiomorpholine-4-carbonyl)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(2-fluoro-3-{6-[4-(4-hydroxy-piperidine-1-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-Bromo-N-(2-fluoro-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(2-fluoro-3-{4-methyl-5-oxo-6-[4-(1-oxo-1λ^4-thiomorpholine-4-carbonyl)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-(1-Hydroxy-1-methyl-ethyl)-N-(2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-{2-methyl-3-[4-methyl-5-oxo-6-(4-thiomorpholin-4-yl-phenylamino)-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide;

4-tert-Butyl-N-{3-[6-(4-imidazol-1-ylmethyl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide;

4-Bromo-N-(2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(2-fluoro-3-{4-methyl-6-[4-([1,4]oxazepane-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-{6-[3-(4-tert-Butyl-benzoylamino)-2-fluoro-phenyl]-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-benzoic acid;

4-tert-Butyl-N-(2-fluoro-3-{4-methyl-5-oxo-6-[4-(4-oxo-piperidine-1-carbonyl)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(2-fluoro-3-{6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(2-fluoro-3-{6-[4-(4-hydroxymethyl-piperidine-1-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(2-fluoro-3-{6-[4-(2-hydroxymethyl-morpholine-4-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-5-oxo-6-[4-(1-oxo-1λ^4-thiomorpholin-4-yl)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(2-fluoro-3-{4-methyl-6-[4-(N-(2,2-Dimethyl-[1,3]dioxolan-4-ylmethyl)aminocarbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

5-tert-Butyl-thiophene-2-carboxylic acid (2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-amide;

4-tert-Butyl-N-{2-fluoro-3-[4-methyl-6-(4-morpholin-4-yl-phenylamino)-5-oxo-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide;

4-tert-Butyl-N-(2-fluoro-3-{4-methyl-6-[4-(N-(2-(2-hydroxy-ethoxy)-ethyl)aminocarbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-{2-fluoro-3-[6-(4-imidazol-1-ylmethyl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide;

4-tert-Butyl-N-(3-{6-[4-(4-hydroxy-piperidine-1-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[4-([1,4]oxazepane-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(2-fluoro-3-{4-methyl-6-[4-(N-(2,3-dihydroxy-propyl)aminocarbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-{2-fluoro-3-[4-methyl-5-oxo-6-(4-thiomorpholin-4-ylmethyl-phenylamino)-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide;

4-tert-Butyl-N-(3-{6-[4-(4-hydroxymethyl-piperidine-1-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-(3-{6-[4-(2-hydroxymethyl-morpholine-4-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-(3-{6-[4-(1,1-dioxo-1λ6-thiomorpholin-4-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-{2-fluoro-3-[4-methyl-5-oxo-6-(4-thiomorpholin-4-yl-phenylamino)-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide;

4-tert-Butyl-cyclohexanecarboxylic acid (2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-amide;

4-tert-Butyl-N-(3-{4-ethyl-5-oxo-6-[4-(1-oxo-1λ^4-thiomorpholin-4-yl)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-Dimethylamino-N-(2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(2-fluoro-3-{4-methyl-5-oxo-6-[4-(1-oxo-1λ^4-thiomorpholin-4-yl)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-5-oxo-6-[4-(4-oxo-4H-pyridin-1-yl)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-Isopropyl-N-(2-methyl-3-{4-methyl-5-oxo-6-[4-(1-oxo-1λ^4-thiomorpholin-4-yl)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-(1-Hydroxy-1-methyl-ethyl)-N-(2-methyl-3-{4-methyl-5-oxo-6-[4-(1-oxo-1λ^4-thiomorpholin-4-yl)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-{2-fluoro-3-[4-methyl-5-oxo-6-(4-pyrrolidin-1-ylmethyl-phenylamino)-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide;

4-tert-Butyl-N-(3-{6-[4-(2-hydroxymethyl-morpholin-4-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-(2-fluoro-3-{4-methyl-5-oxo-6-[4-(1-oxo-1λ^4-thiomorpholin-4-ylmethyl)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(3-{6-[4-(1,1-dioxo-1λ6-thiomorpholin-4-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-(2-fluoro-3-{4-methyl-6-[4-N-(2-Methoxy-ethyl)-N-methylaminocarbonyl-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(2-fluoro-3-{6-[4-(4-methyl-piperazine-1-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(2-fluoro-3-{6-[4-(4-hydroxy-piperidine-1-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

6-tert-Butyl-N-(2-methyl-3-{4-methyl-5-oxo-6-[4-(1-oxo-1λ^4-thiomorpholin-4-yl)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-nicotinamide;

4-{6-[3-(4-tert-Butyl-benzoylamino)-2,4-difluoro-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-benzoic acid;

4-tert-Butyl-N-(2-fluoro-3-{6-[4-(4-methoxy-piperidin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[4-(N-methyl-N-ethylaminocarbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-5-oxo-6-[4-(pyrrolidine-1-carbonyl)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

N-(2-Methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-3-phenyl-acrylamide;

N-(2-Fluoro-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-3-(3-fluoro-phenyl)-acrylamide;

Benzo[b]thiophene-2-carboxylic acid (2-fluoro-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-amide;

Benzo[b]thiophene-2-carboxylic acid (2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-amide;

5-Bromo-thiophene-2-carboxylic acid (2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-amide;

5-Bromo-thiophene-2-carboxylic acid (2-fluoro-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-amide;

N-(2-Fluoro-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-4-methylsulfanyl-benzamide;

N-(2-Methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-4-methylsulfanyl-benzamide;

4-Ethylsulfanyl-N-(2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

Benzofuran-2-carboxylic acid (2-fluoro-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-amide;

4,5-Dibromo-thiophene-2-carboxylic acid (2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-amide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-5-oxo-6-[6-(1-oxo-1λ^4-thiomorpholin-4-yl)-pyridin-3-ylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(2,6-difluoro-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-Cyclopropyl-N-(2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(2-fluoro-3-{4-methyl-5-oxo-6-[4-(1-oxo-1λ^4-thiomorpholin-4-yl)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-{3-[6-(3-fluoro-4-thiomorpholin-4-yl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide;

4-tert-Butyl-N-(3-{6-[3-fluoro-4-(1-oxo-1λ^4-thiomorpholin-4-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

6-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-nicotinamide;

4-tert-Butyl-N-(3-{6-[4-(4-methoxy-piperidin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-(3-{6-[4-(4-methanesulfonyl-piperazin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-(2-fluoro-3-{6-[4-(4-methanesulfonyl-piperazin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-cyclohexanecarboxylic acid (2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-amide;

4-tert-Butyl-N-{2-methyl-3-[4-methyl-6-(4-morpholin-4-yl-phenylamino)-5-oxo-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide;

4-tert-Butyl-N-(3-{6-[4-(ethyl-methyl-amino)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-(3-{6-[4-(ethyl-methyl-amino)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-fluoro-phenyl)-benzamide;

4-tert-Butyl-N-{2-methyl-3-[4-methyl-6-(2-morpholin-4-yl-pyridin-4-ylamino)-5-oxo-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide;

Benzo[b]thiophene-2-carboxylic acid (2-methyl-3-{4-methyl-5-oxo-6-[4-(1-oxo-1λ^4-thiomorpholin-4-yl)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-amide;

N-(3-{6-[4-(4-Acetyl-piperazin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-fluoro-phenyl)-4-tert-butyl-benzamide;

N-(3-{6-[4-(4-Acetyl-piperazin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide;

4-tert-Butyl-N-{3-[6-(4-hydroxymethyl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide;

4-tert-Butyl-N-(3-{6-[4-(4-hydroxy-piperidin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-{2-methyl-3-[4-methyl-5-oxo-6-(4-piperidin-1-yl-phenylamino)-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide;

4-tert-Butyl-N-{2-methyl-3-[4-methyl-5-oxo-6-(4-pyridin-4-yl-phenylamino)-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide;

4-tert-Butyl-N-{2-fluoro-3-[4-methyl-6-(4-methylaminomethyl-phenylamino)-5-oxo-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide;

4-tert-Butyl-N-(3-{6-[4-(3-ethyl-1-methyl-ureidomethyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-fluoro-phenyl)-benzamide;

4-tert-Butyl-N-{3-[6-(3-hydroxymethyl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide;

4-tert-Butyl-N-(3-{6-[4-(3-hydroxy-pyrrolidin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-{2-methyl-3-[4-methyl-5-oxo-6-(4-pyridin-3-yl-phenylamino)-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide;

4-tert-Butyl-N-[2-fluoro-3-(6-{4-[(methanesulfonyl-methyl-amino)-methyl]-phenylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-phenyl]-benzamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-5-oxo-6-[4-(1-oxy-pyridin-3-yl)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

1-(4-{6-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-phenyl)-piperidine-4-carboxylic acid amide;

4-tert-Butyl-N-(2-fluoro-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-N-methyl-benzamide;

N-(3-{6-[4-(4-Acetyl-[1,4]diazepan-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide;

4-tert-Butyl-N-(3-{6-[4-(4-methanesulfonyl-[1,4]diazepan-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-(2-ethyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

1-(4-{6-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-phenyl)-piperidine-3-carboxylic acid amide;

1-(4-{6-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-phenyl)-pyrrolidine-2-carboxylic acid amide;

4-tert-Butyl-N-{2-methyl-3-[4-methyl-5-oxo-6-(pyridin-4-ylamino)-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide;

4-tert-Butyl-N-(3-{6-[4-(1,1-dioxo-1λ6-thiomorpholin-4-yl)-phenylamino]-4-ethyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-{2-methyl-3-[4-methyl-5-oxo-6-(1-oxy-pyridin-3-ylamino)-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide;

4-tert-Butyl-N-{2-methyl-3-[4-methyl-5-oxo-6-(1-oxy-pyridin-4-ylamino)-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide

4-tert-Butyl-N-(3-{6-[4-(1,4-dioxa-8-aza-spiro[4.5]dec-8-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-{3-[6-(4-carbamimidoylmethyl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide;

4-tert-Butyl-N-(3-{4-cyclopropyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-{3-[6-(3-dimethylaminomethyl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[4-(N-(pyridin-4-ylmethyl)aminocarbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[4-(N-(pyridin-3-ylmethyl)aminocarbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

6-tert-Butyl-N-(3-{6-[4-(1,1-dioxo-1λ6-thiomorpholin-4-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-nicotinamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-5-oxo-6-[4-(1-oxy-pyridin-4-yl)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-{3-[6-(1-ethyl-2-oxo-1,2-dihydro-pyridin-4-ylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide;

4-tert-Butyl-N-(3-{4-cyano-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[4-(N-(piperidin-4-yl)aminocarbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-{2-methyl-3-[4-methyl-6-(3-morpholin-4-ylmethyl-phenylamino)-5-oxo-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide;

5,6,7,8-Tetrahydro-naphthalene-2-carboxylic acid (2-methyl-3-{4-methyl-5-oxo-6-[4-(1-oxo-1λ4-thiomorpholin-4-yl)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-amide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[4-(N-(1-ethyl-piperidin-4-yl)aminocarbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-{3-[6-(4-hydroxy-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide;

4-tert-Butyl-N-{2-methyl-3-[4-methyl-6-(3-nitro-phenylamino)-5-oxo-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide;

4-tert-Butyl-N-{3-[6-(4-methanesulfonyl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide;

N-{3-[6-(3-Amino-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-4-tert-butyl-benzamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-5-oxo-6-[4-(piperidin-4-yloxy)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-{3-[6-(3-hydroxy-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[4-(N-(2-pyridin-4-yl-ethyl)aminocarbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[4-(2-methyl-thiazol-4-yl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[4-(2-morpholin-4-yl-ethoxy)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4,5,6,7-Tetrahydro-benzo[b]thiophene-2-carboxylic acid (2-methyl-3-{4-methyl-5-oxo-6-[4-(1-oxo-1λ4-thiomorpholin-4-yl)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-amide;

6-Methyl-4,5,6,7-tetrahydro-benzo[b]thiophene-2-carboxylic acid (2-methyl-3-{4-methyl-5-oxo-6-[4-(1-oxo-1λ4-thiomorpholin-4-yl)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-amide;

N-(2-Methyl-3-{4-methyl-5-oxo-6-[4-(1-oxo-1λ4-thiomorpholin-4-yl)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-4-piperidin-1-yl-benzamide;

6-tert-Butyl-N-{2-methyl-3-[4-methyl-6-(4-morpholin-4-ylmethyl-phenylamino)-5-oxo-4,5-dihydro-pyrazin-2-yl]-phenyl}-nicotinamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[4-(N-(3-amino-phenyl)aminocarbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

N-(3-{6-[4-(4-Amino-piperidine-1-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide;

4-tert-Butyl-N-(3-{6-[4-(1-ethyl-piperidin-4-yloxy)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

N-{3-[6-(Benzothiazol-6-ylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-4-tert-butyl-benzamide;

N-(3-{6-[4-(2-Amino-pyridin-4-ylmethoxy)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide;

4-tert-Butyl-N-[3-(6-{4-[4-(2-hydroxy-ethyl)-piperazine-1-carbonyl]-phenylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-benzamide;

4-tert-Butyl-N-{3-[6-(2,3-dihydro-benzo[1,4]dioxin-6-ylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide;

4,5,6,7-Tetrahydro-benzo[b]thiophene-2-carboxylic acid (2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-amide;

4,5,6,7-Tetrahydro-benzo[b]thiophene-2-carboxylic acid (2-fluoro-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-amide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[4-(2-morpholin-4-yl-acetyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

5-tert-Butyl-pyridine-2-carboxylic acid (2-methyl-3-{4-methyl-5-oxo-6-[4-(1-oxo-1λ4-thiomorpholin-4-yl)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-amide;

N-(2-Methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-4-piperidin-1-yl-benzamide;

N-(2-Fluoro-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-4-piperidin-1-yl-benzamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-5-oxo-6-[4-(pyridin-4-yloxy)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

6-tert-Butyl-N-(2-methyl-3-{4-methyl-5-oxo-6-[4-(pyridin-4-yloxy)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-nicotinamide;

4-tert-Butyl-N-[3-(6-{4-[4-(2-hydroxy-ethyl)-piperazin-1-yl]-phenylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-benzamide;

6-tert-Butyl-N-[3-(6-{4-[4-(2-hydroxy-ethyl)-piperazin-1-yl]-phenylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-nicotinamide;

N-{3-[6-(3-Amino-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-6-tert-butyl-nicotinamide;

3,4,5,6-Tetrahydro-2H-[1,2']bipyridinyl-5'-carboxylic acid (2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-amide;

N-{3-[6-(2-Amino-pyridin-4-ylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-4-tert-butyl-benzamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[4-(N,N-bis-(2-methoxy-ethyl)aminocarbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

5-tert-Butyl-pyridine-2-carboxylic acid (2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-amide;

5-tert-Butyl-pyridine-2-carboxylic acid (2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-amide;

4-Iodo-N-(2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

N-{3-[6-(3-Benzylamino-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-4-tert-butyl-benzamide;

6-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[4-(2-morpholin-4-yl-ethoxy)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-nicotinamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[4-(N-(tetrahydro-pyran-4-yl)aminocarbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-[2-methyl-3-(4-methyl-5-oxo-6-{4-[(tetrahydro-pyran-4-ylamino)-methyl]-phenylamino}-4,5-dihydro-pyrazin-2-yl)-phenyl]-benzamide;

N-(2-Methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-4-pyrrolidin-1-yl-benzamide;

Tetrahydro-furan-2-carboxylic acid (3-{6-[3-(4-tert-butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-phenyl)-amide;

4-tert-Butyl-N-(3-{6-[3-(cyclohexanecarbonyl-amino)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

N-{3-[6-(3-Amino-4-fluoro-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-4-tert-butyl-benzamide;

5,6-Dihydro-4H-cyclopenta[b]thiophene-2-carboxylic acid (2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-amide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[1-(2-morpholin-4-yl-ethyl)-2-oxo-1,2-dihydro-pyridin-4-ylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

N-(2-Methyl-3-{4-methyl-6-[4-(1-methyl-piperidin-4-yloxy)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-4-piperidin-1-yl-benzamide;

6-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[4-(4-methyl-piperazine-1-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-nicotinamide;

6-tert-Butyl-N-(3-{6-[4-(4-ethyl-piperazine-1-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-nicotinamide;

6-tert-Butyl-N-[3-(6-{4-[4-(2-hydroxy-ethyl)-piperazine-1-carbonyl]-phenylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-nicotinamide;

4-(6-{3-[(6-tert-Butyl-pyridine-3-carbonyl)-amino]-2-methyl-phenyl}-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino)-benzoic acid;

Benzo[b]thiophene-5-carboxylic acid (2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-amide;

6-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[4-(4-methyl-[1,4]diazepane-1-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-nicotinamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-5-oxo-6-[3-(pyridin-3-yloxy)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

6-tert-Butyl-N-(2-methyl-3-{4-methyl-5-oxo-6-[3-(pyridin-3-yloxy)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-nicotinamide;

4,4-Dimethyl-chroman-7-carboxylic acid (2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-amide;

6-tert-Butyl-N-(3-{6-[4-(2-hydroxymethyl-morpholin-4-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-nicotinamide;

6-tert-Butyl-N-(2-fluoro-3-{6-[4-(2-hydroxymethyl-morpholin-4-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-nicotinamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-5-oxo-6-[3-(pyridin-4-yloxy)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

6-tert-Butyl-N-(2-methyl-3-{4-methyl-5-oxo-6-[3-(pyridin-4-yloxy)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-nicotinamide;

6-tert-Butyl-N-(3-{6-[4-(2-hydroxymethyl-morpholine-4-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-nicotinamide;

6-tert-Butyl-N-(2-fluoro-3-{6-[4-(2-hydroxymethyl-morpholine-4-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-nicotinamide;

6-tert-Butyl-N-(2-fluoro-3-{4-methyl-6-[4-(4-methyl-[1,4]diazepane-1-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-nicotinamide;

6-tert-Butyl-N-(3-{6-[4-(4-hydroxy-piperidine-1-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-nicotinamide;

6-tert-Butyl-N-(2-fluoro-3-{6-[4-(4-hydroxy-piperidine-1-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-nicotinamide;

4-tert-Butyl-N-{2-methyl-3-[4-methyl-6-(4-nitro-phenylamino)-5-oxo-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide;

N-{3-[6-(4-Amino-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-4-tert-butyl-benzamide;

N-(3-{6-[4-(4-Amino-piperidine-1-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-6-tert-butyl-nicotinamide;;

4-(6-{3-[(6-tert-Butyl-pyridine-3-carbonyl)-amino]-2-fluoro-phenyl}-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino)-benzoic acid;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-5-oxo-6-[4-(pyridin-3-ylmethoxy)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-5-oxo-6-[4-(pyridin-3-yloxy)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

6-tert-Butyl-N-(2-methyl-3-{4-methyl-5-oxo-6-[4-(pyridin-3-yloxy)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-nicotinamide;

6-tert-Butyl-N-(2-methyl-3-{4-methyl-5-oxo-6-[4-(piperazine-1-carbonyl)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-nicotinamide;

6-tert-Butyl-N-[2-fluoro-3-(6-{4-[4-(2-hydroxy-ethyl)-piperazin-1-yl]-phenylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-phenyl]-nicotinamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[4-(4-methyl-piperazin-1-yl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(3-{6-[4-(4-ethyl-piperazin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[4-(N-(hydroxy)aminocarbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

N-{3-[6-(3-Amino-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-4-piperidin-1-yl-benzamide;

6-tert-Butyl-N-[3-(6-{4-[(2-hydroxy-ethyl)-methyl-carbamoyl]-phenylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-nicotinamide;

6-tert-Butyl-N-(3-{6-[4-(cyanomethyl-methyl-carbamoyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-nicotinamide;

6-tert-Butyl-N-(2-methyl-3-{4-methyl-5-oxo-6-[4-(3-oxo-piperazine-1-carbonyl)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-nicotinamide;

N-(3-{6-[4-(4-Ethyl-piperazine-1-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-piperidin-1-yl-benzamide;

6-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[4-(4-methyl-piperazin-1-yl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-nicotinamide;

6-tert-Butyl-N-(3-{6-[4-(4-ethyl-piperazin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-nicotinamide;

N-{2-Methyl-3-[4-methyl-6-(4-morpholin-4-ylmethyl-phenylamino)-5-oxo-4,5-dihydro-pyrazin-2-yl]-phenyl}-4-piperidin-1-yl-benzamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-5-oxo-6-[4-(N-(1-amino-ethylidene))-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-{3-[6-(3-cyclopropylaminomethyl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide;

4-tert-Butyl-N-{2-methyl-3-[4-methyl-5-oxo-6-(3-piperidin-1-ylmethyl-phenylamino)-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide;

4-tert-Butyl-N-[3-(6-{3-[(cyanomethyl-methyl-amino)-methyl]-phenylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-benzamide;

1-(3-{6-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-benzyl)-piperidine-4-carboxylic acid amide;

4-tert-Butyl-N-{3-[6-(3-{[(2-hydroxy-ethyl)-methyl-amino]-methyl}-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide;

4-tert-Butyl-N-[3-(6-{3-[(2-hydroxy-ethylamino)-methyl]-phenylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-benzamide;

4-tert-Butyl-N-(3-{6-[3-(4-hydroxy-piperidin-1-ylmethyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-(3-{6-[3-(2-hydroxymethyl-morpholin-4-ylmethyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

Tetrahydro-furan-2-carboxylic acid (4-{6-[3-(4-tert-butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-phenyl)-amide;

Tetrahydro-furan-3-carboxylic acid (4-{6-[3-(4-tert-butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-phenyl)-amide;

3,4,5,6-Tetrahydro-2H-[1,3']bipyridinyl-6'-carboxylic acid (2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-amide;

6-tert-Butyl-N-(2-fluoro-3-{4-methyl-5-oxo-6-[4-(piperazine-1-carbonyl)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-nicotinamide;

N-(3-{6-[4-(1,1-Dioxo-1l6-thiomorpholin-4-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-piperidin-1-yl-benzamide;

6-tert-Butyl-N-(3-{6-[4-(1,1-dioxo-1l6-thiomorpholin-4-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-fluoro-phenyl)-nicotinamide;

2-tert-Butyl-pyrimidine-5-carboxylic acid (2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-amide;

6-tert-Butyl-N-(2-methyl-3-{4-methyl-5-oxo-6-[4-(pyridin-3-ylmethoxy)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-nicotinamide;

N-(3-{6-[4-(4-Amino-piperidine-1-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-fluoro-phenyl)-6-tert-butyl-nicotinamide;

6-tert-Butyl-N-(2-fluoro-3-{4-methyl-6-[4-(4-methyl-piperazine-1-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-nicotinamide;

5-tert-Butyl-pyrazine-2-carboxylic acid (2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-amide;

6-tert-Butyl-N-(2-fluoro-3-{6-[4-(4-hydroxy-piperidin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-nicotinamide;

N-(2-Methyl-3-{4-methyl-6-[4-(4-methyl-piperazin-1-yl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-4-piperidin-1-yl-benzamide;

N-(3-{6-[4-(4-Ethyl-piperazin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-piperidin-1-yl-benzamide;

6-tert-Butyl-N-(2-fluoro-3-{4-methyl-6-[4-(4-methyl-piperazin-1-yl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-nicotinamide;

6-tert-Butyl-N-(3-{6-[4-(4-ethyl-piperazin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-fluoro-phenyl)-nicotinamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-5-oxo-6-[4-(4-oxo-piperidin-1-yl)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

N-(3-{6-[4-(3-Amino-propylcarbamoyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-fluoro-phenyl)-6-tert-butyl-nicotinamide;

N-(3-{6-[4-(4-Hydroxy-piperidin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-piperidin-1-yl-benzamide

6-tert-Butyl-N-(3-{6-[4-(4-hydroxy-piperidin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-nicotinamide;

4-Azepan-1-yl-N-(2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

5-tert-Butyl-pyridine-2-carboxylic acid (2-fluoro-3-{6-[4-(4-hydroxy-piperidine-1-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-amide;

N-{3-[5-(3-Amino-phenylamino)-1-methyl-6-oxo-1,6-dihydro-pyridin-3-yl]-2-methyl-phenyl}-4-tert-butyl-benzamide;

Tetrahydro-furan-2-carboxylic acid (3-{5-[3-(4-tert-butyl-benzoylamino)-2-methyl-phenyl]-1-methyl-2-oxo-1,2-dihydro-pyridin-3-ylamino}-phenyl)-amide;

4-tert-Butyl-N-{3-[1,4-dimethyl-5-(4-morpholin-4-yl-phenylamino)-6-oxo-1,6-dihydro-pyridin-3-yl]-2-methyl-phenyl}-benzamide;

4-tert-Butyl-N-(3-{5-[4-(1,1-dioxo-1l6-thiomorpholin-4-yl)-phenylamino]-1-methyl-6-oxo-1,6-dihydro-pyridin-3-yl}-2-methyl-phenyl)-benzamide;

6-tert-Butyl-N-(3-{6-[4-(carbamoylmethyl-methyl-carbamoyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-nicotinamide;

6-tert-Butyl-N-{3-[6-(4-hydroxycarbamoyl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-nicotinamide;

5-tert-Butyl-pyridine-2-carboxylic acid (3-{6-[4-(4-ethyl-piperazin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-amide;

N-(3-{6-[4-(4-Amino-piperidin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide;

4-{6-[3-(4-(1-piperidinyl)-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-benzohydroxamic acid;

5-tert-Butyl-pyridine-2-carboxylic acid (3-{6-[4-(1,1-dioxo-1λ^6-thiomorpholin-4-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-amide;

5-tert-Butyl-pyrazine-2-carboxylic acid (2-methyl-3-{4-methyl-6-[4-(4-methyl-piperazine-1-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-amide;

5-tert-Butyl-pyridine-2-carboxylic acid (3-{6-[4-(4-hydroxy-piperidine-1-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-amide;

N-(2-Methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-4-(4-methyl-piperidin-1-yl)-benzamide;

4-tert-Butyl-N-{2-methyl-3-[4-methyl-6-(5-methyl-1H-pyrazol-3-ylamino)-5-oxo-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide;

5-tert-Butyl-pyridine-2-carboxylic acid (3-{6-[4-(2-hydroxymethyl-morpholin-4-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-amide;

N-(2-Methyl-3-{4-methyl-5-oxo-6-[4-(3-oxo-piperazine-1-carbonyl)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-4-piperidin-1-yl-benzamide;

4-(1-Piperidinyl)-N-(3-{4-methyl-6-[4-(2-hydroxyethyl-methyl-carbamoyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-{2-methyl-3-[4-methyl-5-oxo-6-(1H-pyrazol-3-ylamino)-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide;

N-(3-{6-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-phenyl)-isonicotinamide;

5-tert-Butyl-pyrazine-2-carboxylic acid (3-{6-[4-(1,1-dioxo-1λ^6-thiomorpholin-4-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-amide;

Tetrahydro-furan-2-carboxylic acid (3-{6-[3-(4-tert-butyl-benzoylamino)-2-fluoro-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-phenyl)-amide;

5-tert-Butyl-pyridine-2-carboxylic acid (3-{6-[4-(carbamoylmethyl-methyl-carbamoyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-amide;

4,5,6,7-Tetrahydro-benzo[b]thiophene-2-carboxylic acid (3-{6-[4-(carbamoylmethyl-methyl-carbamoyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-amide;

N-(2-Methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-4-(3-methyl-piperidin-1-yl)-benzamide;

N-{3-[6-(3-Acetylamino-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-4-tert-butyl-benzamide;

Tetrahydro-furan-3-carboxylic acid (3-{6-[3-(4-tert-butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-phenyl)-amide;

Thiazole-4-carboxylic acid (3-{6-[3-(4-tert-butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-phenyl)-amide;

(3-{6-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-phenyl)-carbamic acid ethyl ester;

4-tert-Butyl-N-(3-{6-[3-(2-methoxy-acetylamino)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

5-tert-Butyl-pyrimidine-2-carboxylic acid (2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-amide;

4-(Isopropyl-methyl-amino)-N-(2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(2-methyl-3-{6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(3-{6-[4-(1,1-dioxo-1λ^6-thiomorpholin-4-ylmethyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

N-[2-Methyl-3-(4-methyl-5-oxo-6-{4-[(tetrahydro-pyran-4-ylamino)-methyl]-phenylamino}-4,5-dihydro-pyrazin-2-yl)-phenyl]-4-piperidin-1-yl-benzamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[4-(4-methyl-piperazin-1-ylmethyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(3-{6-[4-(4-ethyl-piperazin-1-ylmethyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-{3-[6-(4-{[(2-hydroxy-ethyl)-methyl-amino]-methyl}-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide;

N-[3-(6-{4-[4-(2-Hydroxy-ethyl)-piperazine-1-carbonyl]-phenylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-4-piperidin-1-yl-benzamide;

1-(4-{4-Methyl-6-[2-methyl-3-(4-piperidin-1-yl-benzoylamino)-phenyl]-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-phenyl)-piperidine-4-carboxylic acid amide;

5-tert-Butyl-pyrazine-2-carboxylic acid (3-{6-[4-(4-amino-piperidin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-amide;

N-(2-Methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-4-(4-methyl-piperazin-1-ylmethyl)-benzamide;

4-tert-Butyl-N-[2-fluoro-3-(4-methyl-6-{3-[2-(4-methyl-piperazin-1-yl)-acetylamino]-phenylamino}-5-oxo-4,5-dihydro-pyrazin-2-yl)-phenyl]-benzamide;

N-{3-[6-(3-Amino-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-fluoro-phenyl}-4-tert-butyl-benzamide;

N-{3-[6-(3-Amino-phenylamino)-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-4-tert-butyl-benzamide;

5-tert-Butyl-pyridine-2-carboxylic acid (2-methyl-3-{4-methyl-5-oxo-6-[4-(piperazine-1-carbonyl)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-amide;

Tetrahydro-furan-2-carboxylic acid (3-{6-[3-(4-tert-butyl-benzoylamino)-2-methyl-phenyl]-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-phenyl)-amide;

Tetrahydro-furan-2-carboxylic acid [3-(6-{2-methyl-3-[(4,5,6,7-tetrahydro-benzo[b]thiophene-2-carbonyl)-amino]-phenyl}-3-oxo-3,4-dihydro-pyrazin-2-ylamino)-phenyl]-amide;

Tetrahydro-furan-2-carboxylic acid (5-{6-[3-(4-tert-butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-2-fluoro-phenyl)-amide;

Acetic acid 3-{6-[3-(4-tert-butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-phenyl ester;

N-(2-Methyl-3-{6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-4-piperidin-1-yl-benzamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[4-(morpholin-2-ylmethoxy)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

6-tert-Butyl-pyridazine-3-carboxylic acid (2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-amide;

4-tert-Butyl-N-{2-methyl-3-[4-methyl-5-oxo-6-(3-oxo-3,4-dihydro-2H-benzo[1,4]oxazin-6-ylamino)-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide;

4-Imidazol-1-yl-N-(2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(3-{6-[3-(3-methoxy-propionylamino)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

Furan-2-carboxylic acid (3-{6-[3-(4-tert-butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-phenyl)-amide;

6-tert-Butyl-N-(3-{6-[4-(1,1-dioxo-1λ^6-thiomorpholin-4-yl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-nicotinamide;

4-tert-Butyl-N-[3-(6-{4-[2-(4-ethyl-piperazin-1-yl)-ethoxy]-phenylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-benzamide;

(3-{6-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-phenyl)-carbamic acid tetrahydro-furan-3-yl ester;

Tetrahydro-furan-2-carboxylic acid (3-{6-[3-(4-tert-butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-phenyl)-amide;

Tetrahydro-furan-2-carboxylic acid (3-{6-[3-(4-tert-butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-phenyl)-amide;

N-{3-[6-(5-Amino-pyridin-3-ylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-4-tert-butyl-benzamide;

4-tert-Butyl-N-{3-[6-(1H-indol-5-ylamino)-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide;

Pyrrolidine-2-carboxylic acid (3-{6-[3-(4-tert-butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-phenyl)-amide;

4-tert-Butyl-N-(3-{6-[3-(2-hydroxy-acetylamino)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-[3-(6-cyclopropylamino-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-benzamide;

4-tert-Butyl-N-[3-(6-hydroxy-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-benzamide;

4-tert-Butyl-N-(3-{6-[3-(2-ethoxy-acetylamino)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

N-{3-[6-(3-Amino-4-methyl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-4-tert-butyl-benzamide;

4-tert-Butyl-N-(3-{6-[4-(4-hydroxymethyl-piperidin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-(3-{6-[3-(2-hydroxy-2-methyl-propionylamino)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

Tetrahydro-pyran-4-carboxylic acid (3-{6-[3-(4-tert-butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-phenyl)-amide;

4-tert-Butyl-N-{2-methyl-3-[4-methyl-5-oxo-6-(4-thiomorpholin-4-ylmethyl-phenylamino)-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide;

4-(4-Hydroxy-piperidin-1-yl)-N-(2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

N-{3-[6-(3-Amino-4-chloro-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-4-tert-butyl-benzamide;

N-(3-{6-[3-Amino-4-(morpholine-4-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide;

N-(2-Methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-4-(2-methyl-piperidin-1-yl)-benzamide;

4,5,6,7-Tetrahydro-benzo[b]thiophene-2-carboxylic acid (3-{6-[4-(1,1-dioxo-1λ^6-thiomorpholin-4-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-amide;

4-tert-Butyl-N-{3-[6-(3-dimethylamino-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-5-oxo-6-[4-(piperidin-4-ylmethoxy)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-[3-(6-{4-[(2-hydroxy-ethylamino)-methyl]-phenylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-benzamide;

(3-{6-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-phenyl)-carbamic acid phenyl ester;

4-tert-Butyl-N-{3-[6-(4-cyclopropylaminomethyl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide;

4-tert-Butyl-N-[3-(6-{4-[(carbamoylmethyl-amino)-methyl]-phenylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-benzamide;

4-(4-Methoxymethoxy-piperidin-1-yl)-N-(2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

N-(3-{6-[3-(2-Amino-acetylamino)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide;

Azetidine-2-carboxylic acid (3-{6-[3-(4-tert-butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-phenyl)-amide;

Tetrahydro-furan-2-carboxylic acid (5-{6-[3-(4-tert-butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-2-methyl-phenyl)-amide;

4-tert-Butyl-N-(3-{6-[4-(4-hydroxy-4-methyl-piperidin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

1-Methyl-3-[4-(morpholine-4-carbonyl)-phenylamino]-5-(2-phenyl-benzooxazol-7-yl)-1H-pyrazin-2-one;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[4-(1-methyl-piperidin-2-ylmethoxy)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

5-[2-(4-Methoxy-phenyl)-benzooxazol-7-yl]-1-methyl-3-[4-(morpholine-4-carbonyl)-phenylamino]-1H-pyrazin-2-one;

4-tert-Butyl-N-{3-[6-(1H-indol-5-ylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide;

N-{3-[6-(3-Aminomethyl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-4-tert-butyl-benzamide;

4-tert-Butyl-N-(3-{6-[4-(1-ethyl-piperidin-4-ylmethoxy)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-{2-methyl-3-[4-methyl-5-oxo-6-(1-pyridin-4-ylmethyl-1H-indol-6-ylamino)-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide;

4-Furan-2-yl-N-(2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-(2-Methoxy-1,1-dimethyl-ethyl)-N-(2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(3-{6-[4-(4-hydroxy-4-methyl-piperidine-1-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-(3-{6-[4-(4-hydroxy-4-methyl-piperidin-1-ylmethyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

6-Methyl-4,5,6,7-tetrahydro-benzo[b]thiophene-2-carboxylic acid {3-[6-(3-amino-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-amide;

4-{6-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-2-hydroxy-benzoic acid;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-3-nitro-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

5-Ethyl-4,5,6,7-tetrahydro-benzo[b]thiophene-2-carboxylic acid (2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-amide;

4-Azetidin-1-yl-N-(2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-3-methoxy-N-(2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-{6-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-2-methoxy-benzoic acid;

1,4,4-Trimethyl-1,2,3,4-tetrahydro-quinoline-7-carboxylic acid (2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-amide;

4-(1-Methoxy-1-methyl-ethyl)-N-(2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-(2,2-Dimethyl-propionyl)-N-(2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-(3-{6-[3-methoxy-4-(morpholine-4-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-{6-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-2-methoxy-N-(3-methoxy-propyl)-benzamide;

N-{3-[6-(3-Acryloylamino-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-4-tert-butyl-benzamide;

4-tert-Butyl-N-{3-[6-(1H-indol-4-ylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide;

4-tert-Butyl-N-[3-(6-{4-[(2-methoxy-ethylamino)-methyl]-phenylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-benzamide;

4-tert-Butyl-N-{3-[6-(4-ethylaminomethyl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide;

4-tert-Butyl-N-{3-[6-(4-diethylaminomethyl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide;

4-tert-Butyl-N-[3-(6-{4-[(isopropyl-methyl-amino)-methyl]-phenylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-benzamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[4-(2-methyl-piperidin-1-ylmethyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-[2-methyl-3-(4-methyl-5-oxo-6-{4-[2-(tetrahydro-pyran-4-ylamino)-ethyl]-phenylamino}-4,5-dihydro-pyrazin-2-yl)-phenyl]-benzamide;

5-Amino-2-{6-[3-(4-tert-butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-N-cyclopropyl-benzamide;

5-Amino-benzo[b]thiophene-2-carboxylic acid (2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-amide;

2-Amino-N-{3-[6-(benzothiazol-6-ylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-4-piperidin-1-yl-benzamide;

4-tert-Butyl-N-[3-(6-{2-[(2-hydroxy-ethyl)-methyl-amino]-pyridin-4-ylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-benzamide;

4-tert-Butyl-N-(3-{6-[3-methoxy-4-(4-methyl-piperazine-1-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-{6-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-N-(2-hydroxy-ethyl)-2-methoxy-N-methyl-benzamide;

4-tert-Butyl-N-(3-{6-[3-methoxy-4-(piperidine-1-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

N-{3-[6-(3-Amino-4-morpholin-4-yl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-4-tert-butyl-benzamide;

N-{3-[6-(4-Amino-2-piperidin-1-ylmethyl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-4-tert-butyl-benzamide;

(4-{6-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-benzylamino)-acetic acid;

4-tert-Butyl-N-[3-(6-{4-[(cyclopropylmethyl-amino)-methyl]-phenylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-benzamide;

N-{3-[6-(3-Amino-4-thiomorpholin-4-yl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-4-tert-butyl-benzamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-5-oxo-6-[4-(piperidin-3-ylmethoxy)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

N-(3-{6-[3-Amino-4-(1,1-dioxo-1λ^6-thiomorpholin-4-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide;

N-(3-{6-[3-Amino-4-(piperidine-1-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide;

4-tert-Butyl-N-{2-methyl-3-[4-methyl-5-oxo-6-(1,2,3,4-tetrahydro-isoquinolin-6-ylamino)-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide;

4-tert-Butyl-N-[3-(6-{4-[2-(4-ethyl-piperazin-1-yl)-ethyl]-phenylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-benzamide;

4-tert-Butyl-N-[3-(6-{4-[2-(2-hydroxy-ethylamino)-ethyl]-phenylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-benzamide;

4-tert-Butyl-N-{3-[6-(4-{2-[(2-hydroxy-ethyl)-methyl-amino]-ethyl}-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide;

4-tert-Butyl-N-(3-{6-[4-(2-diethylamino-ethyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

2-Amino-4-{6-[3-(4-tert-butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-N-(2-hydroxy-ethyl)-N-methyl-benzamide;

4-[2-(2-Methoxy-ethoxy)-1,1-dimethyl-ethyl]-N-(2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-(3-Methoxymethoxy-piperidin-1-yl)-N-(2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-{3-[6-(4-hydroxymethyl-3-methoxy-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide;

4-tert-Butyl-N-{3-[6-(1H-indol-6-ylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide;

N-(3-{6-[3-Amino-4-(4-methyl-piperazine-1-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide;

N-(3-{6-[3-Amino-4-(4-ethyl-piperazine-1-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide;

2-Amino-4-{6-[3-(4-tert-butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-N-(2-dimethylamino-ethyl)-benzamide;

4-tert-Butyl-N-{2-methyl-3-[6-(4-morpholin-4-yl-3-nitro-phenylamino)-5-oxo-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide;

4-tert-Butyl-N-{2-methyl-3-[4-methyl-6-(4-morpholin-4-yl-3-nitro-phenylamino)-5-oxo-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide;

N-{3-[6-(3-Amino-4-morpholin-4-yl-phenylamino)-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-4-tert-butyl-benzamide;

2-Amino-4-{6-[3-(4-tert-butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-N-(2-diethylamino-ethyl)-benzamide;

4-tert-Butyl-N-(3-{4-ethyl-6-[4-(phenyl-carbamoyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-(3-{4-ethyl-6-[4-(2-methyl-phenyl-carbamoyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-benzamide;

4-tert-Butyl-N-{3-[6-(4-cyclopropylaminomethyl-3-methoxy-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide;

4-tert-Butyl-N-{3-[6-(4-cyclopropylaminomethyl-3-methoxy-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide;

4-tert-Butyl-N-{3-[6-(3-{2-[(2-hydroxy-ethyl)-methyl-amino]-ethyl}-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide;

N-(3-{6-[3-Amino-4-(1-oxo-1λ^4-thiomorpholine-4-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide;

4-(1-Methyl-cyclobutyl)-N-(2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

N-{3-[6-(4-{[Bis-(2-hydroxy-ethyl)-amino]-methyl}-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-4-tert-butyl-benzamide;

4-tert-Butyl-N-[3-(6-{3-[2-(2-hydroxy-ethylamino)-ethyl]-phenylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-benzamide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[3-(2-morpholin-4-yl-ethyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

4-tert-Butyl-N-[3-(6-{3-[2-(1,1-dioxo-1λ^6-thiomorpholin-4-yl)-ethyl]-phenylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-benzamide;

4-tert-Butyl-N-[3-(6-{3-[2-(4-ethyl-piperazin-1-yl)-ethyl]-phenylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-benzamide;

N-{3-[6-(3-{2-[Bis-(2-hydroxy-ethyl)-amino]-ethyl}-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-4-tert-butyl-benzamide;

4-tert-Butyl-N-{3-[6-(3,4-dihydro-2H-benzo[1,4]oxazin-6-ylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide;

N-(3-{6-[4-(4-Aminomethyl-4-hydroxy-piperidin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide;

2-Amino-4-{6-[3-(4-tert-butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-benzoic acid;

5-(3-Amino-2-methyl-phenyl)-1-methyl-3-(4-morpholin-4-yl-3-nitro-phenylamino)-1H-pyrazin-2-one;

5-tert-Butyl-pyridine-2-carboxylic acid {3-[6-(3-amino-4-morpholin-4-yl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-amide;

4,5,6,7-Tetrahydro-benzo[b]thiophene-2-carboxylic acid {3-[6-(3-amino-4-morpholin-4-yl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-amide;

N-{3-[6-(3-Amino-4-morpholin-4-yl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-4-piperidin-1-yl-benzamide;

N-(2-Methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-4-methylsulfanyl-benzamide;

N-{3-[6-(3-Amino-4-cyclopropylaminomethyl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-4-tert-butyl-benzamide;

5-Methyl-4,5,6,7-tetrahydro-benzo[b]thiophene-2-carboxylic acid (3-{6-[3-amino-4-(morpholine-4-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-amide;

N-(3-{6-[3-Amino-4-(thiomorpholine-4-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide;

2-Amino-4-{6-[3-(4-tert-butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-N-pyridin-3-yl-benzamide;

N-(5-{6-[3-Amino-4-(morpholine-4-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide;

2-Amino-4-{6-[3-(4-tert-butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-N-(2-methoxy-ethyl)-N-methyl-benzamide;

Octahydro-isoquinoline-2-carboxylic acid (2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-amide;

N-(3-{6-[3-Amino-4-(morpholine-4-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-6-tert-butyl-nicotinamide;

N-{3-[6-(2-Amino-indan-5-ylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-4-tert-butyl-benzamide;

N-(3-{6-[3-Amino-4-(morpholine-4-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-fluoro-phenyl)-4-tert-butyl-benzamide;

N-{3-[6-(3-Amino-4-methoxy-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-4-tert-butyl-benzamide;

N-(3-{6-[3-Amino-4-(1-oxo-1λ^4-thiomorpholin-4-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide;

N-(3-{6-[3-Amino-4-(4-hydroxy-piperidin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide;

N-(3-{6-[3-Amino-4-(4-ethyl-piperazin-1-ylmethyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide;

1-(2-Amino-4-{6-[3-(4-tert-butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-phenyl)-piperidine-4-carboxylic acid amide;

N-{3-[6-(3-Amino-4-morpholin-4-yl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-fluoro-phenyl}-4-tert-butyl-benzamide;

N-(3-{6-[3-Amino-4-(4-ethyl-piperazin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide;

N-(3-{6-[4-(4-Aminomethyl-4-hydroxy-piperidine-1-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide;

N-(3-{6-[4-(1,1-Dioxo-1λ^6-thiomorpholin-4-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-pentafluoroethyl-benzamide;

5-Methyl-4,5,6,7-tetrahydro-benzo[b]thiophene-2-carboxylic acid {2-methyl-3-[4-methyl-6-(4-morpholin-4-ylmethyl-phenylamino)-5-oxo-4,5-dihydro-pyrazin-2-yl]-phenyl}-amide;

5-Methyl-4,5,6,7-tetrahydro-benzo[b]thiophene-2-carboxylic acid (3-{6-[3-amino-4-(morpholine-4-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-fluoro-phenyl)-amide;

N-{3-[6-(3-Amino-4-[1,4]oxazepan-4-yl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-4-tert-butyl-benzamide;

5-Methyl-4,5,6,7-tetrahydro-benzo[b]thiophene-2-carboxylic acid (3-{6-[3-amino-4-(4-hydroxy-piperidin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-amide;

N-[3-(6-{3-Amino-4-[4-(2-hydroxy-ethyl)-piperazin-1-yl]-phenylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-4-tert-butyl-benzamide;

4-tert-Butyl-N-{3-[6-(3-methoxy-4-morpholin-4-ylmethyl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide;

N-(3-{6-[3-Amino-4-(4-hydroxy-4-methyl-piperidin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide;

N-(3-{6-[3-Amino-4-(2-morpholin-4-yl-ethoxy)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide;

4,5,6,7-Tetrahydro-benzo[b]thiophene-2-carboxylic acid (3-{6-[3-amino-4-(morpholine-4-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-amide;

N-[3-(6-{3-Amino-4-[(2-methoxy-ethyl)-methyl-amino]-phenylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-4-tert-butyl-benzamide;

4-{6-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-2-methyl-benzoic acid methyl ester;

4-{6-[3-(4-tert-Butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-2-methyl-benzoic acid;

4,5,6,7-Tetrahydro-benzo[b]thiophene-2-carboxylic acid (3-{6-[3-amino-4-(morpholine-4-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-fluoro-phenyl)-amide;

4-tert-Butyl-N-{2-methyl-3-[4-methyl-6-(3-methyl-4-morpholin-4-yl-phenylamino)-5-oxo-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide;

4,5,6,7-Tetrahydro-benzo[b]thiophene-2-carboxylic acid (2-methyl-3-{4-methyl-6-[4-(4-methyl-piperazine-1-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-amide;

5-Methyl-4,5,6,7-tetrahydro-benzo[b]thiophene-2-carboxylic acid [2-methyl-3-(4-methyl-5-oxo-6-{4-[(tetrahydro-pyran-4-ylamino)-methyl]-phenylamino}-4,5-dihydro-pyrazin-2-yl)-phenyl]-amide;

4-tert-Butyl-N-{2-methyl-3-[4-methyl-6-(4-[1,4]oxazepan-4-ylmethyl-phenylamino)-5-oxo-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide;

5-Methyl-4,5,6,7-tetrahydro-benzo[b]thiophene-2-carboxylic acid {3-[6-(4-hydroxymethyl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-amide;

5-Methyl-4,5,6,7-tetrahydro-benzo[b]thiophene-2-carboxylic acid [3-(6-{4-[(carbamoylmethyl-amino)-methyl]-phenylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-amide;

5-Methyl-4,5,6,7-tetrahydro-benzo[b]thiophene-2-carboxylic acid (3-{6-[3-amino-4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-amide;

4,5,6,7-Tetrahydro-benzo[b]thiophene-2-carboxylic acid (3-{6-[3-amino-4-(4-hydroxy-piperidin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-amide;

1-(2-Amino-4-{6-[3-(4-tert-butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-phenyl)-4-hydroxy-pyridinium;

N-[3-(6-{3-Amino-4-[(2-hydroxy-ethyl)-methyl-amino]-phenylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-4-tert-butyl-benzamide;

N-(3-{6-[3-Amino-4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-piperidin-1-yl-benzamide;

N-(3-{6-[3-Amino-4-(4-methyl-piperazin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide;

5,6,7,8-Tetrahydro-naphthalene-2-carboxylic acid (2-methyl-3-{4-methyl-5-oxo-6-[4-(1-oxo-1λ^4-thiomorpholin-4-yl)-phenylamino]-4,5-dihydro-pyrazin-2-yl}-phenyl)-amide;

4,5,6,7-Tetrahydro-benzo[b]thiophene-2-carboxylic acid (2-methyl-3-{4-methyl-6-[4-(4-methyl-piperazine-1-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-amide;

5-Methyl-4,5,6,7-tetrahydro-benzo[b]thiophene-2-carboxylic acid [2-methyl-3-(4-methyl-5-oxo-6-{4-[(tetrahydro-pyran-4-ylamino)-methyl]-phenylamino}-4,5-dihydro-pyrazin-2-yl)-phenyl]-amide;

4-tert-Butyl-N-{2-methyl-3-[4-methyl-6-(4-[1,4]oxazepan-4-ylmethyl-phenylamino)-5-oxo-4,5-dihydro-pyrazin-2-yl]-phenyl}-benzamide;

5-Methyl-4,5,6,7-tetrahydro-benzo[b]thiophene-2-carboxylic acid {3-[6-(4-hydroxymethyl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-amide;

5-Methyl-4,5,6,7-tetrahydro-benzo[b]thiophene-2-carboxylic acid [3-(6-{4-[(carbamoylmethyl-amino)-methyl]-phenylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-amide;

5-Methyl-4,5,6,7-tetrahydro-benzo[b]thiophene-2-carboxylic acid (3-{6-[3-amino-4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-amide;

4,5,6,7-Tetrahydro-benzo[b]thiophene-2-carboxylic acid (3-{6-[3-amino-4-(4-hydroxy-piperidin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-amide;

1-(2-Amino-4-{6-[3-(4-tert-butyl-benzoylamino)-2-methyl-phenyl]-4-methyl-3-oxo-3,4-dihydro-pyrazin-2-ylamino}-phenyl)-4-hydroxy-pyridinium;

N-[3-(6-{3-Amino-4-[(2-hydroxy-ethyl)-methyl-amino]-phenylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-4-tert-butyl-benzamide;

N-(3-{6-[3-Amino-4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-piperidin-1-yl-benzamide;

N-(3-{6-[3-Amino-4-(4-methyl-piperazin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide;

4,5,6,7-Tetrahydro-benzo[b]thiophene-2-carboxylic acid (3-{6-[3-amino-4-(4-hydroxy-piperidine-1-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-amide;

N-(3-{6-[3-Amino-4-(3-hydroxy-piperidin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide;

N-(3-{6-[3-Amino-4-(3-hydroxy-pyrrolidin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide;

N-{3-[6-(3-Amino-4-piperidin-1-yl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-4-tert-butyl-benzamide;

4-(2-Hydroxy-1,1-dimethyl-ethyl)-N-(2-methyl-3-{4-methyl-6-[4-(morpholine-4-carbonyl)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

1-[2-Amino-4-(4-methyl-6-{2-methyl-3-[(4,5,6,7-tetrahydro-benzo[b]thiophene-2-carbonyl)-amino]-phenyl}-3-oxo-3,4-dihydro-pyrazin-2-ylamino)-benzoyl]-piperidine-4-carboxylic acid amide;

4,5,6,7-Tetrahydro-benzo[b]thiophene-2-carboxylic acid (3-{6-[3-amino-4-(3-hydroxy-pyrrolidine-1-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-amide;

4,5,6,7-Tetrahydro-benzo[b]thiophene-2-carboxylic acid (3-{6-[3-amino-4-(4-ethyl-piperazine-1-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-amide;

4,5,6,7-Tetrahydro-benzo[b]thiophene-2-carboxylic acid (3-{6-[3-amino-4-(3-hydroxy-piperidine-1-carbonyl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-amide;

N-(3-{6-[3-Amino-4-(4-methyl-[1,4]diazepan-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide;

N-(3-{6-[3-Amino-4-(2-hydroxymethyl-morpholin-4-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide;

N-(3-{6-[3-Amino-4-(4-hydroxymethyl-piperidin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide;

1-[2-Amino-4-(4-methyl-6-{2-methyl-3-[(4,5,6,7-tetrahydro-benzo[b]thiophene-2-carbonyl)-amino]-phenyl}-3-oxo-3,4-dihydro-pyrazin-2-ylamino)-phenyl]-piperidine-4-carboxylic acid amide;

4,5,6,7-Tetrahydro-benzo[b]thiophene-2-carboxylic acid (3-{6-[3-amino-4-(2-hydroxymethyl-morpholin-4-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-amide;

4,5,6,7-Tetrahydro-benzo[b]thiophene-2-carboxylic acid [3-(6-{3-amino-4-[(2-hydroxy-ethyl)-methyl-carbamoyl]-phenylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-amide;

4-tert-Butyl-N-(2-methyl-3-{4-methyl-6-[3-nitro-4-(pyridin-3-yloxy)-phenylamino]-5-oxo-4,5-dihydro-pyrazin-2-yl}-phenyl)-benzamide;

N-[3-(6-{3-Amino-4-[4-(2-hydroxy-ethyl)-piperidin-1-yl]-phenylamino}-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl)-2-methyl-phenyl]-4-tert-butyl-benzamide;

4,5,6,7-Tetrahydro-benzo[b]thiophene-2-carboxylic acid {2-methyl-3-[4-methyl-5-oxo-6-(pyridin-3-ylamino)-4,5-dihydro-pyrazin-2-yl]-phenyl}-amide;

4-tert-Butyl-N-{3-[6-(3-fluoro-4-morpholin-4-ylmethyl-phenylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-2-methyl-phenyl}-benzamide;

N-(3-{6-[3-Amino-4-(4-methoxy-piperidin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide;

N-(3-{6-[3-Amino-4-(4-cyano-piperidin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide;

1-[2-Amino-4-(4-methyl-6-{2-methyl-3-[(4,5,6,7-tetrahydro-benzo[b]thiophene-2-carbonyl)-amino]-phenyl}-3-oxo-3,4-dihydro-pyrazin-2-ylamino)-phenyl]-piperidine-3-carboxylic acid amide;

N-(3-{6-[3-Amino-4-(3-hydroxymethyl-piperidin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide;

N-(3-{6-[3-Amino-4-(3-methyl-piperazin-1-yl)-phenylamino]-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl}-2-methyl-phenyl)-4-tert-butyl-benzamide; and

4,5,6,7-Tetrahydro-benzo[b]thiophene-2-carboxylic acid {2-methyl-3-[4-methyl-5-oxo-6-(pyridin-4-ylamino)-4,5-dihydro-pyrazin-2-yl]-phenyl}-amide.

91. A pharmaceutical composition, comprising at least one chemical entity of any one of claims 10 to 90, together with at least one pharmaceutically acceptable vehicle chosen from carriers, adjuvants, and excipients.

92. A pharmaceutical composition of claim 91, wherein the composition is formulated in a form chosen from injectable fluids, aerosols, creams, gels, tablets, pills, capsules, syrups, ophthalmic solutions, and transdermal patches.

93. A packaged pharmaceutical composition, comprising
a pharmaceutical composition of claim 91 or 92; and
instructions for using the composition to treat a patient suffering from a disease responsive to inhibition of Btk activity.

94. The packaged pharmaceutical composition of claim 93 wherein the disease responsive to inhibition of Btk activity is cancer.

95. The packaged pharmaceutical composition of claim 93 wherein the disease responsive to inhibition of Btk activity is chosen from allergic disorders, autoimmune diseases, inflammatory diseases, and acute inflammatory reactions.

96. A method for treating a patient having a disease responsive to inhibition of Btk activity, comprising administering to the patient an effective amount of at least one chemical entity of any of claims 10 to 90.

97. The method of claim 96 wherein the patient is a human.

98. The method of claim 96 wherein the patient is chosen from cats and dogs.

99. The method of any one of claims 96 to 98 wherein the disease responsive to inhibition of Btk activity is cancer.

100. The method of claim 99 wherein the disease responsive to inhibition of Btk activity is B-cell lymphoma and leukemia.

101. The method of any one of claims 96 to 100 wherein an effective amount of said at least one chemical entity is administered by a method chosen from intravenously, intramuscularly, and parenterally.

102. The method of any of claims 96 to 100 wherein an effective amount of said at least one chemical entity is administered orally.

103. A method for treating a patient having a disease chosen from cancer, autoimmune diseases, inflammatory diseases, acute inflammatory reactions, and allergic disorders comprising administering to the patient an effective amount of at least one chemical entity of any of claims 10 to 90.

104. The method of claim 103 wherein the patient is a human.

105. The method of claim 103 wherein the patient is chosen from cats and dogs.

106. The method of any one of claims 104 to 106 wherein an effective amount of said at least one chemical entity is administered by a method chosen from intravenously, intramuscularly, and parenterally.

107. The method of any of claims 103 to 105 wherein an effective amount of said at least one chemical entity is administered orally.

108. A method for increasing sensitivity of cancer cells to chemotherapy, comprising administering to a patient undergoing chemotherapy with a chemotherapeutic agent an amount of at least one chemical entity of any of claims 10 to 90, sufficient to increase the sensitivity of cancer cells to the chemotherapeutic agent.

109. A method of reducing medication error and enhancing therapeutic compliance of a patient being treated for a disease responsive to inhibition of Btk activity, the method comprising providing a packaged pharmaceutical preparation of claim 93

wherein the instructions additionally include contraindication and adverse reaction information pertaining to the packaged pharmaceutical composition.

110. A method for inhibiting ATP hydrolysis, the method comprising contacting cells expressing Btk with at least one chemical entity of any one of claims 10 to 90 in an amount sufficient to detectably decrease the level of ATP hydrolysis *in vitro*.

111. The method of claim 110 wherein the cells are present in a mammal.

112. The method of claim 111 wherein the mammal is a human.

113. The method of claim 111 wherein the mammal is chosen from cats and dogs.

114. A method for determining the presence of Btk in a sample, comprising contacting the sample with at least one chemical entity of any one of claims 10 to 90 under conditions that permit detection of Btk activity, detecting a level of Btk activity in the sample, and therefrom determining the presence or absence of Btk in the sample.

115. A method for inhibiting B-cell activity comprising contacting cells expressing Btk with at least one chemical entity, of any one of claims 10 to 90, in an amount sufficient to detectably decrease B-cell activity *in vitro*.