(54) Title: BCL-2-SELECTIVE APOPTOSIS-INDUCING AGENTS FOR THE TREATMENT OF CANCER AND IMMUNE DISEASES

Disclosed are compounds of formula (I) which inhibit the activity of anti-apoptotic Bcl-2 or Bcl-xL proteins, compositions containing the compounds and methods of treating diseases during which are expressed anti-apoptotic Bcl-2 protein.

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Title: SULFONAMIDE DERIVATIVES AS BCL-2-SELECTIVE APOPTOSIS-INDUCING AGENTS FOR THE TREATMENT OF CANCER AND IMMUNE DISEASES

Abstract: Disclosed are compounds of formula (I) which inhibit the activity of anti-apoptotic Bcl-2 or Bcl-xL proteins, compositions containing the compounds and methods of treating diseases during which are expressed anti-apoptotic Bcl-2 protein.
DEMANDES OU BREVETS VOLUMINEUX

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CECI EST LE TOME _1_ DE _3_

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JUMBO APPLICATIONS / PATENTS

THIS SECTION OF THE APPLICATION / PATENT CONTAINS MORE THAN ONE VOLUME.

THIS IS VOLUME _1_ OF _3_

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BCL-2-SELECTIVE APOPTOSIS-INDUCING AGENTS FOR THE TREATMENT OF CANCER AND IMMUNE DISEASES

FIELD OF THE INVENTION

This invention pertains to compounds which selectively inhibit the activity of anti-apoptotic Bcl-2 family proteins, compositions containing the compounds, and methods of treating diseases during which anti-apoptotic Bcl-2 proteins are expressed.

BACKGROUND OF THE INVENTION

Anti-apoptotic Bcl-2 family proteins are associated with a number of diseases and are under investigation as potential therapeutic drug targets. These targets for interventional therapy include, for example, the Bcl-2 family proteins Bcl-2, Bcl-X\textsubscript{L} and Bcl-w. Recently, inhibitors of Bcl-2 family proteins have been reported in commonly-owned PCT/US/2004/36770, published as WO 2005/049593 and PCT/US/2004/367911, published as WO 2005/049594. While this art teaches inhibitors having high binding to the target protein, compound binding affinity is only one of many parameters to be considered. One goal is to produce compounds that preferentially bind to, that is, are selective for, one protein over another protein. To exhibit this selectivity, it is well known that a compound not only displays a high binding affinity to a particular protein but a lower binding affinity for another member as well.

A typical measure of binding affinity of an anti-apoptotic protein inhibitor is the balance between the binding and dissociation processes between the protein and the inhibitor (K\textsubscript{i}). The inhibition constant (K\textsubscript{i}) is the dissociation constant of an enzyme-inhibitor complex or a protein/small molecule complex, wherein the small molecule is inhibiting binding of one protein to another protein. So a large K\textsubscript{i} value indicates a low binding affinity, and a small K\textsubscript{i} value indicates a high binding affinity.

A typical measure of cellular activity of an anti-apoptotic protein inhibitor is the concentration eliciting 50% cellular effect (EC\textsubscript{50}).
Accordingly, the inventors have discovered that while compounds taught in the art have utility for the treatment of various cancers and immune diseases, they are not selective for anti-apoptotic Bcl-2 proteins over anti-apoptotic Bcl-X<sub>L</sub> proteins and thereby result in a higher probability of side effects characterized by inhibition of anti-apoptotic Bcl-X<sub>L</sub> proteins such as, thrombocytopenia.

This invention therefore comprises a series of compounds that demonstrate unexpected properties with respect to their selectivity for binding to, and inhibiting the activity of anti-apoptotic Bcl-2 protein over anti-apoptotic Bcl-X<sub>L</sub> protein as significantly higher than those of the compounds taught in PCT/US/2004/36770 and PCT/US/2004/367911.

**SUMMARY OF THE INVENTION**

One embodiment of this invention, therefore, pertains to compounds or therapeutically acceptable salts, prodrugs or salts of prodrugs thereof, which are useful as selective inhibitors one or more than one anti-apoptotic protein family member, the compounds having Formula (I)

![Chemical Structure](image)

wherein A<sup>1</sup> is N or C(A<sup>2</sup>);

one or two or three or each of A<sup>2</sup>, B<sup>1</sup>, D<sup>1</sup> and E<sup>1</sup> are independently selected R<sup>1</sup>, OR<sup>1</sup>, SR<sup>1</sup>, S(O)R<sup>1</sup>, SO<sub>2</sub>R<sup>1</sup>, C(O)R<sup>1</sup>, C(O)OR<sup>1</sup>, OC(O)R<sup>1</sup>, NHR<sup>1</sup>, N(R<sup>1</sup>)<sub>2</sub>, C(O)NHR<sup>1</sup>, C(O)N(R<sup>1</sup>)<sub>2</sub>, NHC(O)R<sup>1</sup>, NHC(O)OR<sup>1</sup>, NR<sup>1</sup>C(O)NHR<sup>1</sup>, NR<sup>1</sup>C(O)N(R<sup>1</sup>)<sub>2</sub>, SO<sub>2</sub>NHR<sup>1</sup>, SO<sub>2</sub>N(R<sup>1</sup>)<sub>2</sub>, NHSO<sub>2</sub>R<sup>1</sup>, NHSO<sub>2</sub>NHR<sup>1</sup> or N(CH<sub>3</sub>)SO<sub>2</sub>N(CH<sub>3</sub>)R<sup>1</sup>, and the remainder are independently selected H, F, Cl, Br, I, CN, CF<sub>3</sub>, C(O)OH, C(O)NH<sub>2</sub> or C(O)OR<sup>1A</sup>; and

Y<sup>1</sup> is H, CN, NO<sub>2</sub>, C(O)OH, F, Cl, Br, I, CF<sub>3</sub>, OCF<sub>3</sub>, CF<sub>2</sub>CF<sub>3</sub>, OCF<sub>2</sub>CF<sub>3</sub>, R<sup>17</sup>, OR<sup>17</sup>, C(O)R<sup>17</sup>, C(O)OR<sup>17</sup>, SR<sup>17</sup>, NH<sub>2</sub>, NHR<sup>17</sup>, N(R<sup>17</sup>)<sub>2</sub>, NHC(O)R<sup>17</sup>, C(O)NH<sub>2</sub>, C(O)NH<sub>R</sub><sup>17</sup>, C(O)N(R<sup>17</sup>)<sub>2</sub>, NHS(O)R<sup>17</sup> or NHSO<sub>2</sub>R<sup>17</sup>;

or

B<sup>1</sup> and Y<sup>1</sup>, together with the atoms to which they are attached, are imidazole or triazole; and

- 2 -
one or two or each of A, D and E are independently selected R, OR, SR,
S(O)R, SO₂R, C(O)R, C(OR), OC(O)R, NHR, N(R)₂, C(O)NHR, C(O)N(R),
NHC(O)R, NHC(O)OR, NHC(O)NHR, N(CH₂)₂C(O)N(CH₃)R, SO₂NHR, SO₂N(R),
NH₂SO₂R, NH₂SO₂NHR, or N(CH₃)SO₂N(CH₃)R, and the remainder are independently
selected H, F, Cl, Br, I, CF₃, C(O)OH, C(O)NH₂ or C(O)OR₁, A;
R₁ is R₂, R₃, R₄ or R₅;
R₁A is C₁-C₆-alkyl, C₃-C₆-alkenyl or C₅-C₆-alkynyl;
R₂ is phenyl which is unfused or fused with arene, heteroarene or R²A; R²A is
cycloalkane or heterocycloalkane;
R₃ is heteroaryl which is unfused or fused with benzene, heteroarene or R³A; R³A is
cycloalkane or heterocycloalkane;
R₄ is cycloalkyl, cycloalkenyl, heterocycloalkyl or heterocycloalkenyl, each of which
is unfused or fused with arene, heteroarene or R⁴A; R⁴A is cycloalkane, cycloalkene,
heterocycloalkane or heterocycloalkene;
R₅ is alkyl, alkenyl or alkylnyl, each of which is unsubstituted or substituted with one
or two or three independently selected R, NC(R₆A)(R₆B), R₇, OR, SR, S(O)R, SO₂R,
NHR, N(R)₂, C(O)R, C(O)NH₂, C(O)NHR, NHC(O)R, NH₂SO₂R, NH₃C(O)R,
SO₂NH₂, SO₂NHR, SO₂N(R)₂, NH₂C(O)NH₂, NH₂C(O)NH₃R,
NH₂C(O)CH(CH₃)NH₂C(O)CH(CH₃)NH₂, NH₂C(O)CH(CH₃)NH₂C(O)CH(CH₃)NH₃R, OH,
(O), C(O)OH, (O), N₃, CN, NH₂, CF₃, CF₂CF₃, F, Cl, Br or I substituents;
R₆ is C₂-C₅-spiroalkyl, each of which is unsubstituted or substituted with OH, (O),
N₃, CN, CF₃, CF₂CF₃, F, Cl, Br, I, NH₂, NH(CH₃) or N(CH₃)₂;
R₆A and R₆B are independently selected alkyl or, together with the to which they
are attached, R₆C;
R₆C is aziridin-1-yl, azetidin-1-yl, pyrrolidin-1-yl or piperidin-1-yl, each having one
CH₂ moiety unreplaced or replaced with O, C(O), CNOH, CNOCH₂, S, S(O), SO₂ or NH;
R₇ is R₈, R₉, R₁₀ or R₁₁;
R₈ is phenyl which is unfused or fused with arene, heteroarene or R₈A;
R₈A is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;
R^9 is heteroaryl which is unfused or fused with arene, heteroarene or R^{9A}; R^{9A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R^{10} is C_3-C_{10}-cycloalkyl or C_4-C_{10}-cycloalkynyl, each having one or two CH_2 moieties unreplaced or replaced with independently selected O, C(O), CNOH, CNOCH_3, S, S(O), SO_2 or NH and one or two CH moieties unreplaced or replaced with N, and each of which is unfused or fused with arene, heteroarene or R^{10A}; R^{10A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R^{11} is alkyl, alkenyl or alkynyl, each of which is unsubstituted or substituted with one or two or three independently selected R^{12}, OR^{12}, NHR^{12}, N(R^{12})_2, C(O)NH_2, C(O)NHR^{12}, C(O)N(R^{12})_2, OH, (O), C(O)OH, N_3, CN, NH_2, CF_3, CF_2CF_3, F, Cl, Br or I substituents;

R^{12} is R^{13}, R^{14}, R^{15} or R^{16};

R^{13} is phenyl which is unfused or fused with arene, heteroarene or R^{13A}; R^{13A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R^{14} is heteroaryl, each of which is unfused or fused with arene, heteroarene or R^{14A};

R^{14A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R^{15} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene, each of which is unfused or fused with arene, heteroarene or R^{15A}; R^{15A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R^{16} is alkyl, alkenyl or alkynyl;

R^{17} is R^{18}, R^{19}, R^{20} or R^{21};

R^{18} is phenyl which is unfused or fused with arene, heteroarene or R^{18A}; R^{18A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R^{19} is heteroaryl which is unfused or fused with arene, heteroarene or R^{19A}; R^{19A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R^{20} is C_3-C_{10}-cycloalkyl or C_4-C_{10}-cycloalkynyl, each having one or two CH_2 moieties unreplaced or replaced with independently selected O, C(O), CNOH, CNOCH_3, S, S(O), SO_2 or NH and one or two CH moieties unreplaced or replaced with N, and each of which is unfused or fused with arene, heteroarene or R^{20A}; R^{20A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;
R\textsuperscript{21} is alkyl, alkenyl or alkynyl, each of which is unsubstituted or substituted with one or two or three independently selected R\textsuperscript{22}, OR\textsuperscript{22}, NHR\textsuperscript{22}, N(R\textsuperscript{22})\textsubscript{2}, C(O)NH\textsubscript{2}, C(O)NHR\textsuperscript{22}, C(O)N(R\textsuperscript{22})\textsubscript{2}, OH, (O), C(O)OH, N\textsubscript{3}, CN, NH\textsubscript{2}, CF\textsubscript{3}, CF\textsubscript{2}CF\textsubscript{3}, F, Cl, Br or I substituents;
R\textsuperscript{22} is R\textsuperscript{23}, R\textsuperscript{24} or R\textsuperscript{25};

R\textsuperscript{23} is phenyl which is unfused or fused with arene, heteroarene or R\textsuperscript{23A}; R\textsuperscript{23A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R\textsuperscript{24} is heteroarene which is unfused or fused with arene, heteroarene or R\textsuperscript{24A}; R\textsuperscript{24A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R\textsuperscript{25} is C\textsubscript{3}-C\textsubscript{5}-cycloalkyl or C\textsubscript{4}-C\textsubscript{5}-cycloalkenyl, each having one or two CH\textsubscript{2} moieties unreplaced or replaced with independently selected O, C(O), CNOH, CNOCH\textsubscript{3}, S, S(O), SO\textsubscript{2} or NH and one or two CH moieties unreplaced or replaced with N, and each of which is unfused or fused with arene, heteroarene or R\textsuperscript{25A}; R\textsuperscript{25A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

Z\textsuperscript{1} is R\textsuperscript{26} or R\textsuperscript{27}, each of which is substituted with R\textsuperscript{28}, R\textsuperscript{29} or R\textsuperscript{30}, each of which is substituted with F, Cl, Br, I, CH\textsubscript{2}R\textsuperscript{37}, CH(R\textsuperscript{31})(R\textsuperscript{37}), C(R\textsuperscript{31})(R\textsuperscript{31A})(R\textsuperscript{37}), C(O)R\textsuperscript{37}, OR\textsuperscript{37}, SR\textsuperscript{37}, S(O)R\textsuperscript{37}, SO\textsubscript{2}R\textsuperscript{37}, NHR\textsuperscript{37} or N(R\textsuperscript{32})R\textsuperscript{37};

R\textsuperscript{26} is phenyl which is unfused or fused with arene or heteroarene;

R\textsuperscript{27} is heteroarene which is unfused or fused with arene or heteroarene;

R\textsuperscript{28} is phenyl which is unfused or fused with arene, heteroarene or R\textsuperscript{28A}; R\textsuperscript{28A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R\textsuperscript{29} is heteroaryl or R\textsuperscript{29A}; R\textsuperscript{29A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R\textsuperscript{30} is cycloalkyl or cycloalkenyl, each having one or two CH\textsubscript{2} moieties unreplaced or replaced with independently selected O, C(O), CNOH, CNOCH\textsubscript{3}, S, S(O), SO\textsubscript{2} or NH and one or two CH moieties unreplaced or replaced with N, and each of which is unfused or fused with arene, heteroarene or R\textsuperscript{30A}; R\textsuperscript{30A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R\textsuperscript{31} and R\textsuperscript{31A} are independently F, Cl, Br or alkyl or are taken together and are C\textsubscript{2}-C\textsubscript{5}-spiroalkyl;

R\textsuperscript{32} is R\textsuperscript{33}, C(O)R\textsuperscript{33} or C(O)OR\textsuperscript{33};
\( R^{33} \) is \( R^{34} \) or \( R^{35} \);

\( R^{34} \) is phenyl which is unfused or fused with aryl, heteroaryl or \( R^{34A} \); \( R^{34A} \) is
cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

\( R^{35} \) is alkyl which is unsubstituted or substituted with \( R^{36} \);

\( R^{36} \) is phenyl which is unfused or fused with arene, heteroarene or \( R^{36A} \); \( R^{36A} \) is
cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

\( R^{37} \) is \( R^{38} \), \( R^{39} \) or \( R^{40} \), each of which is substituted with F, Cl, Br, I, \( R^{41} \), OR, \( R^{41} \),
NHR, \( N(R^{41})_2 \), NHC(O)OR, SR, S(O)R, or SO2R;

\( R^{38} \) is phenyl which is unfused or fused with arene, heteroarene or \( R^{38A} \); \( R^{38A} \) is
cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

\( R^{39} \) is heteroaryl which is unfused or fused with arene, heteroarene or \( R^{39A} \); \( R^{39A} \) is
cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

\( R^{40} \) is C3-C8-cycloalkyl or C4-C8-cycloalkenyl, each having one or two CH2 moieties
unreplaced or replaced with independently selected O, C(O), CNOH, CNOCH3, S, S(O), SO2
or NH and one or two CH moieties unreplaced or replaced with N, and each of which is
unfused or fused with arene, heteroarene or \( R^{40A} \); \( R^{40A} \) cycloalkane, cycloalkene,
heterocycloalkane or heterocycloalkene;

\( R^{41} \) is \( R^{42} \), \( R^{43} \), \( R^{44} \) or \( R^{45} \);

\( R^{42} \) is phenyl which is unfused or fused with arene, heteroarene or \( R^{42A} \); \( R^{42A} \) is
cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

\( R^{43} \) is heteroaryl which is unfused or fused with arene, heteroarene or \( R^{43A} \); \( R^{43A} \) is
cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

\( R^{44} \) is C3-C9-cycloalkyl or C4-C7-cycloalkenyl, each having one or two CH2 moieties
unreplaced or replaced with independently selected O, C(O), CNOH, CNOCH3, S, S(O), SO2
or NH and one or two CH moieties unreplaced or replaced with N, and each of which is
unfused or fused with arene, heteroarene or \( R^{44A} \); \( R^{44A} \) is cycloalkane, cycloalkene,
heterocycloalkane or heterocycloalkene;

\( R^{45} \) is alkyl, alkenyl or alkynyl, each of which is unsubstituted or substituted with one
or two independently selected \( R^{46} \), OR, \( R^{46} \), NHR, \( N(R^{46})_2 \), C(O)NH2, C(O)NHR,
C(O)N(R^{46})_2, OH, (O), C(O)OH, N3, CN, NH2, CF3, CF2CF3, F, Cl, Br or I substituents;
R^{46} is R^{47}, R^{48} or R^{49};

R^{47} is phenyl which is unfused or fused with arene, heteroarene or R^{47A}; R^{47A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R^{48} is heteroaryl or R^{48A}; R^{48A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R^{49} is C_{3}-C_{6}-cycloalkyl or C_{4}-C_{6}-cycloalkenyl, each having one or two CH_{2} moieties unreplaced or replaced with independently selected O, C(O), CNOH, CNOCH_{3}, S, S(O), SO_{2} or NH and one or two CH moieties unreplaced or replaced with N, and each of which is unfused or fused with arene, heteroarene or R^{49A}; R^{49A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

wherein the moieties represented by R^{26} and R^{27} are further substituted by one or two or three of independently selected R^{50A}, OR^{50A}, SR^{50A}, S(O)R^{50A}, SO_{2}R^{50A} or NHR^{50A}; R^{50A} is R^{51A}, R^{52A}, R^{53A} or R^{54A};

R^{51A} is phenyl which is unfused or fused with benzene, heteroarene or R^{51AA},

wherein R^{51AA} is cycloalkane, cycloalkene or heterocycloalkane heterocycloalkene,

R^{52A} is heteroaryl;

R^{53A} is C_{3}-C_{6}-cycloalkyl or C_{4}-C_{6}-cycloalkenyl; each having one or two CH_{2} moieties unreplaced or replaced with independently selected O, C(O), CNOH, CNOCH_{3}, S, S(O), SO_{2} or NH and one or two CH moieties unreplaced or replaced with N, and each of which is unfused or fused with arene, heteroarene or R^{53AA};

wherein R^{53AA} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R^{54A} is alkyl, alkenyl or alkynyl, each of which is unsubstituted or substituted with one or two or three of independently selected R^{55AA}, OR^{55AA}, SR^{55AA}, S(O)R^{55AA}, SO_{2}R^{55AA}, NHR^{55AA}, N(R^{55AA})_{2}, C(O)R^{55AA}, C(O)NH_{2}, C(O)NHR^{55AA}, NHC(O)R^{55AA},

NH_{2}, NHC(O)OR^{55AA}, SO_{2}NH_{2}, SO_{2}NHR^{55AA}, SO_{2}N(R^{55AA})_{2}, NHC(O)NH_{2},

NHC(O)NHR^{55AA}, OH, (O), C(O)OH, (O), N_{3}, CN, NH_{2}, CF_{3}, OC_{3}, CF_{2}CF_{3}, OCF_{3}, Cl, Br or I substituents;

R^{55AA} is alkyl, alkenyl, alkynyl, phenyl or heteroaryl, or R^{56A};
R^{56A} is C₃-C₆-cycloalkyl or C₄-C₆-cycloalkyl, each having one or two CH₂ moieties unreplaced or replaced with independently selected O, C(O), CONH, CONOCH₃, S, S(O), SO₂ or NH and one or two CH moieties unreplaced or replaced with N;

wherein moieties represented by R² R³ R⁴ R⁶ R⁸ R⁸A R⁹ R¹⁰ R¹³ R¹⁴ R¹⁵ R¹⁸ R¹⁹ R²⁰ R²³ R²⁴ R²⁵ R²⁶ R²⁷ R²⁸ R²⁹ R³⁰ R³⁴ R³⁶ R³⁸ R³⁹ R⁴⁰ R⁴² R⁴³ R⁴⁴ R⁴⁷ R⁴⁸ and R⁴⁹ are independently unsubstituted, further independently unsubstituted, substituted or further substituted with one or two or three or four or five independently selected R⁵⁰, OR⁵⁰, SR⁵⁰, S(O)R⁵⁰, SO₂R⁵⁰, C(O)R⁵⁰, CO(O)R⁵⁰, OC(O)R⁵⁰, OC(O)OR⁵⁰, NH₂, NHR⁵⁰, N(R⁵⁰)₂, C(O)NH₂, C(O)NHR⁵⁰, C(O)N(R⁵⁰)₂, C(O)NHOH, C(O)NHor⁵⁰, C(O)NSO₂R⁵⁰, C(O)NR⁵⁵ SO₂R⁵⁰, SO₂NH₂, SO₂NHR⁵⁰, SO₂N(R⁵⁰)₂, CF₃, CF₂CF₃, C(O)H, C(O)OH, C(N)NH₂, C(N)NHR⁵⁰, C(N)N(R⁵⁰)₂, OH, (O), CN, N₃, NO₂, CF₃, CF₂CF₃, OCF₃, OCF₂CF₃, F, Cl, Br or I substituents;

R⁵₀ is R⁵¹, R⁵², R⁵³ or R⁵⁴;

R⁵¹ is phenyl which is unfused or fused with arene, heteroarene or R⁵¹B; R⁵¹B is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R⁵² is heteroaryl;

R⁵³ is C₃-C₆-cycloalkyl or C₄-C₆-cycloalkenyl, each having one or two CH₂ moieties unreplaced or replaced with independently selected O, C(O), CONH, CONOCH₃, S, S(O), SO₂ or NH and one or two CH moieties unreplaced or replaced with N, and each of which is unfused or fused with arene, heteroarene or R⁵³B;

wherein R⁵³B is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R⁵⁴ is alkyl, alkenyl or alkynyl, each of which is unsubstituted or substituted with one or two or three independently selected R⁵⁵, OR⁵⁵, SR⁵⁵, S(O)R⁵⁵, SO₂R⁵⁵, NHR⁵⁵, N(R⁵⁵)₂, C(O)R⁵⁵, C(O)NH₂, C(O)NHR⁵⁵, NHC(O)R⁵⁵, NH₂SO₂R⁵⁵, NH₂NHR⁵⁵, SO₂NHR⁵⁵, SO₂N(R⁵⁵)₂, NH₂, CF₃, OCF₃, CF₂CF₃, OCF₂CF₃, F, Cl, Br or I substituents;

R⁵⁵ is alkyl, alkenyl, alkynyl, phenyl, heteroaryl or R⁵⁶;

wherein the alkyl, alkenyl, alkynyl are unsubstituted or substituted with OCH₃; and
R^{56} is C₃-C₈-cycloalkyl or C₄-C₆-cycloalkenyl, each having one or two CH₂ moieties unreplaced or replaced with independently selected O, C(O), CNOH, CNOCH₃, S, S(O), SO₂ or NH and one or two CH moieties unreplaced or replaced with N.

Another embodiment of this invention pertains to compounds or therapeutically acceptable salts, prodrugs or salts of prodrugs thereof, which are useful as selective inhibitors of anti-apoptotic Bcl-2 proteins, the compounds having Formula (II)

![Chemical Structure](image)

(II),

wherein

R^{100} is as described for substituents on R^{26};

n is 0, 1, 2, or 3;

A¹ is N or C(A²);

one or two or three or each of A², B¹, D¹ and E¹ are independently selected R¹, OR¹, SR¹, S(O)R¹, SO₂R¹, C(O)R¹, C(O)OR¹, OC(O)R¹, NHR¹, N(R¹)₂, C(O)NHR¹, C(O)N(R¹)₂, NHC(O)R¹, NHC(O)OR¹, NR¹C(O)NHR¹, NR¹C(O)N(R¹)₂, SO₂NHR¹, SO₂N(R¹)₂, NH₂SO₂R¹, NH₂SO₂NHR¹ or N(CH₃)SO₂N(CH₃)R¹, and the remainder are independently selected H, F, Cl, Br, I, CN, CF₃, C(O)OH, C(O)NH₂ or C(O)OR¹A; and

Y¹ is H, CN, NO₂, C(O)OH, F, Cl, Br, I, CF₃, OCF₃, CF₂CF₃, OCF₂CF₃, R¹⁷, OR¹⁷, C(O)R¹⁷, C(O)OR¹⁷, SR¹⁷, NH₂, NHR¹⁷, N(R¹⁷)₂, NH₂(OH), C(O)NH₂, C(O)NHR¹⁷, C(O)N(R¹⁷)₂, NHS(O)R¹⁷ or NH₂SO₂R¹⁷;

or

B¹ and Y¹, together with the atoms to which they are attached, are imidazole or triazole; and
one or two or each of A², D¹ and E¹ are independently selected R¹, OR¹, SR¹, 
S(O)R¹, SO₂R¹, C(O)R¹, C(O)OR¹, OC(O)R¹, NHR¹, N(R¹)₂, C(O)NHR¹, C(O)N(R¹)₂, 
NHC(O)R¹, NHC(O)OR¹, NHC(O)NHR¹, N(CH₃)C(O)N(CH₃)R¹, SO₂NHR¹, SO₂N(R¹)₂, 
NH(SO₂)R¹, NH(SO₂)NHR¹ or N(CH₃)SO₂N(CH₃)R¹, and the remainder are independently 
selected H, F, Cl, Br, I, CF₃, C(O)OH, C(O)NH₂ or C(O)OR¹A;

R¹ is R², R³, R⁴ or R⁵;
R¹A is C₁-C₆-alkyl, C₃-C₆-alkenyl or C₃-C₆-alkynyl;
R² is phenyl which is unfused or fused with arene, heteroarene or R²A; R²A is 
cycloalkane or heterocycloalkane;

R³ is heteroaryl which is unfused or fused with benzene, heteroarene or R³A; R³A is 
cycloalkane or heterocycloalkane;

R⁴ is cycloalkyl, cycloalkenyl, heterocycloalkyl or heterocycloalkenyl, each of which 
is unfused or fused with arene, heteroarene or R⁴A; R⁴A is cycloalkane, cycloalkene, 
heterocycloalkane or heterocycloalkene;

R⁵ is alkyl, alkenyl or alkynyl, each of which is unsubstituted or substituted with one 
or two or three independently selected R⁶, NC(R⁶'A)(R⁶'B), R⁷, OR⁷, SR⁷, S(O)R⁷, SO₂R⁷, 
NHR⁷, N(R⁷)₂, C(O)R⁷, C(O)NH₂, C(O)NHR⁷, NHC(O)R⁷, NH(SO₂)R⁷, NH(C(O)OR⁷, 
SO₂NH₂, SO₂NHR⁷, SO₂N(R⁷)₂, NHC(O)NH₂, NH(C(O)NHR⁷, 
NHC(O)CH(CH₃)NH(C(O)CH(CH₃)NH₂, NHC(O)CH(CH₃)NH(C(O)CH(CH₃)NH₃, NH(O), 
(O), C(O)OH, (O), N₃, CN, NH₂, CF₃, CF₂CF₃, F, Cl, Br or I substituents;

R⁶ is C₂-C₅-spiroalkyl, each of which is unsubstituted or substituted with OH, (O), 
N₃, CN, CF₃, CF₂CF₃, F, Cl, Br, I, NH₂, NH(CH₃) or N(CH₃)₂;

R⁶'A and R⁶'B are independently selected alkyl or, together with the N to which they 
are attached, R⁶'C;

R⁶'C is aziridin-1-y1, azetidin-1-yl, pyrrolidin-1-yl or piperidin-1-yl, each having one 
CH₂ moiety unreplaced or replaced with O, C(O), CNOH, CNOCH₃, S, S(O), SO₂ or NH;

R⁷ is R⁸, R⁹, R¹₀ or R¹₁;
R⁸ is phenyl which is unfused or fused with arene, heteroarene or R⁸'A;
R⁸'A is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;
$R^9$ is heteroaryl which is unfused or fused with arene, heteroarene or $R^{9A}$; $R^{9A}$ is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

$R^{10}$ is C$_3$-C$_{10}$-cycloalkyl or C$_4$-C$_{10}$-cycloalkenyl, each having one or two CH$_2$ moieties unreplaced or replaced with independently selected O, C(O), CNOH, CNOCH$_3$, S, S(O), SO$_2$ or NH and one or two CH moieties unreplaced or replaced with N, and each of which is unfused or fused with arene, heteroarene or $R^{10A}$; $R^{10A}$ is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

$R^{11}$ is alkyl, alkenyl or alkynyl, each of which is unsubstituted or substituted with one or two or three independently selected $R^{12}$, OR$^{12}$, NHR$^{12}$, N(R$^{12}$)$_2$, C(O)NH$_2$, C(O)NHR$^{12}$, C(O)N(R$^{12}$)$_2$, OH, (O), C(O)OH, N$_3$, CN, NH$_2$, CF$_3$, CF$_2$CF$_3$, F, Cl, Br or I substituents;

$R^{12}$ is $R^{13}$, $R^{14}$, $R^{15}$ or $R^{16}$;

$R^{13}$ is phenyl which is unfused or fused with arene, heteroarene or $R^{13A}$; $R^{13A}$ is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

$R^{14}$ is heteroaryl, each of which is unfused or fused with arene, heteroarene or $R^{14A}$;

$R^{14A}$ is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

$R^{15}$ is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene, each of which is unfused or fused with arene, heteroarene or $R^{15A}$; $R^{15A}$ is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

$R^{16}$ is alkyl, alkenyl or alkynyl;

$R^{17}$ is $R^{18}$, $R^{19}$, $R^{20}$ or $R^{21}$;

$R^{18}$ is phenyl which is unfused or fused with arene, heteroarene or $R^{18A}$; $R^{18A}$ is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

$R^{19}$ is heteroaryl which is unfused or fused with arene, heteroarene or $R^{19A}$; $R^{19A}$ is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

$R^{20}$ is C$_3$-C$_{10}$-cycloalkyl or C$_4$-C$_{10}$-cycloalkenyl, each having one or two CH$_2$ moieties unreplaced or replaced with independently selected O, C(O), CNOH, CNOCH$_3$, S, S(O), SO$_2$ or NH and one or two CH moieties unreplaced or replaced with N, and each of which is unfused or fused with arene, heteroarene or $R^{20A}$; $R^{20A}$ is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;
R^{21} is alkyl, alkenyl or alkynyl, each of which is unsubstituted or substituted with one or two or three independently selected R^{22}, OR^{22}, NHR^{22}, N(R^{22})_2, C(O)NH_2, C(O)NHR^{22}, C(O)N(R^{22})_2, OH, (O), C(O)OH, N_3, CN, NH_2, CF_3, CF_2CF_3, F, Cl, Br or I substituents; R^{22} is R^{23}, R^{24} or R^{25}; R^{23} is phenyl which is unfused or fused with arene, heteroarene or R^{23A}; R^{23A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene; R^{24} is heteroarene which is unfused or fused with arene, heteroarene or R^{24A}; R^{24A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene; R^{25} is C_3-C_6-cycloalkyl or C_4-C_6-cycloalkenyl, each having one or two CH_2 moieties unreplaced or replaced with independently selected O, C(O), CNOH, CNOCH_3, S, S(O), SO_2 or NH and one or two CH moieties unreplaced or replaced with N, and each of which is unfused or fused with arene, heteroarene or R^{25A}; R^{25A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene; R^{30} is cycloalkyl or cycloalkenyl, each having one or two CH_2 moieties unreplaced or replaced with independently selected O, C(O), CNOH, CNOCH_3, S, S(O), SO_2 or NH and one or two CH moieties unreplaced or replaced with N, and each of which is unfused or fused with arene, heteroarene or R^{30A}; R^{30A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene; each of which is substituted with F, Cl, Br, I, CH_2R^{37}, CH(R^{31})(R^{37}), C(R^{31})(R^{31A})(R^{37}), C(O)R^{37}, OR^{37}, SR^{37}, S(O)R^{37}, SO_2R^{37}, NHR^{37} or N(R^{32})R^{37}; R^{31} and R^{31A} are independently F, Cl, Br or alkyl or are taken together and are C_2-C_5-spiroalkyl; R^{32} is R^{33}, C(O)R^{33} or C(O)OR^{33}; R^{33} is R^{34} or R^{35}; R^{34} is phenyl which is unfused or fused with aryl, heteroaryl or R^{34A}; R^{34A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene; R^{35} is alkyl which is unsubstituted or substituted with R^{36}; R^{36} is phenyl which is unfused or fused with arene, heteroarene or R^{36A}; R^{36A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene; R^{37} is R^{38}, R^{39} or R^{40}, each of which is substituted with F, Cl, Br, I, R^{41}, OR^{41}, NHR^{41}, N(R^{41})_2, NHC(O)OR^{41}, SR^{41}, S(O)R^{41} or SO_2R^{41};
R^{38} is phenyl which is unfused or fused with arene, heteroarene or R^{38A}; R^{38A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R^{39} is heteroaryl which is unfused or fused with arene, heteroarene or R^{39A}; R^{39A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R^{40} is C_{3-8}-cycloalkyl or C_{4-8}-cycloalkenyl, each having one or two CH2 moieties unreplaced or replaced with independently selected O, C(O), CNOH, CNOCH_3, S, S(O), SO_2 or NH and one or two CH moieties unreplaced or replaced with N, and each of which is unfused or fused with arene, heteroarene or R^{40A}; R^{40A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R^{41} is R^{42}, R^{43}, R^{44} or R^{45};

R^{42} is phenyl which is unfused or fused with arene, heteroarene or R^{42A}; R^{42A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R^{43} is heteroaryl which is unfused or fused with arene, heteroarene or R^{43A}; R^{43A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R^{44} is C_{3-9}-cycloalkyl or C_{4-7}-cycloalkenyl, each having one or two CH2 moieties unreplaced or replaced with independently selected O, C(O), CNOH, CNOCH_3, S, S(O), SO_2 or NH and one or two CH moieties unreplaced or replaced with N, and each of which is unfused or fused with arene, heteroarene or R^{44A}; R^{44A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R^{45} is alkyl, alkenyl or alkynyl, each of which is unsubstituted or substituted with one or two independently selected R^{46}, OR^{46}, NHR^{46}, N(R^{46})_2, C(O)NH_2, C(O)NHR^{46}, C(O)N(R^{46})_2, OH, (O), C(O)OH, N_3, CN, NH_2, CF_3, CF_2CF_3, F, Cl, Br or I substituents;

R^{46} is R^{47}, R^{48} or R^{49};

R^{47} is phenyl which is unfused or fused with arene, heteroarene or R^{47A}; R^{47A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R^{48} is heteroaryl or R^{48A}; R^{48A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R^{49} is C_{3-6}-cycloalkyl or C_{4-6}-cycloalkenyl, each having one or two CH2 moieties unreplaced or replaced with independently selected O, C(O), CNOH, CNOCH_3, S, S(O), SO_2 or NH and one or two CH moieties unreplaced or replaced with N, and each of which is
unfused or fused with arene, heteroarene or R^{49A}; R^{49A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

wherein moieties represented by R^2, R^3, R^4, R^6, R^{6C}, R^8, R^{8A}, R^9, R^{10}, R^{13}, R^{14}, R^{15}, R^{18}, R^{19}, R^{20}, R^{23}, R^{24}, R^{25}, R^{26}, R^{27}, R^{28}, R^{29}, R^{30}, R^{34}, R^{36}, R^{38}, R^{39}, R^{40}, R^{42}, R^{43}, R^{44}, R^{47}, R^{48}, and R^{49} are independently unsubstituted, further unsubstituted, substituted or further substituted with one or two or three or four or five independently selected R^{50}, OR^{50}, SR^{50}, S(O)R^{50}, SO_2R^{50}, C(O)R^{50}, CO(O)R^{50}, OC(O)R^{50}, OC(O)OR^{50}, NH_2, NHR^{50}, N(R^{50})_2, C(O)NH_2, C(O)NHR^{50}, C(O)N(R^{50})_2, C(O)NHOH, C(O)NHOR^{50}, C(O)NHOSO_2R^{50}, C(O)NR^{55}SO_2R^{50}, SO_2NH_2, SO_2NHR^{50}, SO_2N(R^{50})_2, CF_3, CF_2CF_3, C(O)H, C(O)OH, C(N)NH_2, C(N)NHR^{50}, C(N)N(R^{50})_2, OH, (O), CN, N_3, NO_2, CF_3, CF_2CF_3, OCF_3, OCF_2CF_3, F, Cl, Br or I substituents;

R^{50} is R^{51}, R^{52}, R^{53} or R^{54};

R^{51} is phenyl which is unfused or fused with arene, heteroarene or R^{51B}; R^{51B} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R^{52} is heteroaryl;

R^{53} is C_3-C_6-cycloalkyl or C_4-C_6-cycloalkenyl, each having one or two CH_2 moieties unreplaced or replaced with independently selected O, C(O), CNOH, CNOCH_3, S, S(O), SO_2 or NH and one or two CH moieties unreplaced or replaced with N, and each of which is unfused or fused with arene, heteroarene or R^{53B};

wherein R^{53B} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R^{54} is alkyl, alkenyl or alkynyl, each of which is unsubstituted or substituted with one or two or three independently selected R^{55}, OR^{55}, SR^{55}, S(O)R^{55}, SO_2R^{55}, NHR^{55}, N(R^{55})_2, C(O)R^{55}, C(O)NH_2, C(O)NHR^{55}, NHC(O)R^{55}, NHSO_2R^{55}, NHC(O)OR^{55}, SO_2NH_2, SO_2NHR^{55}, SO_2N(R^{55})_2, NHCOH(NH_2), NHCOH(NHR^{55}, OH, (O), C(O)OH, (O), N_3, CN, NH_2, CF_3, OCF_3, CF_2CF_3, OCF_2CF_3, F, Cl, Br or I substituents;

R^{55} is alkyl, alkenyl, alkynyl, phenyl, heteroaryl or R^{56};

wherein the alkyl, alkenyl, alkynyl are unsubstituted or substituted with OCH_3, and
R\textsuperscript{56} is C\textsubscript{3}-C\textsubscript{8}-cycloalkyl or C\textsubscript{4}-C\textsubscript{6}-cycloalkenyl, each having one or two CH\textsubscript{2} moieties unreplace or replaced with independently selected O, C(O), CNOH, CNOCH\textsubscript{3}, S, S(O), SO\textsubscript{2} or NH and one or two CH moieties unreplace or replaced with N.

Another embodiment of this invention pertains to compounds or therapeutically acceptable salts, prodrugs or salts of prodrugs thereof, which are useful as selective inhibitors of anti-apoptotic Bcl-2 proteins, the compounds having Formula (III)

\[
\text{Formula (III),}
\]

wherein

R\textsuperscript{100} is as described for substituents on R\textsuperscript{56};

n is 0, 1, 2, or 3;

A\textsuperscript{1} is N or C(A\textsuperscript{2});

one or two or three or each of A\textsuperscript{2}, B\textsuperscript{1}, D\textsuperscript{1} and E\textsuperscript{1} are independently selected R\textsuperscript{1}, OR\textsuperscript{1},

SR\textsuperscript{1}, S(O)R\textsuperscript{1}, SO\textsubscript{2}R\textsuperscript{1}, C(O)R\textsuperscript{1}, C(O)OR\textsuperscript{1}, OC(O)R\textsuperscript{1}, NHR\textsuperscript{1}, N(R\textsuperscript{1})\textsubscript{2}, C(O)NHR\textsuperscript{1}, C(O)N(R\textsuperscript{1})\textsubscript{2},

NHC(O)R\textsuperscript{1}, NHC(O)OR\textsuperscript{1}, NR\textsuperscript{1}C(O)NHR\textsuperscript{1}, NR\textsuperscript{1}C(O)N(R\textsuperscript{1})\textsubscript{2}, SO\textsubscript{2}NHR\textsuperscript{1}, SO\textsubscript{2}N(R\textsuperscript{1})\textsubscript{2},

NH\textsubscript{2}SO\textsubscript{2}R\textsuperscript{1}, NH\textsubscript{2}SO\textsubscript{2}NHR\textsuperscript{1} or N(CH\textsubscript{3})\textsubscript{2}SO\textsubscript{2}N(CH\textsubscript{3})R\textsuperscript{1}, and the remainder are independently selected H, F, Cl, Br, I, CN, CF\textsubscript{3}, C(O)OH, C(O)NH\textsubscript{2} or C(O)OR\textsuperscript{1A}; and

Y\textsuperscript{1} is H, CN, NO\textsubscript{2}, C(O)OH, F, Cl, Br, I, CF\textsubscript{3}, OCF\textsubscript{3}, CF\textsubscript{2}CF\textsubscript{3}, OCF\textsubscript{2}CF\textsubscript{3}, R\textsuperscript{17}, OR\textsuperscript{17},

C(O)R\textsuperscript{17}, C(O)OR\textsuperscript{17}, SR\textsuperscript{17}, NH\textsubscript{2}, NHR\textsuperscript{17}, N(R\textsuperscript{17})\textsubscript{2}, NHC(O)R\textsuperscript{17}, C(O)NH\textsubscript{2}, C(O)NHR\textsuperscript{17},

C(O)N(R\textsuperscript{17})\textsubscript{2}, NH\textsubscript{2}(O)R\textsuperscript{17} or NH\textsubscript{2}SO\textsubscript{2}R\textsuperscript{17};

or
B\(^1\) and Y\(^1\), together with the atoms to which they are attached, are imidazole or triazole; and

one or two or each of A\(^2\), D\(^1\) and E\(^1\) are independently selected R\(^1\), OR\(^1\), SR\(^1\), S(O)R\(^1\), SO\(_2\)R\(^1\), C(O)R\(^1\), C(OR)\(^1\), OC(O)R\(^1\), NHR\(^1\), N(R\(^1\))\(_2\), C(O)NHR\(^1\), C(O)N(R\(^1\))\(_2\), NHC(O)R\(^1\), NHC(O)OR\(^1\), NHC(O)NHR\(^1\), N(CH\(_3\))C(O)N(CH\(_3\))R\(^1\), SO\(_2\)NHR\(^1\), SO\(_2\)N(R\(^1\))\(_2\), NH\(_2\)SO\(_2\)R\(^1\), NH\(_2\)SO\(_2\)NHR\(^1\) or N(CH\(_3\))SO\(_2\)N(CH\(_3\))R\(^1\), and the remainder are independently selected H, F, Cl, Br, I, CF\(_3\), C(O)OH, C(O)NH\(_2\) or C(O)OR\(^1\)\(^A\);

R\(^1\) is R\(^2\), R\(^3\), R\(^4\) or R\(^5\);

R\(^1\)\(^A\) is C\(_1\)-C\(_6\)-alkyl, C\(_3\)-C\(_6\)-alkenyl or C\(_3\)-C\(_6\)-alkynyl;

R\(^2\) is phenyl which is unfused or fused with arene, heteroarene or R\(^2\)\(^A\); R\(^2\)\(^A\) is cycloalkane or heterocycloalkane;

R\(^3\) is heteroaryl which is unfused or fused with benzene, heteroarene or R\(^3\)\(^A\); R\(^3\)\(^A\) is cycloalkane or heterocycloalkane;

R\(^4\) is cycloalkyl, cycloalkenyl, heterocycloalkyl or heterocycloalkenyl, each of which is unfused or fused with arene, heteroarene or R\(^4\)\(^A\); R\(^4\)\(^A\) is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R\(^5\) is alkyl, alkenyl or alkynyl, each of which is unsubstituted or substituted with one or two or three independently selected R\(^6\), NC(R\(^6\)\(^A\))(R\(^6\)\(^B\)), R\(^7\), OR\(^7\), SR\(^7\), S(O)R\(^7\), SO\(_2\)R\(^7\), NHR\(^7\), N(R\(^7\))\(_2\), C(O)R\(^7\), C(O)NH\(_2\), C(O)NHR\(^7\), NHC(O)R\(^7\), NH\(_2\)SO\(_2\)R\(^7\), NH\(_2\)C(O)OR\(^7\), SO\(_2\)NH\(_2\), SO\(_2\)NHR\(^7\), SO\(_2\)N(R\(^7\))\(_2\), NH\(_2\)C(O)NH\(_2\), NH\(_2\)C(O)NHR\(^7\), NHC(O)CH(CH\(_3\))NHC(O)CH(CH\(_3\))NH\(_2\), NHC(O)CH(CH\(_3\))NHC(O)CH(CH\(_3\))NHR\(^1\), OH, (O), C(O)OH, (O), N\(_3\), CN, NH\(_2\), CF\(_3\), CF\(_2\)CF\(_3\), F, Cl, Br or I substituents;

R\(^6\) is C\(_2\)-C\(_5\)-spiroalkyl, each of which is unsubstituted or substituted with OH, (O), N\(_3\), CN, CF\(_3\), CF\(_2\)CF\(_3\), F, Cl, Br, I, NH\(_2\), NH(CH\(_3\)) or N(CH\(_3\))\(_2\);

R\(^6\)\(^A\) and R\(^6\)\(^B\) are independently selected alkyl or, together with the N to which they are attached, R\(^6\)\(^C\);

R\(^6\)\(^C\) is aziridin-1-yl, azetidin-1-yl, pyrrolidin-1-yl or piperidin-1-yl, each having one CH\(_2\) moiety unreplaced or replaced with O, C(O), CNOH, CNOCH\(_3\), S, S(O), SO\(_2\) or NH;

R\(^7\) is R\(^8\), R\(^9\), R\(^10\) or R\(^11\);
R⁸ is phenyl which is unfused or fused with arene, heteroarene or R⁸A;  
R⁸A is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;
R⁹ is heteroaryl which is unfused or fused with arene, heteroarene or R⁹A; R⁹A is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;
R¹⁰ is C₃-C₁₀-cycloalkyl or C₄-C₁₀-cycloalkenyl, each having one or two CH₂ moieties unreplaced or replaced with independently selected O, C(O), CNOH, CNOCH₃, S, S(O), SO₂ or NH and one or two CH moieties unreplaced or replaced with N, and each of which is unfused or fused with arene, heteroarene or R¹⁰A; R¹⁰A is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;
R¹¹ is alkyl, alkenyl or alkynyl, each of which is unsubstituted or substituted with one or two or three independently selected R¹², OR¹², NHR¹², N(R¹²)₂, C(O)NH₂, C(O)NHR¹², C(O)N(R¹²)₂, OH, (O), C(O)OH, N₃, CN, NH₂, CF₃, CF₂CF₃, F, Cl, Br or I substituents;
R¹² is R¹³, R¹⁴, R¹⁵ or R¹⁶;
R¹³ is phenyl which is unfused or fused with arene, heteroarene or R¹³A; R¹³A is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;
R¹⁴ is heteroaryl, each of which is unfused or fused with arene, heteroarene or R¹⁴A;
R¹⁴A is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;
R¹⁵ is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene, each of which is unfused or fused with arene, heteroarene or R¹⁵A; R¹⁵A is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;
R¹⁶ is alkyl, alkenyl or alkynyl;
R¹⁷ is R¹⁸, R¹⁹, R²⁰ or R²¹;
R¹⁸ is phenyl which is unfused or fused with arene, heteroarene or R¹⁸A; R¹⁸A is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;
R¹⁹ is heteroaryl which is unfused or fused with arene, heteroarene or R¹⁹A; R¹⁹A is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;
R²⁰ is C₃-C₁₀-cycloalkyl or C₄-C₁₀-cycloalkenyl, each having one or two CH₂ moieties unreplaced or replaced with independently selected O, C(O), CNOH, CNOCH₃, S, S(O), SO₂ or NH and one or two CH moieties unreplaced or replaced with N, and each of
which is unfused or fused with arene, heteroarene or R^{20A}; R^{20A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R^{21} is alkyl, alkenyl or alkynyl, each of which is unsubstituted or substituted with one or two or three independently selected R^{22}, OR^{22}, NHR^{22}, N(R^{22})_2, C(O)NH_2, C(O)NHR^{22}, C(O)N(R^{22})_2, OH, (O), C(O)OH, N_3, CN, NH_2, CF_3, CF_2CF_3, F, Cl, Br or I substituents;

R^{22} is R^{23}, R^{24} or R^{25};

R^{23} is phenyl which is unfused or fused with arene, heteroarene or R^{23A}; R^{23A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R^{24} is heteroarene which is unfused or fused with arene, heteroarene or R^{24A}; R^{24A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R^{25} is C_3-C_6-cycloalkyl or C_4-C_6-cycloalkenyl, each having one or two CH_2 moieties unreplaced or replaced with independently selected O, C(O), CNOH, CNOCH_3, S, S(O), SO_2 or NH and one or two CH moieties unreplaced or replaced with N, and each of which is unfused or fused with arene, heteroarene or R^{25A}; R^{25A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R^{30} is cycloalkyl or cycloalkenyl, each having one or two CH_2 moieties unreplaced or replaced with independently selected O, C(O), CNOH, CNOCH_3, S, S(O), SO_2 or NH and one or two CH moieties unreplaced or replaced with N, and each of which is unfused or fused with arene, heteroarene or R^{30A}; R^{30A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene; each of which is substituted with F, Cl, Br, I, CH_2R^{37}, CH(R^{31})(R^{37}), C(R^{31})(R^{31A})(R^{37}), C(O)R^{37}, OR^{37}, SR^{37}, S(O)R^{37}, SO_2R^{37}, NHR^{37} or N(R^{32})R^{37}; R^{31} and R^{31A} are independently F, Cl, Br or alkyl or are taken together and are C_2-C_5-spiroalkyl;

R^{32} is R^{33}, C(O)R^{33} or C(O)OR^{33};

R^{33} is R^{34} or R^{35};

R^{34} is phenyl which is unfused or fused with aryl, heteroaryl or R^{34A}; R^{34A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R^{35} is alkyl which is unsubstituted or substituted with R^{36};

R^{36} is phenyl which is unfused or fused with arene, heteroarene or R^{36A}; R^{36A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;
R^{37} is R^{38}, R^{39} or R^{40}, each of which is substituted with F, Cl, Br, I, R^{41}, OR^{41}, NHR^{41}, N(R^{41})_2, NHC(O)OR^{41}, SR^{41}, S(O)R^{41} or SO_2R^{41};

R^{38} is phenyl which is unfused or fused with arene, heteroarene or R^{38A}; R^{38A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R^{39} is heteroaryl which is unfused or fused with arene, heteroarene or R^{39A}; R^{39A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R^{40} is C_3-C_8-cycloalkyl or C_4-C_8-cycloalkenyl, each having one or two CH_2 moieties unreplace or replaced with independently selected O, C(O), CNOH, CNOCH_3, S, S(O), SO_2 or NH and one or two CH moieties unreplace or replaced with N, and each of which is unfused or fused with arene, heteroarene or R^{40A}; R^{40A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R^{41} is R^{42}, R^{43}, R^{44} or R^{45};

R^{42} is phenyl which is unfused or fused with arene, heteroarene or R^{42A}; R^{42A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R^{43} is heteroaryl which is unfused or fused with arene, heteroarene or R^{43A}; R^{43A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R^{44} is C_3-C_9-cycloalkyl or C_4-C_7-cycloalkenyl, each having one or two CH_2 moieties unreplace or replaced with independently selected O, C(O), CNOH, CNOCH_3, S, S(O), SO_2 or NH and one or two CH moieties unreplace or replaced with N, and each of which is unfused or fused with arene, heteroarene or R^{44A}; R^{44A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R^{45} is alkyl, alkenyl or alkynyl, each of which is unsubstituted or substituted with one or two independently selected R^{46}, OR^{46}, NHR^{46}, N(R^{46})_2, C(O)NH_2, C(O)NHR^{46}, C(O)N(R^{46})_2, OH, (O), C(O)OH, N_3, CN, NH_2, CF_3, CF_2CF_3, F, Cl, Br or I substituents;

R^{46} is R^{47}, R^{48} or R^{49};

R^{47} is phenyl which is unfused or fused with arene, heteroarene or R^{47A}; R^{47A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R^{48} is heteroaryl or R^{48A}; R^{48A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;
R^{49} is C₃-C₆-cycloalkyl or C₄-C₆-cycloalkenyl, each having one or two CH₂ moieties
unreplaced or replaced with independently selected O, C(O), CNOH, CNOCH₃, S, S(O), SO₂
or NH and one or two CH moieties unreplaced or replaced with N, and each of which is
unfused or fused with arene, heteroarene or R^{49A}; R^{49A} is cycloalkane, cycloalkene,
5 heterocycloalkane or heterocycloalkene;

wherein moieties represented by R² R³ R⁴ R⁶ C R⁸ R⁸A R⁹ R¹₀ R¹³ R¹⁴ R¹⁵ R¹⁸ R¹⁹ R²⁰ R²³ R²⁴ R²⁵ R²⁶ R²⁷ R²⁸ R²⁹ R³⁰ R³⁴ R³⁶ R³⁸ R³⁹ R⁴⁰ R⁴² R⁴₃ R⁴₄ R⁴⁷ R⁴₈ and R⁴⁹ are independently unsubstituted, further unsubstituted, substituted or
further substituted with one or two or three or four or five independently selected R⁵₀ OR⁵₀,
10 SR⁵₀, S(O)R⁵₀, SO₂R⁵₀, C(O)R⁵₀, CO(O)R⁵₀, OC(O)R⁵₀, OC(O)OR⁵₀, NH₂, NHR⁵₀,
N(R⁵₀)₂, C(O)NH₂, C(O)NHR⁵₀, C(O)N(R⁵₀)₂, C(O)NHOR⁵₀, C(O)NH₂SO₂R⁵₀,
C(O)NR⁵₅ SO₂R⁵₀, SO₂NH₂, SO₂NHR⁵₀, SO₂N(R⁵₀)₂, CF₃, CF₂CF₃, C(O)H, C(O)OH,
C(N)NH₂, C(N)NHR⁵₀, C(N)N(R⁵₀)₂, OH, (O), CN, N₃, NO₂, CF₃, CF₂CF₃, OCF₃,
OCF₂CF₃, F, Cl, Br or I substituents;
15 R⁵₀ is R⁵₁, R⁵₂, R⁵₃ or R⁵₄;
R⁵₁ is phenyl which is unfused or fused with arene, heteroarene or R⁵₁B; R⁵₁B is
cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R⁵₂ is heteroaryl;
R⁵₃ is C₃-C₆-cycloalkyl or C₄-C₆-cycloalkenyl, each having one or two CH₂ moieties
20 unreplaced or replaced with independently selected O, C(O), CNOH, CNOCH₃, S, S(O), SO₂
or NH and one or two CH moieties unreplaced or replaced with N, and each of which is
unfused or fused with arene, heteroarene or R⁵₃B;

wherein R⁵₃B is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;
R⁵₄ is alkyl, alkenyl or alkynyl, each of which is unsubstituted or substituted with one
or two or three independently selected R⁵₅, OR⁵₅, SR⁵₅, S(O)R⁵₅, SO₂R⁵₅, NHR⁵₅, N(R⁵₅)₂,
C(O)R⁵₅, C(O)NH₂, C(O)NHR⁵₅, C(O)N(R⁵₅)₂, NH₃(O)R⁵₅, NH₂SO₂R⁵₅, NH₃(O)OR⁵₅,
SO₂NH₂, SO₂N(R⁵₅)₂, NH₃(O)NH₂, NH₃(O)NHR⁵₅, OH, (O), C(O)OH, (O), N₃, CN,
NH₂, CF₃, OCF₃, CF₂CF₃, OCF₂CF₃, F, Cl, Br or I substituents;
R⁵₅ is alkyl, alkenyl, alkynyl, phenyl, heteroaryl or R⁵₆;
wherein the alkyl, alkenyl, alkynyl are unsubstituted or substituted with OCH₃; and

R¹⁶ is C₃-C₈-cycloalkyl or C₄-C₆-cycloalkenyl, each having one or two CH₂ moieties
unreplaced or replaced with independently selected O, C(O), CNOH, CNOCH₃, S, S(O), SO₂
or NH and one or two CH moieties unreplaced or replaced with N.

5

Another embodiment of this invention pertains to compounds or therapeutically
acceptable salts, prodrugs or salts of prodrugs thereof, which are useful as selective inhibitors
of anti-apoptotic Bcl-2 proteins, the compounds having Formula (IV)

![Chemical Structure](image)

10

wherein

R¹⁰⁰ is as described for substituents on R²⁶;
n is 0, 1, 2, or 3;
A¹ is N or C(A²);

one or two or three or each of A², B¹, D¹ and E¹ are independently selected R¹, OR¹,
SR¹, S(O)R¹, SO₂R¹, C(O)R¹, C(O)OR¹, OC(O)R¹, NH₂R¹, N(R¹)₂, C(O)NH₂R¹, C(O)N(R¹)₂,
NHC(O)R¹, NHC(O)OR¹, NR¹C(O)NH₂R¹, NR¹C(O)N(R¹)₂, SO₂NH₂R¹, SO₂N(R¹)₂,
NH₂SO₂R¹, NH₂SO₂NH₂R¹ or N(CH₃)SO₂N(CH₃)R¹, and the remainder are independently
selected H, F, Cl, Br, I, CN, CF₃, C(O)OH, C(O)NH₂ or C(O)OR¹A; and

15

Y¹ is H, CN, NO₂, C(O)OH, F, Cl, Br, I, CF₃, OCF₃, CF₂CF₃, OCF₂CF₃, R¹⁷, OR¹⁷,
C(O)R¹⁷, C(O)OR¹⁷, SR¹⁷, NH₂, NHR¹⁷, N(R¹⁷)₂, NHC(O)R¹⁷, C(O)NH₂, C(O)NHR¹⁷,
C(O)N(R¹⁷)₂, NHS(O)R¹⁷ or NH₂SO₂R¹⁷;

or
B¹ and Y¹, together with the atoms to which they are attached, are imidazole or triazole; and

one or two or each of A², D¹ and E¹ are independently selected R¹, OR¹, SR¹, S(O)R¹, SO₂R¹, C(O)R¹, C(O)OR¹, OC(O)R¹, NHR¹, N(R¹)₂, C(O)NHR¹, C(O)N(R¹)₂, NHC(O)R¹, NHC(O)OR¹, NHC(O)NHR¹, N(CH₃)C(O)N(CH₃)R¹, SO₂NHR¹, SO₂N(R¹)₂, NH₂SO₂R¹, NH₂SO₂NHR¹ or N(CH₃)SO₂N(CH₃)R¹, and the remainder are independently selected H, F, Cl, Br, I, CF₃, C(O)OH, C(O)NH₂ or C(O)OR¹⁰⁴;

R¹ is R², R³, R⁴ or R⁵;

R¹⁰⁴ is C₁-C₆-alkyl, C₃-C₆-alkenyl or C₃-C₆-alkynyl;

R² is phenyl which is unfused or fused with arene, heteroarene or R²⁴⁺; R²⁴⁺ is cycloalkane or heterocycloalkane;

R³ is heteroaryl which is unfused or fused with benzene, heteroarene or R³⁴⁺; R³⁴⁺ is cycloalkane or heterocycloalkane;

R⁴ is cycloalkyl, cycloalkenyl, heterocycloalkyl or heterocycloalkenyl, each of which is unfused or fused with arene, heteroarene or R⁴⁴⁺; R⁴⁴⁺ is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R⁵ is alkyl, alkenyl or alkynyl, each of which is unsubstituted or substituted with one or two or three independently selected R⁶, NC(R⁶¹)(R⁶²), R⁷, OR⁷, SR⁷, S(O)R⁷, SO₂R⁷, NHR⁷, N(R⁷)₂, C(O)R⁷, C(O)NH₂, C(O)NHR⁷, NHC(O)R⁷, NH₂SO₂R⁷, NH₂SO₂NHR⁷, NHC(O)CH(CH₃)NHC(O)CH(CH₃)NH₂, NHC(O)CH(CH₃)NHC(O)CH(CH₃)NHR¹, OH, (O), C(O)OH, (O), N₃, CN, NH₂, CF₃, CF₂CF₃, F, Cl, Br or I substituents;

R⁶ is C₂-C₅-spiroalkyl, each of which is unsubstituted or substituted with OH, (O), N₃, CN, CF₃, CF₂CF₃, F, Cl, Br, I, NH₂, NH(CH₃) or N(CH₃)₂;

R⁶¹ and R⁶² are independently selected alkyl or, together with the N to which they are attached, R⁶⁶⁺;

R⁶⁶⁺ is aziridin-1-yl, azetidin-1-yl, pyrrolidin-1-yl or piperidin-1-yl, each having one CH₂ moiety unreplaced or replaced with O, C(O), CNOH, CNOCH₃, S, S(O), SO₂ or NH;

R⁷ is R⁸, R⁹, R¹⁰ or R¹¹;
R^8 is phenyl which is unfused or fused with arene, heteroarene or R^{8A};
R^{8A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;
R^9 is heteroaryl which is unfused or fused with arene, heteroarene or R^{9A}; R^{9A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;
R^{10} is C_3-C_{10}-cycloalkyl or C_4-C_{10}-cycloalkenyl, each having one or two CH_2 moieties unreplaced or replaced with independently selected O, C(O), CNOH, CNOCH_3, S, S(O), SO_2 or NH and one or two CH moieties unreplaced or replaced with N, and each of which is unfused or fused with arene, heteroarene or R^{10A}; R^{10A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;
R^{11} is alkyl, alkenyl or alkynyl, each of which is unsubstituted or substituted with one or two or three independently selected R^{12}, OR^{12}, NHR^{12}, N(R^{12})_2, C(O)NH_2, C(O)NHR^{12}, C(O)N(R^{12})_2, OH, (O), C(O)OH, N_3, CN, NH_2, CF_3, CF_2CF_3, F, Cl, Br or I substituents;
R^{12} is R^{13}, R^{14}, R^{15} or R^{16};
R^{13} is phenyl which is unfused or fused with arene, heteroarene or R^{13A}; R^{13A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;
R^{14} is heteroaryl, each of which is unfused or fused with arene, heteroarene or R^{14A};
R^{14A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;
R^{15} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene, each of which is unfused or fused with arene, heteroarene or R^{15A}; R^{15A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;
R^{16} is alkyl, alkenyl or alkynyl;
R^{17} is R^{18}, R^{19}, R^{20} or R^{21};
R^{18} is phenyl which is unfused or fused with arene, heteroarene or R^{18A}; R^{18A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;
R^{19} is heteroaryl which is unfused or fused with arene, heteroarene or R^{19A}; R^{19A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;
R^{20} is C_3-C_{10}-cycloalkyl or C_4-C_{10}-cycloalkenyl, each having one or two CH_2 moieties unreplaced or replaced with independently selected O, C(O), CNOH, CNOCH_3, S, S(O), SO_2 or NH and one or two CH moieties unreplaced or replaced with N, and each of
which is unfused or fused with arene, heteroarene or R^{20A}; R^{20A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R^{21} is alkyl, alkenyl or alkynyl, each of which is unsubstituted or substituted with one or two or three independently selected R^{22}, OR^{22}, NHR^{22}, N(R^{22})_2, C(O)NH_2, C(O)NHR^{22}, C(O)N(R^{22})_2, OH, (O), C(O)OH, N_3, CN, NH_2, CF_3, CF_2CF_3, F, Cl, Br or I substituents;

R^{22} is R^{23}, R^{24} or R^{25};

R^{23} is phenyl which is unfused or fused with arene, heteroarene or R^{23A}; R^{23A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R^{24} is heteroarene which is unfused or fused with arene, heteroarene or R^{24A}; R^{24A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R^{25} is C_3-C_6-cycloalkyl or C_4-C_6-cycloalkenyl, each having one or two CH_2 moieties unreplaced or replaced with independently selected O, C(O), CNOH, CNOCH_3, S, S(O), SO_2 or NH and one or two CH moieties unreplaced or replaced with N, and each of which is unfused or fused with arene, heteroarene or R^{25A}; R^{25A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R^{30} is cycloalkyl or cycloalkenyl, each having one or two CH_2 moieties unreplaced or replaced with independently selected O, C(O), CNOH, CNOCH_3, S, S(O), SO_2 or NH and one or two CH moieties unreplaced or replaced with N, and each of which is unfused or fused with arene, heteroarene or R^{30A}; R^{30A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene; each of which is substituted with F, Cl, Br, I, CH_2R^{37}, CH(R^{31})(R^{37}), C(R^{31})(R^{31A})(R^{37}), C(O)R^{37}, OR^{37}, SR^{37}, S(O)R^{37}, SO_2R^{37}, NHR^{37} or N(R^{32})R^{37};

R^{31} and R^{31A} are independently F, Cl, Br or alkyl or are taken together and are C_2-C_6-spiroalkyl;

R^{32} is R^{33}, C(O)R^{33} or C(O)OR^{33};

R^{33} is R^{34} or R^{35};

R^{34} is phenyl which is unfused or fused with aryl, heteroaryl or R^{34A}; R^{34A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R^{35} is alkyl which is unsubstituted or substituted with R^{36};

R^{36} is phenyl which is unfused or fused with arene, heteroarene or R^{36A}; R^{36A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;
R^{37} is R^{38}, R^{39} or R^{40}, each of which is substituted with F, Cl, Br, I, R^{41}, OR^{41},
NHR^{41}, N(R^{41})_{2}, NHCOOR^{41}, SR^{41}, S(O)R^{41} or SO_{2}R^{41};
R^{38} is phenyl which is unfused or fused with arene, heteroarene or R^{38A}; R^{38A} is
cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;
R^{39} is heteroaryl which is unfused or fused with arene, heteroarene or R^{39A}; R^{39A} is
cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;
R^{40} is C_{3}-C_{8}-cycloalkyl or C_{4}-C_{8}-cycloalkenyl, each having one or two CH_{2} moieties
unreplaced or replaced with independently selected O, C(O), CNOH, CNOCH_{3}, S, S(O), SO_{2}
or NH and one or two CH moieties unreplaced or replaced with N, and each of which is
unfused or fused with arene, heteroarene or R^{40A}; R^{40A} is
cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;
R^{41} is R^{42}, R^{43}, R^{44} or R^{45};
R^{42} is phenyl which is unfused or fused with arene, heteroarene or R^{42A}; R^{42A} is
cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;
R^{43} is heteroaryl which is unfused or fused with arene, heteroarene or R^{43A}; R^{43A} is
cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;
R^{44} is C_{3}-C_{9}-cycloalkyl or C_{4}-C_{7}-cycloalkenyl, each having one or two CH_{2} moieties
unreplaced or replaced with independently selected O, C(O), CNOH, CNOCH_{3}, S, S(O), SO_{2}
or NH and one or two CH moieties unreplaced or replaced with N, and each of which is
unfused or fused with arene, heteroarene or R^{44A}; R^{44A} is
cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;
R^{45} is alkyl, alkenyl or alkylnyl, each of which is unsubstituted or substituted with one
or two independently selected R^{46}, OR^{46}, NHR^{46}, N(R^{46})_{2}, C(O)NH_{2}, C(O)NHR^{46},
C(O)N(R^{46})_{2}, OH, (O), C(O)OH, N_{3}, CN, NH_{2}, CF_{3}, CF_{2}CF_{3}, F, Cl, Br or I substituents;
R^{46} is R^{47}, R^{48} or R^{49};
R^{47} is phenyl which is unfused or fused with arene, heteroarene or R^{47A}; R^{47A} is
cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;
R^{48} is heteroaryl or R^{48A}; R^{48A} is cycloalkane, cycloalkene, heterocycloalkane or
heterocycloalkene;
R\textsuperscript{49} is C\textsubscript{3}-C\textsubscript{6}-cycloalkyl or C\textsubscript{4}-C\textsubscript{6}-cycloalkenyl, each having one or two CH\textsubscript{2} moieties unreplaced or replaced with independently selected O, C(O), CNOH, CNOCH\textsubscript{3}, S, S(O), SO\textsubscript{2} or NH and one or two CH moieties unreplaced or replaced with N, and each of which is unfused or fused with arene, heteroarene or R\textsuperscript{49A}; R\textsuperscript{49A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

wherein moieties represented by R\textsuperscript{2} R\textsuperscript{3} R\textsuperscript{4} R\textsuperscript{6} R\textsuperscript{6C} R\textsuperscript{8} R\textsuperscript{8A} R\textsuperscript{9} R\textsuperscript{10} R\textsuperscript{13} R\textsuperscript{14} R\textsuperscript{15} R\textsuperscript{18} R\textsuperscript{19} R\textsuperscript{20} R\textsuperscript{23} R\textsuperscript{24} R\textsuperscript{25} R\textsuperscript{26} R\textsuperscript{27} R\textsuperscript{28} R\textsuperscript{29} R\textsuperscript{30} R\textsuperscript{34} R\textsuperscript{36} R\textsuperscript{38} R\textsuperscript{39} R\textsuperscript{40} R\textsuperscript{42} R\textsuperscript{43} R\textsuperscript{44} R\textsuperscript{47} R\textsuperscript{48}, and R\textsuperscript{49} are independently unsubstituted, further unsubstituted, substituted or further substituted with one or two or three or four or five independently selected R\textsuperscript{50}, OR\textsuperscript{50}, SR\textsuperscript{50}, S(O)R\textsuperscript{50}, SO\textsubscript{2}R\textsuperscript{50}, C(O)R\textsuperscript{50}, CO(O)R\textsuperscript{50}, OC(O)R\textsuperscript{50}, OC(O)OR\textsuperscript{50}, NH\textsubscript{2}, NHR\textsuperscript{50}, N(R\textsuperscript{50})\textsubscript{2}, C(O)NH\textsubscript{2}, C(O)NHR\textsuperscript{50}, C(O)N(R\textsuperscript{50})\textsubscript{2}, C(O)NHOH, C(O)NHOR\textsuperscript{50}, C(O)NHSO\textsubscript{2}R\textsuperscript{50}, C(O)NR\textsuperscript{55}SO\textsubscript{2}R\textsuperscript{50}, SO\textsubscript{2}NH\textsubscript{2}, SO\textsubscript{2}NHR\textsuperscript{50}, SO\textsubscript{2}N(R\textsuperscript{50})\textsubscript{2}, CF\textsubscript{3}, CF\textsubscript{2}CF\textsubscript{3}, C(O)H, C(O)OH, C(N)NH\textsubscript{2}, C(N)NHR\textsuperscript{50}, C(N)N(R\textsuperscript{50})\textsubscript{2}, OH, (O), CN, N\textsubscript{3}, NO\textsubscript{2}, CF\textsubscript{3}, CF\textsubscript{2}CF\textsubscript{3}, OCF\textsubscript{3}, OCF\textsubscript{2}CF\textsubscript{3}, F, Cl, Br or I substituents;

R\textsuperscript{50} is R\textsuperscript{51}, R\textsuperscript{52}, R\textsuperscript{53} or R\textsuperscript{54};

R\textsuperscript{51} is phenyl which is unfused or fused with arene, heteroarene or R\textsuperscript{51B}; R\textsuperscript{51B} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R\textsuperscript{52} is heteroaryl;

R\textsuperscript{53} is C\textsubscript{3}-C\textsubscript{6}-cycloalkyl or C\textsubscript{4}-C\textsubscript{6}-cycloalkenyl, each having one or two CH\textsubscript{2} moieties unreplaced or replaced with independently selected O, C(O), CNOH, CNOCH\textsubscript{3}, S, S(O), SO\textsubscript{2} or NH and one or two CH moieties unreplaced or replaced with N, and each of which is unfused or fused with arene, heteroarene or R\textsuperscript{53B};

wherein R\textsuperscript{53B} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R\textsuperscript{54} is alkyl, alkenyl or alkynyl, each of which is unsubstituted or substituted with one or two or three independently selected R\textsuperscript{55}, OR\textsuperscript{55}, SR\textsuperscript{55}, S(O)R\textsuperscript{55}, SO\textsubscript{2}R\textsuperscript{55}, NHR\textsuperscript{55}, N(R\textsuperscript{55})\textsubscript{2}, C(O)R\textsuperscript{55}, C(O)NH\textsubscript{2}, C(O)NHR\textsuperscript{55}, NHHC(O)R\textsuperscript{55}, NHHSO\textsubscript{2}R\textsuperscript{55}, NHHC(O)OR\textsuperscript{55}, SO\textsubscript{2}NH\textsubscript{2}, SO\textsubscript{2}NHR\textsuperscript{55}, SO\textsubscript{2}N(R\textsuperscript{55})\textsubscript{2}, NHHC(O)NH\textsubscript{2}, NHHC(O)NHR\textsuperscript{55}, OH, (O), C(O)OH, (O), N\textsubscript{3}, CN, NH\textsubscript{2}, CF\textsubscript{3}, OCF\textsubscript{3}, CF\textsubscript{2}CF\textsubscript{3}, OCF\textsubscript{2}CF\textsubscript{3}, F, Cl, Br or I substituents;

R\textsuperscript{55} is alkyl, alkenyl, alkynyl, phenyl, heteroaryl or R\textsuperscript{56};
wherein the alkyl, alkenyl, alkynyl are unsubstituted or substituted with OCH₃; and R¹⁶ is C₃-C₈-cycloalkyl or C₄-C₆-cycloalkenyl, each having one or two CH₂ moieties unreplaced or replaced with independently selected O, C(O), CNOH, CNOCH₃, S, S(O), SO₂ or NH and one or two CH moieties unreplaced or replaced with N.

Another embodiment of this invention pertains to compounds or therapeutically acceptable salts, prodrugs or salts of prodrugs thereof, which are useful as selective inhibitors of anti-apoptotic Bcl-2 proteins, the compounds having Formula (V)

![Chemical Structure](image)

(V),

wherein

R¹⁰⁰ is as described for substituents on R²⁶;

n is 0, 1, 2, or 3;

A¹ is N or C(A²);

one or two or three or each of A², B¹, D¹ and E¹ are independently selected R¹, OR¹,

SR¹, S(O)R¹, SO₂R¹, C(O)R¹, C(O)OR¹, OC(O)R¹, NHR¹, N(R¹)₂, C(O)NHR¹, C(O)N(R¹)₂,

NH(C(O))R¹, NH(C(O))OR¹, NR¹C(O)NHR¹, NR¹C(O)N(R¹)₂, SO₂NHR¹, SO₂N(R¹)₂,

NH₂SO₂R¹, NH₂SO₂NHR¹ or N(CH₃)SO₂N(CH₃)R¹, and the remainder are independently selected H, F, Cl, Br, I, CN, CF₃, C(O)OH, C(O)NH₂ or C(O)OR¹¹; and

Y¹ is H, CN, NO₂, C(O)OH, F, Cl, Br, I, CF₃, OCF₃, CF₂CF₃, OCF₂CF₃, R¹⁷, OR¹⁷,

C(O)R¹⁷, C(O)OR¹⁷, SR¹⁷, NH₂, NHR¹⁷, N(R¹⁷)₂, NH(C(O))R¹⁷, C(O)NH₂, C(O)NHR¹⁷,

C(O)N(R¹⁷)₂, NH₂(O)R¹⁷ or NH₂SO₂R¹⁷;
or

B¹ and Y¹, together with the atoms to which they are attached, are imidazole or triazole; and

one or two or each of A², D¹ and E¹ are independently selected R¹, OR¹, SR¹,

5 S(O)R¹, SO₂R¹, C(O)R¹, C(O)OR¹, OC(O)R¹, NHR¹, N(R¹)₂, C(O)NHR¹, C(O)N(R¹)₂,
NHC(O)R¹, NHCO(O)R¹, NH(C₃H₇)C(O)N(CH₃)R¹, SO₂NHR¹, SO₂N(R¹)₂,
NH₂SO₂R¹, NH₂SO₂NHR¹ or N(CH₃)SO₂N(CH₃)R¹, and the remainder are independently
selected H, F, Cl, Br, I, CF₃, C(O)OH, C(O)NH₂ or C(O)OR¹;¹

R¹ is R², R³, R⁴ or R⁵;

10 R¹ is C₁-C₆-alkyl, C₃-C₆-alkenyl or C₃-C₆-alkynyl;

R² is phenyl which is unfused or fused with arene, heteroarene or R²; R² is
cy cloalkane or heterocycloalkane;

R³ is heteroaryl which is unfused or fused with benzene, heteroarene or R³; R³ is
cy cloalkane or heterocycloalkane;

15 R⁴ is cycloalkyl, cycloalkenyl, heterocycloalkyl or heterocycloalkenyl, each of which
is unfused or fused with arene, heteroarene or R⁴; R⁴ is cycloalkane, cycloalkene,
heterocycloalkane or heterocycloalkene;

R⁵ is alkyl, alkenyl or alkynyl, each of which is unsubstituted or substituted with one
or two or three independently selected R⁶, NC(R⁶)(R⁶), R⁷, OR⁷, SR⁷, S(O)R⁷, SO₂R⁷,

20 NHR⁷, N(R⁷)₂, C(O)R⁷, C(O)NH₂, C(O)NHR⁷, NHC(O)R⁷, NH₂SO₂R⁷, NHC(O)OR⁷,
SO₂NH₂, SO₂NHR⁷, SO₂N(R⁷)₂, NHCO(O)NH₂, NHCO(O)NHR⁷,
NHC(O)CH(CH₃)NHCO(O)CH(CH₃)NH₂, NHCO(O)CH(CH₃)NHC(O)CH(CH₃)NH₁, OH,
(O), C(O)OH, (O), N₃, CN, NH₂, CF₃, CF₂CF₃, F, Cl, Br or I substituents;

R⁶ is C₂-C₅-spiroalkyl, each of which is unsubstituted or substituted with OH, (O),

25 N₃, CN, CF₃, CF₂CF₃, F, Cl, Br, I, NH₂, NH(CH₃) or N(CH₃)₂;

R⁶ and R⁶ are independently selected alkyl or, together with the N to which they
are attached, R⁶;³

R⁶ is aziridin-1-yl, azetidin-1-yl, pyrrolidin-1-yl or piperidin-1-yl, each having one
CH₂ moiety unreplaced or replaced with O, C(O), CNOH, CNOCH₃, S, S(O), SO₂ or NH;
R^7 is R^8, R^9, R^{10} or R^{11};

R^8 is phenyl which is unfused or fused with arene, heteroarene or R^{8A};

R^{8A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R^9 is heteroaryl which is unfused or fused with arene, heteroarene or R^{9A}; R^{9A} is

cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R^{10} is C_3-C_{10}-cycloalkyl or C_4-C_{10}-cycloalkeny1, each having one or two CH2
moieties unreplaced or replaced with independently selected O, C(O), CNOH, CNOCH_3, S,
S(O), SO_2 or NH and one or two CH moieties unreplaced or replaced with N, and each of
which is unfused or fused with arene, heteroarene or R^{10A}; R^{10A} is cycloalkane, cycloalkene,
heterocycloalkane or heterocycloalkene;

R^{11} is alkyl, alkenyl or alkynyl, each of which is unsubstituted or substituted with one
or two or three independently selected R^{12}, OR^{12}, NHR^{12}, N(R^{12})_2, C(O)NH_2, C(O)NHR^{12},
C(O)N(R^{12})_2, OH, (O), C(O)OH, N_3, CN, NH_2, CF_3, CF_2CF_3, F, Cl, Br or I substituents;

R^{12} is R^{13}, R^{14}, R^{15} or R^{16};

R^{13} is phenyl which is unfused or fused with arene, heteroarene or R^{13A}; R^{13A} is
cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R^{14} is heteroaryl, each of which is unfused or fused with arene, heteroarene or R^{14A};

R^{14A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R^{15} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene, each of

which is unfused or fused with arene, heteroarene or R^{15A}; R^{15A} is cycloalkane, cycloalkene,
heterocycloalkane or heterocycloalkene;

R^{16} is alkyl, alkenyl or alkynyl;

R^{17} is R^{18}, R^{19}, R^{20} or R^{21};

R^{18} is phenyl which is unfused or fused with arene, heteroarene or R^{18A}; R^{18A} is
cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R^{19} is heteroaryl which is unfused or fused with arene, heteroarene or R^{19A}; R^{19A} is
cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R^{20} is C_3-C_{10}-cycloalkyl or C_4-C_{10}-cycloalkeny1, each having one or two CH2
moieties unreplaced or replaced with independently selected O, C(O), CNOH, CNOCH_3, S,
S(O), SO_2 or NH and one or two CH moieties unreplaced or replaced with N, and each of
which is unfused or fused with arene, heteroarene or $R_{20}^{20A}$; $R_{20}^{20A}$ is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

$R_{21}$ is alkyl, alkenyl or alkynyl, each of which is unsubstituted or substituted with one or two or three independently selected $R_{22}^{22}$, OR$_{22}^{22}$, NR$_{22}^{22}$, N(R$_{22}^{22}$)$_2$, C(O)NH$_2$, C(O)NHR$_{22}^{22}$,

$C(O)N(R_{22}^{22})_2$, OH, (O), C(O)OH, N$_3$, CN, NH$_2$, CF$_3$, CF$_2$CF$_3$, F, Cl, Br or I substituents;

$R_{22}^{22}$ is $R_{23}^{23}$, $R_{24}^{24}$ or $R_{25}^{25}$;

$R_{23}$ is phenyl which is unfused or fused with arene, heteroarene or $R_{23A}^{23A}$; $R_{23A}^{23A}$ is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

$R_{24}$ is heteroarene which is unfused or fused with arene, heteroarene or $R_{24A}^{24A}$; $R_{24A}^{24A}$ is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

$R_{25}$ is C$_3$-C$_6$-cycloalkyl or C$_4$-C$_6$-cycloalkenyl, each having one or two CH$_2$ moieties unreplaced or replaced with independently selected O, C(O), CNOH, CNOCH$_3$, S, S(O), SO$_2$ or NH and one or two CH moieties unreplaced or replaced with N, and each of which is unfused or fused with arene, heteroarene or $R_{25A}^{25A}$; $R_{25A}^{25A}$ is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

$R_{30}$ is cycloalkyl or cycloalkenyl, each having one or two CH$_2$ moieties unreplaced or replaced with independently selected O, C(O), CNOH, CNOCH$_3$, S, S(O), SO$_2$ or NH and one or two CH moieties unreplaced or replaced with N, and each of which is unfused or fused with arene, heteroarene or $R_{30A}^{30A}$; $R_{30A}^{30A}$ is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene; each of which is substituted with F, Cl, Br, I, CH$_2$$R_{37}^{37}$, CH(R$_{31}^{31}$)(R$_{37}^{37}$), C(R$_{31}^{31}$)(R$_{31A}^{31A}$)(R$_{37}^{37}$), C(O)R$_{37}^{37}$, OR$_{37}^{37}$, SR$_{37}^{37}$, S(O)R$_{37}^{37}$, SO$_2$R$_{37}^{37}$, NHR$_{37}^{37}$ or N(R$_{32}^{32}$)R$_{37}^{37}$;

$R_{31}$ and $R_{31A}^{31A}$ are independently F, Cl, Br or alkyl or are taken together and are C$_2$-C$_5$-spiroalkyl;

$R_{32}$ is $R_{33}^{33}$, C(O)OR$_{33}^{33}$ or C(O)OR$_{33}^{33}$;

$R_{33}$ is $R_{34}^{34}$ or $R_{35}^{35}$;

$R_{34}$ is phenyl which is unfused or fused with aryl, heteroaryl or $R_{34A}^{34A}$; $R_{34A}^{34A}$ is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

$R_{35}$ is alkyl which is unsubstituted or substituted with $R_{36}^{36}$;

$R_{36}$ is phenyl which is unfused or fused with arene, heteroarene or $R_{36A}^{36A}$; $R_{36A}^{36A}$ is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;
R\(^{37}\) is R\(^{38}\), R\(^{39}\) or R\(^{40}\), each of which is substituted with F, Cl, Br, I, R\(^{41}\), OR\(^{41}\), NHR\(^{41}\), N(R\(^{41}\))\(_2\), NHCOOR\(^{41}\), SR\(^{41}\), S(O)R\(^{41}\) or SO\(_2\)R\(^{41}\);

R\(^{38}\) is phenyl which is unfused or fused with arene, heteroarene or R\(^{38A}\); R\(^{38A}\) is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R\(^{39}\) is heteroaryl which is unfused or fused with arene, heteroarene or R\(^{39A}\); R\(^{39A}\) is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R\(^{40}\) is C\(_3\)C\(_8\)-cycloalkyl or C\(_4\)-C\(_8\)-cycloalkenyl, each having one or two CH\(_2\) moieties unplaced or replaced with independently selected O, C(O), CNOH, CNOCH\(_3\), S, S(O), SO\(_2\) or NH and one or two CH moieties unplaced or replaced with N, and each of which is unfused or fused with arene, heteroarene or R\(^{40A}\); R\(^{40A}\) is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R\(^{41}\) is R\(^{42}\), R\(^{43}\), R\(^{44}\) or R\(^{45}\);

R\(^{42}\) is phenyl which is unfused or fused with arene, heteroarene or R\(^{42A}\); R\(^{42A}\) is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R\(^{43}\) is heteroaryl which is unfused or fused with arene, heteroarene or R\(^{43A}\); R\(^{43A}\) is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R\(^{44}\) is C\(_3\)-C\(_9\)-cycloalkyl or C\(_4\)-C\(_7\)-cycloalkenyl, each having one or two CH\(_2\) moieties unplaced or replaced with independently selected O, C(O), CNOH, CNOCH\(_3\), S, S(O), SO\(_2\) or NH and one or two CH moieties unplaced or replaced with N, and each of which is unfused or fused with arene, heteroarene or R\(^{44A}\); R\(^{44A}\) is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R\(^{45}\) is alkyl, alkenyl or alkynyl, each of which is unsubstituted or substituted with one or two independently selected R\(^{46}\), OR\(^{46}\), NHR\(^{46}\), N(R\(^{46}\))\(_2\), C(O)NH\(_2\), C(O)NHR\(^{46}\), C(O)N(R\(^{46}\))\(_2\), OH, (O), C(O)OH, N\(_3\), CN, NH\(_2\), CF\(_3\), CF\(_2\)CF\(_3\), F, Cl, Br or I substituents;

R\(^{46}\) is R\(^{47}\), R\(^{48}\) or R\(^{49}\);

R\(^{47}\) is phenyl which is unfused or fused with arene, heteroarene or R\(^{47A}\); R\(^{47A}\) is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R\(^{48}\) is heteroaryl or R\(^{48A}\); R\(^{48A}\) is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;
R^{49} is C_3-C_6-cycloalkyl or C_4-C_6-cycloalkenyl, each having one or two CH_2 moieties unplaced or replaced with independently selected O, C(O), CNOH, CNOCH_3, S, S(O), SO_2 or NH and one or two CH moieties unplaced or replaced with N, and each of which is unfused or fused with arene, heteroarene or R^{49A}; R^{49A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

wherein moieties represented by R^2 R^3, R^4, R^6, R^6C, R^8, R^{8A}, R^9, R^{10}, R^{13}, R^{14}, R^{15}, R^{18}, R^{19}, R^{20}, R^{23}, R^{24}, R^{25}, R^{26}, R^{27}, R^{28}, R^{29}, R^{30}, R^{34}, R^{36}, R^{38}, R^{39}, R^{40}, R^{42}, R^{43}, R^{44}, R^{47}, R^{48}, and R^{49} are independently unsubstituted, further unsubstituted, substituted or further substituted with one or two or three or four or five independently selected R^{50}, OR^{50}, SR^{50}, S(O)R^{50}, SO_2R^{50}, C(O)R^{50}, CO(O)R^{50}, OC(O)R^{50}, OC(O)OR^{50}, NH_2, NHR^{50}, N(R^{50})_2, C(O)NH_2, C(O)NHR^{50}, C(O)N(R^{50})_2, C(O)NHOH, C(O)NHOR^{50}, C(O)NSO_2R^{50}, C(O)NR^{55}, SO_2R^{50}, SO_2NH_2, SO_2NHR^{50}, SO_2N(R^{50})_2, CF_3, CF_2CF_3, C(O)H, C(O)OH, C(N)NH_2, C(N)NHR^{50}, C(N)N(R^{50})_2, OH, (O), CN, N_3, NO_2, CF_3, CF_2CF_3, OCF_3, OCF_2CF_3, F, Cl, Br or I substituents;

R^{50} is R^{51}, R^{52}, R^{53} or R^{54};

R^{51} is phenyl which is unfused or fused with arene, heteroarene or R^{51B}; R^{51B} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R^{52} is heteroaryl;

R^{53} is C_3-C_6-cycloalkyl or C_4-C_6-cycloalkenyl, each having one or two CH_2 moieties unplaced or replaced with independently selected O, C(O), CNOH, CNOCH_3, S, S(O), SO_2 or NH and one or two CH moieties unplaced or replaced with N, and each of which is unfused or fused with arene, heteroarene or R^{53B};

wherein R^{53B} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R^{54} is alkyl, alkenyl or alkynyl, each of which is unsubstituted or substituted with one or two or three independently selected R^{55}, OR^{55}, SR^{55}, S(O)R^{55}, SO_2R^{55}, NHR^{55}, N(R^{55})_2, C(O)R^{55}, C(O)NH_2, C(O)NHR^{55}, NHC(O)R^{55}, NHSO_2R^{55}, NHC(O)OR^{55}, SO_2NH_2, SO_2NHR^{55}, SO_2N(R^{55})_2, NHC(O)NH_2, NHC(O)NHR^{55}, OH, (O), C(O)OH, (O), N_3, CN, NH_2, CF_3, OCF_3, CF_2CF_3, OCF_2CF_3, F, Cl, Br or I substituents;

R^{55} is alkyl, alkenyl, alkynyl, phenyl, heteroaryl or R^{56};
wherein the alkyl, alkenyl, alkylnyl are unsubstituted or substituted with OCH₃; and
R₅⁶ is C₃-C₈-cycloalkyl or C₄-C₆-cycloalkenyl, each having one or two CH₂ moieties
unreplaced or replaced with independently selected O, C(O), CNOH, CNOCH₃, S, S(O), SO₂
or NH and one or two CH moieties unreplaced or replaced with N.

Another embodiment pertains to compounds of Formula (I), Formula (II), Formula
(III), Formula (IV), or Formula (V) wherein A¹ is C(A²); and A² is H.

Another embodiment pertains to compounds of Formula (I), Formula (II), Formula
(III), Formula (IV), or Formula (V) wherein A¹ is C(A²); A² is H; and B¹ is NHR¹.

Another embodiment pertains to compounds of Formula (I), Formula (II), Formula
(III), Formula (IV), or Formula (V) wherein A¹ is C(A²); A² is H; B¹ is NHR¹; and D¹ is H.

Another embodiment pertains to compounds of Formula (I), Formula (II), Formula
(III), Formula (IV), or Formula (V) wherein A¹ is C(A²); A² is H; B¹ is NHR¹; D¹ is H; and E¹
is H.

Another embodiment pertains to compounds of Formula (I), Formula (II), Formula
(III), Formula (IV), or Formula (V) wherein A¹ is C(A²); A² is H; B¹ is NHR¹; D¹ is H; E¹ is
H; and Y¹ is NO₂.

Still another embodiment pertains to compounds having Formula I which are
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((tetrahydro-2H-
pyran-4-ylmethyl)amino)phenyl)sulfonyl)-2-phenoxybenzamide;
benzamide;
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-phenoxy-N-((4-((tetrahydro-2H-
pyran-4-ylmethyl)amino)phenyl)sulfonyl)benzamide;
2-(benzyloxy)-4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((
tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)benzamide;
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((tetrahydro-2H-
pyran-4-ylmethyl)amino)phenyl)sulfonyl)-2-(2-phenylethoxy)benzamide;
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((tetrahydro-2H-
pyran-4-ylmethyl)amino)phenyl)sulfonyl)-2-(phenylthio)benzamide;
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(phenylthio)-N-((4-((tetrahydro-
2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)benzamide;
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-((3-morpholin-4-
ylpropyl)amino)-3-nitrophenyl)sulfonyl)-2-(phenylthio)benzamide;
CA 02744711 2011-05-26

WO 2010/065865

PCT/US2009/066790

4-(4′-(4′-chloro-1,1′-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)-2-(phenylsulfonyl)benzamide;
4-(4′-(4′-chloro-1,1′-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)-2-(phenylsulfinyl)benzamide;
2-benzyl-4-(4′-(4′-chloro-1,1′-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)benzamide;
2-benzyl-4-(4′-(4′-chloro-1,1′-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4′-(3-morpholin-4-ylpropyl)amino)-3-nitrophenyl)sulfonyl)benzamide;
4-(4′-(4′-chloro-1,1′-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)-2-(2-phenylethyl)benzamide;
2-(benzylamino)-4-(4′-(4′-chloro-1,1′-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)benzamide;
2-anilino-4-(4′-(4′-chloro-1,1′-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)benzamide;
2-anilino-4-(4′-(4′-chloro-1,1′-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4′-(2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)benzamide;
4-(4′-(4′-chloro-1,1′-biphenyl-2-yl)methyl)piperazin-1-yl)-2-methoxy-N-((3-nitro-4-((2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)benzamide;
4-(4′-(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-N-((4′-(3-morpholin-4-ylpropyl)amino)-3-nitrophenyl)sulfonyl)-2-phenoxybenzamide;
4-(4′-(2-(4-chlorophenyl)-5,5-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-N-((4′-(3-morpholin-4-ylpropyl)amino)-3-nitrophenyl)sulfonyl)-2-phenoxybenzamide;
4-(4′-(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indazol-5-yl)oxy)-N-((4′-(3-morpholin-4-ylpropyl)amino)-3-nitrophenyl)sulfonyl)benzamide;
4-(4′-(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indazol-5-yl)oxy)-N-((4′-(1-methylpiperidin-4-yl)amino)-3-nitrophenyl)sulfonyl)benzamide;
4-(4′-(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-N-((4′-(3-morpholin-4-ylpropyl)amino)-3-nitrophenyl)sulfonyl)-2-(1,2,3,4-tetrahydroquinolin-6-yl)oxy)benzamide;
4-(4′-(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-N-((4′-(1-methylpiperidin-4-yl)amino)-3-nitrophenyl)sulfonyl)-2-(1,2,3,4-tetrahydroquinolin-6-yl)oxy)benzamide;
4-(4-((4'-chloro-4-(pyrrolidin-1-ylmethyl)-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-yl)methyl)amino)phenyl)sulfonyl)benzamide;
4-(4-((4'-chloro-4-(2-pyrrolidin-1-ylthethyl)-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-yl)methyl)amino)phenyl)sulfonyl)benzamide;
4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-N-((4-((1-cyclopentyl)piperidin-4-yl)amino)-3-nitrophenyl)sulfonyl)-2-(1H-indol-5-yloxy)benzamide
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)-3-isobutylpiperazin-1-yl)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)-2-phenoxybenzamide;
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-(2,4-dioxo-3-azabicyclo(3.2.0)hept-3-yl)phenyl)sulfonyl)-2-phenoxybenzamide;
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-(4-methyl-6-oxo-1,4,5,6-tetrahydropyridazin-3-yl)phenyl)sulfonyl)-2-phenoxybenzamide;
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-(3,3-dimethyl-2-oxazetidin-1-yl)phenyl)sulfonyl)-2-phenoxybenzamide;
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-(4-nitro-2H-1,2,3-triazol-2-yl)phenyl)sulfonyl)-2-phenoxybenzamide;
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-phenoxy-N-((2-(2-piperidin-1-ylethoxy)phenyl)sulfonyl)benzamide;
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-(((1-ethylpyrrolidin-2-yl)methyl)amino)carbonyl)-4-methoxyphenyl)sulfonyl)-2-phenoxybenzamide;
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(1-naphthoxy)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)benzamide;
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(2-naphthoxy)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)benzamide;
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-(3-morpholin-4-ylpropyl)amino)-3-nitrophenyl)sulfonyl)-2-(2-naphthoxy)benzamide;
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(2-naphthoxy)-N-((4-((tetrahydro-2H-pyran-4-ylmethyl)amino)-3-((trifluoromethyl)sulfonyl)phenyl)sulfonyl)benzamide;
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)-2-(quinolin-7-yloxy)benzamide;
4-(4-(4'-chloro-1,1''-biphenyl-2-yl)methyl)pirazin-1-yl)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)-2-(quinolin-6-yloxy)benzamide;  
4-(4-(4'-chloro-1,1''-biphenyl-2-yl)methyl)pirazin-1-yl)-2-(1H-indol-5-yloxy)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)benzamide;  
4-(4-(4'-chloro-1,1''-biphenyl-2-yl)methyl)pirazin-1-yl)-2-(isoquinolin-5-yloxy)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)benzamide;  
4-(4-(4'-chloro-1,1''-biphenyl-2-yl)methyl)pirazin-1-yl)-N-((4-((3-dimethylamino)propyl)amino)-3-nitrophenyl)sulfonyl)-2-(isoquinolin-5-yloxy)benzamide;  
4-(4-(4'-chloro-1,1''-biphenyl-2-yl)methyl)pirazin-1-yl)-N-((4-((3-dimethylamino)propyl)amino)-3-nitrophenyl)sulfonyl)-2-(quinolin-6-yloxy)benzamide;  
4-(4-(4'-chloro-1,1''-biphenyl-2-yl)methyl)pirazin-1-yl)-N-((4-((3-dimethylamino)propyl)amino)-3-nitrophenyl)sulfonyl)-2-(1H-indol-5-yloxy)benzamide;  
4-(4-(4'-chloro-1,1''-biphenyl-2-yl)methyl)pirazin-1-yl)-2-(1H-indol-4-yloxy)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)benzamide;  
4-(4-(4'-chloro-1,1''-biphenyl-2-yl)methyl)pirazin-1-yl)-N-((4-((3-dimethylamino)propyl)amino)-3-nitrophenyl)sulfonyl)-2-(1H-indol-4-yloxy)benzamide;  
4-(4-(4'-chloro-1,1''-biphenyl-2-yl)methyl)pirazin-1-yl)-N-((4-((3-dimethylamino)propyl)amino)-3-nitrophenyl)sulfonyl)-2-(1H-indol-6-yloxy)benzamide;  
4-(4-(4'-chloro-1,1''-biphenyl-2-yl)methyl)pirazin-1-yl)-2-(isoquinolin-7-yloxy)-N-((4-((3-morpholin-4-ylpropyl)amino)-3-nitrophenyl)sulfonyl)benzamide;  
4-(4-(4'-chloro-1,1''-biphenyl-2-yl)methyl)pirazin-1-yl)-N-((4-((3-dimethylamino)propyl)amino)-3-nitrophenyl)sulfonyl)-2-(isoquinolin-7-yloxy)benzamide;  
4-(4-((2-(4-chlorophenyl)-5,5-dimethylcyclohex-1-en-1-yl)methyl)pirazin-1-yl)-2-(1H-indol-5-yloxy)-N-((4-((3-morpholin-4-ylpropyl)amino)-3-nitrophenyl)sulfonyl)benzamide;  
4-(4-((2-(4-chlorophenyl)-5,5-dimethylcyclohex-1-en-1-yl)methyl)pirazin-1-yl)-N-((4-((3-dimethylamino)propyl)amino)-3-nitrophenyl)sulfonyl)-2-(1H-indol-5-yloxy)benzamide;  
4-(4-((2-(4-chlorophenyl)-5,5-dimethylcyclohex-1-en-1-yl)methyl)pirazin-1-yl)-2-(1H-indol-5-yloxy)-N-((4-((3-morpholin-4-ylpropyl)amino)-3-nitrophenyl)sulfonyl)benzamide;  
4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)pirazin-1-yl)-N-((4-((3-dimethylamino)propyl)amino)-3-nitrophenyl)sulfonyl)-2-(1H-indol-5-yloxy)benzamide;  
4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)pirazin-1-yl)-2-(1H-indol-4-yloxy)-N-((4-((3-morpholin-4-ylpropyl)amino)-3-nitrophenyl)sulfonyl)benzamide;  
4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)pirazin-1-yl)-2-(1H-indol-4-yloxy)-N-((4-((3-morpholin-4-ylpropyl)amino)-3-nitrophenyl)sulfonyl)benzamide;
4-(4-((2-(4-chlorophenyl)-5,5-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-N-((4-(3-dimethylamino)propyl)(amine)-3-nitrophenyl)sulfonyl)-2-(1H-indol-4-yloxy)benzamide;
4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-N-((4-(3-dimethylamino)propyl)(amine)-3-nitrophenyl)sulfonyl)-2-(1H-indol-4-yloxy)benzamide;
5 4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((4-((3-morpholin-4-ylpropyl)(amine)-3-nitrophenyl)sulfonyl)benzamide;
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((4-((3-morpholin-4-ylpropyl)(amine)-3-nitrophenyl)sulfonyl)benzamide;
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-methoxyphenyl)sulfonyl)-2-phenoxybenzamide;
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-methylphenyl)sulfonyl)-2-phenoxybenzamide;
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((4-((tetrahydro-2H-pyran-4-ylmethyl)(amine)-3-
((trifluoromethyl)sulfonyl)phenyl)sulfonyl)benzamide;
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((4-((tetrahydro-2H-pyran-4-ylmethyl)(amine)-3-
((trifluoromethyl)sulfonyl)phenyl)sulfonyl)benzamide;
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-((3-dimethylamino)propyl)(amine)-3-((trifluoromethyl)sulfonyl)phenyl)sulfonyl)-2-(1H-indol-5-yloxy)benzamide;
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((4-((3-morpholin-4-ylpropyl)(amine)-3-((trifluoromethyl)sulfonyl)phenyl)sulfonyl)benzamide;
N-((3-((chlorodifluoro)methyl)sulfonyl)-4-((3-
25 (dimethylamino)propyl)(amine)phenyl)sulfonyl)-4-((4-(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)benzamide;
2-(1H-indol-4-yloxy)-4-(4-((2-(4-methoxyphenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((3-pyrrolidin-1-
ylpropyl)(amine)phenyl)sulfonyl)benzamide;
4-(4-(4,4-dimethyl-2-((trifluoromethyl)phenyl)cyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((3-nitro-4-((3-pyrrolidin-1-
ylpropyl)(amine)phenyl)sulfonyl)benzamide;
4-(4-((4,4-dimethyl-2-(4-(trifluoromethoxy)phenyl)cyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((3-nitro-4-((3-pyrrolidin-1-yl)propyl)amino)phenyl)sulfonyl)benzamide;
4-(4-((4,4-dimethyl-2-(3-(trifluoromethyl)phenyl)cyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((3-nitro-4-((3-pyrrolidin-1-yl)propyl)amino)phenyl)sulfonyl)benzamide;
4-(4-((2-(3-fluorophenyl))-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((3-nitro-4-((3-pyrrolidin-1-yl)propyl)amino)phenyl)sulfonyl)benzamide;
4-(4-((2-(4-fluorophenyl))-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((3-nitro-4-((3-pyrrolidin-1-yl)propyl)amino)phenyl)sulfonyl)benzamide;
N-((3-((chloro(difluoro)methyl)sulfonyl))-4-((1-methylpiperidin-4-yl)amino)phenyl)sulfonyl)-4-(4-((2-(4-chlorophenyl))-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)benzamide;
4-(4-((2-(4-chlorophenyl)cyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((4-((1-methylpiperidin-4-yl)amino)-3-nitrophenyl)sulfonyl)benzamide;
4-(4-((2-(4-chlorophenyl))-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((4-((1-methylpiperidin-4-yl)amino)-3-((trifluoromethyl)sulfonyl)phenyl)sulfonyl)benzamide;
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)-2-(phenoxy)methyl)benzamide;
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-((3-morpholin-4-ylpropyl)amino)phenyl)sulfonyl)-2-phenoxybenzamide;
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)-2-(pyridin-3-yloxy)benzamide;
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(pyridin-3-yloxy)-N-((4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)benzamide;
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-((1R)-3-(dimethylamino)-1-((phenylthio)methyl)propyl)amino)-3-nitrophenyl)sulfonyl)-2-phenoxybenzamide;
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)-2-(pyridin-4-yloxy)benzamide;
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-((3-morpholin-4-ylpropyl)amino)-3-nitrophenyl)sulfonyl)-2-(pyridin-3-yloxy)benzamide;
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-((3-morpholin-4-ylpropyl)amino)-3-nitrophenyl)sulfonyl)-2-(pyridin-4-yloxy)benzamide;
4-(4-(4′-chloro-1,1′-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-((2-(4-methylpiperazin-1-yl)ethyl)amino)-3-nitrophenyl)sulfonyl)-2-phenoxybenzamide;
4-(4-(4′-chloro-1,1′-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-((3-(4-methylpiperazin-1-yl)propyl)amino)-3-nitrophenyl)sulfonyl)-2-phenoxybenzamide;
4-(4-(4′-chloro-1,1′-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-((3-(dimethylamino)propyl)(methyl)amino)-3-nitrophenyl)sulfonyl)-2-phenoxybenzamide;
4-(4-(4′-chloro-1,1′-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-((1-methylpiperidin-4-yl)methyl)amino)-3-nitrophenyl)sulfonyl)-2-phenoxybenzamide;
4-(4-(4′-chloro-1,1′-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-((1-methylpiperidin-4-yl)amino)-3-nitrophenyl)sulfonyl)-2-phenoxybenzamide;
4-(4-(4′-chloro-1,1′-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-cyano-4-((3-(dimethylamino)propyl)amino)phenyl)sulfonyl)-2-phenoxybenzamide;
4-(4-(4′-chloro-1,1′-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((3-pyrrolidin-1-yl)propyl)amino)phenyl)sulfonyl)-2-phenoxybenzamide;
4-(4-(4′-chloro-1,1′-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-((3-(dimethylamino)propyl)amino)-3-(trifluoromethyl)phenyl)sulfonyl)-2-phenoxybenzamide;
4-(4-(4′-chloro-1,1′-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-((3-isopropyl(methyl)amino)propyl)amino)-3-nitrophenyl)sulfonyl)-2-phenoxybenzamide;
4-(4-(4′-chloro-1,1′-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-(3-(dimethylamino)propoxy)-3-nitrophenyl)sulfonyl)-2-phenoxybenzamide;
4-(4-(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yl)oxy)-N-((4-(2-(4-methylpiperazin-1-yl)ethyl)amino)-3-nitrophenyl)sulfonyl)benzamide;
4-(4-(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yl)oxy)-N-((4-(3-(4-methylpiperazin-1-yl)propyl)amino)-3-nitrophenyl)sulfonyl)benzamide;
4-(4-(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yl)oxy)-N-((3-nitro-4-((3-pyrrolidin-1-yl)propyl)amino)phenyl)sulfonyl)benzamide;
4-(4-(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yl)oxy)-N-((4-((1-methylpiperidin-4-yl)amino)-3-nitrophenyl)sulfonyl)benzamide;
4-(4-(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yl)oxy)-N-((4-(3-(4-methylpiperazin-1-yl)propyl)amino)-3-nitrophenyl)sulfonyl)benzamide;
4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-N-((4-(3-
(dimethylamino)propoxy)-3-nitrophenyl)sulfonyl)-2-(1H-indol-5-yloxy)benzamide;
4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-
indol-4-yloxy)-N-((3-nitro-4-((3-pyrrolidin-1-yl)propyl)amino)phenyl)sulfonyl)benzamide;
4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-
indol-4-yloxy)-N-((4-((1-methylpiperidin-4-yl)amino)-3-nitrophenyl)sulfonyl)benzamide;
4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-
indol-5-yloxy)-N-((4-(((1-methylpiperidin-4-yl)methyl)amino)-3-nitrophenyl)sulfonyl)benzamide;
4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-
indol-4-yloxy)-N-((4-(((1-methylpiperidin-4-yl)methyl)amino)-3-nitrophenyl)sulfonyl)benzamide;
4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-N-((4-(3-
(dimethylamino)propoxy)-3-nitrophenyl)sulfonyl)-2-(1H-indol-4-yloxy)benzamide;
4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-
indol-5-yloxy)-N-((4-((4-methylpiperazin-1-yl)-3-nitrophenyl)sulfonyl)benzamide;
4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-
indol-4-yloxy)-N-((3-nitro-4-((1-(2,2,2-trifluoroethyl)piperidin-4-yl)amino)phenyl)sulfonyl)benzamide;
4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-N-((4-((4-(dimethylamino)-1-methylpiperidin-4-yl)methyl)amino)-3-nitrophenyl)sulfonyl)-2-
(1H-indol-5-yloxy)benzamide;
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(2,3-dihydro-1,4-benzodioxin-5-
-yl)oxy)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)benzamide;
5-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((tetrahydro-2H-
-pyran-4-ylmethyl)amino)phenyl)sulfonyl)-1,1'-biphenyl-2-carboxamide;
5-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-((3-
(dimethylamino)propyl)amino)-3-nitrophenyl)sulfonyl)-1,1'-biphenyl-2-carboxamide;
4-(4-((4'-chloro-4-((dimethylamino)ethoxy)-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-
((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)-2-phenoxybenzamide;
4-(4'-(3-piperidin-1-ylpropoxy)-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)-2-phenoxybenzamide;
4-(4'-(3-morpholin-4-ylthoxy)-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)-2-phenoxybenzamide;
4-(4'-(3-dimethylamino)propoxy)-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)-2-phenoxybenzamide;
4-(4'-(3-(dimethylamino)propoxy)-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)-2-phenoxybenzamide;
4-(4'-(3-(dimethylamino)propoxy)-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-phenoxy-N-((4-((tetrahydro-2H-pyran-4-ylmethyl)amino)-3-((trifluoromethyl)sulfonyl)phenyl)sulfonyl)benzamide;
4-(4'-(3-(dimethylamino)propoxy)-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-phenoxy-N-((4-((tetrahydro-2H-pyran-4-ylmethyl)amino)-3-((trifluoromethyl)sulfonyl)phenyl)sulfonyl)benzamide;
4-(4'-(3-(dimethylamino)propoxy)-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-phenoxy-N-((4-((tetrahydro-2H-pyran-4-ylmethyl)amino)-3-((trifluoromethyl)sulfonyl)phenyl)sulfonyl)benzamide;
4-(4'-(3-(dimethylamino)propoxy)-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-phenoxy-N-((4-((tetrahydro-2H-pyran-4-ylmethyl)amino)-3-((trifluoromethyl)sulfonyl)phenyl)sulfonyl)benzamide;
4-(4'-(3-pyrrolidin-1-ylpropyl)amino)phenyl)sulfonyl)-2-phenoxybenzamide;
4-(4'-(3-pyrrolidin-1-ylpropyl)amino)phenyl)sulfonyl)-2-phenoxybenzamide;
4-(4'-(3-pyrrolidin-1-ylpropyl)amino)phenyl)sulfonyl)-2-phenoxybenzamide;
4-(4'-(3-pyrrolidin-1-ylpropyl)amino)phenyl)sulfonyl)-2-phenoxybenzamide;
4-(4'-(3-pyrrolidin-1-ylpropyl)amino)phenyl)sulfonyl)-2-phenoxybenzamide;
4-(4'-(3-pyrrolidin-1-ylpropyl)amino)phenyl)sulfonyl)-2-phenoxybenzamide;
4-(4'-(3-pyrrolidin-1-ylpropyl)amino)phenyl)sulfonyl)-2-phenoxybenzamide;
4-(4'-(3-pyrrolidin-1-ylpropyl)amino)phenyl)sulfonyl)-2-phenoxybenzamide;
4-(4'-(3-pyrrolidin-1-ylpropyl)amino)phenyl)sulfonyl)-2-phenoxybenzamide;
4-(4-((4'-chloro-4-(2-morpholin-4-ylethoxy)-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-yl)methyl)amino)phenyl)sulfonyl)benzamide;
4-(4-((4'-chloro-3-(2-(dimethylamino)ethoxy)-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-yl)methyl)amino)phenyl)sulfonyl)benzamide;
4-(4-((4'-chloro-3-(2-((2-(dimethylamino)ethoxy)-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-yl)methyl)amino)phenyl)sulfonyl)benzamide;
4-(4-((4'-chloro-4-(2-morpholin-4-ylethoxy)-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-yl)methyl)amino)phenyl)sulfonyl)benzamide;
4-(4-((4'-chloro-3-(2-morpholin-4-ylethoxy)-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-yl)methyl)amino)phenyl)sulfonyl)benzamide;
4-(4-((4'-chloro-3-(2-morpholin-4-ylethoxy)-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-yl)methyl)amino)phenyl)sulfonyl)benzamide;
4-(4-((4'-chloro-3-(2-morpholin-4-ylethoxy)-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((3-nitro-4-((3-pyrrolidin-1-yl)propyl)amino)phenyl)sulfonyl)benzamide;
4-(4-((4'-chloro-4-(2-(dimethylamino)ethoxy)-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((3-nitro-4-((3-pyrrolidin-1-yl)propyl)amino)phenyl)sulfonyl)benzamide;
4-(4-((4'-chloro-4-(2-(dimethylamino)ethoxy)-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2(1H-indol-5-yloxy)-N-((3-nitro-4-((3-pyrrolidin-1-yl)propyl)amino)phenyl)sulfonyl)benzamide;
4-(4-((4'-chloro-4-(2-((2-(dimethylamino)ethoxy)-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2(1H-indol-5-yloxy)-N-((3-nitro-4-((3-pyrrolidin-1-yl)propyl)amino)phenyl)sulfonyl)benzamide;
4-(4-((4'-chloro-4-(2-(dimethylamino)ethoxy)-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((1-(2,2,2-trifluoroethyl)piperidin-4-yl)amino)phenyl)sulfonyl)-2-phenoxybenzamide;
4-(4-((4'-chloro-4-(2-pyrrolidin-1-ylethoxy)-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-yl)methyl)amino)phenyl)sulfonyl)-2-phenoxybenzamide;
4-(4-((4'-chloro-4-(2-(dimethylamino)ethoxy)-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-yl)methyl)amino)phenyl)sulfonyl)-2-phenoxybenzamide;
4-(4-(4′-chboro-4-(2-diisopropylamino)ethoxy)-1,1′-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-yl)methyl)amino)phenyl)sulfonyl)-2-phenoxybenzamide;
4-(4′-(2,3-dihydro-1H-indol-5-yl))-N-((3-nitro-4-((tetrahydro-2H-pyran-4-yl)methyl)amino)phenyl)sulfonyl)benzamide;
4-(4′-(2,3-dihydro-1H-indol-5-yl)methyl)piperazin-1-yl)-2-((1H-indol-4-yl))-N-((3-nitro-4-((3-pyrrolidin-1-ylpropyl)amino)phenyl)sulfonyl)benzamide;
4-(4′-(2,3-dihydro-1H-indol-5-yl)methyl)piperazin-1-yl)-2-((1H-indol-4-yl))-N-((3-nitro-4-((3-pyrrolidin-1-ylpropyl)amino)phenyl)sulfonyl)benzamide;
4-(4′-(2,3-dihydro-1H-indol-5-yl)methyl)piperazin-1-yl)-2-((1H-indol-4-yl))-N-((3-nitro-4-((3-pyrrolidin-1-ylpropyl)amino)phenyl)sulfonyl)benzamide;
4-(4′-(2,3-dihydro-1H-indol-5-yl)methyl)piperazin-1-yl)-2-((1H-indol-4-yl))-N-((3-nitro-4-((3-pyrrolidin-1-ylpropyl)amino)phenyl)sulfonyl)benzamide;
4-(4′-(2,3-dihydro-1H-indol-5-yl)methyl)piperazin-1-yl)-2-((1H-indol-4-yl))-N-((3-nitro-4-((3-pyrrolidin-1-ylpropyl)amino)phenyl)sulfonyl)benzamide;
4-(4′-(2,3-dihydro-1H-indol-5-yl)methyl)piperazin-1-yl)-2-((1H-indol-4-yl))-N-((3-nitro-4-((3-pyrrolidin-1-ylpropyl)amino)phenyl)sulfonyl)benzamide;
4-(4′-(2,3-dihydro-1H-indol-5-yl)methyl)piperazin-1-yl)-2-((1H-indol-4-yl))-N-((3-nitro-4-((3-pyrrolidin-1-ylpropyl)amino)phenyl)sulfonyl)benzamide;
4-(4′-(2,3-dihydro-1H-indol-5-yl)methyl)piperazin-1-yl)-2-((1H-indol-4-yl))-N-((3-nitro-4-((3-pyrrolidin-1-ylpropyl)amino)phenyl)sulfonyl)benzamide;
4-(4′-(2,3-dihydro-1H-indol-5-yl)methyl)piperazin-1-yl)-2-((1H-indol-4-yl))-N-((3-nitro-4-((3-pyrrolidin-1-ylpropyl)amino)phenyl)sulfonyl)benzamide;
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-((3-dimethylamino)propyl)amino)-3-nitrophenyl)sulfonyl)-2-phenoxypyrazine;
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-((3-morpholin-4-yl)propyl)amino)-3-nitrophenyl)sulfonyl)-2-phenoxypyrazine;
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-((3-dimethylamino)butyl)amino)-3-nitrophenyl)sulfonyl)-2-phenoxypyrazine;
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((1-phenylsulfonyl)piperidin-4-yl)amino)phenyl)sulfonyl)-2-phenoxypyrazine;
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((1-quinolin-8-yl)sulfonyl)piperidin-4-yl)amino)phenyl)sulfonyl)-2-phenoxypyrazine;
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-phenoxypyrazine-N-((4-((3-((trifluoromethyl)sulfonyl)phenyl)sulfonyl)phenyl)sulfonyl)benzamide;
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-phenoxypyrazine-N-((4-((1-quinolin-8-yl)sulfonyl)piperidin-4-yl)amino)-3-((trifluoromethyl)sulfonyl)phenyl)sulfonyl)benzamide;
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-phenoxypyrazine-N-((4-((1S)-3-(dimethylamino)-1-thien-2-yl)propyl)amino)-3-nitrophenyl)sulfonyl)-2-phenoxypyrazine;
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((1-quinolin-8-yl)methyl)amino)phenyl)sulfonyl)-2-phenoxypyrazine;
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-phenoxypyrazine-N-((4-((tetrahydro-2H-pyran-4-yl)methyl)amino)-3-((trifluoromethyl)sulfonyl)phenyl)sulfonyl)benzamide;
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((2-(1H,1,2,3-triazol-1-yl)ethyl)amino)phenyl)sulfonyl)-2-phenoxypyrazine;
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((2-(2H-1,2,3-triazol-2-yl)ethyl)amino)phenyl)sulfonyl)-2-phenoxypyrazine;
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-((3-dimethylamino)propyl)amino)-3-nitrophenyl)sulfonyl)-2-(2-naphthoxy)benzamide;
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((2-(2-oxopyridin-1(2H)-yl)ethyl)amino)phenyl)sulfonyl)-2-phenoxypyrazine;
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((2-pyridin-2-yl)oxy)ethyl)amino)phenyl)sulfonyl)-2-phenoxypyrazine;
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((2-pyridin-4-ylethyl)amino)phenyl)sulfonyl)-2-phenoxypyrazine;
4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-N-((4-(3- (dimethylamino)propyl)amino)-3-(trifluoromethyl)sulfonyl)phenyl)sulfonyl)-2-(1H-indol-5-yloxy)benzamide;
4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-N-((4-(3-(dimethylamino)propyl)amino)-3-(trifluoromethyl)phenyl)sulfonyl)-2-(1H-indol-5-yloxy)benzamide;
4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-N-((3-cyano-4-((3-(dimethylamino)propyl)amino)phenyl)sulfonyl)-2-(1H-indol-5-yloxy)benzamide;
4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H- indol-5-yloxy)-N-((3-nitro-4-((1-tetrahydro-2H-pyran-4-yl)piperidin-4-yl)amino)phenyl)sulfonyl)benzamide;
4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H- indol-5-yloxy)-N-((4-(4-methylpiperazin-1-yl)amino)-3-nitrophenyl)sulfonyl)benzamide;
4-(4-(1-(4'-chloro-1,1'-biphenyl-2-yl)ethyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((3-nitro- 4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)benzamide;
N-((4-(((4-aminotetrahydro-2H-pyran-4-yl)methyl)amino)-3-nitrophenyl)sulfonyl)-4-(4-((2- (4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy) benzamide;
4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H- indol-5-yloxy)-N-((3-nitro-4-((tetahydoro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)benzamide;
Trans-4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2- (1H-indol-5-yloxy)-N-((4-[4-[[4-morpholin-4-ylcycloheyl]amino]-3-nitrophenyl}sulfonyl)benzamide;
4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H- indol-5-yloxy)-N-((4-[[2-methoxyethyl]amino]-3-nitrophenyl)sulfonyl)benzamide;
4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H- indol-5-yloxy)-N-((3-nitro-4-((3S)-tetrahydro-2H-pyran-3-yl)methyl)amino)phenyl)sulfonyl)benzamide;
4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H- indol-5-yloxy)-N-((3-nitro-4-((3R)-tetrahydro-2H-pyran-3-yl)methyl)amino)phenyl)sulfonyl)benzamide;
4-(4-[[4-(4-chlorophenyl)-6,6-dimethyl-5,6-dihydro-2H-pyran-3-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-[{(3-nitro-4-[(tetrahydro-2H-pyran-4-yl)methyl]amino)phenyl}sulfonyl]benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcycohex-1-en-1-yl]methyl]piperazin-1-yl)-N-{(4-[[4-hydroxy-1-methylpiperidin-4-yl]methyl]amino]-3-nitrophenyl}sulfonyl]-2-(1H-indol-5-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcycohex-1-en-1-yl]methyl]piperazin-1-yl)-3-fluoro-2-(1H-indol-5-yloxy)-N-{(4-[[1-methylpiperidin-4-yl]amino]-3-nitrophenyl}sulfonyl]benzamide;
N-{[4-[[3S,4R]-1-benzyl-3-hydroxy-piperidin-4-yl]amino]-3-nitrophenyl}sulfonyl]-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcycohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)benzamide;
N-{(4-[[4-aminotetrahydro-2H-pyran-4-yl]methyl]amino]-3-nitrophenyl}sulfonyl]-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcycohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcycohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-[{(4-[[1-(2-methoxyethyl)piperidin-4-yl]amino]-3-nitrophenyl}sulfonyl]benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcycohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-{[4-[[1-2-hydroxyethyl)piperidin-4-yl]amino]-3-nitrophenyl}sulfonyl]-2-(1H-indol-4-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcycohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-{[4-[[1-(2-methoxyethyl)piperidin-4-yl]amino]-3-nitrophenyl}sulfonyl]benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4-[[1-(3-hydroxypropyl)piperidin-4-yl]amino]-3-nitrophenyl]sulfonyl]-2-(1H-indol-4-yloxy)benzamide;
4-4-[(4'-chloro-3-[3-(dimethylamino)propyl]-1',l'-biphenyl-2-yl)methyl]piperazin-1-yl]-2-(1H-indol-4-yloxy)-N-[[3-nitro-4-[(tetrahydro-2H-pyran-4-ylmethyl)amino]phenyl]sulfonyl]benzamide;
4-4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4-[[1-(3-hydroxypropyl)piperidin-4-yl]amino]-3-nitrophenyl]sulfonyl]-2-(1H-indol-5-yloxy)benzamide;
4-4-[(4'-chloro-4-morpholin-4-yl-1,1'-biphenyl-2-yl)methyl]piperazin-1-yl]-2-(1H-indol-4-yloxy)-N-[[3-nitro-4-[(tetrahydro-2H-pyran-4-ylmethyl)amino]phenyl]sulfonyl]benzamide;
4-4-[(4'-chloro-3-[2-(dimethylamino)ethoxy]-1,1'-biphenyl-2-yl)methyl]piperazin-1-yl]-2-(1H-indol-4-yloxy)-N-[[3-nitro-4-[(1-tetrahydro-2H-pyran-4-yl)piperidin-4-yl]amino]phenyl]sulfonyl]benzamide;
4-4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4-[[4-diethylamino)cyclohexyl]amino]-3-nitrophenyl]sulfonyl]-2-(1H-indol-5-yloxy)benzamide;
4-4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4-[[4-(dimethylamino)cyclohexyl]amino]-3-nitrophenyl]sulfonyl]-2-(1H-indol-4-yloxy)benzamide;
4-4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4-[[4-diethylamino)cyclohexyl]amino]-3-nitrophenyl]sulfonyl]-2-(1H-indol-4-yloxy)benzamide;
4-4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4-[[4-(dimethylamino)cyclohexyl]amino]-3-nitrophenyl]sulfonyl]-2-(1H-indol-4-yloxy)-N-[[4-[(4-morpholin-4-yl)cyclohexyl]amino]-3-nitrophenyl]sulfonyl]benzamide;
4-4-[(4'-chloro-3-[2-(dimethylamino)ethoxy]-1,1'-biphenyl-2-yl)methyl]piperazin-1-yl]-2-(1H-indol-4-yloxy)-N-[[4-[(1-methyl)piperidin-4-yl]amino]-3-nitrophenyl]sulfonyl]benzamide;
4-4-[[1-(4'-chloro-1,1'-biphenyl-2-yl)ethyl]piperazin-1-yl]-2-(1H-indol-4-yloxy)-N-[[4-[[1-methyl)piperidin-4-yl]amino]-3-nitrophenyl]sulfonyl]benzamide;
4-4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4-[[4-(dimethylamino)tetrahydro-2H-pyran-4-yl]methyl]amino]-3-nitrophenyl]sulfonyl]-2-(1H-indol-5-yloxy)benzamide;
N-((4-[[2-(aminocyclohexyl)amino]-3-nitrophenyl]sulfonyl)-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yl oxy) benzamide;  
4-(4-[[4'-chloro-4-[3-(dimethylamino)prop-1-ynyl]-1,1'-biphenyl-2-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((3-nitro-4-[1-(4,4,4-trifluorobutyl)piperidin-4-yl]amino)phenyl)sulfonyl]benzamide;  
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-((4-[[2-(4-hydroxy-1-methylpiperidin-4-yl)ethyl]amino]-3-nitrophenyl)sulfonyl]-2-(1H-indol-5-yloxy) benzamide;  
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((3-nitro-4-[[1-(1,3-thiazol-2-yl)piperidin-4-yl]amino]phenyl)sulfonyl]benzamide;  
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-((4-[[1-cyclopropylmethyl]piperidin-4-yl]amino)-3-nitrophenyl)sulfonyl]-2-(1H-indol-5-yloxy) benzamide;  
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((4-[4-(4-methylpiperazin-1-yl)amino]-3 trifluoromethyl)sulfonyl]phenyl)benzamide;  
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((3-nitro-4-[[1-(4,4,4-trifluorobutyl)piperidin-4-yl]amino]phenyl)sulfonyl]benzamide;  
4-[[4-[[1-(4'-chloro-1,1'-biphenyl-2-yl)ethyl]piperazin-1-yl]-2-(1H-indol-4-yloxy)-N-((4-[4-(4methylpiperazin-1-yl)amino]-3-nitrophenyl]sulfonyl]benzamide;  
4-[[4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]-3-(hydroxymethyl)piperazin-1-yl]-2-(1H-indol-5-yloxy)-N-((3-nitro-4-[[1-(tetrahydro-2Hpyran-4-yl)piperidin-4-yl]amino]phenyl)sulfonyl]benzamide;  

- 48 -
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-([4-[(4-methylpiperazin-1-yl)amino]-3-[(trifluoromethyl)sulfonyl]phenyl]sulfonyl)benzamide;
4-(4-[[4'-chloro-4-(2-hydroxyethoxy)-1,1'-biphenyl-2-yl]methyl]piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-([4-[(1-methylpiperidin-4-yl)amino]-3-nitrophenyl]sulfonyl)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-([3-nitro-4-[[3-(3-oxopiperazin-1-yl)propyl]amino]phenyl]sulfonyl)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-([3-nitro-4-[[3-(3-oxopiperazin-1-yl)propyl]amino]phenyl]sulfonyl)benzamide;
4-(4-[[2-(4-chlorophenyl)-5-hydroxycyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-([4-[(1-methylpiperidin-4-yl)amino]-3-nitrophenyl]sulfonyl)benzamide;
4-(4-[[2-(4-chlorophenyl)-5-hydroxycyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-([4-[(4-methylpiperazin-1-yl)amino]-3-nitrophenyl]sulfonyl)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-([4-[[1-(2,3-dihydro-1H-inden-2-yl)piperidin-4-yl]amino]-3-nitrophenyl]sulfonyl]-2-(1H-indol-4-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4-[[1-(2,3-dihydro-1H-inden-2-yl)piperidin-4-yl]amino]-3-nitrophenyl]sulfonyl]-2-(1H-indol-5-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-([4-[(1-morpholin-4-ylcyclohexyl)methyl]amino]-3-nitrophenyl)sulfonyl]benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-([3-nitro-4-[[1-(1,3-thiazol-2-ylmethyl)piperidin-4-yl]amino]phenyl]sulfonyl)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4-((4-(hydroxymethyl)tetrahydro-2H-pyran-4-yl)methyl]amino]-3-nitrophenyl]sulfonyl]-2-(1H-indol-5-yloxy)benzamide;

4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4-[[2-(hydroxyethyl)piperazin-1-yl]amino]-3-nitrophenyl]sulfonyl]-2-(1H-indol-5-yloxy)benzamide;

4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-[[4-[[3S]-1-methylpyrrolidin-3-yl]amino]-3-nitrophenyl]sulfonyl]benzamide;

4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]-3-(hydroxymethyl)piperazin-1-yl]-2-(1H-indol-5-yloxy)-N-((3-nitro-4-[(tetrahydro-2H-pyran-4-ylmethyl]amino)phenyl] sulfonyl]benzamide;

N-[[4-[[4-aminotetrahydro-2H-pyran-4-yl)methyl]amino]-3-nitrophenyl]sulfonyl]-4-[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]-3-(hydroxymethyl)piperazin-1-yl]-2-(1H-indol-5-yloxy)benzamide;

4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[1-(hydroxycyclohexyl)methyl]amino]-3-nitrophenyl]sulfonyl]-2-(1H-indol-5-yloxy)benzamide;

4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]-2-(1H-indol-4-yloxy)-N-((4-(4-(methoxyethyl)amino)-3-nitrophenyl] sulfonyl]benzamide;

4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((4-(4-(hydroxymethyl)tetrahydro-2H-pyran-4-yl]amino)-3-nitrophenyl] sulfonyl]benzamide;

4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((4-(4-(hydroxymethyl)tetrahydro-2H-pyran-4-yl]amino)-3-nitrophenyl] sulfonyl]benzamide;

4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-((4-((2-hydroxy-1-tetrahydro-2H-pyran-4-yethyl)amino]-3-nitrophenyl] sulfonyl]benzamide;

4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-((4-[(2-hydroxy-1-tetrahydro-2H-pyran-4-yethyl)amino]-3-nitrophenyl] sulfonyl]benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-[[4-(methylamino)-3-nitrophenyl]sulfonfonyl]benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-[[4-(methylamino)-3-nitrophenyl]sulfonfonyl]benzamide;
4-[[1-(4'-chloro-1',1'-biphenyl-2-yl)ethyl]piperazin-1-yl]-2-(1H-indol-4-yloxy)-N-[[4-[[3-morpholin-4-ylpropyl]amino]-3-nitrophenyl]sulfonfonyl]benzamide;
N-[[4-[[1-amino cyclohexyl]methyl]amino]-3-nitrophenyl]sulfonfonyl]-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)benzamide;
4-(4-[[1-2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]ethyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-[[4-[4-methylpiperazin-1-yl]amino]-3-nitrophenyl]sulfonfonyl]benzamide;
4-[[1R-1-(4'-chloro-1',1'-biphenyl-2-yl)ethyl]piperazin-1-yl]-2-(1H-indol-4-yloxy)-N-[[3-nitro-4-[[tetrahydro-2H-pyran-4-ylmethyl]amino]phenyl]sulfonfonyl]benzamide;
4-[(1S)-1-(4'-chloro-1,1'-biphenyl-2-yl)ethyl]piperazin-1-yl]-2-(1H-indol-4-yloxy)-N-[(3-nitro-4-[(tetrahydro-2H-pyran-4-ylmethyl)amino]phenyl)sulfonyl]benzamide;
4-(2-[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]ethyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-[(4-[3-morpholin-4-yl(propyl)amino]-3-nitrophenvl)sulfonyl]benzamide;
4-(2-[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]ethyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-[(3-nitro-4-[(1-tetrahydro-2H-pyran-4-yl)piperidin-4-yl]amino]phenyl)sulfonyl]benzamide;
4-(2-[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl)piperazin-1-yl)-N-[(4-[cyclohexylmethyl)amino]-3-nitrophenvl)sulfonyl]-2-(1H-indol-5-yloxy)benzamide;
4-(2-[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-[(4-[morpholin-4-ylamino]-3-nitrophenvl)sulfonyl]benzamide;
4-(2-[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-[(3-nitro-4-[(tetrahydro-2H-pyran-3-yl)methylamino]phenyl)sulfonyl]benzamide;
4-(2-[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-[(4-[morpholin-4-ylamino]-3-nitrophenvl)sulfonyl]benzamide;
4-(2-[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-[(3-nitro-4-[(tetrahydro-2H-pyran-4-ylamino)phenyl)sulfonyl]benzamide;
4-(2-[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-[(4-[[3-methyloxetan-3-yl)methyl]amino]-3-nitrophenvl)sulfonyl]benzamide;
4-(2-[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-[(4-[4-methoxy[cyclohexyl)amino]-3-nitrophenvl)sulfonyl]benzamide;
4-(2-[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl)piperazin-1-yl)-N-[(3-[1,1-dioxidothiomorpholin-4-yl]propyl]amino]-3-nitrophenvl)sulfonyl]-2-(1H-indol-5-yloxy)benzamide;
4-(2-[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-[(3-nitro-4-[(2-(oxopiperidin-1-yl)ethyl]amino)phenyl)sulfonyl]benzamide;
4-(2-[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-[(3-nitro-4-[(2-(oxoimidazolidin-1-yl)ethyl]amino)phenyl)sulfonyl]benzamide;
4-(2-[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-[(3-nitro-4-[(2-pyridin-4-yethyl)amino]phenyl)sulfonyl]benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-[[4-morpholin-4-yl-3-nitrophenyl]sulfonyl]benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-[[4-[4-methoxy-piperidin-1-yl]-3-nitrophenyl]sulfonyl]benzamide;
4-[[4-(4-chloro-4-((dimethy lamino)ethoxy)-1,1'-biphenyl-2-yl]methyl]piperazin-1-yl]-2-(1H-indol-4-yloxy)-N-[[4-[[4-(methyl)piperazin-1-yl]amino]-3-nitrophenyl]sulfonyl]benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[1,1-dioxidotetrahydrothien-3-yl]methyl]amino]-3-nitrophenyl)sulfonyl]-2-(1H-indol-5-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[1,1-dioxidotetrahydrothien-3-yl]amino]-3-nitrophenyl)sulfonyl]-2-(1H-indol-5-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-[[4-(tetrahydro-2H-pyran-4-ylmethyl)amino]-3-(trifluoromethyl)phenyl]sulfonyl]benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4-[[2-(1,3-dioxolan-2-yl)ethyl]-3-nitrophenyl]sulfonyl]-2-(1H-indol-5-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-[[4-[[1-methyl-5-oxopyrrolidin-3-yl]amino]-3-nitrophenyl]sulfonyl]benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-([4-[[1-methyl-6-oxopiperidin-3-yl]amino]-3-nitrophenyl]sulfonyle)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-[[3-nitro-4-(piperidin-1-ylamino)phenyl]sulfonyle]benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-([3-nitro-4-(piperidin-1-ylamino)phenyl]sulfonyle)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-([4-[[3-methyloxetan-3-yl]methoxy]-3-nitrophenyl]sulfonyle)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-([3-nitro-4-[(1-oxidotetrahydro-2H-thiopyran-4-yl)methyl]amino]phenyl]sulfonyle)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-([3-nitro-4-[[1,3-thiazol-5-ylmethyl]amino]phenyl]sulfonyle)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-[[3-nitro-4-(tetrahydro-2H-pyran-4-ylmethoxy)phenyl]sulfonyle]benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-([4-[[3-(methylsulfonyl)propyl]amino]-3-nitrophenyl]sulfonyle]benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4-[[3-[1,1-dioxidothiomorpholin-4-yl]propyl]amino]-3-nitrophenyl]sulfonyl]-2-(1H-indol-4-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4-[[1,4-dioxan-2-ylmethoxy]-3-nitrophenyl]sulfonyl]-2-(1H-indol-5-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[1,1-dioxidotetrahydrothien-3-yl]amino]-3-nitrophenyl]sulfonyl]-2-(1H-indol-4-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4-[[1,1-dioxidotetrahydro-2H-thiopyran-4-yl]methyl]amino]-3-nitrophenyl]sulfonyl]-2-(1H-indol-4-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[2,2-difluoroethyl]amino]-3-nitrophenyl]sulfonyl]-2-(1H-indol-5-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4,4-difluorocyclohexyl]amino]-3-nitrophenyl]sulfonyl]-2-(1H-indol-5-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4-fluorotetrahydro-2H-pyran-4-ylmethoxy]-3-nitrophenyl]sulfonyl]-2-(1H-indol-4-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-4-[[4-hydroxy(cyclohexyl)methyl]amino]-3-nitrophenyl]sulfonyl]-2-(1H-indol-5-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-4-[[4-methoxy(cyclohexyl)methyl]amino]-3-nitrophenyl]sulfonyl]benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-4-[[3-nitro-4-(2-tetrahydro-2H-pyran-4-ylethoxy)phenyl]sulfonyl]benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-4-[[3-(methylsulfonyl)propoxy]-3-nitrophenyl]sulfonyl]benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-4-[[3-(methoxypropyl)amino]-3-nitrophenyl]sulfonyl]benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-4-[[3-(methoxypropyl)amino]-3-nitrophenyl]sulfonyl]benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[4-[[2-cyanoethyl]amino]-3-nitrophenyl]sulfonyl]-2-(1H-indol-5-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[4-[[2-cyanoethyl]amino]-3-nitrophenyl]sulfonyl]-2-(1H-indol-4-yloxy)benzamide;
4-[(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl)-N-[(3R)-4-hydroxy-1-adamantyl)methyl] amino)-3-nitrophenyl]sulfonyl]-2-(1H-indol-5-yloxy)benzamide;
4-{[(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl}-N-[(Cis-4-hydroxy-1-adamantyl)methyl] amino)-3-nitrophenyl]sulfonyl]-2-(1H-indol-5-yloxy)benzamide;
4-(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-[(3-nitro-4-[(3,3,3-trifluoropropyl)amino]phenyl] sulfonyl]benzamide;
4-(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-[(3-nitro-4-[(3,3,3-trifluoropropyl)amino]phenyl] sulfonyl]benzamide;
N-[(5-bromo-6-[tetrahydro-2H-pyran-4-ylmethyl]amino]pyridin-3-yl] sulfonyl]-4-(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl)-2-(1H-indol-4-yloxy)benzamide;
4-(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl)-N-[(1,1-dioxidotetrahydrothien-3-yl)methyl] amino)-3-nitrophenyl]sulfonyl]-2-(1H-indol-4-yloxy)benzamide;
4-(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl)-N-[(4-(methylamino)-3-[(trifluoromethyl)sulfonyl]phenyl] sulfonyl]benzamide;
N-[(5-bromo-6-[tetrahydro-2H-pyran-4-ylmethoxy]pyridin-3-yl] sulfonyl]-4-(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)benzamide;
4-(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-[(4-(methylamino)-3-[(trifluoromethyl)sulfonyl]phenyl] sulfonyl]benzamide;
4-(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-[(6-[tetrahydro-2H-pyran-4-ylmethoxy]-5-(1,3-thiazol-2-yl)pyridin-3-yl] sulfonyl]benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[5-cyano-6-(tetrahydro-2H-pyran-4-ylmethoxy)pyridin-3-yl]sulfonyl]-2-(1H-indol-5-yloxy)benzamide;
N-[[4-[[1-acetyl]piperidin-4-yl]amino]-3-nitrophenyl]sulfonyl]-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-[[4-[[1-(methylsulfonyl)piperidin-4-yl]amino]-3-nitrophenyl]sulfonyl]benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4-[[1,4-dioxan-2-ylmethyl]amino]-3-nitrophenyl]sulfonyl]-2-(1H-indol-5-yloxy)benzamide;
N-[[4-[[1-acetyl]piperidin-4-yl]amino]-3-nitrophenyl]sulfonyl]-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-4-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-[[4-[[1-(methylsulfonyl)piperidin-4-yl]amino]-3-nitrophenyl]sulfonyl]benzamide;
4-[[4-(5-tert-butyl-4'-chloro-1,1'-biphenyl-2-yl)methyl]piperazin-1-yl]-2-(1H-indol-5-yloxy)-N-[[3-nitro-4-[(tetrahydro-2H-pyran-4-ylmethyl)amino]phenyl]sulfonyl]benzamide;
4-[[4-(5-tert-butyl-4'-chloro-1,1'-biphenyl-2-yl)methyl]piperazin-1-yl]-2-(1H-indol-5-yloxy)-N-[[3-nitro-4-(tetrahydro-2H-pyran-4-ylmethoxy)phenyl]sulfonyl]benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4-[(2R)-1,4-dioxan-2-ylmethoxy]-3-nitrophenyl]sulfonyl]-2-(1H-indol-5-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-(4-[(2S)-1,4-dioxan-2-ylmethoxy]-3-nitrophenyl)sulfonyl)-2-(1H-indol-5-yloxy)benzamide;
N-(5-bromo-6-[[tetrahydro-2H-pyran-4-ylmethyl]amino]pyridin-3-yl)sulfonyl)-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-{5-cyano-6-[[tetrahydro-2H-pyran-4-ylmethyl]amino]pyridin-3-yl}sulfonyl)-2-(1H-indol-5-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-{4-[[1-methylpiperidin-4-yl]oxy]-3-nitrophenyl]sulfonyl]benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-{4-[[1-methylpiperidin-4-yl]methoxy]-3-nitrophenyl]sulfonyl]benzamide;
4-(4-[[2-(4-chlorophenyl)-1-(3-hydroxypropyl)-1,2,5,6-tetrahydropyridin-3-yl]methyl]piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-(3-nitro-4-[[tetrahydro-2H-pyran-4-ylmethyl]amino]phenyl]sulfonyl]benzamide;
benzyl 4-[[4-[[4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl]-2-(1H-indol-5-yloxy)benzoyl]amino]sulfonyl]-2-nitrophenyl)methyl)piperidine-1-carboxylate;
N-{3-(aminocarbonyl)-4-[[tetrahydro-2H-pyran-4-ylmethoxy]phenyl]sulfonyl]-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)benzamide;
4-[(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl)-N-{(4-
{(1R)-1-(hydroxymethyl)-2-methylpropyl}amino)-3-nitrophenyl}sulfonyl]-2-(1H-indol-5-
ol-5-yloxy)benzamide;
4-[(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl)-2-(1H-
indol-5-yloxy)-N-{(4-[(4-methoxyphenyl)amino]-3-nitrophenyl}sulfonyl]benzamide;
N-[(4-[(2-(1,3-benzodioxol-5-yl)ethyl]amino)-3-nitrophenyl]sulfonyl]-4-[(2-
(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl)-2-(1H-indol-5-
ol-5-yloxy)benzamide;
4-[(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl)-2-(1H-
indol-5-yloxy)-N-[(3-nitro-4-[[3-(2-oxopyrrolidin-1-
(4-[(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl)-N-{(4-
[3-(1H-imidazol-1-yl)propyl]amino]-3-nitrophenyl}sulfonyl]-2-(1H-indol-5-
ol-5-yloxy)benzamide;
4-[(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl)-N-[(4-
[3-(1H-imidazol-1-yl)propyl]amino]-3-nitrophenyl}sulfonyl]-2-(1H-indol-5-
ol-5-yloxy)benzamide;
4-[(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl)-2-(1H-
indol-5-yloxy)-N-[(3-nitro-4-[[1S]-1-phenylethyl]amino]-phenyl]sulfonyl]benzamide;
N-[(2-chloro-5-fluoro-4-[(tetrahydro-2H-pyran-4-ylmethyl]amino}phenyl]sulfonyl]-4-[(2-
(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl)-2-(1H-indol-5-
ol-5-yloxy)benzamide;
4-[(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl)-2-(1H-
indol-5-yloxy)-N-[(4-[(2-(methoxyethoxy)ethyl]thio]-3-nitrophenyl)sulfonyl]benzamide;
4-[(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl)-2-(1H-
indol-4-yloxy)-N-[(4-[(2-(methoxyethoxy)ethyl]thio]-3-nitrophenyl)sulfonyl]benzamide;
4-[(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl)-2-(1H-
indol-5-yloxy)-N-[(4-(methylsulfonyl)phenyl]sulfonyl]benzamide;
4-[(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl)-2-(1H-
indol-4-yloxy)-N-[(4-(methylsulfonyl)phenyl]sulfonyl]benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-((4-
[(2,2-dimethyltetrahydro-2H-pyran-4-yl)methoxy]-3-nitrophenoxy)sulfonyl)-2-(1H-indol-5-
yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-([5-
cyano-6-[(4-fluorotetrahydro-2H-pyran-4-yl)methoxy]pyridin-3-yl]sulfonyl)-2-(1H-indol-5-
yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-([5-
cyano-6-(tetrahydro-2H-pyran-4-yl)methoxy]pyridin-3-yl]sulfonyl)-2-(1H-indol-4-
yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-([5-
chloro-6-(tetrahydro-2H-pyran-4-yl)methoxy]pyridin-3-yl]sulfonyl)-2-(1H-indol-4-
yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-([5-
cyano-6-(2-morpholin-4-ylethoxy)pyridin-3-yl]sulfonyl)-2-(1H-indol-5-yl oxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-(3-nitro-4-[(1-tetrahydro-2H-pyran-4-yl)piperidin-4-
yl]oxy)phenyl] sulfonyl) benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-
indol-5-yl)oxy)-N-(4-[(4-morpholin-4-ylbut-2-ynyl oxy)-3-nitrophenoxy)sulfonyl) benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-([5-
ethynyl-6-(tetrahydro-2H-pyran-4-yl)methoxy]pyridin-3-yl]sulfonyl)-2-(1H-indol-4-
yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-([5-
cyano-6-(2-morpholin-4-ylethoxy)pyridin-3-yl]sulfonyl)-2-(1H-indol-4-yl oxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-([5-
cyano-6-[(4-fluorotetrahydro-2H-pyran-4-yl)methoxy]pyridin-3-yl] sulfonyl)-2-(1H-indol-4-
yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-((4-
[(3-hydroxy-4-methoxyphenyl) amino]-3-nitrophenoxy)sulfonyl)-2-(1H-indol-5-
yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(2,3-
dihydro-1H-indol-4-yl)oxy)-N-(4-[(1-methylpiperidin-4-yl)amino]-3-
nitrophenoxy)sulfonyl) benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-({4-[(1-methylpiperidin-4-yl)amino]-3-nitrophenyl}sulfonyl)-2-(pyridin-3-ylamino)benzamide;  
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-({3-nitro-4-[(1-tetrahydro-2H-pyran-4-yl)piperidin-4-yl]amino}[phenyl]sulfonyl)-2-(pyridin-3-yloxy)benzamide;  
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-({3-nitro-4-[(tetrahydro-2H-pyran-4-ylmethyl]amino}[phenyl]sulfonyl)-2-(1,2,3,4-tetrahydroisoquinolin-5-yloxy)benzamide;  
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-[(1H-indazol-4-yloxy)-N-({3-nitro-4-[(tetrahydro-2H-pyran-4-ylmethyl]amino}[phenyl]sulfonyl)benzamide;  
Trans-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indazol-4-yloxy)-N-({4-[(4-morpholin-4-ylcyclohexyl]amino]-3-nitrophenyl}sulfonyl)benzamide;  
2-(1H-benzimidazol-4-yloxy)-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-({3-nitro-4-[(tetrahydro-2H-pyran-4-ylmethyl]amino}[phenyl]sulfonyl)benzamide;  
N-({5-chloro-6-[(4-fluorotetrahydro-2H-pyran-4-yl)methoxy]pyridin-3-yl}sulfonyl)-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indazol-4-yloxy)benzamide;  
N-({5-chloro-6-[(4-fluorotetrahydro-2H-pyran-4-yl)methoxy]pyridin-3-yl}sulfonyl)-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-4-yloxy)benzamide;  
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-({5-cyano-6-[(4-fluorotetrahydro-2H-pyran-4-yl)methoxy]pyridin-3-yl}sulfonyl)-2-(1H-indazol-4-yloxy)benzamide;
2-(1H-benzimidazol-4-yloxy)-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4-[[3R]-1-(2,2-difluoroethyl)pyrrolidin-3-yl]amino]-3-nitrophenyl]sulfonyl]benzamide;

2-(1H-benzimidazol-4-yloxy)-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[(4-[4-fluorotetrahydro-2H-pyran-4-yl]methoxy)-3-nitrophenyl]sulfonyl]benzamide;

4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4-[[4-fluorotetrahydro-2H-pyran-4-yl]methyl]amino]-3-nitrophenyl]sulfonyl]-2-(1H-indazol-4-yloxy)benzamide;

4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[6-[4-fluorotetrahydro-2H-pyran-4-yl]methoxy]-5-(trifluoromethyl)pyridin-3-yl]sulfonyl]-2-(1H-indazol-4-yloxy)benzamide;

4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4-[[4-cyclopropylmorpholin-2-yl]methyl]amino]-3-nitrophenyl]sulfonyl]-2-(1H-indazol-4-yloxy)benzamide;

4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4-[[4,4-difluorocyclohexyl]methyl]amino]-3-nitrophenyl]sulfonyl]-2-(1H-indazol-4-yloxy)benzamide;

N-[[5-chloro-6-[[4-fluorotetrahydro-2H-pyran-4-yl]methyl]amino]pyridin-3-yl]sulfonyl]-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indazol-4-yloxy)benzamide;

Trans-N-[[5-chloro-6-[[4-methoxycyclohexyl]methoxy]pyridin-3-yl]sulfonyl]-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indazol-4-yloxy)benzamide;


4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[5-fluoro-6-[[4-fluorotetrahydro-2H-pyran-4-yl]methoxy]pyridin-3-yl]sulfonyl]-2-(1H-indazol-4-yloxy)benzamide;

2-(1H-benzimidazol-4-yloxy)-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[3-nitro-4-[(1-tetrahydro-2H-pyran-4-yl)piperidin-4-yl]amino]phenyl]sulfonyl]benzamide;
2-(1H-benzimidazol-4-yl)oxy)-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[4-[[1-methylpiperidin-4-yl]amino]-3-nitrophenyl]sulfonyl]benzamide;

N-[[5-chloro-6-[[1-(cyanomethyl)-4-fluoropiperidin-4-yl]methoxy]pyridin-3-yl]sulfonyl]-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indazol-4-yloxy)benzamide;

4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[5-chloro-6-(tetrahydrofuran-3-ylmethoxy)pyridin-3-yl]sulfonyl]-2-(1H-indazol-4-yloxy)benzamide;

Trans-N-[(5-chloro-6-[[4-hydroxycyclohexyl]methoxy]pyridin-3-yl]sulfonyl]-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indazol-4-yloxy)benzamide;

N-[[5-chloro-6-[[3R]-1-(2,2-difluoroethyl)pyrrolidin-3-yl]oxy]pyridin-3-yl]sulfonyl]-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indazol-4-yloxy)benzamide;

2-(1H-benzimidazol-4-yl)oxy)-N-[[5-chloro-6-[[2S]-4-(N,N-dimethylglycyl)morpholin-2-yl]methoxy]pyridin-3-yl]sulfonyl]-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)benzamide;

2-(1H-benzimidazol-4-yl)oxy)-N-[[5-chloro-6-[[2S]-4-(N,N-dimethylglycyl)morpholin-2-yl]methoxy]pyridin-3-yl]sulfonyl]-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indazol-4-yloxy)benzamide;

N-[[5-chloro-6-[[2S]-4-(N,N-dimethylglycyl)morpholin-2-yl]methoxy]pyridin-3-yl]sulfonyl]-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indazol-4-yloxy)benzamide;

N-[[5-chloro-6-[[2R]-4-(N,N-dimethylglycyl)morpholin-2-yl]methoxy]pyridin-3-yl]sulfonyl]-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indazol-4-yloxy)benzamide;

4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[5-chloro-6-(tetrahydro-2H-pyran-4-ylmethoxy)pyridin-3-yl]sulfonyl]-2-(1H-indazol-4-yloxy)benzamide;

2-(1H-benzimidazol-4-yl)oxy)-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4-[[3R]-1-(cyanomethyl)pyrrolidin-3-yl]amino]-3-nitrophenyl]sulfonyl]benzamide;
2-(1H-benzimidazol-4-yloxy)-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4-((3R)-1-[2-(2-methoxyethoxy)ethyl]pyrrolidin-3-yl]amino)-3-nitrophenyl]sulfonyl]benzamide;
2-(1H-benzimidazol-4-yloxy)-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4-((3R)-1-(N,N-dimethylglycyl)pyrrolidin-3-yl)amino]-3-nitrophenyl]sulfonyl]benzamide;
2-(1H-benzimidazol-4-yloxy)-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4-((4-(cyanomethyl)morpholin-2-yl)methyl)amino]-3-nitrophenyl]sulfonyl]benzamide;
2-(1H-benzimidazol-4-yloxy)-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4-(3-nitro-4-[[4-oxetan-3-ylmorpholin-2-yl]methyl]amino]-3-nitrophenyl]sulfonyl]benzamide;
N-[[5-chloro-6-((3R)-1-[2-fluoro-1-(fluoromethyl)ethyl]pyrrolidin-3-yl]oxy)pyridin-3-yl]sulfonyl]-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indazol-4-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4-((3R)-1-[2-fluoro-1-(fluoromethyl)ethyl]pyrrolidin-3-yl)amino]-3-nitrophenyl]sulfonyl]-2-(1H-indazol-4-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4-[[1-cyclopropylpiperidin-4-yl]amino]-3-nitrophenyl]sulfonyl]-2-(1H-indazol-4-yloxy)benzamide;
Trans-2-(1H-benzimazidol-4-yloxy)-4-(4-\{2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl\}methyl)piperazin-1-yl)-N-\{(4-\{(4-methoxy)cyclohexyl\}methyl)amino\}-3-nitrophenyl)sulfonyl]benzamide;
2-(1H-benzimazidol-4-yloxy)-4-(4-\{2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl\}methyl)piperazin-1-yl)-N-(4-\{(4-fluorotetrahydro-2H-pyran-4-yl)\}methyl)amino\}-3-nitrophenyl)sulfonyl]benzamide;
2-(1H-benzimazidol-4-yloxy)-4-(4-\{2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl\}methyl)piperazin-1-yl)-N-(\{5-fluoro-6-\{(4-fluorotetrahydro-2H-pyran-4-yl\}methoxy\}pyridin-3-yl\}sulfonyl)benzamide;
2-(1H-benzimazidol-4-yloxy)-N-(\{5-chloro-6-\{(4-fluorotetrahydro-2H-pyran-4-yl\}methoxy\}pyridin-3-yl\}sulfonyl)-4-(4-\{2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl\}methyl)piperazin-1-yl)-2-(1H-indazol-4-yloxy)benzamide;
N-(\{5-chloro-6-\{(3R)-1-\{2-fluoro-1-(fluoromethyl)\}pyrrolidin-3-yl\}methoxy\}pyridin-3-yl\}sulfonyl)-4-(4-\{2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl\}methyl)piperazin-1-yl)-2-(1H-indazol-4-yloxy)benzamide;
Trans-4-(4-\{2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl\}methyl)piperazin-1-yl)-2-(1H-indazol-4-yloxy)-N-(\{4-\{(4-methoxy)cyclohexyl\}methylamino\}-3-nitrophenyl)sulfonyl]benzamide;
4-(4-\{2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl\}methyl)piperazin-1-yl)-N-(\{4-(1,4-dioxan-2-yl)methoxy\}3-nitrophenyl)sulfonyl]-2-(1H-indazol-4-yloxy)benzamide;
N-(\{5-chloro-6-\{(1-cyclopropyl)piperidin-4-yl\}amino\}pyridin-3-yl\}sulfonyl)-4-(4-\{2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl\}methyl)piperazin-1-yl)-2-(1H-indazol-4-yloxy)benzamide;
2-(1H-benzimazidol-4-yloxy)-N-(\{5-chloro-6-\{(1-cyclopropyl)piperidin-4-yl\}amino\}pyridin-3-yl\}sulfonyl)-4-(4-\{2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl\}methyl)piperazin-1-yl)-2-(1H-indazol-4-yloxy)benzamide;
2-(1H-benzimazidol-4-yloxy)-4-(4-\{2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl\}methyl)piperazin-1-yl)-N-(\{4-\{(1,4-dioxan-2-yl)methylamino\}-3-nitrophenyl)sulfonyl]benzamide;
2-(1H-benzimidazol-4-yloxy)-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4-[(1-cyclopropylpiperidin-4-yl)amino]-3-nitrophenyl]sulfonyl]benzamide;
Trans-2-(1H-benzimidazol-4-yloxy)-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4-[(4-morpholin-4-yl)cyclohexyl]amino]-3-nitrophenyl]sulfonyl]benzamide;
2-(1H-benzimidazol-4-yloxy)-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4-[(4-methylpiperazin-1-yl)amino]-3-nitrophenyl]sulfonyl]benzamide;
2-(1H-benzimidazol-4-yloxy)-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4-[(1-methylpiperidin-4-yl)methyl]amino]-3-nitrophenyl]sulfonyl]benzamide;
2-(1H-benzimidazol-4-yloxy)-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4-[(4,4-difluorocyclohexyl)methyl]amino]-3-nitrophenyl]sulfonyl]benzamide;
N-[[4-[(4-acetylmorpholin-2-yl)methyl]amino]-3-nitrophenyl]sulfonyl]-2-(1H-benzimidazol-4-yloxy)-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl]benzamide;
2-(1H-benzimidazol-4-yloxy)-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4-[(4-(methylsulfonyl)morpholin-2-yl)methyl]amino]-3-nitrophenyl]sulfonyl]benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[6-(4-fluoro-1-[2-fluoro-1-(fluoromethyl)ethyl]piperidin-4-yl)methoxy]-5-(trifluoromethyl)pyridin-3-yl)sulfonyl]-2-(1H-indazol-4-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[5-chloro-6-(2-tetrahydrofuran-2-ylethoxy)pyridin-3-yl]sulfonyl]-2-(1H-indazol-4-yloxy)benzamide;
Trans-2-(1H-benzimidazol-4-yloxy)-4-(4-\{(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl\}piperazin-1-yl)-N-\{(4-\{(4-cyanocyclohexyl)methyl\}amino\}-3-nitrophenyl)sulfonyl]benzamide;

2-(1H-benzimidazol-4-yloxy)-N-(\{5-chloro-6-\{(4,4-difluorocyclohexyl)methoxy\}pyridin-3-yl\}sulfonyl)-4-(4-\{(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl\}piperazin-1-yl)benzamide;

N-(\{3-chloro-4-\{(4-fluorotetrahydro-2H-pyran-4-yl)methoxy\}phenyl\}sulfonyl)-4-(4-\{(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl\}piperazin-1-yl)-2-(1H-indazol-4-yloxy)benzamide;

N-(\{5-chloro-6-\{(4-fluorotetrahydro-2H-pyran-4-yl)methoxy\}pyridin-3-yl\}sulfonyl)-4-(4-\{(4-(4-chlorophenyl)-6,6-dimethyl-5,6-dihydro-2H-pyran-3-yl)methyl\}piperazin-1-yl)-2-(1H-indazol-4-yloxy)benzamide;

4-(4-\{(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl\}piperazin-1-yl)-N-(\{5-cyano-6-\{(2-tetrahydro-2H-pyran-4-ylethoxy\}pyridin-3-yl\}sulfonyl)-2-(1H-indazol-4-yloxy)benzamide;

4-(4-\{(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl\}piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-(\{4-\{[(1R,5S)-8-methyl-8-azabicyclo[3.2.1]oct-3-yl]amino\}-3-nitrophenyl\}sulfonyl]benzamide;

N-(\{3-nitro-4-\{\{tetrahydro-2H-pyran-4-ylmethyl\}amino\}phenyl\}sulfonyl)-2-phenoxy-4-(4-(\{(3-phenylpropanoyl\}\{(1S,2S,3S,5R)-2,6,6-trimethylbicyclo[3.1.1]hept-3-yl\}amino\}piperidin-1-yl)benzamide;

N-(\{4-\{(3-morpholin-4-ylpropyl\}amino\}-3-nitrophenyl\}sulfonyl)-2-phenoxy-4-(4-\{(3-phenylpropanoyl\}\{(1S,2S,3S,5R)-2,6,6-trimethylbicyclo[3.1.1]hept-3-yl\}amino\}piperidin-1-yl)benzamide;

N-(\{3-nitro-4-\{\{tetrahydro-2H-pyran-4-ylmethyl\}amino\}phenyl\}sulfonyl)-2-phenoxy-4-(4-(\{(3-phenylpropyl\}\{(1S,2S,3S,5R)-2,6,6-trimethylbicyclo[3.1.1]hept-3-yl\}amino\}piperidin-1-yl)benzamide;

N-(\{4-\{(3-morpholin-4-ylpropyl\}amino\}-3-nitrophenyl\}sulfonyl)-2-phenoxy-4-(4-(\{(3-phenylpropyl\}\{(1S,2S,3S,5R)-2,6,6-trimethylbicyclo[3.1.1]hept-3-yl\}amino\}piperidin-1-yl)benzamide;

4-[4-(2-\{[(1R,5S)-8-methyl-8-azabicyclo[3.2.1]oct-3-yl]amino\}benzyl)piperazin-1-yl]-N-(\{4-\{3-morpholin-4-ylpropyl\}amino\}-3-nitrophenyl\}sulfonyl)-2-phenoxybenzamide;

4-[4-(2-\{[(1R,5S)-8-methyl-8-azabicyclo[3.2.1]oct-3-yl]amino\}benzyl)piperazin-1-yl]-N-(\{3-nitro-4-\{\{tetrahydro-2H-pyran-4-ylmethyl\}amino\}phenyl\}sulfonyl)-2-phenoxybenzamide;
4-[(2-(3-azabicyclo[3.2.2]non-3-yl)benzyl)piperazin-1-yl]-N-(3-nitro-4-[(tetrahydro-2H-pyran-4-ylmethyl)amino]phenyl)sulfonfonyl)-2-phenoxybenzamide; 
4-[(2-(3-azabicyclo[3.2.2]non-3-yl)benzyl)piperazin-1-yl]-2-phenoxy-N-(4-[(tetrahydro-2H-pyran-4-ylmethyl)amino]-3-(trifluoromethyl)sulfonfonyl)phenyl)sulfonfonyl)benzamide; 
4-[(2-(3-azabicyclo[3.2.2]non-3-yl)benzyl)piperazin-1-yl]-2-phenoxy-N-(4-[(tetrahydro-2H-pyran-4-ylmethyl)amino]phenyl)sulfonfonyl)benzamide; 
4-[(2-(3-azabicyclo[3.2.2]non-3-yl)benzyl)piperazin-1-yl]-N-(4-[(3-morpholin-4-yl)propyl]amino]-3-nitrophenyl)sulfonfonyl)-2-phenoxybenzamide; 
4-(2-[(4R,7S)-2,3,3a,4,7,7a-hexahydro-1H-4,7-methanoinden-5-yl]benzyl)piperazin-1-yl)-N-(3-nitro-4-[(tetrahydro-2H-pyran-4-ylmethyl)amino]phenyl)sulfonfonyl)-2-phenoxybenzamide; 
and therapeutically acceptable salts, prodrugs, salts of prodrugs and metabolites thereof.

Another embodiment pertains to a composition for treating bladder cancer, brain cancer, breast cancer, bone marrow cancer, cervical cancer, chronic lymphocytic leukemia, colorectal cancer, esophageal cancer, hepatocellular cancer, lymphoblastic leukemia, follicular lymphoma, lymphoid malignancies of T-cell or B-cell origin, melanoma, myelogenous leukemia, myeloma, oral cancer, ovarian cancer, non-small cell lung cancer, chronic lymphocytic leukemia, myeloma, prostate cancer, small cell lung cancer or spleen cancer, said composition comprising an excipient and a therapeutically effective amount of the compound of Formula (I).

Another embodiment pertains to a method of treating bladder cancer, brain cancer, breast cancer, bone marrow cancer, cervical cancer, chronic lymphocytic leukemia, colorectal cancer, esophageal cancer, hepatocellular cancer, lymphoblastic leukemia, follicular lymphoma, lymphoid malignancies of T-cell or B-cell origin, melanoma, myelogenous leukemia, myeloma, oral cancer, ovarian cancer, non-small cell lung cancer, chronic lymphocytic leukemia, myeloma, prostate cancer, small cell lung cancer or spleen cancer in a
patient, said method comprising administering to the patient a therapeutically effective amount of Formula (I).

Another embodiment pertains to a method of treating bladder cancer, brain cancer, breast cancer, bone marrow cancer, cervical cancer, chronic lymphocytic leukemia, colorectal cancer, esophageal cancer, hepatocellular cancer, lymphoblastic leukemia, follicular lymphoma, lymphoid malignancies of T-cell or B-cell origin, melanoma, myelogenous leukemia, myeloma, oral cancer, ovarian cancer, non-small cell lung cancer, chronic lymphocytic leukemia, myeloma, prostate cancer, small cell lung cancer or spleen cancer in a patient, said method comprising administering to the patient therapeutically effective amount of the compound of Formula (I) and a therapeutically effective amount of one additional therapeutic agent or more than one additional therapeutic agent.

DETAILED DESCRIPTION OF THE INVENTION

Variable moieties herein are represented by identifiers (capital letters with numerical and/or alphabetical superscripts) and may be specifically embodied.

It is meant to be understood that proper valences are maintained for all moieties and combinations thereof, that monovalent moieties having more than one atom are drawn from left to right and are attached through their left ends, and that divalent moieties are also drawn from left to right.

It is also meant to be understood that a specific embodiment of a variable moiety herein may be the same or different as another specific embodiment having the same identifier.

The term "alkenyl" as used herein, means a straight or branched hydrocarbon chain containing from 2 to 10 carbons and containing at least one carbon-carbon double bond. The term “C<sub>x</sub>-C<sub>y</sub> alkyl” means a straight or branched hydrocarbon chain containing at least one carbon-carbon double bond containing x to y carbon atoms. The term “C<sub>3</sub>-C<sub>6</sub> alkenyl” means an alkenyl group containing 3-6 carbon atoms. Representative examples of alkenyl include, but are not limited to, buta-2,3-dienyl, ethenyl, 2-propenyl, 2-methyl-2-propenyl, 3-butenyl, 4-pentenyl, 5-hexenyl, 2-heptenyl, 2-methyl-1-heptenyl, and 3-decenyl.

The term "alkenylene" means a divalent group derived from a straight or branched chain hydrocarbon of 2 to 4 carbon atoms and contains at least one carbon-carbon double bond. The term “C<sub>x</sub>-C<sub>y</sub> alkylene” means a divalent group derived from a straight or branched hydrocarbon chain containing at least one carbon-carbon double bond and containing x to y
carbon atoms. Representative examples of alkenylene include, but are not limited to, -CH=CH- and -CH₂CH=CH-.

The term "alkyl" as used herein, means a straight or branched, saturated hydrocarbon chain containing from 1 to 10 carbon atoms. The term “Cₓ-Cᵧ alkyl" means a straight or branched chain, saturated hydrocarbon containing x to y carbon atoms. For example “C₁-C₆ alkyl” means a straight or branched chain, saturated hydrocarbon containing 2 to 6 carbon atoms. Representative examples of alkyl include, but are not limited to, methyl, ethyl, n-propyl, iso-propyl, n-butyl, sec-butyl, iso-butyl, tert-butyl, n-pentyl, isopentyl, neopentyl, n-hexyl, 3-methylhexyl, 2,2-dimethylpentyl, 2,3-dimethylpentyl, n-heptyl, n-octyl, n-nonyl, and n-decyl.

The term "alkylene" means a divalent group derived from a straight or branched, saturated hydrocarbon chain of 1 to 10 carbon atoms, for example, of 1 to 4 carbon atoms. The term “Cₓ-Cᵧ alkylene” means a divalent group derived from a straight or branched chain, saturated hydrocarbon containing x to y carbon atoms. For example “C₂-C₆ alkylene” means a straight or branched chain, saturated hydrocarbon containing 2 to 6 carbon atoms. Representative examples of alkenylene include, but are not limited to, -CH₂-, -CH₂CH₂-, -CH₂CH₂CH₂-, and -CH₂CH(CH₃)CH₂-.

The term "alkynyl" as used herein, means a straight or branched chain hydrocarbon group containing from 2 to 10 carbon atoms and containing at least one carbon-carbon triple bond. The term “Cₓ-Cᵧ alkynyl” means a straight or branched chain hydrocarbon group containing from x to y carbon atoms. For example “C₃-C₆ alkynyl” means a straight or branched chain hydrocarbon group containing from 3 to 6 carbon atoms and containing at least one carbon-carbon triple bond. Representative examples of alkynyl include, but are not limited to, acetylenyl, 1-propynyl, 2-propynyl, 3-butylnyl, 2-pentylnyl, and 1-butylnyl.

The term "alkynylene," as used herein, means a divalent radical derived from a straight or branched chain hydrocarbon group containing from 2 to 10 carbon atoms and containing at least one carbon-carbon triple bond.

The term "aryl" as used herein, means phenyl.

The term "cyclic moiety," as used herein, means benzene, phenyl, phenylene, cycloalkane, cycloalkyl, cycloalkylene, cycloalkene, cycloalkenyl, cycloalkenylene, cycloalkyne, cycloalkynyl, cycloalkynylene, heteroarene, heteroaryl, heterocycloalkane, heterocycloalkyl, heterocycloalkene, heterocycloalkenyl and spiroalkyl.

The term "cycloalkylene" or cycloalkyl" or “cycloalkane” as used herein, means a monocyclic or bridged hydrocarbon ring system. The monocyclic cycloalkyl is a carbo cyclic
ring system containing three to ten carbon atoms, zero heteroatoms and zero double bonds. Examples of monocyclic ring systems include cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, and cyclooctyl. The monocyclic ring may contain one or two alkylene bridges, each consisting of one, two, or three carbon atoms, each linking two non-adjacent carbon atoms of the ring system. Representative examples of such bridged cycloalkyl ring systems include, but are not limited to, bicyclo[3.1.1]heptane, bicyclo[2.2.1]heptane, bicyclo[2.2.2]octane, bicyclo[3.2.1]octane, bicyclo[3.2.2]nonane, bicyclo[3.3.1]nonane, bicyclo[4.2.1]nonane, tricyclo[3.3.1.0^3,7]nonane (octahydro-2,5-methanopentalene or noradamantane), and tricyclo[3.3.1.1^3,7]decane (adamantane). The monocyclic and bridged cycloalkyl can be attached to the parent molecular moiety through any substitutable atom contained within the ring system.

The term "cycloalkenylene," or "cycloalkenyl" or "cycloalkene" as used herein, means a monocyclic or a bridged hydrocarbon ring system. The monocyclic cycloalkenyl has four to ten carbon atoms and zero heteroatoms. The four-membered ring systems have one double bond, the five-or six-membered ring systems have one or two double bonds, the seven- or eight-membered ring systems have one, two, or three double bonds, and the nine- or ten-membered rings have one, two, three, or four double bonds. Representative examples of monocyclic cycloalkenyl groups include, but are not limited to, cyclobutenyl, cyclopentenyl, cyclohexenyl, cycloheptenyl, and cyclooctenyl. The monocyclic cycloalkenyl ring may contain one or two alkylene bridges, each consisting of one, two, or three carbon atoms, each linking two non-adjacent carbon atoms of the ring system. Representative examples of the bridged cycloalkenyl groups include, but are not limited to, bicyclo[2.2.1]hept-2-ene, 4,5,6,7-tetrahydro-3H-indene, octahydronaphthalenyl, and 1,6-dihydro-pentalene. The monocyclic and bridged cycloalkenyl can be attached to the parent molecular moiety through any substitutable atom contained within the ring systems.

The term "cycloalkyne," or "cycloalkynyl," or "cycloalkynylene," as used herein, means a monocyclic or a bridged hydrocarbon ring system. The monocyclic cycloalkynyl has eight or more carbon atoms, zero heteroatoms, and one or more triple bonds. The monocyclic cycloalkynyl ring may contain one or two alkylene bridges, each consisting of one, two, or three carbon atoms, each linking two non-adjacent carbon atoms of the ring system. The monocyclic and bridged cycloalkynyl can be attached to the parent molecular moiety through any substitutable atom contained within the ring systems.

The term "heteroarene," or "heteroaryl," or "heteroarylene," as used herein, means a five-membered or six-membered aromatic ring having at least one carbon atom and one or
more than one independently selected nitrogen, oxygen or sulfur atom. The heteroarenes of this invention are connected through any adjacent atoms in the ring, provided that proper valences are maintained. Representative examples of heteroaryl include, but are not limited to, furanyl (including, but not limited thereto, furan-2-y1), imidazolyl (including, but not limited thereto, 1H-imidazol-1-y1), isoxazolyl, isothiazolyl, oxadiazolyl, 1,3-oxazolyl, pyridinyl (e.g. pyridin-4-y1, pyridin-2-y1, pyridin-3-y1), pyridazinyl, pyrimidinyl, pyrazinyl, pyrazolyl, pyrrolyl, tetrazolyl, thiadiazolyl, 1,3-thiazolyl, thienyl (including, but not limited thereto, thien-2-y1, thien-3-y1), triazolyl, and triazinyl.

The term "heterocycloalkane," or "heterocycloalkyl," or "heterocycloalkylene," as used herein, means monocyclic or bridged three-, four-, five-, six-, seven-, or eight-membered ring containing at least one heteroatom independently selected from the group consisting of O, N, and S and zero double bonds. The monocyclic and bridged heterocycloalkane are connected to the parent molecular moiety through any substitutable carbon atom or any substitutable nitrogen atom contained within the rings. The nitrogen and sulfur heteroatoms in the heterocycle rings may optionally be oxidized and the nitrogen atoms may optionally be quarternized. Representative examples of heterocycloalkane groups include, but are not limited to, 8-azabicyclo[3.2.1]octane, 3-azabicyclo[3.2.2]nonane, morpholinyl, tetrahydropyranyl, pyrrolidinyl, piperidinyl, dioxolanyl, tetrahydrofuranyl, thiomorpholinyl, 1,4-dioxanyl, tetrahydrothienyl, tetrahydrothiopyranyl, oxetanyl, piperazinyl, imidazolidinyl, azetidine, azepanyl, aziridinyl, diazepanyl, dithiolanyl, dithianyl, isoxazolidinyl, isothiazolidinyl, oxadiazolidinyl, oxazolidinyl, pyrazolidinyl, tetrahydrothiencyl, thiadiazolidinyl, thiazolidinyl, thiomorpholinyl, trithianyl, and trithianyl.

The term "heterocycloalkene," or "heterocycloalkenyl," or "heterocycloalkenyleny," as used herein, means monocyclic or bridged three-, four-, five-, six-, seven-, or eight-membered ring containing at least one heteroatom independently selected from the group consisting of O, N, and S and one or more double bonds. The monocyclic and bridged heterocycloalkene are connected to the parent molecular moiety through any substitutable carbon atom or any substitutable nitrogen atom contained within the rings. The nitrogen and sulfur heteroatoms in the heterocycle rings may optionally be oxidized and the nitrogen atoms may optionally be quarternized. Representative examples of heterocycloalkene groups include, but are not limited to, 1,4,5,6-tetrahydropyridazinyl, 1,2,3,6-tetrahydropyridinyl, dihydropyranyl, imidazolinyl, isothiazolinyl, oxadiazolinyl, isoxazolinyl, oxazolinyl, pyranyl, pyrazolinyl, pyrrolinyl, thiadiazolinyl, thiazolinyl, and thiopyranyl.
The term "phenylene," as used herein, means a divalent radical formed by removal of a hydrogen atom from phenyl.

The term "spiroalkyl," as used herein, means alkylene, both ends of which are attached to the same carbon atom and is exemplified by C₂-spiroalkyl, C₃-spiroalkyl, C₄-spiroalkyl, C₅-spiroalkyl, C₆-spiroalkyl, C₇-spiroalkyl, C₈-spiroalkyl, C₉-spiroalkyl and the like.

The term "spiroheteroalkyl," as used herein, means spiroalkyl having one or two CH₂ moieties replaced with independently selected O, C(O), CNOH, CNOCH₃, S, S(O), SO₂ or NH and one or two CH moieties unreplaced or replaced with N.

The term "spiroheteroalkenyl," as used herein, means spiroalkenyl having one or two CH₂ moieties replaced with independently selected O, C(O), CNOH, CNOCH₃, S, S(O), SO₂ or NH and one or two CH moieties unreplaced or replaced with N and also means spiroalkenyl having one or two CH₂ moieties unreplaced or replaced with independently selected O, C(O), CNOH, CNOCH₃, S, S(O), SO₂ or NH and one or two CH moieties replaced with N.

The term, "spirocyclo," as used herein, means two substituents on the same carbon atom, that, together with the carbon atom to which they are attached, form a cycloalkane, heterocycloalkane, cycloalkene, or heterocycloalkene ring.

The term "C₂-C₅-spiroalkyl," as used herein, means C₂-spiroalkyl, C₃-spiroalkyl, C₄-spiroalkyl, and C₅-spiroalkyl.

The term "C₂-spiroalkyl," as used herein, means eth-1,2-ylene, both ends of which replace hydrogen atoms of the same CH₂ moiety.

The term "C₃-spiroalkyl," as used herein, means prop-1,3-ylene, both ends of which replace hydrogen atoms of the same CH₂ moiety.

The term "C₄-spiroalkyl," as used herein, means but-1,4-ylene, both ends of which replace hydrogen atoms of the same CH₂ moiety.

The term "C₅-spiroalkyl," as used herein, means pent-1,5-ylene, both ends of which replace hydrogen atoms of the same CH₂ moiety.

The term "C₆-spiroalkyl," as used herein, means hex-1,6-ylene, both ends of which replace hydrogen atoms of the same CH₂ moiety.
The term "NH protecting group," as used herein, means trichloroethoxycarbonyl, tribromoethoxycarbonyl, benzzyloxy carbonyl, para-nitrobenzyl carbonyl, ortho-bromobenzyloxy carbonyl, chloroacetyl, dichloroacetyl, trichloroacetyl, trifluoro acetyl, phenylacetyl, formyl, acetyl, benzoyl, tert-amlyoxycarbonyl, tert-butoxycarbonyl, para-methoxybenzyl oxy carbonyl, 3,4-dimethoxybenzyl-oxycarbonyl, 4-(phenylazo)benzyl oxy carbonyl, 2-furfuryl-oxycarbonyl, diphenylmethoxycarbonyl, 1,1-dimethylpropoxy-carbonyl, isopropanoxy carbonyl, phthaloyl, succinyl, alanyl, leucyl, 1-adaman myloxy carbonyl, 8-quinolyloxycarbonyl, benzyl, diphenylmethyl, triphenylmethyl, 2-nitrophenylthio, methanesulfonyl, para-toluensulfonyl, N,N-dimethylaminomethylene, benzyldene, 2-hydroxybenzylidene, 2-hydroxy-5-chlorobenzylidene, 2-hydroxy-1-naphthylmethylene, 3-hydroxy-4-pyridylmethylene, cyclohexyldiene, 2-ethoxycarbonylcyclohexyldiene, 2-ethoxycarbonylcyclopentylidene, 2-acetyl-cyclohexyldiene, 3,3-dimethyl-5-oxycyclo-hexyldene, diphenylphosphoryl, dibenzylphosphoryl, 5-methyl-2-oxo-2H-1,3-dioxol-4-yl-methyl, trimethylsilyl, triethylsilyl, and triphenylsilyl.

The term "C(O)OH protecting group," as used herein, means methyl, ethyl, n-propyl, isopropyl, 1,1-dimethyl propyl, n-butyl, tert-butyl, phenyl, naphthyl, benzyl, diphenylmethyl, triphenylmethyl, para-nitrobenzyl, para-methoxybenzyl, bis(para-methoxyphenyl)methyl, acetylmethyl, benzoylmethyl, para-nitrobenzoylmethyl, para-bromobenzoymethyl, para-methanesulfonylbenzoylmethyl, 2-tetrahdropryanyl 2-tetrahdrofuranyl, 2,2,2-trichloroethyl, 2-(trimethylsilyl)ethyl, acetoxy methyl, propionyloxymethyl, pivaloyloxymethyl, phthalimidomethyl, succinimidomethyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, methoxymethyl, methoxyethoxymethyl, 2-(trimethylsilyl)ethoxymethyl, benzoxymethyl, methylthiomethyl, 2-methylthioethyl, phenylthiomethyl, 1,1-dimethyl-2-propenyl, 3-methyl-3-but enyl, allyl, trimethylsilyl, triethyisilyl, triisopropylsilyl, diethylisopropylsilyl, tert- butyldimethylsilyl, tert-butylidiphenylsilyl, diphenylmethyisilyl, and tert-butylmethoxyphenylsilyl.

The term "OH or SH protecting group," as used herein, means benzzyloxy carbonyl, 4-nitrobenzyloxy carbonyl, 4-bromobenzyloxy carbonyl, 4-methoxybenzyloxy carbonyl, 3,4-dimethoxybenzyloxy carbonyl, methoxycarbonyl, ethoxycarbonyl, tert-butoxycarbonyl, 1,1-dimethylpropoxycarbonyl, isopropanoxy carbonyl, isobutyloxycarbonyl, diphenylmethoxycarbonyl, 2,2,2-trichloroethoxycarbonyl, 2,2,2-tribromoethoxycarbonyl, 2-(trimethylsilyl)ethoxycarbonyl, 2-(phenylsulfonyl)ethoxycarbonyl, 2-(triphenylphosphonio)ethoxycarbonyl, 2-furfuryloxy carbonyl, 1-adaman tyloxy carbonyl,
vinyl氧carbonyl, allyloxy carbonyl, S-benzyl thiocarbonyl, 4-ethoxy-1-naphthoxy carbonyl, 8-quinolyl oxycarbonyl, acetyl, formyl, chloro acetyl, dichloro acetyl, trichloro acetyl, trifluoro acetyl, methoxy acetyl, phenoxy acetyl, pivaloyl, benzoyl, methyl, tert-butyl, 2,2,2-trichloro ethyl, 2-trimethyl silyl ethyl, 1,1-dimethyl-2-propenyl, 3-methyl-3-butenyl, allyl, benzyl (phenylmethyl), para-methoxy benzyl, 3,4-dimethoxy benzyl, diphenyl methyl, triphenyl methyl, tetrahydro furanyl, tetrahydro pyranyl, tetrahydro thiopyranyl, methoxymethyl, methyl thiomethyl, benzyloxymethyl, 2-methoxy ethoxymethyl, 2,2,2-trichloro ethoxymethyl, 2-(trimethyl silyl) ethoxymethyl, 1-ethoxy ethyl, methanesulfon yl, para-toluene sulfonyl, trimethyl silyl, triethyl silyl, triisopropyl silyl, diethyl isopropyl silyl, tert-butyl dimethyl silyl, tert-butyl diphenyl silyl, diphenyl methyl silyl, and tert-butyl methoxy phenyl silyl.

Compounds

Geometric isomers may exist in the present compounds. Compounds of this invention may contain carbon-carbon double bonds or carbon-nitrogen double bonds in the E or Z configuration, wherein the term “E” represents higher order substituents on opposite sides of the carbon-carbon or carbon-nitrogen double bond and the term “Z” represents higher order substituents on the same side of the carbon-carbon or carbon-nitrogen double bond as determined by the Cahn-Ingold-Prelog Priority Rules. The compounds of this invention may also exist as a mixture of “E” and “Z” isomers. Substituents around a cyclo alkyl or heterocyclo alkyl are designated as being of cis or trans configuration. Furthermore, the invention contemplates the various isomers and mixtures thereof resulting from the disposal of substituents around an adamantane ring system. Two substituents around a single ring within an adamantane ring system are designated as being of Z or E relative configuration.


Compounds of this invention contain asymmetrically substituted carbon atoms in the R or S configuration, in which the terms "R" and "S" are as defined by the IUPAC 1974 Recommendations for Section E, Fundamental Stereochemistry, Pure Appl. Chem. (1976) 45, 13-10. Compounds having asymmetrically substituted carbon atoms with equal amounts of R and S configurations are racemic at those carbon atoms. Atoms with an excess of one configuration over the other are assigned the configuration present in the higher amount, preferably an excess of about 85%-90%, more preferably an excess of about 95%-99%, and still more preferably an excess greater than about 99%. Accordingly, this invention includes
r racemic mixtures, relative and absolute stereoisomers, and mixtures of relative and absolute stereoisomers.

Compounds of this invention containing NH, C(O)OH, OH or SH moieties may have attached thereto prodrug-forming moieties. The prodrug-forming moieties are removed by metabolic processes and release the compounds having the freed hydroxyl, amino or carboxylic acid in vivo. Prodrugs are useful for adjusting such pharmacokinetic properties of the compounds as solubility and/or hydrophobicity, absorption in the gastrointestinal tract, bioavailability, tissue penetration, and rate of clearance.

*Isotope Enriched or Labeled Compounds*

Compounds of the invention can exist in isotope-labeled or -enriched form containing one or more atoms having an atomic mass or mass number different from the atomic mass or mass number most abundantly found in nature. Isotopes can be radioactive or non-radioactive isotopes. Isotopes of atoms such as hydrogen, carbon, phosphorous, sulfur, fluorine, chlorine, and iodine include, but are not limited to, $^2$H, $^3$H, $^{13}$C, $^{14}$C, $^{15}$N, $^{16}$O, $^{32}$P, $^{35}$S, $^{18}$F, $^{36}$Cl, and $^{125}$I. Compounds that contain other isotopes of these and/or other atoms are within the scope of this invention.

In another embodiment, the isotope-labeled compounds contain deuterium ($^2$H), tritium ($^3$H) or $^{14}$C isotopes. Isotope-labeled compounds of this invention can be prepared by the general methods well known to persons having ordinary skill in the art. Such isotope-labeled compounds can be conveniently prepared by carrying out the procedures disclosed in the Examples disclosed herein and Schemes by substituting a readily available isotope-labeled reagent for a non-labeled reagent. In some instances, compounds may be treated with isotope-labeled reagents to exchange a normal atom with its isotope, for example, hydrogen for deuterium can be exchanged by the action of a deuteric acid such as D$_2$SO$_4$/D$_2$O. In addition to the above, relevant procedures and intermediates are disclosed, for instance, in Lizondo, J et al., *Drugs Fut.*, 21(11), 1116 (1996); Brickner, S J et al., *J Med Chem.*, 39(3), 673 (1996); Mallesham, B et al., *Org Lett.*, 5(7), 963 (2003); PCT publications WO1997010223, WO2005099353, WO1995007271, WO2006008754; US Patent Nos. 7534819; 7534819; 7531685; 7528131; 7521421; 7514068; 7511013; and US Patent Application Publication Nos. 20090137457; 20090131485; 20090131363; 20090118238; 2009011840; 20090105338; 20090105307; 20090105147; 20090093422; 20090088416; and 20090082471.

The isotope-labeled compounds of the invention may be used as standards to determine the effectiveness of Bcl-2 inhibitors in binding assays. Isotope containing
compounds have been used in pharmaceutical research to investigate the in vivo metabolic fate of the compounds by evaluation of the mechanism of action and metabolic pathway of the nonisotope-labeled parent compound (Blake et al. *J. Pharm. Sci.* 64, 3, 367-391 (1975)). Such metabolic studies are important in the design of safe, effective therapeutic drugs, either because the in vivo active compound administered to the patient or because the metabolites produced from the parent compound prove to be toxic or carcinogenic (Foster et al., Advances in Drug Research Vol. 14, pp. 2-36, Academic press, London, 1985; Kato et al., *J. Labelled Comp. Radiopharmaceut.*, 36(10):927-932 (1995); Kushner et al., *Can. J. Physiol. Pharmacol.*, 77, 79-88 (1999).

In addition, non-radio active isotope containing drugs, such as deuterated drugs called “heavy drugs,” can be used for the treatment of diseases and conditions related to Bcl-2 activity. Increasing the amount of an isotope present in a compound above its natural abundance is called enrichment. Examples of the amount of enrichment include from about 0.5, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 16, 21, 25, 29, 33, 37, 42, 46, 50, 54, 58, 63, 67, 71, 75, 79, 84, 88, 92, 96, to about 100 mol %. Replacement of up to about 15% of normal atom with a heavy isotope has been effected and maintained for a period of days to weeks in mammals, including rodents and dogs, with minimal observed adverse effects (Czajka D M and Finkel A J, Ann. N.Y. Acad. Sci. 1960 84: 770; Thomson J F, Ann. New York Acad. Sci 1960 84: 736; Czakja D M et al., Am. J. Physiol. 1961 201: 357). Acute replacement of as high as 15%-23% in human fluids with deuterium was found not to cause toxicity (Blagojevic N et al. in "Dosimetry & Treatment Planning for Neutron Capture Therapy", Zamenhof R, Solares G and Harling O Eds. 1994. Advanced Medical Publishing, Madison Wis. pp.125-134; Diabetes Metab. 23: 251 (1997)).

Stable isotope labeling of a drug can alter its physico-chemical properties such as pKa and lipid solubility. These effects and alterations can affect the pharmacodynamic response of the drug molecule if the isotopic substitution affects a region involved in a ligand-receptor interaction. While some of the physical properties of a stable isotope-labeled molecule are different from those of the unlabeled one, the chemical and biological properties are the same, with one important exception: because of the increased mass of the heavy isotope, any bond involving the heavy isotope and another atom will be stronger than the same bond between the light isotope and that atom. Accordingly, the incorporation of an isotope at a site of metabolism or enzymatic transformation will slow said reactions potentially altering the pharmcokinetic profile or efficacy relative to the non-istopic compound.
Amides, Esters and Prodrugs

Prodrugs are derivatives of an active drug designed to ameliorate some identified, undesirable physical or biological property. The physical properties are usually solubility (too much or not enough lipid or aqueous solubility) or stability related, while problematic biological properties include too rapid metabolism or poor bioavailability which itself may be related to a physicochemical property.

Prodrugs are usually prepared by: a) formation of ester, hemi esters, carbonate esters, nitrate esters, amides, hydroxamic acids, carbamates, imines, Mannich bases, and enamines of the active drug, b) functionalizing the drug with azo, glycoside, peptide, and ether functional groups, c) use of polymers, salts, complexes, phosphoramides, acetals, hemiacetals, and ketal forms of the drug. For example, see Andrejus Korolkovas’s, "Essentials of Medicinal Chemistry", John Wiley-Interscience Publications, John Wiley and Sons, New York (1988), pp. 97-118.

Esters can be prepared from substrates of formula (I) containing either a hydroxyl group or a carboxy group by general methods known to persons skilled in the art. The typical reactions of these compounds are substitutions replacing one of the heteroatoms by another atom, for example:

Scheme 1

\[
\begin{align*}
\text{Acyl Chloride} & \quad + \Theta \text{OCH}_2\text{CH}_3 & \rightarrow & \quad \text{Ester} \\
\text{Alkoxide} & \\
\end{align*}
\]

Amides can be prepared from substrates of formula (I) containing either an amino group or a carboxy group in similar fashion. Esters can also react with amines or ammonia to form amides.

Scheme 2

Another way to make amides from compounds of formula (I) is to heat carboxylic acids and amines together.

Scheme 3
In Schemes 2 and 3 above, R and R' are independently substrates of formula (I), alkyl or hydrogen.

Suitable groups for $A^1$, $B^1$, $D^1$, $E^1$, $Y^1$, and $Z^1$ in compounds of Formula (I) are independently selected. The described embodiments of the present invention may be combined. Such combination is contemplated and within the scope of the present invention. For example, it is contemplated that embodiments for any of $A^1$, $B^1$, $D^1$, $E^1$, $Y^1$, and $Z^1$ can be combined with embodiments defined for any other of $A^1$, $B^1$, $D^1$, $E^1$, $Y^1$, and $Z^1$.

One embodiment of this invention, therefore, pertains to compounds or therapeutically acceptable salts, prodrugs or salts of prodrugs thereof, which are useful as selective inhibitors one or more than one anti-apoptotic protein family member, the compounds having formula (I)

![Chemical Structure](image)

wherein $A^1$ is N or C(A)²;

one or two or three or each of $A^2$, $B^1$, $D^1$ and $E^1$ are independently selected $R^1$, OR¹, SR¹, S(O)R¹, SO₂R¹, C(O)R¹, C(O)OR¹, OC(O)R¹, NH²R¹, N(R¹)₂, C(O)NHR¹, C(O)N(R¹)₂, NH(C)OR¹, NH(C)OR¹, NR¹C(O)NHR¹, NR¹C(O)N(R¹)₂, SO₂NHR¹, SO₂N(R¹)₂, NH₅SO₂R¹, NH₅SO₂NHR¹ or N(CH₃)SO₂N(CH₃)R¹, and the remainder are independently selected H, F, Cl, Br, I, CN, CF₃, C(O)OH, C(O)NH₂ or C(O)OR¹; and

$Y^1$ is H, CN, NO₂, C(O)OH, F, Cl, Br, I, CF₃, OF₃, CF₂OF₃, OCF₂OF₃, R¹, OR¹, C(O)R¹, C(O)OR¹, SR¹, NH₂, NH²R¹, N(R¹)₂, CH(C)R¹, C(O)NH₂, C(O)NHR¹, C(O)N(R¹)₂, NH₅SO₂R¹ or NH₅SO₂R¹;

or

$B^1$ and $Y^1$, together with the atoms to which they are attached, are imidazole or triazole; and

one or two or each of $A^2$, $D^1$ and $E^1$ are independently selected $R^1$, OR¹, SR¹, S(O)R¹, SO₂R¹, C(O)R¹, C(O)OR¹, OC(O)R¹, NH²R¹, N(R¹)₂, C(O)NHR¹, C(O)N(R¹)₂,
NHC(O)R^1, NHC(O)OR^1, NHC(O)NHR^1, N(CH_3)C(O)N(CH_3)R^1, SO_2NHR^1, SO_2N(R^1)_2, NHSO_2R^1, NHSO_2NHR^1 or N(CH_3)SO_2N(CH_3)R^1, and the remainder are independently selected H, F, Cl, Br, I, CF_3, C(O)OH, C(O)NH_2 or C(O)OR^{1A};

R^1 is R^2, R^3, R^4 or R^5;

R^{1A} is C_1-C_6-alkyl, C_3-C_6-alkenyl or C_3-C_6-alkynyl;

R^2 is phenyl which is unfused or fused with arene, heteroarene or R^{2A}; R^{2A} is cycloalkane or heterocycloalkane;

R^3 is heteroaryl which is unfused or fused with benzene, heteroarene or R^{3A}; R^{3A} is cycloalkane or heterocycloalkane;

R^4 is cycloalkyl, cycloalkenyl, heterocycloalkyl or heterocycloalkenyl, each of which is unfused or fused with arene, heteroarene or R^{4A}; R^{4A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R^5 is alkyl, alkenyl or alkynyl, each of which is unsubstituted or substituted with one or two or three independently selected R^6, NC(R^{6A})(R^{6B}), R^7, OR^7, SR^7, S(O)R^7, SO_2R^7, NHR^7, N(R^7)_2, C(O)R^7, C(O)NH_2, C(O)NHR^7, NHC(O)R^7, NH_2SO_2R^7, NHCO_2R^7, NHC(O)OR^7, SO_2NH_2, SO_2NHR^7, SO_2N(R^7)_2, NHC(O)NH_2, NHC(O)NHR^7, NHC(O)CH(CH_3)NHC(O)CH(CH_3)NH_2, NHC(O)CH(CH_3)NHC(O)CH(CH_3)NHR^1, OH, (O), C(O)OH, (O), N_3, CN, NH_2, CF_3, CF_2CF_3, F, Cl, Br or I substituents;

R^6 is C_2-C_5-spiroalkyl, each of which is unsubstituted or substituted with OH, (O), N_3, CN, CF_3, CF_2CF_3, F, Cl, Br, I, NH_2, NH(CH_3) or N(CH_3)_2;

R^{6A} and R^{6B} are independently selected alkyl or, together with the N to which they are attached, R^{6C};

R^{6C} is aziridin-1-yl, azetidin-1-yl, pyrrolidin-1-yl or piperidin-1-yl, each having one CH_2 moiety unreplaced or replaced with O, C(O), CNOH, CNOCH_3, S, S(O), SO_2 or NH;

R^7 is R^8, R^9, R^{10} or R^{11};

R^8 is phenyl which is unfused or fused with arene, heteroarene or R^{8A};

R^{8A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R^9 is heteroaryl which is unfused or fused with arene, heteroarene or R^{9A}; R^{9A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;
R^{10} is C_{3}-C_{10}-cycloalkyl or C_{4}-C_{10}-cycloalkenyl, each having one or two CH_{2} moieties unreplaced or replaced with independently selected O, C(O), CNOH, CNOCH_{3}, S, S(O), SO_{2} or NH and one or two CH moieties unreplaced or replaced with N, and each of which is unfused or fused with arene, heteroarene or R^{10A}; R^{10A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R^{11} is alkyl, alkenyl or alkynyl, each of which is unsubstituted or substituted with one or two or three independently selected R^{12}, OR^{12}, NHR^{12}, N(R^{12})_{2}, C(O)NH_{2}, C(O)NHR^{12}, C(O)N(R^{12})_{2}, OH, (O), C(O)OH, N_{3}, CN, NH_{2}, CF_{3}, CF_{2}CF_{3}, F, Cl, Br or I substituents; R^{12} is R^{13}, R^{14}, R^{15} or R^{16};

R^{13} is phenyl which is unfused or fused with arene, heteroarene or R^{13A}; R^{13A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R^{14} is heteroaryl, each of which is unfused or fused with arene, heteroarene or R^{14A}; R^{14A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R^{15} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene, each of which is unfused or fused with arene, heteroarene or R^{15A}; R^{15A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R^{16} is alkyl, alkenyl or alkynyl;

R^{17} is R^{18}, R^{19}, R^{20} or R^{21};

R^{18} is phenyl which is unfused or fused with arene, heteroarene or R^{18A}; R^{18A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R^{19} is heteroaryl which is unfused or fused with arene, heteroarene or R^{19A}; R^{19A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R^{20} is C_{3}-C_{10}-cycloalkyl or C_{4}-C_{10}-cycloalkenyl, each having one or two CH_{2} moieties unreplaced or replaced with independently selected O, C(O), CNOH, CNOCH_{3}, S, S(O), SO_{2} or NH and one or two CH moieties unreplaced or replaced with N, and each of which is unfused or fused with arene, heteroarene or R^{20A}; R^{20A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R^{21} is alkyl, alkenyl or alkynyl, each of which is unsubstituted or substituted with one or two or three independently selected R^{22}, OR^{22}, NHR^{22}, N(R^{22})_{2}, C(O)NH_{2}, C(O)NHR^{22}, C(O)N(R^{22})_{2}, OH, (O), C(O)OH, N_{3}, CN, NH_{2}, CF_{3}, CF_{2}CF_{3}, F, Cl, Br or I substituents;
R\(^{22}\) is R\(^{23}\), R\(^{24}\) or R\(^{25}\);

R\(^{23}\) is phenyl which is unfused or fused with arene, heteroarene or R\(^{23A}\); R\(^{23A}\) is
cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R\(^{24}\) is heteroarene which is unfused or fused with arene, heteroarene or R\(^{24A}\); R\(^{24A}\) is
cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R\(^{25}\) is C\(_{3-6}\)-cycloalkyl or C\(_{4-6}\)-cycloalkenyl, each having one or two CH\(_2\) moieties
unreplaced or replaced with independently selected O, C(O), CNOH, CNO\(_2\)H, S, S(O), SO\(_2\)
or NH and one or two CH moieties unreplaced or replaced with N, and each of which is
unfused or fused with arene, heteroarene or R\(^{25A}\); R\(^{25A}\) is cycloalkane, cycloalkene,
heterocycloalkane or heterocycloalkene;

Z\(^1\) is R\(^{26}\) or R\(^{27}\), each of which is substituted with R\(^{28}\), R\(^{29}\) or R\(^{30}\), each of which is
substituted with F, Cl, Br, I, CH\(_2\)R\(^{37}\), CH(R\(^{31}\))(R\(^{37}\)), C(R\(^{31}\))(R\(^{31A}\))(R\(^{37}\)), C(O)R\(^{37}\), OR\(^{37}\),
SR\(^{37}\), S(O)R\(^{37}\), SO\(_2\)R\(^{37}\), NHR\(^{37}\) or N(R\(^{32}\))R\(^{37}\);

R\(^{26}\) is phenyl which is unfused or fused with arene or heteroarene;

R\(^{27}\) is heteroarene which is unfused or fused with arene or heteroarene;

R\(^{28}\) is phenyl which is unfused or fused with arene, heteroarene or R\(^{28A}\); R\(^{28A}\) is
cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene

R\(^{29}\) is heteroaryl or R\(^{29A}\); R\(^{29A}\) is cycloalkane, cycloalkene, heterocycloalkane or
heterocycloalkene;

R\(^{30}\) is cycloalkyl or cycloalkenyl, each having one or two CH\(_2\) moieties unreplaced or
replaced with independently selected O, C(O), CNOH, CNO\(_2\)H, S, S(O), SO\(_2\) or NH and
one or two CH moieties unreplaced or replaced with N, and each of which is unfused or fused
with arene, heteroarene or R\(^{30A}\); R\(^{30A}\) is cycloalkane, cycloalkene, heterocycloalkane or
heterocycloalkene;

R\(^{31}\) and R\(^{31A}\) are independently F, Cl, Br or alkyl or are taken together and are
C\(_{2-5}\)-spiroalkyl;

R\(^{32}\) is R\(^{33}\), C(O)R\(^{33}\) or C(O)OR\(^{33}\);

R\(^{33}\) is R\(^{34}\) or R\(^{35}\);

R\(^{34}\) is phenyl which is unfused or fused with aryl, heteroaryl or R\(^{34A}\); R\(^{34A}\) is
cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;
R^{35} is alkyl which is unsubstituted or substituted with R^{36};

R^{36} is phenyl which is unfused or fused with arene, heteroarene or R^{36A}; R^{36A} is
cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R^{37} is R^{38}, R^{39} or R^{40}, each of which is substituted with F, Cl, Br, I, R^{41}, OR^{41},

NHR^{41}, N(R^{41})_2, NHC(O)OR^{41}, SR^{41}, S(O)R^{41} or SO_2R^{41};

R^{38} is phenyl which is unfused or fused with arene, heteroarene or R^{38A}; R^{38A} is
cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R^{39} is heteroaryl which is unfused or fused with arene, heteroarene or R^{39A}; R^{39A} is
cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R^{40} is C_3-C_8-cycloalkyl or C_4-C_8-cycloalkenyl, each having one or two CH_2 moieties
unreplaced or replaced with independently selected O, C(O), CNOH, CNOCH_3, S, S(O), SO_2
or NH and one or two CH moieties unreplaced or replaced with N, and each of which is
unfused or fused with arene, heteroarene or R^{40A}; R^{40A} cycloalkane, cycloalkene,
heterocycloalkane or heterocycloalkene;

R^{41} is R^{42}, R^{43}, R^{44} or R^{45};

R^{42} is phenyl which is unfused or fused with arene, heteroarene or R^{42A}; R^{42A} is
cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R^{43} is heteroaryl which is unfused or fused with arene, heteroarene or R^{43A}; R^{43A} is
cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R^{44} is C_3-C_9-cycloalkyl or C_4-C_7-cycloalkenyl, each having one or two CH_2 moieties
unreplaced or replaced with independently selected O, C(O), CNOH, CNOCH_3, S, S(O), SO_2
or NH and one or two CH moieties unreplaced or replaced with N, and each of which is
unfused or fused with arene, heteroarene or R^{44A}; R^{44A} is cycloalkane, cycloalkene,
heterocycloalkane or heterocycloalkene;

R^{45} is alkyl, alkenyl or alkynyl, each of which is unsubstituted or substituted with one
or two independently selected R^{46}, OR^{46}, NHR^{46}, N(R^{46})_2, C(O)NH_2, C(O)NHR^{46},
C(O)N(R^{46})_2, OH, (O), C(O)OH, N_3, CN, NH_2, CF_3, CF_2CF_3, F, Cl, Br or I substituents;

R^{46} is R^{47}, R^{48} or R^{49};

R^{47} is phenyl which is unfused or fused with arene, heteroarene or R^{47A}; R^{47A} is

cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;
R^{48} is heteroaryl or R^{48A}; R^{48A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R^{49} is C_{3-6}-cycloalkyl or C_{4-6}-cycloalkenyl, each having one or two CH_{2} moieties unreplaced or replaced with independently selected O, C(O), CNOH, CNOCH_{3}, S, S(O), SO_{2} or NH and one or two CH moieties unreplaced or replaced with N, and each of which is unfused or fused with arene, heteroarene or R^{49A}; R^{49A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

wherein the moieties represented by R^{26} and R^{27} are further substituted by one or two or three of independently selected R^{50A}, OR^{50A}, SR^{50A}, S(O)R^{50A}, SO_{2}R^{50A} or NHR^{50A}, R^{50A} is R^{51A}, R^{52A}, R^{53A} or R^{54A};

R^{51A} is phenyl which is unfused or fused with benzene, heteroarene or R^{51AA},

wherein R^{51AA} is cycloalkane, cycloalkene or heterocycloalkane heterocycloalkene, R^{52A} is heteroaryl;

R^{53A} is C_{3}-C_{6}-cycloalkyl or C_{4}-C_{6}-cycloalkenyl; each having one or two CH_{2} moieties unreplaced or replaced with independently selected O, C(O), CNOH, CNOCH_{3}, S, S(O), SO_{2} or NH and one or two CH moieties unreplaced or replaced with N, and each of which is unfused or fused with arene, heteroarene or R^{53AA};

wherein R^{53AA} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R^{54A} is alkyl, alkenyl or alkynyl, each of which is unsubstituted or substituted with one or two or three of independently selected R^{55AA}, OR^{55AA}, SR^{55AA}, S(O)R^{55AA}, SO_{2}R^{55AA}, NHR^{55AA}, N(R^{55AA})_{2}, C(O)R^{55AA}, C(O)NH_{2}, C(O)NHR^{55AA}, NHC(O)R^{55AA}, NHSO_{2}R^{55AA}, NHC(O)OR^{55AA}, SO_{2}NH_{2}, SO_{2}NHR^{55AA}, SO_{2}N(R^{55AA})_{2}, NHC(O)NH_{2}, NHC(O)NHR^{55AA}, OH, (O), C(O)OH, (O), N_{3}, CN, NH_{2}, CF_{3}, OCF_{3}, CF_{2}CF_{3}, OCF_{2}CF_{3}, F, Cl, Br or I substituents;

R^{55AA} is alkyl, alkenyl, alkynyl, phenyl or heteroaryl, or R^{56A};

R^{56A} is C_{3}-C_{6}-cycloalkyl or C_{4}-C_{6}-cycloalkyl, each having one or two CH_{2} moieties unreplaced or replaced with independently selected O, C(O), CNOH, CNOCH_{3}, S, S(O), SO_{2} or NH and one or two CH moieties unreplaced or replaced with N;
wherein moieties represented by \( R^2 \), \( R^3 \), \( R^4 \), \( R^6 \), \( R^{6C} \), \( R^8 \), \( R^{8A} \), \( R^9 \), \( R^{10} \), \( R^{13} \), \( R^{14} \), \( R^{15} \), \( R^{18} \), \( R^{19} \), \( R^{20} \), \( R^{23} \), \( R^{24} \), \( R^{25} \), \( R^{26} \), \( R^{27} \), \( R^{28} \), \( R^{29} \), \( R^{30} \), \( R^{34} \), \( R^{36} \), \( R^{38} \), \( R^{39} \), \( R^{40} \), \( R^{42} \), \( R^{43} \), \( R^{44} \), \( R^{47} \), \( R^{48} \), and \( R^{49} \) are independently unsubstituted, further unsubstituted, substituted or further substituted with one or two or three or four or five independently selected \( R^{50} \), \( OR^{50} \), \( SR^{50} \), \( S(O)R^{50} \), \( SO_2R^{50} \), \( C(O)R^{50} \), \( CO(O)R^{50} \), \( OC(O)R^{50} \), \( OC(O)OR^{50} \), \( NH_2 \), \( NHR^{50} \), \( N(R^{50})_2 \), \( C(O)NH_2 \), \( C(O)NHR^{50} \), \( C(O)N(R^{50})_2 \), \( C(O)NHOR^{50} \), \( C(O)NHSO_2R^{50} \), \( C(O)NR^{50} \), \( SO_2R^{50} \), \( SO_2NH_2 \), \( SO_2NHR^{50} \), \( SO_2N(R^{50})_2 \), \( CF_5 \), \( CF_2CF_3 \), \( C(O)H \), \( C(O)OH \), \( C(N)NH_2 \), \( C(N)NHR^{50} \), \( C(N)N(R^{50})_2 \), \( OH \), \( (O) \), \( CN \), \( N_3 \), \( NO_2 \), \( CF_3 \), \( CF_2CF_3 \), \( OFC_3 \), \( OCF_2CF_3 \), \( F \), \( Cl \), \( Br \) or \( I \) substituents;

5

\( R^{50} \) is \( R^{51} \), \( R^{52} \), \( R^{53} \) or \( R^{44} \);

\( R^{51} \) is phenyl which is unfused or fused with arene, homoarene or \( R^{51B} \); \( R^{51B} \) is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

\( R^{52} \) is heteroaryl;

\( R^{53} \) is \( C_3-C_6 \)-cycloalkyl or \( C_4-C_6 \)-cycloalkenyl, each having one or two \( CH_2 \) moieties unreplaced or replaced with independently selected \( O \), \( C(O) \), \( CNOH \), \( CNOCH_3 \), \( S \), \( S(O) \), \( SO_2 \) or \( NH \) and one or two \( CH \) moieties unreplaced or replaced with \( N \), and each of which is unfused or fused with arene, homoarene or \( R^{53B} \);

wherein \( R^{53B} \) is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

\( R^{54} \) is alkyl, alkenyl or alkynyl, each of which is unsubstituted or substituted with one or two or three independently selected \( R^{55} \), \( OR^{55} \), \( SR^{55} \), \( S(O)R^{55} \), \( SO_2R^{55} \), \( NHR^{55} \), \( N(R^{55})_2 \), \( C(O)R^{55} \), \( C(O)NH_2 \), \( C(O)NHR^{55} \), \( NHC(O)R^{55} \), \( NHSO_2R^{55} \), \( NH(O)OR^{55} \), \( SO_2NH_2 \), \( SO_2N(R^{55})_2 \), \( NHC(O)NH_2 \), \( NHC(O)NHR^{55} \), \( OH \), \( (O) \), \( C(O)OH \), \( (O) \), \( N_3 \), \( CN \), \( NH_2 \), \( CF_3 \), \( OCF_3 \), \( CF_2CF_3 \), \( OCF_2CF_3 \), \( F \), \( Cl \), \( Br \) or \( I \) substituents;

\( R^{55} \) is alkyl, alkenyl, alkynyl, phenyl, heteroaryl or \( R^{56} \); and

wherein the alkyl, alkenyl, alkynyl are unsubstituted or substituted with \( OCH_3 \); and

\( R^{56} \) is \( C_3-C_8 \)-cycloalkyl or \( C_4-C_6 \)-cycloalkenyl, each having one or two \( CH_2 \) moieties unreplaced or replaced with independently selected \( O \), \( C(O) \), \( CNOH \), \( CNOCH_3 \), \( S \), \( S(O) \), \( SO_2 \) or \( NH \) and one or two \( CH \) moieties unreplaced or replaced with \( N \).

Another embodiment of this invention pertains to compounds of Formula (I), wherein
wherein A$^1$ is N or C(A$^2$);

one or two or three or each of A$^2$, B$^1$, D$^1$ and E$^1$ are independently selected R$^1$, OR$^1$, SR$^1$, S(O)R$^1$, SO$_2$R$^1$, C(O)R$^1$, C(O)OR$^1$, OC(O)R$^1$, NHR$^1$, N(R$^1$)$_2$, C(O)NHR$^1$, C(O)N(R$^1$)$_2$, NHC(O)R$^1$, NHC(O)OR$^1$, NR$^1$C(O)NHR$^1$, NR$^1$C(O)N(R$^1$)$_2$, SO$_2$NHR$^1$, SO$_2$N(R$^1$)$_2$.

NH$_2$SO$_2$R$^1$, NH$_2$SO$_2$NHR$^1$ or Ni(CH$_3$)$_2$SO$_2$Ni(CH$_3$)R$^1$, and the remainder are independently selected H, F, Cl, Br, I, CN, CF$_3$, C(O)OH, C(O)NH$_2$ or C(O)OR$^1$A; and

Y$^1$ is H, CN, NO$_2$, C(O)OH, F, Cl, Br, I, CF$_3$, OCF$_3$, CF$_2$CF$_3$, OCF$_2$CF$_3$, R$^{17}$, OR$^{17}$, C(O)R$^{17}$, C(O)OR$^{17}$, SR$^{17}$, NH$_2$, NHR$^{17}$, N(R$^{17}$)$_2$, NHC(O)R$^{17}$, C(O)NH$_2$, C(O)NHR$^{17}$, C(O)N(R$^{17}$)$_2$, NH$_2$SO$_2$R$^{17}$ or NH$_2$SO$_2$NHR$^{17}$;

or

B$^1$ and Y$^1$, together with the atoms to which they are attached, are imidazole or triazole; and

one or two or each of A$^2$, D$^1$ and E$^1$ are independently selected R$^1$, OR$^1$, SR$^1$, S(O)R$^1$, SO$_2$R$^1$, C(O)R$^1$, C(O)OR$^1$, OC(O)R$^1$, NHR$^1$, N(R$^1$)$_2$, C(O)NHR$^1$, C(O)N(R$^1$)$_2$.

NHC(O)R$^1$, NHC(O)OR$^1$, NHC(O)NHR$^1$, N(CH$_3$)$_2$C(O)N(CH$_3$)R$^1$, SO$_2$NHR$^1$, SO$_2$N(R$^1$)$_2$, NH$_2$SO$_2$R$^1$, NH$_2$SO$_2$NHR$^1$ or Ni(CH$_3$)$_2$SO$_2$Ni(CH$_3$)R$^1$, and the remainder are independently selected H, F, Cl, Br, I, CF$_3$, C(O)OH, C(O)NH$_2$ or C(O)OR$^1$A;

R$^1$ is R$^2$, R$^3$, R$^4$ or R$^5$;

R$^{1A}$ is C$_1$-C$_6$-alkyl, C$_3$-C$_6$-alkenyl or C$_3$-C$_6$-alkynyl;

R$^2$ is phenyl which is unfused or fused with arene, heteroarene or R$^{2A}$; R$^{2A}$ is cycloalkane or heterocycloalkane;

R$^3$ is heteroaryl which is unfused or fused with benzene, heteroarene or R$^{3A}$; R$^{3A}$ is cycloalkane or heterocycloalkane;

R$^4$ is cycloalkyl, cycloalkeny, heterocycloalkyl or heterocycloalkenyl, each of which is unfused or fused with arene, heteroarene or R$^{4A}$; R$^{4A}$ is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R$^5$ is alkyl, alkenyl or alkynyl, each of which is unsubstituted or substituted with one or two or three independently selected R$^6$, NC(R$^{6A}$)(R$^{6B}$), R$^7$, OR$^7$, SR$^7$, S(O)R$^7$, SO$_2$R$^7$, NHR$^7$, N(R$^7$)$_2$, C(O)R$^7$, C(O)NH$_2$, C(O)NHR$^7$, NHC(O)R$^7$, NH$_2$SO$_2$R$^7$, NH$_2$SO$_2$NHR$^7$. 

- 88 -
SO₂NH₂, SO₂NHR, SO₂N(R₇)₂, NHC(O)NH₂, NHC(O)NHR,
NHC(O)CH(CH₃)NHC(O)CH(CH₃)NH₂, NHC(O)CH(CH₃)NHC(O)CH(CH₃)NHR, OH,
(O), C(O)OH, (O), N₃, CN, NH₂, CF₃, CF₂CF₃, F, Cl, Br or I substituents;
R⁶ is C₂-C₅-spiroalkyl, each of which is unsubstituted or substituted with OH, (O),
N₃, CN, CF₃, CF₂CF₃, F, Cl, Br, I, NH₂, NH(CH₃) or N(CH₃)₂;
R⁶A and R⁶B are independently selected alkyl or, together with the N to which they
are attached, R⁶C;
R⁶C is aziridin-1-yl, azetidin-1-yl, pyrrolidin-1-yl or piperidin-1-yl, each having one
CH₂ moiety unreplaced or replaced with O, C(O), CNOH, CNOCH₃, S, S(O), SO₂ or NH;
R⁷ is R⁸, R⁹, R¹⁰ or R¹¹;
R⁸ is phenyl which is unfused or fused with arene, heteroarene or R⁸A;
R⁸A is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;
R⁹ is heteroaryl which is unfused or fused with arene, heteroarene or R⁹A; R⁹A is
cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;
R¹⁰ is C₃-C₁₀-cycloalkyl or C₄-C₁₀-cycloalkenyl, each having one or two CH₂
moieties unreplaced or replaced with independently selected O, C(O), CNOH, CNOCH₃, S,
S(O), SO₂ or NH and one or two CH moieties unreplaced or replaced with N, and each of
which is unfused or fused with arene, heteroarene or R¹⁰A; R¹⁰A is cycloalkane, cycloalkene,
heterocycloalkane or heterocycloalkene;
R¹¹ is alkyl, alkenyl or alkynyl, each of which is unsubstituted or substituted with one
or two or three independently selected R¹², OR¹², NHR¹², N(R¹²)₂, C(O)NH₂, C(O)NHR¹²,
C(O)N(R¹²)₂, OH, (O), C(O)OH, N₃, CN, NH₂, CF₃, CF₂CF₃, F, Cl, Br or I substituents;
R¹² is R¹³, R¹⁴, R¹⁵ or R¹⁶;
R¹³ is phenyl which is unfused or fused with arene, heteroarene or R¹³A; R¹³A is
cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;
R¹⁴ is heteroaryl, each of which is unfused or fused with arene, heteroarene or R¹⁴A;
R¹⁴A is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;
R\(^{15}\) is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene, each of which is unfused or fused with arene, heteroarene or R\(^{15A}\); R\(^{15A}\) is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R\(^{16}\) is alkyl, alkenyl or alkynyl;

R\(^{17}\) is R\(^{18}\), R\(^{19}\), R\(^{20}\) or R\(^{21}\);

R\(^{18}\) is phenyl which is unfused or fused with arene, heteroarene or R\(^{18A}\); R\(^{18A}\) is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R\(^{19}\) is heteroaryl which is unfused or fused with arene, heteroarene or R\(^{19A}\); R\(^{19A}\) is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R\(^{20}\) is C\(_3\)-C\(_{10}\)-cycloalkyl or C\(_4\)-C\(_{10}\)-cycloalkenyl, each having one or two CH\(_2\) moieties unreplaced or replaced with independently selected O, C(O), CNOH, CNOCH\(_3\), S, S(O), SO\(_2\) or NH and one or two CH moieties unreplaced or replaced with N, and each of which is unfused or fused with arene, heteroarene or R\(^{20A}\); R\(^{20A}\) is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R\(^{21}\) is alkyl, alkenyl or alkynyl, each of which is unsubstituted or substituted with one or two or three independently selected R\(^{22}\), OR\(^{22}\), NHR\(^{22}\), N(R\(^{22}\))\(_2\), C(O)NH\(_2\), C(O)NHR\(^{22}\), C(O)N(R\(^{22}\))\(_2\), OH, (O), C(O)OH, N\(_3\), CN, NH\(_2\), CF\(_3\), CF\(_2\)CF\(_3\), F, Cl, Br or I substituents;

R\(^{22}\) is R\(^{23}\), R\(^{24}\) or R\(^{25}\);

R\(^{23}\) is phenyl which is unfused or fused with arene, heteroarene or R\(^{23A}\); R\(^{23A}\) is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R\(^{24}\) is heteroarene which is unfused or fused with arene, heteroarene or R\(^{24A}\); R\(^{24A}\) is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R\(^{25}\) is C\(_3\)-C\(_6\)-cycloalkyl or C\(_4\)-C\(_6\)-cycloalkenyl, each having one or two CH\(_2\) moieties unreplaced or replaced with independently selected O, C(O), CNOH, CNOCH\(_3\), S, S(O), SO\(_2\) or NH and one or two CH moieties unreplaced or replaced with N, and each of which is unfused or fused with arene, heteroarene or R\(^{25A}\); R\(^{25A}\) is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

Z\(^1\) is R\(^{26}\) or R\(^{27}\), each of which is substituted with R\(^{28}\), R\(^{29}\) or R\(^{30}\), each of which is substituted with F, Cl, Br, I, CH\(_2\)R\(^{37}\), CH(R\(^{31}\))(R\(^{37}\)), C(R\(^{31}\))(R\(^{31A}\))(R\(^{37}\)), C(O)R\(^{37}\), OR\(^{37}\), SR\(^{37}\), S(O)R\(^{37}\), SO\(_2\)R\(^{37}\), NHR\(^{37}\) or N(R\(^{32}\))R\(^{37}\);
R^{26} is phenyl which is unfused or fused with arene or heteroarene;
R^{27} is heteroarene which is unfused or fused with arene or heteroarene;
R^{28} is phenyl which is unfused or fused with arene, heteroarene or R^{28A}; R^{28A} is
cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene
5
R^{29} is heteroaryl or R^{29A}; R^{29A} is cycloalkane, cycloalkene, heterocycloalkane or
heterocycloalkene;
R^{30} is cycloalkyl or cycloalkenyl, each having one or two CH\_2 moieties unreplaced or
replaced with independently selected O, C(O), CNOH, CNOCH\_3, S, S(O), SO\_2 or NH and
one or two CH moieties unreplaced or replaced with N, and each of which is unfused or fused
with arene, heteroarene or R^{30A}; R^{30A} is cycloalkane, cycloalkene, heterocycloalkane or
heterocycloalkene;
10
R^{31} and R^{31A} are independently F, Cl, Br or alkyl or are taken together and are
C\_2-C\_5-spiroalkyl;
R^{32} is R^{33}, C(O)R^{33} or C(O)OR^{33};
R^{33} is R^{34} or R^{35};
15
R^{34} is phenyl which is unfused or fused with aryl, heteroaryl or R^{34A}; R^{34A} is
cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;
R^{35} is alkyl which is unsubstituted or substituted with R^{36};
R^{36} is phenyl which is unfused or fused with arene, heteroarene or R^{36A}; R^{36A} is
cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;
20
R^{37} is R^{38}, R^{39} or R^{40}, each of which is substituted with F, Cl, Br, I, R^{41}, OR^{41},
NHR^{41}, N(R^{41})\_2, NHC(O)OR^{41}, SR^{41}, S(O)R^{41} or SO\_2R^{41};
R^{38} is phenyl which is unfused or fused with arene, heteroarene or R^{38A}; R^{38A} is
cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;
25
R^{39} is heteroaryl which is unfused or fused with arene, heteroarene or R^{39A}; R^{39A} is
cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;
R^{40} is C\_5-C\_8-cycloalkyl or C\_4-C\_8-cycloalkenyl, each having one or two CH\_2 moieties
unreplaced or replaced with independently selected O, C(O), CNOH, CNOCH\_3, S, S(O), SO\_2
or NH and one or two CH moieties unreplaced or replaced with N, and each of which is
unfused or fused with arene, heteroarene or R_{40A}; R_{40A} cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R_{41} is R_{42}, R_{43}, R_{44} or R_{45};

R_{42} is phenyl which is unfused or fused with arene, heteroarene or R_{42A}; R_{42A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R_{43} is heteroaryl which is unfused or fused with arene, heteroarene or R_{43A}; R_{43A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R_{44} is C_{3-9}-cycloalkyl or C_{4-7}-cycloalkenyl, each having one or two CH_{2} moieties unreplaced or replaced with independently selected O, C(O), CNOH, CNOCH_{3}, S, S(O), SO_{2} or NH and one or two CH moieties unreplaced or replaced with N, and each of which is unfused or fused with arene, heteroarene or R_{44A}; R_{44A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R_{45} is alkyl, alkenyl or alkynyl, each of which is unsubstituted or substituted with one or two independently selected R_{46}, OR_{46}, NHR_{46}, N(R_{46})_{2}, C(O)NH_{2}, C(O)NHR_{46},

C(O)N(R_{46})_{2}, OH, (O), C(O)OH, N_{3}, CN, NH_{2}, CF_{3}, CF_{2}CF_{3}, F, Cl, Br or I substituents;

R_{46} is R_{47}, R_{48} or R_{49};

R_{47} is phenyl which is unfused or fused with arene, heteroarene or R_{47A}; R_{47A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R_{48} is heteroaryl or R_{48A}; R_{48A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R_{49} is C_{3-9}-cycloalkyl or C_{4-7}-cycloalkenyl, each having one or two CH_{2} moieties unreplaced or replaced with independently selected O, C(O), CNOH, CNOCH_{3}, S, S(O), SO_{2} or NH and one or two CH moieties unreplaced or replaced with N, and each of which is unfused or fused with arene, heteroarene or R_{49A}; R_{49A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

wherein the moieties represented by R_{26} and R_{27} are further substituted with OR_{50A};

R_{50A} is R_{51A};

R_{51A} is phenyl which is fused with heteroarene;

wherein moieties represented by R_{2}, R_{3}, R_{4}, R_{6}, R_{6C}, R_{8}, R_{8A}, R_{9}, R_{10}, R_{13}, R_{14}, R_{15}, R_{18}, R_{19}, R_{20}, R_{23}, R_{24}, R_{25}, R_{26}, R_{27}, R_{28}, R_{29}, R_{30}, R_{34}, R_{36}, R_{38}, R_{39}, R_{40}, R_{42}, R_{43},
R^44, R^47, R^48, and R^49 are independently unsubstituted, further unsubstituted, substituted or further substituted with one or two or three or four or five independently selected R^50, OR^50, 
SR^50, S(O)R^50, SO_2R^50, C(O)R^50, CO(O)R^50, OC(O)R^50, OC(O)OR^50, NH_2, NHR^50, 
N(R^50)_2, C(O)NH_2, C(O)NHR^50, C(O)N(NR^50)_2, C(O)NHOH, C(O)NHOR^50, C(O)NHSO_2R^50, 
C(O)NR^55, SO_2R^50, SO_2NH_2, SO_2NHR^50, SO_2N(R^50)_2, CF_3, CF_2CF_3, C(O)H, C(O)OH, 
C(N)NH_2, C(N)NHR^50, C(N)N(NR^50)_2, OH, (O), CN, N_3, NO_2, CF_3, CF_2CF_3, OCF_3, 
OCF_2CF_3, F, Cl, Br or I substituents;
R^50 is R^51, R^52, R^53 or R^54;
R^51 is phenyl which is unfused or fused with arene, heteroarene or R^51B; R^51B is 
cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;
R^52 is heteroaryl;
R^53 is C_3-C_6-cycloalkyl or C_4-C_6-cycloalkenyl, each having one or two CH_2 moieties 
unreplaced or replaced with independently selected O, C(O), CNOH, CNOCH_3, S, S(O), SO_2 
and NH or one or two CH moieties unreplaced or replaced with N, and each of which is 
unfused or fused with arene, heteroarene or R^53B;
wherein R^53B is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;
R^54 is alkyl, alkenyl or alkynyl, each of which is unsubstituted or substituted with one 
or two or three independently selected R^55, OR^55, SR^55, S(O)R^55, SO_2R^55, NHR^55, N(R^55)_2, 
C(O)R^55, C(O)NH_2, C(O)NHR^55, NHC(O)R^55, NHSO_2R^55, NH(C(O)OR)^55, SO_2NH_2, 
SO_2NHR^55, SO_2N(R^55)_2, NH(C(O)NH}_2, NH(C(O)NHR^55, OH, (O), C(O)OH, (O), N_3, CN, 
NH_2, CF_3, OCF_3, CF_2CF_3, OCF_2CF_3, F, Cl, Br or I substituents;
R^55 is alkyl, alkenyl, alkynyl, phenyl, heteroaryl or R^56; and 
wherein the alkyl, alkenyl are unsubstituted or substituted with OCH_3; and 
R^56 is C_3-C_8-cycloalkyl or C_4-C_6-cycloalkenyl, each having one or two CH_2 moieties 
unreplaced or replaced with independently selected O, C(O), CNOH, CNOCH_3, S, S(O), SO_2 
or NH and one or two CH moieties unreplaced or replaced with N.
In one embodiment of Formula (I), A^1 is N or C(A^2);
one or two or three or each of A^2, B^1, D^1 and E^1 are independently selected R^1, OR^1, SR^1, SO_2R^1, NHR^1, N(R^1)_2, or C(O)NHR^1, and the remainder are independently selected H, F, Cl, Br, or I;

Y^1 is H, CN, NO_2, F, Cl, Br, I, CF_3, R^17, NHC(O)R^17, or C(O)NH_2;

R^1 is R^2, R^3, R^4 or R^5;

R^2 is phenyl;

R^3 is heteroaryl;

R^4 is cycloalkyl, heterocycloalkyl or heterocycloalkenyl, each of which is unfused or fused with R^{4A}; R^{4A} is cycloalkane;

R^5 is alkyl, or alkenyl, each of which is unsubstituted or substituted with one or two or three independently selected R^6, R^7, OR^7, SR^7, SO_2R^7, N(R^7)_2, OH, CN, CF_3, F, Cl, Br or I substituents;

R^6 is C_2-C_5-spiroalkyl;

R^7 is R^8, R^9, R^{10} or R^{11};

R^8 is phenyl which is unfused or fused with R^{8A};

R^{8A} is heterocycloalkane;

R^9 is heteroaryl;

R^{10} is C_3-C_10-cycloalkyl, each having one or two CH_2 moieties unreplaced or replaced with independently selected O, S(O), SO_2 or NH and one or two CH moieties unreplaced or replaced with N;

R^{11} is alkyl, each of which is unsubstituted or substituted with one or two or three independently selected OR^{12}, F, Cl, Br or I substituents;

R^{12} is R^{16};

R^{16} is alkyl;

R^{17} is R^{19} or R^{21};

R^{19} is heteroaryl which is unfused or fused with arene, heteroarene or R^{19A}; R^{19A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R^{21} is alkenyl;
Z\(^1\) is R\(^{26}\), each of which is substituted with R\(^{30}\), each of which is substituted with F, Cl, Br, I, CH\(_2\)R\(^{37}\), or CH(R\(^{31}\))(R\(^{37}\));

R\(^{26}\) is phenyl;
R\(^{30}\) is cycloalkyl, each having two CH\(_2\) moieties unreplaced or replaced with NH;

5 R\(^{31}\) and R\(^{31A}\) are independently alkyl;
R\(^{37}\) is R\(^{38}\), R\(^{39}\) or R\(^{40}\), each of which is substituted with F, Cl, Br, I, NHR\(^{41}\), or R\(^{41}\);
R\(^{38}\) is phenyl;
R\(^{39}\) is heteroaryl;
R\(^{40}\) is C\(_3\)-C\(_8\)-cycloalkyl or C\(_4\)-C\(_8\)-cycloalkenyl, each having one or two CH\(_2\) moieties unreplaced or replaced with independently selected O, C(O), CNOH, CNOCH\(_3\), S, S(O), SO\(_2\) or NH;

10 R\(^{41}\) is R\(^{42}\), R\(^{43}\), or R\(^{44}\);
R\(^{42}\) is phenyl;
R\(^{43}\) is heteroaryl;

R\(^{44}\) is C\(_3\)-C\(_9\)-cycloalkyl or C\(_4\)-C\(_7\)-cycloalkenyl, each having one or two CH\(_2\) moieties unreplaced or replaced with independently selected NH and one or two CH moieties unreplaced or replaced with N, and each of which is unfused or fused with R\(^{44A}\); R\(^{44A}\) is cycloalkane;

wherein the moiety represented by R\(^{26}\) is further substituted by one or two or three of

20 independently selected R\(^{50A}\), OR\(^{50A}\), SR\(^{50A}\), S(O)R\(^{50A}\), SO\(_2\)R\(^{50A}\) or NHR\(^{50A}\);

R\(^{50A}\) is R\(^{51A}\), R\(^{52A}\) or R\(^{54A}\);
R\(^{51A}\) is phenyl which is unfused or fused with benzene, heteroarene or R\(^{51AA}\);

wherein R\(^{51AA}\) is heterocycloalkane;
R\(^{52A}\) is heteroaryl;

R\(^{54A}\) is alkyl, each of which is unsubstituted or substituted with one or two or three of

25 independently selected R\(^{55AA}\), or OR\(^{55AA}\);

R\(^{55AA}\) is phenyl;

wherein moieties represented by R\(^2\) R\(^3\) R\(^4\), R\(^6\), R\(^6C\), R\(^8\), R\(^{8A}\) R\(^7\), R\(^{10}\), R\(^{13}\), R\(^{14}\), R\(^{15}\), R\(^{18}\), R\(^{19}\), R\(^{20}\), R\(^{23}\), R\(^{24}\), R\(^{25}\), R\(^{26}\), R\(^{27}\), R\(^{28}\), R\(^{29}\), R\(^{30}\), R\(^{34}\), R\(^{36}\), R\(^{38}\), R\(^{39}\), R\(^{40}\), R\(^{42}\), R\(^{43}\),
R^{44}, R^{47}, R^{48}, and R^{49} are independently unsubstituted, further unsubstituted, substituted or further substituted with one or two or three or four or five independently selected R^{50}, OR^{50}, SR^{50}, S(O)R^{50}, SO_2R^{50}, C(O)R^{50}, CO(O)R^{50}, NH_2, NHR^{50}, SO_2NH_2, OH, (O), CN, CF_3, OCF_3, F, Cl, Br or I substituents;

R^{50} is R^{51}, R^{52}, or R^{54}.

R^{51} is phenyl which is unfused or fused with arene, heteroarene or R^{51B}; R^{51B} is heterocycloalkane;

R^{52} is heteroaryl;

R^{53} is C_3-C_6-cycloalkyl, each having one or two CH_2 moieties unreplaced or replaced with independently selected O, and one or two CH moieties unreplaced or replaced with N;

R^{54} is alkyl, each of which is unsubstituted or substituted with one or two or three independently selected R^{55}, OR^{55}, N(R^{55})_2, OH, CN, F, Cl, Br or I substituents; and

R^{55} is alkyl or phenyl;

wherein the alkyl is unsubstituted or substituted with OCH_3; and

R^{56} is C_3-C_8-cycloalkyl, each having one or two CH_2 moieties unreplaced or replaced with independently selected NH and one or two CH moieties unreplaced or replaced with N.

In one embodiment of Formula (I), A^1 is N. In another embodiment of Formula (I), A^1 is C(A^2). In another embodiment of Formula (I), A^1 is C(A^2), and A^2 is H.

In one embodiment of Formula (I), B^1 is R^1, OR^1, SR^1, SO_2R^1, NHR^1, N(R^1)_2, or C(O)NHR^1. In another embodiment of Formula (I), B^1 is NHR^1. In another embodiment of Formula (I), B^1 is NHR^1, and A^1 is C(A^2), and A^2 is H. In another embodiment of Formula (I), B^1 is OR^1. In another embodiment of Formula (I), B^1 is OR^1, and A^1 is C(A^2), and A^2 is H.

In one embodiment of Formula (I), D^1 and E^1 are H. In another embodiment of Formula (I), B^1 is NHR^1, and A^1 is C(A^2), A^2 is H, and D^1 and E^1 are H. In another embodiment of Formula (I), B^1 is OR^1, and A^1 is C(A^2), A^2 is H, and D^1 and E^1 are H.

In one embodiment of Formula (I), Y^1 is H, CN, NO_2, F, Cl, Br, I, CF_3, R^{17}, NHC(O)R^{17}, or C(O)NH_2. In another embodiment of Formula (I), Y^1 is NO_2. In another embodiment of Formula (I), Y^1 is Cl. In another embodiment of Formula (I), B^1 is NHR^1,
and A¹ is C(A²), A² is H, D¹ and E¹ are H, and Y¹ is NO₂. In another embodiment of Formula (I), B¹ is OR¹, and A¹ is C(A²), A² is H, D¹ and E¹ are H, and Y¹ is Cl.

In one embodiment of Formula (I), R¹ is R², R³, R⁴ or R⁵. In another embodiment of Formula (I), R¹ is R², and R² is phenyl.

In one embodiment of Formula (I), R¹ is R³, and R³ is heteroaryl. In another embodiment of Formula (I), R³ is triazolyl.

In one embodiment of Formula (I), R¹ is R⁴. In another embodiment of Formula (I), R¹ is R⁴ and R⁴ is cycloalkyl. In another embodiment of Formula (I), R¹ is R⁴, and R⁴ is cyclohexyl. In another embodiment of Formula (I), R¹ is R⁴, and R⁴ is heterocycloalkyl. In another embodiment of Formula (I), R¹ is R⁴, and R⁴ is 8-azabicyclo[3.2.1]octane, azetidinyl, piperidinyl, piperazinyl, pyrrolidinyl, morpholinyl, tetrahydropyranyl, or tetrahydrothiophenyl. In another embodiment of Formula (I), R¹ is R⁴, and R⁴ is heterocycloalkenyl. In another embodiment of Formula (I), R¹ is R⁴, and R⁴ is tetrahydropyridazinyl.

In one embodiment of Formula (I), R¹ is R⁵. In another embodiment of Formula (I), R¹ is R⁵ and R⁵ is alkyl or alkenyl. In another embodiment of Formula (I), R¹ is R⁵ and R⁵ is alkyl which is unsubstituted. In another embodiment of Formula (I), R¹ is R⁵ and R⁵ is alkyl which is substituted with one or two or three independently selected R⁶, R⁷, OR⁷, SR⁷, SO₂R⁷, N(R⁷)₂, OH, CN, CF₃, F, Cl, Br or I substituents. In another embodiment of Formula (I), R¹ is R⁵ and R⁵ is alkyl which is substituted with R⁷.

In one embodiment of Formula (I), R⁷ is R⁸, R⁹, R¹⁰ or R¹¹. In another embodiment of Formula (I), R⁷ is R⁸, and R⁸ is phenyl which is unfused or fused with R⁸A, and R⁸A is heterocycloalkane. In another embodiment of Formula (I), R⁷ is R⁸, and R⁸ is phenyl which is unfused. In another embodiment of Formula (I), R⁷ is R⁸, and R⁸ is heteroaryl. In another embodiment of Formula (I), R⁷ is R⁸, and R⁸ is furanyl, imidazolyl, isothiazolyl, isoxazolyl, 1,2,3-oxadiazoyl, 1,2,5-oxadiazoyl, oxazolyl, pyrazinyl, pyrazolyl, pyridazinyl, pyridinyl, pyrimidinyl, pyrrolyl, tetrazolyl, thiazolyl, thiophenyl, triazinyl or 1,2,3-triazolyl. In another embodiment of Formula (I), R⁷ is R⁸, and R⁸ is pyridinyl, thiazolyl, imidazoyl, and 1,2,3-triazolyl. In another embodiment of Formula (I), R⁷ is R¹⁰, and R¹⁰ is C₃-C₁₀-cycloalkyl. In another embodiment of Formula (I), R⁷ is R¹⁰, and R¹⁰ is C₆ or C₁₀-cycloalkyl. In another embodiment of Formula (I), R⁷ is R¹⁰, and R¹⁰ is cyclohexyl or adamantanyll. In another embodiment of Formula (I), R⁷ is R¹⁰, and R¹⁰ is morpholinyl,
piperazinyl, piperidinyl, tetrahydro-2H-pyranyl, 1,2-dihydropyridinyl, pyranyl, pyridin-1(H)-yl, pyrrolidinyl, oxetanyl, thiomorpholinyl, imidazolidinyl, tetrahydrothiophenyl, dioxolanyl, tetrahydrothiopyrany1, dioxany1, or tetrahydrofurany1. In another embodiment of Formula (I), R₇ is R₁₀, and R₁₀ is morpholinyl, piperazinyl, piperidinyl, tetrahydro-2H-pyranyl, 1,2-

dihydropyridinyl, pyrrolidinyl, oxetanyl, thiomorpholinyl, imidazolidinyl, tetrahydrothiophenyl, dioxolanyl, tetrahydrothiopyrany1, dioxany1, or tetrahydrofurany1. In another embodiment of Formula (I), R₇ is R₁₁, and R₁₁ is alkyl which is unsubstituted or substituted. In another embodiment of Formula (I), R₇ is R₁₁, and R₁₁ is alkyl which is unsubstituted. In another embodiment of Formula (I), R₇ is R₁₁, and R₁₁ is alkyl which is substituted. In another embodiment of Formula (I), R₇ is R₁₁, and R₁₁ is alkyl which is substituted with one or two or three independently selected OR₁₂, F, Cl, Br or I substituents. In another embodiment of Formula (I), R₇ is R₁₁, R₁₁ is alkyl which is substituted with OR₁₂, R₁₂ is R₁₆, and R₁₆ is alkyl.

In one embodiment of Formula (I), R₁₇ is R₁₉ or R₂₁. In another embodiment of Formula (I), R₁₇ is R₁₉, and R₁₉ is heteroaryl. In another embodiment of Formula (I), R₁₇ is R₁₉, and R₁₉ is thiazolyl. In another embodiment of Formula (I), R₁₇ is R₂₁, and R₂₁ is alkynyl. In another embodiment of Formula (I), R₁₇ is R₂₁, and R₂₁ is ethynyl.

Still another embodiment pertains to compounds having Formula I which are 4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)-2-phenoxybenzamide;

benzamide;

4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-phenoxy-N-((4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonoyl)benzamide;

2-(benzyloxy)-4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)benzamide;

4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonoyl)-2-(2-phenylethoxy)benzamide;

4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonoyl)-2-(phenylthio)benzamide;

4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(phenylthio)-N-((4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonoyl)benzamide;
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-((3-morpholin-4-
ylpropyl)amino)-3-nitrophenyl)sulfonyl)-2-(phenylthio)benzamide;
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((tetrahydro-2H-
pyran-4-ylmethyl)amino)phenyl)sulfonyl)-2-(phenylsulfonyl)benzamide;
2-benzyl-4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-
(tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)benzamide;
2-benzyl-4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-((tetrahydro-2H-
pyran-4-ylmethyl)amino)phenyl)sulfonyl)benzamide;
2-benzyl-4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-((3-morpholin-4-
ylpropyl)amino)-3-nitrophenyl)sulfonyl)benzamide;
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((tetrahydro-2H-
pyran-4-ylmethyl)amino)phenyl)sulfonyl)-2-(2-phenylethyl)benzamide;
2-benzyl-4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-((3-morpholin-4-
ylpropyl)amino)-3-nitrophenyl)sulfonyl)benzamide;
2-anilino-4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-
(tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)benzamide;
2-anilino-4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-((tetrahydro-2H-
pyran-4-ylmethyl)amino)phenyl)sulfonyl)benzamide;
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-methoxy-N-((3-nitro-4-
(tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)benzamide;
4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-N-((4-((3-
morpholin-4-ylpropyl)amino)-3-nitrophenyl)sulfonyl)-2-phenoxybenzamide;
4-(4-((2-(4-chlorophenyl)-5,5-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-N-((4-((3-
morpholin-4-ylpropyl)amino)-3-nitrophenyl)sulfonyl)-2-phenoxybenzamide;
4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-
indazol-5-yloxy)-N-((4-((3-morpholin-4-ylpropyl)amino)-3-nitrophenyl)sulfonyl)benzamide;
4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-
indazol-5-yloxy)-N-((4-((1-methylpiperidin-4-yl)amino)-3-nitrophenyl)sulfonyl)benzamide;
4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-N-((4-((3-
morpholin-4-ylpropyl)amino)-3-nitrophenyl)sulfonyl)-2-(1,2,3,4-tetrahydroquinolin-6-
yloxy)benzamide;
4-(4-((2-(4-chloro-2H-pyran-4-ylmethyl)amino)-3-nitrophenyl)sulfonyl)-2-(1H-indol-4-yloxy)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)benzamide;  
4-(4-((2-(4-chloro-2H-pyran-4-ylmethyl)amino)-3-nitrophenyl)sulfonyl)-2-(1H-indol-4-yloxy)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)benzamide;  
4-(4-((2-(4-chloro-2H-pyran-4-ylmethyl)amino)-3-nitrophenyl)sulfonyl)-2-(1H-indol-4-yloxy)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)benzamide;  
4-(4-((2-(4-chloro-2H-pyran-4-ylmethyl)amino)-3-nitrophenyl)sulfonyl)-2-(1H-indol-4-yloxy)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)benzamide;  
4-(4-((2-(4-chloro-2H-pyran-4-ylmethyl)amino)-3-nitrophenyl)sulfonyl)-2-(1H-indol-4-yloxy)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)benzamide;  
4-(4-((2-(4-chloro-2H-pyran-4-ylmethyl)amino)-3-nitrophenyl)sulfonyl)-2-(1H-indol-4-yloxy)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)benzamide;  
4-(4-((2-(4-chloro-2H-pyran-4-ylmethyl)amino)-3-nitrophenyl)sulfonyl)-2-(1H-indol-4-yloxy)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)benzamide;  
4-(4-((2-(4-chloro-2H-pyran-4-ylmethyl)amino)-3-nitrophenyl)sulfonyl)-2-(1H-indol-4-yloxy)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)benzamide;  
4-(4-((2-(4-chloro-2H-pyran-4-ylmethyl)amino)-3-nitrophenyl)sulfonyl)-2-(1H-indol-4-yloxy)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)benzamide;  
4-(4-((2-(4-chloro-2H-pyran-4-ylmethyl)amino)-3-nitrophenyl)sulfonyl)-2-(1H-indol-4-yloxy)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)benzamide;  
4-(4-((2-(4-chloro-2H-pyran-4-ylmethyl)amino)-3-nitrophenyl)sulfonyl)-2-(1H-indol-4-yloxy)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)benzamide;  
4-(4-((2-(4-chloro-2H-pyran-4-ylmethyl)amino)-3-nitrophenyl)sulfonyl)-2-(1H-indol-4-yloxy)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)benzamide;  
4-(4-((2-(4-chloro-2H-pyran-4-ylmethyl)amino)-3-nitrophenyl)sulfonyl)-2-(1H-indol-4-yloxy)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)benzamide;  
4-(4-((2-(4-chloro-2H-pyran-4-ylmethyl)amino)-3-nitrophenyl)sulfonyl)-2-(1H-indol-4-yloxy)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)benzamide;  
4-(4-((2-(4-chloro-2H-pyran-4-ylmethyl)amino)-3-nitrophenyl)sulfonyl)-2-(1H-indol-4-yloxy)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)benzamide;  
4-(4-((2-(4-chloro-2H-pyran-4-ylmethyl)amino)-3-nitrophenyl)sulfonyl)-2-(1H-indol-4-yloxy)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)benzamide;  
4-(4-((2-(4-chloro-2H-pyran-4-ylmethyl)amino)-3-nitrophenyl)sulfonyl)-2-(1H-indol-4-yloxy)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)benzamide;  
4-(4-((2-(4-chloro-2H-pyran-4-ylmethyl)amino)-3-nitrophenyl)sulfonyl)-2-(1H-indol-4-yloxy)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)benzamide;  
4-(4-((2-(4-chloro-2H-pyran-4-ylmethyl)amino)-3-nitrophenyl)sulfonyl)-2-(1H-indol-4-yloxy)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)benzamide;  
4-(4-((2-(4-chloro-2H-pyran-4-ylmethyl)amino)-3-nitrophenyl)sulfonyl)-2-(1H-indol-4-yloxy)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)benzamide;  
4-(4-((2-(4-chloro-2H-pyran-4-ylmethyl)amino)-3-nitrophenyl)sulfonyl)-2-(1H-indol-4-yloxy)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)benzamide;  
4-(4-((2-(4-chloro-2H-pyran-4-ylmethyl)amino)-3-nitrophenyl)sulfonyl)-2-(1H-indol-4-yloxy)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)benzamide;  
4-(4-((2-(4-chloro-2H-pyran-4-ylmethyl)amino)-3-nitrophenyl)sulfonyl)-2-(1H-indol-4-yloxy)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)benzamide;  
4-(4-((2-(4-chloro-2H-pyran-4-ylmethyl)amino)-3-nitrophenyl)sulfonyl)-2-(1H-indol-4-yloxy)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)benzamide;  
4-(4-((2-(4-chloro-2H-pyran-4-ylmethyl)amino)-3-nitrophenyl)sulfonyl)-2-(1H-indol-4-yloxy)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)benzamide;
4-(4-((4′-chloro-1,1′-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)-2-quinolin-7-yloxy)benzamide;
4-(4-((4′-chloro-1,1′-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)-2-(quinolin-6-yloxy)benzamide;
4-(4-((4′-chloro-1,1′-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)benzamide;
4-(4-((4′-chloro-1,1′-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(isoquinolin-5-yloxy)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)benzamide;
4-(4-((4′-chloro-1,1′-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-((3-dimethylamino)propyl)amino)-3-nitrophenyl)sulfonyl)-2-(isoquinolin-5-yloxy)benzamide;
4-(4-((4′-chloro-1,1′-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-((3-dimethylamino)propyl)amino)-3-nitrophenyl)sulfonyl)-2-(quinolin-6-yloxy)benzamide;
4-(4-((4′-chloro-1,1′-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-((3-dimethylamino)propyl)amino)-3-nitrophenyl)sulfonyl)-2-(1H-indol-5-yloxy)benzamide;
4-(4-((4′-chloro-1,1′-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)benzamide;
4-(4-((4′-chloro-1,1′-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-((3-dimethylamino)propyl)amino)-3-nitrophenyl)sulfonyl)-2-(1H-indol-4-yloxy)benzamide;
4-(4-((4′-chloro-1,1′-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-((3-dimethylamino)propyl)amino)-3-nitrophenyl)sulfonyl)-2-(1H-indol-6-yloxy)benzamide;
4-(4-((4′-chloro-1,1′-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(isoquinolin-7-yloxy)-N-((4-((3-morpholin-4-ylpropyl)amino)-3-nitrophenyl)sulfonyl)benzamide;
4-(4-((4′-chloro-1,1′-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-((3-dimethylamino)propyl)amino)-3-nitrophenyl)sulfonyl)-2-(isoquinolin-7-yloxy)benzamide;
4-(4-((2-(4-chlorophenyl)-5,5-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((4-((3-morpholin-4-ylpropyl)amino)-3-nitrophenyl)sulfonyl)benzamide;
4-(4-((2-(4-chlorophenyl)-5,5-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-N-((4-((3dimethylamino)propyl)amino)-3-nitrophenyl)sulfonyl)-2-(1H-indol-5-yloxy)benzamide;
4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((4-((3-morpholin-4-ylpropyl)amino)-3-nitrophenyl)sulfonyl)benzamide;
4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-N-((4-((3dimethylamino)propyl)amino)-3-nitrophenyl)sulfonyl)-2-(1H-indol-5-yloxy)benzamide;
4-(4-((2-(4-chlorophenyl)-5,5-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((4-((3-morpholin-4-ylpropyl)amino)-3-nitrophenyl)sulfonyl)benzamide;
4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((4-((3-morpholin-4-ylpropyl)amino)-3-nitrophenyl)sulfonyl)benzamide;  
4-(4-((2-(4-chlorophenyl)-5,5-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-N-((4-((3-dimethylamino)propyl)amino)-3-nitrophenyl)sulfonyl)-2-(1H-indol-4-yloxy)benzamide;  
4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-N-((4-((3-dimethylamino)propyl)amino)-3-nitrophenyl)sulfonyl)-2-(1H-indol-4-yloxy)benzamide;  
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((4-((3-morpholin-4-ylpropyl)amino)-3-nitrophenyl)sulfonyl)benzamide;  
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-methoxyphenyl)sulfonyl)-2-phenoxybenzamide;  
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-methylphenyl)sulfonyl)-2-phenoxybenzamide;  
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((4-((tetrahydro-2H-pyran-4-ylmethyl)amino)-3-((trifluoromethyl)sulfonyl)phenyl)sulfonyl)benzamide;  
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((4-((tetrahydro-2H-pyran-4-ylmethyl)amino)-3-((trifluoromethyl)sulfonyl)phenyl)sulfonyl)benzamide;  
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-((3-morpholin-4-ylpropyl)amino)-3-((trifluoromethyl)sulfonyl)phenyl)sulfonyl)benzamide;  
N-((3-((chloro(dimfluoro)methyl)sulfonyl)-4-((3-(dimethylamino)propyl)amino)phenyl)sulfonyl)-4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)benzamide;  
4-(4-((4,4-dimethyl-2-(4-(trifluoromethyl)phenyl)cyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((3-nitro-4-((3-pyrrolidin-1-ylpropyl)amino)phenyl)sulfonyl)benzamide;  
4-(4-((4,4-dimethyl-2-(4-(trifluoromethyl)phenyl)cyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((3-nitro-4-((3-pyrrolidin-1-ylpropyl)amino)phenyl)sulfonyl)benzamide;
4-(4-(4,4-dimethyl-2-(4-(trifluoromethoxy)phenyl)cyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yl)oxy)-N-((3-nitro-4-((3-pyrrolidin-1-yl)propyl)amino)phenyl)sulfonyl)benzamide;
4-(4-(4,4-dimethyl-2-(3-(trifluoromethyl)phenyl)cyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yl)oxy)-N-((3-nitro-4-((3-pyrrolidin-1-yl)propyl)amino)phenyl)sulfonyl)benzamide;
4-(4-(2-(3-fluorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yl)oxy)-N-((3-nitro-4-((3-pyrrolidin-1-yl)propyl)amino)phenyl)sulfonyl)benzamide;
4-(4-(2-(4-fluorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yl)oxy)-N-((3-nitro-4-((3-pyrrolidin-1-yl)propyl)amino)phenyl)sulfonyl)benzamide;
N-((3-((chloro(di fluoro)methyl)sulfonyl)-4-((1-methylpiperidin-4-yl)amino)phenyl)sulfonyl)-4-(4-(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yl)oxy)benzamide;
4-(4-(2-(4-chlorophenyl)cyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yl)oxy)-N-((4-((1-methylpiperidin-4-yl)amino)-3-nitrophenyl)sulfonyl)benzamide;
4-(4-(4-(4-chloro-1',1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yl)oxy)-N-((4-((1-methylpiperidin-4-yl)amino)-3-nitrophenyl)sulfonyl)benzamide;
4-(4-(4-chloro-1',1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-yl)methyl)amino)phenyl)sulfonyl)-2-(phenoxymethyl)benzamide;
4-(4-(4-chloro-1',1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-((3-morpholin-4-yl)propyl)amino)phenyl)sulfonyl)-2-phenoxymethylbenzamide;
4-(4-(4-chloro-1',1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-yl)methyl)amino)phenyl)sulfonyl)-2-(pyridin-3-yl)oxy)benzamide;
4-(4-(4-chloro-1',1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(pyridin-3-yl)oxy)-N-((4-((tetrahydro-2H-pyran-4-yl)methyl)amino)phenyl)sulfonyl)benzamide;
4-(4-(4-chloro-1',1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-(1R)-3-(dimethylamino)-1-((phenylthio)methyl)propyl)amino)-3-nitrophenyl)sulfonyl)-2-phenoxymethylbenzamide;
4-(4-(4-chloro-1',1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-yl)methyl)amino)phenyl)sulfonyl)-2-(pyridin-4-yl)oxy)benzamide;
4-(4-(4-chloro-1',1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-((3-morpholin-4-yl)propyl)amino)-3-nitrophenyl)sulfonyl)-2-(pyridin-3-yl)oxy)benzamide;
4-(4-(4-chloro-1',1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-((3-morpholin-4-yl)propyl)amino)-3-nitrophenyl)sulfonyl)-2-(pyridin-4-yl)oxy)benzamide;
4-(4-((4′-chloro-1,1′-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-((2-(4-methylpiperazin-1-yl)ethyl)amino)-3-nitrophenyl)sulfonfonyl)-2-phenoxybenzamide; 
4-(4-((4′-chloro-1,1′-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-((3-(4-methylpiperazin-1-yl)propyl)amino)-3-nitrophenyl)sulfonfonyl)-2-phenoxybenzamide; 
4-(4-((4′-chloro-1,1′-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-((3-(dimethylamino)propyl)(methyl)amino)-3-nitrophenyl)sulfonfonyl)-2-phenoxybenzamide; 
4-(4-((4′-chloro-1,1′-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-((1-methylpiperidin-4-yl)methyl)amino)-3-nitrophenyl)sulfonfonyl)-2-phenoxybenzamide; 
4-(4-((4′-chloro-1,1′-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-((1-methylpiperidin-4-yl)amino)-3-nitrophenyl)sulfonfonyl)-2-phenoxybenzamide; 
4-(4-((4′-chloro-1,1′-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-cyano-4-((3-(dimethylamino)propyl)amino)phenyl)sulfonfonyl)-2-phenoxybenzamide; 
4-(4-((4′-chloro-1,1′-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((3-pyrrolidin-1-yl)propyl)amino)phenyl)sulfonfonyl)-2-phenoxybenzamide; 
4-(4-((4′-chloro-1,1′-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-((3-(dimethylamino)propyl)amino)-3-((trifluoromethyl)phenyl)sulfonfonyl)-2-phenoxybenzamide; 
4-(4-((4′-chloro-1,1′-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-((3-isopropyl(methyl)amino)propyl)amino)-3-nitrophenyl)sulfonfonyl)-2-phenoxybenzamide; 
4-(4-((4′-chloro-1,1′-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-(3-(dimethylamino)propoxy)-3-nitrophenyl)sulfonfonyl)-2-phenoxybenzamide; 
4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((4-(2-(4-methylpiperazin-1-yl)ethyl)amino)-3-nitrophenyl)sulfonfonyl)benzamide; 
4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((4-(3-(4-methylpiperazin-1-yl)propyl)amino)-3-nitrophenyl)sulfonfonyl)benzamide; 
4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((3-nitro-4-((3-pyrrolidin-1-yl)propyl)amino)phenyl)sulfonfonyl)benzamide 
4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((4-(1-methylpiperidin-4-yl)amino)-3-nitrophenyl)sulfonfonyl)benzamide; 
4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((4-(3-(4-methylpiperazin-1-yl)propyl)amino)-3-nitrophenyl)sulfonfonyl)benzamide;
4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-N-((4-(3-(dimethylamino)propoxy)-3-nitrophenyl)sulfonyl)-2-(1H-indol-5-yloxy)benzamide;
4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((4-(2-(4-methylpiperazin-1-yl)ethyl)amino)-3-nitrophenyl)sulfonyl)benzamide;
4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((3-nitro-4-((3-pyrrolidin-1-yl)propyl)amino)phenyl)sulfonyl)benzamide;
4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-(((1-methylpiperidin-4-yl)amino)-3-nitrophenyl)sulfonyl)benzamide;
4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((4-(((1-methylpiperidin-4-yl)methyl)amino)-3-nitrophenyl)sulfonyl)benzamide;
4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((4-(((1-methylpiperidin-4-yl)methyl)amino)-3-nitrophenyl)sulfonyl)benzamide;
4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-N-((4-(3-(dimethylamino)propoxy)-3-nitrophenyl)sulfonyl)-2-(1H-indol-4-yloxy)benzamide;
4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((4-(4-methylpiperazin-1-yl)-3-nitrophenyl)sulfonyl)benzamide;
4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((3-nitro-4-((1-2,2,2-trifluoroethyl)piperidin-4-yl)amino)phenyl)sulfonyl)benzamide;
4-(4-(4-(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-N-((4-(((4-(dimethylamino)-1-methylpiperidin-4-yl)methyl)amino)-3-nitrophenyl)sulfonyl)-2-(1H-indol-5-yloxy)benzamide;
4-(4-(4-chloro-1,1′-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(2,3-dihydro-1,4-benzodioxin-5-yloxy)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)benzamide;
5-(4-(4-chloro-1,1′-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)-1,1′-biphenyl-2-carboxamide;
5-(4-(4-chloro-1,1′-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-(3-(dimethylamino)propyl)amino)-3-nitrophenyl)sulfonyl)-1,1′-biphenyl-2-carboxamide;
4-(4-(4-chloro-4-(2-(dimethylamino)ethoxy)-1,1′-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)-2-phenoxybenzamide;
4-(4'-(4-chloro-4-(3-piperidin-1-ylpropoxy)-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((tetrahydro-2H-pyranyl-4-ylmethyl)amino)phenyl)sulfonyl)-2-phenoxybenzamide;  
4-(4'-(4-chloro-4-(2-morpholin-4-ylethoxy)-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((tetrahydro-2H-pyranyl-4-ylmethyl)amino)phenyl)sulfonyl)-2-phenoxybenzamide;  
4-(4'-(4-chloro-4-(3-(dimethylamino)propoxy)-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((tetrahydro-2H-pyranyl-4-ylmethyl)amino)phenyl)sulfonyl)-2-phenoxybenzamide;  
4-(4'-(4-chloro-4-(2-morpholin-4-ylethoxy)-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-phenoxy-N-((4-((tetrahydro-2H-pyranyl-4-ylmethyl)amino)-3-((trifluoromethyl)sulfonyl)phenyl)sulfonyl)benzamide;  
4-(4'-(4-chloro-4-(3-(dimethylamino)propoxy)-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-phenoxy-N-((4-((tetrahydro-2H-pyranyl-4-ylmethyl)amino)-3-((trifluoromethyl)sulfonyl)phenyl)sulfonyl)benzamide;  
4-(4'-(4-chloro-4-(2-(dimethylamino)ethoxy)-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-phenoxy-N-((4-((tetrahydro-2H-pyranyl-4-ylmethyl)amino)-3-((trifluoromethyl)sulfonyl)phenyl)sulfonyl)benzamide;  
4-(4'-(4-chloro-4-(2-(dimethylamino)ethoxy)-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((3-pyrrolidin-1-ylpropyl)amino)phenyl)sulfonyl)-2-phenoxybenzamide;  
4-(4'-(4-chloro-3-(2-(dimethylamino)ethoxy)-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((tetrahydro-2H-pyranyl-4-ylmethyl)amino)phenyl)sulfonyl)-2-phenoxybenzamide;  
4-(4'-(4-chloro-3-(2-(dimethylamino)ethoxy)-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((3-pyrrolidin-1-ylpropyl)amino)phenyl)sulfonyl)-2-phenoxybenzamide;  
4-(4'-(4-chloro-3-(2-(dimethylamino)ethoxy)-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-phenoxy-N-((4-((tetrahydro-2H-pyranyl-4-ylmethyl)amino)-3-((trifluoromethyl)sulfonyl)phenyl)sulfonyl)benzamide;  
4-(4'-(4-chloro-4-(2-(dimethylamino)ethoxy)-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yl)oxy)-N-((3-nitro-4-((tetrahydro-2H-pyranyl-4-ylmethyl)amino)phenyl)sulfonyl)benzamide;  
4-(4'-(4-chloro-4-(2-(dimethylamino)ethoxy)-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yl)oxy)-N-((3-nitro-4-((tetrahydro-2H-pyranyl-4-ylmethyl)amino)phenyl)sulfonyl)benzamide;
4-((4'-chloro-4-(2-morpholin-4-yloxy)-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-yl)methyl)amino)phenyl)sulfonyl)benzamide;
4-((4'-chloro-3-(2-(dimethylamino)ethoxy)-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-yl)methyl)amino)phenyl)sulfonyl)benzamide;
4-((4'-chloro-3-(2-(dimethylamino)ethoxy)-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-yl)methyl)amino)phenyl)sulfonyl)benzamide;
4-((4'-chloro-4-(2-morpholin-4-yloxy)-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-yl)methyl)amino)phenyl)sulfonyl)benzamide;
4-((4'-chloro-3-(2-morpholin-4-yloxy)-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-yl)methyl)amino)phenyl)sulfonyl)benzamide;
4-((4'-chloro-3-(2-morpholin-4-yloxy)-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-yl)methyl)amino)phenyl)sulfonyl)benzamide;
4-((4'-chloro-4-(2-(dimethylamino)ethoxy)-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-(((4-((1-methylpiperidin-4-yl)amino)-3-nitrophenyl)sulfonyl)-2-phenoxybenzamide;
4-((4'-chloro-3-(2-(dimethylamino)ethoxy)-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((3-nitro-4-((3-pyrrolidin-1-yl)propyl)amino)phenyl)sulfonyl)benzamide;
4-((4'-chloro-4-(2-(dimethylamino)ethoxy)-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((3-nitro-4-((3-pyrrolidin-1-yl)propyl)amino)phenyl)sulfonyl)benzamide;
4-((4'-chloro-4-(2-morpholin-4-yloxy)-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((3-nitro-4-((3-pyrrolidin-1-yl)propyl)amino)phenyl)sulfonyl)benzamide;
4-((4'-chloro-4-(2-(dimethylamino)ethoxy)-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-(((3-nitro-4-((1-(2,2,2-trifluoroethyl)piperidin-4-yl)amino)phenyl)sulfonyl)-2-phenoxybenzamide;
4-((4'-chloro-4-(2-pyrrolidin-1-yloxy)-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-(((3-nitro-4-((tetrahydro-2H-pyran-4-yl)methyl)amino)phenyl)sulfonyl)-2-phenoxybenzamide;
4-(4'-chloro-4-(2-diisopropylamino)ethoxy)-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)-2-phenoxypyrimidamide; 4-(4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(2,3-dihydro-1H-indol-5-ylxylo)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)benzamide; 4-(4-(2-(4-chlorophenyl)cyclohept-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-ylxylo)-N-((3-nitro-4-((3-pyrrolidin-1-ylpropyl)amino)phenyl)sulfonyl)benzamide; 4-(4-(2-(4-chlorophenyl)cyclooct-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-ylxylo)-N-((3-nitro-4-((3-pyrrolidin-1-ylpropyl)amino)phenyl)sulfonyl)benzamide; 4-(4-(2-(4-chlorophenyl)cyclopent-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-ylxylo)-N-((3-nitro-4-((3-pyrrolidin-1-ylpropyl)amino)phenyl)sulfonyl)benzamide; 4-(4-(2-(4-chlorophenyl)cyclopent-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-ylxylo)-N-((4-((1-methylpiperidin-4-yl)amino)-3-nitrophenyl)sulfonyl)benzamide; 4-(4-(4-(4-chlorophenyl)-6,6-dimethyl-5,6-dihydro-2H-pyran-3-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-ylxylo)-N-((4-((1-methylpiperidin-4-yl)amino)-3-nitrophenyl)sulfonyl)benzamide; 4-(4-(2-(4-chlorophenyl)cyclohept-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-ylxylo)-N-((4-((1-methylpiperidin-4-yl)amino)-3-nitrophenyl)sulfonyl)benzamide; 4-(4-(2-(4-chlorophenyl)cyclopent-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-ylxylo)-N-((4-((1-methylpiperidin-4-yl)amino)-3-nitrophenyl)sulfonyl)benzamide; 4-(4-(2-(4-chlorophenyl)cyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-ylxylo)-N-((4-((1-methylpiperidin-4-yl)amino)-3-nitrophenyl)sulfonyl)benzamide; 4-(4-(4-(4-chlorophenyl)-6,6-dimethyl-5,6-dihydro-2H-pyran-3-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-ylxylo)-N-((4-((1-methylpiperidin-4-yl)amino)-3-nitrophenyl)sulfonyl)benzamide; 4-(4-(2-(4-chlorophenyl)cyclohept-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-ylxylo)-N-((4-((1-methylpiperidin-4-yl)amino)-3-nitrophenyl)sulfonyl)benzamide; 4-(4-(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-N-((4-((1-methylpiperidin-4-yl)amino)-3-nitrophenyl)sulfonyl)-2-phenoxypyrimidamide; 4-(4'-(4-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-(2-(dimethylamino)ethyl)amino)-3-nitrophenyl)sulfonyl)-2-phenoxypyrimidamide;
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-(3-((dimethylamino)propyl)amino)-3-nitrophenyl)sulfonyl)-2-phenoxybenzamide;
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-(3-morpholin-4-ylpropyl)amino)-3-nitrophenyl)sulfonyl)-2-phenoxybenzamide;
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-(3-(dimethylamino)butyl)amino)-3-nitrophenyl)sulfonyl)-2-phenoxybenzamide;
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((1-phenylsulfonyl)piperidin-4-yl)amino)phenyl)sulfonyl)-2-phenoxybenzamide;
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((1-(quinolin-8-yl)sulfonyl)piperidin-4-yl)amino)phenyl)sulfonyl)-2-phenoxybenzamide;
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-phenoxy-N-((4-(3-(phenylsulfonyl)piperidin-4-yl)amino)-3-((trifluoromethyl)sulfonyl)phenyl)sulfonyl)benzamide;
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-phenoxy-N-((4-(1-(quinolin-8-yl)sulfonyl)piperidin-4-yl)amino)-3-((trifluoromethyl)sulfonyl)phenyl)sulfonyl)benzamide;
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-((1S)-3-((dimethylamino)1-thien-2-yl)propyl)amino)-3-nitrophenyl)sulfonyl)-2-phenoxybenzamide;
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((thien-2-ylmethyl)amino)phenyl)sulfonyl)-2-phenoxybenzamide;
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-phenoxy-N-((4-((tetrahydro-2H-pyran-4-yl)methyl)amino)-3-((trifluoromethyl)sulfonyl)phenyl)sulfonyl)benzamide;
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((2-(1H,1,2,3-triazol-1-yl)ethyl)amino)phenyl)sulfonyl)-2-phenoxybenzamide;
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((2H-1,2,3-triazol-2-yl)ethyl)amino)phenyl)sulfonyl)-2-phenoxybenzamide;
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-(3-(dimethylamino)propyl)amino)-3-nitrophenyl)sulfonyl)-2-(2-naphthoxy)benzamide;
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((2-(2-oxopyridin-1(2H)-yl)ethyl)amino)phenyl)sulfonyl)-2-phenoxybenzamide;
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((2-pyridin-2-yloxy)ethyl)amino)phenyl)sulfonyl)-2-phenoxybenzamide;
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((2-pyridin-4-ylethyl)amino)phenyl)sulfonyl)-2-phenoxybenzamide;
4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-N-(4-((3-(dimethylamino)propyl)amino)-3-((trifluoromethyl)sulfonyl)phenyl)sulfonyl)-2-(1H-indol-5-yloxy)benzamide;

4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-N-(4-((3-(dimethylamino)propyl)amino)-3-((trifluoromethyl)phenyl)sulfonyl)-2-(1H-indol-5-yloxy)benzamide;

4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-N-(3-cyano-4-((3-(dimethylamino)propyl)amino)phenyl)sulfonyl)-2-(1H-indol-5-yloxy)benzamide;

4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-(3-nitro-4-((1-tetrahydro-2H-pyran-4-yl)piperidin-4-yl)amino)phenyl)sulfonyl)benzamide;

4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-(4-((4-methylpiperazin-1-yl)amino)-3-nitrophenyl)sulfonyl)benzamide;

4-(4-((1'-4'-chloro-1,1'-biphenyl-2-yl)ethyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-(3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)benzamide;

N-(4-(((4-aminotetrahydro-2H-pyran-4-yl)methyl)amino)-3-nitrophenyl)sulfonyl)-4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)benzamide;

4-(4-{{2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl}methyl}piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-({3-nitro-4-{{(tetrahydro-2H-pyran-4-ylmethyl)amino}phenyl}sulfonyl}benzamide;

Trans-4-(4-{{2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl}methyl}piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-{{4-{{4-morpholin-4-ylcyclohexyl}amino}}-3-nitrophenyl}sulfonyl)benzamide;

4-(4-{{2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl}methyl}piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-{{4-{{2-methoxyethyl}amino}}-3-nitrophenyl}sulfonyl)benzamide;

4-(4-{{2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl}methyl}piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-{{3-nitro-4-{{(3S)-tetrahydro-2H-pyran-3-yl}methyl}amino}phenyl}sulfonyl)benzamide;

4-(4-{{2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl}methyl}piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-{{3-nitro-4-{{(3R)-tetrahydro-2H-pyran-3-yl}methyl}amino}phenyl}sulfonyl)benzamide;
4-(4-[[4-(4-chlorophenyl)-6,6-dimethyl-5,6-dihydro-2H-pyran-3-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-([3-nitro-4-[(tetrahydro-2H-pyran-4-yl)methyl]amino]phenyl)sulfonyl)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4-[(4-hydroxy-1-methylpiperidin-4-yl)methyl]amino]-3-nitrophenyl)sulfonyl]-2-(1H-indol-5-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-3-fluoro-2-(1H-indol-5-yloxy)-N-([4-[(1-methylpiperidin-4-yl)amino]-3-nitrophenyl)sulfonyl]benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-3-fluoro-2-(1H-indol-5-yloxy)-N-([3-nitro-4-[(1-tetrahydro-2H-pyran-4-yl)piperidin-4-yl]amino]phenyl)sulfonyl)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4-[(4-hydroxy-1-methylpiperidin-4-yl)methyl]amino]-3-nitrophenyl)sulfonyl]-2-(1H-indol-4-yloxy)benzamide;
N-[[4-[(3S,4R)-1-benzyl-3-hydroxypiperidin-4-yl]amino]-3-nitrophenyl)sulfonyl]-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)benzamide;
N-[[4-[(4-aminotetrahydro-2H-pyran-4-yl)methyl]amino]-3-nitrophenyl)sulfonyl]-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-[[4-[[1-(2-methoxyethyl)piperidin-4-yl]amino]-3-nitrophenyl)sulfonyl]benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-[[4-[[4-methylpiperazin-1-yl]amino]-3-nitrophenyl)sulfonyl]benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4-[(1-(2-hydroxyethyl)piperidin-4-yl)amino]-3-nitrophenyl)sulfonyl]-2-(1H-indol-4-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-[[4-[[1-(2-methoxyethyl)piperidin-4-yl]amino]-3-nitrophenyl)sulfonyl]benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[4-[[1-(3-hydroxypropyl)piperidin-4-yl]amino]-3-nitrophenyl)sulfonyl]-2-(1H-indol-4-yloxy)benzamide;
4-(4-[[4'-chloro-3-[3-(dimethylamino)propyl]-1,1'-biphenyl-2-yl]methyl]piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-(3-nitro-4-[(tetrahydro-2H-pyran-4-ylmethyl]amino)phenyl)sulfonyl)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[4-[[1-(3-hydroxypropyl)piperidin-4-yl]amino]-3-nitrophenyl)sulfonyl]-2-(1H-indol-5-yloxy)benzamide;
4-(4-[[4'-chloro-4-morpholin-4-yl-1,1'-biphenyl-2-yl]methyl]piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-(3-nitro-4-[(tetrahydro-2H-pyran-4-ylmethyl]amino)phenyl)sulfonyl)benzamide;
4-(4-[[4'-chloro-3-[2-(dimethylamino)ethoxy]-1,1'-biphenyl-2-yl]methyl]piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-(3-nitro-4-[(1-tetrahydro-2H-pyran-4-yl)piperidin-4-yl]amino)phenyl)sulfonyl)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[4-[[4-(diethylamino)cyclohexyl]amino]-3-nitrophenyl)sulfonyl]-2-(1H-indol-5-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[4-[[4-(dimethylamino)cyclohexyl]amino]-3-nitrophenyl)sulfonyl]-2-(1H-indol-4-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[4-[[4-(diethylamino)cyclohexyl]amino]-3-nitrophenyl)sulfonyl]-2-(1H-indol-4-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[4-[[4-(morpholin-4-yl)cyclohexyl]amino]-3-nitrophenyl)sulfonyl)benzamide;
4-[4-[[4'-chloro-3-[2-(dimethylamino)ethoxy]-1,1'-biphenyl-2-yl]methyl]piperazin-1-yl]-2-(1H-indol-4-yloxy)-N-[4-[[1-methylpiperidin-4-yl]amino]-3-nitrophenyl)sulfonyl)benzamide;
4-(4-[[1-(4'-chloro-1,1'-biphenyl-2-yl)ethyl]piperazin-1-yl]-2-(1H-indol-4-yloxy)-N-[4-[[1-methylpiperidin-4-yl]amino]-3-nitrophenyl)sulfonyl)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[4-[[4-(dimethylamino)tetrahydro-2H-pyran-4-yl]methyl]amino]-3-nitrophenyl)sulfonyl]-2-(1H-indol-5-yloxy)benzamide;
N-[[4-[[2-(4-aminocyclohexyl)amino]-3-nitrophenyl]sulfonyl]-4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl]-2-(1H-indol-5-yloxy)benzamide;

4-[[4'-chloro-4-[[3-(dimethylamino)prop-1-yny]-1,1'-biphenyl-2-yl]methyl]piperazin-1-yl]-2-(1H-indol-5-yloxy)-N-[[3-nitro-4-[[1-(4,4,4-trifluorobutyl)piperidin-4-yl]amino]phenyl]sulfonyl]benzamide;

4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl]-N-[[4-[[2-(4-hydroxy-4-methyl)piperidin-4-yl]ethyl]amino]-3-nitrophenyl]sulfonyl]-2-(1H-indol-5-yloxy)benzamide;

4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl]-2-(1H-indol-5-yloxy)-N-[[3-nitro-4-[[1-(1,3-thiazol-2-yl)piperidin-4-yl]amino]phenyl]sulfonyl]benzamide;

4-[[4'-chloro-4-[[2-(hydroxyethoxy)-1,1'-biphenyl-2-yl]methyl]piperazin-1-yl]-2-(1H-indol-5-yloxy)-N-[[3-nitro-4-[[1-(4,4,4-trifluorobutyl)piperidin-4-yl]amino]phenyl]sulfonyl]benzamide;

4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl]-N-[[4-[[1-(cyclopropylmethyl)piperidin-4-yl]amino]-3-nitrophenyl]sulfonyl]-2-(1H-indol-5-yloxy)benzamide;


4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl]-2-(1H-indol-5-yloxy)-N-[[3-nitro-4-[[1-(4,4,4-trifluorobutyl)piperidin-4-yl]amino]phenyl]sulfonyl]benzamide;

4-[[4-[[4'-chloro-1,1'-biphenyl-2-yl]ethyl]piperazin-1-yl]-2-(1H-indol-5-yloxy)-N-[[4-[[4-methylpiperazin-1-yl]amino]-3-nitrophenyl]sulfonyl]benzamide;

4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]-3-(hydroxymethyl)piperazin-1-yl]-2-(1H-indol-5-yloxy)-N-[[3-nitro-4-[[1-(4,4,4-trifluorobutyl)piperidin-4-yl]amino]phenyl]sulfonyl]benzamide;

4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]-3-(hydroxymethyl)piperazin-1-yl]-2-(1H-indol-5-yloxy)-N-[[3-nitro-4-[[1-(4,4,4-trifluorobutyl)piperidin-4-yl]amino]phenyl]sulfonyl]benzamide;
4-(4-[(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-(4-[(4-methylpiperazin-1-yl)amino]-3-[(trifluoromethyl)sulfonyl]phenyl)sulfonyl]benzamide;
4-(4-[(4'-chloro-4-(2-hydroxyethoxy)-1,1'-biphenyl-2-yl)methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-(4-[(1-methylpiperidin-4-yl)amino]-3-nitrophenyl)sulfonyl]benzamide;
4-(4-[(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-(3-nitro-4-[(3-(3-oxopiperazin-1-yl)propyl]amino]phenyl)sulfonyl]benzamide;
4-(4-[(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-(3-nitro-4-[(3-(3-oxopiperazin-1-yl)propyl]amino]phenyl)sulfonyl]benzamide;
4-(4-[(2-(4-chlorophenyl)-5-hydroxycyclohex-1-en-1-yl)methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-(4-[(1-methylpiperidin-4-yl)amino]-3-nitrophenyl)sulfonyl]benzamide;
4-(4-[(2-(4-chlorophenyl)-5-hydroxycyclohex-1-en-1-yl)methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-(3-nitro-4-[(1-tetrahydro-2H-pyran-4-yl)piperidin-4-yl]amino]phenyl)sulfonyl]benzamide;
4-(4-[(2-(4-chlorophenyl)-5-hydroxycyclohex-1-en-1-yl)methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-(4-[(4-methylpiperazin-1-yl)amino]-3-nitrophenyl)sulfonyl]benzamide;
4-(4-[(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl)-N-(4-[(1-(2,3-dihydro-1H-inden-2-yl)piperidin-4-yl]amino]-3-nitrophenyl)sulfonyl]-2-(1H-indol-4-yloxy)benzamide;
4-(4-[(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl)-N-[(4-[(1-(2,3-dihydro-1H-inden-2-yl)piperidin-4-yl]amino]-3-nitrophenyl)sulfonyl]-2-(1H-indol-5-yloxy)benzamide;
4-(4-[(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-[(4-[(1-morpholin-4-ylcyclohexyl)methyl]amino]-3-nitrophenyl)sulfonyl]benzamide;
4-(4-[(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-[(3-nitro-4-[(1-(1,3-thiazol-2-ylmethyl)piperidin-4-yl]amino]phenyl)sulfonyl]benzamide;
4-(4-[(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-[(3-nitro-4-[(1-(1,3-thiazol-4-ylmethyl)piperidin-4-yl]amino]phenyl)sulfonyl]benzamide;
4-[(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl]-N-\{(4-\{(4-(hydroxymethyl)tetrahydro-2H-pyran-4-yl)methyl\}amino)-3-nitrophenyl\}sulfonfonyl]-2-(1H-indol-5-yloxy)benzamide;
4-[(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl]-N-\{(4-\{(2-hydroxyethyl)piperazin-1-yl\}amino)-3-nitrophenyl\}sulfonfonyl]-2-(1H-indol-5-yloxy)benzamide;
4-[(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl]-2-(1H-indol-5-yloxy)-N-\{(4-\{(3S)-1-methylpyrrolidin-3-yl\}amino\}3-nitrophenyl\}sulfonfonyl]benzamide;
4-[(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]-3-(hydroxymethyl)piperazin-1-yl]-2-(1H-indol-5-yloxy)-N-\{(3-nitro-4-[\{tetrahydro-2H-pyran-4-yl\}methyl\}amino\}phenyl\}sulfonfonyl]benzamide;
N-\{(4-\{(4-aminotetrahydro-2H-pyran-4-yl)methyl\}amino\}3-nitrophenyl\}sulfonfonyl]-4-[(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]-3-(hydroxymethyl)piperazin-1-yl]-2-(1H-indol-5-yloxy)benzamide;
4-[(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl]-N-\{\{(1-hydroxycyclohexyl)methyl\}amino\}3-nitrophenyl\}sulfonfonyl]-2-(1H-indol-5-yloxy)benzamide;
4-[(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl]-2-(1H-indol-4-yloxy)-N-\{\{(2-methoxyethyl)amino\}3-nitrophenyl\}sulfonfonyl]benzamide;
4-[(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl]-N-\{(4-\{(4-hydroxymethyl)tetrahydro-2H-pyran-4-yl\}amino\}3-nitrophenyl\}sulfonfonyl]-2-(1H-indol-5-yloxy)benzamide;
4-[(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl]-N-\{(4-\{(4-hydroxymethyl)tetrahydro-2H-pyran-4-yl\}amino\}3-nitrophenyl\}sulfonfonyl]-2-(1H-indol-4-yloxy)benzamide;
4-[(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl]-N-\{(4-\{(2-hydroxy-1-tetrahydro-2H-pyran-4-yl)eth)amino\}3-nitrophenyl\}sulfonfonyl]-2-(1H-indol-5-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-[[4-(methylamino)-3-nitrophenyl]sulfonyle]benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-[[4-(methylamino)-3-nitrophenyl]sulfonyle]benzamide;
4-{4-[1-(4'-chloro-1,1'-biphenyl-2-yl)ethyl]piperazin-1-yl}-2-(1H-indol-4-yloxy)-N-[[4-{3-morpholin-4-ylpropyl)amino]-3-nitrophenyl]sulfonyle]benzamide;
N-[[4-{[(1-aminocyclohexyl)methyl]amino}-3-nitrophenyl]sulfonyle]-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-[[3-nitro-4-[[2-(2-oxopyrrolidin-1-yl)ethyl](amino)phenyl]sulfonyle]benzamide;
4-{4-[1-(4'-chloro-1,1'-biphenyl-2-yl)ethyl]piperazin-1-yl}-2-(1H-indol-5-yloxy)-N-[[3-nitro-4-[(tetrahydro-2H-pyran-4-ylmethyl)amino]phenyl]sulfonyle]benzamide;
4-{4-[[1R]-1-(4'-chloro-1,1'-biphenyl-2-yl)ethyl]piperazin-1-yl}-2-(1H-indol-4-yloxy)-N-[[3-nitro-4-[(tetrahydro-2H-pyran-4-ylmethyl)amino]phenyl]sulfonyle]benzamide;
4-{[1S]-1-(4'-chloro-1,1'-biphenyl-2-yl)ethyl]piperazin-1-yl}-2-(1H-indol-4-yl)oxy)-N-{3-nitro-4-[tetrahydro-2H-pyran-4-ylmethyl]amino}phenyl}sulfonyl]benzamide;
4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]ethyl]piperazin-1-yl}-2-(1H-indol-5-yl)oxy)-N-{4-[(3-morpholin-4-ylpropyl)amino]-3-nitrophenyl}sulfonyl]benzamide;
4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]ethyl]piperazin-1-yl}-2-(1H-indol-5-yl)oxy)-N-{3-nitro-4-[(1-tetrahydro-2H-pyran-4-yl)piperidin-4-yl]amino}phenyl}sulfonyl]benzamide;
4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl}-N-{4-[(cyclohexylmethyl)amino]-3-nitrophenyl}sulfonyl]-2-(1H-indol-5-yl)oxy]benzamide;
4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl}-2-(1H-indol-5-yl)oxy)-N-{4-(morpholin-4-ylamino)-3-nitrophenyl}sulfonyl]benzamide;
4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl}-2-(1H-indol-5-yl)oxy)-N-{3-nitro-4-[(tetrahydro-2H-pyran-3-ylmethyl)amino]phenyl}sulfonyl]benzamide;
4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl}-2-(1H-indol-4-yl)oxy)-N-{4-(morpholin-4-ylamino)-3-nitrophenyl}sulfonyl]benzamide;
4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl}-2-(1H-indol-5-yl)oxy)-N-{3-nitro-4-(tetrahydro-2H-pyran-4-ylamino)phenyl}sulfonyl]benzamide;
4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl}-2-(1H-indol-5-yl)oxy)-N-{4-[(3-methyloxetan-3-yl)methyl]amino}-3-nitrophenyl}sulfonyl]benzamide;
4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl}-2-(1H-indol-5-yl)oxy)-N-{4-[(4-methyloxycyclohexyl)amino]-3-nitrophenyl}sulfonyl]benzamide;
4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl}-N-{4-{[3-(1,1-dioxidothiomorpholin-4-yl)propyl]amino}-3-nitrophenyl}sulfonyl]-2-(1H-indol-5-yl)oxy]benzamide;
4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl}-2-(1H-indol-5-yl)oxy)-N-{[3-nitro-4-{[2-(2-oxopiperidin-1-yl)ethyl]amino}]phenyl}sulfonyl]benzamide;
4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl}-2-(1H-indol-5-yl)oxy)-N-{[3-nitro-4-{[2-(2-oxoimidazolidin-1-yl)ethyl]amino}]phenyl}sulfonyl]benzamide;
4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl}-2-(1H-indol-5-yl)oxy)-N-{[3-nitro-4-{[2-pyridin-4-yl]ethy]amino}]phenyl}sulfonyl]benzamide;
4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-{[4-morpholin-4-yl-3-nitrophenyl]sulfonyl}benzamide;
4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-{[4-(4-methoxy)piperidin-1-yl]-3-nitrophenyl}sulfonyle]benzamide;
4-(4-{[2-(4-chlorophenyl)-5-pyrrolidin-1-ylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-{[3-nitro-4-{[tetrahydro-2H-pyran-4-ylmethyl]amino}phenyl}sulfonyle]benzamide;
4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-{[3-nitro-4-{[2-(3-oxopiperazin-1-
10 y)ethyl]amino}phenyl}sulfonyle]benzamide;
4-{4-[(4′-chloro-4-{(dimethylamino)ethoxy}-1,1′-biphenyl-2-yl]methyl}piperazin-1-yl]-2-(1H-indol-4-yloxy)-N-{4-{[(4-methyl)piperazin-1-yl]amino}-3-nitrophenyl}sulfonyle]benzamide;
4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-{[(1,1-dioxidotetrahydrothien-3-yl)methyl]amino}-3-nitrophenyl}sulfonyle]2-(1H-indol-5-yloxy)benzamide;
4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-{[(1,1-dioxidotetrahydrothien-3-yl)amino]-3-nitrophenyl}sulfonyle]2-(1H-indol-5-yloxy)benzamide;
4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-{[4-((trifluoromethyl)phenyl)sulfonyle]benzamide;
4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-{[4-[(1,3-dioxolan-2-yl)ethyl]-3-nitrophenyl}sulfonyle]2-(1H-indol-5-yloxy)benzamide;
4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-{[3-nitro-4-{[tetrahydro-2H-pyran-4-ylmethoxy]phenyl}sulfonyle]benzamide;
4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-{[3-nitro-4-{[2-(3-oxopiperazin-1-
10 y)ethyl]amino}phenyl}sulfonyle]benzamide;
4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-{[4-{[1-methyl-5-oxopyrrolidin-3-yl]amino]-3-nitrophenyl}sulfonyle]benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-[[4-[[1-methyl-6-oxopiperidin-3-yl]amino]-3-nitrophenyl]sulfonyl]benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-[[3-nitro-4-(piperidin-1-ylamino)phenyl]sulfonyl]benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-[[3-nitro-4-(piperidin-1-ylamino)phenyl]sulfonyl]benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-[[4-[[3-methyloxetan-3-yl]methoxy]-3-nitrophenyl]sulfonyl]benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-[[3-nitro-4-[(1,3-thiazol-5-yl)methyl]amino]phenyl]sulfonyl]benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-[[3-nitro-4-(tetrahydro-2H-pyran-4-ylmethoxy)phenyl]sulfonyl]benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-[[4-[[2-(methoxyethoxy)ethyl]amino]-3-nitrophenyl]sulfonyl]benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-[[4-[[3-(methylsulfonyl)propyl]amino]-3-nitrophenyl]sulfonyl]benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4-[[3-(1,1-dioxidothiomorpholin-4-yl)propyl]amino]-3-nitrophenyl]sulfonyl]-2-(1H-indol-4-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4-[(1,4-dioxan-2-ylmethoxy)-3-nitrophenyl]sulfonyl]-2-(1H-indol-5-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4-[[1,1-dioxidotetrahydrothien-3-yl]amino]-3-nitrophenyl]sulfonyl]-2-(1H-indol-4-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4-[[1,1-dioxidotetrahydro-2H-thiopyran-4-yl]methyl]amino]-3-nitrophenyl]sulfonyl]-2-(1H-indol-4-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4-[[2,2-difluoroethyl]amino]-3-nitrophenyl]sulfonyl]-2-(1H-indol-5-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4-[[4,4-difluorocyclohexyl]amino]-3-nitrophenyl]sulfonyl]-2-(1H-indol-5-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4-[[fluorotetrahydro-2H-pyran-4-ylmethoxy]-3-nitrophenyl]sulfonyl]-2-(1H-indol-4-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-([4-(2-methoxyethyl)amino]-3-[(trifluoromethyl)sulfonyl]phenyl)sulfonyl]benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[(4-[(4-hydroxycyclohexyl)methyl]amino]-3-nitrophenyl)sulfonyl]-2-(1H-indol-5-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-[(4-[(4-methoxy cyclohexyl)methyl]amino]-3-nitrophenyl)sulfonyl]benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-[(3-nitro-4-(2-tetrahydro-2H-pyran-4-yloxy)phenyl)sulfonyl]benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-([4-(2-methoxyethyl)amino]-3-[(trifluoromethyl)sulfonyl]phenyl)sulfonyl]benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-([4-3-(methylsulfonyl)propoxy]-3-nitrophenyl)sulfonyl]benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-([4-[(3-methoxypropyl)amino]-3-nitrophenyl)sulfonyl]benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-([4-[(3-methoxypropyl)amino]-3-nitrophenyl)sulfonyl]benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-([4-[[2-cyanoethyl]amino]-3-nitrophenyl)sulfonyl]-2-(1H-indol-5-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-([4-[[2-cyanoethyl]amino]-3-nitrophenyl)sulfonyl]-2-(1H-indol-4-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4-
{(3R)-4-hydroxy-1-adamantyl[methyl]amino}-3-nitrophenyl]sulfonyl]-2-(1H-indol-5-
yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4-
{{Cis-4-hydroxy-1-adamantyl[methyl]amino}-3-nitrophenyl]sulfonyl}-2-(1H-indol-5-
yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-
indol-4-yloxy)-N-{{3-nitro-4-[(3,3,3-trifluoropropyl)amino]phenyl}sulfonyl}benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-
indol-5-yloxy)-N-{{3-nitro-4-[(3,3,3-trifluoropropyl)amino]phenyl}sulfonyl}benzamide;
N-{{5-bromo-6-[(tetrahydro-2H-pyran-4-ylmethyl)amino]pyridin-3-yl}sulfonyl}-4-(4-[[2-(4-
chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-4-
yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4-
{(1,1-dioxidotetrahydrothien-3-yl)methyl]amino}-3-nitrophenyl)sulfonyl]-2-(1H-indol-4-
yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-{{4-
[(trifluoromethyl)sulfonyl]phenyl}sulfonyl}benzamide;
N-{{5-bromo-6-(tetrahydro-2H-pyran-4-ylmethoxy)pyridin-3-yl}sulfonyl}-4-(4-[[2-(4-
chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-
yloxy)benzamide;
4-(4-[[4-(4-chlorophenyl)-6-isopropanylpyridin-3-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-
yloxy)-N-{{3-nitro-4-[(tetrahydro-2H-pyran-4-ylmethyl)amino]phenyl}sulfonyl}benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-
indol-5-yloxy)-N-{{5-(tetrahydro-2H-pyran-4-ylmethoxy)-5-(1,3-thiazol-2-yl)pyridin-3-
yl}sulfonyl}benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-
indol-5-yloxy)-N-{{4-[(2-methoxyethyl)amino]carbonyl[phenyl]sulfonyl}benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[5-cyano-6-(tetrahydro-2H-pyran-4-ylmethoxy)pyridin-3-yl]sulfonyl]-2-(1H-indol-5-yloxy)benzamide;
N-[(1-acetyl)piperidin-4-yl]amino]-3-nitrophenyl]sulfonyl]-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)benzamide;
N-[(4-[[1-(methyl)sulfonyl]piperidin-4-yl]amino]-3-nitrophenyl]sulfonyl]benzamide;
N-[(4-[[1-(dioxan-2-ylmethyl)amino]-3-nitrophenyl]sulfonyl]-2-(1H-indol-5-yloxy)benzamide;
N-[(4-[[1-acetyl)piperidin-4-yl]amino]-3-nitrophenyl]sulfonyl]-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-4-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-4-yloxy)N-[(4-[[1-(methyl)sulfonyl]piperidin-4-yl]amino]-3-nitrophenyl]sulfonyl]benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[(4-[[2R]-1,4-dioxan-2-ylmethoxy]-3-nitrophenyl]sulfonyl]-2-(1H-indol-5-yloxy)benzamide;
4-(4-\{2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl\}methyl)piprazin-1-yl)-N-(\{4-\[(2S)-1,4-dioxan-2-ylmethoxy]-3-nitrophenyl\}sulfonyl)-2-(1H-indol-5-yloxy)benzamide;
4-(4-\{2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl\}methyl)piprazin-1-yl)-2-(1H-indol-5-yloxy)-N-(\{4-[3-morpholin-4-ylpropyl]amino\}3-\[(trifluoromethyl)sulfonyl]phenyl\}sulfonyl)benzamide;
N-(\{5-bromo-6-[(tetrahydro-2H-pyran-4-ylmethyl)amino]pyridin-3-yl\}sulfonyl)-4-(4-\{2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl\}methyl)piprazin-1-yl)-2-(1H-indol-5-yloxy)benzamide;
4-(4-\{2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl\}methyl)piprazin-1-yl)-2-(1H-indol-5-yloxy)-N-(\{4-[2-morpholin-4-yylethyl]amino\}3-\[(trifluoromethyl)sulfonyl]phenyl\}sulfonyl)benzamide;
4-(4-\{2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl\}methyl)piprazin-1-yl)-N-(\{5-cyano-6-[(tetrahydro-2H-pyran-4-ylmethyl)amino]pyridin-3-yl\}sulfonyl)-2-(1H-indol-5-yloxy)benzamide;
4-(4-\{2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl\}methyl)piprazin-1-yl)-2-(1H-indol-5-yloxy)-N-(\{4-[(1-methylpiperidin-4-yl)oxy]-3-nitrophenyl\}sulfonyl)benzamide;
4-(4-\{2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl\}methyl)piprazin-1-yl)-2-(1H-indol-5-yloxy)-N-(\{4-[1-methylpiperidin-4-ylmethoxy]-3-nitrophenyl\}sulfonyl)benzamide;
4-(4-\{2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl\}methyl)piprazin-1-yl)-2-(1H-indol-5-yloxy)-N-(\{3-nitro-4-[(tetrahydro-2H-pyran-4-ylmethyl)amino]phenyl\}sulfonyl)benzamide;
25 benzyl 4-(\{4-\{(4-\{4-(4-\{2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl\}methyl)piprazin-1-yl\}-2-(1H-indol-5-yloxy)benzoyl]amino\}sulfonyl\}2-nitrophenyl)methyl)piperidine-1-carboxylate;
N-(\{3-(aminocarbonyl)-4-[(tetrahydro-2H-pyran-4-ylmethoxy)phenyl]sulfonyl\}-4-(4-\{2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl\}methyl)piprazin-1-yl)-2-(1H-indol-5-yloxy)benzamide;
4-(4-\{4'-chloro-5-(trifluoromethyl)-1,1'-biphenyl-2-yl\}methyl)piprazin-1-yl)-2-(1H-indol-5-yloxy)-N-(\{3-nitro-4-[(1-tetrahydro-2H-pyran-4-yl)piperidin-4-yl]amino\}phenyl\}sulfonyl)benzamide;
4-[(5-tert-butyl-4'-chloro-1,1'-biphenyl-2-yl)methyl]piperazin-1-yl]-2-(1H-indol-5-yloxy)-N-(3-nitro-4-[(1-tetrahydro-2H-pyran-4-yl)piperazin-4-yl]amino)phenyl)sulfonyl)benzamide;
4-[(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((4-[(1-methyl-1H-imidazol-5-yl)methyl]amino)-3-nitrophenyl)sulfonyl)benzamide;
4-[(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((4-[morpholin-4-yl]sulfonyl)phenyl)sulfonyl)benzamide;
4-[(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl)-N-((4-[(1,1-dioxidothiomorpholin-4-yl)amino]-3-nitrophenyl)sulfonyl)-2-(1H-indol-5-yloxy)benzamide;
4-[(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl)-2-(1H-indol-4-yloxy)benzamide;
4-[(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((4-[morpholin-4-yl)cyclohexyl]amino)-3-nitrophenyl)sulfonyl)benzamide;
N-[(5-bromo-6-(tetrahydro-2H-pyran-4-ylmethoxy)pyridin-3-yl)sulfonyl]-4-[(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl)-2-(1H-indol-4-yloxy)benzamide;
4-[(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-[(6-[(tetrahydro-2H-pyran-4-yl)amino]-5-(1,3-thiazol-2-yl)pyridin-3-yl)sulfonyl]benzamide;
4-[(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl)-N-((3-cyano-4-[(tetrahydro-2H-pyran-4-yl)methyl]amino)phenyl)sulfonyl)-2-(1H-indol-4-yloxy)benzamide;
4-[(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl)-N-((3-cyano-4-[(tetrahydro-2H-pyran-4-yl)methyl]amino)phenyl)sulfonyl)-2-(1H-indol-5-yloxy)benzamide;
4-[(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl)-N-((4-[3,3-dimethylbutyl]amino)-3-nitrophenyl)sulfonyl)-2-(1H-indol-5-yloxy)benzamide;
4-[(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl)-N-[(4-[(1S)-1-(hydroxymethyl)-3-methylbutyl]amino]-3-nitrophenyl)sulfonyl)-2-(1H-indol-5-yloxy)benzamide;
4-[(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-[(3-nitro-4-[(2R)-tetrahydrofuran-2-ylmethyl]amino}phenyl)sulfonyl]benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[(4-[(1R)-1-(hydroxymethyl)-2-methylpropyl]amino]-3-nitrophenyl)sulfonyl]-2-(1H-indol-5-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-[(4-[(4-methoxyphenyl)amino]-3-nitrophenyl)sulfonyl]benzamide;
N-[(4-[[2-(1,3-benzodioxol-5-yl)ethyl]amino]-3-nitrophenyl)sulfonyl]-4-(4-[[2(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-[(3-nitro-4-[[3-(2-oxopyrrolidin-1-yl)propyl]amino]phenyl)sulfonyl]benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[(4-[(4-hydroxyphenyl)amino]-3-nitrophenyl)sulfonyl]-2-(1H-indol-5-yloxy)benzamide;
N-[(4-[[2-(4-aminosulfonyl)phenyl]ethyl]amino]-3-nitrophenyl)sulfonyl]-4-(4-[[2(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[(4-[[3-(1H-imidazol-1-yl)propyl]amino]-3-nitrophenyl)sulfonyl]-2-(1H-indol-5-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-[(3-nitro-4-[[1S]-1-phenylethyl]amino]phenyl)sulfonyl]benzamide;
N-[[2-chloro-5-fluoro-4-[(tetrahydro-2H-pyran-4-ylmethyl)amino]phenyl]sulfonyl]-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-[(4-[[2-(methoxyethoxy)ethyl]thio]-3-nitrophenyl)sulfonyl]benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-[(4-[[2-(methoxyethoxy)ethyl]thio]-3-nitrophenyl)sulfonyl]benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-[(4-(methylsulfonyl)phenyl)sulfonyl]benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-[(4-(methylsulfonyl)phenyl)sulfonyl]benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-{{4-[(2,2-dimethyltetrahydro-2H-pyran-4-yl)methoxy]-3-nitrophenyl}sulfonyl}-2-(1H-indol-5-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-{{5-cyano-6-[(4-fluorotetrahydro-2H-pyran-4-yl)methoxy]pyridin-3-yl}sulfonyl}-2-(1H-indol-5-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-{{5-cyano-6-(tetrahydro-2H-pyran-4-ylmethoxy)pyridin-3-yl}sulfonyl}-2-(1H-indol-4-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-{{5-chloro-6-(tetrahydro-2H-pyran-4-ylmethoxy)pyridin-3-yl}sulfonyl}-2-(1H-indol-4-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-{{5-cyano-6-(2-morpholin-4-ylethoxy)pyridin-3-yl}sulfonyl}-2-(1H-indol-5-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-{{3-nitro-4-[(1-tetrahydro-2H-pyran-4-yl)piperidin-4-yl]oxy}phenyl}sulfonyl}benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-{{4-[(4-morpholin-4-ylbut-2-ynyl)oxy]-3-nitrophenyl}sulfonyl}benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-{{5-ethynyl-6-(tetrahydro-2H-pyran-4-ylmethoxy)pyridin-3-yl}sulfonyl}-2-(1H-indol-4-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-{{5-cyano-6-(2-morpholin-4-ylethoxy)pyridin-3-yl}sulfonyl}-2-(1H-indol-4-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-{{5-cyano-6-[(4-fluorotetrahydro-2H-pyran-4-yl)methoxy]pyridin-3-yl}sulfonyl}-2-(1H-indol-4-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-{{4-[(3-hydroxy-4-methoxyphenyl)amino]-3-nitrophenyl}sulfonyl}-2-(1H-indol-5-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(2,3-dihydro-1H-indol-4-yloxy)-N-{{4-[(1-methylpiperidin-4-yl)amino]-3-nitrophenyl}sulfonyl}benzamide;
4-(4-{{2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl}methyl}piperazin-1-yl)-N-{{4-[(1-methylpiperidin-4-yl)amino]-3-nitrophenyl}sulfonyle}2-(pyridin-3-ylamino)benzamide;
4-(4-{{2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl}methyl}piperazin-1-yl)-N-{{3-nitro-4-[(1-tetrahydro-2H-pyran-4-yl)piperidin-4-yl]amino}phenyl}sulfonyle}2-(pyridin-3-ylamino)benzamide;
4-(4-{{2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl}methyl}piperazin-1-yl)-N-{{3-nitro-4-[(tetrahydro-2H-pyran-4-yl)methyl]amino}phenyl}sulfonyle}2-(1,2,3,4-tetrahydroisoquinolin-5-ylamino)benzamide;
4-(4-{{2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl}methyl}piperazin-1-yl)-2-(1H-indazol-4-ylamino)N-{{3-nitro-4-[(tetrahydro-2H-pyran-4-yl)methyl]amino}phenyl}sulfonyle}benzamide;
Trans-4-(4-{{2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl}methyl}piperazin-1-yl)-2-(1H-indazol-4-ylamino)N-{{4-[(4-morpholin-4-yl)cyclohexyl]amino}3-nitrophenyl}sulfonyle}benzamide;
2-(1H-benzimidazol-4-ylamino)4-(4-{{2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl}methyl}piperazin-1-yl)N-{{3-nitro-4-[(tetrahydro-2H-pyran-4-yl)methyl]amino}phenyl}sulfonyle}benzamide;
N-{{5-chloro-6-[(4-fluorotetrahydro-2H-pyran-4-yl)methoxy]pyridin-3-yl}sulfonyle}4-(4-{{2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl}methyl}piperazin-1-yl)-2-(1H-indazol-4-ylamino)benzamide;
N-{{5-chloro-6-[(4-fluorotetrahydro-2H-pyran-4-yl)methoxy]pyridin-3-yl}sulfonyle}4-(4-{{2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl}methyl}piperazin-1-yl)-2-(1H-indol-4-ylamino)benzamide;
4-(4-{{2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl}methyl}piperazin-1-yl)-N-{{5-cyano-6-[(4-fluorotetrahydro-2H-pyran-4-yl)methoxy]pyridin-3-yl}sulfonyle}2-(1H-indazol-4-ylamino)benzamide;
2-(1H-benzimidazol-4-yloxy)-4-4-
{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-
yl]methyl}piperazin-1-yl)-N-[(4-
{[(3R)-1-(2,2-difluoroethyl)pyrrolidin-3-yl]amino}-3-
nitrophenyl)sulfonyl]benzamide;
2-(1H-benzimidazol-4-yloxy)-4-4-
{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-
yl]methyl}piperazin-1-yl)-N-[(4-
{[4-fluorotetrahydro-2H-pyran-4-yl]methoxy}-3-
nitrophenyl)sulfonyl]benzamide;
4-4-
{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-
yl]methyl}piperazin-1-yl)-N-[(4-
{[4-fluorotetrahydro-2H-pyran-4-yl]methyl}amino}-3-nitrophenyl)sulfonyl]-2-(1H-indazol-
4-yloxy)benzamide;
4-4-
{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-
yl]methyl}piperazin-1-yl)-N-[(4-
{[(4-cyclopropylmorpholin-2-yl)methyl]amino}-3-nitrophenyl)sulfonyl]-2-(1H-indazol-
4-yloxy)benzamide;
4-4-
{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-
yl]methyl}piperazin-1-yl)-N-[(4-
{[(4,4-difluorocyclohexyl)methyl]amino}-3-nitrophenyl)sulfonyl]-2-(1H-indazol-4-
 yloxy)benzamide;
N-[(5-chloro-6-
{[4-fluorotetrahydro-2H-pyran-4-yl)methyl]amino}pyridin-3-yl)sulfonyl]-4-
(4-
{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-
yl]methyl}piperazin-1-yl)-2-(1H-
indazol-4-yloxy)benzamide;
Trans-N-((5-chloro-6-
{[4-methoxycyclohexyl]methoxy}pyridin-3-yl)sulfonyl)-4-4-
{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-
yl]methyl}piperazin-1-yl)-2-(1H-indazol-4-
yloxy)benzamide;
2-(1H-benzimidazol-4-yloxy)-4-4-
{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-
yl]methyl}piperazin-1-yl)-N-[(4-
{[(4,2-difluoroethyl)morpholin-2-yl]methyl}amino)-3-
nitrophenyl)sulfonyl]benzamide;
4-4-
{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-
yl]methyl}piperazin-1-yl)-N-[(5-
fluoro-6-
{[4-fluorotetrahydro-2H-pyran-4-yl)methoxy}pyridin-3-yl)sulfonyl]-2-(1H-indazol-
4-yloxy)benzamide;
2-(1H-benzimidazol-4-yloxy)-4-4-
{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-
yl]methyl}piperazin-1-yl)-N-[(3-nitro-4-
{[1-tetrahydro-2H-pyran-4-yl]pip eridin-4-
yl)amino]phenyl}sulfonyl]benzamide;
2-(1H-benzimidazol-4-yloxy)-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4-[(1-methylpiperidin-4-yl)amino]-3-nitrophenyl]sulfonyl]benzamide;
N-[[5-chloro-6-{{[1-(cyanomethyl)-4-fluoropiperidin-4-yl]methoxy}pyridin-3-yl}sulfonyl]4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indazol-4-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[5-chloro-6-(tetrahydrofuran-3-ylmethoxy)pyridin-3-yl]sulfonyl]-2-(1H-indazol-4-yloxy)benzamide;
Trans-N-{{5-chloro-6-[(4-hydroxycyclohexyl)methoxy]pyridin-3-yl}sulfonyl]4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indazol-4-yloxy)benzamide;
N-[[5-chloro-6-{{[(3R)-1-(2,2-difluoroethyl)pyrrolidin-3-yl]oxy}pyridin-3-yl}sulfonyl]4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indazol-4-yloxy)benzamide;
2-(1H-benzimidazol-4-yloxy)-N-{{5-chloro-6-[[{(2S)-4-(N,N-dimethylglycyl)morpholin-2-yl]methoxy}pyridin-3-yl}sulfonyl]4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)benzamide;
2-(1H-benzimidazol-4-yloxy)-N-{{5-chloro-6-{{[(2R)-4-(N,N-dimethylglycyl)morpholin-2-yl]methoxy}pyridin-3-yl}sulfonyl]4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indazol-4-yloxy)benzamide;
N-{{5-chloro-6-{{[(2S)-4-(N,N-dimethylglycyl)morpholin-2-yl]methoxy}pyridin-3-yl}sulfonyl]4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indazol-4-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-{{5-chloro-6-(tetrahydro-2H-pyran-4-ylmethoxy)pyridin-3-yl}sulfonyl]2-(1H-indazol-4-yloxy)benzamide;
2-(1H-benzimidazol-4-yloxy)-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-{{4-[(3R)-1-(cyanomethyl)pyrrolidin-3-yl]amino}-3-nitrophenyl}sulfonyl]benzamide;
2-(1H-benzimidazol-4-yloxy)-4-(4-[(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl)-N-[(4-((3R)-1-[2-(2-methoxyethoxy)ethyl]pyrrolidin-3-yl)amino)-3-nitrophenyl]sulfonyl]benzamide;
2-(1H-benzimidazol-4-yloxy)-4-(4-[(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl)-N-[(4-((3R)-1-(N,N-dimethylglycyl)pyrrolidin-3-yl)amino)-3-nitrophenyl]sulfonyl]benzamide;
2-(1H-benzimidazol-4-yloxy)-4-(4-[(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl)-N-[(4-[(4-(cyanomethyl)morpholin-2-yl)methyl]amino)-3-nitrophenyl]sulfonyl]benzamide;
2-(1H-benzimidazol-4-yloxy)-4-(4-[(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl)-N-[(4-[(4-cyclopropyl)morpholin-2-yl)methyl]amino]-3-nitrophenyl]sulfonyl]benzamide;
2-(1H-benzimidazol-4-yloxy)-4-(4-[(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl)-N-[(3-nitro-4-[[4-oxetan-3-ylmorpholin-2-yl)methyl]amino]phenyl)sulfonyl]benzamide;
N-[[5-chloro-6-((3R)-1-[2-fluoro-1-(fluoromethyl)ethyl]pyrrolidin-3-yl)oxy]pyridin-3-yl]sulfonyl]-4-(4-[(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl)-2-(1H-indazol-4-yloxy)benzamide;
4-(4-[(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl)-N-[(4-((3R)-1-[2-fluoro-1-(fluoromethyl)ethyl]pyrrolidin-3-yl)amino)-3-nitrophenyl]sulfonyl]-2-(1H-indazol-4-yloxy)benzamide;
4-(4-[(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl)-N-[(4-[(1-cyclopropyl)piperidin-4-yl)amino]-3-nitrophenyl]sulfonyl)-2-(1H-indazol-4-yloxy)benzamide;
2-(1H-benzimidazol-4-yloxy)-4-(4-[(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl)-N-[(4-((2R)-4-(N,N-dimethylglycyl)morpholin-2-yl)methyl]amino]-3-nitrophenyl]sulfonyl]benzamide;
2-(1H-benzimidazol-4-yloxy)-4-(4-[(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl)-N-[(4-((2S)-4-(N,N-dimethylglycyl)morpholin-2-yl)methyl]amino)-3-nitrophenyl]sulfonyl]benzamide;
2-(1H-benzimidazol-4-yloxy)-4-(4-[(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl)-N-(3-nitro-4-[(tetrahydrofuran-3-yl)methyl]amino]phenyl)sulfonyl]benzamide;
Trans-2-(1H-benzimidazol-4-yloxy)-4-(4-[(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl)-N-[(4-[(4-methoxy)cyclohexyl]methyl]amino]-3-nitrophenyl)sulfonyl]benzamide;

2-(1H-benzimidazol-4-yloxy)-4-(4-[(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl)-N-[(4-[(4-fluorotetrahydro-2H-pyran-4-yl)methyl]amino]-3-nitrophenyl)sulfonyl]benzamide;

2-(1H-benzimidazol-4-yloxy)-4-(4-[(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl)-N-[(5-fluoro-6-[(4-fluorotetrahydro-2H-pyran-4-yl)methoxy]pyridin-3-yl)sulfonyl]benzamide;

2-(1H-benzimidazol-4-yloxy)-N-[(5-chloro-6-[(4-fluorotetrahydro-2H-pyran-4-yl)methoxy]pyridin-3-yl)sulfonyl]-4-(4-[(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl)benzamide;

N-[(5-chloro-6-[(3R)-1-[2-fluoro-1-(fluoromethyl)ethyl]pyrrolidin-3-yl]methoxy]pyridin-3-yl)sulfonyl]-4-(4-[(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl)-2-(1H-indazol-4-yloxy)benzamide;

Trans-4-(4-[(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl)-2-(1H-indazol-4-yloxy)-N-[(4-[(4-methoxy)cyclohexyl]methyl]amino]-3-nitrophenyl)sulfonyl]benzamide;

4-(4-[(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl)-N-[(4-(1,4-dioxan-2-yl)methoxy)-3-nitrophenyl)sulfonyl]-2-(1H-indazol-4-yloxy)benzamide;

N-[(5-chloro-6-[(1-cyclopropyl)piperidin-4-yl]amino]pyridin-3-yl)sulfonyl]-4-(4-[(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl)-2-(1H-indazol-4-yloxy)benzamide;

2-(1H-benzimidazol-4-yloxy)-N-[(5-chloro-6-[(1-cyclopropyl)piperidin-4-yl]amino]pyridin-3-yl)sulfonyl]-4-(4-[(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl)benzamide;

2-(1H-benzimidazol-4-yloxy)-4-(4-[(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl)-N-[(4-[(1,4-dioxan-2-yl)methoxy]amino]-3-nitrophenyl)sulfonyl]benzamide;
2-(1H-benzimidazol-4-yloxy)-4-(4-\{2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl\}methyl)piperazin-1-yl)-N-(4-\{[1-cyclopropylpiperidin-4-yl]amino\}-3-nitrophenyl)sulfonyl)benzamide;

Trans-2-(1H-benzimidazol-4-yloxy)-4-(4-\{2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl\}methyl)piperazin-1-yl)-N-(4-\{[4-morpholin-4-ylcyclohexyl]amino\}-3-nitrophenyl)sulfonyl)benzamide;

2-(1H-benzimidazol-4-yloxy)-4-(4-\{2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl\}methyl)piperazin-1-yl)-N-(4-\{[4-methylpiperazin-1-yl]amino\}-3-nitrophenyl)sulfonyl)benzamide;

2-(1H-benzimidazol-4-yloxy)-4-(4-\{2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl\}methyl)piperazin-1-yl)-N-(4-\{[(1-methylpiperidin-4-yl)methyl]amino\}-3-nitrophenyl)sulfonyl)benzamide;

2-(1H-benzimidazol-4-yloxy)-4-(4-\{2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl\}methyl)piperazin-1-yl)-N-(4-\{[(4,4-difluorocyclohexyl)methyl]amino\}-3-nitrophenyl)sulfonyl)benzamide;

N-[(4-\{[(4-acetyl)morpholin-2-yl]methyl]amino\}-3-nitrophenyl)sulfonyl]-2-(1H-benzimidazol-4-yloxy)-4-(4-\{2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl\}methyl)piperazin-1-yl)benzamide;

2-(1H-benzimidazol-4-yloxy)-4-(4-\{2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl\}methyl)piperazin-1-yl)-N-(4-\{[(4-(methylsulfonyl)morpholin-2-yl)methyl]amino\}-3-nitrophenyl)sulfonyl)benzamide;

4-(4-\{2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl\}methyl)piperazin-1-yl)-N-\{6-\{4-fluoro-1-[2-fluoro-1-(fluoromethyl)ethyl]piperidin-4-yl\}-methoxy\}-5-(trifluoromethyl)pyridin-3-yl)sulfonyl)-2-(1H-indazol-4-yloxy)benzamide;

4-(4-\{2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl\}methyl)piperazin-1-yl)-N-(3-nitro-4-[tetrahydro-2H-pyran-4-ylmethyl]amino)[phenyl]sulfonyl)-2-phenoxybenzamide;

4-(4-\{2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl\}methyl)piperazin-1-yl)-N-[5-chloro-6-(2-tetrahydrofuran-2-ylethoxy)pyridin-3-yl]sulfonyl)-2-(1H-indazol-4-yloxy)benzamide;
Trans-2-(1H-benzimidazol-4-yloxy)-4-(4-{{2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl}methyl}piperazin-1-yl)-N-{{4-{{(4-cyanocyclohexyl)methyl}amino}-3-nitrophenyl}sulfonyle]benzamide;
2-(1H-benzimidazol-4-yloxy)-N-{{5-chloro-6-[(4,4-difluorocyclohexyl)methoxy]pyridin-3-yl}sulfonyle]4-(4-{{2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl}methyl}piperazin-1-yl)benzamide;
N-{{3-chloro-4-[(4-fluorotetrahydro-2H-pyran-4-yl)methoxy]phenyl}sulfonyle]4-(4-{{2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl}methyl}piperazin-1-yl)-2-(1H-indazol-4-yloxy)benzamide;
N-{{5-chloro-6-[(4-fluorotetrahydro-2H-pyran-4-yl)methoxy]pyridin-3-yl}sulfonyle]4-(4-{{4-(4-chlorophenyl)-6,6-dimethyl-5,6-dihydro-2H-pyran-3-yl}methyl}piperazin-1-yl)-2-(1H-indazol-4-yloxy)benzamide;
4-(4-{{2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl}methyl}piperazin-1-yl)-N-{{5-cyano-6-[(2-tetrahydro-2H-pyran-4-ylthoxy)pyridin-3-yl]sulfonyle]2-(1H-indazol-4-yloxy)benzamide;
4-(4-{{2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl}methyl}piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-{{4-{{[(1R,5S)-8-methyl-8-azabicyclo[3.2.1]oct-3-yl]amino}-3-nitrophenyl}sulfonyle]benzamide;
N-{{3-nitro-4-[(tetrahydro-2H-pyran-4-ylmethyl)amino]phenyl}sulfonyle]2-phenoxy-4-(4-{{(3-phenylpropanoyl)}[(1S,2S,3S,5R)-2,6,6-trimethylbicyclo[3.1.1]hept-3-yl]amino}piperidin-1-yl)benzamide;
N-{{4-{{3-morpholin-4-ylpropyl}amino}-3-nitrophenyl}sulfonyle]2-phenoxy-4-(4-{{3-phenylpropanoyl}{[(1S,2S,3S,5R)-2,6,6-trimethylbicyclo[3.1.1]hept-3-yl]amino}piperidin-1-yl)benzamide;
N-{{3-nitro-4-[(tetrahydro-2H-pyran-4-ylmethyl)amino]phenyl}sulfonyle]2-phenoxy-4-(4-{{3-phenylpropyl}{[(1S,2S,3S,5R)-2,6,6-trimethylbicyclo[3.1.1]hept-3-yl]amino}piperidin-1-yl)benzamide;
N-{{4-{{3-morpholin-4-ylpropyl}amino}-3-nitrophenyl}sulfonyle]2-phenoxy-4-(4-{{3-phenylpropyl}{[(1S,2S,3S,5R)-2,6,6-trimethylbicyclo[3.1.1]hept-3-yl]amino}piperidin-1-yl)benzamide;
4-(4-{{[(1R,5S)-8-methyl-8-azabicyclo[3.2.1]oct-3-yl]amino}benzyl}piperazin-1-yl)-N-{{4-{{3-morpholin-4-ylpropyl}amino}-3-nitrophenyl}sulfonyle]2-phenoxybenzamide;
4-(4-{{[(1R,5S)-8-methyl-8-azabicyclo[3.2.1]oct-3-yl]amino}benzyl}piperazin-1-yl)-N-{{3-nitro-4-[(tetrahydro-2H-pyran-4-ylmethyl)amino]phenyl}sulfonyle]2-phenoxybenzamide;
4-{4-[2-(3-azabicyclo[3.2.2]non-3-yl)benzyl]piperazin-1-yl}-N-(3-nitro-4-{[(tetrahydro-2H-pyran-4-ylmethyl)amino]phenyl}sulfonyl)-2-phenoxybenzamide;
4-{4-[2-(3-azabicyclo[3.2.2]non-3-yl)benzyl]piperazin-1-yl}-2-phenoxy-N-(4-[(tetrahydro-2H-pyran-4-ylmethyl)amino]-3-[(trifluoromethyl)sulfonyl]phenyl)sulfonyl)benzamide;
4-{4-[2-(3-azabicyclo[3.2.2]non-3-yl)benzyl]piperazin-1-yl}-2-phenoxy-N-(4-[(tetrahydro-2H-pyran-4-ylmethyl)amino]phenyl)sulfonyl)benzamide;
4-{4-[2-(3-azabicyclo[3.2.2]non-3-yl)benzyl]piperazin-1-yl}-N-(4-[3-morpholin-4-yl(propyl)amino]-3-nitrophenyl)sulfonyl)-2-phenoxybenzamide;
4-(4-2-[(4R,7S)-2,3,3a,4,7,7a-hexahydro-1H-4,7-methanoindene-5-yl]benzyl]piperazin-1-yl)-N-(3-nitro-4-{[(tetrahydro-2H-pyran-4-ylmethyl)amino]phenyl}sulfonyl)-2-phenoxybenzamide;
and therapeutically acceptable salts, prodrugs, salts of prodrugs and metabolites thereof.

In another aspect, the present invention provides compounds of Formula (II)
and therapeutically acceptable salts, prodrugs, salts of prodrugs and metabolites thereof, wherein $A^1, B^1, D^1, E^1, Y^1, R^{20},$ and $R^{37}$ are as described herein for Formula (I), $n$ is 0, 1, 2, or 3; describing the number of substituents on $R^{26}$, and $R^{100}$ is as described for substituents on $R^{26}$.

5 In one embodiment of Formula (II), $A^1$ is N. In another embodiment of Formula (II), $A^1$ is C($A^2$). In another embodiment of Formula (II), $A^1$ is C($A^2$), and $A^2$ is H.

In one embodiment of Formula (II), $B^1$ is $R^1, OR^1, SR^1, SO_2R^1, NHR^1, N(R^1)_2,$ or C(O)NHR$^1$. In another embodiment of Formula (II), $B^1$ is NHR$^1$. In another embodiment of Formula (II), $B^1$ is NHR$^1$, and $A^1$ is C($A^2$), and $A^2$ is H. In another embodiment of Formula (II), $B^1$ is OR$^1$. In another embodiment of Formula (II), $B^1$ is OR$^1$, and $A^1$ is C($A^2$), and $A^2$ is H.

In one embodiment of Formula (II), $D^1$ and $E^1$ are H. In another embodiment of Formula (II), $B^1$ is NHR$^1$, and $A^1$ is C($A^2$), $A^2$ is H, and $D^1$ and $E^1$ are H. In another embodiment of Formula (II), $B^1$ is OR$^1$, and $A^1$ is C($A^2$), $A^2$ is H, and $D^1$ and $E^1$ are H.

10 In one embodiment of Formula (II), $Y^1$ is H, CN, NO$_2$, F, Cl, Br, I, CF$_3$, R$^{17},$ NHC(O)R$^{17}$, or C(O)NH$_2$. In another embodiment of Formula (II), $Y^1$ is NO$_2$. In another embodiment of Formula (II), $B^1$ is NHR$^1$, and $A^1$ is C($A^2$), $A^2$ is H, D$^1$ and E$^1$ are H, and $Y^1$ is NO$_2$. In another embodiment of Formula (II), $Y^1$ is Cl. In another embodiment of Formula (II), $B^1$ is OR$^1$, and $A^1$ is C($A^2$), $A^2$ is H, D$^1$ and E$^1$ are H, and $Y^1$ is Cl.

15 In one embodiment of Formula (II), $R^1$ is $R^2, R^3, R^4$ or $R^5$. In another embodiment of Formula (II), $R^1$ is $R^2$, and $R^2$ is phenyl.

In one embodiment of Formula (II), $R^1$ is $R^2$, and $R^3$ is heteroaryl. In another embodiment of Formula (II), $R^3$ is triazolyl.

In one embodiment of Formula (II), $R^1$ is $R^2$. In another embodiment of Formula (II), $R^1$ is $R^4$, and $R^4$ is cycloalkyl. In another embodiment of Formula (II), $R^1$ is $R^4$, and $R^4$ is cyclohexyl. In another embodiment of Formula (II), $R^1$ is $R^4$, and $R^4$ is heterocycloalkyl. In another embodiment of Formula (II), $R^1$ is $R^4$, and $R^4$ is 8-azabicyclo[3.2.1]octane, azetidinyl, piperidinyl, piperazinyl, pyrrolidinyl, morpholinyl, tetrahydropryranyl, or tetrahydrothiophenyl. In another embodiment of Formula (II), $R^1$ is $R^4$, and $R^4$ is heterocycloalkenyl. In another embodiment of Formula (II), $R^1$ is $R^4$, and $R^4$ is tetrahydropryridazinyl.
In one embodiment of Formula (II), $R^1$ is $R^5$. In another embodiment of Formula (II), $R^1$ is $R^5$ and $R^5$ is alkyl or alkenyl. In another embodiment of Formula (II), $R^1$ is $R^5$ and $R^5$ is alkyl which is unsubstituted. In another embodiment of Formula (II), $R^1$ is $R^5$ and $R^5$ is alkyl which is substituted with one or two or three independently selected $R^6$, $R^7$, $OR^7$, $SR^7$, $SO_2R^7$, $N(R^7)_2$, OH, CN, CF$_3$, F, Cl, Br or I substituents. In another embodiment of Formula (II), $R^1$ is $R^5$ and $R^5$ is alkyl which is substituted with $R^7$.

In one embodiment of Formula (II), $R^7$ is $R^8$, $R^9$, $R^{10}$ or $R^{11}$. In another embodiment of Formula (II), $R^7$ is $R^8$, and $R^8$ is phenyl which is unfused or fused with $R^{8A}$, and $R^{8A}$ is heterocycloalkane. In another embodiment of Formula (II), $R^7$ is $R^8$, and $R^8$ is phenyl which is unfused. In another embodiment of Formula (II), $R^7$ is $R^9$, and $R^9$ is heteroaryl. In another embodiment of Formula (II), $R^7$ is $R^9$, and $R^9$ is furanyl, imidazolyl, isothiazolyl, isoxazolyl, 1,2,3-oxadiazolyl, 1,2,5-oxadiazolyl, oxazolyl, pyrazinyl, pyrazolyl, pyridazinyl, pyridinyl, pyrimidinyl, pyrrolyl, tetrazolyl, thiazolyl, thiophenyl, triazinyl or 1,2,3-triazolyl. In another embodiment of Formula (II), $R^7$ is $R^9$, and $R^9$ is pyridinyl, thiazolyl, imidazolyl, and 1,2,3-triazolyl. In another embodiment of Formula (II), $R^7$ is $R^{10}$, and $R^{10}$ is C$_3$-C$_{10}$-cycloalkyl. In another embodiment of Formula (II), $R^7$ is $R^{10}$, and $R^{10}$ is C$_6$ or C$_{10}$-cycloalkyl. In another embodiment of Formula (II), $R^7$ is $R^{10}$, and $R^{10}$ is cyclohexyl or adamantanyl. In another embodiment of Formula (II), $R^7$ is $R^{10}$, and $R^{10}$ is morpholinyl, piperazinyl, piperidinyl, tetrahydro-2H-pyranyl, 1,2-dihydropyridinyl, pyranyl, pyridin-1(H)-yl, pyrrolidinyl, oxetanyl, thiomorpholinyl, imidazolidinyl, tetrahydrothiophenyl, dioxolanyl, tetrahydrothiopyranyl, dioxanyl, or tetrahydrofuranyl. In another embodiment of Formula (II), $R^7$ is $R^{10}$, and $R^{10}$ is morpholinyl, piperazinyl, piperidinyl, tetrahydro-2H-pyranyl, 1,2-dihydropyridinyl, pyrrolidinyl, oxetanyl, thiomorpholinyl, imidazolidinyl, tetrahydrothiophenyl, dioxolanyl, tetrahydrothiopyranyl, dioxanyl, or tetrahydrofuranyl. In another embodiment of Formula (II), $R^7$ is $R^{11}$, and $R^{11}$ is alkyl which is unsubstituted or substituted. In another embodiment of Formula (II), $R^7$ is $R^{11}$, and $R^{11}$ is alkyl which is unsubstituted. In another embodiment of Formula (II), $R^7$ is $R^{11}$, and $R^{11}$ is alkyl which is substituted. In another embodiment of Formula (II), $R^7$ is $R^{11}$, and $R^{11}$ is alkyl which is substituted with one or two or three independently selected OR$^{12}$, F, Cl, Br or I substituents.

In another embodiment of Formula (II), $R^7$ is $R^{11}$, $R^{11}$ is alkyl which is substituted with OR$^{12}$, $R^{12}$ is $R^{16}$, and $R^{16}$ is alkyl.
In one embodiment of Formula (II), \( R^{17} \) is \( R^{19} \) or \( R^{21} \). In another embodiment of Formula (II), \( R^{17} \) is \( R^{19} \), and \( R^{19} \) is heteroaryl. In another embodiment of Formula (II), \( R^{17} \) is \( R^{19} \), and \( R^{19} \) is thiazoyl. In another embodiment of Formula (II), \( R^{17} \) is \( R^{21} \), and \( R^{21} \) is alkylnyl. In another embodiment of Formula (II), \( R^{17} \) is \( R^{21} \), and \( R^{21} \) is ethynyl.

Still another embodiment pertains to compounds having Formula II which are

\[
4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-N-((4-((1-cyclopentyl)piperidin-4-yl)amino)-3-nitrophenyl)sulfonyl)-2-(1H-indol-5-yloxy)benzamide
\]

\[
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-yl)methyl)amino)phenyl)sulfonyl)benzamide;
\]

\[
4-(4-(3-(dimethylamino)propyl)amino)-3-nitrophenyl)sulfonyl)-2-(1H-indol-5-yloxy)benzamide;
\]

\[
4-(4-((2-(4-chlorophenyl)-5,5-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((4-((3-morpholin-4-yl)propyl)amino)-3-nitrophenyl)sulfonyl)benzamide;
\]

\[
4-(4-((2-(4-chlorophenyl)-5,5-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-N-((4-(3-(dimethylamino)propyl)amino)-3-nitrophenyl)sulfonyl)-2-(1H-indol-5-yloxy)benzamide;
\]

\[
4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((4-((3-morpholin-4-yl)propyl)amino)-3-nitrophenyl)sulfonyl)benzamide;
\]

\[
4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-N-((4-((3-(dimethylamino)propyl)amino)-3-nitrophenyl)sulfonyl)-2-(1H-indol-5-yloxy)benzamide;
\]

\[
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((4-((3-morpholin-4-yl)propyl)amino)-3-nitrophenyl)sulfonyl)benzamide;
\]

\[
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((4-((3-morpholin-4-yl)propyl)amino)-3-nitrophenyl)sulfonyl)benzamide;
\]

\[
4-(4-((3-(dimethylamino)propyl)amino)-3-nitrophenyl)sulfonyl)phenyl)sulfonyl)benzamide;
\]

\[
4-(4-((3-(dimethylamino)propyl)amino)-3-((trifluoromethyl)sulfonyl)phenyl)sulfonyl)benzamide;
\]

\[
N-((3-(chloro(difluoro)methyl)sulfonyl)-4-((3-(dimethylamino)propyl)amino)phenyl)sulfonyl)-2-(1H-indol-5-yloxy)benzamide;
\]

\[
N-((3-(chloro(difluoro)methyl)sulfonyl)-4-((1-methyl)piperidin-4-yl)amino)phenyl)sulfonyl)-4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)benzamide;
\]

\[
N-((3-(chloro(difluoro)methyl)sulfonyl)-4-((1-methyl)piperidin-4-yl)amino)phenyl)sulfonyl)-4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)benzamide;
\]
4-(4-((2-(4-chlorophenyl)cyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((4-((1-methylpiperidin-4-yl)amino)-3-nitrophenyl)sulfonyl)benzamide;  
4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((4-((1-methylpiperidin-4-yl)amino)-3-(trifluoromethyl)sulfonyl)phenyl)sulfonyl)benzamide;  
4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((4-((2-(4-methylpiperazin-1-yl)ethyl)amino)-3-nitrophenyl)sulfonyl)benzamide;  
4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((4-((3-(4-methylpiperazin-1-yl)propyl)amino)-3-nitrophenyl)sulfonyl)benzamide;  
4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((3-nitro-4-((3-pyrrrolidin-1-yl)propyl)amino)phenyl)sulfonyl)benzamide  
4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((4-(1-methylpiperidin-4-yl)amino)-3-nitrophenyl)sulfonyl)benzamide;  
4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((4-(3-(dimethylamino)propoxy)-3-nitrophenyl)sulfonyl)-2-(1H-indol-5-yloxy)benzamide;  
4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((4-((1-methylpiperidin-4-yl) methyl)amino)-3-nitrophenyl)sulfonyl)benzamide;  
4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((4-(3-(dimethylamino)-1-methylpiperidin-4-yl) methyl)amino)-3-nitrophenyl)sulfonyl)-2-(1H-indol-5-yloxy)benzamide;  
4-(4-((4′-chboro-4-((2-(dimethylamino)ethoxy)-1,1′-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-yl)methyl)amino)phenyl)sulfonyl)benzamide;  
4-(4-((4′-chboro-4-((2-morpholin-4-yloxy)-1,1′-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-yl)methyl)amino)phenyl)sulfonyl)benzamide;  
4-(4-((4′-chboro-3-((2-(dimethylamino)ethoxy)-1,1′-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-yl)methyl)amino)phenyl)sulfonyl)benzamide;
4-((4'-chloro-3-(2-morpholin-4-yloxy)-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-yl)methyl)amino)phenyl)sulfonyl)benzamide;
4-((4'-chloro-3-(2-(dimethylamino)ethoxy)-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((3-nitro-4-((3-pyrrolidin-1-ylpropyl)amino)phenyl)sulfonyl)benzamide;
4-((4'-chloro-4-(2-(dimethylamino)ethoxy)-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((3-nitro-4-((3-pyrrolidin-1-ylpropyl)amino)phenyl)sulfonyl)benzamide;
4-((4'-chloro-4-(2-morpholin-4-yloxy)-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((3-nitro-4-((3-pyrrolidin-1-ylpropyl)amino)phenyl)sulfonyl)benzamide;
4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(2,3-dihydro-1H-indol-5-yloxy)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-yl)methyl)amino)phenyl)sulfonyl)benzamide;
4-((4-(4-chlorophenyl)-6,6-dimethyl-5,6-dihydro-2H-pyran-3-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((4-((1-methylpiperidin-4-yl)amino)-3-nitrophenyl)sulfonyl)benzamide;
4-((4-(2-(4-chlorophenyl)cyclohept-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((4-((1-methylpiperidin-4-yl)amino)-3-nitrophenyl)sulfonyl)benzamide;
4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-N-((4-((3-dimethylamino)propyl)amino)-3-((trifluoromethyl)sulfonyl)phenyl)sulfonyl)-2-(1H-indol-5-yloxy)benzamide;
4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-N-((4-((3-dimethylamino)propyl)amino)-3-((trifluoromethyl)phenyl)sulfonyl)-2-(1H-indol-5-yloxy)benzamide;
4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-N-((3-cyano-4-((3-dimethylamino)propyl)amino)phenyl)sulfonyl)-2-(1H-indol-5-yloxy)benzamide;
4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((3-nitro-4-((1-tetrahydro-2H-pyran-4-yl)piperidin-4-yl)amino)phenyl)sulfonyl)benzamide;
4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((4-((4-methylpiperazin-1-yl)amino)-3-nitrophenyl)sulfonyl)benzamide;

Trans-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-[[4-[[4-morpholin-4-ylcyclohexyl]amino]-3-nitrophenyl]sulfonyl]benzamide;


4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4-[(4-hydroxy-1-methylpiperidin-4-yl)methyl]amino]-3-nitrophenyl]sulfonyl]-2-(1H-indol-5-yloxy)benzamide;

4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-3-fluoro-2-(1H-indol-5-yloxy)-N-[[4-[(1-methylpiperidin-4-yl)amino]-3-nitrophenyl]sulfonyl]benzamide;


N-[[4-[[3S,4R]-1-benzyl-3-hydroxypiperidin-4-yl]amino]-3-nitrophenyl]sulfonyl]-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)benzamide;

N-[[4-[[4-aminotetrahydro-2H-pyran-4-yl)methyl]amino]-3-nitrophenyl]sulfonyl]-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-
indol-5-yloxy)-N-[[4-[(1-(2-methoxyethyl)piperidin-4-yl)amino]-3-
nitropheryl)sulfonyl]benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-5-fluoro-
2-(1H-indol-5-yloxy)-N-((4-[(1-methylpiperidin-4-yl)amino]-3-
nitropheryl)sulfonyl)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-5-fluoro-
2-(1H-indol-5-yloxy)-N-((3-nitro-4-[(1-tetrahydro-2H-pyran-4-yl)piperidin-4-
yl]amino)[phenyl]sulfonyl)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4-
[(1-(3-hydroxypropyl)piperidin-4-yl)amino]-3-nitropheryl)sulfonyl]-2-(1H-indol-5-
yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4-
[(4-(diethylamino)cyclohexyl)amino]-3-nitropheryl)sulfonyl]-2-(1H-indol-5-
yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4-
[(4-(dimethylamino)tetrahydro-2H-pyran-4-yl)methyl]amino]-3-nitropheryl)sulfonyl]-
2-(1H-indol-5-yloxy)benzamide;
N-((4-[2-amino)cyclohexyl)amino]-3-nitropheryl)sulfonyl)-4-(4-[[2-(4-chlorophenyl)-4,4-
dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4-
[(2-(4-hydroxy-1-methyl)piperidin-4-yl)ethyl]amino]-3-nitropheryl)sulfonyl]-2-(1H-indol-5-
yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-
indol-5-yloxy)-N-((3-nitro-4-[[1-(1,3-thiazol-2-yl)piperidin-4-
yl]amino]phenyl)sulfonyl]benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4-
[(1-cyclopropyl)methyl)piperidin-4-yl]amino]-3-nitropheryl)sulfonyl]-2-(1H-indol-5-
yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-
indol-5-yloxy)-N-((3-nitro-4-[[1-(4,4-trifluorobutyl)piperidin-4-
yl]amino]phenyl)sulfonyl]benzamide;
4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]-3-(hydroxymethyl)piperazin-1-yl]-2-(1H-indol-5-yl)oxy)-N-([4-[(1-methylpiperidin-4-yl)amino]-3-nitrophenyl]sulfonfonyl)benzamide;
4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]-3-(hydroxymethyl)piperazin-1-yl]-2-(1H-indol-5-yl)oxy)-N-([3-nitro-4-[(1-tetrahydro-2H-pyran-4-yl)piperidin-4-yl]amino]phenyl)sulfonfonyl)benzamide;
4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl]-2-(1H-indol-5-yl)oxy)-N-([4-[(4-methylpiperazin-1-yl)amino]-3-(trifluoromethyl)sulfonfonyl]phenyl)sulfonfonyl)benzamide;
4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl]-2-(1H-indol-5-yl)oxy)-N-([3-nitro-4-[(3-oxopiperazin-1-yl)propyl]amino]phenyl)sulfonfonyl)benzamide;
4-[[2-(4-chlorophenyl)-5-hydroxycyclohex-1-en-1-yl]methyl]piperazin-1-yl]-2-(1H-indol-5-yl)oxy)-N-([4-[(1-methylpiperidin-4-yl)amino]-3-nitrophenyl]sulfonfonyl)benzamide;
4-[[2-(4-chlorophenyl)-5-hydroxycyclohex-1-en-1-yl]methyl]piperazin-1-yl]-2-(1H-indol-5-yl)oxy)-N-([3-nitro-4-[(1-tetrahydro-2H-pyran-4-yl)piperidin-4-yl]amino]phenyl)sulfonfonyl)benzamide;
4-[[2-(4-chlorophenyl)-5-hydroxycyclohex-1-en-1-yl]methyl]piperazin-1-yl]-2-(1H-indol-5-yl)oxy)-N-([4-[(4-methylpiperazin-1-yl)amino]-3-nitrophenyl]sulfonfonyl)benzamide;
4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl]-N-([4-[(1,2,3-dihydro-1H-inden-2-yl)piperidin-4-yl]amino]-3-nitrophenyl)sulfonfonyl)-2-(1H-indol-5-yl)oxy)-N-([4-[(1-morpholin-4-ylyclohexyl)methyl]amino]-3-nitrophenyl)sulfonfonyl)benzamide;
4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl]-N-([3-nitro-4-[[1-(1,3-thiazol-2-yl)methyl]piperidin-4-yl]amino]phenyl)sulfonfonyl)benzamide;
4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl]-N-([3-nitro-4-[[1-(1,3-thiazol-4-yl)methyl]piperidin-4-yl]amino]phenyl)sulfonfonyl)benzamide;
4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl]-N-([4-[[4-(hydroxymethyl)tetrahydro-2H-pyran-4-yl]methyl]amino]-3-nitrophenyl)sulfonfonyl)-2-(1H-indol-5-yl)oxy)benzamide;

4-(4-[(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl)-N-{(4-
[4-(2-hydroxyethyl)piperazin-1-yl]amino}-3-nitrophenyl)sulfonyl]-2-(1H-indol-5-
yloxy)benzamide;
4-(4-[(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl)-2-(1H-
indol-5-yloxy)-N-{[(3S)-1-methylpyrrolidin-3-yl]amino}-3-
nitrophenyl)sulfonyl]benzamide;
4-(4-[(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl)-N-{(4-
[1-(3-fluoropropyl)piperidin-4-yl]amino}-3-nitrophenyl)sulfonyl]-2-(1H-indol-5-
yloxy)benzamide;
4-[4-[(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]-3-(hydroxymethyl)piperazin-1-
yl]-2-(1H-indol-5-yloxy)-N-{(3-nitro-4-[(tetrahydro-2H-pyran-
4-ylmethyl]amino}phenyl]sulfonyl]benzamide;
N-{[(4-aminotetrahydro-2H-pyran-4-yl)methyl]amino}-3-nitrophenyl)sulfonyl]-4-[4-[(2-
(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]-3-(hydroxymethyl)piperazin-1-
yl]-2-(1H-indol-5-yloxy)benzamide;
4-(4-[(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl)-N-{(4-
[(1-hydroxycyclohexyl)methyl]amino}-3-nitrophenyl)sulfonyl]-2-(1H-indol-5-
yloxy)benzamide;
4-(4-[(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl)-N-{(4-
[(4-hydroxymethyl]tetrahydro-2H-pyran-4-yl]amino}-3-nitrophenyl)sulfonyl]-2-(1H-indol-
5-yloxy)benzamide;
4-(4-[(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl)-N-{(4-
[2-hydroxy-1-tetrahydro-2H-pyran-4-ylethyl]amino}-3-nitrophenyl)sulfonyl]-2-(1H-indol-5-
yloxy)benzamide;
4-(4-[(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl)-2-(1H-
indol-5-yloxy)-N-{[3-nitro-4-[(1-[2-(1H-pyrazol-1-yl)ethyl]piperidin-4-
yl]amino}phenyl]sulfonyl]benzamide;
4-(4-[(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl)-2-(1H-
indol-5-yloxy)-N-{[(methylamino)-3-nitrophenyl]sulfonyl]benzamide;
4-(4-[(2-(4-chlorophenyl)-5-hydroxycyclohex-1-en-1-yl)methyl]piperazin-1-yl)-2-(1H-indol-
5-yloxy)-N-{(3-nitro-4-[(tetrahydro-2H-pyran-4-
ylmethyl]amino}phenyl]sulfonyl]benzamide;
N-[[4-[[1-aminocyclohexyl]methyl]amino]-3-nitrophenyl]sulfonyle-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-[[3-nitro-4-[(2-oxopyrrolidin-1-yl)ethyl]amino]phenyl]sulfonylebenzamide;
4-[[1-(4'-chloro-1,1'-biphenyl-2-yl)ethyl]piperazin-1-yl]-2-(1H-indol-5-yloxy)-N-[[3-nitro-4-[(tetrahydro-2H-pyran-4-yl)methyl]amino]phenyl]sulfonylebenzamide;
4-(4-[[1-2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]ethyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-[[4-[[4-methyl]piperazin-1-yl]amino]-3-nitrophenyl]sulfonylebenzamide;
4-(4-[[1-2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]ethyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-[[4-[[3-morpholin-4-yl]propyl]amino]-3-nitrophenyl]sulfonylebenzamide;
4-(4-[[1-2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]ethyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-[[3-nitro-4-[(1-tetrahydro-2H-pyran-4-ylpiperidin-4-yl)amino]phenyl]sulfonylebenzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4-[[cyclohexyl]methyl]amino]-3-nitrophenyl]sulfonylebenzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-[[4-[(morpholin-4-ylamino)]-3-nitrophenyl]sulfonylebenzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-[[3-nitro-4-[(tetrahydro-2H-pyran-4-ylamino)]phenyl]sulfonylebenzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-[[4-[(3-methyloxetan-3-yl)methyl]amino]-3-nitrophenyl]sulfonylebenzamide;

4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-[[4-[(1-methyl-5-oxopyrrolidin-3-yl)amino]-3-nitrophenyl]sulfonyl]benzamide;

4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-[[4-[(1-methyl-6-oxopiperidin-3-yl)amino]-3-nitrophenyl]sulfonyl]benzamide;

4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-[[3-nitro-4-(piperidin-1-ylamino)phenyl]sulfonyl]benzamide;


4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-[[4-(1,4-dioxan-2-ylmethoxy)-3-nitrophenyl]sulfonyl]benzamide;

4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((3-nitro-4-[[2-(trifluoromethoxy)ethyl]amino]phenyl)sulfonyl)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-((4-[[2,2-difluoroethyl]amino]-3-nitrophenoxy)sulfonyl)-2-(1H-indol-5-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((4-((tetrahydro-2H-pyran-4-ylmethyl)amino)-3-(trifluoromethyl)sulfonyl)phenyl)sulfonyl)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((4-[[4,4-difluorocyclohexyl]amino]-3-nitrophenoxy)sulfonyl)-2-(1H-indol-5-yloxy)benzamide;
4-(4-[[4-(4-chlorophenyl)-1-isopropyl-6-oxo-1,6-dihydropyridin-3-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)-3-(trifluoromethyl)sulfonyl)phenyl)sulfonyl)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((4-((tetrahydro-2H-pyran-4-ylmethyl)amino)carbonyl)phenyl)sulfonyl)sulfonyl)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-((4-[[4-hydroxycyclohexyl]methyl]amino)-3-nitrophenoxy)sulfonyl)-2-(1H-indol-5-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((4-[[4-methoxycyclohexyl]methyl]amino)-3-nitrophenoxy)sulfonyl)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-((4-[[4-hydroxycyclohexyl]methyl]amino)-3-nitrophenoxy)sulfonyl)-2-(1H-indol-5-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((4-[[4-methoxycyclohexyl]methyl]amino)-3-nitrophenoxy)sulfonyl)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((4-[[2-methoxyethyl]amino]-3-nitrophenoxy)sulfonyl)phenyl)sulfonyl)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((4-[[3-methoxypropyl]amino]-3-nitrophenoxy)sulfonyl)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-((4-[[2-cyanoethyl]amino]-3-nitrophenoxy)sulfonyl)-2-(1H-indol-5-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[(3R)-4-hydroxy-1-adamantyl[methyl]amino]-3-nitrophenyl)sulfonfonyl]-2-(1H-indol-5-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[(3R)-4-hydroxy-1-adamantyl[methyl]amino]-3-nitrophenyl)sulfonfonyl]-2-(1H-indol-5-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-(3-nitro-4-[[3,3,3-trifluoropropyl]amino][phenyl]sulfonfonyl)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-(4-fluorotetrahydro-2H-pyran-4-ylmethoxy)-3-nitrophenyl)sulfonfonyl]-2-(1H-indol-5-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-(4-(methylamino)-3-[(trifluoromethyl)sulfonfonyl][phenyl]sulfonfonyl)benzamide;
N-(5-bromo-6-(tetrahydro-2H-pyran-4-ylmethoxy)pyridin-3-yl)sulfonfonyl]-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-[[6-(tetrahydro-2H-pyran-4-ylmethoxy)-5-(1,3-thiazol-2-yl)]pyridin-3-yl]sulfonfonyl)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-[[2-methoxyethyl]amino][carbonyl][phenyl]sulfonfonyl)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-(5-cyano-6-(tetrahydro-2H-pyran-4-ylmethoxy)pyridin-3-yl)sulfonfonyl]-2-(1H-indol-5-yloxy)benzamide;
N-(4-[[1-acetyl]pyridin-4-yl]amino)-3-nitrophenyl)sulfonfonyl]-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-[[4-[1-(methylsulfonyl)pyridin-4-yl]amino]-3-nitrophenyl)sulfonfonyl)]benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4-[[1,4-dioxan-2-ylmethyl]amino]-3-nitrophenyl]sulfonfonyl]-2-(1H-indol-5-yloxy)benzamide;
4-(4-[[4’-chloro-5-(trifluoromethyl)-1,1’-biphenyl-2-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-(3-nitro-4-((tetrahydro-2H-pyran-4-y1methoxy)phenyl)sulfonyl)benzamide;
4-{4-[[tert-butyl-4’-chboro-1,1’-biphenyl-2-yl]methyl]piperazin-1-yl}-2-(1H-indol-5-yloxy)-N-(3-nitro-4-[(tetrahydro-2H-pyran-4-y1methoxy)amino][phenyl]sulfonyl)benzamide;
4-{4-[[tert-butyl-4’-chboro-1,1’-biphenyl-2-yl]methyl]piperazin-1-yl}-2-(1H-indol-5-yloxy)-N-(3-nitro-4-((tetrahydro-2H-pyran-4-y1methoxy)phenyl)sulfonyl)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-(3-nitro-4-[(2,2,2-trifluoroethyl)amino][phenyl]sulfonyl)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-(3-[[tetrahydro-2H-pyran-4-y1methyl]amino][carbonyl][phenyl]sulfonyl)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-(4-[[2R]-1,4-dioxan-2-y1methoxy]-3-nitrophenyl)sulfonyl)-2-(1H-indol-5-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-(4-[[2S]-1,4-dioxan-2-y1methoxy]-3-nitrophenyl)sulfonyl)-2-(1H-indol-5-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-(4-[[3-morpholin-4-y1propyl]amino]-3-[[trifluoromethyl]sulfonyl][phenyl]sulfonyl)benzamide;
N-(5-bromo-6-[(tetrahydro-2H-pyran-4-y1methoxy)amino][pyridin-3-yl]sulfonyl)-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-(4-[[2-morpholin-4-y1ethyl]amino]-3-[[trifluoromethyl]sulfonyl][phenyl]sulfonyl)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-(5-cyano-6-[(tetrahydro-2H-pyran-4-y1methoxy)amino][pyridin-3-yl]sulfonyl)-2-(1H-indol-5-yloxy)benzamide;
benzyl 4-({4-(1H-indol-5-yloxy)benzoyl}1-amino)benzamide; N-3-(aminocarbonyl)-4-(tetrahydro-2H-pyran-4-ylmethoxy)phenyl)sulfonyl}-4-(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)benzamide;
4-(4-{{4'-chloro-5-(trifluoromethyl)-1,1'-biphenyl}-2-yl}methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-3-nitro-4-(1-tetrahydro-2H-pyran-4-ylpiperidin-4-yl)amino]phenyl]sulfonyl]benzamide;
4-(4-{{5-tert-butyl-4'-chloro-1,1'-biphenyl}-2-yl}methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-3-nitro-4-(1-tetrahydro-2H-pyran-4-ylpiperidin-4-yl)amino]phenyl]sulfonyl]benzamide;
4-(4-{{2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl}methyl}piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-4-(1,1-dioxidospiromorpholin-4-yl)amino]-3-nitrophenyl]sulfonyl]benzamide;
4-(4-{{2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl}methyl}piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-4-(4-morpholin-4-ylsulfonyl)phenyl]sulfonyl]benzamide;
4-(4-{{2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl}methyl}piperazin-1-yl)-N-3-cyano-4-(tetrahydro-2H-pyran-4-ylmethyl)amino]phenyl]sulfonyl]-2-(1H-indol-5-yloxy)benzamide;
4-(4-{{2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl}methyl}piperazin-1-yl)-N-3-(3,3-dimethylbutyl)amino]-3-nitrophenyl]sulfonyl]benzamide;
4-(4-{{2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl}methyl}piperazin-1-yl)-N-1-(hydroxymethyl)-3-methylbutyl]amino]-3-nitrophenyl)sulfonyl]-2-(1H-indol-5-yloxy)benzamide;
4-(4-{{2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl}methyl}piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-3-nitro-4-(1[(2R)-tetrahydrofuran-2-ylmethyl]amino]phenyl]sulfonyl]benzamide;
4-(4-{{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl}-N-[[4-[(1R)-1-(hydroxymethyl)-2-methylpropyl]amino]-3-nitrophenyl]sulfonyl]-2-(1H-indol-5-yloxy)benzamide;

4-(4-{{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl}-2-(1H-indol-5-yloxy)-N-{{4-[(4-methoxyphenyl)amino]-3-nitrophenyl}sulfonyl}benzamide;

N-{{4-{{[2-(1,3-benzodioxol-5-yl)ethyl]amino}-3-nitrophenyl}sulfonyl}-4-(4-{{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl}-2-(1H-indol-5-yloxy)benzamide;

4-(4-{{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl}-2-(1H-indol-5-yloxy)-N-{{3-nitro-4-[[3-(2-oxoypyrrolidin-1-yl)propyl]amino]phenyl}sulfonyl}benzamide;

4-(4-{{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl}-N-{{4-[(4-hydroxyphenyl)amino]-3-nitrophenyl}sulfonyl}-2-(1H-indol-5-yloxy)benzamide;

N-{{4-{{[2-[(4-aminosulfonyl)phenyl]ethyl]amino}-3-nitrophenyl}sulfonyl}-4-(4-{{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl}-2-(1H-indol-5-yloxy)benzamide;

4-(4-{{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl}-N-{{4-{{[3-(1H-imidazol-1-yl)propyl]amino}-3-nitrophenyl}sulfonyl}-2-(1H-indol-5-yloxy)benzamide;

4-(4-{{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl}-2-(1H-indol-5-yloxy)-N-{{3-nitro-4-[[1S]-1-phenylethyl]amino]phenyl}sulfonyl}benzamide;

N-{{2-chloro-5-fluoro-4-[(tetrahydro-2H-pyran-4-ylmethyl)amino]phenyl}sulfonyl}-4-(4-{{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl}-2-(1H-indol-5-yloxy)benzamide;

4-(4-{{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl}-2-(1H-indol-5-yloxy)-N-{{4-[(2-methoxyethoxy)ethyl]thio}-3-nitrophenyl}sulfonyl}benzamide;

4-(4-{{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl}-2-(1H-indol-5-yloxy)-N-{{4-(methylsulfonyl)phenyl}sulfonyl}benzamide;

4-(4-{{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl}-N-{{4-[(2,2-dimethyltetrahydro-2H-pyran-4-yl)methoxy]-3-nitrophenyl}sulfonyl}-2-(1H-indol-5-yloxy)benzamide;

4-(4-{{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl}-N-{{5-cyano-6-[(4-fluorotetrahydro-2H-pyran-4-yl)methoxy]pyridin-3-yl}sulfonyl}-2-(1H-indol-5-yloxy)benzamide;
4-(4-[(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl)-N-[[5-cyano-6-(2-morpholin-4-yloxy)pyridin-3-yl]sulfonyl]-2-(1H-indol-5-yloxy)benzamide; 4-(4-[(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-[[3-nitro-4-[(1-tetrahydro-2H-pyran-4-ylpiperidin-4-yl)oxy]phenyl]sulfonyl]benzamide; 4-(4-[(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-[[4-[(4-morpholin-4-ylbut-2-ynyl)oxy]-3-nitrophenyl]sulfonyl]benzamide; 4-(4-[(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl)-N-[[4-[(3-hydroxy-4-methoxyphenyl)amino]-3-nitrophenyl]sulfonyl]-2-(1H-indol-5-yloxy)benzamide; 4-(4-[(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-[[4-[[1R,5S]-8-methyl-8-azabicyclo[3.2.1]oct-3-yl]amino]-3-nitrophenyl]sulfonyl]benzamide; and therapeutically acceptable salts, prodrugs, salts of prodrugs and metabolites thereof.

In another aspect, the present invention provides compounds of Formula (III)

![Formula (III)](image_url)

and therapeutically acceptable salts, prodrugs, salts of prodrugs and metabolites thereof, wherein A^1, B^1, D^1, E^1, Y^1, R^30, and R^37 are as described herein for Formula (I), n is 0, 1, 2, or 3; describing the number of substituents on R^26, and R^100 is as described for substituents on R^26.

In one embodiment of Formula (III), A^1 is N. In another embodiment of Formula (III), A^1 is C(A^2). In another embodiment of Formula (III), A^1 is C(A^2), and A^2 is H.
In one embodiment of Formula (III), B\(^1\) is R\(^1\), OR\(^1\), SR\(^1\), SO\(_2\)R\(^1\), NHR\(^1\), N(R\(^1\))\(_2\), or C(O)NHR\(^1\). In another embodiment of Formula (III), B\(^1\) is NHR\(^1\). In another embodiment of Formula (III), B\(^1\) is NHR\(^1\), and A\(^1\) is C(A\(^2\)), and A\(^2\) is H. In another embodiment of Formula (III), B\(^1\) is OR\(^1\). In another embodiment of Formula (III), B\(^1\) is OR\(^1\), and A\(^1\) is C(A\(^2\)), and A\(^2\) is H.

In one embodiment of Formula (III), D\(^1\) and E\(^1\) are H. In another embodiment of Formula (III), B\(^1\) is NHR\(^1\), and A\(^1\) is C(A\(^2\)), A\(^2\) is H, and D\(^1\) and E\(^1\) are H. In another embodiment of Formula (III), B\(^1\) is OR\(^1\), and A\(^1\) is C(A\(^2\)), A\(^2\) is H, and D\(^1\) and E\(^1\) are H.

In one embodiment of Formula (III), Y\(^1\) is H, CN, NO\(_2\), F, Cl, Br, I, CF\(_3\), R\(^{17}\), NHC(O)R\(^{17}\), or C(O)NH\(_2\). In another embodiment of Formula (III), Y\(^1\) is NO\(_2\). In another embodiment of Formula (III), B\(^1\) is NHR\(^1\), and A\(^1\) is C(A\(^2\)), A\(^2\) is H, D\(^1\) and E\(^1\) are H, and Y\(^1\) is NO\(_2\). In another embodiment of Formula (III), Y\(^1\) is Cl. In another embodiment of Formula (III), B\(^1\) is OR\(^1\), and A\(^1\) is C(A\(^2\)), A\(^2\) is H, D\(^1\) and E\(^1\) are H, and Y\(^1\) is Cl.

In one embodiment of Formula (III), R\(^1\) is R\(^2\), R\(^3\), R\(^4\) or R\(^5\). In another embodiment of Formula (III), R\(^1\) is R\(^2\), and R\(^2\) is phenyl.

In one embodiment of Formula (III), R\(^1\) is R\(^3\), and R\(^3\) is heteroaryl. In another embodiment of Formula (III), R\(^1\) is triazolyl.

In one embodiment of Formula (III), R\(^1\) is R\(^4\). In another embodiment of Formula (III), R\(^1\) is R\(^3\), and R\(^4\) is cycloalkyl. In another embodiment of Formula (III), R\(^1\) is R\(^4\), and R\(^4\) is cyclohexyl. In another embodiment of Formula (III), R\(^1\) is R\(^3\), and R\(^4\) is heterocycloalkyl. In another embodiment of Formula (III), R\(^1\) is R\(^3\), and R\(^4\) is 8-azabicyclo[3.2.1]octane, azetidinyl, piperidinyl, piperazinyl, pyrrolidinyl, morpholinyl, tetrahydropyranyl, or tetrahydrothiophenyl. In another embodiment of Formula (III), R\(^1\) is R\(^4\), and R\(^4\) is heterocycloalkenyl. In another embodiment of Formula (III), R\(^1\) is R\(^4\), and R\(^4\) is tetrahydropyridazinyl.

In one embodiment of Formula (III), R\(^1\) is R\(^5\). In another embodiment of Formula (III), R\(^1\) is R\(^3\) and R\(^5\) is alkyl or alkynyl. In another embodiment of Formula (III), R\(^1\) is R\(^5\) and R\(^5\) is alkyl which is unsubstituted. In another embodiment of Formula (III), R\(^1\) is R\(^5\) and R\(^5\) is alkyl which is substituted with one or two or three independently selected R\(^6\), R\(^7\), OR\(^7\), SR\(^7\), SO\(_2\)R\(^7\), N(R\(^7\))\(_2\), OH, CN, CF\(_3\), F, Cl, Br or I substituents. In another embodiment of Formula (III), R\(^1\) is R\(^5\) and R\(^5\) is alkyl which is substituted with R\(^7\).
In one embodiment of Formula (III), \( R^7 \) is \( R^8, R^9, R^{10} \) or \( R^{11} \). In another embodiment of Formula (III), \( R^7 \) is \( R^8 \), and \( R^8 \) is phenyl which is unfused or fused with \( R^{8A} \), and \( R^{8A} \) is heterocycloalkane. In another embodiment of Formula (III), \( R^7 \) is \( R^8 \), and \( R^8 \) is phenyl which is unfused. In another embodiment of Formula (III), \( R^7 \) is \( R^9 \), and \( R^9 \) is heteroaryl. In another embodiment of Formula (III), \( R^7 \) is \( R^9 \), and \( R^9 \) is furanyl, imidazolyl, isothiazolyl, isoxazolyl, 1,2,3-oxadiazolyl, 1,2,5-oxadiazolyl, oxazolyl, pyrazinyl, pyrazolyl, pyridazinyl, pyridinyl, pyrimidinyl, pyrrolyl, tetrazolyl, thiazolyl, thiophenyl, triazinyl or 1,2,3-triazolyl. In another embodiment of Formula (III), \( R^7 \) is \( R^9 \), and \( R^9 \) is pyridinyl, thiazolyl, imidazolyl, and 1,2,3-triazolyl. In another embodiment of Formula (III), \( R^7 \) is \( R^{10} \), and \( R^{10} \) is 

\[
C_3-C_{10}\text{-cycloalkyl. In another embodiment of Formula (III), } R^7 \text{ is } R^{10}, \text{ and } R^{10} \text{ is } C_6 \text{ or } C_{10}\text{-cycloalkyl. In another embodiment of Formula (III), } R^7 \text{ is } R^{10}, \text{ and } R^{10} \text{ is cyclohexyl or adamantanyl. In another embodiment of Formula (III), } R^7 \text{ is } R^{10}, \text{ and } R^{10} \text{ is morpholinyl, piperezinyl, piperidinyl, tetrahydro-2H-pyranyl, 1,2-dihydropyridinyl, pyranyl, pyridin-1(H)-yl, pyrrolidinyl, oxetanyl, thiomorpholinyl, imidazolidinyl, tetrahydrothiophenyl, dioxolanyl, tetrahydrothiopyrany1, dioxanyl, or tetrahydrofuranyl. In another embodiment of Formula (III), } R^7 \text{ is } R^{10}, \text{ and } R^{10} \text{ is morpholinyl, piperezinyl, piperidinyl, tetrahydro-2H-pyranyl, 1,2-dihydropyridinyl, pyrrolidinyl, oxetanyl, thiomorpholinyl, imidazolidinyl, tetrahydrothiophenyl, dioxolanyl, tetrahydrothiopyrany1, dioxanyl, or tetrahydrofuranyl. In another embodiment of Formula (III), } R^7 \text{ is } R^{11}, \text{ and } R^{11} \text{ is alkyl which is unsubstituted or substituted. In another embodiment of Formula (III), } R^7 \text{ is } R^{11}, \text{ and } R^{11} \text{ is alkyl which is unsubstituted. In another embodiment of Formula (III), } R^7 \text{ is } R^{11}, \text{ and } R^{11} \text{ is alkyl which is substituted. In another embodiment of Formula (III), } R^7 \text{ is } R^{11}, \text{ and } R^{11} \text{ is alkyl which is substituted with one or two or three independently selected OR}^{12}, \text{ F, Cl, Br or I substituents. In another embodiment of Formula (III), } R^7 \text{ is } R^{11}, \text{ and } R^{11} \text{ is alkyl which is substituted with OR}^{12}, \text{ R}^{12} \text{ is } R^{16}, \text{ and } R^{16} \text{ is alkyl.}
\]

In one embodiment of Formula (III), \( R^{17} \) is \( R^{19} \) or \( R^{21} \). In another embodiment of Formula (III), \( R^{17} \) is \( R^{19} \), and \( R^{19} \) is heteroaryl. In another embodiment of Formula (III), \( R^{17} \) is \( R^{19} \), and \( R^{19} \) is thiazolyl. In another embodiment of Formula (III), \( R^{17} \) is \( R^{21} \), and \( R^{21} \) is alkynyl. In another embodiment of Formula (III), \( R^{17} \) is \( R^{21} \), and \( R^{21} \) is ethynyl.
Still another embodiment pertains to compounds having Formula (III) which are

4-(4-((4'-chloro-4-(pyrrolidin-1-ylmethyl)-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-yl)methyl)amino)phenyl)sulfonyl)benzamide;

5 4-(4-((4'-chloro-4-(2-pyrrolidin-1-ylethyl)-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-yl)methyl)amino)phenyl)sulfonyl)benzamide;

4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)benzamide;

10 4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-((3-(dimethylamino)propyl)amino)-3-nitrophenyl)sulfonyl)-2-(1H-indol-4-yloxy)benzamide;

4-(4-((2-(4-chlorophenyl)-5,5-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((4-((3-morpholin-4-ylpropyl)amino)-3-nitrophenyl)sulfonyl)benzamide;

4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((4-((3-morpholin-4-ylpropyl)amino)-3-nitrophenyl)sulfonyl)benzamide;

15 4-(4-((2-(4-chlorophenyl)-5,5-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-N-((4-((3-(dimethylamino)propyl)amino)-3-nitrophenyl)sulfonyl)-2-(1H-indol-4-yloxy)benzamide;

4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-N-((4-((3-(dimethylamino)propyl)amino)-3-nitrophenyl)sulfonyl)-2-(1H-indol-4-yloxy)benzamide;

4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((4-((3-morpholin-4-ylpropyl)amino)-3-nitrophenyl)sulfonyl)benzamide;

4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((4-((tetrahydro-2H-pyran-4-ylmethyl)amino)-3-((trifluoromethyl)sulfonyl)phenyl)sulfonyl)benzamide;

20 4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((4-((3-morpholin-4-ylpropyl)amino)-3-((trifluoromethyl)sulfonyl)phenyl)sulfonyl)benzamide;

2-(1H-indol-4-yloxy)-4-(4-((2-(4-methoxyphenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((3-pyrrolidin-1-ylpropyl)amino)phenyl)sulfonyl)benzamide;

25 4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((4-((3-morpholin-4-ylpropyl)amino)-3-((trifluoromethyl)sulfonyl)phenyl)sulfonyl)benzamide;

4-(4,4-dimethyl-2-(4-(trifluoromethyl)phenyl)cyclohex-1-en-1-ylmethyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((3-nitro-4-((3-pyrrolidin-1-ylpropyl)amino)phenyl)sulfonyl)benzamide;
4-(4-((4,4-dimethyl-2-(4-(trifluoromethoxy)phenyl)cyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((3-nitro-4-((3-pyrrolidin-1-yl)propyl)amino)phenyl)sulfonyl)benzamide;  
4-(4-(4,4-dimethyl-2-(3-(trifluoromethyl)phenyl)cyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((3-nitro-4-((3-pyrrolidin-1-yl)propyl)amino)phenyl)sulfonyl)benzamide;  
4-(4-((2-(3-fluorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((3-nitro-4-((3-pyrrolidin-1-yl)propyl)amino)phenyl)sulfonyl)benzamide;  
4-(4-(4-(2-(4-fluorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((3-nitro-4-((3-pyrrolidin-1-yl)propyl)amino)phenyl)sulfonyl)benzamide;  
4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((4-((3-(4-methyl)piperazin-1-yl)propyl)amino)-3-nitrophenyl)sulfonyl)benzamide;  
4-(4-(4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((4-((2-(4-methyl)piperazin-1-yl)ethyl)amino)-3-nitrophenyl)sulfonyl)benzamide;  
4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((3-nitro-4-((3-pyrrolidin-1-yl)propyl)amino)phenyl)sulfonyl)benzamide;  
4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((4-((1-methyl)piperazin-4-yl)amino)-3-nitrophenyl)sulfonyl)benzamide;  
4-(4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((4-((1-methyl)piperazin-4-yl)methyl)amino)-3-nitrophenyl)sulfonyl)benzamide;  
4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((4-((3-dimethylamino)propoxy)-3-nitrophenyl)sulfonyl)benzamide;  
4-(4-(4-(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((3-nitro-4-(1-(2,2,2-trifluoroethyl)piperidin-4-yl)amino)phenyl)sulfonyl)benzamide;  
4-(4-((4'-chloro-4-(2(dimethylamino)ethoxy)-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-yl)methyl)amino)phenyl)sulfonyl)benzamide;  
4-(4-(4'-chloro-3-(2(dimethylamino)ethoxy)-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-yl)methyl)amino)phenyl)sulfonyl)benzamide;
4-(4-((4'-chloro-4-(2-morpholin-4-yloxy)-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((3-nitro-4-((tetrahydro-2H-pyrano-4-yl)methyl)amino)phenyl)sulfonyl)benzamide;
4-(4-((4'-chloro-3-(2-morpholin-4-yloxy)-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((3-nitro-4-((tetrahydro-2H-pyrano-4-yl)methyl)amino)phenyl)sulfonyl)benzamide;
4-(4-((2-(4-chlorophenyl)cyclohept-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((3-nitro-4-((3-pyrrolidin-1-ylpropyl)amino)phenyl)sulfonyl)benzamide;
4-(4-((2-(4-chlorophenyl)cyclooct-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((3-nitro-4-((3-pyrrolidin-1-ylpropyl)amino)phenyl)sulfonyl)benzamide;
4-(4-((2-(4-chlorophenyl)cyclopent-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((3-nitro-4-((3-pyrrolidin-1-ylpropyl)amino)phenyl)sulfonyl)benzamide;
4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclopent-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((4-((1-methyl)piperidin-4-yl)amino)-3-nitrophenyl)sulfonyl)benzamide;
4-(4-((4-(4-chlorophenyl)-6,6-dimethyl-5,6-dihydro-2H-pyrano-3-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((4-((1-methyl)piperidin-4-yl)amino)-3-nitrophenyl)sulfonyl)benzamide;
4-(4-((2-(4-chlorophenyl)cyclooct-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((4-((1-methyl)piperidin-4-yl)amino)-3-nitrophenyl)sulfonyl)benzamide;
4-(4-((2-(4-chlorophenyl)cyclohept-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((4-((1-methyl)piperidin-4-yl)amino)-3-nitrophenyl)sulfonyl)benzamide;
4-(4-((2-(4-chlorophenyl)cyclopent-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((4-((1-methyl)piperidin-4-yl)amino)-3-nitrophenyl)sulfonyl)benzamide;
4-(4-((2-(4-chlorophenyl)cyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((4-((1-methyl)piperidin-4-yl)amino)-3-nitrophenyl)sulfonyl)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-[[4-[[4-methylpiperazin-1-yl]amino]-3-nitrophenyl]sulfonyl]benzamide;

4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-[[4-[[1-(2-hydroxyethyl)piperidin-4-yl]amino]-3-nitrophenyl]sulfonyl]-2-(1H-indol-4-yloxy)benzamide;

4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-[[4-[[1-(3-hydroxypropyl)piperidin-4-yl]amino]-3-nitrophenyl]sulfonyl]-2-(1H-indol-4-yloxy)benzamide;

4-[4-[[4'-chloro-3-[3-(dimethylamino)propyl]-1,1'-biphenyl-2-yl]methyl]piperazin-1-yl]-2-(1H-indol-4-yloxy)-N-[[3-nitro-4-[(tetrahydro-2H-pyran-4-y1)methyl]amino]phenyl]sulfonyl]benzamide;

4-[[4'-chloro-4-morpholin-4-yl-1,1'-biphenyl-2-yl]methyl]piperazin-1-yl]-2-(1H-indol-4-yloxy)-N-[[3-nitro-4-[(tetrahydro-2H-pyran-4-yl)methyl]amino]phenyl]sulfonyl]benzamide;

4-[4-[[4'-chloro-3-[2-(dimethylamino)ethoxy]-1,1'-biphenyl-2-yl]methyl]piperazin-1-yl]-2-(1H-indol-4-yloxy)-N-[[3-nitro-4-[(1-tetrahydro-2H-pyran-4-yl)piperidin-4-y1]amino]phenyl]sulfonyl]benzamide;

4-[4-[[1-(4'-chloro-1,1'-biphenyl-2-yl)ethyl]piperazin-1-yl]-2-(1H-indol-4-yloxy)-N-[[3-nitro-4-[(tetrahydro-2H-pyran-4-yl)methyl]amino]phenyl]sulfonyl]benzamide;

4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl]-2-(1H-indol-4-yloxy)-N-[[4-[[4-(dimethylamino)cyclohexyl]amino]-3-nitrophenyl]sulfonyl]-2-(1H-indol-4-yloxy)benzamide;

4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-[[4-[[4-(diethylamino)cyclohexyl]amino]-3-nitrophenyl]sulfonyl]-2-(1H-indol-4-yloxy)benzamide;

4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-[[4-[[4-(methylamino)cyclohexyl]amino]-3-nitrophenyl]sulfonyl]-2-(1H-indol-4-yloxy)benzamide;

4-[4-[[4'-chloro-3-[2-(dimethylamino)ethoxy]-1,1'-biphenyl-2-yl]methyl]piperazin-1-yl]-2-(1H-indol-4-yloxy)-N-[[4-[[1-methylpiperidin-4-yl]amino]-3-nitrophenyl]sulfonyl]benzamide;
4-{[1-(4'-chloro-1,1'-biphenyl-2-yl)ethyl]piperazin-1-yl}-2-(1H-indol-4-yl)oxy)-N-(4-[(1-methylpiperidin-4-yl)amino]-3-nitrophenyl)sulfonyl)benzamide;
4-{[1-(4'-chloro-4-[3-(dimethylamino)prop-1-ynyl]-1,1'-biphenyl-2-yl)methyl]piperazin-1-yl}]-2-(1H-indol-4-yl)oxy)-N-(3-nitro-4-[(tetrahydro-2H-pyran-4-yl)methyl]phenyl)sulfonyl)benzamide;
4-{[2-(1H-indol-4-yl)oxy]-N-(3-nitro-4-{[(1-4,4,4-trifluorobutyl)piperidin-4-yl]amino}phenyl)sulfonyl)benzamide;
4-{[(4'-chloro-4-(2-hydroxyethoxy)-1,1'-biphenyl-2-yl)methyl]piperazin-1-yl}]-2-(1H-indol-4-yl)oxy)-N-(3-nitro-4-[(tetrahydro-2H-pyran-4-yl)methyl]phenyl)sulfonyl)benzamide;
4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl}-2-(1H-indol-4-yl)oxy)-N-(4-{[(4-methylpiperazin-1-yl)amino]-3-[(trifluoromethyl)phenyl)sulfonyl]benzamide;
4-{[1-(4'-chloro-1,1'-biphenyl-2-yl)ethyl]piperazin-1-yl}]-2-(1H-indol-4-yl)oxy)-N-(4-[(4-methylpiperazin-1-yl)amino]-3-nitrophenyl)sulfonyl)benzamide;
4-{[4'-chloro-2-(2-hydroxyethoxy)-1,1'-biphenyl-2-yl]methyl}piperazin-1-yl}]-2-(1H-indol-4-yl)oxy)-N-(4-{[1-(methylpiperidin-4-yl)amino]-3-nitrophenyl)sulfonyl)benzamide;
4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl}]-2-(1H-indol-4-yl)oxy)-N-(3-nitro-4-{[(3-(3-oxopiperazin-1-yl)propyl]amino}phenyl)sulfonyl)benzamide;
4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl}]-2-(1H-indol-4-yl)oxy)-N-(4-{[1-(2,3-dihydro-1H-inden-2-yl)piperidin-4-yl]amino}-3-nitrophenyl)sulfonyl)benzamide;
4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl}]-2-(1H-indol-4-yl)oxy)-N-(4-{[(4-hydroxymethyl)tetrahydro-2H-pyran-4-yl]amino}-3-nitrophenyl)sulfonyl)benzamide;
4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl}]-2-(1H-indol-4-yl)oxy)-N-(3-nitro-4-{[(tetrahydro-2H-pyran-4-yl)methyl]amino}phenyl)sulfonyl)benzamide;
4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl}]-2-(1H-indol-4-yl)oxy)-N-{[4-(methylamino)-3-nitrophenyl)sulfonyl]benzamide;
4-[[1-(4'-chloro-1,1'-biphenyl-2-yl)ethyl]piperazin-1-yl]-2-(1H-indol-4-yl)oxy]-N-[[4-[(3-morpholin-4-ylpropyl)amino]-3-nitrophenyl]sulfonyl]benzamide;
4-[[1R]-1-(4'-chloro-1,1'-biphenyl-2-yl)ethyl]piperazin-1-yl]-2-(1H-indol-4-yl)oxy]-N-[[3-nitro-4-[(tetrahydro-2H-pyran-4-ylmethyl)amino]phenyl]sulfonyl]benzamide;
4-[[1S]-1-(4'-chloro-1,1'-biphenyl-2-yl)ethyl]piperazin-1-yl]-2-(1H-indol-4-yl)oxy]-N-[[3-nitro-4-[(tetrahydro-2H-pyran-4-ylmethyl)amino]phenyl]sulfonyl]benzamide;
4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl]-2-(1H-indol-4-yl)oxy]-N-[[4-(morpholin-4-ylamino)-3-nitrophenyl]sulfonyl]benzamide;
4-[[4'-(4'-chloro-4-[2-(dimethylamino)ethoxy]-1,1'-biphenyl-2-yl)methyl]piperazin-1-yl]-2-(1H-indol-4-yl)oxy]-N-[[4-[(4-methylpiperazin-1-yl)amino]-3-nitrophenyl]sulfonyl]benzamide;
4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl]-2-(1H-indol-4-yl)oxy]-N-[[3-nitro-4-[2-(3-oxopiperazin-1-yl)ethyl]amino]phenyl]sulfonyl]benzamide;
4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl]-2-(1H-indol-4-yl)oxy]-N-[[3-nitro-4-[piperidin-1-ylamino]phenyl]sulfonyl]benzamide;
4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl]-2-(1H-indol-4-yl)oxy]-N-[[3-nitro-4-[tetrahydro-2H-pyran-4-ylmethoxy]phenyl]sulfonyl]benzamide;
4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl]-2-(1H-indol-4-yl)oxy]-N-[[3-nitro-4-[2-(trifluoromethoxy)ethyl]amino]phenyl]sulfonyl]benzamide;
4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl]-2-(1H-indol-4-yl)oxy]-N-[[4-[[2-(2-methoxyethoxy)ethyl]amino]-3-nitrophenyl]sulfonyl]benzamide;
4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl]-2-(1H-indol-4-yl)oxy]-N-[[4-[[3-(methylsulfonyl)propyl]amino]-3-nitrophenyl]sulfonyl]benzamide;
4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl]-2-(1H-indol-4-yl)oxy]-N-[[4-[[3-(1,1-dioxidothiomorpholin-4-yl)propyl]amino]-3-nitrophenyl]sulfonyl]benzamide;
4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl]-2-(1H-indol-4-yl)oxy]-N-[[4-[[1,1-dioxide(tetrahydrothien-3-yl)amino]-3-nitrophenyl]sulfonyl]benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4-[(1,1-dioxidotetrahydro-2H-thiopyran-4-yl)methyl]amino]-3-nitrophenyl)sulfonyl]-2-(1H-indol-4-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4-[(4-fluorotetrahydro-2H-pyran-4-ylmethoxy]-3-nitrophenyl] sulfonyl]-2-(1H-indol-4-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-[[4-[(3-methoxypropyl]amino]-3-nitrophenyl] sulfonyl]benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-[[4-[(2-cyanoethyl]amino]-3-nitrophenyl] sulfonyl]-2-(1H-indol-4-yloxy)benzamide;
N-[[5-bromo-6-[(tetrahydro-2H-pyran-4-ylmethyl]amino]pyridin-3-yl] sulfonyl]-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-4-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4-[(1,1-dioxidotetrahydrothien-3-yl)methyl]amino]-3-nitrophenyl)sulfonyl]-2-(1H-indol-4-yloxy)benzamide;
N-[[4-[(1-acetyl]piperidin-4-yl]amino]-3-nitrophenyl] sulfonyl]-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-4-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-[[4-[(1)-(methyl)sulfonyl]piperidin-4-yl]amino]-3-nitrophenyl] sulfonyl]benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-[[4-[[3-morpholin-4-ylpropyl]amino]phenyl]sulfonyl]benzamide;
4-(4-[[2-(4-chlorophenyl)-1-(3-hydroxypropyl)-1,2,5,6-tetrahydropyridin-3-yl]methyl]piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-[[3-nitro-4-[[tetrahydro-2H-pyran-4-ylmethyl]amino]phenyl]sulfonyl]benzamide;
N-[[5-bromo-6-(tetrahydro-2H-pyran-4-ylmethoxy)pyridin-3-yl]sulfonyl]-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-4-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[3-cyano-4-[[tetrahydro-2H-pyran-4-ylmethyl]amino]phenyl]sulfonyl]-2-(1H-indol-4-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-[[4-[[2-(methoxyethoxy)ethyl]thio]-3-nitrophenyl]sulfonyl]benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-[[4-(methylsulfonyl)phenyl]sulfonyl]benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[5-cyano-6-(tetrahydro-2H-pyran-4-ylmethoxy)pyridin-3-yl]sulfonyl]-2-(1H-indol-4-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[5-chloro-6-(tetrahydro-2H-pyran-4-ylmethoxy)pyridin-3-yl]sulfonyl]-2-(1H-indol-4-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[5-ethynyl-6-(tetrahydro-2H-pyran-4-ylmethoxy)pyridin-3-yl]sulfonyl]-2-(1H-indol-4-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[5-cyano-6-(2-morpholin-4-ylethoxy)pyridin-3-yl]sulfonyl]-2-(1H-indol-4-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[(5-cyano-6-[(4-fluorotetrahydro-2H-pyran-4-yl)methoxy]pyridin-3-yl)sulfonyl]-2-(1H-indol-4-yloxy)benzamide;

N-((5-chloro-6-[(4-fluorotetrahydro-2H-pyran-4-yl)methoxy]pyridin-3-yl)sulfonyl)-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-4-yloxy)benzamide;

and therapeutically acceptable salts, prodrugs, salts of prodrugs and metabolites thereof.

In another aspect, the present invention provides compounds of Formula (IV)

![Chemical Structure](image)

and therapeutically acceptable salts, prodrugs, salts of prodrugs and metabolites thereof, wherein A<sup>1</sup>, B<sup>1</sup>, D<sup>1</sup>, E<sup>1</sup>, Y<sup>1</sup>, R<sup>20</sup>, and R<sup>37</sup> are as described herein for Formula (I), n is 0, 1, 2, or 3; describing the number of substituents on R<sup>26</sup>, and R<sup>100</sup> is as described for substituents on R<sup>26</sup>.

In one embodiment of Formula (IV), A<sup>1</sup> is N. In another embodiment of Formula (IV), A<sup>1</sup> is C(A<sup>2</sup>). In another embodiment of Formula (IV), A<sup>1</sup> is C(A<sup>2</sup>), and A<sup>2</sup> is H.

In one embodiment of Formula (IV), B<sup>1</sup> is R<sup>1</sup>, OR<sup>1</sup>, SR<sup>1</sup>, SO<sub>2</sub>R<sup>1</sup>, NHR<sup>1</sup>, N(R<sup>1</sup>)<sub>2</sub>, or C(O)NHR<sup>1</sup>. In another embodiment of Formula (IV), B<sup>1</sup> is NHR<sup>1</sup>. In another embodiment of Formula (IV), B<sup>1</sup> is NHR<sup>1</sup>, and A<sup>1</sup> is C(A<sup>2</sup>), and A<sup>2</sup> is H. In another embodiment of Formula (IV), B<sup>1</sup> is OR<sup>1</sup>. In another embodiment of Formula (IV), B<sup>1</sup> is OR<sup>1</sup>, and A<sup>1</sup> is C(A<sup>2</sup>), and A<sup>2</sup> is H.

In one embodiment of Formula (IV), D<sup>1</sup> and E<sup>1</sup> are H. In another embodiment of Formula (IV), B<sup>1</sup> is NHR<sup>1</sup>, and A<sup>1</sup> is C(A<sup>2</sup>), A<sup>2</sup> is H, and D<sup>1</sup> and E<sup>1</sup> are H. In another embodiment of Formula (IV), B<sup>1</sup> is OR<sup>1</sup>, and A<sup>1</sup> is C(A<sup>2</sup>), A<sup>2</sup> is H, and D<sup>1</sup> and E<sup>1</sup> are H.
In one embodiment of Formula (IV), $Y^1$ is H, CN, NO$_2$, F, Cl, Br, I, CF$_3$, R$_{17}$, NHC(O)R$_{17}$, or C(O)NH$_2$. In another embodiment of Formula (IV), $Y^1$ is NO$_2$. In another embodiment of Formula (IV), $B^1$ is NHR$_1$, and $A^1$ is C(A$_2$), A$_2$ is H, D$_1$ and E$_1$ are H, and $Y^1$ is NO$_2$. In another embodiment of Formula (IV), $Y^1$ is Cl. In another embodiment of Formula (I), $B^1$ is OR$_1$, and $A^1$ is C(A$_2$), A$_2$ is H, D$_1$ and E$_1$ are H, and $Y^1$ is Cl.

In one embodiment of Formula (IV), $R^1$ is R$_2$, R$_3$, R$_4$ or R$_5$. In another embodiment of Formula (IV), $R^1$ is R$_2$, and R$_2$ is phenyl.

In one embodiment of Formula (IV), $R^1$ is R$_3$, and R$_3$ is heteroaryl. In another embodiment of Formula (IV), R$_3$ is triazolyl.

In one embodiment of Formula (IV), $R^1$ is R$_4$. In another embodiment of Formula (IV), $R^1$ is R$_4$, and R$_4$ is cycloalkyl. In another embodiment of Formula (IV), $R^1$ is R$_4$, and R$_4$ is cyclohexyl. In another embodiment of Formula (IV), $R^1$ is R$_4$, and R$_4$ is heterocycloalkyl. In another embodiment of Formula (IV), $R^1$ is R$_4$, and R$_4$ is 8-azabicyclo[3.2.1]octane, azetidinyl, piperidinyl, piperazinyl, pyrrolidinyl, morpholinyl, tetrahydropyranyl, or tetrahydrothiophenyl. In another embodiment of Formula (IV), $R^1$ is R$_4$, and R$_4$ is heterocycloalkenyl. In another embodiment of Formula (IV), $R^1$ is R$_4$, and R$_4$ is tetrahydropyridazinyl.

In one embodiment of Formula (IV), $R^1$ is R$_5$. In another embodiment of Formula (IV), $R^1$ is R$_5$ and R$_5$ is alkyl or alkylnyl. In another embodiment of Formula (IV), $R^1$ is R$_5$ and R$_5$ is alkyl which is unsubstituted. In another embodiment of Formula (IV), $R^1$ is R$_5$ and R$_5$ is alkyl which is substituted with one or two or three independently selected R$_6$, R$_7$, OR$_7$, SR$_7$, SO$_2$R$_7$, N(R$_7$)$_2$, OH, CN, CF$_3$, F, Cl, Br or I substituents. In another embodiment of Formula (IV), $R^1$ is R$_5$ and R$_5$ is alkyl which is substituted with R$_7$.

In one embodiment of Formula (IV), $R^7$ is R$_8$, R$_9$, R$_{10}$ or R$_{11}$. In another embodiment of Formula (IV), $R^7$ is R$_8$, and R$_8$ is phenyl which is unfused or fused with R$_{8A}$, and R$_{8A}$ is heterocycloalkane. In another embodiment of Formula (IV), $R^7$ is R$_9$, and R$_9$ is phenyl which is unfused. In another embodiment of Formula (IV), $R^7$ is R$_9$, and R$_9$ is heteroaryl. In another embodiment of Formula (IV), $R^7$ is R$_9$, and R$_9$ is furanyl, imidazolyl, isothiazolyl, isoxazolyl, 1,2,3-oxadiazoyl, 1,2,5-oxadiazoyl, oxazolyl, pyrazinyl, pyrazolyl, pyridazinyl, pyridinyl, pyrimidinyl, pyrrol, tetrazolyl, thiazolyl, thiophenyl, triazinyl or 1,2,3-triazolyl. In another embodiment of Formula (IV), $R^7$ is R$_9$, and R$_9$ is pyridinyl, thiazolyl, imidazolyl, and 1,2,3-triazolyl. In another embodiment of Formula (IV), $R^7$ is R$_{10}$, and R$_{10}$ is
C3-C10-cycloalkyl. In another embodiment of Formula (IV), R7 is R10, and R10 is C6 or
C10-cycloalkyl. In another embodiment of Formula (IV), R7 is R10, and R10 is cyclohexyl or
adamantanyl. In another embodiment of Formula (IV), R7 is R10, and R10 is morpholinyl,
piperazinyl, piperidinyl, tetrahydro-2H-pyranyl, 1,2-dihydropyridinyl, pyranyl, pyridin-1(H)-
yl, pyrrolidinyl, oxetanyl, thiomorpholinyl, imidazolidinyl, tetrahydrothiophenyl, dioxolanyl,
tetrahydrothiopyranyl, dioxanyl, or tetrahydrofuranyl. In another embodiment of Formula
(IV), R7 is R10, and R10 is morpholinyl, piperazinyl, piperidinyl, tetrahydro-2H-pyranyl, 1,2-
dihydropyridinyl, pyrrolidinyl, oxetanyl, thiomorpholinyl, imidazolidinyl, tetrahydrothiophenyl,
dioxolanyl, tetrahydrothiopyranyl, dioxanyl, or tetrahydrofuranyl. In
another embodiment of Formula (IV), R7 is R11, and R11 is alkyl which is unsubstituted or
substituted. In another embodiment of Formula (IV), R7 is R11, and R11 is alkyl which is
unsubstituted. In another embodiment of Formula (IV), R7 is R11, and R11 is alkyl which is
substituted. In another embodiment of Formula (IV), R7 is R11, and R11 is alkyl which is
substituted with one or two or three independently selected OR12, F, Cl, Br or I substituents.
In another embodiment of Formula (IV), R7 is R11, R11 is alkyl which is substituted with
OR12, R12 is R16, and R16 is alkyl.

In one embodiment of Formula (IV), R17 is R19 or R21. In another embodiment of
Formula (IV), R17 is R19, and R19 is heteroaryl. In another embodiment of Formula (IV), R17
is R19, and R19 is thiazolyl. In another embodiment of Formula (IV), R17 is R21, and R21 is
alkynyl. In another embodiment of Formula (IV), R17 is R21, and R21 is ethynyl.

Still another embodiment pertains to compounds having Formula (IV) which are
2-(1H-benzimidazol-4-yl)oxy)-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-([3-nitro-4-[(tetrahydro-2H-pyran-4-
ylmethyl)amino]phenyl}sulfonyl)benzamide;
2-(1H-benzimidazol-4-yl)oxy)-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[(4-((3R)-1-(2,2-difluoroethyl)pyrrolidin-3-yl)amino)-3-
nitrophenyl}sulfonyl]benzamide;
2-(1H-benzimidazol-4-yl)oxy)-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4-[(4-fluorotetrahydro-2H-pyran-4-yl)]methoxy]-3-
nitrophenyl}sulfonyl]benzamide;
2-(1H-benzimidazol-4-yl)oxy)-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4-[[4-(2,2-difluoroethyl)morpholin-2-yl]methyl]amino]-3-nitrophenyl]sulfonyl]benzamide;
2-(1H-benzimidazol-4-yl)oxy)-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-((3-nitro-4-[[1-tetrahydro-2H-pyran-4-yl]piperidin-4-yl]phenyl)sulfonyl]benzamide;
2-(1H-benzimidazol-4-yl)oxy)-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4-[[1-methylpiperidin-4-yl]amino]-3-nitrophenyl]sulfonyl]benzamide;
2-(1H-benzimidazol-4-yl)oxy)-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[5-chloro-6-[[2S]-4-(N,N-dimethylglycyl)morpholin-2-yl]methoxy]pyridin-3-yl]sulfonyl]-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)benzamide;
2-(1H-benzimidazol-4-yl)oxy)-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4-[[3R]-1-(cyanomethyl)pyrroolidin-3-yl]amino]-3-nitrophenyl]sulfonyl]benzamide;
2-(1H-benzimidazol-4-yl)oxy)-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4-((3R)-1-[2-(2-methoxyethoxy)ethyl]pyrroolidin-3-yl]amino]-3-nitrophenyl]sulfonyl]benzamide;
2-(1H-benzimidazol-4-yl)oxy)-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4-((3R)-1-(N,N-dimethylglycyl)pyrroolidin-3-yl]amino]-3-nitrophenyl]sulfonyl]benzamide;
2-(1H-benzimidazol-4-yl)oxy)-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4-((cyanomethyl)morpholin-2-yl]methyl]amino]-3-nitrophenyl]sulfonyl]benzamide;
2-(1H-benzimidazol-4-yl)oxy)-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4-((4-cyclopropyl)morpholin-2-yl)methyl]amino]-3-nitrophenyl]sulfonyl]benzamide;
2-(1H-benzimidazol-4-yl)oxy)-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[3-nitro-4-[[4-(oxetan-3-yl)morpholin-2-yl]methyl]amino]phenyl)sulfonyl]benzamide;

- 167 -
2-(1H-benzimidazol-4-yloxy)-4-((2-[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-y]methyl)piperazin-1-yl)-N-[(4-((2S)-4-(N,N-dimethylglycyl)morpholin-2-yl)methyl]amino]-3-nitrophenyl)sulfonyl]benzamide;

5 2-(1H-benzimidazol-4-yloxy)-4-((2-[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-y]methyl)piperazin-1-yl)-N-[(4-((2S)-4-(N,N-dimethylglycyl)morpholin-2-yl)methyl]amino]-3-nitrophenyl)sulfonyl]benzamide;

2-(1H-benzimidazol-4-yloxy)-4-((2-[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-y]methyl)piperazin-1-yl)-N-((3-nitro-4-[(tetrahydrofuran-3-yl)methyl]amino)phenyl) sulfonyl]benzamide;

10 Trans-2-(1H-benzimidazol-4-yloxy)-4-((2-[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-y]methyl)piperazin-1-yl)-N-[(4-((4-methoxy)cyclohexyl)methyl]amino]-3-nitrophenyl)sulfonyl]benzamide;

2-(1H-benzimidazol-4-yloxy)-4-((2-[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-y]methyl)piperazin-1-yl)-N-((5-fluoro-6-[(4-fluorotetrahydro-2H-pyran-4-yl)methoxy]pyridin-3-yl)sulfonyl]benzamide;

2-(1H-benzimidazol-4-yloxy)-N-((5-chloro-6-[(4-fluorotetrahydro-2H-pyran-4-yl)methoxy]pyridin-3-yl)sulfonyl]-4-((2-[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-y]methyl)piperazin-1-yl)benzamide;

20 2-(1H-benzimidazol-4-yloxy)-N-((5-chloro-6-[(1-cyclopropyl)piperidin-4-yl]amino)pyridin-3-yl)sulfonyl]-4-((2-[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-y]methyl)piperazin-1-yl)benzamide;

2-(1H-benzimidazol-4-yloxy)-4-((2-[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-y]methyl)piperazin-1-yl)-N-((4-((1,4-dioxan-2-yl)methyl]amino)3-nitrophenyl)sulfonyl]benzamide;

2-(1H-benzimidazol-4-yloxy)-4-((2-[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-y]methyl)piperazin-1-yl)-N-((4-((1-cyclopropyl)piperidin-4-yl]amino)-3-nitrophenyl)sulfonyl]benzamide;

Trans-2-(1H-benzimidazol-4-yloxy)-4-((2-[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-y]methyl)piperazin-1-yl)-N-((4-((4-morpholin-4-yl)cyclohexyl]amino]-3-nitrophenyl)sulfonyl]benzamide;
2-(1H-benzimidazol-4-yloxy)-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[(4-[((4-methylpiperazin-1-yl)amino]-3-nitrophenyl)sulfonyl]benzamide;
2-(1H-benzimidazol-4-yloxy)-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[(4-[[1-methylpiperidin-4-yl]methyl]amino]-3-nitrophenyl)sulfonyl]benzamide;
2-(1H-benzimidazol-4-yloxy)-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[(4-[(2R)-4-[2-(methoxyethoxy)ethyl]morpholin-2-yl]methyl)amino]-3-nitrophenyl)sulfonyl]benzamide;
2-(1H-benzimidazol-4-yloxy)-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[(4-[[4,4-difluorocyclohexyl]methyl]amino]-3-nitrophenyl)sulfonyl]benzamide;
N-[(4-[[4-acetylmorpholin-2-yl]methyl]amino]-3-nitrophenyl)sulfonyl]-2-(1H-benzimidazol-4-yloxy)-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)benzamide;
2-(1H-benzimidazol-4-yloxy)-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[(4-[[4-(methylsulfonyl)morpholin-2-yl]methyl]amino]-3-nitrophenyl)sulfonyl]benzamide;
Trans-2-(1H-benzimidazol-4-yloxy)-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[(4-[[4-cyanocyclohexyl]methyl]amino]-3-nitrophenyl)sulfonyl]benzamide;
2-(1H-benzimidazol-4-yloxy)-N-{(5-chloro-6-[[4,4-difluorocyclohexyl]methoxy]pyridin-3-yl)sulfonyl]-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)benzamide;
and therapeutically acceptable salts, prodrugs, salts of prodrugs and metabolites thereof.

In another aspect, the present invention provides compounds of Formula (V)
and therapeutically acceptable salts, prodrugs, salts of prodrugs and metabolites thereof,
wherein A', B', D', E', Y', R', R', and R' are as described herein for Formula (I), n is 0, 1, 2,
or 3; describing the number of substituents on R', and R' is as described for substituents on
R'.

In one embodiment of Formula (V), A' is N. In another embodiment of Formula (V),
A' is C(A'). In another embodiment of Formula (V), A' is C(A'), and A' is H.

In one embodiment of Formula (V), B' is R', OR', SR', SO₂R', NHR', N(R')₂, or
C(O)NHR'. In another embodiment of Formula (V), B' is NHR'. In another embodiment of
Formula (V), B' is NHR', and A' is C(A'), and A' is H. In another embodiment of Formula
(V), B' is OR'. In another embodiment of Formula (V), B' is OR', and A' is C(A'), and A' is
H.

In one embodiment of Formula (V), D' and E' are H. In another embodiment of
Formula (V), B' is NHR', and A' is C(A'), A' is H, and D' and E' are H. In another
embodiment of Formula (V), B' is OR', and A' is C(A'), A' is H, and D' and E' are H.

In one embodiment of Formula (V), Y' is H, CN, NO₂, F, Cl, Br, I, CF₃, R'₁₇,
NHC(O)R'₁₇, or C(O)NH₂. In another embodiment of Formula (V), Y' is NO₂. In another
embodiment of Formula (V), B' is NHR', and A' is C(A'), A' is H, D', E' are H, and Y' is
NO₂. In another embodiment of Formula (V), Y' is Cl. In another embodiment of Formula
(I), B' is OR', and A' is C(A'), A' is H, D' and E' are H, and Y' is Cl.
In one embodiment of Formula (V), R¹ is R², R³, R⁴ or R⁵. In another embodiment of Formula (V), R¹ is R², and R² is phenyl.

In one embodiment of Formula (V), R¹ is R³, and R³ is heteroaryl. In another embodiment of Formula (V), R³ is triazolyl.

In one embodiment of Formula (V), R¹ is R⁴. In another embodiment of Formula (V), R¹ is R⁴, and R⁴ is cycloalkyl. In another embodiment of Formula (V), R¹ is R⁴, and R⁴ is cyclohexyl. In another embodiment of Formula (V), R¹ is R⁴, and R⁴ is heterocycloalkyl. In another embodiment of Formula (V), R¹ is R⁴, and R⁴ is 8-azabicyclo[3.2.1]octane, azetidinyl, piperidinyl, piperazinyl, pyrrolidinyl, morpholinyl, tetrahydropyranyl, or tetrahydrothiophenyl. In another embodiment of Formula (V), R¹ is R⁴, and R⁴ is heterocycloalkenyl. In another embodiment of Formula (V), R¹ is R⁴, and R⁴ is tetrahydropyridazinyl.

In one embodiment of Formula (V), R¹ is R⁵. In another embodiment of Formula (V), R¹ is R⁵ and R⁵ is alkyl or alkynyl. In another embodiment of Formula (V), R¹ is R⁵ and R⁵ is alkyl which is unsubstituted. In another embodiment of Formula (V), R¹ is R⁵ and R⁵ is alkyl which is substituted with one or two or three independently selected R⁶, R⁷, OR⁷, SR⁷, SO₂R⁷, N(R⁷)₂, OH, CN, CF₃, F, Cl, Br or I substituents. In another embodiment of Formula (V), R¹ is R⁵ and R⁵ is alkyl which is substituted with R⁷.

In one embodiment of Formula (V), R⁷ is R⁸, R⁹, R¹⁰ or R¹¹. In another embodiment of Formula (V), R⁷ is R⁸, and R⁸ is phenyl which is unfused or fused with R⁸⁸A, and R⁸⁸A is heterocycloalkane. In another embodiment of Formula (V), R⁷ is R⁸, and R⁸ is phenyl which is unfused. In another embodiment of Formula (V), R⁷ is R⁹, and R⁹ is heteroaryl. In another embodiment of Formula (V), R⁷ is R⁹, and R⁹ is furanyl, imidazolyl, isothiazolyl, isoxazolyl, 1,2,3-oxadiazoyl, 1,2,5-oxadiazoyl, oxazolyl, pyrazinyl, pyrazolyl, pyridazinyl, pyridinyl, pyrimidinyl, pyrrolyl, tetrazolyl, thiazolyl, thiophenyl, triazinyl or 1,2,3-triazolyl. In another embodiment of Formula (V), R⁷ is R⁹, and R⁹ is pyridinyl, thiazolyl, imidazolyl, and 1,2,3-triazolyl. In another embodiment of Formula (V), R⁷ is R¹⁰, and R¹⁰ is C₃-C₁₀-cycloalkyl. In another embodiment of Formula (V), R⁷ is R¹⁰, and R¹⁰ is C₆ or C₁₀-cycloalkyl. In another embodiment of Formula (V), R⁷ is R¹⁰, and R¹⁰ is cyclohexyl or adamantantyl. In another embodiment of Formula (V), R⁷ is R¹⁰, and R¹⁰ is morpholinyl, piperazinyl, piperidinyl, tetrahydro-2H-pyranyl, 1,2-dihydropyridinyl, pyranyl, pyridin-1(H)-yl, pyrrolidinyl, oxetanyl, thiomorpholinyl, imidazolidinyl, tetrahydrothiophenyl, dioxolanyl,
tetrahydrothiopyranyl, dioxanyl, or tetrahydrofuranyl. In another embodiment of Formula (V), R⁷ is R¹⁰, and R¹⁰ is morpholinyl, piperazinyl, piperidinyl, tetrahydro-2H-pyranyl, 1,2-dihydropyridinyl, pyrrolidinyl, oxetanyl, thiomorpholinyl, imidazolidinyl, tetrahydrothiophenyl, dioxolanyl, tetrahydrothiopyranyl, dioxanyl, or tetrahydrofuranyl. In another embodiment of Formula (V), R⁷ is R¹¹, and R¹¹ is alkyl which is unsubstituted or substituted. In another embodiment of Formula (V), R⁷ is R¹¹, and R¹¹ is alkyl which is unsubstituted. In another embodiment of Formula (V), R⁷ is R¹¹, and R¹¹ is alkyl which is substituted. In another embodiment of Formula (V), R⁷ is R¹¹, and R¹¹ is alkyl which is substituted with one or two or three independently selected OR¹², F, Cl, Br or I substituents.

In another embodiment of Formula (V), R⁷ is R¹¹, R¹¹ is alkyl which is substituted with OR¹², R¹² is R¹⁶, and R¹⁶ is alkyl.

In one embodiment of Formula (V), R¹⁷ is R¹⁹ or R²¹. In another embodiment of Formula (V), R¹⁷ is R¹⁹, and R¹⁹ is heteroaryl. In another embodiment of Formula (V), R¹⁷ is R¹⁹, and R¹⁹ is thiazolyl. In another embodiment of Formula (V), R¹⁷ is R²¹, and R²¹ is alkynyl. In another embodiment of Formula (V), R¹⁷ is R²¹, and R²¹ is ethynyl.

Still another embodiment pertains to compounds having Formula (V) which are N-((5-chloro-6-[(4-fluorotetrahydro-2H-pyran-4-yl)methoxy]pyridin-3-yl)sulfonyl)-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylocyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indazol-4-yloxy)benzamide; 4-(4-[[2-(4-chlorophenyl)-4,4-dimethylocyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-((5-cyano-6-[(4-fluorotetrahydro-2H-pyran-4-yl)methoxy]pyridin-3-yl)sulfonyl)-2-(1H-indazol-4-yloxy)benzamide; 4-(4-[[2-(4-chlorophenyl)-4,4-dimethylocyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[(4-[[4-fluorotetrahydro-2H-pyran-4-yl)methyl]amino]-3-nitrophenyl)sulfonyl]-2-(1H-indazol-4-yloxy)benzamide; 4-(4-[[2-(4-chlorophenyl)-4,4-dimethylocyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[6-[(4-fluorotetrahydro-2H-pyran-4-yl)methoxy]-5-(trifluoromethyl)pyridin-3-yl)sulfonyl]-2-(1H-indazol-4-yloxy)benzamide; 4-(4-[[2-(4-chlorophenyl)-4,4-dimethylocyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[(4-[[4-cyclopropylmorpholin-2-yl)methyl]amino]-3-nitrophenyl)sulfonyl]-2-(1H-indazol-4-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4-
[[4,4-difluorocyclohexyl]methyl]amino]-3-nitrophenyl)sulfonyl]2-(1H-indazol-4-
yloxy)benzamide;

N-[[5-chloro-6-[[((4-fluorotetrahydro-2H-pyran-4-yl)methyl]amino}pyridin-3-yl)sulfonyl]-4-
(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-
diazol-4-yloxy)benzamide;

Trans-N-[[5-chloro-6-[[4-methoxycyclohexyl]methoxy}pyridin-3-yl)sulfonyl]4-(4-[[2-(4-
chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indazol-4-
yloxy)benzamide;

4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[5-
fluoro-6-[[4-fluorotetrahydro-2H-pyran-4-yl]methoxy}pyridin-3-yl)sulfonyl]2-(1H-indazol-
4-yloxy)benzamide;

N-[[5-chloro-6-[[1-(cyanomethyl)-4-fluoropiperidin-4-yl]methoxy}pyridin-3-yl)sulfonyl]-4-
(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-
diazol-4-yloxy)benzamide;

4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[5-
chloro-6-(tetrahydrofuran-3-ylmethoxy}pyridin-3-yl)sulfonyl]-2-(1H-indazol-4-
yloxy)benzamide;

Trans-N-[[5-chloro-6-[[4-hydroxycyclohexyl]methoxy}pyridin-3-yl)sulfonyl]-4-(4-[[2-(4-
chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indazol-4-
yloxy)benzamide;

N-[[5-chloro-6-[[3(R)-1-(2,2-difluoroethyl}pyrrolidin-3-yl]oxy}pyridin-3-yl)sulfonyl]-4-(4-
[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indazol-
4-yloxy)benzamide;

N-[[5-chloro-6-[[[2S]-4-(N,N-diethylglycyl)morpholin-2-yl]methoxy}pyridin-3-
yl)sulfonyl]-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-
yl)-2-(1H-indazol-4-yloxy)benzamide;

N-[[5-chloro-6-[[[2R]-4-(N,N-diethylglycyl)morpholin-2-yl]methoxy}pyridin-3-
yl)sulfonyl]-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-
yl)-2-(1H-indazol-4-yloxy)benzamide;

4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[5-
chloro-6-(tetrahydro-2H-pyran-4-ylmethoxy}pyridin-3-yl)sulfonyl]-2-(1H-indazol-4-
yloxy)benzamide;
N-[[5-chloro-6-[[3R]-1-[2-fluoro-1-(fluoromethyl)ethyl]pyrrolidin-3-yl]sulfonyl]-4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl]-2-(1H-indazol-4-yloxy)benzamide;
4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[3R]-1-[2-fluoro-1-(fluoromethyl)ethyl]pyrrolidin-3-yl]amino)-3-nitrophenyl]sulfonyl]-2-(1H-indazol-4-yloxy)benzamide;
4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[1-cyclopropylpiperidin-4-yl]amino]-3-nitrophenyl]sulfonyl]-2-(1H-indazol-4-yloxy)benzamide;

Trans-4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl]-2-(1H-indazol-4-yloxy)-N-[[4-[[4-methoxy(cyclohexyl)methyl]amino]-3-nitrophenyl]sulfonyl]benzamide;
4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl]-N-[[4-(1,4-dioxan-2-ylmethoxy)-3-nitrophenyl]sulfonyl]-2-(1H-indazol-4-yloxy)benzamide;
N-[[5-chloro-6-[[1-cyclopropylpiperidin-4-yl]amino]pyrindin-3-yl]sulfonyl]-4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indazol-4-yloxy)benzamide;
2-(1H-benzimidazol-4-yloxy)-N-[[5-chloro-6-[[1-cyclopropylpiperidin-4-yl]amino]pyridin-3-yl]sulfonyl]-4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl]benzamide;
4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl]-N-[[6-(1,4-fluoro-1-[2-fluoro-1-(fluoromethyl)ethyl]piperidin-4-yl]methoxy]-5-(trifluoromethyl)pyridin-3-yl]sulfonyl]-2-(1H-indazol-4-yloxy)benzamide;
4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl]-N-[[5-chloro-6-(2-tetrahydrofuran-2-ylethoxy)pyridin-3-yl]sulfonyl]-2-(1H-indazol-4-yloxy)benzamide;
N-[[3-chloro-4-[(4-fluorotetrahydro-2H-pyran-4-yl)methoxy]phenyl]sulfonyl]-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indazol-4-yloxy)benzamide;
N-[[5-chloro-6-[(4-fluorotetrahydro-2H-pyran-4-yl)methoxy]pyridin-3-yl]sulfonyl]-4-(4-[[4-(4-chlorophenyl)-6,6-dimethyl-5,6-dihydro-2H-pyran-3-yl]methyl]piperazin-1-yl)-2-(1H-indazol-4-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[5-cyano-6-(2-tetrahydro-2H-pyran-4-yloxy)pyridin-3-yl]sulfonyl]-2-(1H-indazol-4-yloxy)benzamide;
and therapeutically acceptable salts, prodrugs, salts of prodrugs and metabolites thereof.

Pharmaceutical Compositions, Combination Therapies, Methods of Treatment, and Administration

Another embodiment comprises pharmaceutical compositions comprising a compound having Formula (I) and an excipient.

Still another embodiment comprises methods of treating cancer in a mammal comprising administering thereto a therapeutically acceptable amount of a compound having Formula (I).

Still another embodiment comprises methods of treating autoimmune disease in a mammal comprising administering thereto a therapeutically acceptable amount of a compound having Formula (I).

Still another embodiment pertains to compositions for treating diseases during which anti-apoptotic Bcl-2 proteins are expressed, said compositions comprising an excipient and a therapeutically effective amount of the compound having Formula (I).

Still another embodiment pertains to methods of treating disease in a patient during which anti-apoptotic Bcl-2 proteins are expressed, said methods comprising administering to the patient a therapeutically effective amount of a compound having Formula (I).

Still another embodiment pertains to compositions for treating bladder cancer, brain cancer, breast cancer, bone marrow cancer, cervical cancer, chronic lymphocytic leukemia, colorectal cancer, esophageal cancer, hepatocellular cancer, lymphoblastic leukemia, follicular lymphoma, lymphoid malignancies of T-cell or B-cell origin, melanoma, myelogenous leukemia, myeloma, oral cancer, ovarian cancer, non-small cell lung cancer, prostate cancer, small cell lung cancer or spleen cancer, said compositions comprising an excipient and a therapeutically effective amount of the compound having Formula (I).
Still another embodiment pertains to methods of treating bladder cancer, brain cancer, breast cancer, bone marrow cancer, cervical cancer, chronic lymphocytic leukemia, colorectal cancer, esophageal cancer, hepatocellular cancer, lymphoblastic leukemia, follicular lymphoma, lymphoid malignancies of T-cell or B-cell origin, melanoma, myelogenous leukemia, myeloma, oral cancer, ovarian cancer, non-small cell lung cancer, prostate cancer, small cell lung cancer or spleen cancer in a patient, said methods comprising administering to the patient a therapeutically effective amount of a compound having Formula (I).

Still another embodiment pertains to compositions for treating diseases during which are expressed anti-apoptotic Bcl-2 proteins, said compositions comprising an excipient and a therapeutically effective amount of the compound having Formula (I) and a therapeutically effective amount of one additional therapeutic agent or more than one additional therapeutic agent.

Still another embodiment pertains to methods of treating disease in a patient during which are expressed anti-apoptotic Bcl-2 proteins, said methods comprising administering to the patient a therapeutically effective amount of a compound having Formula (I) and a therapeutically effective amount of one additional therapeutic agent or more than one additional therapeutic agent.

Still another embodiment pertains to compositions for treating bladder cancer, brain cancer, breast cancer, bone marrow cancer, cervical cancer, chronic lymphocytic leukemia, colorectal cancer, esophageal cancer, hepatocellular cancer, lymphoblastic leukemia, follicular lymphoma, lymphoid malignancies of T-cell or B-cell origin, melanoma, myelogenous leukemia, myeloma, oral cancer, ovarian cancer, non-small cell lung cancer, chronic lymphocytic leukemia, myeloma, prostate cancer, small cell lung cancer or spleen cancer, said compositions comprising an excipient and a therapeutically effective amount of the compound having Formula (I) and a therapeutically effective amount of one additional therapeutic agent or more than one additional therapeutic agent.

Still another embodiment pertains to methods of treating bladder cancer, brain cancer, breast cancer, bone marrow cancer, cervical cancer, chronic lymphocytic leukemia, colorectal cancer, esophageal cancer, hepatocellular cancer, lymphoblastic leukemia, follicular lymphoma, lymphoid malignancies of T-cell or B-cell origin, melanoma, myelogenous leukemia, myeloma, oral cancer, ovarian cancer, non-small cell lung cancer, chronic lymphocytic leukemia, myeloma, prostate cancer, small cell lung cancer or spleen cancer in a patient, said methods comprising administering to the patient a therapeutically effective
amount of the compound having Formula (I) and a therapeutically effective amount of one additional therapeutic agent or more than one additional therapeutic agent.

Metabolites of compounds having Formula I, produced by in vitro or in vivo metabolic processes, may also have utility for treating diseases associated with anti-apoptotic Bcl-2 protein.

Certain precursor compounds which may be metabolized in vitro or in vivo to form compounds having Formula I may also have utility for treating diseases associated with expression of anti-apoptotic Bcl-2 protein.

Compounds having Formula I may exist as acid addition salts, basic addition salts or zwitterions. Salts of the compounds are prepared during isolation or following purification of the compounds. Acid addition salts of the compounds are those derived from the reaction of the compounds with an acid. For example, the acetate, adipate, alginate, bicarbonate, citrate, aspartate, benzoate, benzenesulfonate, bisulfate, butyrate, camphorate, camphorsulfonate, digluconate, formate, fumarate, glycerophosphate, glutamate, hemisulfate, heptanoate, hexanoate, hydrochloride, hydrobromide, hydroiodide, lactobionate, lactate, maleate, mesitylenesulfonate, methanesulfonate, naphthylenesulfonate, nicotinate, oxalate, pamoate, pectinate, persulfate, phosphate, picrate, propionate, succinate, tartrate, thiocyanate, trichloroacetic, trifluoroacetic, para-toluenesulfonate, and undecanoate salts of the compounds and prodrugs thereof are contemplated as being embraced by this invention.

Basic addition salts of the compounds are those derived from the reaction of the compounds with the hydroxide, carbonate or bicarbonate of cations such as lithium, sodium, potassium, calcium, and magnesium.

The compounds having Formula I may be administered, for example, buccally, ophthalmically, orally, osmotically, parenterally (intramuscularly, intraperitoneally intrasternally, intravenously, subcutaneously), rectally, topically, transdermally, or vaginally.

Therapeutically effective amounts of compounds having Formula I depend on the recipient of the treatment, the disorder being treated and the severity thereof, the composition containing the compound, the time of administration, the route of administration, the duration of treatment, the compound potency, its rate of clearance and whether or not another drug is co-administered. The amount of a compound of this invention having Formula I used to make a composition to be administered daily to a patient in a single dose or in divided doses is from about 0.03 to about 200 mg/kg body weight. Single dose compositions contain these amounts or a combination of submultiples thereof.
Compounds having Formula I may be administered with or without an excipient. Excipients include, for example, encapsulating materials or additives such as absorption accelerators, antioxidants, binders, buffers, coating agents, coloring agents, diluents, disintegrating agents, emulsifiers, extenders, fillers, flavoring agents, humectants, lubricants, perfumes, preservatives, propellants, releasing agents, sterilizing agents, sweeteners, solubilizers, wetting agents and mixtures thereof.

Excipients for preparation of compositions comprising a compound having Formula I to be administered orally in solid dosage form include, for example, agar, alginic acid, aluminum hydroxide, benzyl alcohol, benzyl benzoate, 1,3-butylene glycol, caromers, castor oil, cellulose, cellulose acetate, cocoa butter, corn starch, corn oil, cottonseed oil, cross-povidone, diglycerides, ethanol, ethyl cellulose, ethyl laureate, ethyl oleate, fatty acid esters, gelatin, germ oil, glucose, glycerol, groundnut oil, hydroxypropylmethyl cellulose, isopropanol, isotonic saline, lactose, magnesium hydroxide, magnesium stearate, malt, mannitol, monoglycerides, olive oil, peanut oil, potassium phosphate salts, potato starch, povidone, propylene glycol, Ringer's solution, safflower oil, sesame oil, sodium carboxymethyl cellulose, sodium phosphate salts, sodium lauryl sulfate, sodium sorbitol, soybean oil, stearic acids, stearyl fumarate, sucrose, surfactants, talc, tragacanth, tetrahydrofurfuryl alcohol, triglycerides, water, and mixtures thereof. Excipients for preparation of compositions comprising a compound of this invention having Formula I to be administered ophthalmically or orally in liquid dosage forms include, for example, 1,3-butylene glycol, castor oil, corn oil, cottonseed oil, ethanol, fatty acid esters of sorbitan, germ oil, groundnut oil, glycerol, isopropanol, olive oil, polyethylene glycols, propylene glycol, sesame oil, water and mixtures thereof. Excipients for preparation of compositions comprising a compound of this invention having Formula I to be administered osmotically include, for example, chlorofluorohydrocarbons, ethanol, water and mixtures thereof.

Excipients for preparation of compositions comprising a compound of this invention having Formula I to be administered parenterally include, for example, 1,3-butanediol, castor oil, corn oil, cottonseed oil, dextrose, germ oil, groundnut oil, liposomes, oleic acid, olive oil, peanut oil, Ringer's solution, safflower oil, sesame oil, soybean oil, U.S.P. or isotonic sodium chloride solution, water and mixtures thereof. Excipients for preparation of compositions comprising a compound of this invention having Formula I to be administered rectally or vaginally include, for example, cocoa butter, polyethylene glycol, wax and mixtures thereof.

Compounds having Formula (I) are expected to be useful when used with alkylating agents, angiogenesis inhibitors, antibodies, antimetabolites, antimitotics, antiproliferatives,
antivirals, aurora kinase inhibitors, other apoptosis promoters (for example, Bcl-xL, Bcl-w and Bfl-1) inhibitors, activators of death receptor pathway, Bcr-Abl kinase inhibitors, BiTE (Bi-Specific T cell Engager) antibodies, antibody drug conjugates, biologic response modifiers, cyclin-dependent kinase inhibitors, cell cycle inhibitors, cyclooxygenase-2 inhibitors, DVDs, leukemia viral oncogene homolog (ErbB2) receptor inhibitors, growth factor inhibitors, heat shock protein (HSP)-90 inhibitors, histone deacetylase (HDAC) inhibitors, hormonal therapies, immunologicals, inhibitors of inhibitors of apoptosis proteins (IAPs), intercalating antibiotics, kinase inhibitors, kinesin inhibitors, Jak2 inhibitors, mammalian target of rapamycin inhibitors, microRNA’s, mitogen-activated extracellular signal-regulated kinase inhibitors, multivalent binding proteins, non-steroidal anti-inflammatory drugs (NSAIDs), poly ADP (adenosine diphosphate)-ribose polymerase (PARP) inhibitors, platinum chemotherapeutics, polo-like kinase (Plk) inhibitors, phosphoinositide-3 kinase (PI3K) inhibitors, proteosome inhibitors, purine analogs, pyrimidine analogs, receptor tyrosine kinase inhibitors, etinoids/deltoids plant alkaloids, small inhibitory ribonucleic acids (siRNAs), topoisomerase inhibitors, ubiquitin ligase inhibitors, and the like, and in combination with one or more of these agents.

BiTE antibodies are bi-specific antibodies that direct T-cells to attack cancer cells by simultaneously binding the two cells. The T-cell then attacks the target cancer cell. Examples of BiTE antibodies include adecatumumab (Micromet MT201), blinatumomab (Micromet MT103) and the like. Without being limited by theory, one of the mechanisms by which T-cells elicit apoptosis of the target cancer cell is by exocytosis of cytolytic granule components, which include perforin and granzyme B. In this regard, Bcl-2 has been shown to attenuate the induction of apoptosis by both perforin and granzyme B. These data suggest that inhibition of Bcl-2 could enhance the cytotoxic effects elicited by T-cells when targeted to cancer cells (V.R. Sutton, D.L. Vaux and J.A. Trapani, J. of Immunology 1997, 158 (12), 5783).

SiRNAs are molecules having endogenous RNA bases or chemically modified nucleotides. The modifications do not abolish cellular activity, but rather impart increased stability and/or increased cellular potency. Examples of chemical modifications include phosphorothioate groups, 2'-deoxynucleotide, 2'-OCH3-containing ribonucleotides, 2'-F-ribonucleotides, 2'-methoxyethyl ribonucleotides, combinations thereof and the like. The siRNA can have varying lengths (e.g., 10-200 bps) and structures (e.g., hairpins, single/double strands, bulges, nicks/gaps, mismatches) and are processed in cells to provide active gene silencing. A double-stranded siRNA (dsRNA) can have the same number of
nucleotides on each strand (blunt ends) or asymmetric ends (overhangs). The overhang of 1-2 nucleotides can be present on the sense and/or the antisense strand, as well as present on the 5'- and/or the 3'-ends of a given strand. For example, siRNAs targeting McI-1 have been shown to enhance the activity of ABT-263, (i.e., N-(4-(4-((2-(4-chlorophenyl))-5,5-dimethyl-1-cyclohex-1-en-1-yl)methyl) piperazin-1-yl)benzoyl)-4-(((1R)-3-(morpholin-4-yl)-1-((phenylsulfanyl)methyl)propyl)amino)-3-((trifluoromethyl)sulfonyl)benzenesulfonamide) or ABT-737 (i.e., N-(4-(4-((4'-chloro(1,1'-biphenyl)-2-yl)methyl)piperazin-1-yl)benzoyl)-4-(((1R)-3-(dimethylamino)-1-((phenylsulfanyl)methyl)propyl)amino)-3-nitrobenzenesulfonamide) in multiple tumor cell lines (Tse et al., Cancer Research 2008, 68(9), 3421 and references therein).

Multivalent binding proteins are binding proteins comprising two or more antigen binding sites. Multivalent binding proteins are engineered to have the three or more antigen binding sites and are generally not naturally occurring antibodies. The term “multispecific binding protein” means a binding protein capable of binding two or more related or unrelated targets. Dual variable domain (DVD) binding proteins are tetravalent or multivalent binding proteins binding proteins comprising two or more antigen binding sites. Such DVDs may be monospecific (i.e., capable of binding one antigen) or multispecific (i.e., capable of binding two or more antigens). DVD binding proteins comprising two heavy chain DVD polypeptides and two light chain DVD polypeptides are referred to as DVD Ig's. Each half of a DVD Ig comprises a heavy chain DVD polypeptide, a light chain DVD polypeptide, and two antigen binding sites. Each binding site comprises a heavy chain variable domain and a light chain variable domain with a total of 6 CDRs involved in antigen binding per antigen binding site. Multispecific DVDs include DVD binding proteins that bind DLL4 and VEGF, or C-met and EGFR or ErbB3 and EGFR.

Alkylation agents include altretamine, AMD-473, AP-5280, apaziquone, bendamustine, brostallicin, busulfan, carboquone, carmustine (BCNU), chlorambucil, CLORETAZINE® (laromustine, VNP 40101M), cyclophosphamide, decarbazine, estramustine, fotemustine, glufosfamide, ifosfamide, KW-2170, lomustine (CCNU), mafosfamide, melphalan, mitobronitol, mitolactol, nimustine, nitrogen mustard N-oxide, ranimustine, temozolomide, thiotepa, TREANDA® (bendamustine), treosulfan, rofosfamide and the like.

Angiogenesis inhibitors include endothelial-specific receptor tyrosine kinase (Tie-2) inhibitors, epidermal growth factor receptor (EGFR) inhibitors, insulin growth factor-2 receptor (IGFR-2) inhibitors, matrix metalloproteinase-2 (MMP-2) inhibitors, matrix
metalloproteinase-9 (MMP-9) inhibitors, platelet-derived growth factor receptor (PDGFR) inhibitors, thrombospondin analogs, vascular endothelial growth factor receptor tyrosine kinase (VEGFR) inhibitors and the like.

Antimetabolites include ALIMTA® (pemetrexed disodium, LY231514, MTA), 5-azacitidine, XELODA® (capecitabine), carmofur, LEUSTAT® (cladribine), clofarabine, cytarabine, cytarabine ocosfate, cytosine arabinoside, decitabine, deferoxamine, doxifluridine, eflophos, EICAR (5-ethyl-1-β-D-ribofuranosylimidazole-4-carboxamide), enocitabine, ethynylcytidine, fludarabine, 5-fluorouracil alone or in combination with leucovorin, GEMZAR® (gemcitabine), hydroxyurica, ALKERAN® (melphalan), mercaptopurine, 6-mercaptopurine riboside, methotrexate, mycophenolic acid, nelarabine, nolatrexed, ocsfate, pelitrexol, pentostatin, raltitrexed, Ribvirin, triapine, trimetrexate, S-1, tiazofurin, tegafur, TS-1, vidarabine, UFT and the like.

Antivirals include ritonavir, hydroxychloroquine and the like.

Aurora kinase inhibitors include ABT-348, AZD-1152, MLN-8054, VX-680, Aurora A-specific kinase inhibitors, Aurora B-specific kinase inhibitors and pan-Aurora kinase inhibitors and the like.

Bcl-2 protein inhibitors include AT-101 ((-)gossypol), GENASENSE® (G3139 or oblimersen (Bcl-2-targeting antisense oligonucleotide)), IPI-194, IPI-565, N-(4-(4-((4′-chboro(1,1′-biphenyl)-2-yl)methyl)piperazin-1-yl)benzoyl)-4-(((1R)-3-(dimethylamino)-1-((phenylsulfonyl)methyl)propyl)amino)-3-nitrobenzenesulfonamide) (ABT-737), N-(4-(4-(2-(4-chlorophenyl)-5,5-dimethyl-1-cyclohex-1-en-1-yl)methyl)piperazin-1-yl)benzoyl)-4-(((1R)-3-(morpholin-4-yl)-1-((phenylsulfonyl)methyl)propyl)amino)-3-((trifluoromethyl)sulfonyl)benzenesulfonamide (ABT-263), GX-070 (obatoclax) and the like.

Bcr-Abl kinase inhibitors include DASATINIB® (BMS-354825), GLEEVEC® (imatinib) and the like.

CDK inhibitors include AZD-5438, BMI-1040, BMS-032, BMS-387, CVT-2584, flavopyridol, GPC-286199, MCS-5A, PD0332991, PHA-690509, seliciclib (CYC-202, R-roscovitine), ZK-304709 and the like.

COX-2 inhibitors include ABT-963, ARCOXIA® (etoricoxib), BEXTRA® (valdecoxib), BMS347070, CELEBREX® (celecoxib), COX-189 (lumiracoxib), CT-3, DERAMAXX® (deracoxib), JTE-522, 4-methyl-2-(3,4-dimethylphenyl)-1-(4-sulfamoylphenyl-1H-pyrrole), MK-663 (etoricoxib), NS-398, parecoxib, RS-57067, SC-58125, SD-8381, SVE-2016, S-2474, T-614, VIOXX® (rofecoxib) and the like.
EGFR inhibitors include ABX-EGF, anti-EGFR immunoliposomes, EGF-vaccine, EMD-7200, ERBITUX® (cetuximab), HR3, IgA antibodies, IRESSA® (gefitinib), TARCEVA® (erlotinib or OSI-774), TP-38, EGFR fusion protein, TYKERB® (lapatinib) and the like.

ErbB2 receptor inhibitors include CP-724-714, CI-1033 (canertinib), HERCEPTIN® (trastuzumab), TYKERB® (lapatinib), OMNITARG® (2C4, pertuzumab), TAK-165, GW-572016 (ionafarnib), GW-282974, EKB-569, PI-166, dHER2 (HER2 vaccine), APC-8024 (HER-2 vaccine), anti-HER/2neu bispecific antibody, B7.her2IgG3, AS HER2 trifunctional bispecific antibodies, mAB AR-209, mAB 2B-1 and the like.

Histone deacetylase inhibitors include depsipeptide, LAQ-824, MS-275, trapoxin, suberoylanilide hydroxamic acid (SAHA), TSA, valproic acid and the like.

HSP-90 inhibitors include 17-AAG-nab, 17-AAG, CNF-101, CNF-1010, CNF-2024, 17-DMAG, geldanamycin, IPI-504, KOS-953, MYCOGRAB® (human recombinant antibody to HSP-90), NCS-683664, PU24FC1, PU-3, radicicol, SNX-2112, STA-9090 VER49009 and the like.

Inhibitors of inhibitors of apoptosis proteins include HGS1029, GDC-0145, GDC-0152, LCL-161, LBW-242 and the like.


Activators of death receptor pathway include TRAIL, antibodies or other agents that target TRAIL or death receptors (e.g., DR4 and DR5) such as Apomab, conatumumab, ETR2-ST01, GDC0145, (lexatumumab), HGS-1029, LBY-135, PRO-1762 and trastuzumab.

Kinesin inhibitors include Eg5 inhibitors such as AZD4877, ARRY-520; CENPE inhibitors such as GSK923295A and the like.

JAK-2 inhibitors include CEP-701 (lesaurtinib), XL019 and INCB018424 and the like.

MEK inhibitors include ARRY-142886, ARRY-438162 PD-325901, PD-98059 and the like.

mTOR inhibitors include AP-23573, CCI-779, everolimus, RAD-001, rapamycin, temsirolimus, ATP-competitive TORC1/TORC2 inhibitors, including PI-103, PP242, PP30, Torin 1 and the like.

Non-steroidal anti-inflammatory drugs include AMIGESIC® (salsalate), DOLOBID® (diflunisal), MOTRIN® (ibuprofen), ORUDIS® (ketoprofen), RELAFEN® (nabumetone),
FELDENE® (piroxicam), ibuprofen cream, ALEVE® (naproxen) and NAPROSYN® (naproxen), VOLTAREN® (diclofenac), INDOCIN® (indomethacin), CLINORIL® (sulindac), TOLECTIN® (tolmetin), LODINE® (etodolac), TORADOL® (ketorolac), DAYPRO® (oxaprozin) and the like.

PDGFR inhibitors include C-451, CP-673, CP-868596 and the like.

Platinum chemotherapeutics include cisplatin, ELOXATIN® (oxaliplatin) eptaplatin, lobaplatin, nedaplatin, PARAPLATIN® (carboplatin), satraplatin, picoplatin and the like.

Polo-like kinase inhibitors include BI-2536 and the like.

Phosphoinositide-3 kinase (PI3K) inhibitors include wortmannin, LY294002, XL-147, CAL-120, ONC-21, AEZS-127, ETP-45658, PX-866, GDC-0941, BGT226, BEZ235, XL765 and the like.

Thrombospondin analogs include ABT-510, ABT-567, ABT-898, TSP-1 and the like.

VEGFR inhibitors include AVASTIN® (bevacizumab), ABT-869, AEE-788, ANGIOZYME™ (a ribozyme that inhibits angiogenesis (Ribozyme Pharmaceuticals (Boulder, CO.) and Chiron, (Emeryville, CA)), axitinib (AG-13736), AZD-2171, CP-547,632, IM-862, MACUGEN (pegaptanib), NEXAVAR® (sorafenib, BAY43-9006), pazopanib (GW-786034), vatalanib (PTK-787, ZK-222584), SUTENT® (sunitinib, SU-11248), VEGF trap, ZACTIMA™ (vandetanib, ZD-6474), GA101, ofatumumab, ABT-806 (mAb-806), ErbB3 specific antibodies, BSG2 specific antibodies, DLL4 specific antibodies and C-met specific antibodies, and the like.

Antibiotics include intercalating antibiotics aclacinomycin aclarubicin, actinomycin D, amrubcin, annamycin, adriamycin, BLENDOXANE® (bleomycin), daunorubicin, CAELYX® or MYOCET® (liposomal doxorubicin), elasmicrin, epirubicin, glarubicin, ZAVEDOS® (idarubicin), mitomycin C, nemorubicin, neocarzinostatin, peplomycin, pirarubicin, rebeccamycin, stimulamer, streptozocin, VALSTAR® (valrubicin), zinostatin and the like.

Topoisomerase inhibitors include aclacinomycin, 9-aminocamptothecin, amonafide, amsacrine, becactecarin, belotecan, BN-80915, CAMPTOSAR® (irinotecan hydrochloride), camptothecin, CARDIOXAN® (dextrazoxine), diplomotecan, edotecarin, ELENCE® or PHARMORUBICIN® (epirubicin), etoposide, exatecan, 10-hydroxycamptothecin, gimatecan, lurtotecan, mitoxantrone, orathecin, pirarubicin, pixantrone, rubitecan, sobuzoxane, SN-38, tafluposide, topotecan and the like.

Antibodies include AVASTIN® (bevacizumab), CD40-specific antibodies, chTNT-1/B, denosumab, ERBITUX® (cetuximab), HUMAX-CD4® (zanolimumab), IGF1R-specific
antibodies, lintuzumab, PANOREX® (edrecolomab), RENCAREX® (WX G250),
RITUXAN® (rituximab), ticilimumab, trastuzumab, CD20 antibodies types I and II and the like.

Hormonal therapies include ARIMIDEX® (anastrozole), AROMASIN® (exemestane),
arzoxifene, CASODEX® (bicalutamide), CETROTIDE® (cetrorelix), degarelix, deslorelin,
DESOPAN® (trilostane), dexamethasone, DROGENIL® (flutamide), EVISTA® (raloxifene),
AFEMA™ (fadrozole), FARESTON® (toremifene), FASLODEX® (fulvestrant), FEMARA®
(letrozole), formestane, glucocorticoids, HECTOROL® (doxercalciferol), RENAGEL®
(sevelamer carbonate), lasofoxifene, leuprolide acetate, MEGACE® (megestrol),
MIFEPREX® (mifepristone), NILANDRON™ (nilutamide), NOLVADEX® (tamoxifen citrate),
PLENAXISTM (abarelix), prednisone, PROPECIA® (finasteride), rilostane,
SUPREFACT® (buserelin), TRELSTAR® (luteinizing hormone releasing hormone (LHRH)),
VANTAS® (Histrelin implant), VETORYL® (trilostane or modrastane), ZOLADEX®
(fosrelin, goserelin) and the like.

Deltoids and retinoids include seocalcitol (EB1089, CB1093), lexacalcitrol
(KH1060), fenretinide, PANRETIN® (aliretinoin), ATRAGEN® (liposomal tretinoin),
TARGETET® (bexarotene), LGD-1550 and the like.

PARP inhibitors include ABT-888 (veliparib), olaparib, KU-59436, AZD-2281, AG-
014699, BSI-201, BGP-15, INO-1001, ONO-2231 and the like.

Plant alkaloids include, but are not limited to, vincristine, vinblastine, vindesine,
vinorelbine and the like.

Proteasome inhibitors include VELCADE® (bortezomib), MG132, NPI-0052, PR-171
and the like.

Examples of immunologicals include interferons and other immune-enhancing agents.

Interferons include interferon alpha, interferon alpha-2a, interferon alpha-2b, interferon beta,
interferon gamma-1a, ACTIMMUNE® (interferon gamma-1b) or interferon gamma-n1,
combinations thereof and the like. Other agents include ALFAFERONE®,(IFN-α), BAM-
002 (oxidized glutathione), BEROMUN® (tasonermin), BEXXAR® (tositumomab),
CAMPATH® (alemtuzumab), CTLA4 (cytotoxic lymphocyte antigen 4), decarbazine,
denileukin, epratuzumab, GRANOCYTE® (lenograstim), lentinan, leukocyte alpha
interferon, imiquimod, MDX-010 (anti-CTLA-4), melanoma vaccine, mitomomab,
molgramostim, MYLOTARG™ (gemtuzumab ozogamicin), NEUPOGEN® (filgrastim),
OncoVAC-CL, OVAREX® (oregovomab), pemtumomab (Y-muHMFG1), PROVENGE®
(sipuleucel-T), sargaramostim, sizofiran, teceleukin, THERACYSTM (Bacillus Calmette-Guerin), ubenimex, VIRULIZINSTM (immunotherapeutic, Lorus Pharmaceuticals), Z-100 (Specific Substance of Maruyama (SSM)), WF-10 (Tetrachlorodecto dine (TCDO)), PROLEUKINSTM (aldesleukin), ZADAXINSTM (thymalfasin), ZENAPAXSTM (daclizumab), ZEVALINSTM (90Y-Ibritumomab tiuxetan) and the like.

Biological response modifiers are agents that modify defense mechanisms of living organisms or biological responses, such as survival, growth or differentiation of tissue cells to direct them to have anti-tumor activity and include krestin, lentini an, sizofiran, picibanil PF-3512676 (CpG-8954), ubenimex and the like.

Pyrimidine analogs include cytarabine (ara C or Arabinoside C), cytosine arabinoside, doxifluoridine, FLUDARA® (fludarabine), 5-FU (5-fluorouracil), floxuridine, GEMZARSTM (gemcitabine), TOMUDEXSTM (ratitrexed), TROXATYL™ (triacetyluridine troxacitabine) and the like.

Purine analogs include LANVISSTM (thioguanine) and PURI-NETHOLSTM (mercaptopurine).

Antimitotic agents include batabulin, epothilone D (KOS-862), N-(2-((4-hydroxyphenyl)amino)pyridin-3-yl)-4-methoxybenzenesulfonamide, ixabepilone (BMS 247550), paclitaxel, TAXOTERESTM (docetaxel), PNU100940 (109881), patupilone, XRP-9881 (larotaxel), vinflunine, ZK-EPO (synthetic epothilone) and the like.

Ubiquitin ligase inhibitors include MDM2 inhibitors, such as nutlins, NEDD8 inhibitors such as MLN4924 and the like.

Compounds of this invention can also be used as radiosensitizers that enhance the efficacy of radiotherapy. Examples of radiotherapy include external beam radiotherapy, teletherapy, brachytherapy and sealed, unsealed source radiotherapy and the like.

Additionally, compounds having Formula (I) may be combined with other chemotherapeutic agents such as ABRAXANESTM (ABI-007), ABT-100 (farnesyl transferase inhibitor), ADVEXINSTM (Ad5CMV-p53 vaccine), ALTOCORSTM or MEVACORSTM (lovastatin), AMPLIGENSTM (poly L:poly C12U, a synthetic RNA), APTSYSSTM (exisulind), AREDJSTM (pamidronic acid), arglabin, L-asparaginase, atamestane (1-methyl-3,17-dione-androsta-1,4-diene), AVAGESTM (tazarotene), AVE-8062 (combreastatin derivative) BEC2 (mitomobab), cachectin or cachexin (tumor necrosis factor), canaxvin (vaccine), CEAVACSTM (cancer vaccine), CELEUKSTM (celmoleukin), CEPLENESTM (histamine dihydrochloride), CERVARIXTM (human papillomavirus vaccine), CHOPSTM (C: CYTOXANSTM (cyclophosphamide); H: ADRIAMYCINSTM (hydroxydoxorubicin); O: Vincristine (ONCOVINSTM); P: prednisone),
CYPAT™ (cyproterone acetate), combrestatin A4P, DAB(389)EGF (catalytic and translocation domains of diphtheria toxin fused via a His-Ala linker to human epidermal growth factor) or TransMID-107R™ (diphtheria toxins), dacarbazine, dactinomycin, 5,6-dimethylxanthene-4-acetic acid (DMXAA), eniluracil, EVIZON™ (squalamine lactate), DIMERICINE® (T4N5 liposome lotion), discodermolide, DX-8951f (exatecan mesylate), enzastaurin, EPO906 (epithilone B), GARDASIL® (quadrivalent human papillomavirus (Types 6, 11, 16, 18) recombinant vaccine), GASTRIMMUNE®, GENASENSE®, GMK (ganglioside conjugate vaccine), GVAX® (prostate cancer vaccine), halofuginone, histerelin, hydroxycarbamide, ibandronic acid, IGN-101, IL-13-PE38, IL-13-PE38QQR (cintredekin besudotox), IL-13-pseudomonas exotoxin, interferon-α, interferon-γ, JUNOVAN™ or MEPACT™ (mifamurtide), lonafarnib, 5,10-methylenetetrahydrofolate, miltefosine (hexadecylphosphocholine), NEOVASTAT®(AE-941), NEUTREXIN® (trimetrexate glucuronate), NIPENT® (pentostatin), ONCONASE® (a ribonuclease enzyme), ONCOPHAGE® (melanoma vaccine treatment), ONCOVAX® (IL-2 Vaccine), ORATHECIN™ (rubitecan), OSIDEM® (antibody-based cell drug), OVAREX® MAb (murine monoclonal antibody), paclitaxel, PANDIMEX™ (aglycone saponins from ginseng comprising 20(S)protopanaxadiol (aPPD) and 20(S)protopanaxatriol (aPPT)), panitumumab, PANVAC®-VF (investigational cancer vaccine), pegasparagase, PEG Interferon A, phenoxodiol, procarbazine, rebimastat, REMOVAB® (catumaxomab), REVLIMID® (lenalidomide), RSR13 (efaproxiral), SOMATULINE® LA (lanreotide), SORIATANE® (acitretin), staurosporine (Streptomyces staurospores), talabostat (PT100), TARGRETIN® (bexarotene), TAXOPREXIN® (DHA-paclitaxel), TELCYTA® (canfosfamide, TLK286), temilifene, TEMODAR® (temozolomide), tesmilifene, thalidomide, THERATOPE® (STnKLH), thymitaq (2-amino-3,4-dihydro-6-methyl-4-oxo-5-(4-pyridylthio)quinazoline dihydrochloride), TNFERADE™ (adenovector: DNA carrier containing the gene for tumor necrosis factor-α), TRACLEER® or ZAVESCA® (bosentan), tretinoin (Retin-A), tetrandrine, TRISENOX® (arsenic trioxide), VIRULIZIN®, ukrain (derivative of alkaloids from the greater celandine plant), vitaxin (anti-alpha-beta3 antibody), XCYTRIN® (motexafin gadolinium), XINLAY™ (atrasentan), XYOTAX™ (paclitaxel poliglumex), YONDELIS® (trabectedin), ZD-6126, ZINECARD® (dextrazoxane), ZOMETA® (zolendronic acid), zorubicin and the like.

Data

Determination of the utility of compounds having Formula I as binders to and inhibitors of anti-apoptotic Bcl-2 and Bcl-xL proteins was performed using the Time
Resolved-Fluorescence Resonance Energy Transfer (TR-FRET) Assay. Tb-anti-GST antibody was purchased from Invitrogen (Catalog No. PV4216).

**Probe Synthesis**

All reagents were used as obtained from the vendor unless otherwise specified.

Peptide synthesis reagents including diisopropylethylamine (DIEA), dichloromethane (DCM), N-methylpyrrolidone (NMP), 2-((H-benzotriazole-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate (HBTU), N-hydroxybenzotriazole (HOBt) and piperidine were obtained from Applied Biosystems, Inc. (ABI), Foster City, CA or American Bioanalytical, Natick, MA. Preloaded 9-Fluorenylmethyloxycarbonyl (Fmoc) amino acid cartridges (Fmoc-Ala-OH, Fmoc-Cys(Trt)-OH, Fmoc-Asp(tBu)-OH, Fmoc-Glu(tBu)-OH, Fmoc-Phe-OH, Fmoc-Gly-OH, Fmoc-His(Trt)-OH, Fmoc-Ile-OH, Fmoc-Leu-OH, Fmoc-Lys(Boc)-OH, Fmoc-Met-OH, Fmoc-Asn(Trt)-OH, Fmoc-Pro-OH, Fmoc-Gln(Trt)-OH, Fmoc-Arg(Pbf)-OH, Fmoc-Ser(tBu)-OH, Fmoc-Thr(tBu)-OH, Fmoc-Val-OH, Fmoc-Trp(Boc)-OH, Fmoc-Tyr(tBu)-OH) were obtained from ABI or Anaspec, San Jose, CA. The peptide synthesis resin (Fmoc-Rink amide MBHA resin) and Fmoc-Lys(Mtt)-OH were obtained from Novabiochem, San Diego, CA. Single-isomer 6-carboxyfluorescein succinimidyl ester (6-FAM-NHS) was obtained from Anaspec. Trifluoroacetic acid (TFA) was obtained from Oakwood Products, West Columbia, SC. Thioanisole, phenol, triisopropylsilane (TIS), 3,6-dioxo-1,8-octanedithiol (DODT) and isopropanol were obtained from Aldrich Chemical Co., Milwaukee, WI.

Matrix-assisted laser desorption ionization mass-spectra (MALDI-MS) were recorded on an Applied Biosystems Voyager DE-PRO MS. Electrospray mass-spectra (ESI-MS) were recorded on Finnigan SSQ7000 (Finnigan Corp., San Jose, CA) in both positive and negative ion mode.

**General Procedure For Solid-Phase Peptide Synthesis (SPPS)**

Peptides were synthesized with, at most, 250 μmol preloaded Wang resin/vessel on an ABI 433A peptide synthesizer using 250 μmol scale Fastmoc™ coupling cycles. Preloaded cartridges containing 1 mmol standard Fmoc-amino acids, except for the position of attachment of the fluorophore, where 1 mmol Fmoc-Lys(Mtt)-OH was placed in the cartridge, were used with conductivity feedback monitoring. N-terminal acetylation was accomplished by using 1 mmol acetic acid in a cartridge under standard coupling conditions.

**Removal of 4-Methyltrityl (Mtt) From Lysine**

The resin from the synthesizer was washed thrice with dichloromethane and kept wet. 150 mL of 95:4:1 dichloromethane:triisopropylsilane:trifluoroacetic acid was flowed through the resin bed over 30 minutes. The mixture turned deep yellow then faded to pale yellow.
100 mL of DMF was flowed through the bed over 15 minutes. The resin was then washed thrice with DMF and filtered. Ninhydrin tests showed a strong signal for primary amine.

Resin Labeling With 6-Carboxyfluorescein-NHS (6-FAM-NHS)

The resin was treated with 2 equivalents 6-FAM-NHS in 1% DIEA/DMF and stirred or shaken at ambient temperature overnight. When complete, the resin was drained, washed thrice with DMF, thrice with (1% DCM and 1% methanol) and dried to provide an orange resin that was negative by ninhydrin test.

General Procedure For Cleavage And Deprotection Of Resin-Bound Peptide

Peptides were cleaved from the resin by shaking for 3 hours at ambient temperature in a cleavage cocktail consisting of 80% TFA, 5% water, 5% thioanisole, 5% phenol, 2.5% TIS, and 2.5% EDT (1 mL/0.1 g resin). The resin was removed by filtration and rinsing twice with TFA. The TFA was evaporated from the filtrates, and product was precipitated with ether (10 mL/0.1 g resin), recovered by centrifugation, washed twice with ether (10 mL/0.1 g resin) and dried to give the crude peptide.

General Procedure For Purification Of Peptides

The crude peptides were purified on a Gilson preparative HPLC system running Unipoint® analysis software (Gilson, Inc., Middleton, WI) on a radial compression column containing two 25 × 100 mm segments packed with Delta-Pak™ C18 15 µm particles with 100 Å pore size and eluted with one of the gradient methods listed below. One to two milliliters of crude peptide solution (10 mg/mL in 90% DMSO/water) was purified per injection. The peaks containing the product(s) from each run were pooled and lyophilized. All preparative runs were run at 20 mL/min with eluents as buffer A: 0.1% TFA-water and buffer B: acetonitrile.

General Procedure For Analytical HPLC

Analytical HPLC was performed on a Hewlett-Packard 1200 series system with a diode-array detector and a Hewlett-Packard 1046A fluorescence detector running HPLC 3D ChemStation software version A.03.04 (Hewlett-Packard, Palo Alto, CA) on a 4.6 × 250 mm YMC column packed with ODS-AQ 5 µm particles with a 120 Å pore size and eluted with one of the gradient methods listed below after pre-equilibrating at the starting conditions for 7 minutes. Eluents were buffer A: 0.1% TFA-water and buffer B: acetonitrile. The flow rate for all gradients was 1 mL/min.

F-Bak: Peptide Probe: Acetyl-{(SEQ ID NO: 1)GQVGRQAIIGDK(6-FAM)-(SEQ ID NO: 2) INR-NH₂}
Fmoc-Rink amide MBHA resin was extended using the general peptide synthesis procedure to provide the protected resin-bound peptide (1.020 g). The Mtt group was removed, labeled with 6-FAM-NHS and cleaved and deprotected as described hereinabove to provide the crude product as an orange solid (0.37 g). This product was purified by RP-HPLC. Fractions across the main peak were tested by analytical RP-HPLC, and the pure fractions were isolated and lyophilized, with the major peak providing the title compound (0.0802 g) as a yellow solid; MALDI-MS m/z = 2137.1 ((M+H)+).

Alternative Synthesis of Peptide Probe F-Bak: Acetyl--(SEQ ID NO: 1)GQVGRQLAIIGDK(6-FAM)--(SEQ ID NO: 2)INR-NH2

The protected peptide was assembled on 0.25 mmol Fmoc-Rink amide MBHA resin (Novabiochem) on an Applied Biosystems 433A automated peptide synthesizer running Fastmoc™ coupling cycles using pre-loaded 1 mmol amino acid cartridges, except for the fluorescein(6-FAM)-labeled lysine, where 1 mmol Fmoc-Lys(4-methyltrityl) was weighed into the cartridge. The N-terminal acetyl group was incorporated by putting 1 mmol acetic acid in a cartridge and coupling as described hereinabove. Selective removal of the 4-methyltrityl group was accomplished with a solution of 95:4:1 DCM:TIS:TFA (v/v/v) flowed through the resin over 15 minutes, followed by quenching with a flow of dimethylformamide. Single-isomer 6-carboxyfluorescein-NHS was reacted with the lysine side-chain in 1% DIEA in DMF and confirmed complete by ninhydrin testing. The peptide was cleaved from the resin and side-chains deprotected by treating with 80:5:5:5:2.5:2.5 TFA:water:phenol:thioanisole:triisopropylsilane:3,6-dioxo-1,8-octanediethiol (v/v/v/v/v/v/v), and the crude peptide was recovered by precipitation with diethyl ether. The crude peptide was purified by reverse-phase high-performance liquid chromatography, and its purity and identity were confirmed by analytical reverse-phase high-performance liquid chromatography and matrix-assisted laser-desorption mass-spectrometry (m/z = 2137.1 ((M+H)+)).

Time Resolved-Fluorescence Resonance Energy Transfer (TR-FRET) Assay

Representative compounds were serially diluted in dimethyl sulfoxide (DMSO) starting at 50 µM (2× starting concentration; 10% DMSO) and 10 µL were transferred into a 384-well plate. Then 10 µL of a protein/probe/antibody mix was added to each well at final concentrations listed in TABLE 1.
TABLE 1. Protein, Probe And Antibody Used For TR-FRET Assays

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<tr>
<th>Protein</th>
<th>Probe</th>
<th>Protein (nM)</th>
<th>Probe (nM)</th>
<th>Antibody</th>
<th>Antibody (nM)</th>
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<td>Tb-anti-GST</td>
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6-FAM = 6-carboxyfluorescein; Tb = terbium; GST = glutathione S-transferase

The samples were then mixed on a shaker for 1 minute and incubated for an additional 3 hours at room temperature. For each assay, the probe/antibody and protein/probe/antibody were included on each assay plate as negative and positive controls, respectively. Fluorescence was measured on the Envision (Perkin Elmer) using a 340/35 nm excitation filter and 520/525 (F-Bak peptide) and 495/510 nm (Tb-labeled anti-Histidine antibody) emission filters.

Inhibition constants ($K_i$) for compounds according to the invention and ABT-737, and the binding selectivity ratio ($Bcl-X_1$ $K_i$:Bcl-2 $K_i$) for each are shown in TABLE 2 below. The inhibition constant ($K_i$) is the dissociation constant of an enzyme-inhibitor complex or a protein/small molecule complex, wherein the small molecule is inhibiting binding of one protein to another protein or peptide. Where the $K_i$ for a compound is represented as “>” (greater than) a certain numerical value, it is intended to mean that the binding affinity value (e.g., for Bcl-X1) is greater than the limits of detection of the assay used. Where the binding selectivity ratio for a compound is represented as “>” (greater than) a certain numerical value, it is intended to mean that the selectivity of a particular compound for Bcl-2 over Bcl-X1 is at least as great as the number indicated. Where the $K_i$ for a compound is represented as “<” (less than) a certain numerical value, it is intended to mean that the binding affinity value (e.g., for Bcl-2) is lower than the limit of detection of the assay used. Inhibition constants were determined using Wang’s equation (Wang Z-X., An Exact Mathematical Expression For Describing Competitive Binding Of Two Different Ligands To A Protein Molecule. FEBS Lett. 1995, 360:111-4).
### TABLE 2. TR-FRET Binding Affinity

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<tr>
<th>Example</th>
<th>Bcl-2 $K_i$ (µM)</th>
<th>Bcl-X$_L$ $K_i$ (µM)</th>
<th>Binding selectivity ratio (Bcl-X$_L$ $K_i$/Bcl-2 $K_i$)</th>
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TABLE 2 shows the utility of compounds having Formula I to functionally inhibit anti-apoptotic Bcl-2 protein. It also surprisingly demonstrates these compounds having comparatively less affinity for anti-apoptotic Bcl-xL protein, which in turn gives rise to high binding selectivity ratios (Bcl-xL $K_i$ / Bcl-2 $K_i$) ranging from $>2$ to $>263$, 263. This selectivity for Bcl-2 protein is significantly greater than compounds previously disclosed in PCT US 2004/36770 and PCT US 2004/367911, as exemplified by ABT-737 in TABLE 2.

For some compounds (e.g., 192 and 193), the assay did not detect any activity against either Bcl-2 or Bcl-XL under the conditions stated above in the experimental description for the FRET assay. As those skilled in the art will appreciate, the upper and lower limits of detection in an assay are influenced by the assay conditions, and for the FRET assay specifically, by the concentration of the probe that is used. Since compounds represented by Examples 192 and 193 show $K_i$ values that are greater than the limits of detection in the assay format used, it can be stated that their affinity for Bcl-2 and Bcl-XL is less than the upper limit of detection of the assays. However, they may still have affinity for one or both proteins, and the inventors expect that they also have selectivity for Bcl-2.

Platelet Cell Viability Assay

Platelet-rich plasma (PRP) (prepared in-house according to conventional techniques) was incubated with ABT-737 (4-(4-((4′-chloro-1,1′-biphenyl-2-yl)methyl)piperazin-1-yl)-N-(((1R)-3-(dimethylamino)-1-((phenylthio)methyl)propyl)amino)-3-nitrophenyl)sulfonyl)benzamide) or compounds of the invention at various concentrations for five hours at 37°C. After the incubation, platelets were equilibrated to room temperature for 20 minutes and then an equal volume of Cell Titer Glo reagent (Promega Corporation) was added. Samples were mixed for two minutes and then allowed to equilibrate for an additional 10 minutes at room temperature. The luminescence generated from the samples was quantitated using an LJI Analyst plate reader. IC$_{50}$ values are concentrations of compound needed for 50% inhibition of cellular viability.

FL5.12/Bcl-2 cell viability assay

FL5.12 is an IL-3 dependent prolymphocytic murine cell line that undergoes apoptosis upon IL-3 withdrawal as a result of the upregulation of pro-apoptotic Bcl-2 proteins such as Bim and Puma. Stable overexpression of anti-apoptotic Bcl-2 protein (FL5.12/Bcl-2) protects against apoptosis induced by IL-3 withdrawal by sequestration of Bim and Puma.
[Refs. Harada, et.al. PNAS 101, 15313 (2004); Certo, et.al. Cancer Cell 9, 351 (2006).] The ability of compounds to kill FL5.12/Bcl-2 cells upon IL-3 withdrawal is a direct measure of the compounds’ ability to inhibit anti-apoptotic Bcl-2 protein function.

Wild type FL5.12/Bcl-2 overexpressing stable transfectants were cultured in RPMI-1640 supplemented with 2 mM L-glutamine, 10% FBS, 1 mM sodium pyruvate, 2 mM HEPES, 1% penicillin/streptomycin (Invitrogen), 57 μM β-ME, and 10% WEHI-3B conditioned medium (source of IL-3) and maintained at 37 °C containing 5% CO₂. 1x10⁶ cells/ml were washed 1 x PBS and resuspended in medium not supplemented with 10% WEHI-3B for 48 hrs prior to cytotoxicity assays. Cells were then treated for an additional 24 hrs in the presence of various concentrations of the indicated compounds. Cell viability was assessed by CellTitre Glo assay (Promega Corp.) according to the manufacturer’s recommendations.

Data analysis was performed using GraphPad Prism 4.0 and results are shown in TABLE 3 below.

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nd = not determined

TABLE 3 shows the utility of compounds having Formula I to functionally inhibit anti-apoptotic Bcl-2 protein in a cellular context. FL5.12 is an IL-3 dependent prolymphocytic murine cell line that undergoes apoptosis upon IL-3 withdrawal as a result of the upregulation of pro-apoptotic Bcl-2 family proteins such as Bim and Puma. Stable overexpression of anti-apoptotic Bcl-2 protein (FL5.12/Bcl-2) protects against apoptosis induced by IL-3 withdrawal by sequestration of Bim and Puma. (Refs. Harada, et.al. PNAS 2004, 101, 15313; Certo, et.al. Cancer Cell 2006, 9, 351.) The ability of compounds to kill FL5.12/Bcl-2 cells upon IL-3 withdrawal is a direct measure of the compounds ability to
inhibit anti-apoptotic Bcl-2 protein function. Compounds of Formula I are very effective in killing FL5.12/Bcl-2 cells under IL-3 withdrawal as demonstrated by low EC\textsubscript{50} values.

Compounds of this invention bind to anti-apoptotic Bcl-2 proteins with high affinity and potently inhibit the function of anti-apoptotic Bcl-2 protein in a cellular context and are therefore expected to have utility in treatment of diseases during which anti-apoptotic Bcl-2 protein is expressed.

The anti-apoptotic Bcl-xL protein has been disclosed elsewhere (Cell March 23, 2007, 128, 1173-1176.) to be the major regulator of the survival of circulating platelets in animals. Genetic mutations to Bcl-xL protein that decrease Bcl-xL protein stability and half-life causes a decrease in platelet survival and life-span in mice bearing these mutations. A potent pharmacologic inhibitor of Bcl-xL, ABT-737, causes a rapid, concentration dependant decrease in circulating platelets following injection into C57BL/6 mice or in beagle canines (Cell March 23, 2007, 128, 1173-1176.; Cell Death Differ. May 2007;14(5), 943-51). Thus, without being limited by theory, compounds of this invention that have reduced affinity for Bcl-xL can be expected to show lower levels of platelet apoptosis than previously reported compounds with higher Bcl-xL affinity.

The effect of compounds on platelet survival can be directly evaluated ex vivo by examining the viability of isolated canine platelets in the presence of various concentrations of compound. The data in Table 3 shows that compounds of Formula I have significantly less to no effect on the viability of isolated canine platelets ex vivo (higher EC\textsubscript{50} values) compared to compounds previously disclosed in PCT US 2004/36770 and PCT US 2004/367911, as exemplified by ABT-737. Furthermore, the functional selectivity ratio (canine platelet EC\textsubscript{50} : FL5.12/Bcl-2 EC\textsubscript{50}) for compounds of Formula I ranges from 32 to 4849, which is significantly higher than that for compounds previously disclosed in PCT US 2004/36770 and PCT US 2004/367911, as exemplified by ABT-737.

Because compounds having Formula I bind to anti-apoptotic Bcl-2 protein with comparatively lower binding to anti-apoptotic Bcl-X\textsubscript{L} protein, the compounds would have utility as medicaments for the treatment of cancer and autoimmune and immune diseases with reduction of the side effect of thrombocytopenia (i.e., they would be circulating platelet-sparing). Involvement of Bcl-X\textsubscript{L} in thrombocytopenia is disclosed in Cell March 23, 2007, 128, 1173-1176. As described herein and elsewhere, a potent inhibitor of Bcl-X\textsubscript{L}, ABT-737, causes a dose-dependent decrease in circulating platelets following injection into C57BL/6 mice or in canines (Cell Death Differ. May 2007;14(5), 943-51). Compounds with reduced Bcl-X\textsubscript{L} affinity exhibit substantially less to no decrease in circulating platelets. Thus, without
being limited by theory, compounds of this invention that have reduced affinity for Bcl- X\textsubscript{L} can be expected to show lower levels of platelet apoptosis than previously reported compounds with higher Bcl- X\textsubscript{L} affinity. The EC\textsubscript{50} data in TABLE 2 show the effects of administration of compounds of this invention, compared to ABT-737, on canine platelets.


Involvement of Bcl-2 protein in arthritis is disclosed in commonly-owned United States Provisional Patent Application Serial No. 60/988,479.

Involvement of Bcl-2 protein in bone marrow transplant rejection is disclosed in commonly-owned United States Patent Application Serial No. 11/941,196 (now U.S. Published Application 20080182845A1).

Overexpression of Bcl-2 protein correlates with resistance to chemotherapy, clinical outcome, disease progression, overall prognosis or a combination thereof in various cancers and disorders of the immune system. Cancers include, but are not limited to, hematologic and solid tumor types such as acoustic neuroma, acute leukemia, acute lymphoblastic leukemia, acute myelogenous leukemia (monocytic, myeloblastic, adenocarcinoma, angiosarcoma, astrocytoma, myelomonocytic and promyelocytic), acute t-cell leukemia, basal cell carcinoma, bile duct carcinoma, bladder cancer, brain cancer, breast cancer (including estrogen-receptor positive breast cancer), bronchogenic carcinoma, Burkitt's lymphoma, cervical cancer, chondrosarcoma, chordoma, choriocarcinoma, chronic leukemia, chronic lymphocytic leukemia, chronic myelocytic (granulocytic) leukemia, chronic myelogenous leukemia, colon cancer, colorectal cancer, craniopharyngioma, cystadenocarcinoma, dysproliferative changes (dysplasias and metaplasias), embryonal carcinoma, endometrial

It is also expected that compounds having Formula I would inhibit growth of cells expressing Bcl-2 protein derived from a pediatric cancer or neoplasm including embryonal rhabdomyosarcoma, pediatric acute lymphoblastic leukemia, pediatric acute myelogenous leukemia, pediatric alveolar rhabdomyosarcoma, pediatric anaplastic ependymoma, pediatric anaplastic large cell lymphoma, pediatric anaplastic medulloblastoma, pediatric atypical teratoid/rhabdoid tumor of the central nervous system, pediatric biphenotypic acute leukemia, pediatric Burkitts lymphoma, pediatric cancers of Ewing’s family of tumors such as primitive neuroectodermal tumors, pediatric diffuse anaplastic Wilm’s tumor, pediatric favorable histology Wilm’s tumor, pediatric glioblastoma, pediatric medulloblastoma, pediatric neuroblastoma, pediatric neuroblastoma-derived myelocytomatosis, pediatric pre-B-cell cancers (such as leukemia), pediatric psteosarcoma, pediatric rhabdoid kidney tumor, pediatric rhabdomyosarcoma, and pediatric T-cell cancers such as lymphoma and skin cancer and the like.
Autoimmune disorders include acquired immunodeficiency disease syndrome (AIDS), autoimmune lymphoproliferative syndrome, hemolytic anemia, inflammatory diseases, and thrombocytopenia, acute or chronic immune disease associated with organ transplantation, Addison's disease, allergic diseases, alopecia, alopecia areata, atheromatous disease/arteriosclerosis, atherosclerosis, arthritis (including osteoarthritis, juvenile chronic arthritis, septic arthritis, Lyme arthritis, psoriatic arthritis and reactive arthritis), autoimmune bullous disease, abetalipoproteinaemia, acquired immunodeficiency-related diseases, acute immune disease associated with organ transplantation, acquired acrocyanosis, acute and chronic parasitic or infectious processes, acute pancreatitis, acute renal failure, acute rheumatic fever, acute transverse myelitis, adenocarcinomas, aerial ectopic beats, adult (acute) respiratory distress syndrome, AIDS dementia complex, alcoholic cirrhosis, alcohol-induced liver injury, alcohol-induced hepatitis, allergic conjunctivitis, allergic contact dermatitis, allergic rhinitis, allergy and asthma, allograft rejection, alpha-1-antitrypsin deficiency, Alzheimer's disease, amyotrophic lateral sclerosis, anemia, angina pectoris, ankylosing spondylitis associated lung disease, anterior horn cell degeneration, antibody mediated cytotoxicity, antiphospholipid syndrome, anti-receptor hypersensitivity reactions, aortic and peripheral aneurysms, aortic dissection, arterial hypertension, arteriosclerosis, arteriovenous fistula, arthropathy, asthenia, asthma, ataxia, atopic allergy, atrial fibrillation (sustained or paroxysmal), atrial flutter, atrioventricular block, atrophic autoimmune hypothyroidism, autoimmune haemolytic anaemia, autoimmune hepatitis, type-1 autoimmune hepatitis (classical autoimmune or lupoid hepatitis), autoimmune mediated hypoglycaemia, autoimmune neutropaenia, autoimmune thrombocytopaenia, autoimmune thyroid disease, B cell lymphoma, bone graft rejection, bone marrow transplant (BMT) rejection, bronchiolitis obliterans, bundle branch block, burns, cachexia, cardiac arrhythmias, cardiac stun syndrome, cardiac tumors, cardiomyopathy, cardiopulmonary bypass inflammation response, cartilage transplant rejection, cerebellar cortical degenerations, cerebellar disorders, chaotic or multifocal atrial tachycardia, chemotherapy associated disorders, chlamydia, cholecsatatis, chronic alcoholism, chronic active hepatitis, chronic fatigue syndrome, chronic immune disease associated with organ transplantation, chronic eosinophilic pneumonia, chronic inflammatory pathologies, chronic mucocutaneous candidiasis, chronic obstructive pulmonary disease (COPD), chronic salicylate intoxication, colorectal common varied immunodeficiency (common variable hypogammaglobulinaemia), conjunctivitis, connective tissue disease associated interstitial lung disease, contact dermatitis, Coombs positive haemolytic anaemia, cor pulmonale, Creutzfeldt-Jakob disease, cryptogenic autoimmune
hepatitis, cryptogenic fibrosing alveolitis, culture negative sepsis, cystic fibrosis, cytokine therapy associated disorders, Crohn's disease, dementia pugilistica, demyelinating diseases, dengue hemorrhagic fever, dermatitis, dermatitis scleroderma, dermatologic conditions, dermatomyositis/polymyositis associated lung disease, diabetes, diabetic arteriosclerotic disease, diabetes mellitus, Diffuse Lewy body disease, dilated cardiomyopathy, dilated congestive cardiomyopathy, discoid lupus erythematosus, disorders of the basal ganglia, disseminated intravascular coagulation, Down's Syndrome in middle age, drug-induced interstitial lung disease, drug-induced hepatitis, drug-induced movement disorders induced by drugs which block CNS dopamine, receptors, drug sensitivity, eczema, encephalomyelitis, endocarditis, endocrinopathy, enteropathic synovitis, epiglottitis, Epstein-Barr virus infection, erythromelalgia, extrapyramidal and cerebellar disorders, familial hematophagocytic lymphohistiocytosis, fetal thymus implant rejection, Friedreich's ataxia, functional peripheral arterial disorders, female infertility, fibrosis, fibrotic lung disease, fungal sepsis, gangrene, gastric ulcer, giant cell arteritis, glomerular nephritis, glomerulonephritis,
histiocytosis, malignant melanoma, meningitis, meningococcemia, microscopic vasculitis of the kidneys, migraine headache, mitochondrial multi-system disorder, mixed connective tissue disease, mixed connective tissue disease associated lung disease, monoclonal gammopathy, multiple myeloma, multiple systems degenerations (Mencel Dejerine-Thomas Shi-Drager and Machado-Joseph), myalgic encephalitis/Royal Free Disease, myasthenia gravis, microscopic vasculitis of the kidneys, mycobacterium avium intracellulare, mycobacterium tuberculosis, myelodyplastic syndrome, myocardial infarction, myocardial ischemic disorders, nasopharyngeal carcinoma, neonatal chronic lung disease, nephritis, nephrosis, nephrotic syndrome, neurodegenerative diseases, neurogenic I muscular atrophies, neutropenic fever, Non-alcoholic Steatohepatitis, occlusion of the abdominal aorta and its branches, occlusive arterial disorders, organ transplant rejection, orchitis/epididymitis, orchitis vasectomy reversal procedures, organomegaly, osteoarthritis, osteoporosis, ovarian failure, pancreas transplant rejection, parasitic diseases, parathyroid transplant rejection, Parkinson's disease, pelvic inflammatory disease, pemphigus vulgaris, pemphigus foliaceus, pemphigoid, perennial rhinitis, pericardial disease, peripheral atherosclerotic disease, peripheral vascular disorders, peritonitis, pernicious anemia, phacogenic uveitis, pneumocystis carinii pneumonia, pneumonia, POEMS syndrome (polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy, and skin changes syndrome), post perfusion syndrome, post pump syndrome, post-MI cardiomyopathy syndrome, postinfectious interstitial lung disease, premature ovarian failure, primary biliary cirrhosis, primary sclerosing hepatitis, primary myxoedema, primary pulmonary hypertension, primary sclerosing cholangitis, primary vasculitis, Progressive supranuclear Palsy, psoriasis, psoriasis type 1, psoriasis type 2, psoriatic arthropathy, pulmonary hypertension secondary to connective tissue disease, pulmonary manifestation of polyarteritis nodosa, post-infiltratory interstitial lung disease, radiation fibrosis, radiation therapy, Raynaud's phenomenon and disease, Refsum's disease, regular narrow QRS tachycardia, Reiter's disease, renal disease NOS, renovascular hypertension, reperfusion injury, restrictive cardiomyopathy, rheumatoid arthritis associated interstitial lung disease, rheumatoid spondylitis, sarcoidosis, Schmidt's syndrome, scleroderma, senile chorea, Senile Dementia of Lewy body type, sepsis syndrome, septic shock, seronegative arthropathies, shock, sickle cell anemia, Sjögren's disease associated lung disease, Sjögren's syndrome, skin allograft rejection, skin changes syndrome, small bowel transplant rejection, sperm autoimmunity, multiple sclerosis (all subtypes), spinal ataxia, spinocerebellar degenerations, spondyloarthritis, sporadic, polyglandular deficiency type I sporadic, polyglandular
deficiency type II, Still's disease, streptococcal myositis, stroke, structural lesions of the cerebellum, Subacute sclerosing panencephalitis, sympathetic ophthalmia, Syncope, syphilis of the cardiovascular system, systemic anaphylaxis, systemic inflammatory response syndrome, systemic onset juvenile rheumatoid arthritis, systemic lupus erythematosus, systemic lupus erythematosus-associated lung disease, systemic sclerosis, systemic sclerosis-associated interstitial lung disease, T-cell or FAB ALL, Takayasu's disease/arteritis, Telangiectasia, Th2 Type and Th1 Type mediated diseases, thromboangitis obliterans, thrombocytopenia, thyroiditis, toxicity, toxic shock syndrome, transplants, trauma/hemorrhage, type-2 autoimmune hepatitis (anti-LKM antibody hepatitis), type B insulin resistance with acanthosis nigricans, type III hypersensitivity reactions, type IV hypersensitivity, ulcerative colitic arthropathy, ulcerative colitis, unstable angina, uremia, urosepsis, urticaria, uveitis, valvular heart diseases, varicose veins, vasculitis, vasculitic diffuse lung disease, venous diseases, venous thrombosis, ventricular fibrillation, vitiligo acute liver disease, viral and fungal infections, vital encephalitis/aseptic meningitis, vital-associated hemaphagocytic syndrome, Wegener's granulomatosis, Wernicke-Korsakoff syndrome, Wilson's disease, xenograft rejection of any organ or tissue, yersinia and salmonella-associated arthropathy and the like.

Schemes and Experimental

The following schemes are presented to provide what is believed to be the most useful and readily understood description of procedures and conceptual aspects of this invention. Compounds of this invention may be made by synthetic chemical processes, examples of which are shown herein. It is meant to be understood that the order of the steps in the processes may be varied, that reagents, solvents and reaction conditions may be substituted for those specifically mentioned, and that vulnerable moieties may be protected and deprotected, as necessary.

The following abbreviations have the meanings indicated. ADDP means 1,1'- (azodicarbonyl)dipiperidine; AD-mix-β means a mixture of (DHQD)$_2$PHAL, K$_3$Fe(CN)$_6$, K$_2$CO$_3$, and K$_2$SO$_4$; 9-BBN means 9-borabicyclo(3.3.1)nonane; Boc means tert-butoxycarbonyl; (DHQD)$_2$PHAL means hydroquinidine 1,4-phthalazinediyl diethyl ether; DBU means 1,8-diazabicyclo(5.4.0)undec-7-ene; DIBAL means diisobutylaluminum hydride; DIEA means diisopropylethylamine; DMAP means N,N-dimethylaminopropylamine; DMF means N,N-dimethylformamide; dmpe means 1,2-bis(dimethylphosphino)ethane; DMSO means DMSO; dppb means 1,4-bis(diphenylphosphino)-butane; dppe means 1,2-
bis(diphenylphosphino)ethane; dppf means 1,1'-bis(diphenylphosphino)ferrocene; dppe means 1,1'-bis(diphenylphosphino)methane; EDAC·HCl means 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride; Fmoc means fluorenlymethoxycarbonyl; HATU means O-(7-azabenzotriazol-1-yl)-N,N',N''-tetramethyluronium hexafluorophosphate; HMPA means hexamethylphosphoramide; IPA means isopropyl alcohol; MP-BH₃ means macroporous triethylammonium methylpolystyrene cyanoborohydride; TEA means triethylamine; TFA means trifluoroacetic acid; THF means tetrahydrofuran; NCS means N-chlorosuccinimide; NMM means N-methylmorpholine; NMP means N-methylpyrrolidine; PPh₃ means triphenylphosphine.

**SCHEME 1**

Compounds of Formula (4) can be prepared as shown in SCHEME 1, and can be used as described in SCHEME 7 to prepare compounds of Formula (1), which are representative of the compounds of the present invention. Compounds of Formula (1) wherein R is alkyl, R<sup>100</sup> is as described for substituents on R<sup>26</sup>, and n is 1, 2, or 3; can be converted to compounds of Formula (2) using R<sup>37</sup>CH₂MgX<sup>1</sup>, wherein X<sup>1</sup> is a halide, in a solvent such as but not limited to ether or tetrahydrofuran. Compounds of Formula (3) can be prepared from compounds of Formula (2) using a strong base such as NaH and R<sup>50</sup>X<sup>2</sup>, wherein X<sup>2</sup> is a halide and R<sup>50</sup>a is as described herein. Compounds of Formula (3), when treated with aqueous NaOH or LiOH, will provide compounds of Formula (4).

**SCHEME 2**
As shown in SCHEME 2, compounds of Formula (5) can be reacted with compounds of Formula (6) and a reducing agent to provide compounds of Formula (7). Examples of reducing agents include sodium borohydride, sodium cyanoborohydride, sodium triacetoxyborohydride, polymer supported cyanoborohydride, and the like. The reaction is typically performed in a solvent such as but not limited to methanol, tetrahydrofuran, and dichloromethane or mixtures thereof. Compounds of Formula (8) can be prepared from compounds of Formula (7) as described in SCHEME 1, and can be used as described in SCHEME 7 to prepare compounds of Formula (I).

SCHEME 3

Compounds of Formula (9), when reacted with a compound a Formula (10) wherein X is a halide or triflate, and a base will provide a compound of Formula (11). Bases useful in the reaction include triethylamine, diisopropylethylamine and the like. Compounds of Formula (13), wherein R^{41} is as described herein for substituents on R^{37}, can be prepared from compounds of Formula (11) and compounds of Formula (12) using Suzuki coupling conditions known to those skilled in the art and readily available in the literature. Compounds of Formula (14) can be prepared from compounds of Formula (13) as described in SCHEME 1, and can be used as described in SCHEME 7 to prepare compounds of Formula (I).
shown in SCHEME 4, compounds of Formula (17) can be prepared from compounds of
Formula (15) and compounds of Formula (16), wherein R is alkyl and R^{41} is as described
herein, using Suzuki coupling conditions known to those skilled in the art and readily
available in the literature. Compounds of Formula (17) can be reduced to compounds of
Formula (18) using a reducing agent such as LiAlH_{4} in a solvent such as but not limited to
diethyl ether or THF. Compounds of Formula (19) can be prepared from compounds of
Formula (18) using Dess-Martin periodinane or Swern oxidation conditions known to those
skilled in the art and readily available in the literature. Compounds of Formula (19) can be
reacted with a compound of Formula (5) and a reducing agent to provide compounds of
Formula (20). Examples of reducing agents include sodium borohydride, sodium
cyanoborohydride, sodium triacetoxyborohydride, polymer supported cyanoborohydride, and
the like. The reaction is typically performed in a solvent such as but not limited to methanol,
tetrahydrofuran, 1,2-dichloroethane, and dichloromethane or mixtures thereof. Compounds of
Formula (21) can be prepared from compounds of Formula (20) as described in SCHEME 1,
and can be used as described in SCHEME 7 to prepare compounds of Formula (I).
As shown in Scheme 5, compounds of Formula (22), wherein R is alkyl, may be converted to compounds of Formula (23) by reacting the former, wherein X is Cl, Br, I, or CF$_3$SO$_3$-$,$ and compounds of Formula R$_{50A}$-OH and a catalyst, with or without a first base. Examples of catalysts include copper(I) trifluoromethanesulfonate toluene complex, PdCl$_2$, Pd(OAc)$_2$, and Pd$_3$(dba)$_3$. Examples of first bases include triethylamine, N,N-diisopropylethylamine, Cs$_2$CO$_3$, Na$_2$CO$_3$, K$_3$PO$_4$, and mixtures thereof.

Compounds of Formula (22) may also be converted to compounds of Formula (23) by reacting the former, when X is Cl, F, or NO$_2$, and compounds of Formula R$_{50A}$-OH with a first base. Examples of first bases include triethylamine, N,N-diisopropylethylamine, Cs$_2$CO$_3$, Na$_2$CO$_3$, K$_3$PO$_4$, and mixtures thereof.

Compounds of Formula (18) can be reacted with mesyl chloride and a base such as but not limited to triethylamine, followed by N-t-butoxycarbonylpiperazine, to provide
compounds of Formula (24). Compounds of Formula (25) can be prepared by reacting compounds of Formula (24) with triethylsilane and trifluoroacetic acid. Compounds of Formula (25) can be reacted with compounds of Formula (26) and HK₂PO₄ to provide compounds of Formula (27) in a solvent such as but not limited to dimethylsulfoxide.

Compounds of Formula (28) can be prepared from compounds of Formula (27) as described in SCHEME 1, and can be used as described in SCHEME 7 to prepare compounds of Formula (I).

SCHEME 7

shown in SCHEME 7, compounds of Formula (32), which can be prepared as described herein, may be converted to compounds of Formula (33) by reacting the former with ammonia. Compounds of Formula (33) may be converted to compounds of Formula (I) by reacting the former and compounds of Formula (4), (8), (14), (21), (23), (28), or (38) and a coupling agent, with or without a first base. Examples of coupling agents include 1-ethyl-3-[3-(dimethylamino)propyl]-carbodiimide hydrochloride, 1,1'-carbonyldiimidazole, and benzotriazol-1-yl-oxytritylpyrrolidinophosphonium hexafluorophosphate. Examples of first bases include triethylamine, N,N-diisopropylethylamine, 4-(dimethylamino)pyridine, and mixtures thereof.

SCHEME 8

Compounds of Formula (33), prepared as described in SCHEME 7, can also be converted to compounds of Formula (I) by reacting the former and compounds of Formula (34) and a first base. Examples of first bases include but are not limited to sodium hydride, triethylamine, N,N-diisopropylethylamine, 4-(dimethylamino)pyridine, and mixtures thereof.
As shown in SCHEME 9, compounds of Formula (35), wherein L is a bond, alkyl, O, S, S(O), S(O)\textsubscript{2}, NH, etc., can be reacted with compounds of Formula (36), to provide compounds of Formula (37). The reaction is typically performed at elevated temperatures in a solvent such as but not limited to dimethylsulfoxide, and may require the use of a base such as but not limited to potassium phosphate, potassium carbonate, and the like. Compounds of Formula (38) can be prepared from compounds of Formula (37) as described in SCHEME 1, and can be used as described in SCHEME 7 to prepare compounds of Formula (I).

Compounds of Formula (39), wherein Y is as described herein for substituents on R\textsuperscript{37}, can be prepared from compounds of Formula (39A) wherein X is a halide or triflate, and Y-B(OH)\textsubscript{2} using Suzuki coupling conditions known to those skilled in the art and readily available in the literature. Compounds of Formula (39) can be reacted with tert-butyl piperazine-1-carboxylate and a reducing agent such as sodium triacetoxyborohydride to provide compounds of Formula (40). The reaction is typically performed in a solvent such as but not limited to methylene chloride. Compounds of Formula (41) can be prepared from compounds of Formula (40) by reacting the latter with R\textsuperscript{50}X, wherein X is a halide, and NaH in a solvent such as N,N-dimethylformamide, and then the resulting material can be treated...
with triethylsilane and trifluoroacetic acid in dichloromethane. Compounds of Formula (41) can be used as described in Scheme 9 wherein \( R^{37} \) is as shown in Formula (41).

**SCHEME 11**

As shown in SCHEME 11, substituted piperazin-2-ones wherein \( R^{50} \) is alkyl, can be reacted with compounds of Formula (6a) and a reducing agent such as sodium triacetoxyborohydride in dichloromethane to provide compounds of Formula (42). Compounds of Formula (42) can be reduced to compounds of Formula (43) using a reducing agent such as but not limited to lithium aluminum hydride in a solvent such as but not limited to tetrahydrofuran. Compounds of Formula (43) can be used as described in Scheme 9 wherein \( CH_2R^{37} \) is as shown in Formula (43).

The following examples are presented to provide what is believed to be the most useful and readily understood description of procedures and conceptual aspects of this invention. The exemplified compounds were named using ACD/ChemSketch Version 5.06 (05 June 2001, Advanced Chemistry Development Inc., Toronto, Ontario), or ChemDraw® Ver. 9.0.5 (CambridgeSoft, Cambridge, MA). Intermediates were named using ChemDraw® Ver. 9.0.5 (CambridgeSoft, Cambridge, MA).

**EXAMPLE 1**

4-\{4\-[\(4'\)-chloro-1,1'-biphenyl-2-yl]methyl\]piperazin-1-yl\}N-\{3-nitro-4-[(tetrahydro-2H-pyran-4-ylmethyl)amino]phenyl\]sulfonyl\}-2-phenoxybenzamide

**EXAMPLE 1A**

tert-butyl 4-\{(4'-chlorobiphenyl-2-yl)amethyl\}piperazine-1-carboxylate

4'-Chlorobiphenyl-2-carbaldehyde (EXAMPLE 27C) (4.1 g), tert-butyl piperazine-1-carboxylate (4.23 g), and sodium triacetoxyborohydride (5.61 g) in \( CH_2Cl_2 \) (60 mL) were combined stirred for 24 hours. The reaction was quenched with methanol and poured into
ether. The solution was washed with water and brine, concentrated, and chromatographed on silica gel with 2-25% ethyl acetate/hexanes.

EXAMPLE 1B
1-((4′-chlorobiphenyl-2-yl)methyl)piperazine
EXAMPLE 1A (3.0 g) and triethyilsilane (1 mL) were stirred in CH₂Cl₂ (30 mL) and trifluoroacetic acid (30 mL) for 2 hours, and the reaction was concentrated, and then taken up in ether and concentrated again. The product was used without further purification.

EXAMPLE 1C
methyl 4-fluoro-2-phenoxybenzoate
Methyl 2-bromo-4-fluorobenzoate (1 g), phenol (0.565 g), cesium carbonate (1.96 g), copper(I) triflate toluene complex (0.087 g), and ethyl acetate (0.034 mL) in toluene (12 mL) was stirred at 110°C for 24 hours. The reaction was cooled and chromatographed on silica gel with 5% ethyl acetate/hexanes.

EXAMPLE 1D
methyl 4-(4-((4′-chlorobiphenyl-2-yl)methyl)piperazin-1-yl)-2-phenoxybenzoate
EXAMPLE 1C (630 mg), EXAMPLE 1B, and K₂CO₃ (707 mg) were stirred in dimethylsulfoxide at 125°C for 5 hours. The reaction was cooled and chromatographed on silica gel with 10% ethyl acetate/hexanes.

EXAMPLE 1E
4-(4-((4′-chlorobiphenyl-2-yl)methyl)piperazin-1-yl)-2-phenoxybenzoic acid
EXAMPLE 1D (600 mg) was stirred in 25 mL 2:1 dioxane/1M NaOH at 60°C for 24 hours. The solution was cooled and adjusted to pH 4 with NaH₂PO₄ solution and concentrated HCl, and extracted with ethyl acetate. The extract was washed with brine and dried (Na₂SO₄), filtered and concentrated.

EXAMPLE 1F
3-nitro-4-((tetrahydro-2H-pyran-4-yl)methylamino)benzenesulfonamide
4-Fluoro-3-nitrobenzenesulfonamide (2.18 g), (tetrahydropyran-4-yl)methylamine (1.14 g), and triethylamine (1 g) were stirred in tetrahydrofuran (30 mL) for 24 hours. The
solution was diluted with ethyl acetate, washed with NaH₂PO₄ solution and brine, and dried (Na₂SO₄), filtered and concentrated. The product was triturated from ethyl acetate.

EXAMPLE 1G

4-{4'-[4-chloro-1,1'-biphenyl-2-yl]methyl}piperazin-1-yl)-N-{3-nitro-4-[(tetrahydro-2H-pyran-4-ylmethyl)amino]phenyl}sulfonyle-2-phenoxybenzamide

EXAMPLE 1E (90 mg), EXAMPLE 1F (45 mg), 1-ethyl-3-[3-(dimethylamino)propyl]-carbodiimide hydrochloride (65 mg), and 4-dimethylaminopyridine (22 mg) were stirred in CH₂Cl₂ (4 mL) for 24 hours. The reaction was cooled and chromatographed on silica gel with 20-100% ethyl acetate/hexanes. ¹H NMR (300MHz, dimethylsulfoxide-d₆) δ 11.55 (brs, 1H), 8.63 (t, 1H), 8.47 (d, 1H), 7.75 (d, 1H), 7.46 (m, 6H), 7.35 (m, 2H), 7.24 (m, 3H), 7.15 (d, 1H), 6.99 (dd, 1H), 6.82 (d, 2H), 6.75 (d, 1H), 6.38 (d, 1H), 3.86 (br d, 2H), 3.49 (m, 2H), 3.37 (br s, 2H), 3.15 (br s, 4H), 2.34 (br s, 4H), 1.91 (br s, 4H), 1.64 (br d, 2H), 1.29 (m, 3H).

EXAMPLE 2

4-{4'-[4-chloro-1,1'-biphenyl-2-yl]methyl}piperazin-1-yl)-2-phenoxy-N-{4-[(tetrahydro-2H-pyran-4-ylmethyl)amino]phenyl}sulfonylebemzamide

EXAMPLE 2A

4-((tetrahydro-2H-pyran-4-yl)methylamino)benzenesulfonamide

4-Aminobenzenesulfonamide (6.80 g), tetrahydropyran-4-carboxaldehyde (4.96 g), and sodium triacetoxypyrroloxyborohydride (16.74 g) in tetrahydrofuran (300 mL) and acetic acid (15 mL) were stirred in for 24 hours. The reaction was concentrated and taken up in ethyl acetate. The resulting solution was washed with water and brine, concentrated, and chromatographed on silica gel with 50% ethyl acetate/hexanes.

EXAMPLE 2B

4-{4'-[4-chloro-1,1'-biphenyl-2-yl]methyl}piperazin-1-yl)-2-phenoxy-N-{4-[(tetrahydro-2H-pyran-4-ylmethyl)amino]phenyl}sulfonylebemzamide

This example was prepared by substituting EXAMPLE 2A for EXAMPLE 1F in EXAMPLE 1G. ¹H NMR (500MHz, dimethylsulfoxide-d₆/D₂O) δ 7.54 (d, 1H), 7.46 (m, 8H), 7.36 (m, 4H), 7.24 (d, 1H), 7.13 (dd, 1H), 6.93 (d, 2H), 6.75 (d, 1H), 6.55 (d, 2H), 6.30
(d, 1H), 3.86 (dd, 2H), 3.36 (s, 2H), 3.28 (t, 2H), 3.10 (br s, 4H), 2.96 (d, 2H), 2.32 (br s, 4H),
1.76 (m, 1H), 1.64 (d, 2H), 1.20 (m, 2H).

**EXAMPLE 3**

2-(benzyloxy)-4-{4-[(4′-chloro-1,1′-biphenyl-2-yl)methyl]piperazin-1-yl}·N-(3-nitro-4-
[(tetrahydro-2H-pyran-4-ylmethyl)amino]phenyl)sulfonyl)benzamide

**EXAMPLE 3A**

methyl 2-(benzyloxy)-4-fluorobenzoate

Methyl 4-fluoro-2-hydroxybenzoate (2.00 g), benzyl bromide (1.54 mL), and
cesium carbonate (4.60 g) in N,N-dimethylformamide (50 mL) were stirred for 24 hours. The
reaction was taken up in ether and washed with 3x 1M NaOH solution, and brine, then
concentrated to give the pure product.

**EXAMPLE 3B**

methyl 2-(benzyloxy)-4-(4-((4′-chlorobiphenyl-2-yl)methyl)piperazin-1-yl)benzoate

This example was prepared by substituting EXAMPLE 3A for EXAMPLE 1C in EXAMPLE 1D.

**EXAMPLE 3C**

2-(benzyloxy)-4-(4-((4′-chlorobiphenyl-2-yl)methyl)piperazin-1-yl)benzoic acid

This example was prepared by substituting EXAMPLE 3B for EXAMPLE 1D in EXAMPLE 1E.

**EXAMPLE 3D**

2-(benzyloxy)-4-{4-[(4′-chloro-1,1′-biphenyl-2-yl)methyl]piperazin-1-yl}·N-(3-nitro-4-
[(tetrahydro-2H-pyran-4-ylmethyl)amino]phenyl)sulfonyl)benzamide

This example was prepared by substituting EXAMPLE 3C for EXAMPLE 1E in EXAMPLE 1G. \(^1\)H NMR (300MHz, dimethylsulfoxide-d6) δ 10.90 (br s, 1H), 8.66 (m, 1H), 8.59 (s, 1H), 7.82 (d, 1H), 7.33-7.55 (m, 12H), 7.18-7.27 (m, 3H), 6.61 (s, 1H), 6.56 (d, 1H), 5.22 (s, 2H), 3.86 (br d, 2H), 3.40 (m, 2H), 3.31 (m, 8H), 2.34 (br s, 4H), 1.91 (br s, 2H), 1.64 (br d, 2H), 1.29 (m, 3H).
EXAMPLE 4
4-[(4'-chloro-1,1'-biphenyl-2-yl)methyl]piperazin-1-yl]-N-{3-nitro-4-[(tetrahydro-2H-pyran-4-ylmethyl)amino]phenyl}sulfonyl)-2-(2-phenylethoxy)benzamide

EXAMPLE 4A
methyl 4-fluoro-2-phenethoxybenzoate

Methyl 4-fluoro-2-hydroxybenzoate (1.00 g) and phenethyl alcohol (0.64 mL) were added to triphenylphosphine (1.54 g) and diisopropylazodicarboxylate (1.04 mL) in tetrahydrofuran (20 mL) at 0°C, and the reaction was stirred at room temperature for 24 hours. The mixture was chromatographed on silica gel with 5% ethyl acetate/hexanes.

EXAMPLE 4B
methyl 4-[(4'-chlorobiphenyl-2-yl)methyl]piperazin-1-yl]-2-phenethoxybenzoate

This example was prepared by substituting EXAMPLE 4A for EXAMPLE 1C in EXAMPLE 1D.

EXAMPLE 4C
4-[(4'-chlorobiphenyl-2-yl)methyl]piperazin-1-yl]-2-phenethoxybenzoic acid

This example was prepared by substituting EXAMPLE 4B for EXAMPLE 1D in EXAMPLE 1E.

EXAMPLE 4D
4-[(4'-chloro-1,1'-biphenyl-2-yl)methyl]piperazin-1-yl]-N-{3-nitro-4-[(tetrahydro-2H-pyran-4-ylmethyl)amino]phenyl}sulfonyl)-2-(2-phenylethoxy)benzamide

This example was prepared by substituting EXAMPLE 4C for EXAMPLE 1E in EXAMPLE 1G. $^1$H NMR (300MHz, dimethylsulfoxide-d$_6$) δ 10.75 (br s, 1H), 8.66 (m, 2H), 7.91 (d, 1H), 7.47 (m, 6H), 7.20-7.40 (m, 8H), 6.53 (d, 1H), 6.47 (s, 1H), 4.35 (t, 2H), 4.03 (m, 1H), 3.85 (br d, 2H), 3.38 (s, 2H), 3.25 (m, 8H), 3.13 (t, 2H), 2.36 (br s, 4H), 2.21 (br s, 2H), 1.62 (br d, 2H), 1.20 (m, 2H), 1.17 (m, 1H).

EXAMPLE 5
4-[(4'-chloro-1,1'-biphenyl-2-yl)methyl]piperazin-1-yl]-N-{3-nitro-4-[(tetrahydro-2H-pyran-4-ylmethyl)amino]phenyl}sulfonyl)-2-(phenylthio)benzamide
EXAMPLE 5A
methyl 4-fluoro-2-(phenylthio)benzoate
5-Fluoro-2-(methoxycarbonyl)phenylboronic acid (1.00 g), 2-
(phenylthio)isoindoline-1,3-dione (0.86 g), and (2-hydroxy-3,5-
diisopropylbenzoyloxy)copper (0.29 g) were stirred in dioxane (15 mL) at 50°C for 24 hours. The reaction mixture was chromatographed on silica gel with 5% ethyl acetate/hexanes.

EXAMPLE 5B
10 methyl 4-((4'-chlorobiphenyl-2-yl)methyl)piperazin-1-yl)-2-(phenylthio)benzoate
This example was prepared by substituting EXAMPLE 5A for EXAMPLE 1C in EXAMPLE 1D.

EXAMPLE 5C
15 4-((4'-chlorobiphenyl-2-yl)methyl)piperazin-1-yl)-2-(phenylthio)benzoic acid
This example was prepared by substituting EXAMPLE 5B for EXAMPLE 1D in EXAMPLE 1E.

EXAMPLE 5D
20 4-{(4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl}-N-{(3-nitro-4-{[tetrahydro-2H-
pyran-4-ylmethyl]amino}[phenyl]sulfonyl)-2-(phenylthio)benzamide
This example was prepared by substituting EXAMPLE 5C for EXAMPLE 1E in EXAMPLE 1G. 1H NMR (300MHz, dimethylsulfoxide-d6) δ 11.95 (br s, 1H), 8.59 (m,
2H), 7.93 (d, 1H), 7.63 (d, 1H), 7.15-7.50 (m, 14H), 6.73 (d, 1H), 6.18 (s, 1H), 3.82 (dd, 2H),
3.36 (m, 4H), 3.32 (m, 2H), 2.94 (br s, 4H), 2.30 (br s, 4H), 1.64 (m, 1H), 1.61 (m, 2H), 1.25
(m, 2H).

EXAMPLE 6
30 4-{(4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl}-2-(phenylthio)-N-{(4-[
[tetrahydro-2H-pyran-4-ylmethyl]amino][phenyl]sulfonyl)benzamide
This example was prepared by substituting EXAMPLE 5C for EXAMPLE 1E and EXAMPLE 2A for EXAMPLE 1F in EXAMPLE 1G. 1H NMR (500MHz,
dimethylsulfoxide-d6/D2O) δ 7.65 (d, 2H), 7.55 (d, 1H), 7.33-7.48 (m, 12H), 7.24 (m, 2H),
6.73 (d, 1H), 6.66 (d, 2H), 6.17 (d, 1H), 3.85 (dd, 2H), 3.34 (s, 2H), 3.26 (t, 2H), 2.98 (d, 2H), 2.92 (br s, 4H), 2.25 (br s, 4H), 1.78 (m, 1H), 1.63 (d, 2H), 1.20 (m, 2H).

EXAMPLE 7

4-{{4'chloro-1,1'-biphenyl-2-yl}methyl}piperazin-1-yl}N-{{4-[3-morpholin-4-yl]propyl}amino}-3-nitrophenyl{sulfonyl}-2-(phenylthio)benzamide

EXAMPLE 7A

4-(3-morpholinopropylamino)-3-nitrobenzenesulfonamide

This example was prepared by substituting 3-(N-morpholiny)-1-propylamine for (tetrahydropropyran-4-yl)methyamine in EXAMPLE 1F.

EXAMPLE 7B

4-{{4'chloro-1,1'-biphenyl-2-yl}methyl}piperazin-1-yl}N-{{4-[3-morpholin-4-yl]propyl}amino}-3-nitrophenyl{sulfonyl}-2-(phenylthio)benzamide

This example was prepared by substituting EXAMPLE 5C for EXAMPLE 1E and EXAMPLE 7A for EXAMPLE 1F in EXAMPLE 1G. \(^{1}H\) NMR (300MHz, dimethylsulfoxide-d\(_6\)) \(\delta\) 10.20 (br s, 1H), 8.69 (m, 1H), 8.57 (d, 1H), 7.95 (dd, 2H), 7.71 (m, 1H), 7.31-7.51 (m, 10H), 7.12-7.26 (m, 3H), 6.68 (dd, 1H), 6.07 (m, 1H), 4.06 (s, 2H), 3.68 (m, 4H), 3.50 (m, 2H), 3.32 (m, 6H), 2.88 (m, 4H), 2.27 (m, 4H), 1.91 (m, 2H).

EXAMPLE 8

4-{{4'chloro-1,1'-biphenyl-2-yl}methyl}piperazin-1-yl}N-{{3-nitro-4-[(tetrahydro-2H-pyran-4-yl)methyl]amino}phenyl{sulfonyl}-2-(phenylsulfonyl)benzamide

EXAMPLE 8A

methyl 4-fluoro-2-(phenylsulfonyl)benzoate

EXAMPLE 5A (0.30 g) and KMnO\(_4\) (1.80 g) were stirred in acetic acid (40 mL) at 60°C for 24 hours. The reaction mixture was filtered through a plug of silica gel, concentrated, and chromatographed on silica gel with 50% ethyl acetate/hexanes.

EXAMPLE 8B

methyl 4-((4'-chlorobiphenyl-2-yl)methyl)piperazin-1-yl}-2-(phenylsulfonyl)benzoate
This example was prepared by substituting EXAMPLE 8A for EXAMPLE 1C in EXAMPLE 1D.

**EXAMPLE 8C**

4-(4′-chlorobiphenyl-2-yl)methylpiperazin-1-yl)-2-(phenylsulfonyl)benzoic acid

This example was prepared by substituting EXAMPLE 8B for EXAMPLE 1D in EXAMPLE 1E.

**EXAMPLE 8D**

4-{4′-[4′-chlo-ro-1,1′-biphenyl-2-yl]methyl}[piperazin-1-yl]-N-{3-nitro-4-[(tetrahydro-2H-pyran-4-yl)methyl]amino}[phenyl]sulfonyl)-2-(phenylsulfonyl)benzamide

This example was prepared by substituting EXAMPLE 8C for EXAMPLE 1E in EXAMPLE 1G. $^1$H NMR (500MHz, dimethylsulfoxide-d$_6$) δ 11.95 (br s, 1H), 8.54 (s, 1H), 8.41 (dd, 1H), 7.90 (m, 2H), 7.82 (d, 1H), 7.76 (d, 1H), 7.66 (m, 1H), 7.46 (m, 5H), 7.40 (m, 4H), 7.11 (m, 2H), 6.67 (dd, 1H), 6.62 (m, 1H), 4.36 (m, 1H), 3.82 (dd, 2H), 3.39 (m, 6H), 3.19 (m, 6H), 2.37 (br s, 4H), 1.91 (m, 1H), 1.63 (m, 2H), 1.26 (m, 2H).

**EXAMPLE 9**

4-{4′-[4′-chlo-ro-1,1′-biphenyl-2-yl]methyl}[piperazin-1-yl]-N-{3-nitro-4-[(tetrahydro-2H-pyran-4-yl)methyl]amino}[phenyl]sulfonyl)-2-(phenylsulfinyl)benzamide

**EXAMPLE 9A**

methyl 4-fluoro-2-(phenylsulfinyl)benzoate

OXONE® (Dupont) (5.60 g) was added portionwise over 1 hour to EXAMPLE 5A (1.00 g) in a mixture of acetic acid (30 mL), water (30 mL) and CH$_2$Cl$_2$ (20 mL), and the reaction was stirred for an additional 1 hour. The reaction mixture was taken up in ethyl acetate, washed with Na$_2$S$_2$O$_3$ solution, water, and brine, concentrated, and chromatographed on silica gel with 5-25% ethyl acetate/hexanes.

**EXAMPLE 9B**

methyl 4-(4′-(4′-chlorobiphenyl-2-yl)methyl)piperazin-1-yl)-2-(phenylsulfinyl)benzoate

This example was prepared by substituting EXAMPLE 9A for EXAMPLE 1C in EXAMPLE 1D.
EXAMPLE 9C
4-(4-((4'-chlorobiphenyl-2-yl)methyl)piperazin-1-yl)-2-(phenylsulfinyl)benzoic acid

This example was prepared by substituting EXAMPLE 9B for EXAMPLE 1D

EXAMPLE 9D
4-{(4'-chloro-1,1'-biphenyl-2-yl)methyl}piperazin-1-yl]-N-{(3-nitro-4-[(tetrahydro-2H-pyran-4-yl)methyl]amino}phenyl)sulfonyl)-2-(phenylsulfinyl)benzamide

This example was prepared by substituting EXAMPLE 9C for EXAMPLE 1E in EXAMPLE 1G. \( ^1 \)H NMR (500MHz, dimethylsulfoxide-\( d_6/D_2O \)) \( \delta \) 8.51 (s, 1H), 7.85 (dd, 2H), 7.64 (d, 2H), 7.48 (m, 8H), 7.32 (m, 1H), 7.23 (m, 1H), 7.14 (m, 4H), 6.97 (d, 1H), 3.85 (dd, 2H), 3.35 (d, 2H), 3.34 (m, 6H), 3.27 (t, 2H), 2.74 (br s, 4H), 1.93 (m, 1H), 1.64 (d, 2H), 1.28 (m, 2H).

EXAMPLE 10
2-benzyl-4-{4-[4'-chloro-1,1'-biphenyl-2-yl)methyl}piperazin-1-yl]-N-{(3-nitro-4-[(tetrahydro-2H-pyran-4-yl)methyl]amino}phenyl)sulfonyl)benzamide

EXAMPLE 10A
methyl 2-benzyl-4-fluorobenzoate

5-Fluoro-2-(methoxycarbonyl)phenylboronic acid (1.00 g), benzyl bromide (0.50 mL), \( K_2CO_3 \) (1.75 g), and [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(II) (PdCl\(_2\)(dppf)) (0.17 g) were stirred in tetrahydrofuran (20 mL) at 60°C for 24 hours. The reaction mixture was chromatographed on silica gel with 2% ethyl acetate/hexanes.

EXAMPLE 10B
methyl 2-benzyl-4-(4-((4'-chlorobiphenyl-2-yl)methyl)piperazin-1-yl)benzoate

This example was prepared by substituting EXAMPLE 10A for EXAMPLE 1C in EXAMPLE 1D.

EXAMPLE 10C
2-benzyl-4-(4-((4'-chlorobiphenyl-2-yl)methyl)piperazin-1-yl)benzoic acid
This example was prepared by substituting EXAMPLE 10B for EXAMPLE 1D in EXAMPLE 1E.

EXAMPLE 10D

2-benzyl-4-{4-[4'-chloro-1,1'-biphenyl-2-yl]methyl)piperazin-1-yl}N-(3-nitro-4-
[(tetrahydro-2H-pyran-4-ylmethyl)amino]phenyl)sulfonyl)benzamide

This example was prepared by substituting EXAMPLE 10C for EXAMPLE 1E in EXAMPLE 1G. 1H NMR (500MHz, dimethylsulfoxide-d6/D2O) δ 8.55 (d, 1H), 7.90 (d, 1H), 7.38-7.56 (m, 10H), 7.25 (m, 2H), 6.96 (d, 2H), 6.83 (s, 2H), 6.75 (d, 1H), 4.06 (s, 2H), 3.85 (dd, 2H), 3.48 (s, 2H), 3.37 (d, 2H), 3.25 (t, 2H), 3.20 (br s, 4H), 2.44 (br s, 4H), 1.91 (m, 1H), 1.63 (d, 2H), 1.29 (m, 2H).

EXAMPLE 11

2-benzyl-4-{4-[4'-chloro-1,1'-biphenyl-2-yl]methyl)piperazin-1-yl}N-(4-{[(tetrahydro-2H-
pyran-4-ylmethyl)amino]phenyl}sulfonyl)benzamide

This example was prepared by substituting EXAMPLE 10C for EXAMPLE 1E and EXAMPLE 2A for EXAMPLE 1F in EXAMPLE 1G. 1H NMR (300MHz, dimethylsulfoxide-d6) δ 11.70 (br s, 1H), 7.48 (m, 6H), 6.88 (m, 6H), 6.62 (m, 6H), 6.42 (dd, 2H), 3.83 (dd, 4H), 3.24 (m, 6H), 2.96 (m, 4H), 1.82 (m, 2H), 1.63 (m, 3H), 1.18 (m, 4H).

EXAMPLE 12

2-benzyl-4-{4-[4'-chloro-1,1'-biphenyl-2-yl]methyl)piperazin-1-yl}N-(4-{[3-morpholin-4-
ylpropyl]amino]3-nitrophenyl}sulfonyl)benzamide

This example was prepared by substituting EXAMPLE 10C for EXAMPLE 1E and EXAMPLE 7A for EXAMPLE 1F in EXAMPLE 1G. 1H NMR (300MHz, dimethylsulfoxide-d6) δ 11.90 (br s, 1H), 8.80 (m, 1H), 8.54 (d, 1H), 7.91 (dd, 1H), 7.48 (m, 7H), 7.40 (d, 2H), 7.26 (d, 2H), 6.97 (dd, 2H), 6.86 (m, 2H), 6.76 (d, 1H), 4.04 (m, 5H), 3.72 (m, 4H), 3.56 (m, 2H), 3.40 (m, 8H), 3.21 (m, 4H), 2.34 (m, 2H), 1.98 (m, 2H).

EXAMPLE 13

4-{4-[4'-chloro-1,1'-biphenyl-2-yl]methyl)piperazin-1-yl}N-(3-nitro-4-{[(tetrahydro-2H-
pyran-4-ylmethyl)amino]phenyl}sulfonyl)-2-(2-phenylethyl)benzamide
EXAMPLE 13A
methyl 4-fluoro-2-phenethylbenzoate
Methyl 2-bromo-4-fluorobenzoate (1.00 g), (E)-styrylboronic acid (0.89 g),
tetrakis(triphenylphosphine)palladium(0) (0.50 g), and K$_3$PO$_4$ (2.28 g) were stirred in
dioxane (17 mL) at 90°C for 24 hours. The reaction mixture chromatographed on silica gel
with 1-5% ethyl acetate/hexanes. The product in methanol (10 ml) was added to 20 wt% of
fresh dry 5% Pd-C and stirred 4 days with H$_2$ in a pressure bottle. The mixture was filtered
through a nylon membrane and concentrated.

EXAMPLE 13B
methyl 4-(4-((4'-chlorobiphenyl-2-y1)methyl)piperazin-1-yl)-2-phenethylbenzoate
This example was prepared by substituting EXAMPLE 13A for EXAMPLE 1C
in EXAMPLE 1D.

EXAMPLE 13C
4-(4-((4'-chlorobiphenyl-2-y1)methyl)piperazin-1-yl)-2-phenethylbenzoic acid
This example was prepared by substituting EXAMPLE 13B for EXAMPLE 1D
in EXAMPLE 1E.

EXAMPLE 13D
4-(4-((4'-chlorobiphenyl-2-y1)methyl)piperazin-1-yl)-N-(3-nitro-4-((tetrahydro-2H-pyran-4-
yl)methylamino)phenylsulfonyl)-2-phenethylbenzamide
This example was prepared by substituting EXAMPLE 13C for EXAMPLE 1E
in EXAMPLE 1G. $^1$H NMR (500MHz, dimethylsulfoxide-d$_6$/D$_2$O) δ 8.62 (d, 1H), 7.95 (d,
1H), 7.91 (m, 1H), 7.35-7.52 (m, 6H), 7.19 (m, 2H), 7.13 (m, 2H), 6.99 (m, 4H), 6.83 (d, 1H),
6.70 (d, 1H), 6.65 (s, 1H), 3.80 (m, 2H), 3.24 (m, 2H), 3.18 (t, 2H), 3.11 (br s, 4H), 2.91 (t,
2H), 2.48 (m, 2H), 2.38 (br s, 4H), 1.81 (m, 1H), 1.54 (d, 2H), 1.23 (m, 2H).

EXAMPLE 14
2-(benzylamino)-4-{4-[(4'-chloro-1,1'-biphenyl-2-y1)methyl]piperazin-1-yl}-N-{(3-nitro-4-[(tetrahydro-2H-pyran-4-ylmethylamino)phenyl]sulfonyl)benzamide
EXAMPLE 14A
methyl 2-(benzylamino)-4-fluorobenzoate

Methyl 2-amino-4-fluorobenzoate (0.90 g), benzaldehyde (0.54 mL), sodium triacetoxyborohydride (1.58 g) and acetic acid (0.3 mL) in CH₂Cl₂ (20 mL) were stirred for 3 hours. The reaction was quenched with methanol, concentrated, and chromatographed on silica gel with 5% ethyl acetate/hexanes.

EXAMPLE 14B
methyl 2-(benzylamino)-4-(4-((4′-chlorobiphenyl-2-yl)methyl)piperazin-1-yl)benzoate

This example was prepared by substituting EXAMPLE 14A for EXAMPLE 1C in EXAMPLE 1D.

EXAMPLE 14C
2-(benzylamino)-4-(4-((4′-chlorobiphenyl-2-yl)methyl)piperazin-1-yl)benzoic acid

This example was prepared by substituting EXAMPLE 14B for EXAMPLE 1D in EXAMPLE 1E.

EXAMPLE 14D
2-(benzylamino)-4-{(4′-chloro-1,1′-biphenyl-2-yl)methyl}piperazin-1-yl}-N-{(3-nitro-4-[[tetrahydro-2H-pyran-4-ylmethyl]amino]phenyl} sulfonyl benzamide

This example was prepared by substituting EXAMPLE 14C for EXAMPLE 1E in EXAMPLE 1G. ¹H NMR (500MHz, dimethylsulfoxide-d₆/D₂O) δ 8.58 (d, 1H), 7.92 (d, 1H), 7.87 (m, 1H), 7.59 (d, 2H), 7.48 (m, 2H), 7.43 (m, 4H), 7.20-7.29 (m, 8H), 6.15 (d, 1H), 4.32 (s, 2H), 3.85 (m, 2H), 3.49 (m, 2H), 3.33 (m, 2H), 3.26 (t, 2H), 3.12 (br s, 4H), 2.39 (br s, 4H), 1.90 (m, 1H), 1.62 (d, 2H), 1.27 (m, 2H).

EXAMPLE 15
2-anilino-4-{(4′-chloro-1,1′-biphenyl-2-yl)methyl}piperazin-1-yl}-N-{(3-nitro-4-[[tetrahydro-2H-pyran-4-ylmethyl]amino]phenyl} sulfonyl benzamide

EXAMPLE 15A
methyl 4-fluoro-2-(phenylamino) benzoate
Methyl 2-bromo-4-fluorobenzoate (1.00 g), aniline (0.47 mL), palladium(II) acetate (0.048 g), 2,2'-bis(diphenylphosphino)-1,1'-binaphthyl (0.214 g) and Cs₂CO₃ (2.08 g) in toluene (12 mL) were stirred at 90°C for 24 hours. The reaction was concentrated and chromatographed on silica gel with 5-50% ethyl acetate/hexanes.

EXAMPLE 15B
methyl 4-(4-((4'-chlorobiphenyl-2-yl)methyl)piperazin-1-yl)-2-(phenylamino)benzoate

This example was prepared by substituting EXAMPLE 15A for EXAMPLE 1C in EXAMPLE 1D.

EXAMPLE 15C
4-(4-((4'-chlorobiphenyl-2-yl)methyl)piperazin-1-yl)-2-(phenylamino)benzoic acid

This example was prepared by substituting EXAMPLE 15B for EXAMPLE 1D in EXAMPLE 1E.

EXAMPLE 15D
2-anilino-4-{4-[(4'-chboro-1,1'-biphenyl-2-yl)methyl]piperazin-1-yl}-N-[(3-nitro-4-

This example was prepared by substituting EXAMPLE 15C for EXAMPLE 1E in EXAMPLE 1G. ¹H NMR (300MHz, dimethylsulfoxide-d₆) δ 11.55 (br s, 1H), 8.56 (m, 2H), 7.92 (d, 1H), 7.72 (d, 1H), 7.47 (m, 6H), 7.25 (m, 4H), 7.12 (d, 2H), 6.95 (m, 2H), 6.53 (s, 1H), 6.38 (dd, 1H), 3.81 (dd, 2H), 3.37 (br s, 4H), 3.12 (br s, 4H), 2.41 (br s, 4H), 1.91 (m, 1H), 1.61 (br d, 2H), 1.23 (m, 4H).

EXAMPLE 16
2-anilino-4-{4-[(4'-chloro-1,1'-biphenyl-2-yl)methyl]piperazin-1-yl}-N-[(4-[(tetrahydro-2H-
pyran-4-ylmethyl]amino]phenyl)sulfonyl]benzamide

This example was prepared by substituting EXAMPLE 15C for EXAMPLE 1E and EXAMPLE 2A for EXAMPLE 1F in EXMAPLE 1G. ¹H NMR (500MHz, dimethylsulfoxide-d₆/D₂O) δ 7.78 (d, 1H), 7.52 (d, 2H), 7.47 (m, 6H), 7.36 (m, 3H), 7.27 (m, 3H), 7.11 (m, 2H), 6.90 (m, 1H), 6.61 (s, 1H), 6.53 (d, 1H), 6.31 (d, 1H), 4.46 (s, 1H), 3.82 (m, 2H), 3.37 (s, 2H), 3.26 (t, 2H), 3.05 (br s, 4H), 2.93 (d, 2H), 2.37 (br s, 4H), 1.77 (m, 1H), 1.63 (d, 2H), 1.20 (m, 2H).
EXAMPLE 17
4-{4-[(4'-chloro-1,1'-biphenyl-2-yl)methyl]piperazin-1-yl}-2-methoxy-N-((3-nitro-4-[(tetrahydro-2H-pyran-4-ylmethyl)amino]phenyl)sulfonyl)benzamide

EXAMPLE 17A
methyl 4-((4'-chlorobiphenyl-2-yl)methyl)piperazin-1-yl)-2-methoxybenzoate

Methyl 4-bromo-2-methoxybenzoic acid (700 mg), EXAMPLE 1B (983 mg), K$_3$PO$_4$ (909 mg), tris(dibenzylideneacetone)dipalladium(0) (78 mg), and 2-(di-t-butylphosphino)biphenyl (102 mg) were stirred in 1,2-dimethoxyethane (10 mL) at 80°C for 24 hours. The reaction mixture was chromatographed on silica gel with 20-50% ethyl acetate/hexanes.

EXAMPLE 17B
4-((4'-chlorobiphenyl-2-yl)methyl)piperazin-1-yl)-2-methoxybenzoic acid

This example was prepared by substituting EXAMPLE 17A for EXAMPLE 1D in EXAMPLE 1E.

EXAMPLE 17C
4-{4-[(4'-chloro-1,1'-biphenyl-2-yl)methyl]piperazin-1-yl}-2-methoxy-N-((3-nitro-4-[(tetrahydro-2H-pyran-4-ylmethyl)amino]phenyl)sulfonyl)benzamide

This example was prepared by substituting EXAMPLE 17B for EXAMPLE 1E in EXAMPLE 1G. $^1$H NMR (300MHz, dimethylsulfoxide-d$_6$) δ 10.81 (br s, 1H), 8.64 (m, 2H), 7.96 (d, 1H), 7.20-7.54 (m, 10H), 6.52 (d, 1H), 6.46 (s, 1H), 3.90 (s, 3H), 3.40 (m, 4H), 3.27 (br s, 4H), 2.39 (br s, 4H), 1.91 (m, 1H), 1.62 (br d, 2H), 1.27 (m, 4H).

EXAMPLE 18
4-{4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl}-N-((4-[(3-morpholin-4-ylpropyl)amino]-3-nitrophenyl)sulfonyl)-2-phenoxybenzamide

EXAMPLE 18A
methyl 4,4-dimethyl-2-( trifluoromethylsulfonyloxy)cyclohex-1-enecarboxylate

To a suspension of hexane washed NaH (17 g) in dichloromethane (700 mL), 5,5-dimethyl-2-methoxycarbonylcyclohexanone (38.5 g) was added dropwise at 0°C. After
stirring for 30 minutes, the mixture was cooled to −78°C and trifluoromethanesulfonic anhydride (40 mL) was added. The reaction mixture was warmed to room temperature and stirred for 24 hours. The organic layer was washed with brine, dried, and concentrated to give the product.

EXAMPLE 18B
methyl 2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-enecarboxylate

EXAMPLE 18A (62.15g), 4-chlorophenylboronic acid (32.24 g), CsF (64 g) and tetrakis(triphenylphosphine)palladium(0) (2g) in 2:1 1,2-dimethoxyethane/methanol (600 mL) were heated to 70°C for 24 hours. The mixture was concentrated. Ether (4x 200 mL) was added and the mixture was filtered. The combined ether solution was concentrated to give the product.

EXAMPLE 18C
(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-enyl)methanol

To a mixture of LiBH₄ (13g), EXAMPLE 18B (53.8 g) and ether (400 mL), methanol (25 mL) was added slowly by syringe. The mixture was stirred at room temperature for 24 hours. The reaction was quenched with 1N HCl with ice-cooling. The mixture was diluted with water and extracted by ether (3x 100mL). The extracts were dried, and concentrated. The crude product was chromatographed on silica gel with 0-30% ethyl acetate/hexanes.

EXAMPLE 18D
methyl 2-bromo-4-(piperazin-1-yl)benzoate

This example was prepared by substituting piperazine for EXAMPLE 1B and methyl 2-bromo-4-fluorobenzoate for EXAMPLE 1C in EXAMPLE 1D.

EXAMPLE 18E
methyl 2-bromo-4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-enyl)methyl)piperazin-1-yl)benzoate

MsCl (7.5 mL) was added via syringe to EXAMPLE 18C (29.3 g) and triethylamine (30 mL) in CH₂Cl₂ (500 mL) at 0°C, and the mixture was stirred for 1 minute. EXAMPLE 18D (25 g) was added and the reaction was stirred at room temperature for 24
hours. The suspension was washed with brine, dried, and concentrated. The crude product was chromatographed on silica gel with 10-20% ethyl acetate/hexanes.

EXAMPLE 18F

methyl 4-((4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-enyl)ethyl)piperazin-1-yl)-2-phenoxybenzoate

EXAMPLE 18E (500 mg), phenol (195 mg), Cs₂CO₃ (674 mg), 1-naphthoic acid (356 mg), copper (I) triflate-toluene complex (45 mg), ethyl acetate (0.016 mL), and 4A sieves (50 mg) in toluene (2 mL) was stirred at 105°C for 24 hours. The reaction was cooled and taken up in ethyl acetate (100 mL) and water (40 mL). The layers were separated and the organic layer was washed with 2x Na₂CO₃ solution and brine, dried, and concentrated. The crude product was chromatographed on silica gel with 20% ethyl acetate/hexanes.

EXAMPLE 18G

4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-enyl)ethyl)piperazin-1-yl)-2-phenoxybenzoic acid

This example was prepared by substituting EXAMPLE 18F for EXAMPLE 1D in EXAMPLE 1G.

EXAMPLE 18H

4-(4-{{2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl}methyl}piperazin-1-yl)-N-({4-[[3-morpholin-4-ylpropyl]amino]-3-nitrophenyl}sulfonfonyl)-2-phenoxybenzamide

This example was prepared by substituting EXAMPLE 18G for EXAMPLE 1E and EXAMPLE 7A for EXAMPLE 1F in EXAMPLE 1G. ¹H NMR (300MHz, dimethylsulfoxide-δ₆) δ 11.10 (br s, 1H), 8.76 (m, 1H), 8.46 (d, 1H), 7.76 (dd, 1H), 7.50 (d, 1H), 7.35 (d, 2H), 7.23 (d, 2H), 7.06 (dd, 2H), 6.99 (dd, 1H), 6.81 (d, 2H), 6.74 (d, 1H), 6.34 (s, 1H), 3.62 (m, 4H), 3.46 (m, 2H), 3.13 (m, 4H), 2.76 (m, 2H), 2.48 (m, 2H), 2.22 (m, 6H), 1.97 (m, 2H), 1.82 (m, 2H), 1.40 (t, 2H), 1.06 (m, 7H), 0.94 (s, 3H).

EXAMPLE 19

4-(4-{{2-(4-chlorophenyl)-5,5-dimethylcyclohex-1-en-1-yl}methyl}piperazin-1-yl)-N-({4-[[3-morpholin-4-ylpropyl]amino]-3-nitrophenyl}sulfonfonyl)-2-phenoxybenzamide
EXAMPLE 19A
methyl 5,5-dimethyl-2-(trifluoromethylsulfonyl oxy)cyclohex-1-enecarboxylate
This example was prepared by substituting 4,4-dimethyl-2-
methoxycarbonylcyclohexanone for 5,5-dimethyl-2-methoxycarbonylcyclohexanone in

EXAMPLE 19B
methyl 2-(4-chlorophenyl)-5,5-dimethylcyclohex-1-enecarboxylate
This example was prepared by substituting EXAMPLE 19A for

EXAMPLE 19C
(2-(4-chlorophenyl)-5,5-dimethylcyclohex-1-enyl)methanol
This example was prepared by substituting EXAMPLE 19B for

EXAMPLE 19D
methyl 2-bromo-4-(4-(2-(4-chlorophenyl)-5,5-dimethylcyclohex-1-enyl)methyl)piperazin-1-
yl)benzoate

EXAMPLE 19E
methyl 4-(4-((2-(4-chlorophenyl)-5,5-dimethylcyclohex-1-enyl)methyl)piperazin-1-yl)-2-
phenoxybenzoate

EXAMPLE 19F
4-(4-((2-(4-chlorophenyl)-5,5-dimethylcyclohex-1-enyl)methyl)piperazin-1-yl)-2-
phenoxybenzoic acid
This example was prepared by substituting EXAMPLE 19E for EXAMPLE 1D in

EXAMPLE 1E.
EXAMPLE 19G
4-(4-[[2-(4-chlorophenyl)-5,5-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[(4-[(3-morpholin-4-ylpropyl)amino]-3-nitrophenyl)sulfonyl]-2-phenoxybenzamide

This example was prepared by substituting EXAMPLE 19F for EXAMPLE 1E and EXAMPLE 7A for EXAMPLE 1F in EXAMPLE 1G. $^1$H NMR (300MHz, dimethylsulfoxide-d$_6$) δ 11.10 (br s, 1H), 8.71 (m, 1H), 8.42 (d, 1H), 7.73 (dd, 1H), 7.53 (d, 1H), 7.34 (d, 2H), 7.21 (dd, 2H), 7.10 (d, 2H), 6.96 (dd, 1H), 6.78 (d, 2H), 6.70 (d, 1H), 6.32 (s, 1H), 3.61 (m, 4H), 3.44 (m, 2H), 3.09 (m, 4H), 2.71 (m, 2H), 2.44 (m, 4H), 2.21 (m, 4H), 1.96 (m, 2H), 1.79 (m, 2H), 1.47 (t, 2H), 1.17 (m, 3H), 1.08 (m, 4H), 0.95 (s, 3H).

EXAMPLE 20
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indazol-5-yloxy)-N-[(4-[(3-morpholin-4-ylpropyl)amino]-3-nitrophenyl)sulfonyl]benzamide

EXAMPLE 20A
ethyl 2-(1H-indazol-5-yloxy)-4-fluorobenzoate
Ethyl 2,4-difluorobenzoate (1.14 g), K$_2$PO$_4$ (1.30 g) and 5-hydroxyindazole (0.90 g) were stirred at 110°C in diglyme (12 mL) for 24 hours. The reaction was cooled and poured into ether. The solution was washed three times with 1M NaOH solution, and brine, and dried. The solution was then concentrated, and the crude product was chromatographed on silica gel with 20% ethyl acetate/hexanes.

EXAMPLE 20B
tert-butyl 4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-enyl)methyl)piperazine-1-carboxylate

This example was prepared by substituting N-t-butoxycarbonylpiperazine for EXAMPLE 18D in EXAMPLE 18E.

EXAMPLE 20C
1-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-enyl)methyl)piperazine

This EXAMPLE was prepared by substituting EXAMPLE 20B for EXAMPLE 1A in EXAMPLE 1B.
EXAMPLE 20D

ethyl 2-(1H-indazol-5-yloxy)-4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-enyl)methyl)piperazin-1-yl)benzoate

EXAMPLE 20A (330 mg), EXAMPLE 20C (335 mg), and HK2PO4 (191 mg) were stirred in dimethylsulfoxide (5 mL) at 140℃ for 24 hours. The reaction was diluted with ethyl acetate, washed three times with water, washed with brine, dried, and concentrated. The crude product was chromatographed on silica gel with 30% ethyl acetate/hexanes.

EXAMPLE 20E

2-(1H-indazol-5-yloxy)-4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-enyl)methyl)piperazin-1-yl)benzoic acid

This example was prepared by substituting EXAMPLE 20D for EXAMPLE 1D in EXAMPLE 1E.

EXAMPLE 20F

4-(4-{{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl}-2-(1H-indazol-5-yloxy)-N-{{4-[(3-morpholin-4-ylpropyl)amino]-3-nitrophenyl}sulfonyl}benzamide

This example was prepared by substituting EXAMPLE 20E for EXAMPLE 1E and EXAMPLE 7A for EXAMPLE 1F in EXAMPLE 1G. 1H NMR (300MHz, dimethylsulfoxide-d6) δ 13.03 (br s, 1H), 11.25 (br s, 1H), 8.70 (m, 1H), 8.48 (d, 1H), 7.94 (dd, 1H), 7.68 (dd, 1H), 7.52 (m, 2H), 7.34 (d, 2H), 7.06 (m, 4H), 6.96 (dd, 1H), 6.88 (d, 1H), 6.23 (s, 1H), 3.61 (m, 4H), 3.44 (m, 2H), 3.05 (m, 4H), 2.73 (m, 2H), 2.42 (m, 4H), 2.18 (m, 4H), 1.99 (m, 2H), 1.91 (d, 2H), 1.78 (m, 2H), 1.39 (t, 2H), 1.17 (m, 2H), 0.93 (s, 6H).

EXAMPLE 21

4-(4-{{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl}-2-(1H-indazol-5-yloxy)-N-{{4-[(1-methylpiperidin-4-yl)amino]-3-nitrophenyl}sulfonyl}benzamide

EXAMPLE 21A

4-(1-methylpiperidin-4-ylamino)-3-nitrobenzenesulfonamide

This example was prepared by substituting 4-amino-N-methylpiperidine for (tetrahydropyran-4-yl)methylamine in EXAMPLE 1F.
EXAMPLE 21B

4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indazol-5-yl)oxy)-N-[[4-[[1-methylpiperidin-4-yl]amino]-3-nitrophenyl]sulfonyl]benzamide

This example was prepared by substituting EXAMPLE 20E for EXAMPLE 1E and EXAMPLE 21A for EXAMPLE 1F in EXAMPLE 1G. $^1$H NMR (300MHz, dimethylsulfoxide-d$_6$) $\delta$ 12.80 (br s, 1H), 10.70 (br s, 1H), 8.34 (s, 1H), 8.02 (d, 1H), 7.87 (d, 1H), 7.70 (dd, 1H), 7.55 (m, 2H), 7.36 (d, 2H), 7.06 (m, 2H), 6.95 (m, 1H), 6.72 (d, 1H), 6.62 (d, 1H), 6.24 (s, 1H), 3.35 (m, 4H), 3.18 (m, 2H), 3.00 (m, 2H), 2.80 (m, 4H), 2.73 (m, 2H), 2.20 (m, 4H), 1.99 (m, 2H), 1.91 (s, 3H), 1.54 (m, 1H), 1.41 (t, 2H), 1.22 (m, 2H), 1.09 (s, 6H).

EXAMPLE 22

4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4-[(3-morpholin-4-ylpropyl)amino]-3-nitrophenyl]sulfonyl]-2-(1,2,3,4-tetrahydroquinolin-6-yl)oxy]benzamide

EXAMPLE 22A

ethyl 4-fluoro-2-(1,2,3,4-tetrahydroquinolin-6-yl)oxy)benzoate

This example was prepared by substituting 5-hydroxy-1,2,3,4-tetrahydroquinoline for 5-hydroxyindazole in EXAMPLE 20A.

EXAMPLE 22B

ethyl 4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-enyl)methyl)piperazin-1-yl)-2-(1,2,3,4-tetrahydroquinolin-6-yl)oxy)benzoate

This example was prepared by substituting EXAMPLE 22A for EXAMPLE 20A in EXAMPLE 20D.

EXAMPLE 22C

4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-enyl)methyl)piperazin-1-yl)-2-(1,2,3,4-tetrahydroquinolin-6-yl)oxy)benzoic acid

This example was prepared by substituting EXAMPLE 22B for EXAMPLE 1D in EXAMPLE 1E.
EXAMPLE 22D

4-([2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl)piperazin-1-yl)-N-([4-(3-morpholin-4-ylpropyl)amino]-3-nitrophenyl)sulfonyl)-2-(1,2,3,4-tetrahydroquinolin-6-yloxy)benzamide

This example was prepared by substituting EXAMPLE 22C for EXAMPLE 1E and EXAMPLE 7A for EXAMPLE 1F in EXAMPLE 1G. $^1$H NMR (300MHz, dimethylsulfoxide-$d_6$) $\delta$ 10.95 (br s, 1H), 8.83 (m, 1H), 8.60(d, 1H), 7.90 (dd, 1H), 7.46 (d, 1H), 7.35 (d, 2H), 7.21 (dd, 2H), 7.06 (d, 2H), 6.62 (m, 2H), 6.42 (d, 1H), 6.11 (d, 1H), 5.61 (br s, 1H), 4.02 (m, 1H), 3.61 (m, 4H), 3.48 (m, 2H), 3.17 (m, 2H), 3.07 (m, 4H), 2.74 (m, 2H), 2.63 (m, 2H), 2.44 (m, 4H), 2.19 (m, 4H), 1.97 (m, 4H), 1.79 (m, 4H), 1.41 (t, 2H), 1.17 (m, 4H), 0.94 (s, 6H).

EXAMPLE 23

4-([2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl)piperazin-1-yl)-N-([4-[(1-methylpiperidin-4-yl)amino]-3-nitrophenyl)sulfonyl]-2-(1,2,3,4-tetrahydroquinolin-6-yloxy)benzamide

This example was prepared by substituting EXAMPLE 22C for EXAMPLE 1E and EXAMPLE 21A for EXAMPLE 1F in EXAMPLE 1G. $^1$H NMR (300MHz, dimethylsulfoxide-$d_6$) $\delta$ 11.10 (br s, 1H), 8.71(m, 1H), 8.42 (d, 1H), 7.73 (dd, 1H), 7.53 (d, 1H), 7.34 (d, 2H), 7.21 (dd, 2H), 7.10 (d, 2H), 6.96 (dd, 1H), 6.78 (d, 2H), 6.70 (d, 1H), 6.32 (s, 1H), 3.61 (m, 4H), 3.44 (m, 2H), 3.09 (m, 4H), 2.71 (m, 2H), 2.44 (m, 4H), 2.21 (m, 4H), 1.96 (m, 2H), 1.79 (m, 2H), 1.47 (t, 2H), 1.17 (m, 3H), 1.08 (m, 4H), 0.95 (s, 3H).

EXAMPLE 24

4-([4'-chboro-4-(pyrrolidin-1-ylmethyl)-1,1'-biphenyl-2-yl)methyl]piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-([3-nitro-4-[(tetrahydro-2H-pyran-4-ylmethyl)amino]phenyl)sulfonyl]benzamide

EXAMPLE 24A

methyl 5-formyl-2-(trifluoromethylsulfonyloxy)benzoate

Triflic anhydride (7.74 mL) was added to methyl 5-formyl-2-hydroxybenzoate (7.5 g) in 150 mL CH$_2$Cl$_2$ at 0°C, and the reaction was stirred and allowed to warm to room.
temperature over 3 hours. The reaction was diluted with CH₂Cl₂ (150 mL), washed with 3x brine, dried over Na₂SO₄, and concentrated. The product was used without further purification.

EXAMPLE 24B
methyl 4’-chloro-4-formylbiphenyl-2-carboxylate

EXAMPLE 24A (14.5 g), 4-chlorophenylboronic acid (6.88 g) CsF (12.2 g), and tetrakis(triphenylphosphine)palladium(0) were stirred at 70°C for 24 hours. The reaction was cooled, filtered, and concentrated. The crude product was taken up in ethyl acetate (250 mL), washed with 3x 1M NaOH, and brine, concentrated, and chromatographed on silica gel with 10% ethyl acetate/hexanes.

EXAMPLE 24C
methyl 4’-chloro-4-(pyrrolidin-1-ylmethyl)biphenyl-2-carboxylate

This example was prepared by substituting EXAMPLE 24B for 4’-chlorobiphenyl-2-carboxaldehyde and pyrrolidine for tert-butyl piperazine-1-carboxylate in EXAMPLE 1A.

EXAMPLE 24D
(4’-chloro-4-(pyrrolidin-1-ylmethyl)biphenyl-2-yl)methanol

DIBAL in hexanes (1M, 5.9 mL) was added to EXAMPLE 24C (650 mg) in CH₂Cl₂ (30 mL) at 0°C, and the reaction was stirred for 20 minutes. The reaction was quenched by the slow addition of methanol (2 mL), and 1M NaOH (10 mL), and the resulting solution was extracted twice with ethyl acetate. The extracts were washed with brine, dried over Na₂SO₄, and concentrated. The product was used without further purification.

EXAMPLE 24E
4’-chloro-4-(pyrrolidin-1-ylmethyl)biphenyl-2-carbaldehyde

Dess-Martin periodinane (1.30 g) was added to EXAMPLE 24D (770 mg) in CH₂Cl₂ (30 mL) at room temperature and the reaction was stirred for 24 hours. The reaction mixture was concentrated and chromatographed on silica gel with 1% triethylamine in 25% ethyl acetate/hexanes.
EXAMPLE 24F
methyl 2-(1H-indol-4-yloxy)-4-fluorobenzoate
This example was prepared by substituting 4-hydroxyindole for 5-
hydroxyindazole and methyl 2,4-difluorobenzoate for ethyl 2,4-difluorobenzoate in

EXAMPLE 20A.

EXAMPLE 24G
tert-butyl 4-(3-(1H-indol-4-yloxy)-4-(methoxycarbonyl)phenyl)piperazine-1-carboxylate
This example was prepared by substituting EXAMPLE 24F for EXAMPLE

20A and tert-butyl piperazine-1-carboxylate for EXAMPLE 20C in EXAMPLE 20D.

EXAMPLE 24H
methyl 2-(1H-indol-4-yloxy)-4-(piperazin-1-yl)benzoate
This example was prepared by substituting EXAMPLE 24G for EXAMPLE 1A

in EXAMPLE 1B.

EXAMPLE 24I
methyl 2-(1H-indol-4-yloxy)-4-(4-((4'-chloro-4-(pyrrolidin-1-ylmethyl)biphenyl-2-
yl)methyl)piperazin-1-yl)benzoate
This example was prepared by substituting EXAMPLE 24E for 4'-chlorobiphenyl-2-carboxaldehyde and EXAMPLE 24H for tert-butyl piperazine-1-carboxylate in EXAMPLE 1A.

EXAMPLE 24J
2-(1H-indol-4-yloxy)-4-(4-((4'-chloro-4-(pyrrolidin-1-ylmethyl)biphenyl-2-
yl)methyl)piperazin-1-yl)benzoic acid
This example was prepared by substituting EXAMPLE 24I for EXAMPLE 1D in

EXAMPLE 1E.

EXAMPLE 24K
4-(4-[[4'-chloro-4-(pyrrolidin-1-ylmethyl)-1,1'-biphenyl-2-yl]methyl]piperazin-1-yl)-2-(1H-
indol-4-yloxy)-N-([3-nitro-4-[(tetrahydro-2H-pyran-4-
yl)methyl]amino]phenyl)sulfonylebenzamide
This example was prepared by substituting EXAMPLE 24J for EXAMPLE 1E in EXAMPLE 1G. $^1$H NMR (300MHz, dimethylsulfoxide-d$_6$) δ 11.52 (br s, 1H), 11.26 (s, 1H), 10.68 (br s, 1H), 8.61 (dd, 1H), 8.49 (s, 1H), 8.19 (br s, 1H), 7.66 (d, 2H), 7.54 (m, 3H), 7.36 (m, 2H), 7.28 (s, 1H), 7.24 (d, 1H), 7.05 (d, 1H), 6.95 (dd, 1H), 6.75 (d, 1H), 6.35 (m, 2H), 6.26 (s, 1H), 4.38 (m, 3H), 3.85 (dd, 2H), 3.61 (m, 4H), 3.24 (m, 4H), 3.09 (m, 4H), 2.85 (m, 2H), 2.35 (m, 2H), 2.02 (m, 2H), 1.87 (m, 4H), 1.60 (m, 2H), 1.25 (m, 2H).

EXAMPLE 25
4-(4-[(4'-chloro-4-(2-pyrrolidin-1-yl ethyl)-1,1'-biphenyl-2-yl]methyl]piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-(3-nitro-4-[(tetrahydro-2H-pyran-4-ylmethyl)amino]phenyl)sulfonyl)benzamide

EXAMPLE 25A
methyl 4'-chboro-4-(2-oxoethyl)biphenyl-2-carboxylate

To a solution of (methoxymethyl)diphenylphosphine oxide (1.62 g) in 40 mL tetrahydrofuran at -78°C, was added lithium diisopropylamide (2M, 3.3 mL), and after stirring 3 minutes, EXAMPLE 24B (1.57 g) was added, and the solution was warmed to room temperature. NaH (230 mg), and 40 mL N,N-dimethylformamide were added, and the mixture was heated to 60°C for 1 hours. The reaction was cooled and poured into NaH$_2$PO$_4$ solution. The resulting solution was extracted twice with ether, and the combined extracts were washed twice with water, and brine, and concentrated. The crude mixture of enol ethers was taken up in 1M HCl (50 mL) and dioxane (50 mL), and stirred at 60°C for 3 hours. The reaction was cooled and poured into NaHCO$_3$ solution. The resulting solution was extracted twice with ether, and the combined extracts were washed with water, and brine, and concentrated. The product was used without further purification.

EXAMPLE 25B
methyl 4'-chloro-4-(2-(pyrrolidin-1-yl)ethyl)biphenyl-2-carboxylate

This example was prepared by substituting EXAMPLE 25A for 4'-chlorobiphenyl-2-carboxaldehyde and pyrrolidine for tert-butyl piperazine-1-carboxylate in EXAMPLE 1A.
DEMANDES OU BREVETS VOLUMINEUX

LA PRÉSENTE PARTIE DE CETTE DEMANDE OU CE BREVETS COMPREND PLUS D'UN TOME.

CECI EST LE TOME _1__ DE _3__

NOTE: Pour les tomes additionnels, veillez contacter le Bureau Canadien des Brevets.

________________________________________________________________________

JUMBO APPLICATIONS / PATENTS

THIS SECTION OF THE APPLICATION / PATENT CONTAINS MORE THAN ONE VOLUME.

THIS IS VOLUME _1__ OF _3__

NOTE: For additional volumes please contact the Canadian Patent Office.
What is claimed is:

1. A compound having formula I

\[
\text{O} \quad \text{O} \quad \text{E}^1
\]
\[
\text{Z}^1 \quad \text{N} \quad \text{S} \quad \text{A}^1 \quad \text{B}^1
\]
\[
\text{D}^1 \quad \text{Y}^1
\]

(I)

or a therapeutically acceptable salt thereof,

wherein \( A^1 \) is N or C(A^2);

one or two or three or each of A^2, B^1, D^1 and E^1 are independently selected from R^1, OR^1,

SR^1, S(O)R^1, SO_2R^1, C(O)R^1, C(O)OR^1, OC(O)R^1, NHR^1, N(R^1)\_2, C(O)NHR^1, C(O)N(R^1)\_2,

NHC(O)R^1, NHC(O)OR^1, NR^1C(O)NHR^1, NR^1C(O)N(R^1)\_2, SO_2NHR^1, SO_2N(R^1)\_2, NHSO_2R^1,

NHSO_2NHR^1 and N(CH_3)SO_2N(CH_3)R^1, and the remainder of A^2, B^1, D^1 and E^1 are

independently selected from H, F, Cl, Br, I, CN, CF_3, C(O)OH, C(O)NH_2 and C(O)OR^1A;

Y^1 is H, CN, NO_2, C(O)OH, F, Cl, Br, I, CF_3, OCF_3, CF_2CF_3, OCF_2CF_3, R^1\_7, OR^1\_7,

C(O)R^1\_7, C(O)OR^1\_7, SR^1\_7, NH_2, NHR^1\_7, N(R^1)\_7\_2, NHC(O)R^1\_7, C(O)NH_2, C(O)NHR^1\_7,

C(O)N(R^1)\_7\_2, NHSO_2R^1\_7 or NHSO_2R^1\_7;

R^1 is R^2, R^3, R^4 or R^5;

R^1A is C_1-C_6-alkyl, C_3-C_6-alkenyl or C_3-C_6-alkynyl;

R^2 is phenyl which is optionally fused with arene, heteroarene or R^2A; R^2A is cycloalkane

or heterocycloalkane;

R^3 is heteroaryl which is optionally fused with benzene, heteroarene or R^3A; R^3A is cycloalkane or heterocycloalkane;

R^4 is cycloalkyl, cycloalkenyl, heterocycloalkyl or heterocycloalkenyl, each of which is

optionally fused with arene, heteroarene or R^4A; R^4A is cycloalkane, cycloalkene,

heterocycloalkane or heterocycloalkene;

R^5 is alkyl, alkenyl or alkynyl, each of which is optionally substituted with one or two or

three independently selected R^6, R^7, OR^7, SR^7, S(O)R^7, SO_2R^7, NHR^7, N(R^7)\_2, C(O)R^7,

C(O)NH_2, C(O)NHR^7, NHC(O)R^7, NHSO_2R^7, NHC(O)OR^7, SO_2NH_2, SO_2NHR^7, SO_2N(R^7)\_2,

NHC(O)NH_2, NHC(O)NHR^7, NHC(O)CH(CH_3)\_2NHC(O)CH(CH_3)NH_2, OH, (O), C(O)OH, N\_1, CN, NH_2, CF_3, CF_2CF_3, F, Cl, Br or I substituents;

560
R^6 is C2-C5-spiroalkyl, each of which is optionally substituted with OH, (O), N3, CN, CF3, CF2CF3, F, Cl, Br, l, NH2, NH(CH3) or N(CH3)2, wherein spiroalkyl means alkylene, both ends of which are attached to the same carbon atom;

R^7 is R^8, R^9, R^10 or R^11;

R^8 is phenyl which is optionally fused with arene, heteroarene or R^8A;

R^8A is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R^9 is heteroaryl which is optionally fused with arene, heteroarene or R^9A; R^9A is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R^10 is C3-C10-cycloalkyl or C4-C10-cycloalkenyl, each having one or two CH2 moieties unreplaced or replaced with independently selected O, C(O), CNOH, CNOCH3, S, S(O), SO2 or NH and one or two CH moieties unreplaced or replaced with N, and each of which is optionally fused with arene, heteroarene or R^10A; R^10A is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R^11 is alkyl, alkenyl or alkynyl, each of which is optionally substituted with one or two or three independently selected R^12, OR^12, NHR^12, N(R^12)2, C(O)NH2, C(O)NHR^12, C(O)N(R^12)2, OH, (O), C(O)OH, N3, CN, NH2, CF3, CF2CF3, F, Cl, Br or l substituents;

R^12 is R^13, R^14, R^15 or R^16;

R^13 is phenyl which is optionally fused with arene, heteroarene or R^13A; R^13A is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R^14 is heteroaryl, each of which is optionally fused with arene, heteroarene or R^14A; R^14A is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R^15 is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene, each of which is optionally fused with arene, heteroarene or R^15A; R^15A is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R^16 is alkyl, alkenyl or alkynyl;

R^17 is R^18, R^19, R^20 or R^21;

R^18 is phenyl which is optionally fused with arene, heteroarene or R^18A; R^18A is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R^19 is heteroaryl which is optionally fused with arene, heteroarene or R^19A; R^19A is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;
R²⁰ is C₃-C₁₀-cycloalkyl or C₄-C₁₀-cycloalkenyl, each having one or two CH₂ moieties un replaced or replaced with independently selected O, C(O), CNOH, CNOCH₃, S, S(O), SO₂ or NH and one or two CH moieties un replaced or replaced with N, and each of which is optionally fused with arene, heteroarene or R²⁰A; R²⁰A is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R²¹ is alkyl, alkenyl or alkynyl, each of which is optionally substituted with one or two or three independently selected R²², OR²², NHR²², N(R²²)₂, C(O)NH₂, C(O)NHRC(O)N(R²²)₂, OH, (O), C(O)OH, N₃, CN, NH₂, CF₃, CF₂CF₃, F, Cl, Br or I substituents;
R²² is R²³, R²⁴ or R²⁵;
R²³ is phenyl which is optionally fused with arene, heteroarene or R²³A; R²³A is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R²⁴ is heteroarene which is optionally fused with arene, heteroarene or R²⁴A; R²⁴A is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R²⁵ is C₃-C₅-cycloalkyl or C₄-C₅-cycloalkenyl, each having one or two CH₂ moieties un replaced or replaced with independently selected O, C(O), CNOH, CNOCH₃, S, S(O), SO₂ or NH and one or two CH moieties un replaced or replaced with N, and each of which is optionally fused with arene, heteroarene or R²⁵A; R²⁵A is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

Z¹ is R²⁶ substituted with R³⁰, which is substituted with CH₂R²⁷ or CH(R³¹)(R³⁷);
R²⁶ is phenyl;
R³⁰ is cycloalkyl having one or two CH₂ moieties un replaced or replaced with independently selected O, C(O), CNOH, CNOCH₃, S, S(O), SO₂ or NH and one or two CH moieties un replaced or replaced with N;
R³¹ is F, Cl, Br or alkyl;
R³⁷ is R³⁸ or R⁴⁰, each of which is substituted with R⁴¹;
R³⁸ is phenyl;
R⁴⁰ is C₃-C₈-cycloalkyl or C₄-C₈-cycloalkenyl, each having one or two CH₂ moieties un replaced or replaced with independently selected O, C(O), CNOH, CNOCH₃, S, S(O), SO₂ or NH and one or two CH moieties un replaced or replaced with N;
R⁴¹ is R⁴²;
R⁴² is substituted phenyl;
wherein the phenyl represented by \( R^{26} \) is further substituted by one or two or three substituents independently selected from \( OR^{50, A} \), \( SR^{50, A} \), \( S(O)R^{50, A} \), \( SO_2R^{50, A} \) and \( NHR^{50, A} \), \( R^{50, A} \) is \( R^{51, A} \), \( R^{52, A} \), or \( R^{53, A} \);

\( R^{51, A} \) is phenyl which is optionally fused with benzene, heteroarene or \( R^{51, AA} \),

wherein \( R^{51, AA} \) is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene,

\( R^{52, A} \) is heteroaryl;

\( R^{53, A} \) is \( C_3-C_6 \)-cycloalkyl or \( C_4-C_6 \)-cycloalkenyl; each having one or two \( CH_2 \) moieties unplaced or replaced with independently selected \( O, C(O), CNOH, CNOCH_3, S, S(O), SO_2 \) or \( NH \) and one or two \( CH \) moieties unplaced or replaced with \( N \), and each of which is optionally fused with arene, heteroarene or \( R^{53, AA} \);

wherein \( R^{53, AA} \) is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

wherein \( R^{2}, R^{3}, R^{4}, R^{6}, R^{8, A}, R^{9}, R^{10}, R^{12}, R^{14}, R^{15}, R^{18}, R^{19}, R^{20}, R^{23}, R^{24}, R^{25}, R^{26}, R^{30}, R^{38}, R^{40}, \) and \( R^{42} \) are independently optionally substituted with one or two or three or four or five independently selected \( R^{50, A} \), \( OR^{50, A} \), \( SR^{50, A} \), \( S(O)R^{50, A} \), \( SO_2R^{50, A} \), \( C(O)R^{50, A} \), \( CO(O)R^{50, A} \), \( OC(O)OR^{50, A} \), \( NH_2 \), \( NHR^{50, A} \), \( N(NR^{50, A})_2 \), \( C(O)NH, C(O)NH_2, C(O)NHR^{50, A}, C(O)N(R^{50, A})_2, C(O)NOH, C(O)NHOH, C(O)NHOR^{50, A}, C(O)NHSO_2R^{50, A}, C(O)NR^{55}SO_2R^{50, A}, SO_2NH_2, SO_2NHR^{50, A}, SO_2N(R^{50, A}), CF_3, CF_2CF_3, C(O)H, C(O)OH, OH, (O), CN, N_3, NO_2, OCF_3, OCF_2CF_3, F, Cl, Br or I substituents;

\( R^{50} \) is \( R^{51, A} \), \( R^{52, A} \) or \( R^{53, A} \);

\( R^{51} \) is phenyl which is optionally fused with arene, heteroarene or \( R^{51, B} \); \( R^{51, B} \) is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

\( R^{52} \) is heteroaryl;

\( R^{53} \) is \( C_3-C_6 \)-cycloalkyl or \( C_4-C_6 \)-cycloalkenyl, each having one or two \( CH_2 \) moieties unplaced or replaced with independently selected \( O, C(O), CNOH, CNOCH_3, S, S(O), SO_2 \) or \( NH \) and one or two \( CH \) moieties unplaced or replaced with \( N \), and each of which is optionally fused with arene, heteroarene or \( R^{53, B} \);

wherein \( R^{53, B} \) is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

\( R^{54} \) is alkyl, alkenyl or alkynyl, each of which is optionally substituted with one or two or three independently selected \( R^{55, A} \), \( OR^{55, A} \), \( SR^{55, A} \), \( S(O)R^{55, A} \), \( SO_2R^{55, A} \), \( NHR^{55, A} \), \( N(NR^{55, A})_2 \), \( C(O)R^{55, A} \), \( C(O)NH, C(O)NH_2, C(O)NHR^{55, A}, C(O)NHR^{55, A}, NHC(O)R^{55, A}, NHC(O)OR^{55, A}, SO_2NH_2, SO_2NHR^{55, A}, SO_2N(R^{55, A}), NHC(O)NH_2, NHC(O)NHR^{55, A}, OH, (O), C(O)OH, N_3, CN, NH_2, CF_3, OCF_3, CF_2CF_3, OCF_2CF_3, F, Cl, Br or I substituents;
R^{55} is alkyl, alkenyl, alkynyl, phenyl, heteroaryl or R^{56};
wherein the alkyl, alkenyl, alkynyl are optionally substituted with OCH_{3}; and
R^{56} is C_{3}-C_{6}-cycloalkyl or C_{4}-C_{6}-cycloalkenyl, each having one or two CH\_2 moieties unresolved or replaced with independently selected O, C(O), CNOH, CNOCH_{3}, S, S(O), SO\_2 or NH and one or two CH moieties unresolved or replaced with N.

2. The compound of claim 1 having formula II

![Chemical Structure](image)

or therapeutically acceptable salt thereof,
wherein

R^{100} is R^{50}, OR^{50}, SR^{50}, S(O)R^{50}, SO\_2R^{50}, C(O)R^{50}, CO(O)R^{50}, OC(O)R^{50}, OC(O)OR^{50},
NH\_2, NHR^{50}, N(R^{50})_2, C(O)NH\_2, C(O)NHR^{50}, C(O)NR^{50}, C(O)N(R^{50})_2, C(O)NHOH, C(O)NH\_2R^{50},
C(O)NHSO\_2R^{50}, C(O)NR^{55}SO\_2R^{50}, SO\_2NH\_2, SO\_2NHR^{50}, SO\_2N(R^{50})_2, CF\_3, CF\_2CF\_3, C(O)H,
C(O)OH, OH, (O), CN, N\_2, NO\_2, OCF\_3, OCF\_2CF\_3, F, Cl, Br or I;
n is 0, 1, 2, or 3;
A\_1 is N or C(A\_2);
one or two or three or each of A\_2, B\_1, D\_1 and E\_1 are independently selected from R\_1, OR\_1,
SR\_1, S(O)R\_1, SO\_2R\_1, C(O)R\_1, C(O)OR\_1, OC(O)R\_1, NHR\_1, N(R\_1)_2, C(O)NHR\_1, C(O)N(R\_1)_2,
NHC(O)R\_1, NHC(O)OR\_1, NR\_1C(O)NHR\_1, NR\_1C(O)N(R\_1)_2, SO\_2NHR\_1, SO\_2N(R\_1)_2, NHSO\_2R\_1,
NH\_2R\_1 and N(CH\_3)SO\_2N(CH\_3)R\_1, and the remainder of A\_2, B\_1, D\_1 and E\_1 are
independently selected from H, F, Cl, Br, I, CN, CF\_3, C(O)OH, C(O)NH\_2 and C(O)OR\_1A\_2.
Y is H, CN, NO₂, C(O)OH, F, Cl, Br, I, CF₃, OCF₃, CF₂CF₃, OCF₂CF₃, R¹⁷, OR¹⁷, C(O)R¹⁷, C(O)OR¹⁷, SR¹⁷, NH₂, NHR¹⁷, NR¹⁷, NHC(O)R¹⁷, C(O)NH₂, C(O)NHR¹⁷,
C(O)N(R¹⁷)₂, NHS(O)R¹⁷ or NHSO₂R¹⁷;
R¹ is R², R³, R⁴ or R⁵;
R¹A is C₁-C₆-alkyl, C₃-C₆-alkenyl or C₃-C₆-alkynyl;
R² is phenyl which is optionally fused with arene, heteroarene or R²A; R²A is cycloalkane or heterocycloalkane;
R³ is heteroaryl which is optionally fused with benzene, heteroarene or R³A; R³A is cycloalkane or heterocycloalkane;
R⁴ is cycloalkyl, cycloalkenyl, heterocycloalkyl or heterocycloalkenyl, each of which is optionally fused with arene, heteroarene or R⁴A; R⁴A is cycloalkane, cycloalkene,
heterocycloalkane or heterocycloalkene;
R⁵ is alkyl, alkenyl or alkynyl, each of which is optionally substituted with one or two or three independently selected R⁶, R⁷, OR⁷, SR⁷, S(O)R⁷, SO₂R⁷, NHR⁷, N(R⁷)₂, C(O)R⁷,
C(O)NH₂, C(O)NHR⁷, NHC(O)R⁷, NHSO₂R⁷, NHC(O)OR⁷, SO₂NH₂, SO₂NHR⁷, SO₂N(R⁷)₂,
NHC(O)NH₂, NHC(O)NHR⁷, NHC(O)CH(CH₃)NH₂, OH, (O), C(O)OH, N₃, CN, NH₂, CF₃, CF₂CF₃, F, Cl, Br or I substituents;
R⁶ is C₂-C₅-spiroalkyl, each of which is optionally substituted with OH, (O), N₃, CN, CF₃, CF₂CF₃, F, Cl, Br, I, NH₂, NH(CH₃) or N(CH₃)₂, wherein spiroalkyl means alkylene, both ends of which are attached to the same carbon atom;
R⁷ is R⁸, R⁹, R¹⁰ or R¹¹;
R⁸ is phenyl which is optionally fused with arene, heteroarene or R⁸A;
R⁸A is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;
R⁹ is heteroaryl which is optionally fused with arene, heteroarene or R⁹A; R⁹A is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;
R¹⁰ is C₃-C₅-cycloalkyl or C₄-C₅-cycloalkenyl, each having one or two CH₃ moieties unreplaced or replaced with independently selected O, C(O), CNOH, CNOCH₃, S, S(O), SO₂ or NH and one or two CH moieties unreplaced or replaced with N, and each of which is optionally fused with arene, heteroarene or R¹⁰A; R¹⁰A is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

565
$R^{11}$ is alkyl, alkenyl or alkylnyl, each of which is optionally substituted with one or two or three independently selected $R^{12}$, OR$^{12}$, NHR$^{12}$, N(R$^{12}$)$_2$, C(O)NH$_2$, C(O)NHR$^{12}$, C(O)N(R$^{12}$)$_2$, OH, (O), C(O)OH, N$_3$, CN, NH$_2$, CF$_3$, CF$_2$CF$_3$, F, Cl, Br or I substituents;

$R^{12}$ is $R^{13}$, $R^{14}$, $R^{15}$ or $R^{16}$;

$R^{13}$ is phenyl which is optionally fused with arene, heteroarene or $R^{13A}$, $R^{13A}$ is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

$R^{14}$ is heteroaryl, each of which is optionally fused with arene, heteroarene or $R^{14A}$, $R^{14A}$ is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

$R^{15}$ is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene, each of which is optionally fused with arene, heteroarene or $R^{15A}$; $R^{15A}$ is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

$R^{16}$ is alkyl, alkenyl or alkylnyl;

$R^{17}$ is $R^{18}$, $R^{19}$, $R^{20}$ or $R^{21}$;

$R^{18}$ is phenyl which is optionally fused with arene, heteroarene or $R^{18A}$, $R^{18A}$ is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

$R^{19}$ is heteroaryl which is optionally fused with arene, heteroarene or $R^{19A}$; $R^{19A}$ is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

$R^{20}$ is C$_3$-C$_{10}$-cycloalkyl or C$_4$-C$_{10}$-cycloalkenyl, each having one or two CH$_2$ moieties unreplaced or replaced with independently selected O, C(O), CNOH, CNOCH$_3$, S, S(O), SO$_2$ or NH and one or two CH moieties unreplaced or replaced with N, and each of which is optionally fused with arene, heteroarene or $R^{20A}$; $R^{20A}$ is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

$R^{21}$ is alkyl, alkenyl or alkylnyl, each of which is optionally substituted with one or two or three independently selected $R^{22}$, OR$^{22}$, NHR$^{22}$, N(R$^{22}$)$_2$, C(O)NH$_2$, C(O)NHR$^{22}$, C(O)N(R$^{22}$)$_2$, OH, (O), C(O)OH, N$_3$, CN, NH$_2$, CF$_3$, CF$_2$CF$_3$, F, Cl, Br or I substituents;

$R^{22}$ is $R^{23}$, $R^{24}$ or $R^{25}$;

$R^{23}$ is phenyl which is optionally fused with arene, heteroarene or $R^{23A}$; $R^{23A}$ is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

$R^{24}$ is heteroarene which is optionally fused with arene, heteroarene or $R^{24A}$; $R^{24A}$ is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;
$R^{25}$ is $C_3$-$C_6$-cycloalkyl or $C_4$-$C_8$-cycloalkenyl, each having one or two CH$_2$ moieties unrepraced or replaced with independently selected O, C(O), CNOH, CNOCH$_3$, S, S(O), SO$_2$ or NH and one or two CH moieties unrepraced or replaced with N, and each of which is optionally fused with arene, heteroarene or $R^{25A}$; $R^{25A}$ is cycloalkane, cycloalkene, heterocycloalkane or heterocycoalkene;

$R^{30}$ is cycloalkyl having one or two CH$_2$ moieties unrepraced or replaced with independently selected O, C(O), CNOH, CNOCH$_3$, S, S(O), SO$_2$ or NH and one or two CH moieties unrepraced or replaced with N; $R^{37}$ is $R^{38}$ or $R^{40}$, each of which is substituted with $R^{41}$; $R^{38}$ is phenyl; $R^{40}$ is $C_3$-$C_6$-cycloalkyl or $C_4$-$C_8$-cycloalkenyl, each having one or two CH$_2$ moieties unrepraced or replaced with independently selected O, C(O), CNOH, CNOCH$_3$, S, S(O), SO$_2$ or NH and one or two CH moieties unrepraced or replaced with N; $R^{51}$ is $R^{42}$; $R^{42}$ is substituted phenyl; wherein $R^2$, $R^3$, $R^4$, $R^6$, $R^8$, $R^{8A}$, $R^9$, $R^{10}$, $R^{13}$, $R^{14}$, $R^{15}$, $R^{18}$, $R^{19}$, $R^{20}$, $R^{23}$, $R^{24}$, $R^{25}$, $R^{30}$, $R^{38}$, $R^{40}$, and $R^{42}$ are independently optionally substituted with one or two or three or four or five independently selected $R^{50}$, OR$_2$, SR$_2$, S(O)R$_2$, SO$_2$R$_2$, C(O)R$_2$, OR, CO(O)R$_2$, OC(O)R$_2$, OC(O)OR, NH$_2$, NHR$_2$, N(R$_5$)$_2$, C(O)NH$_2$, C(O)NHR$_2$, C(O)N(R$_5$)$_2$, C(O)NHOH, C(O)NHOR$_2$, C(O)NH$_2$SO$_2$R$_2$, C(O)NR$_5$SO$_2$R$_2$, SO$_2$NH$_2$, SO$_2$NHR$_2$, SO$_2$N(R$_5$)$_2$, CF$_3$, CF$_2$CF$_3$, C(O)H, C(O)OH, OH, (O), CN, N$_3$, NO$_2$, OCF$_3$, OCF$_2$CF$_3$, F, Cl, Br or I substituents; $R^{50}$ is $R^{51}$, $R^{52}$, $R^{53}$ or $R^{54}$; $R^{51}$ is phenyl which is optionally fused with arene, heteroarene or $R^{51B}$; $R^{51B}$ is cycloalkane, cycloalkene, heterocycloalkane or heterocycoalkene; $R^{52}$ is heteroaryl; $R^{53}$ is $C_3$-$C_6$-cycloalkyl or $C_4$-$C_6$-cycloalkenyl, each having one or two CH$_2$ moieties unrepraced or replaced with independently selected O, C(O), CNOH, CNOCH$_3$, S, S(O), SO$_2$ or NH and one or two CH moieties unrepraced or replaced with N, and each of which is optionally fused with arene, heteroarene or $R^{53B}$; wherein $R^{53B}$ is cycloalkane, cycloalkene, heterocycloalkane or heterocycoalkene;
R^{54} is alkyl, alkenyl or alkynyl, each of which is optionally substituted with one or two or three independently selected R^{55}, OR^{55}, SR^{55}, S(O)R^{55}, SO_2R^{55}, NHR^{55}, N(R^{55})_2, C(O)R^{55}, C(O)NH_2, C(O)NHR^{55}, NH(C(O))R^{55}, NHSO_2R^{55}, NHC(O)OR^{55}, SO_2NH_2, SO_2NHR^{55}, SO_2N(R^{55})_2, NH(C(O))NH_2, NHC(O)NHR^{55}, OH, (O), C(O)OH, N_3, CN, NH_2, CF_3, OCF_3, CF_2CF_3, OCF_2CF_3, F, Cl, Br or I substituents;

R^{55} is alkyl, alkenyl, alkynyl, phenyl, heteroaryl or R^{56};

wherein the alkyl, alkenyl, alkynyl are optionally substituted with OCH_3; and

R^{56} is C_3-C_6-cycloalkyl or C_4-C_6-cycloalkenyl, each having one or two CH_2 moieties unreplaced or replaced with independently selected O, C(O), CNOH, CNOCH_3, S, S(O), SO_2 or NH and one or two CH moieties unreplaced or replaced with N.

3. The compound of claim 1 having formula III

\[
\text{(III),}
\]

or therapeutically acceptable salt thereof,

wherein

\[ R^{100} \] is R^{50}, OR^{50}, SR^{50}, S(O)R^{50}, SO_2R^{50}, C(O)R^{50}, CO(O)R^{50}, OC(O)R^{50}, OC(O)OR^{50}, NH_2, NHR^{50}, N(R^{50})_2, C(O)NH_2, C(O)NHR^{50}, C(O)N(R^{50})_2, C(O)NHOH, C(O)NHOR^{50}, C(O)NHSO_2R^{50}, C(O)NR^{55}SO_2R^{50}, SO_2NH_2, SO_2NHR^{50}, SO_2N(R^{50})_2, CF_3, CF_2CF_3, C(O)H, C(O)OH, OH, (O), CN, N_3, NO_2, OCF_3, OCF_2CF_3, F, Cl, Br or I;

\[ n = 0, 1, 2, \text{ or } 3; \]
A\(^1\) is N or C(A\(^2\));

one or two or three or each of A\(^2\), B\(^1\), D\(^1\) and E\(^1\) are independently selected from R\(^1\), OR\(^1\),
SR\(^1\), S(O)R\(^1\), SO\(_2\)R\(^1\), C(O)R\(^1\), C(O)OR\(^1\), OC(O)R\(^1\), NHR\(^1\), N(R\(^1\))\(_2\), C(O)NHR\(^1\), C(O)N(R\(^1\))\(_2\),
NH(C)OR\(^1\), NH(C)OR\(^1\), NR\(^1\)C(O)NHR\(^1\), NR\(^1\)C(O)N(R\(^1\))\(_2\), SO\(_2\)NH\(^1\), SO\(_2\)N(R\(^1\))\(_2\), NHSO\(_2\)R\(^1\),
NHSO\(_2\)NHR\(^1\) and N(CH\(_3\))SO\(_2\)N(CH\(_3\))R\(^1\); and the remainder of A\(^2\), B\(^1\), D\(^1\) and E\(^1\) are
independently selected from H, F, Cl, Br, I, CN, CF\(_3\), C(O)OH, C(O)NH\(_2\) and C(O)OR\(^{1A}\);

Y\(^1\) is H, CN, NO\(_2\), C(O)OH, F, Cl, Br, I, CF\(_3\), OCF\(_3\), CF\(_2\)CF\(_3\), OCF\(_2\)CF\(_3\), R\(^{17}\), OR\(^{17}\),
C(O)R\(^{17}\), C(O)OR\(^{17}\), SR\(^{17}\), NH\(_2\), NHR\(^{17}\), N(R\(^{17}\))\(_2\), NH(C)OR\(^{17}\), C(O)NH\(_2\), C(O)NHR\(^{17}\),
C(O)N(R\(^{17}\))\(_2\), NHS(O)R\(^{17}\) or NHSO\(_2\)R\(^{17}\);

R\(^1\) is R\(^2\), R\(^3\), R\(^4\) or R\(^5\);

R\(^{1A}\) is C\(_1\)-C\(_6\)-alkyl, C\(_3\)-C\(_6\)-alkenyl or C\(_3\)-C\(_6\)-alkynyl;

R\(^2\) is phenyl which is optionally fused with arene, heteroarene or R\(^{2A}\); R\(^{2A}\) is cycloalkane
or heterocycloalkane;

R\(^3\) is heteroaryl which is optionally fused with benzene, heteroarene or R\(^{3A}\); R\(^{3A}\) is
cycloalkane or heterocycloalkane;

R\(^4\) is cycloalkyl, cycloalkenyl, heterocycloalkyl or heterocycloalkenyl, each of which is
optionally fused with arene, heteroarene or R\(^{4A}\); R\(^{4A}\) is cycloalkane, cycloalkene,
heterocycloalkane or heterocycloalkene;

R\(^5\) is alkyl, alkenyl or alkynyl, each of which is optionally substituted with one or two or
three independently selected R\(^6\), R\(^7\), OR\(^7\), SR\(^7\), S(O)R\(^7\), SO\(_2\)R\(^7\), NHR\(^7\), N(R\(^7\))\(_2\), C(O)R\(^7\),
C(O)NH\(_2\), C(O)NHR\(^7\), NH(C)OR\(^7\), NH(C)OR\(^7\), SO\(_2\)NH\(_2\), SO\(_2\)NHR\(^7\), SO\(_2\)N(R\(^7\))\(_2\),
NH(C)OH\(_2\), NH(C)OH\(_2\), NH(C)CH(CH\(_3\))NH(C)CH(CH\(_3\))NH\(_2\), OH, (O), C(O)OH, N\(_2\),
CN, NH\(_2\), CF\(_3\), CF\(_2\)CF\(_3\), F, Cl, Br or I substituents;

R\(^6\) is C\(_2\)-C\(_5\)-spiroalkyl, each of which is optionally substituted with OH, (O), N\(_2\), CN,
CF\(_3\), CF\(_2\)CF\(_3\), F, Cl, Br, I, NH\(_2\), NH(CH\(_3\)) or N(CH\(_3\))\(_2\), wherein spiroalkyl means alkylene, both
ends of which are attached to the same carbon atom;

R\(^7\) is R\(^8\), R\(^9\), R\(^{10}\) or R\(^{11}\);

R\(^8\) is phenyl which is optionally fused with arene, heteroarene or R\(^{8A}\);

R\(^{8A}\) is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R\(^9\) is heteroaryl which is optionally fused with arene, heteroarene or R\(^{9A}\); R\(^{9A}\) is
cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;
R\(^{10}\) is C\(_3\)-C\(_{10}\)-cycloalkyl or C\(_4\)-C\(_{10}\)-cycloalkenyl, each having one or two CH\(_2\) moieties unreplaced or replaced with independently selected O, C(O), CN=O, CNOH, C=NOCH\(_3\), S, S(O), SO\(_2\) or NH and one or two CH moieties unreplaced or replaced with N, and each of which is optionally fused with arene, heteroarene or R\(^{10A}\); R\(^{10A}\) is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R\(^{11}\) is alkyl, alkenyl or alkynyl, each of which is optionally substituted with one or two or three independently selected R\(^{12}\), OR\(^{12}\), NHR\(^{12}\), N(R\(^{12}\))\(_2\), C(O)NH\(_2\), C(O)NHR\(^{12}\), C(O)N(R\(^{12}\))\(_2\), OH, (O), C(O)OH, N\(_3\), CN, NH\(_2\), CF\(_3\), CF\(_2\)CF\(_3\), F, Cl, Br or I substituents;

R\(^{12}\) is R\(^{13}\), R\(^{14}\), R\(^{15}\) or R\(^{16}\);

R\(^{13}\) is phenyl which is optionally fused with arene, heteroarene or R\(^{13A}\); R\(^{13A}\) is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R\(^{14}\) is heteroaryl, each of which is optionally fused with arene, heteroarene or R\(^{14A}\); R\(^{14A}\) is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R\(^{15}\) is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene, each of which is optionally fused with arene, heteroarene or R\(^{15A}\); R\(^{15A}\) is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R\(^{16}\) is alkyl, alkenyl or alkynyl;

R\(^{17}\) is R\(^{18}\), R\(^{19}\), R\(^{20}\) or R\(^{21}\);

R\(^{18}\) is phenyl which is optionally fused with arene, heteroarene or R\(^{18A}\); R\(^{18A}\) is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R\(^{19}\) is heteroaryl which is optionally fused with arene, heteroarene or R\(^{19A}\); R\(^{19A}\) is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R\(^{20}\) is C\(_3\)-C\(_{10}\)-cycloalkyl or C\(_4\)-C\(_{10}\)-cycloalkenyl, each having one or two CH\(_2\) moieties unreplaced or replaced with independently selected O, C(O), CN=O, CNOH, C=NOCH\(_3\), S, S(O), SO\(_2\) or NH and one or two CH moieties unreplaced or replaced with N, and each of which is optionally fused with arene, heteroarene or R\(^{20A}\); R\(^{20A}\) is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R\(^{21}\) is alkyl, alkenyl or alkynyl, each of which is optionally substituted with one or two or three independently selected R\(^{22}\), OR\(^{22}\), NHR\(^{22}\), N(R\(^{22}\))\(_2\), C(O)NH\(_2\), C(O)NHR\(^{22}\), C(O)N(R\(^{22}\))\(_2\), OH, (O), C(O)OH, N\(_3\), CN, NH\(_2\), CF\(_3\), CF\(_2\)CF\(_3\), F, Cl, Br or I substituents;

R\(^{22}\) is R\(^{23}\), R\(^{24}\) or R\(^{25}\);
R_{23}^\text{is phenyl which is optionally fused with arene, heteroarene or R}_{23}^{2A}, R_{23}^{2A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene; \\
R_{24}^\text{is heteroarene which is optionally fused with arene, heteroarene or R}_{24}^{2A}, R_{24}^{2A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene; \\
R_{25}^\text{is C}_3^-C_6^-\text{-cycloalkyl or C}_4^-C_6^-\text{-cycloalkenyl, each having one or two CH}_2\text{ moieties unreplaced or replaced with independently selected O, C(O), CNOH, CNOCH}_3\text{, S, S(O), SO}_2\text{ or NH and one or two CH moieties unreplaced or replaced with N, and each of which is optionally fused with arene, heteroarene or R}_{25}^{2A}, R_{25}^{2A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene; \\
R_{30}^\text{is cycloalkyl having one or two CH}_2\text{ moieties unreplaced or replaced with independently selected O, C(O), CNOH, CNOCH}_3\text{, S, S(O), SO}_2\text{ or NH and one or two CH moieties unreplaced or replaced with N; } \\
R_{37}^\text{is } R_{38}^{38} \text{ or } R_{40}^{40}, \text{ each of which is substituted with } R_{41}^{41}; \\
R_{38}^{38} \text{ is phenyl; } \\
R_{40}^{40} \text{ is C}_3^-C_8^-\text{-cycloalkyl or C}_4^-C_8^-\text{-cycloalkenyl, each having one or two CH}_2\text{ moieties unreplaced or replaced with independently selected O, C(O), CNOH, CNOCH}_3\text{, S, S(O), SO}_2\text{ or NH and one or two CH moieties unreplaced or replaced with N; } \\
R_{41}^{41} \text{ is } R_{42}^{42}; \\
R_{42}^{42} \text{ is substituted phenyl; } \\
\text{wherein } R_2, R_3, R_4, R_6, R_8, R_8^A, R_9, R_{10}, R_{13}, R_{14}, R_{15}, R_{18}, R_{19}, R_{20}, R_{23}, R_{24}, R_{25}, R_{30}, R_{38}, R_{40}, \text{ and } R_{42}^{42} \text{ are independently optionally substituted with one or two or three or four or five independently selected } R_{50}^{50}, \text{ OR}_{50}^{50}, \text{ SR}_{50}^{50}, S(O)R_{50}^{50}, \text{ SO}_2R_{50}^{50}, \text{ C(O)R}_{50}^{50}, \text{ CO(O)R}_{50}^{50}, \text{ OC(O)R}_{50}^{50}, \text{ OC(O)OR}_{50}^{50}, \text{ NHR}_{50}^{50}, N(R_{50}^{50})_2, \text{ C(O)NH}_2, \text{ C(O)NHR}_{50}^{50}, \text{ C(O)N(R}_{50}^{50})_2, \text{ C(O)NH}_{OH}, \text{ C(O)NHOR}_{50}^{50}, \text{ C(O)NHSO}_2R_{50}^{50}, \text{ C(O)NR}_{55}^{55}SO_2R_{50}^{50}, \text{ SO}_2NH}_2, \text{ SO}_2NHR}_{50}^{50}, \text{ SO}_2N(R_{50}^{50})_2, CF_3, CF_2CF_3, \text{ C(O)H, C(O)OH, OH, (O), CN, N}_3, \text{ NO}_2, OCF}_3, OCF}_2CF_3, F, Cl, Br or 1 substituents; } \\
R_{50}^{50} \text{ is } R_{51}^{51}, R_{52}^{52}, R_{53}^{53} \text{ or } R_{54}^{54}; \\
R_{51}^{51} \text{ is phenyl which is optionally fused with arene, heteroarene or R}_{51}^{51B}, R_{51}^{51B} \text{ is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene; } \\
R_{52}^{52} \text{ is heteroaryl; } \\
R_{53}^{53} \text{ is C}_3^-C_8^-\text{-cycloalkyl or C}_4^-C_8^-\text{-cycloalkenyl, each having one or two CH}_2\text{ moieties unreplaced or replaced with independently selected O, C(O), CNOH, CNOCH}_3\text{, S, S(O), SO}_2\text{ or}
NH and one or two CH moieties unreplaced or replaced with N, and each of which is optionally fused with arene, heteroarene or $R^{53B}$;

wherein $R^{53B}$ is cycloalkane, cycloalkene, heterocycloalkane or heterocyclooalkene;

$R^{54}$ is alkyl, alkenyl or alkynyl, each of which is optionally substituted with one or two or three independently selected $R^{55}$, OR$^{55}$, SR$^{55}$, S(O)R$^{55}$, SO$_2$R$^{55}$, NHR$^{55}$, N(R$^{55})_2$, C(O)R$^{55}$, C(O)NH$_2$, C(O)NHR$^{55}$, NHC(O)R$^{55}$, NHSO$_2$R$^{55}$, NHC(O)OR$^{55}$, SO$_2$NH$_2$, SO$_2$NIIR$^{55}$, SO$_2$N(R$^{55})_2$, NHC(O)NH$_2$, NHC(O)NHR$^{55}$, OH, (O), C(O)OH, N$_3$, CN, NH$_2$, CF$_3$, OCF$_3$, CF$_2$CF$_3$, OCF$_2$CF$_3$, F, Cl, Br or I substituents;

$R^{55}$ is alkyl, alkenyl, alkynyl, phenyl, heteroaryl or $R^{56}$;

wherein the alkyl, alkenyl, alkynyl are optionally substituted with OCH$_3$; and

$R^{56}$ is C$_3$-C$_6$-cycloalkyl or C$_4$-C$_5$-cycloalkenyl, each having one or two CH moieties unreplaced or replaced with independently selected O, C(O), CNOH, CNOCH$_3$, S, S(O), SO$_2$ or NH and one or two CH moieties unreplaced or replaced with N.

4. The compound of claim 1 having formula IV

![Chemical Structure](image)

or therapeutically acceptable salt thereof,

wherein

$R^{100}$ is $R^{50}$, OR$^{50}$, SR$^{50}$, S(O)R$^{50}$, SO$_2$R$^{50}$, C(O)R$^{50}$, CO(O)R$^{50}$, OC(O)R$^{50}$, OC(O)OR$^{50}$, NH$_2$, NHR$^{50}$, N(R$^{50})_2$, C(O)NH$_2$, C(O)NHR$^{50}$, C(O)N(R$^{50})_2$, C(O)NHOH, C(O)NHor$^{50}$,
C(O)NHSO₂R', C(O)NR₅SO₂R', SO₂NH₂, SO₂NHR₅', SO₂N(R₅')₂, CF₃, CF₂CF₃, C(O)H, C(O)OH, OH, (O), CN, N₃, NO₂, OCF₃, OCF₂CF₃, F, Cl, Br or I;
n is 0, 1, 2, or 3;
A¹ is N or C(A²);
one or two or three or each of A², B¹, D¹ and E¹ are independently selected from R¹, OR¹, SR¹, S(O)R¹, SO₂R¹, C(O)R¹, C(O)OR¹, OC(O)R¹, NH₃R¹, N(R¹)₂, C(O)NHR¹, C(O)N(R¹)₂, NHC(O)R¹, NHC(O)OR¹, NR¹C(O)NHR¹, NR¹C(O)N(R¹)₂, SO₂NHR¹, SO₂N(R¹)₂, NHSO₂R¹, NHSO₂NHR¹ and N(CH₃)₂SO₂N(CH₃)R¹, and the remainder of A², B¹, D¹ and E¹ are independently selected from H, F, Cl, Br, I, CN, CF₃, C(O)OH, C(O)NH₂ and C(O)OR¹;
Y¹ is H, CN, NO₂, C(O)OH, F, Cl, Br, I, CF₃, OCF₃, CF₂CF₃, OCF₂CF₃, R¹, OR¹, C(O)R¹, C(O)OR¹, SR¹, NH₂, NHR¹, N(R¹)₂, NHC(O)R¹, C(O)NH₂, C(O)NHR¹, C(O)N(R¹)₂, NH₃R¹, SO₂R¹ or NHSO₂R¹;
R¹ is R², R³, R⁴ or R⁵;
R¹A is C₁-C₆-alkyl, C₅-C₆-alkenyl or C₃-C₆-alkynyl;
R² is phenyl which is optionally fused with arene, heteroarene or R²A; R²A is cycloalkane or heterocycloalkane;
R³ is heteroaryl which is optionally fused with benzene, heteroarene or R³A; R³A is cycloalkane or heterocycloalkane;
R⁴ is cycloalkyl, cycloalkenyl, heterocycloalkyl or heterocycloalkenyl, each of which is optionally fused with arene, heteroarene or R⁴A; R⁴A is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;
R⁵ is alkyl, alkenyl or alkynyl, each of which is optionally substituted with one or two or three independently selected R⁶, R⁷, OR⁷, SR⁷, S(O)R⁷, SO₂R⁷, NHR⁷, N(R⁷)₂, C(O)R⁷, C(O)NH₂, C(O)NHR⁷, NH₂C(O)R⁷, SO₂NHR², SO₂N(R⁷)₂, NH₂C(O)NH₂, NHC(O)NHR², NHC(O)CH(CH₃)₂NHC(O)CH(CH₃)₂NH₂, OH, (O), C(O)OH, N₃, CN, NH₂, CF₃, CF₂CF₃, F, Cl, Br or I substituents;
R⁶ is C₂-C₅-spiroalkyl, each of which is optionally substituted with OH, (O), N₃, CN, CF₃, CF₂CF₃, F, Cl, Br, I, NH₂, NH(CH₃)₂ or N(CH₃)₂, wherein spiroalkyl means alkylene, both ends of which are attached to the same carbon atom;
R⁷ is R⁸, R⁹, R¹⁰ or R¹¹;
R⁸ is phenyl which is optionally fused with arene, heteroarene or R⁸A;
R^{8A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;
R^{9} is heteroaryl which is optionally fused with arene, heteroarene or R^{9A}; R^{9A} is
cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;
R^{10} is C_{3-10}-cycloalkyl or C_{4-10}-cycloalkenyl, each having one or two CH_{2} moieties
unreplaced or replaced with independently selected O, C(O), CNOH, CNOCH_{3}, S, S(O), SO_{2} or
NH and one or two CH moieties unreplaced or replaced with N, and each of which is optionally
fused with arene, heteroarene or R^{10A}; R^{10A} is cycloalkane, cycloalkene, heterocycloalkane or
heterocycloalkene;
R^{11} is alkyl, alkenyl or alkynyl, each of which is optionally substituted with one or two or
three independently selected R^{12}, OR^{12}, NHR^{12}, N(R^{12})_{2}, C(O)NH_{2}, C(O)NHR^{12}, C(O)N(R^{12})_{2},
OH, (O), C(O)OH, N_{3}, CN, NH_{2}, CF_{3}, CF_{2}CF_{3}, F, Cl, Br or I substituents;
R^{12} is R^{13}, R^{14}, R^{15} or R^{16};
R^{13} is phenyl which is optionally fused with arene, heteroarene or R^{13A}; R^{13A} is
cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;
R^{14} is heteroaryl, each of which is optionally fused with arene, heteroarene or R^{14A}; R^{14A}
is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;
R^{15} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene, each of which is
optionally fused with arene, heteroarene or R^{15A}; R^{15A} is cycloalkane, cycloalkene,
heterocycloalkane or heterocycloalkene;
R^{16} is alkyl, alkenyl or alkynyl;
R^{17} is R^{18}, R^{19}, R^{20} or R^{21};
R^{18} is phenyl which is optionally fused with arene, heteroarene or R^{18A}; R^{18A} is
cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;
R^{19} is heteroaryl which is optionally fused with arene, heteroarene or R^{19A}; R^{19A} is
cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;
R^{20} is C_{3-10}-cycloalkyl or C_{4-10}-cycloalkenyl, each having one or two CH_{2} moieties
unreplaced or replaced with independently selected O, C(O), CNOH, CNOCH_{3}, S, S(O), SO_{2} or
NH and one or two CH moieties unreplaced or replaced with N, and each of which is optionally
fused with arene, heteroarene or R^{20A}; R^{20A} is cycloalkane, cycloalkene, heterocycloalkane or
heterocycloalkene;
R^{21} is alkyl, alkenyl or alkynyl, each of which is optionally substituted with one or two or three independently selected R^{22}, OR^{22}, NHR^{22}, N(R^{22})_2, C(O)NH_2, C(O)NHR^{22}, C(O)N(R^{22})_2, OH, (O), C(O)OH, N_3, CN, NH_2, CF_3, CF_2CF_3, F, Cl, Br or 1 substituents;
R^{22} is R^{23}, R^{24} or R^{25};
R^{23} is phenyl which is optionally fused with arene, heteroarene or R^{23A}; R^{23A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;
R^{24} is heteroarene which is optionally fused with arene, heteroarene or R^{24A}; R^{24A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;
R^{25} is C_3-C_8-cycloalkyl or C_4-C_8-cycloalkenyl, each having one or two CH_2 moieties unreplaced or replaced with independently selected O, C(O), CNOH, CNOCH_3, S, S(O), SO_2 or NH and one or two CH moieties unreplaced or replaced with N, and each of which is optionally fused with arene, heteroarene or R^{25A}; R^{25A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;
R^{30} is cycloalkyl having one or two CH_2 moieties unreplaced or replaced with independently selected O, C(O), CNOH, CNOCH_3, S, S(O), SO_2 or NH and one or two CH moieties unreplaced or replaced with N;
R^{37} is R^{38} or R^{40}, each of which is substituted with R^{41};
R^{38} is phenyl;
R^{40} is C_3-C_8-cycloalkyl or C_4-C_8-cycloalkenyl, each having one or two CH_2 moieties unreplaced or replaced with independently selected O, C(O), CNOH, CNOCH_3, S, S(O), SO_2 or NH and one or two CH moieties unreplaced or replaced with N;
R^{41} is R^{42};
R^{42} is substituted phenyl;
wherein R^2, R^3, R^4, R^6, R^8, R^8A, R^9, R^{10}, R^{13}, R^{14}, R^{15}, R^{18}, R^{19}, R^{20}, R^{23}, R^{24}, R^{25}, R^{30}, R^{38}, R^{40}, and R^{42} are independently optionally substituted with one or two or three or four or five independently selected R^{50}, OR^{50}, SR^{50}, S(O)R^{50}, SO_2R^{50}, C(O)R^{50}, CO(O)R^{50}, OC(O)R^{50}, OC(O)OR^{50}, NH_2, NHR^{50}, N(R^{50})_2, C(O)NH_2, C(O)NHR^{50}, C(O)N(R^{50})_2, C(O)NHOH, C(O)NHOH^{50}, C(O)NHSO_2R^{50}, C(O)NR^{55}SO_2R^{50}, SO_2NH_2, SO_2NHR^{50}, SO_2N(R^{50})_2, CF_3, CF_2CF_3, C(O)OH, C(O)OH, OH, (O), CN, N_3, NO_2, OCF_3, OCF_2CF_3, F, Cl, Br or 1 substituents;
R^{50} is R^{51}, R^{52}, R^{53} or R^{54};

575
R^{51} is phenyl which is optionally fused with arene, heteroarene or R^{51B}; R^{51B} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R^{52} is heteroaryl;

R^{53} is C_{3-6}-cycloalkyl or C_{4-6}-cycloalkenyl, each having one or two CH2 moieties unreplaced or replaced with independently selected O, C(O), CNOH, CNOCH3, S, S(O), SO2 or NH and one or two CH moieties unreplaced or replaced with N, and each of which is optionally fused with arene, heteroarene or R^{53B};

wherein R^{53B} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R^{54} is alkyl, alkenyl or alkynyl, each of which is optionally substituted with one or two or three independently selected R^{55}, OR^{55}, S\cdot R^{55}, S\cdot O\cdot R^{55}, SO2R^{55}, NHR^{55}, N(\cdot R^{55})2, C(O)\cdot R^{55}, C(O)NH2, C(O)\cdot NHR^{55}, NHC(O)\cdot R^{55}, NH\cdot SO2\cdot R^{55}, NH\cdot C(O)\cdot OR^{55}, SO2NH2, SO2NHR^{55}, SO2N(\cdot R^{55})2, NH\cdot (O)\cdot NH\cdot NHR^{55}, OH\cdot (O), C(O)\cdot OH, N3, CN, NH2, CF3, OCF3, CF2CF3, OCF2CF3, F, Cl, Br or I substituents;

R^{55} is alkyl, alkenyl, alkynyl, phenyl, heteroaryl or R^{56};

wherein the alkyl, alkenyl, alkynyl are optionally substituted with OCH3; and

R^{56} is C_{3-6}-cycloalkyl or C_{4-6}-cycloalkenyl, each having one or two CH2 moieties unreplaced or replaced with independently selected O, C(O), CNOH, CNOCH3, S, S(O), SO2 or NH and one or two CH moieties unreplaced or replaced with N.

5. The compound of claim 1 having formula V

![Chemical structure](image-url)
(V),

or therapeutically acceptable salt thereof,

wherein

\[ R^{100} \text{ is } R^{50}, \text{ OR}^{50}, \text{ SR}^{50}, S(O)R^{50}, \text{ SO}_{2}R^{50}, \text{ C}(O)R^{50}, \text{ CO}(O)R^{50}, \text{ OC}(O)R^{50}, \text{ OC}(O)\text{OR}^{50}, \]

\[ \text{NH}_{2}, \text{ NHR}^{50}, N(\text{R}^{50})_{2}, \text{ C}(O)\text{NH}_{2}, \text{ C}(O)\text{NHR}^{50}, \text{ C}(O)\text{N}(\text{R}^{50})_{2}, \text{ C}(O)\text{NHOH}, \text{ C}(O)\text{NHOR}^{50}, \]

\[ \text{C}(O)\text{NH}_{2}\text{R}^{50}, \text{ C}(O)\text{NR}^{50}\text{SO}_{2}R^{50}, \text{ SO}_{2}\text{NH}_{2}, \text{ SO}_{2}\text{NHR}^{50}, \text{ SO}_{2}\text{N}(\text{R}^{50})_{2}, \text{ C}(O)\text{H}, \text{ C}(O)\text{OH}, \text{ OH}, \]

\[ \text{O}, \text{ CN}, \text{ N}_{3}, \text{ NO}_{2}, \text{ CF}_{3}, \text{ CF}_{2}\text{CF}_{3}, \text{ OCF}_{3}, \text{ OCF}_{2}\text{CF}_{3}, \text{ F}, \text{ Cl}, \text{ Br or I}; \]

\[ n \text{ is } 0, 1, 2, \text{ or } 3; \]

\[ A^{1} \text{ is } N \text{ or } C(A^{2}); \]

one or two or three or each of \( A^{2}, B^{1}, D^{1} \) and \( E^{1} \) are independently selected from \( R^{1}, \text{ OR}^{1}, \)

\[ \text{SR}^{1}, S(O)R^{1}, \text{ SO}_{2}R^{1}, \text{ C}(O)R^{1}, \text{ C}(O)\text{OR}^{1}, \text{ OC}(O)R^{1}, \text{ NHR}^{1}, N(\text{R}^{1})_{2}, \text{ C}(O)\text{NHR}^{1}, \text{ C}(O)\text{N}(\text{R}^{1})_{2}, \]

\[ \text{NH}^{2}, \text{ NHC}(O)R^{1}, \text{ NHC}(O)\text{OR}^{1}, \text{ NR}^{1}\text{C}(O)\text{NH}^{1}, \text{ NR}^{1}\text{C}(O)\text{N}(\text{R}^{1})_{2}, \text{ SO}_{2}\text{NHR}^{1}, \text{ SO}_{2}\text{N}(\text{R}^{1})_{2}, \text{ NH}^{2}\text{SO}_{2}R^{1}, \]

\[ \text{NHC}(O)\text{NH}_{2} \text{ and } C(O)\text{OR}^{1A}, N(\text{CH}_{3})\text{SO}_{2}N(\text{CH}_{3})R^{1}, \text{ and the remainder of } A^{2}, B^{1}, D^{1} \text{ and } E^{1} \text{ are } \]

independently selected from \( H, F, \text{ Cl}, \text{ Br}, I, \text{ CN}, \text{ CF}_{3}, \text{ C}(O)\text{OH}, \text{ C}(O)\text{NH}_{2} \text{ and } C(O)\text{OR}^{1A}; \)

\[ Y^{1} \text{ is } H, \text{ CN}, \text{ NO}_{2}, C(O)\text{OH}, F, \text{ Cl}, \text{ Br}, I, \text{ CF}_{3}, \text{ OCF}_{3}, \text{ CF}_{2}\text{CF}_{3}, \text{ OCF}_{2}\text{CF}_{3}, R^{17}, \text{ OR}^{17}, \]

\[ C(O)\text{R}^{17}, C(O)\text{OR}^{17}, \text{ SR}^{17}, \text{ NH}_{2}, \text{ NHR}^{17}, N(\text{R}^{17})_{2}, \text{ NHC}(O)\text{R}^{17}, \text{ C}(O)\text{NH}_{2}, \text{ C}(O)\text{NHR}^{17}, \]

\[ C(O)\text{N}(\text{R}^{17})_{2}, \text{ NH}^{2}\text{SO}(O)\text{R}^{17} \text{ or } \text{NH}^{2}\text{SO}_{2}R^{17}; \]

\[ R^{1} \text{ is } R^{2}, R^{3}, R^{4} \text{ or } R^{5}; \]

\[ R^{1A} \text{ is } C_{1}-C_{6}-\text{alkyl}, C_{3}-C_{6}-\text{alkenyl or } C_{3}-C_{6}-\text{alkynyl}; \]

\[ R^{2} \text{ is phenyl which is optionally fused with arene, heteroarene or } R^{2A}, R^{2A} \text{ is cycloalkane or heterocycloalkane; } \]

\[ R^{3} \text{ is heteroaryl which is optionally fused with benzene, heteroarene or } R^{3A}; R^{3A} \text{ is cycloalkane or heterocycloalkane; } \]

\[ R^{4} \text{ is cycloalkyl, cycloalkenyl, heterocycloalkyl or heterocycloalkenyl, each of which is } \]

optionally fused with arene, heteroarene or \( R^{4A}, R^{4A} \text{ is cycloalkane, cycloalkene, } \]

heterocycloalkane or heterocycloalkene; \]

\[ R^{5} \text{ is alkyl, alkenyl or alkynyl, each of which is optionally substituted with one or two or } \]

three independently selected \( R^{6}, R^{7}, \text{ OR}^{7}, \text{ SR}^{7}, S(O)R^{7}, \text{ SO}_{2}R^{7}, \text{ NHR}^{7}, N(\text{R}^{7})_{2}, \text{ C}(O)R^{7}, \]

\[ \text{C}(O)\text{NH}_{2}, \text{ C}(O)\text{NHR}^{7}, \text{ NHC}(O)\text{R}^{7}, \text{ NH}^{2}\text{SO}_{2}R^{7}, \text{ NHC}(O)\text{OR}^{7}, \text{ SO}_{2}\text{NH}_{2}, \text{ SO}_{2}\text{NHR}^{7}, \text{ SO}_{2}\text{N}(\text{R}^{7})_{2}, \]

577
NHC(O)NH₂, NHC(O)NHR², NHC(O)CH(CH₃)NH₂, NHC(O)CH(CH₃)NH₂, OH, (O), C(O)OH, N₃, CN, NH₂, CF₃, CF₂CF₃, F, Cl, Br or I substituents;

R⁶ is C₂-C₅-spiroalkyl, each of which is optionally substituted with OH, (O), N₃, CN, CF₃, CF₂CF₃, F, Cl, Br, I, NH₂, NH(CH₃) or N(CH₃)₂, wherein spiroalkyl means alkylene, both ends of which are attached to the same carbon atom;

R⁷ is R⁸, R⁹, R¹⁰ or R¹¹;

R⁸ is phenyl which is optionally fused with arene, heteroarene or R⁸⁺;

R⁸⁺ is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R⁹ is heteroaryl which is optionally fused with arene, heteroarene or R⁹⁺; R⁹⁺ is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R¹⁰ is C₃-C₁₀-cycloalkyl or C₄-C₁₀-cycloalkenyl, each having one or two CH₂ moieties unreplaced or replaced with independently selected O, C(O), CNOH, CNOCH₃, S, S(O), SO₂ or NH and one or two CH moieties unreplaced or replaced with N, and each of which is optionally fused with arene, heteroarene or R¹⁰⁺; R¹⁰⁺ is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R¹¹ is alkyl, alkenyl or alkynyl, each of which is optionally substituted with one or two or three independently selected R¹², OR¹², NHR¹², N(R¹²)₂, C(O)NH₂, C(O)NHR¹², C(O)N(R¹²)₂, OH, (O), C(O)OH, N₃, CN, NH₂, CF₃, CF₂CF₃, F, Cl, Br or I substituents;

R¹² is R¹³, R¹⁴, R¹⁵ or R¹⁶;

R¹³ is phenyl which is optionally fused with arene, heteroarene or R¹³⁺; R¹³⁺ is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R¹⁴ is heteroaryl, each of which is optionally fused with arene, heteroarene or R¹⁴⁺; R¹⁴⁺ is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R¹⁵ is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene, each of which is optionally fused with arene, heteroarene or R¹⁵⁺; R¹⁵⁺ is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R¹⁶ is alkyl, alkenyl or alkynyl;

R¹⁷ is R¹⁸, R¹⁹, R²⁰ or R²¹;

R¹⁸ is phenyl which is optionally fused with arene, heteroarene or R¹⁸⁺; R¹⁸⁺ is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;
R¹⁹ is heteroaryl which is optionally fused with arene, heteroarene or R¹⁹A; R¹⁹A is
cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R²⁰ is C₃-C₁₀-cycloalkyl or C₄-C₁₀-cycloalkenyl, each having one or two CH₂ moieties
unreplaced or replaced with independently selected O, C(O), CNOH, CNOCH₃, S, S(O), SO₂ or
NH and one or two CH moieties unreplaced or replaced with N, and each of which is optionally
fused with arene, heteroarene or R²⁰A; R²⁰A is cycloalkane, cycloalkene, heterocycloalkane or
heterocycloalkene;

R²¹ is alkyl, alkenyl or alkynyl, each of which is optionally substituted with one or two or
three independently selected R²², OR²², NHR²², N(R²²)₂, C(O)NH₂, C(O)NHR²², C(O)N(R²²)₂,
OH, (O), C(O)OH, N₃, CN, NH₂, CF₃, CF₂CF₃, F, Cl, Br or I substituents;
R²² is R²², R²⁴ or R²⁵;
R²³ is phenyl which is optionally fused with arene, heteroarene or R²³A; R²³A is
cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R²⁴ is heteroarene which is optionally fused with arene, heteroarene or R²⁴A; R²⁴A is
cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R²⁵ is C₃-C₅-cycloalkyl or C₄-C₆-cycloalkenyl, each having one or two CH₂ moieties
unreplaced or replaced with independently selected O, C(O), CNOH, CNOCH₃, S, S(O), SO₂ or
NH and one or two CH moieties unreplaced or replaced with N, and each of which is optionally
fused with arene, heteroarene or R²⁵A; R²⁵A is cycloalkane, cycloalkene, heterocycloalkane or
heterocycloalkene;

R³⁰ is cycloalkyl having one or two CH₂ moieties unreplaced or replaced with
independently selected O, C(O), CNOH, CNOCH₃, S, S(O), SO₂ or NH and one or two CH
moieties unreplaced or replaced with N;
R³⁷ is R³⁸ or R⁴⁰, each of which is substituted with R⁴¹;
R³⁸ is phenyl;
R⁴⁰ is C₃-C₆-cycloalkyl or C₄-C₈-cycloalkenyl, each having one or two CH₂ moieties
unreplaced or replaced with independently selected O, C(O), CNOH, CNOCH₃, S, S(O), SO₂ or
NH and one or two CH moieties unreplaced or replaced with N;
R⁴¹ is R⁴²;
R⁴² is substituted phenyl;
wherein R², R³, R⁴, R⁶, R⁸, R⁸A, R⁹, R¹⁰, R¹³, R¹⁴, R¹⁵, R¹⁸, R¹⁹, R²⁰, R²³, R²⁴, R²⁵, R³¹, R³⁸, R⁴⁰, and R⁴² are independently optionally substituted with one or two or three or four or five independently selected R⁵⁰, OR⁵⁰, SR⁵⁰, S(O)R⁵⁰, SO₂R⁵⁰, C(O)R⁵⁰, CO(O)R⁵⁰, OC(O)R⁵⁰, OC(O)OR⁵⁰, NH₂, NHR⁵⁰, N(R⁵⁰)₂, C(O)NH₂, C(O)NHR⁵⁰, C(O)N(NH₂)₂, C(O)NHOH, C(O)NHOR⁵⁰, C(O)NHSO₂R⁵⁰, C(O)NR⁵⁵SO₃R⁵⁰, SO₂NH₂, SO₂NHR⁵⁰, SO₂N(NH₂)₂, CF₃, CF₂CF₃, C(O)H, C(O)OH, OH, (O), CN, N₁, NO₂, OCF₃, OCF₂CF₃, F, Cl, Br or I substituents; R⁵⁰ is R⁵¹, R⁵², R⁵³ or R⁵⁴;
R⁵¹ is phenyl which is optionally fused with arene, heteroarene or R⁵¹B, R⁵¹B is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;
R⁵² is heteroaryl;
R⁵³ is C₃-C₆-cycloalkyl or C₄-C₆-cycloalkenyl, each having one or two CH₂ moieties unreplaced or replaced with independently selected O, C(O), CNOH, CNOCH₃, S, S(O), SO₂ or NH and one or two CH moieties unreplaced or replaced with N, and each of which is optionally fused with arene, heteroarene or R⁵¹B;
wherein R⁵¹B is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;
R⁵⁴ is alkyl, alkenyl or alkylnyl, each of which is optionally substituted with one or two or three independently selected R⁵⁵, OR⁵⁵, SR⁵⁵, S(O)R⁵⁵, SO₂R⁵⁵, NHR⁵⁵, N(R⁵⁵)₂, C(O)R⁵⁵, C(O)NH₂, C(O)NHR⁵⁵, NHC(O)R⁵⁵, NHSO₂R⁵⁵, NH(C(O))R⁵⁵, SO₂NH₂, SO₂NHR⁵⁵, SO₂N(R⁵⁵)₂, NHC(O)NH₂, NHC(O)NHR⁵⁵, OH, (O), C(O)OH, N₃, CN, NH₂, CF₃, OCF₃, CF₂CF₃, OCF₂CF₃, F, Cl, Br or I substituents; R⁵⁵ is alkyl, alkenyl, alkylnyl, phenyl, heteroaryl or R⁵⁶;
wherein the alkyl, alkenyl, alkylnyl are optionally substituted with OCH₃; and
R⁵⁶ is C₃-C₆-cycloalkyl or C₄-C₆-cycloalkenyl, each having one or two CH₂ moieties unreplaced or replaced with independently selected O, C(O), CNOH, CNOCH₃, S, S(O), SO₂ or NH and one or two CH moieties unreplaced or replaced with N.

6. The compound or therapeutically acceptable salt according to any one of claims 1, 2, 3, 4 and 5, wherein
A¹ is C(A²); and
A² is H.
7. The compound or therapeutically acceptable salt according to any one of claims 1, 2, 3, 4 and 5, wherein

\[ A^1 \text{ is } C(A^2); \]
\[ A^2 \text{ is } H; \text{ and} \]
\[ B^1 \text{ is } \text{NHR}^1. \]

8. The compound or therapeutically acceptable salt according to any one of claims 1, 2, 3, 4 and 5, wherein

\[ A^1 \text{ is } C(A^2); \]
\[ A^2 \text{ is } H; \]
\[ B^1 \text{ is } \text{NHR}^1; \text{ and} \]
\[ D^1 \text{ is } H. \]

9. The compound or therapeutically acceptable salt according to any one of claims 1, 2, 3, 4 and 5, wherein

\[ A^1 \text{ is } C(A^2); \]
\[ A^2 \text{ is } H; \]
\[ B^1 \text{ is } \text{NHR}^1; \]
\[ D^1 \text{ is } H; \text{ and} \]
\[ E^1 \text{ is } H. \]

10. The compound or therapeutically acceptable salt according to any one of claims 1, 2, 3, 4 and 5, wherein

\[ A^1 \text{ is } C(A^2); \]
\[ A^2 \text{ is } H; \]
\[ B^1 \text{ is } \text{NHR}^1; \]
\[ D^1 \text{ is } H; \]
\[ E^1 \text{ is } H; \text{ and} \]
\[ Y^1 \text{ is } \text{NO}_2. \]

11. A compound or therapeutically acceptable salt wherein the compound is chosen from:
4-(4-(4′-chloro-1,1′-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)-2-phenoxybenzamide;
4-(4-(4′-chloro-1,1′-biphenyl-2-yl)methyl)piperazin-1-yl)-2-phenoxy-N-((4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)benzamide;
4-(4-(4′-chloro-1,1′-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)-2-(phenylthio)benzamide;
4-(4-(4′-chloro-1,1′-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(phenylthio)-N-((4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)benzamide;
4-(4-(4′-chloro-1,1′-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-((3-morpholin-4-ylpropyl)amino)-3-nitrophenyl)sulfonyl)-2-(phenylthio)benzamide;
4-(4-(4′-chloro-1,1′-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)-2-(phenylsulfonyl)benzamide;
4-(4-(4′-chloro-1,1′-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)-2-(phenylsulfonyl)benzamide;
2-anilino-4-(4-(4′-chloro-1,1′-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)benzamide;
2-anilino-4-(4-(4′-chloro-1,1′-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)benzamide;
4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-N-((4-((3-morpholin-4-ylpropyl)amino)-3-nitrophenyl)sulfonyl)-2-phenoxybenzamide;
4-(4-((2-(4-chlorophenyl)-5,5-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-N-((4-((3-morpholin-4-ylpropyl)amino)-3-nitrophenyl)sulfonyl)-2-phenoxybenzamide;
4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indazol-5-yloxy)-N-((4-((3-morpholin-4-ylpropyl)amino)-3-nitrophenyl)sulfonyl)benzamide;
4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indazol-5-yloxy)-N-((4-((1-methylpiperidin-4-yl)amino)-3-nitrophenyl)sulfonyl)benzamide;
4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-N-((4-((3-morpholin-4-ylpropyl)amino)-3-nitrophenyl)sulfonyl)-2-(1,2,3,4-tetrahydroquinolin-6-yl)oxo)benzamide;
4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-N-((4-((1-methylpiperidin-4-yl)amino)-3-nitrophenyl)sulfonyl)-2-(1,2,3,4-tetrahydroquinolin-6-yloxy)benzamide;

4-(4-((4'-chloro-4-(pyrrolidin-1-ylmethyl)-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)benzamide;

4-(4-((4'-chloro-4-(2-pyrrolidin-1-ylethyl)-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)benzamide;

4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-N-((4-((1-cyclo pentyl)piperidin-4-yl)amino)-3-nitrophenyl)sulfonyl)-2-(1H-indol-5-yloxy)benzamide

4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)-3-isobutylpiperazin-1-yl)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)-2-phenoxybenzamide;

4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-(2,4-dioxo-3-azabicyclo(3.2.0)hept-3-yl)phenyl)sulfonyl)-2-phenoxybenzamide;

4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-(4-methyl-6-oxo-1,4,5,6-tetrahydropyridazin-3-yl)phenyl)sulfonyl)-2-phenoxybenzamide;

4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-(3,3-dimethyl-2-oxoazetidin-1-yl)phenyl)sulfonyl)-2-phenoxybenzamide;

4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-(4-nitro-2H-1,2,3-triazol-2-yl)phenyl)sulfonyl)-2-phenoxybenzamide;

4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-phenoxy-N-((2-(2-piperidin-1-ylethoxy)phenyl)sulfonyl)benzamide;

4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-((((1-ethylpyrrolidin-2-yl)methyl)amino)carbonyl)-4-methoxyphenyl)sulfonyl)-2-phenoxybenzamide;

4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(1-naphthyloxy)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)benzamide;

4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(2-naphthyloxy)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)benzamide;

4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-((3-morpholin-4-ylpropyl)amino)-3-nitrophenyl)sulfonyl)-2-2-naphthyloxy)benzamide;
4-(4'-(4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(2-naphthoxy)-N-((4-
((tetrahydro-2H-pyran-4-ylmethyl)amino)-3-
((trifluoromethyl)sulfonyl)phenyl)sulfonyl)benzamide;
4-(4'-(4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((tetrahydro-2H-
pyran-4-ylmethyl)amino)phenyl)sulfonyl)-2-(quinolin-7-yl)oxy)benzamide;
4-(4'-(4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((tetrahydro-2H-
pyran-4-ylmethyl)amino)phenyl)sulfonyl)-2-(quinolin-6-yl)oxy)benzamide;
4-(4'-(4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yl)oxy)-N-((3-
nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)benzamide;
4-(4'-(4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(isoquinolin-5-yl)oxy)-N-((3-
nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)benzamide;
4-(4'-(4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-(3-
(dimethylamino)propyl)amino)-3-nitrophenyl)sulfonyl)-2-(isoquinolin-5-yl)oxy)benzamide;
4-(4'-(4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-(3-
(dimethylamino)propyl)amino)-3-nitrophenyl)sulfonyl)-2-(quinolin-6-yl)oxy)benzamide;
4-(4'-(4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-(3-
(dimethylamino)propyl)amino)-3-nitrophenyl)sulfonyl)-2-(1H-indol-5-yl)oxy)benzamide;
4-(4'-(4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yl)oxy)-N-((3-
nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)benzamide;
4-(4'-(4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-(3-
(dimethylamino)propyl)amino)-3-nitrophenyl)sulfonyl)-2-(1H-indol-4-yl)oxy)benzamide;
4-(4'-(4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-(3-
(dimethylamino)propyl)amino)-3-nitrophenyl)sulfonyl)-2-(1H-indol-6-yl)oxy)benzamide;
4-(4'-(4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(isoquinolin-7-yl)oxy)-N-((4-
((3-morpholin-4-ylpropyl)amino)-3-nitrophenyl)sulfonyl)benzamide;
4-(4'-(4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-(3-
(dimethylamino)propyl)amino)-3-nitrophenyl)sulfonyl)-2-(isoquinolin-7-yl)oxy)benzamide;
4-(4'-(2-(4-chlorophenyl)-5,5-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-
indol-5-yl)oxy)-N-((4-((3-morpholin-4-ylpropyl)amino)-3-nitrophenyl)sulfonyl)benzamide;
4-(4'-(2-(4-chlorophenyl)-5,5-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-N-((4-
((3-(dimethylamino)propyl)amino)-3-nitrophenyl)sulfonyl)-2-(1H-indol-5-yl)oxy)benzamide;
4-(4-(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((4-((3-morpholin-4-ylpropyl)amino)-3-nitrophenyl)sulfonyle)benzamide;
4-(4-(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-N-((4-((3-(dimethylamino)propyl)amino)-3-nitrophenyl)sulfonyle)-2-(1H-indol-5-yloxy)benzamide;
4-(4-((2-(4-chlorophenyl)-5,5-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((4-((3-morpholin-4-ylpropyl)amino)-3-nitrophenyl)sulfonyle)benzamide;
4-(4-(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((4-((3-morpholin-4-ylpropyl)amino)-3-nitrophenyl)sulfonyle)benzamide;
4-(4-((3-(dimethylamino)propyl)amino)-3-nitrophenyl)sulfonyle)-2-(1H-indol-4-yloxy)benzamide;
4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-N-((4-((3-(dimethylamino)propyl)amino)-3-nitrophenyl)sulfonyle)-2-(1H-indol-4-yloxy)benzamide;
4-(4-(4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((4-((3-morpholin-4-ylpropyl)amino)-3-nitrophenyl)sulfonyle)benzamide;
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((4-((3-morpholin-4-ylpropyl)amino)-3-nitrophenyl)sulfonyle)benzamide;
4-(4-(4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-methoxyphenyl)sulfonyle)-2-phenoxybenzamide;
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-methylphenyl)sulfonyle)-2-phenoxybenzamide;
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((4-((tetrahydro-2H-pyran-4-ylmethyl)amino)-3-((trifluoromethyl)sulfonyle)phenyl)sulfonyle)benzamide;
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((4-((tetrahydro-2H-pyran-4-ylmethyl)amino)-3-((trifluoromethyl)sulfonyle)phenyl)sulfonyle)benzamide;
4-(4-(4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-((3-(dimethylamino)propyl)amino)-3-((trifluoromethyl)sulfonyle)phenyl)sulfonyle)-2-(1H-indol-5-yloxy)benzamide;
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((4-((3-morpholin-4-ylpropyl)amino)-3-((trifluoromethyl)sulfonyle)phenyl)sulfonyle)benzamide;
N-((3-((chloro(difluoromethyl)sulfonyl)-4-((3-dimethylamino)propyl)amino)phenyl)sulfonyl)-4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yl)oxy)benzamide;

2-(1H-indol-4-yl)oxy)-4-(4-((2-(4-methoxyphenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((3-pyrrolidin-1-yl)propyl)amino)phenyl)sulfonyl)benzamide;

4-(4-(4,4-dimethyl-2-(4-(trifluoromethyl)phenyl)cyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yl)oxy)-N-((3-nitro-4-((3-pyrrolidin-1-yl)propyl)amino)phenyl)sulfonyl)benzamide;

4-(4-((4,4-dimethyl-2-(4-(trifluoromethoxy)phenyl)cyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yl)oxy)-N-((3-nitro-4-((3-pyrrolidin-1-yl)propyl)amino)phenyl)sulfonyl)benzamide;

4-(4-((4,4-dimethyl-2-(3-(trifluoromethyl)phenyl)cyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yl)oxy)-N-((3-nitro-4-((3-pyrrolidin-1-yl)propyl)amino)phenyl)sulfonyl)benzamide;

4-(4-((2-(3-fluorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yl)oxy)-N-((3-nitro-4-((3-pyrrolidin-1-yl)propyl)amino)phenyl)sulfonyl)benzamide;

4-(4-((2-(4-fluorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yl)oxy)-N-((3-nitro-4-((3-pyrrolidin-1-yl)propyl)amino)phenyl)sulfonyl)benzamide;

N-((3-((chloro(difluoromethyl)methyl)sulfonyl)-4-(1-methylpiperidin-4-yl)amino)phenyl)sulfonyl)-4-(4-(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yl)oxy)benzamide;

4-(4-((2-(4-chlorophenyl)cyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yl)oxy)-N-((4-((1-methylpiperidin-4-yl)amino)-3-nitrophenyl)sulfonyl)benzamide;

4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yl)oxy)-N-((4-((1-methylpiperidin-4-yl)amino)-3-((trifluoromethyl)sulfonyl)phenyl)sulfonyl)benzamide;

4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-((3-morpholin-4-yl)propyl)amino)phenyl)sulfonyl)-2-phenoxybenzamide;

4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)-2-(pyridin-3-yl)oxy)benzamide;
4-(4'-(4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(pyridin-3-ylmethoxy)-N-((4-
(tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)benzamide;
4-(4'-(4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-(((1R)-3-
(dimethylamino)-1-((phenylthio)methyl)propyl)amino)-3-nitrophenyl)sulfonyl)-2-
phenoxybenzamide;
4-(4'-(4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((tetrahydro-2H-
pyran-4-ylmethyl)amino)phenyl)sulfonyl)-2-(pyridin-4-ylmethoxy)benzamide;
4-(4'-(4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-((3-morpholin-4-
ylpropyl)amino)-3-nitrophenyl)sulfonyl)-2-(pyridin-3-ylmethoxy)benzamide;
4-(4'-(4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-((3-morpholin-4-
ylpropyl)amino)-3-nitrophenyl)sulfonyl)-2-(pyridin-4-ylmethoxy)benzamide;
4-(4'-(4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-((2-(4-methylpiperazin-
1-yl)ethyl)amino)-3-nitrophenyl)sulfonyl)-2-phenoxybenzamide;
4-(4'-(4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-((3-4-methylpiperazin-
1-yl)propyl)amino)-3-nitrophenyl)sulfonyl)-2-phenoxybenzamide;
4-(4'-(4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-((3-dimethylamino)propyl)(methyl)amino)-3-nitrophenyl)sulfonyl)-2-phenoxybenzamide;
4-(4'-(4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-(((1-methylpiperidi-
4-yl)methyl)amino)-3-nitrophenyl)sulfonyl)-2-phenoxybenzamide;
4-(4'-(4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-((1-methylpiperidi-
4-yl)methyl)amino)-3-nitrophenyl)sulfonyl)-2-phenoxybenzamide;
4-(4'-(4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-((3-
(dimethylamino)propyl)methyl)amino)-3-nitrophenyl)sulfonyl)-2-phenoxybenzamide;
4-(4'-(4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-cyano-4-((3-
(dimethylamino)propyl)amino)phenyl)sulfonyl)-2-phenoxybenzamide;
4-(4'-(4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((3-pyrroli-
1-ylpropyl)amino)phenyl)sulfonyl)-2-phenoxybenzamide;
4-(4'-(4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-((3-
(dimethylamino)propyl)amino)-3-(trifluoromethyl)phenyl)sulfonyl)-2-phenoxybenzamide;
4-(4'-(4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-((3-
isopropyl(methyl)amino)propyl)amino)-3-nitrophenyl)sulfonyl)-2-phenoxybenzamide;
4-(4'-(4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-((3-
(dimethylamino)propoxy)-3-nitrophenyl)sulfonyl)-2-phenoxybenzamide;
4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((4-(2-(4-methylpiperazin-1-yl)ethyl)amino)-3-nitrophenyl)sulfonyl)benzamide;

4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((4-((3-(4-methylpiperazin-1-yl)propyl)amino)-3-nitrophenyl)sulfonyl)benzamide;

4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((3-nitro-4-((3-pyrrolidin-1-yl)propyl)amino)phenyl)sulfonyl)benzamide;

4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((4-((1-methylpiperidin-4-yl)amino)-3-nitrophenyl)sulfonyl)benzamide;

4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((4-((3-(4-methylpiperazin-1-yl)propyl)amino)-3-nitrophenyl)sulfonyl)benzamide;

4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-N-((4-(3-(dimethylamino)propoxy)-3-nitrophenyl)sulfonyl)-2-(1H-indol-5-yloxy)benzamide;

4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((4-((2-(4-methylpiperazin-1-yl)ethyl)amino)-3-nitrophenyl)sulfonyl)benzamide;

4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((3-nitro-4-((3-pyrrolidin-1-yl)propyl)amino)phenyl)sulfonyl)benzamide;

4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((4-((1-methylpiperidin-4-yl)amino)-3-nitrophenyl)sulfonyl)benzamide;

4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((4-((1-methylpiperidin-4-yl)methyl)amino)-3-nitrophenyl)sulfonyl)benzamide;

4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((4-(((1-methylpiperidin-4-yl)methyl)amino)-3-nitrophenyl)sulfonyl)benzamide;

4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-N-((4-(3-(dimethylamino)propoxy)-3-nitrophenyl)sulfonyl)-2-(1H-indol-4-yloxy)benzamide;
4-[(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yl)oxy]-N-((4-(4-methylpiperazin-1-yl)-3-nitrophenyl)sulfonyl)benzamide;

4-[(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yl)oxy]-N-((3-nitro-4-((1-(2,2,2-trifluoroethyl)piperidin-4-yl)amino)phenyl)sulfonyl)benzamide;

4-[(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-N-((4-((4-(dimethylamino)-1-methylpiperidin-4-yl)methyl)amino)-3-nitrophenyl)sulfonyl)-2-(1H-indol-5-yl)oxy]benzamide;

4-[(4-(4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(2,3-dihydro-1,4-benzodioxin-5-yl)oxy]-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)benzamide;

4-[(4-((4'-chloro-4-(2-(dimethylamino)ethoxy)-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)-2-phenoxybenzamide;

4-[(4-((4'-chloro-4-(3-piperidin-1-ylpropoxy)-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)-2-phenoxybenzamide;

4-[(4-((4'-chloro-4-(2-morpholin-4-yloethoxy)-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)-2-phenoxybenzamide;

4-[(4-((4'-chloro-4-(3-(dimethylamino)propoxy)-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)-2-phenoxybenzamide;

4-[(4-((4'-chloro-4-(2-morpholin-4-yloethoxy)-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-phenoxy-N-((4-((tetrahydro-2H-pyran-4-ylmethyl)amino)-3-((trifluoromethyl)sulfonyl)phenyl)sulfonyl)benzamide;

4-[(4-((4'-chloro-4-(3-piperidin-1-ylpropoxy)-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-phenoxy-N-((4-((tetrahydro-2H-pyran-4-ylmethyl)amino)-3-((trifluoromethyl)sulfonyl)phenyl)sulfonyl)benzamide;

4-[(4-((4'-chloro-4-(3-(dimethylamino)propoxy)-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-phenoxy-N-((4-((tetrahydro-2H-pyran-4-ylmethyl)amino)-3-((trifluoromethyl)sulfonyl)phenyl)sulfonyl)benzamide;
4-(4'-(4-chloro-4-(2-(dimethylamino)ethoxy)-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-phenoxy-N-((4-(tetrahydro-2H-pyran-4-ylmethyl)amino)-3-((trifluoromethyl)sulfonyl)phenyl)sulfonyl)benzamide;

4-(4'-(4-chloro-4-(2-(dimethylamino)ethoxy)-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((3-pyrrolidin-1-ylpropyl)amino)phenyl)sulfonyl)-2-phenoxybenzamide;

4-(4'-(4-chloro-3-(2-(dimethylamino)ethoxy)-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)-2-phenoxybenzamide;

4-(4'-(4-chloro-3-(2-(dimethylamino)ethoxy)-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((3-pyrrolidin-1-ylpropyl)amino)phenyl)sulfonyl)-2-phenoxybenzamide;

4-(4'-(4-chloro-3-(2-(dimethylamino)ethoxy)-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-phenoxy-N-((4-(tetrahydro-2H-pyran-4-ylmethyl)amino)-3-((trifluoromethyl)sulfonyl)phenyl)sulfonyl)benzamide;

4-(4'-(4-chloro-4-(2-(dimethylamino)ethoxy)-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)benzamide;

4-(4'-(4-chloro-4-(2-(dimethylamino)ethoxy)-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)benzamide;

4-(4'-(4-chloro-4-(2-morpholin-4-yloxy)-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)benzamide;

4-(4'-(4-chloro-3-(2-(dimethylamino)ethoxy)-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)benzamide;

4-(4'-(4-chloro-3-(2-(dimethylamino)ethoxy)-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)benzamide;

4-(4'-(4-chloro-4-(2-morpholin-4-yloxy)-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)benzamide;
4-((4′-chloro-3-(2-morpholin-4-yloxy)-1,1′-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)benzamide;
4-((4′-chloro-3-(2-morpholin-4-yloxy)-1,1′-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)benzamide;
4-((4′-chloro-4-((2-(dimethylamino)ethoxy)-1,1′-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-((1-methylpiperidin-4-yl)amino)-3-nitrophenyl)sulfonyl)-2-phenoxybenzamide;
4-((4′-chloro-3-(2-(dimethylamino)ethoxy)-1,1′-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((3-nitro-4-((3-pyrrolidin-1-ylpropyl)amino)phenyl)sulfonyl)benzamide;
4-((4′-chloro-4-((2-(dimethylamino)ethoxy)-1,1′-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((3-nitro-4-((3-pyrrolidin-1-ylpropyl)amino)phenyl)sulfonyl)benzamide;
4-((4′-chloro-4-((2-(dimethylamino)ethoxy)-1,1′-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((3-nitro-4-((3-pyrrolidin-1-ylpropyl)amino)phenyl)sulfonyl)benzamide;
4-((4′-chloro-4-((2-(dimethylamino)ethoxy)-1,1′-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((1-(2,2,2-trifluoroethyl)piperidin-4-yl)amino)phenyl)sulfonyl)-2-phenoxybenzamide;
4-((4′-chloro-4-((2-pyrrolidin-1-ylthio)-1,1′-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)-2-phenoxybenzamide;
4-((4′-chloro-4-((2-diisopropylamino)ethoxy)-1,1′-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)-2-phenoxybenzamide;
4-((4′-chloro-1,1′-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(2,3-dihydro-1H-indol-5-yloxy)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)benzamide;
4-((2-(4-chlorophenyl)cyclohept-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((3-nitro-4-((3-pyrrolidin-1-ylpropyl)amino)phenyl)sulfonyl)benzamide;
4-((2-(4-chlorophenyl)cyclooct-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((3-nitro-4-((3-pyrrolidin-1-ylpropyl)amino)phenyl)sulfonyl)benzamide;
4-((2-(4-chlorophenyl)cyclopent-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((3-nitro-4-((3-pyrrolidin-1-ylpropyl)amino)phenyl)sulfonyl)benzamide;
4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclopent-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yl)oxy)-N-((4-((1-methylpiperidin-4-yl)amino)-3-nitrophenyl)sulfonyl)benzamide;

4-(4-((2-(4-chlorophenyl)cyclooct-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yl)oxy)-N-((4-((1-methylpiperidin-4-yl)amino)-3-nitrophenyl)sulfonyl)benzamide;

4-(4-((2-(4-chlorophenyl)cyclohept-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yl)oxy)-N-((4-((1-methylpiperidin-4-yl)amino)-3-nitrophenyl)sulfonyl)benzamide;

4-(4-((2-(4-chlorophenyl)cyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yl)oxy)-N-((4-((1-methylpiperidin-4-yl)amino)-3-nitrophenyl)sulfonyl)benzamide;

4-(4-((2-(4-chlorophenyl)-6,6-dimethyl-5,6-dihydro-2H-pyran-3-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yl)oxy)-N-((4-((1-methylpiperidin-4-yl)amino)-3-nitrophenyl)sulfonyl)benzamide;

4-(4-((2-(4-chlorophenyl)cyclohept-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yl)oxy)-N-((4-((1-methylpiperidin-4-yl)amino)-3-nitrophenyl)sulfonyl)benzamide;

4-(4-((2-(4-chlorophenyl)cyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yl)oxy)-N-((4-((1-methylpiperidin-4-yl)amino)-3-nitrophenyl)sulfonyl)-2-phenoxybenzamide;

4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-((2-(dimethylamino)ethyl)amino)-3-nitrophenyl)sulfonyl)-2-phenoxybenzamide;

4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-((3-(dimethylamino)propyl)amino)-3-nitrophenyl)sulfonyl)-2-phenoxybenzamide;

4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-((3-morpholin-4-ylpropyl)amino)-3-nitrophenyl)sulfonyl)-2-phenoxybenzamide;

4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-((4-(dimethylamino)butyl)amino)-3-nitrophenyl)sulfonyl)-2-phenoxybenzamide;

4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((1-phenylsulfonyl)piperidin-4-yl)amino)phenyl)sulfonyl)-2-phenoxybenzamide;

592
4-(4-(4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((1-(quinolin-8-ylsulfonyl)piperidin-4-yl)amino)phenyl)sulfonyl)-2-phenoxybenzamide;

4-(4-(4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-phenoxy-N-((4-(1-(phenylsulfonyl)piperidin-4-yl)amino)-3-((trifluoromethyl)sulfonyl)phenyl)sulfonyl)benzamide;

4-(4-(4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-phenoxy-N-((4-(1-(quinolin-8-ylsulfonyl)piperidin-4-yl)amino)-3-((trifluoromethyl)sulfonyl)phenyl)sulfonyl)benzamide;

4-(4-(4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-phenoxy-N-((4-(1-(dimethylamino)-1-thien-2-ylpropyl)amino)-3-nitrophenyl)sulfonyl)-2-phenoxybenzamide;

4-(4-(4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((thien-2-ylmethyl)amino)phenyl)sulfonyl)-2-phenoxybenzamide;

4-(4-(4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-phenoxy-N-((4-((tetrahydro-2H-pyran-4-yl)methyl)amino)-3-((trifluoromethyl)sulfonyl)phenyl)sulfonyl)benzamide;

4-(4-(4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((2-(1H-1,2,3-triazol-1-yl)ethyl)amino)phenyl)sulfonyl)-2-phenoxybenzamide;

4-(4-(4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((2-(1H-1,2,3-triazol-2-yl)ethyl)amino)phenyl)sulfonyl)-2-phenoxybenzamide;

4-(4-(4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((4-((3-(dimethylamino)propyl)amino)-3-nitrophenyl)sulfonyl)-2-(2-naphthoxy)benzamide;

4-(4-(4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((2-(2-oxopyridin-1(2H)-yl)ethyl)amino)phenyl)sulfonyl)-2-phenoxybenzamide;

4-(4-(4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((2-(pyridin-2-yloxy)ethyl)amino)phenyl)sulfonyl)-2-phenoxybenzamide;

4-(4-(4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-N-((3-nitro-4-((2-pyridin-4-ythethyl)amino)phenyl)sulfonyl)-2-phenoxybenzamide;

4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-N-((4-((3-(dimethylamino)propyl)amino)-3-((trifluoromethyl)sulfonyl)phenyl)sulfonyl)-2-(1H-indol-5-yloxy)benzamide;

4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-N-((4-((3-(dimethylamino)propyl)amino)-3-(trifluoromethyl)phenyl)sulfonyl)-2-(1H-indol-5-yloxy)benzamide;
4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-N-((3-cyano-4-(((dimethylamino)propyl)amino)phenyl)sulfonyl)-2-(1H-indol-5-yloxy)benzamide;

4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-(((3-nitro-4-((1-tetrahydro-2H-pyran-4-yl)piperidin-4-yl)amino)phenyl)sulfonyl)benzamide;

4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-(((4-((4-methyl(piperazin-1-yl)amino)-3-nitrophenyl)sulfonyl)benzamide;

4-(4-((1-(4′-chboro-1,1′-biphenyl-2-yl)ethyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-(((3-nitro-4-((tetrahydro-2H-pyran-4-yl)methyl)amino)phenyl)sulfonyl)benzamide;

N-(((4-((4-aminotetrahydro-2H-pyran-4-yl)methyl)amino)-3-nitrophenyl)sulfonyl)-4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)benzamide;

4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-(((3-nitro-4-((tetrahydro-2H-pyran-4-yl)methyl)amino)phenyl)sulfonyl)benzamide;

4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((4-((4-morpholin-4-yl)cyclohexyl)amino)-3-nitrophenyl)sulfonyl)benzamide;

4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-(((4-((2-methoxyethyl)amino)-3-nitrophenyl)sulfonyl)benzamide;

4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-(((3-nitro-4-(((3S)-tetrahydro-2H-pyran-3-yl)methyl)amino)phenyl)sulfonyl)benzamide;

4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-(((3-nitro-4-(((3R)-tetrahydro-2H-pyran-3-yl)methyl)amino)phenyl)sulfonyl)benzamide;

4-(4-((4-(4-chlorophenyl)-6,6-dimethyl-5,6-dihydro-2H-pyran-3-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-(((3-nitro-4-((tetrahydro-2H-pyran-4-yl)methyl)amino)phenyl)sulfonyl)benzamide;
4-((4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[(4-[[4-hydroxy-1-methylpiperidin-4-yl]methyl]amino]-3-nitrophenyl)sulfonyl]-2-(1H-indol-5-yloxy)benzamide;

4-((4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-3-fluoro-2-(1H-indol-5-yloxy)-N-((4-[[1-methylpiperidin-4-yl]amino]-3-nitrophenyl)sulfonyl)benzamide;


4-((4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[(4-[[4-hydroxy-1-methylpiperidin-4-yl]methyl]amino]-3-nitrophenyl)sulfonyl]-2-(1H-indol-4-yloxy)benzamide;

N-[(4-[[3S,4R]-1-benzyl-3-hydroxypiperidin-4-yl]amino]-3-nitrophenyl)sulfonyl]-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)benzamide;

N-[(4-[[4-aminotetrahydro-2H-pyran-4-yl]methyl]amino]-3-nitrophenyl)sulfonyl]-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)benzamide;

4-((4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((4-[[1-(2-methoxyethyl)piperidin-4-yl]amino]-3-nitrophenyl)sulfonyl)benzamide;

4-((4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((4-[[4-methylpiperazin-1-yl]amino]-3-nitrophenyl)sulfonyl)benzamide;

4-((4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[(4-[[1-(2-hydroxyethyl)piperidin-4-yl]amino]-3-nitrophenyl)sulfonyl]-2-(1H-indol-4-yloxy)benzamide;

4-((4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((4-[[1-(2-methoxyethyl)piperidin-4-yl]amino]-3-nitrophenyl)sulfonyl)benzamide;

595
4-[(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl]-N-[(4-[[1-(3-hydroxypropyl)piperidin-4-yl]amino]-3-nitrophenyl)sulfonyl]-2-(1H-indol-4-yloxy)benzamide;

4-[(4′-choloro-3-[3-(dimethylamino)propyl]-1,1′-biphenyl-2-yl)methyl]piperazin-1-yl]-2-(1H-indol-4-yloxy)-N-[(3-nitro-4-[(tetrahydro-2H-pyran-4-ylmethyl]amino)[phenyl] sulfonyl]benzamide;

4-[(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl]-N-[(4-[[1-(3-hydroxypropyl)piperidin-4-yl]amino]-3-nitrophenyl)sulfonyl]-2-(1H-indol-5-yloxy)benzamide;

4-[(4′-choloro-4-morpholin-4-yl-1,1′-biphenyl-2-yl)methyl]piperazin-1-yl]-2-(1H-indol-4-yloxy)-N-[(3-nitro-4-[(tetrahydro-2H-pyran-4-ylmethyl]amino)[phenyl] sulfonyl]benzamide;

4-[(4′-choloro-3-[2-(dimethylamino)ethoxy]-1,1′-biphenyl-2-yl)methyl]piperazin-1-yl]-2-(1H-indol-4-yloxy)-N-[(3-nitro-4-[(1-tetrahydro-2H-pyran-4-ylpiperidin-4-yl]amino)[phenyl] sulfonyl]benzamide;

4-[(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl]-N-[(4-[[4-(diethylamo)cylohexyl]amino]-3-nitrophenyl)sulfonyl]-2-(1H-indol-5-yloxy)benzamide;

4-[(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl]-N-[(4-[[4-(dimethylamino)cyclohexyl]amino]-3-nitrophenyl)sulfonyl]-2-(1H-indol-4-yloxy)benzamide;

4-[(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl]-N-[(4-[[4-(diethylamino)cyclohexyl]amino]-3-nitrophenyl)sulfonyl]-2-(1H-indol-4-yloxy)benzamide;

4-[(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl]-2-(1H-indol-4-yloxy)-N-[(4-[[4-morpholin-4-ylcyclohexyl]amino]-3-nitrophenyl)sulfonyl]benzamide;

4-[(4′-choloro-3-[2-(dimethylamino)ethoxy]-1,1′-biphenyl-2-yl)methyl]piperazin-1-yl]-2-(1H-indol-4-yloxy)-N-[(4-[[1-methylpiperidin-4-yl]amino]-3-nitrophenyl)sulfonyl]benzamide;
4-[(1-(4′-chloro-1,1′-biphenyl-2-yl)ethyl)piperazin-1-yl]-2-(1H-indol-4-yloxy)-N-((4-[(1-methylpiperidin-4-yl)amino]-3-nitrophenyl)sulfonyl)benzamide;

4-[(2-(4-chlorophenyl))-4,4-dimethylcyclohex-1-en-1-yl]methyl)piperazin-1-yl]-N-[(4-[(4-dimethylamino)tetrahydro-2H-pyran-4-yl]methyl)amino]-3-nitrophenyl)sulfonyl]-2-(1H-indol-5-yloxy)benzamide;

N-((4-[(2-aminocyclohexyl)amino]-3-nitrophenyl)sulfonyl)-4-[(2-(4-chlorophenyl))-4,4-dimethylcyclohex-1-en-1-yl]methyl)piperazin-1-yl]-2-(1H-indol-5-yloxy)benzamide;

4-[(4′-chlooro-4-[(3-(dimethylamino)prop-1-ynyl]-1,1′-biphenyl-2-yl)methyl)piperazin-1-yl]-2-(1H-indol-4-yloxy)-N-((3-nitro-4-[(tetrahydro-2H-pyran-4-yl)methyl]amino]phenyl)sulfonyl)benzamide;

4-[(2-(4-chlorophenyl))-4,4-dimethylcyclohex-1-en-1-yl]methyl)piperazin-1-yl]-2-(1H-indol-4-yloxy)-N-[(3-nitro-4-[(1-(4,4,4-trifluorobutyl)piperidin-4-yl)amino]phenyl)sulfonyl]benzamide;

4-[(2-(4-chlorophenyl))-4,4-dimethylcyclohex-1-en-1-yl]methyl)piperazin-1-yl]-N-[(4-[(2-(4-hydroxy-1-methylpiperidin-4-yl)ethyl]amino]-3-nitrophenyl)sulfonyl]-2-(1H-indol-5-yloxy)benzamide;

4-[(2-(4-chlorophenyl))-4,4-dimethylcyclohex-1-en-1-yl]methyl)piperazin-1-yl]-N-[(3-nitro-4-[(1-(1,3-thiazol-2-yl)piperidin-4-yl)amino]phenyl)sulfonyl]benzamide;

4-[(4′-chlooro-4-(2-hydroxyethoxy)-1,1′-biphenyl-2-yl)methyl]piperazin-1-yl]-2-(1H-indol-4-yloxy)-N-((3-nitro-4-[(tetrahydro-2H-pyran-4-yl)methyl]amino]phenyl)sulfonyl)benzamide;

4-[(2-(4-chlorophenyl))-4,4-dimethylcyclohex-1-en-1-yl]methyl)piperazin-1-yl]-N-[(4-[(1-cyclopropylmethyl)piperidin-4-yl]amino]-3-nitrophenyl)sulfonyl]-2-(1H-indol-5-yloxy)benzamide;

4-[(2-(4-chlorophenyl))-4,4-dimethylcyclohex-1-en-1-yl]methyl)piperazin-1-yl]-2-(1H-indol-4-yloxy)-N-((4-[(4-methylpiperazin-1-yl)amino]-3-[(trifluoromethyl)sulfonyl]phenyl)sulfonyl)benzamide;

4-[(2-(4-chlorophenyl))-4,4-dimethylcyclohex-1-en-1-yl]methyl)piperazin-1-yl]-2-(1H-indol-5-yloxy)-N-[(3-nitro-4-[(1-(4,4,4-trifluorobutyl)piperidin-4-yl)amino]phenyl)sulfonyl]benzamide;

597
4-{[1-(4'-chloro-1,1'-biphenyl-2-yl)ethyl]piperazin-1-yl}-2-(1H-indol-4-yloxy)-N-{(4-[(3-methyl)piperazin-1-yl)]amino}-3-nitrophenyl}sulfonylbemadme;

4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-y]methyl}-3-(hydroxymethyl)piperazin-1-yl]-2-(1H-indol-5-yloxy)-N-{(4-[(1-methyl)piperidin-4-yl)amino]-3-nitrophenyl}sulfonylbemadme;

4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-y]methyl}-3-(hydroxymethyl)piperazin-1-yl]-2-(1H-indol-5-yloxy)-N-{(3-nitro-4-[[1-tetrahydro-2H-pyran-4-yl)piperidin-4-yl]amino]phenyl}sulfonylbemadme;

4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-y]methyl}piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-{(4-[(4-methyl)piperazin-1-yl)]amino}-3-[(trifluoromethyl)sulfonyl]phenyl}sulfonylbemadme;

4-{[4'-chloro-4-(2-hydroxyethoxy)-1,1'-biphenyl-2-yl)methyl]piperazin-1-yl]-2-(1H-indol-4-yloxy)-N-{(4-[(1-methyl)piperidin-4-yl)amino]-3-nitrophenyl}sulfonylbemadme;

4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-y]methyl}piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-{(3-nitro-4-[[3-(3-oxopiperazin-1-yl)propyl]amino]phenyl}sulfonylbemadme;

4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-y]methyl}piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-{(3-nitro-4-[[3-(3-oxopiperazin-1-yl)propyl]amino]phenyl}sulfonylbemadme;

4-{[2-(4-chlorophenyl)-5-hydroxyycyclohex-1-en-1-y]methyl}piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-{(4-[(1-methyl)piperidin-4-yl)amino]-3-nitrophenyl}sulfonylbemadme;

4-{[2-(4-chlorophenyl)-5-hydroxyycyclohex-1-en-1-y]methyl}piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-{(3-nitro-4-[[1-tetrahydro-2H-pyran-4-yl)piperidin-4-yl]amino]phenyl}sulfonylbemadme;

4-{[2-(4-chlorophenyl)-5-hydroxyycyclohex-1-en-1-y]methyl}piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-{(4-[(4-methyl)piperazin-1-yl)]amino}-3-nitrophenyl}sulfonylbemadme;

4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-y]methyl}piperazin-1-yl)-N-{(4-[[1-(2,3-dihydro-1H-inden-2-yl)piperidin-4-yl]amino]-3-nitrophenyl}sulfonylbemadme;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[(4-[[1-(2,3-dihydro-1H-inden-2-yl)piperidin-4-yl]amino]-3-nitrophenyl)sulfonyl]-2-(1H-indol-5-yloxy)benzamide;

4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-[[1-(1,3-thiazol-2-ylmethyl)piperidin-4-yl]amino]phenyl)sulfonyl]benzamide;

4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-[[3-nitro-4-[[1-(1,3-thiazol-2-ylmethyl)piperidin-4-yl]amino]phenyl)sulfonyl]benzamide;

4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-[[4-(hydroxymethyl)tetrahydro-2H-pyran-4-yl]methyl]amino)-3-nitrophenyl)sulfonyl]-2-(1H-indol-5-yloxy)benzamide;

4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4-(2-hydroxyethyl)piperazin-1-yl]amino]-3-nitrophenyl)sulfonyl]-2-(1H-indol-5-yloxy)benzamide;

4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-[[4-[(3S)-1-methylpyrrolidin-3-yl]amino]-3-nitrophenyl)sulfonyl]benzamide;

4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4-[[1-(3-fluoropropyl)piperidin-4-yl]amino]-3-nitrophenyl)sulfonyl]-2-(1H-indol-5-yloxy)benzamide;


N-[(4-[[4-aminotetrahydro-2H-pyran-4-yl]methyl]amino]-3-nitrophenyl)sulfonyl]-4-[4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]-3-(hydroxymethyl)piperazin-1-yl]-2-(1H-indol-5-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[(4-[[1-hydroxycyclohexyl]methyl]amino]-3-nitrophenyl)sulfonyl]-2-(1H-indol-5-yl)oxy)benzamide;

4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-4-yl)oxy)-N-[(4-[[2-methoxyethyl]amino]-3-nitrophenyl)sulfonyl]benzamide;

4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[(4-[[4-(hydroxymethyl)tetrahydro-2H-pyran-4-yl]amino]-3-nitrophenyl)sulfonyl]-2-(1H-indol-5-yl)oxy)benzamide;

4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[(4-[[4-(hydroxymethyl)tetrahydro-2H-pyran-4-yl]amino]-3-nitrophenyl)sulfonyl]-2-(1H-indol-4-yl)oxy)benzamide;

4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-{{2-hydroxy-1-tetrahydro-2H-pyran-4-yl]ethy]amino]-3-nitrophenyl{sulfonyl}-2-(1H-indol-5-yl)oxy)benzamide;

4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yl)oxy)-N-{{3-nitro-4-{{1-[2-(1H-pyrazol-1-yl)ethyl]piperidin-4-yl]amino}phenyl{sulfonyl}benzamide;

4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-4-yl)oxy)-N-{{3-nitro-4-{{(tetrahydro-2H-pyran-4-yl)methyl]amino}phenyl{sulfonyl}benzamide;

4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yl)oxy)-N-{{4-(methylamino)-3-nitrophenyl{sulfonyl}benzamide;

4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-4-yl)oxy)-N-{{4-(methylamino)-3-nitrophenyl{sulfonyl}benzamide;

4-(4-[[1-(4′-chboro-1,1′-biphenyl-2-yl]ethy]piperazin-1-yl)-2-(1H-indol-4-yl)oxy)-N-{{3-morpholin-4-ylpropyl]amino]-3-nitrophenyl{sulfonyl}benzamide;

4-(4-[[2-(4-chlorophenyl)-5-hydroxycyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yl)oxy)-N-{(1-nitro-4-{{(tetrahydro-2H-pyran-4-yl)methyl]amino}phenyl{sulfonyl}benzamide;
4-(4-[(2-(4-chlorophenyl)-5-morpholin-4-yl)cyclohex-1-en-1-yl]methyl)piperazin-1-yl)-
2-(1H-indol-5-yloxy)-N-(3-nitro-4-[(tetrahydro-2H-pyran-4-ylmethyl)amino]phenyl)sulfonylel benzamide;
N-(4-[(1-amino(cyclohexyl)methyl)amino]-3-nitrophenyl)sulfonylel 4-(4-[(2-(4-
chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-
yloxy)benzamide;
4-(4-[(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-
(1H-indol-5-yloxy)-N-(3-nitro-4-[(2-(oxopyrrolidin-1-
yl)ethyl)amino]phenyl)sulfonylel benzamide;
4-(4-[(1-(4'-chloro-1,1'-biphenyl)-2-yl)ethyl)piperazin-1-yl]-2-(1H-indol-5-yloxy)-N-(3-
nitro-4-[(tetrahydro-2H-pyan-4-ylmethyl)amino]phenyl)sulfonylel benzamide;
4-4-[(4-[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]ethyl)piperazin-1-yl]-2-
(1H-indol-5-yloxy)-N-(4-4-[(4-methylpiperazin-1-yl)amino]-3-nitrophenyl)sulfonylel benzamide;
4-4-[(1R)-1-(4'-chloro-1,1'-biphenyl)-2-yl]ethyl)piperazin-1-yl]-2-(1H-indol-4-yloxy)-
N-(3-nitro-4-[(tetrahydro-2H-pyran-4-ylmethyl)amino]phenyl)sulfonylel benzamide;
4-4-[(1S)-1-(4'-chloro-1,1'-biphenyl)-2-yl]ethyl)piperazin-1-yl]-2-(1H-indol-4-yloxy)-N-
(3-nitro-4-[(tetrahydro-2H-pyran-4-ylmethyl)amino]phenyl)sulfonylel benzamide;
4-4-[(1-[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]ethyl)piperazin-1-yl]-2-
(1H-indol-5-yloxy)-N-(4-[(3-morpholin-4-ylpropyl)amino]-3-nitrophenyl)sulfonylel benzamide;
4-4-[(1-[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]ethyl)piperazin-1-yl]-2-
(1H-indol-5-yloxy)-N-(3-nitro-4-[(1-tetrahydro-2H-pyran-4-yl)piperidin-4-
yl)amino]phenyl)sulfonylel benzamide;
4-4-[(2-(4-chlorophenyl)-4,4-dimehylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-N-
(4-[(cyclohexylmethyl)amino]-3-nitrophenyl)sulfonylel 2-(1H-indol-5-yloxy)benzamide;
4-4-[(2-(4-chlorophenyl)-4,4-dimehylcyclohex-1-en-1-yl)methyl)piperazin-1-yl]-2-
(1H-indol-5-yloxy)-N-(4-[(morphiol-4-ylmethyl)-3-nitrophenyl)sulfonylel benzamide;

4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-[[4-(morpholin-4-ylamino)-3-nitrophenyl]sulfonyl]benzamide;

4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-[[3-nitro-4-(tetrahydro-2H-pyran-4-ylamino)phenyl]sulfonyl]benzamide;

4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-[[4-[[3-methyloxetan-3-yl]methyl]amino]-3-nitrophenyl]sulfonyl]benzamide;

4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-[[4-[[4-methoxy(cyclohexyl)amino]-3-nitrophenyl]sulfonyl]benzamide;

4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4-[[3-(1,1-dioxido-thiomorpholin-4-yl)propyl]amino]-3-nitrophenyl]sulfonyl]-2-(1H-indol-5-yloxy)benzamide;


4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-[[4-morpholin-4-yl-3-nitrophenyl]sulfonyl]benzamide;

4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-[[4-(methoxypiperidin-1-yl)-3-nitrophenyl]sulfonyl]benzamide;


4-[[4'-chloro-4-[[2-(dimethylamino)ethoxy]-1,1'-biphenyl-2-yl]methyl]piperazin-1-yl]-2-(1H-indol-4-yloxy)-N-[[4-[[4-methylpiperazin-1-yl]amino]-3-nitrophenyl]sulfonyl]benzamide;

4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl]-N-[[4-[[1,1-dioxidotetrahydrothien-3-yl]methyl]amino]-3-nitrophenyl]sulfonyl]-2-(1H-indol-5-yloxy)benzamide;

4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl]-N-[[4-[[1,1-dioxidotetrahydrothien-3-yl]amino]-3-nitrophenyl]sulfonyl]-2-(1H-indol-5-yloxy)benzamide;


4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl]-N-[[4-[[2-(1,3-dioxolan-2-yl)ethyl]3-nitrophenyl]sulfonyl]-2-(1H-indol-5-yloxy)benzamide;


4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl]-2-(1H-indol-5-yloxy)-N-[[4-[[1-methyl-5-oxopyrrolidin-3-yl]amino]-3-nitrophenyl]sulfonyl]benzamide;

4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl]-2-(1H-indol-5-yloxy)-N-[[4-[[1-methyl-6-oxopiperidin-3-yl]amino]-3-nitrophenyl]sulfonyl]benzamide;

4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl]-2-(1H-indol-4-yloxy)-N-[[3-nitro-4-(piperidin-1-ylamino)phenyl]sulfonyl]benzamide;
4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((3-nitro-4-((piperidin-1-ylamino)phenyl)sulfonyl)benzamide;

4-(4-((4-(4-chlorophenyl)-1-methyl-1H-pyrazol-5-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)benzamide;

4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((4-((3-methyloxetan-3-yl)methoxy)-3-nitrophenyl)sulfonyl)benzamide;

4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((3-nitro-4-((1-oxidotetrahydro-2H-thiopyran-4-yl)methyl)amino)phenyl)sulfonyl)benzamide;

4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((3-nitro-4-((1,3-thiazol-5-yl)methyl)amino)phenyl)sulfonyl)benzamide;

4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethoxy)phenyl)sulfonyl)benzamide;

4-(4-((2-(4-chlorophenyl)-5,5-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)benzamide;

4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((3-nitro-4-((2-tetrahydro-2H-pyran-4-yl)ethyl)amino)phenyl)sulfonyl)benzamide;

4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((3-nitro-4-((2-(trifluoromethoxy)ethyl)amino)phenyl)sulfonyl)benzamide;

4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((4-((2-(methoxyethoxy)ethyl)amino)-3-nitrophenyl)sulfonyl)benzamide;

4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((4-((3-(methylsulfonyl)propyl)amino)-3-nitrophenyl)sulfonyl)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[(4-[[3-(1,1-dioxidothiomorpholin-4-yi)propyl]amino]-3-nitrophenyl)sulfonyle]-2-(1H-indol-4-yloxy)benzamide;


4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4-(1,4-dioxan-2-ylmethoxy)-3-nitrophenyl]sulfonyle]-2-(1H-indol-5-yloxy)benzamide;


4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4-[[1,1-dioxidotetrahydrothien-3-yl]amino]-3-nitrophenyl]sulfonyle]-2-(1H-indol-4-yloxy)benzamide;


4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4-[[1,1-dioxidotetrahydro-2H-thiopyran-4-yl]methyl]amino]-3-nitrophenyl]sulfonyle]-2-(1H-indol-4-yloxy)benzamide;

4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4-[[2,2-difluoroethyl]amino]-3-nitrophenyl]sulfonyle]-2-(1H-indol-5-yloxy)benzamide;


4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4-[[4,4-difluorocyclohexyl]amino]-3-nitrophenyl]sulfonyle]-2-(1H-indol-5-yloxy)benzamide;
4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-({4-[(4-fluorotetrahydro-2H-pyran-4-ylmethoxy)-3-nitrophenyl]sulfonyl}-2-(1H-indol-4-yloxy)benzamide;

4-(4-{[4-(4-chlorophenyl)-1-isopropyl-6-oxo-1,6-dihydropyridin-3-yl]methyl}piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-({3-nitro-4-(tetrahydro-2H-pyran-4-ylmethyl)amino}phenyl)sulfonyl)benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-({4-{(tetrahydro-2H-pyran-4-ylmethyl)amino}carbonyl}phenyl)sulfonyl)benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-{4-{[2-methoxyethyl]amino}-3-[(trifluoromethyl)sulfonyl]phenyl}sulfonyl)benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-[(4-[[4-hydroxycyclohexyl]methyl]amino]-3-nitrophenyl]sulfonyl)benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-{4-[[4-methoxy(cyclohexyl)methyl]amino]-3-nitrophenyl}sulfonyl)benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-[(4-[[4-hydroxycyclohexyl]methyl]amino]-3-nitrophenyl]sulfonyl)benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-{4-[[4-methoxy(cyclohexyl)methyl]amino]-3-nitrophenyl}sulfonyl)benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-{3-nitro-4-(2-tetrahydro-2H-pyran-4-yloxy)phenyl}sulfonyl)benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-{4-{[2-methoxyethyl]amino}-3-[(trifluoromethyl)sulfonyl]phenyl}sulfonyl)benzamide;
4-((2-(4-chlorophenyl)-4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-((3-nitrophenyl)sulfonyl)benzamide;
4-((2-(4-chlorophenyl)-4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-((3-nitrophenyl)sulfonyl)benzamide;
4-((2-(4-chlorophenyl)-4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-N-((3-nitrophenyl)sulfonyl)-2-(1H-indol-5-yloxy)benzamide;
4-((2-(4-chlorophenyl)-4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-N-((3-nitrophenyl)sulfonyl)-2-(1H-indol-5-yloxy)benzamide;
4-((2-(4-chlorophenyl)-4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-N-((3-nitrophenyl)sulfonyl)-2-(1H-indol-5-yloxy)benzamide;
4-((2-(4-chlorophenyl)-4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-N-((3-nitrophenyl)sulfonyl)-2-(1H-indol-5-yloxy)benzamide;
4-((2-(4-chlorophenyl)-4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-N-((3-nitrophenyl)sulfonyl)-2-(1H-indol-5-yloxy)benzamide;
4-((2-(4-chlorophenyl)-4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-N-((3-nitrophenyl)sulfonyl)-2-(1H-indol-5-yloxy)benzamide;
4-((2-(4-chlorophenyl)-4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-N-((3-nitrophenyl)sulfonyl)-2-(1H-indol-5-yloxy)benzamide;
4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl)piperazin-1-yl}-2-(1H-indol-5-yloxy)-N-({4-(methylamino)-3-[(trifluoromethyl)sulfonyl]phenyl}sulfonyl)benzamide;

N-{[5-bromo-6-(tetrahydro-2H-pyran-4-ylmethoxy)pyridin-3-yl]sulfonyl}-4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl)piperazin-1-yl}-2-(1H-indol-5-yloxy)benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl)piperazin-1-yl}-2-(1H-indol-5-yloxy)-N-{[3-nitro-4-[(tetrahydro-2H-pyran-4-ylmethyl)amino]phenyl}sulfonyl)benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl)piperazin-1-yl}-2-(1H-indol-5-yloxy)-N-{{6-(tetrahydro-2H-pyran-4-ylmethoxy)-5-(1,3 thiazol-2-yl)pyridin-3-yl}sulfonyl}benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl)piperazin-1-yl}-2-(1H-indol-5-yloxy)-N-{[4-{[2-(methoxyethyl)amino]carbonyl}phenyl]sulfonyl}benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl)piperazin-1-yl}-N-{{5-cyano-6-(tetrahydro-2H-pyran-4-ylmethoxy)pyridin-3-yl}sulfonyl}2-(1H-indol-5-yloxy)benzamide;

N-{[4-{[1-acetyl]piperidin-4-yl]amino}-3-nitrophenyl}sulfonyl]-4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl)piperazin-1-yl}-2-(1H-indol-5-yloxy)-N-{[4-{1-(methylsulfonyl)piperidin-4-yl]amino}-3-nitrophenyl}sulfonyl]benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl)piperazin-1-yl}-N-{[4-{1,4-dioxan-2-ylmethy]amino}-3-nitrophenyl}sulfonyl]-2-(1H-indol-5-yloxy)benzamide;

N-{[4-{[1-acetyl]piperidin-4-yl]amino}-3-nitrophenyl}sulfonyl]-4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl)piperazin-1-yl}-2-(1H-indol-4-yloxy)-N-{[4-{1-(methylsulfonyl)piperidin-4-yl]amino}-3-nitrophenyl}sulfonyl]benzamide;

608
4-(4-({4′-chboro-5-(trifluoromethyl)-1,1′-biphenyl-2-yl}methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-([3-nitro-4-({tetrahydro-2H-pyran-4-ylmethyl}amino)phenyl]sulfonyl)benzamide;

4-(4-({4′-chloro-5-(trifluoromethyl)-1,1′-biphenyl-2-yl}methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-([3-nitro-4-({tetrahydro-2H-pyran-4-ylmethyl}amino)phenyl]sulfonyl)benzamide;

4-(4-((5-tert-butyl-4′-chloro-1,1′-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-([3-nitro-4-({tetrahydro-2H-pyran-4-ylmethyl}amino)phenyl]sulfonyl)benzamide;

4-(4-((5-tert-butyl-4′-chloro-1,1′-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-([3-nitro-4-({tetrahydro-2H-pyran-4-ylmethyl}amino)phenyl]sulfonyl)benzamide;

4-(4-((2-(4-chlorophenyl))-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-([3-nitro-4-((2,2,2-trifluoromethyl)amino)phenyl]sulfonyl)benzamide;

4-(4-((2-(4-chlorophenyl))-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-([3-nitro-4-((2,2,2-trifluoromethyl)amino)phenyl]sulfonyl)benzamide;

4-(4-((2-(4-chlorophenyl))-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-([3-nitro-4-((2,2,2-trifluoromethyl)amino)phenyl]sulfonyl)benzamide;

4-(4-((2-(4-chlorophenyl))-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-([3-nitro-4-((2,2,2-trifluoromethyl)amino)phenyl]sulfonyl)benzamide;

4-(4-((2-(4-chlorophenyl))-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-([3-nitro-4-((2,2,2-trifluoromethyl)amino)phenyl]sulfonyl)benzamide;

4-(4-((2-(4-chlorophenyl))-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-([3-nitro-4-((2,2,2-trifluoromethyl)amino)phenyl]sulfonyl)benzamide;

4-(4-((2-(4-chlorophenyl))-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-([3-nitro-4-((2,2,2-trifluoromethyl)amino)phenyl]sulfonyl)benzamide;

4-(4-((2-(4-chlorophenyl))-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-([3-nitro-4-((2,2,2-trifluoromethyl)amino)phenyl]sulfonyl)benzamide;

4-(4-((2-(4-chlorophenyl))-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-([3-nitro-4-((2,2,2-trifluoromethyl)amino)phenyl]sulfonyl)benzamide;

4-(4-((2-(4-chlorophenyl))-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-([3-nitro-4-((2,2,2-trifluoromethyl)amino)phenyl]sulfonyl)benzamide;

4-(4-((2-(4-chlorophenyl))-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-([3-nitro-4-((2,2,2-trifluoromethyl)amino)phenyl]sulfonyl)benzamide;

4-(4-((2-(4-chlorophenyl))-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-([3-nitro-4-((2,2,2-trifluoromethyl)amino)phenyl]sulfonyl)benzamide;

4-(4-((2-(4-chlorophenyl))-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-([3-nitro-4-((2,2,2-trifluoromethyl)amino)phenyl]sulfonyl)benzamide;

4-(4-((2-(4-chlorophenyl))-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-([3-nitro-4-((2,2,2-trifluoromethyl)amino)phenyl]sulfonyl)benzamide;

4-(4-((2-(4-chlorophenyl))-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-([3-nitro-4-((2,2,2-trifluoromethyl)amino)phenyl]sulfonyl)benzamide;

4-(4-((2-(4-chlorophenyl))-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-([3-nitro-4-((2,2,2-trifluoromethyl)amino)phenyl]sulfonyl)benzamide;

4-(4-((2-(4-chlorophenyl))-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-([3-nitro-4-((2,2,2-trifluoromethyl)amino)phenyl]sulfonyl)benzamide;

4-(4-((2-(4-chlorophenyl))-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-([3-nitro-4-((2,2,2-trifluoromethyl)amino)phenyl]sulfonyl)benzamide;

4-(4-((2-(4-chlorophenyl))-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-([3-nitro-4-((2,2,2-trifluoromethyl)amino)phenyl]sulfonyl)benzamide;

4-(4-((2-(4-chlorophenyl))-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-([3-nitro-4-((2,2,2-trifluoromethyl)amino)phenyl]sulfonyl)benzamide;

4-(4-((2-(4-chlorophenyl))-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-([3-nitro-4-((2,2,2-trifluoromethyl)amino)phenyl]sulfonyl)benzamide;

4-(4-((2-(4-chlorophenyl))-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-([3-nitro-4-((2,2,2-trifluoromethyl)amino)phenyl]sulfonyl)benzamide;

4-(4-((2-(4-chlorophenyl))-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-([3-nitro-4-((2,2,2-trifluoromethyl)amino)phenyl]sulfonyl)benzamide;

N-(5-bromo-6-({tetrahydro-2H-pyran-4-ylmethyl}amino)pyridin-3-yl)sulfonyl)-4-(4-((2-(4-chlorophenyl))-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)benzamide;
4-[2-(4-chlorophenyl)-4,4-dime hycyclohex-1-en-1-yl]methylpiperazin-1-yl)-2-(1H-indol-5-yloxy)-N-(4-[(2-morpholin-4-yethyl)amino]-3-[[trifluoromethyl]sulfonyl]phenyl] sulfonyl benzamide;

4-[2-(4-chlorophenyl)-4,4-dime hycyclohex-1-en-1-yl]methylpiperazin-1-yl)-N-[(5-cyano-6-[(tetrahydro-2H-pyran-4-ylmethy l)amino]pyridin-3-yl]sulfonyl]-2-(1H-indol-5-yloxy)benzamide;

4-[2-(4-chlorophenyl)-4,4-dime hycyclohex-1-en-1-yl]methylpiperazin-1-yl)-2-(1H-indol-5-yloxy)-N-[(1-methylpiperidine-4-yl)methoxy]-3-nitrophenyl] sulfonyl benzamide;

4-[2-(4-chlorophenyl)-4,4-dime hycyclohex-1-en-1-yl]methylpiperazin-1-yl)-2-(1H-indol-5-yloxy)-N-[(4-[[1-methylpiperi.dine-4-yl]methoxy]-3-nitrophenyl] sulfonyl benzamide;

4-[2-(4-chlorophenyl)-4,4-dime hycyclohex-1-en-1-yl]methylpiperazin-1-yl)-2-(1H-indol-5-yloxy)-N-[(4-[[1-methylpiperidine-4-yl]methoxy]-3-nitrophenyl] sulfonyl benzamide;

4-[2-(4-chlorophenyl)-1-(3-hydroxypropyl)-1,2,5,6-tetrahydropyridin-3-yl]methylpiperazin-1-yl)-2-(1H-indol-4-yloxy)-N-[(3-nitro-4-[tetrahydro-2H-pyran-4-ylmethyl)amino]phenyl] sulfonyl benzamide;

benzyl 4-(4-[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)benzoylamino)sulfonyl]benzamide;N-[(3-(aminocarbonyl)-4-(tetrahydro-2H-pyran-4-ylmethoxy)phenyl)sulfonyl]-4-(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)benzamide;

4-[2-(4-chlorophenyl)-1,1'-biphenyl-2-yl]methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-[(3-nitro-4-[(1-tetrahydro-2H-pyran-4-yl)piperidin-4-yl]amino]phenyl] sulfonyl benzamide;

4-[2-(4-chlorophenyl)-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-[(3-nitro-4-[(1-tetrahydro-2H-pyran-4-yl)piperidin-4-yl]amino]phenyl] sulfonyl benzamide;

4-[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-[(4-[(1-methyl-1H-imidazol-5-yl)methyl]amino]-3-nitrophenyl] sulfonyl benzamide;

4-[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl)piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-[(4-[(morpholin-4-yl)sulfonyl]phenyl)sulfonyl] benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-([4-[[1,1-dioxidothiomorpholin-4-yl]amino]-3-nitrophenyl]sulfonyl)-2-(1H-indol-5-yloxy)benzamide;

4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-([4-[[4-morpholin-4-ylcyclohexyl]amino]-3-nitrophenyl]sulfonyl)benzamide;

N-[[5-bromo-6-(tetrahydro-2H-pyran-4-ylmethoxy)pyridin-3-yl]sulfonyl]-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-4-yloxy)benzamide;

4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-[[6-[[tetrahydro-2H-pyran-4-ylmethyl]amino]-5-(1,3-thiazol-2-yl)pyridin-3-yl]sulfonyl]benzamide;


4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-([4-[[3,3-dimethylbutyl]amino]-3-nitrophenyl]sulfonyl)-2-(1H-indol-5-yloxy)benzamide;

4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4-[[1S]-1-(hydroxymethyl)-3-methylbutyl]amino]-3-nitrophenyl]sulfonyl]-2-(1H-indol-5-yloxy)benzamide;


4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4-[[1R]-1-(hydroxymethyl)-2-methylpropyl]amino]-3-nitrophenyl]sulfonyl]-2-(1H-indol-5-yloxy)benzamide;

4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-[[4-[(4-methoxyphenyl)amino]-3-nitrophenyl]sulfonyl]benzamide;
N-[(4-[(2-(1,3-benzodioxol-5-yl)ethyl]amino)-3-nitrophenyl)sulfonyl]-4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(1H-indol-5-yloxy)benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-[3-nitro-4-[[3-(2-oxopyrrolidin-1-yl)propyl]amino]phenyl]sulfonyl]benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-[(4-[(4-hydroxyphenyl)amino]-3-nitrophenyl)sulfonyl]-2-(1H-indol-5-yloxy)benzamide;

N-[(4-{[2-(3-(1H-imidazol-1-yl)propyl]amino}-3-nitrophenyl)sulfonyl]-2-(1H-indol-5-yloxy)benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-[(4-[[3-(1H-imidazol-1-yl)propyl]amino]-3-nitrophenyl)sulfonyl]-2-(1H-indol-5-yloxy)benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-[3-nitro-4-{[(1S)-1-phenylethyl]amino]phenyl}sulfonyl]benzamide;

N-[(2-chloro-5-fluoro-4-{[tetrahydro-2H-pyran-4-ylmethyl]amino}phenyl)sulfonyl]-4-(4-{(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(1H-indol-5-yloxy)benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-[4-{[2-(methoxyethoxy)ethyl]thio}-3-nitrophenyl)sulfonyl]benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-[4-[[2-(methoxyethoxy)ethyl]thio]-3-nitrophenyl]sulfonyl]benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-[[4-(methyl)sulfonyl]phenyl]sulfonyl]benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(1H-indol-4-yloxy)-N-[[4-(methyl)sulfonyl]phenyl]sulfonyl]benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-[[4-(2,2-dimethyltetrahydro-2H-pyran-4-y) methoxy]-3-nitrophenyl]sulfonyl]-2-(1H-indol-5-yloxy)benzamide;
4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-\((\{5-cyano-6-\{4-fluorotetrahydro-2H-pyran-4-yl\}methoxy\}pyridin-3-yl\)sulfonyl\)-2-(1H-indol-5-yloxy)benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-\((\{5-cyano-6-(tetrahydro-2H-pyran-4-ylmethoxy)\}pyridin-3-yl\)sulfonyl\)-2-(1H-indol-4-yloxy)benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-\((\{5-chloro-6-(tetrahydro-2H-pyran-4-ylmethoxy)\}pyridin-3-yl\)sulfonyl\)-2-(1H-indol-4-yloxy)benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-\((\{5-cyano-6-(2-morpholin-4-ylmethoxy)\}pyridin-3-yl\)sulfonyl\)-2-(1H-indol-5-yloxy)benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-(\{4-[(1-tetrahydro-2H-pyran-4-yl)\}piperidin-4-yl\}oxygen)\}sulfonyl\)benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-(\{4-[(4-morpholin-4-ylbut-2-ynyl)oxy]-3-nitrophenyl\}sulfonyl\)benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-\((\{5-ethynyl-6-(tetrahydro-2H-pyran-4-ylmethoxy)\}pyridin-3-yl\)sulfonyl\)-2-(1H-indol-4-yloxy)benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-\((\{5-cyano-6-(2-morpholin-4-ylmethoxy)\}pyridin-3-yl\)sulfonyl\)-2-(1H-indol-4-yloxy)benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-\((\{5-cyano-6-(4-fluorotetrahydro-2H-pyran-4-yl)methoxy\}pyridin-3-yl\)sulfonyl\)-2-(1H-indol-4-yloxy)benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-\((\{4-[(3-hydroxy-4-methoxyphenyl)\}amino]-3-nitrophenyl\}sulfonyl\)-2-(1H-indol-5-yloxy)benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(2,3-dihydro-1H-indol-4-yloxy)-N-(\{4-[(1-methylpiperidin-4-yl)amino]-3-nitrophenyl\}sulfonyl) benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-
(4-[[1-methylpiperidin-4-yl]amino]-3-nitrophenyl)sulfonyl)-2-(pyridin-3-ylamino)benzamide;

4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-
(3-nitro-4-[[1-tetrahydro-2H-pyran-4-ylpiperidin-4-yl]amino]phenyl)sulfonyl)-2-(pyridin-3-
ylamino)benzamide;

4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-
(3-nitro-4-[[1-tetrahydro-2H-pyran-4-ylmetil]amino]phenyl)sulfonyl)-2-(1,2,3,4-
tetrahydroisoquinolin-5-yloxy)benzamide;

4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-
(1H-indazol-4-yloxy)-N-(3-nitro-4-[[tetrahydro-2H-pyran-4-
ylmethyl]amino]phenyl)sulfonyl)benzamide;

4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-
(1H-indazol-4-yloxy)-N-(3-nitro-4-[[1-tetrahydro-2H-pyran-4-ylpiperidin-4-
yl]amino]phenyl)sulfonyl)benzamide;

Trans-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-
yl)-2-(1H-indazol-4-yloxy)-N-(4-[[4-morpholin-4-ylicyclohexyl]amino]-3-
nitrophenyl)sulfonyl)benzamide;

2-(1H-benzimidazol-4-yloxy)-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-
yl]methyl]piperazin-1-yl)-N-(3-nitro-4-[[tetrahydro-2H-pyran-4-
ylmethyl]amino]phenyl)sulfonyl)benzamide;

N-(5-chloro-6-[[4-fluorotetrahydro-2H-pyran-4-yl]methoxy]pyridin-3-yl)sulfonyl)-4-
(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indazol-
4-yloxy)benzamide;

N-(5-chloro-6-[[4-fluorotetrahydro-2H-pyran-4-yl]methoxy]pyridin-3-yl)sulfonyl)-4-
(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indol-4-
yloxy)benzamide;
4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-
{(5-cyano-6-{[4-fluorotetrahydro-2H-pyranyl-4-yl]methoxy}[pyridin-3-yl]sulfonyl)-2-(1H-indazol-
4-yloxy)benzamide;

2-(1H-benzimidazol-4-yloxy)-4-(4- [2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-
yl]methyl}piperazin-1-yl)-N-(4-{[(3R)-1-{2,2-difluoroethyl}pyrrolidin-3-yl]amino}-3-
nitrophenyl)sulfonyl]benzamide;

2-(1H-benzimidazol-4-yloxy)-4-(4- [2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-
yl]methyl}piperazin-1-yl)-N-(4-{[(4-fluorotetrahydro-2H-pyranyl-4-yl)methoxy]-3-
nitrophenyl}sulfonyl]benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-
{(4-{[4-fluorotetrahydro-2H-pyranyl-4-yl]methyl}amino}-3-nitrophenyl)sulfonyl]-2-(1H-indazol-
4-yloxy)benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-
{(5-{[4-fluorotetrahydro-2H-pyranyl-4-yl]methoxy}-5-(trifluoromethyl)pyridin-3-yl]sulfonyl})-2-
(1H-indazol-4-yloxy)benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-
{(4-{[4-cyclopropylmorpholin-2-yl]methyl}amino}-3-nitrophenyl)sulfonyl]-2-(1H-indazol-4-
yloxy)benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-
{(4-{[4,4-difluorocyclohexyl]methyl}amino}-3-nitrophenyl)sulfonyl]-2-(1H-indazol-4-
yloxy)benzamide;

N-{[5-chloro-6-{[4-fluorotetrahydro-2H-pyranyl-4-yl]methyl}amino]pyridin-3-
yl}sulfonyl]-4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-
2-(1H-indazol-4-yloxy)benzamide;

Trans-N-{[5-chloro-6-{(4-methoxy)cyclohexyl]methoxy}[pyridin-3-yl]sulfonyl]-4-(4-{[2-
(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(1H-indazol-4-
yloxy)benzamide;

2-(1H-benzimidazol-4-yloxy)-4-(4- [2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-
yl]methyl}piperazin-1-yl)-N-(4-{[(4-(2,2-difluoroethyl)morpholin-2-yl]methyl}amino)-3-
nitrophenyl)sulfonyl]benzamide;

615
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-
({5-fluoro-6-[4-fluorotetrahydro-2H-pyran-4-yl]methoxy}pyridin-3-yl)sulfonyl)-2-(1H-indazol-
4-yl)benzamide;

2-(1H-benzimidazol-4-yl)oxy)-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-
yl]methyl]piperazin-1-yl)-N-({3-nitro-4-[[1-tetrahydro-2H-pyran-4-yl]piperidin-4-
yl]amino}phenyl)sulfonyl)benzamide;

2-(1H-benzimidazol-4-yl)oxy)-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-
yl]methyl]piperazin-1-yl)-N-({4-[[1-methylpiperidin-4-yl]amino]-3-nitrophenyl}sulfonyl)benzamide;

N-({5-chloro-6-[[1-(cyanomethyl)-4-fluoropiperidin-4-yl]methoxy}pyridin-3-
ylsulfonyl]-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-
2-(1H-indazol-4-yl)benzamide;

Trans-N-({5-chloro-6-[4-hydroxycyclohexyl]methoxy}pyridin-3-yl)sulfonyl)-4-(4-[[2-
(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indazol-4-
yl)benzamide;

N-({5-chloro-6-[[3R]-1-(2,2-difluoroethyl)pyrrolidin-3-yl]oxy}pyridin-3-yl)sulfonyl]-4-
(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl)piperazin-1-yl)-2-(1H-indazol-
4-yl)benzamide;

2-(1H-benzimidazol-4-yl)oxy)-N-({5-chloro-6-[[2S]-4-(N,N-dimethylglycyl)morpholin-
2-yl]methoxy}pyridin-3-yl)sulfonyl]-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-
1-yl]methyl]piperazin-1-yl)benzamide;

2-(1H-benzimidazol-4-yl)oxy)-N-({5-chloro-6-[[2R]-4-(N,N-dimethylglycyl)morpholin-
2-yl]methoxy}pyridin-3-yl)sulfonyl]-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-
1-yl]methyl]piperazin-1-yl)benzamide;

N-({5-chloro-6-[[2S]-4-(N,N-dimethylglycyl)morpholin-2-yl]methoxy}pyridin-3-
ylsulfonyl]-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-
2-(1H-indazol-4-yl)benzamide;
N-[(5-chloro-6-\{(2R)-4-(N,N-dimethylglycyl)morpholin-2-yl\}methoxy)pyridin-3-yl]sulfonyl]-4-(4-\{(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl\}methyl)piperazin-1-yl)-2-(1H-indazol-4-yl)benzamide;

4-(4-\{(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl\}methyl)piperazin-1-yl)-N-\{(5-chloro-6-(tetrahydro-2H-pyran-4-ylmethoxy)pyridin-3-yl\}sulfonyl]-2-(1H-indazol-4-yl)benzamide;

2-(1H-benzimidazol-4-yl)oxy]-4-(4-\{(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl\}methyl)piperazin-1-yl)-N-\{(4-\{(3R)-1-(cyanomethyl)pyrrolidin-3-yl\}amino\}3-nitrophenyl)sulfonyl]benzamide;

2-(1H-benzimidazol-4-yl)oxy]-4-(4-\{(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl\}methyl)piperazin-1-yl)-N-\{(4-\{(3R)-1-(N,N-dimethylglycyl)pyrrolidin-3-yl\}amino\}3-nitrophenyl)sulfonyl]benzamide;

2-(1H-benzimidazol-4-yl)oxy]-4-(4-\{(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl\}methyl)piperazin-1-yl)-N-\{(4-\{(3R)-1-(N,N-dimethylglycyl)pyrrolidin-3-yl\}amino\}3-nitrophenyl)sulfonyl]benzamide;

2-(1H-benzimidazol-4-yl)oxy]-4-(4-\{(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl\}methyl)piperazin-1-yl)-N-\{(4-\{(4-(cyanomethyl)morpholin-2-yl\}methyl)\}amino\}3-nitrophenyl)sulfonyl]benzamide;

2-(1H-benzimidazol-4-yl)oxy]-4-(4-\{(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl\}methyl)piperazin-1-yl)-N-\{(4-\{(4-(4-cyclopropylmorpholin-2-yl\}methyl)\}amino\}3-nitrophenyl)sulfonyl]benzamide;

2-(1H-benzimidazol-4-yl)oxy]-4-(4-\{(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl\}methyl)piperazin-1-yl)-N-\{(3-nitro-4-\{(4-oxetan-3-ylmorpholin-2-yl\}methyl)\}amino\}phenyl)sulfonyl]benzamide;

N-\{(5-chloro-6-\{(3R)-1-[2-fluoro-1-(fluoromethyl)ethyl]pyrrolidin-3-yl\}oxy)pyridin-3-yl\}sulfonyl]-4-(4-\{(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl\}methyl)piperazin-1-yl)-2-(1H-indazol-4-yl)benzamide;

4-(4-\{(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl\}methyl)piperazin-1-yl)-N-\{(4-\{(3R)-1-[2-fluoro-1-(fluoromethyl)ethyl]pyrrolidin-3-yl\}amino\}3-nitrophenyl)sulfonyl]2-(1H-indazol-4-yl)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-(4-[[1-cyclopropylpiperidin-4-yl]amino]-3-nitrophenyl)sulfonyl)-2-(1H-indazol-4-yloxy)benzamide;

2-(1H-benzimidazol-4-yloxy)-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[4-([2R]-4-(N,N-dimethylglycyl)morpholin-2-yl)methyl]amino)-3-nitrophenyl)sulfonyl]benzamide;

2-(1H-benzimidazol-4-yloxy)-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[4-([2S]-4-(N,N-dimethylglycyl)morpholin-2-yl)methyl]amino)-3-nitrophenyl)sulfonyl]benzamide;

2-(1H-benzimidazol-4-yloxy)-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[3-nitro-4-[[tetrahydrofuran-3-ylmethyl]amino][phenyl]sulfonyl]benzamide;

Trans-2-(1H-benzimidazol-4-yloxy)-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[4-[[4-methoxyhexyl]methyl]amino]-3-nitrophenyl)sulfonyl]benzamide;

2-(1H-benzimidazol-4-yloxy)-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[4-[[4-fluorotetrahydro-2H-pyran-4-yl]methyl]amino]-3-nitrophenyl)sulfonyl]benzamide;

2-(1H-benzimidazol-4-yloxy)-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-(5-fluoro-6-[[4-fluorotetrahydro-2H-pyran-4-yl]methoxy]pyridin-3-yl]sulfonyl]benzamide;

2-(1H-benzimidazol-4-yloxy)-N-(5-chloro-6-[[4-fluorotetrahydro-2H-pyran-4-yl]methoxy]pyridin-3-yl]sulfonyl)-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl]benzamide;

N-[[5-chloro-6-([3R]-1-[2-fluoro-1-(fluoromethyl)ethyl]pyrrolidin-3-yl]methoxy]pyridin-3-yl]sulfonyl]-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indazol-4-yloxy)benzamide;

N-[[5-chloro-6-([3R]-1-(2,2-difluoroethyl)pyrrolidin-3-yl]methoxy]pyridin-3-yl]sulfonyl]-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indazol-4-yloxy)benzamide;
Trans-4-{[2-(4-chlorophenyl)-4,6-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(1H-indazol-4-yloxy)-N-[[4-[[4-methoxy(cyclohexyl)methyl]amino]-3-nitrophenyl]sulfonyl]benzamide;

4-([2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4-(1,4-dioxan-2-ylmethoxy)-3-nitrophenyl]sulfonyl]-2-(1H-indazol-4-yloxy)benzamide;

N-[[5-chloro-6-[[1-cyclopropylpiperidin-4-yl]amino]pyridin-3-yl]sulfonyl]-4-([2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indazol-4-yloxy)benzamide;

2-(1H-benzimidazol-4-yloxy)-N-[[5-chloro-6-[[1-cyclopropylpiperidin-4-yl]amino]pyridin-3-yl]sulfonyl]-4-([2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)benzamide;

2-(1H-benzimidazol-4-yloxy)-4-([2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4-(1,4-dioxan-2-ylmethyl)amino]-3-nitrophenyl]sulfonyl]benzamide;

2-(1H-benzimidazol-4-yloxy)-4-([2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4-[(1-cyclopropylpiperidin-4-yl)amino]-3-nitrophenyl]sulfonyl]benzamide;

Trans-2-(1H-benzimidazol-4-yloxy)-4-([2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4-[[4-morpholin-4-ylcyclohexyl]amino]-3-nitrophenyl]sulfonyl]benzamide;

2-(1H-benzimidazol-4-yloxy)-4-([2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4-[(4-methylpiperazin-1-yl)amino]-3-nitrophenyl]sulfonyl]benzamide;

2-(1H-benzimidazol-4-yloxy)-4-([2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[4-[[1-methylpiperidin-4-yl]methyl]amino]-3-nitrophenyl]sulfonyl]benzamide;

2-(1H-benzimidazol-4-yloxy)-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-{{4-[(4,4-difluorocyclohexyl)methyl]amino}-3-nitrophenyl}sulfonyl]benzamide;
N-{{4-[(4-acetilmorpholin-2-yl)methyl]amino}-3-nitrophenyl}sulfonyl]-2-(1H-benzimidazol-4-yloxy)-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl]benzamide;
2-(1H-benzimidazol-4-yloxy)-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-{{4-[(4-(methylsulfonyl)morpholin-2-yl)methyl]amino}-3-nitrophenyl}sulfonyl]benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dime:yclcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-{{6-[[4-fluoro-1-[2-fluoro-1-(fluoromethy1)ethyl]piperidin-4-yl]methoxy]-5-(trifluoromethyl)pyridin-3-yl]sulfonyl}-2-(1H-indazol-4-yloxy)benzamide;
4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-[[5-chloro-6-((2-tetrahydrofuran-2-y1)ethoxy)pyridin-3-yl]sulfonyl]-2-(1H-indazol-4-yloxy)benzamide;
2-(1H-benzimidazol-4-yloxy)-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-N-{{4-[(4-cyanocyclohexyl)methyl]amino}-3-nitrophenyl}sulfonyl]benzamide;
2-(1H-benzimidazol-4-yloxy)-N-{{5-chloro-6-[(4,4-difluorocyclohexyl)methoxy]pyridin-3-yl}sulfonyl]-4-(4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl]benzamide;
N-{{3-chloro-4-[(4-fluorotetrahydro-2H-pyran-4-yl)methoxy]phenyl}sulfonyl]-4-((4-[[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl]piperazin-1-yl)-2-(1H-indazol-4-yloxy)benzamide;
N-{{5-chloro-6-[(4-fluorotetrahydro-2H-pyran-4-yl)methoxy]pyridin-3-yl}sulfonyl]-4-(4-[[4-(4-chlorophenyl)-6,6-dimethyl-5,6-dihydro-2H-pyran-3-yl]methyl]piperazin-1-yl)-2-(1H-indazol-4-yloxy)benzamide;
4-[(2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl)methyl]piperazin-1-yl)-N-[(5-cyano-6-(2-tetrahydro-2H-pyran-4-ylethoxy)pyridin-3-yl)sulfonyl]-2-(1H-indazol-4-yloxy)benzamide; and

12. A compound or therapeutically acceptable salt wherein the compound is chosen from:
2-(benzyloxy)-4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl))-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)benzamide;
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl))-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)-2-(2-phenylethoxy)benzamide;
2-benzyl-4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl))-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)benzamide;
2-benzyl-4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl))-N-((4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)benzamide;
2-benzyl-4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl))-N-((4-((3-morpholin-4-ylpropyl)amino)-3-nitrophenyl)sulfonyl)benzamide;
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl))-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)-2-(2-phenylethyl)benzamide;
2-(benzylamino)-4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl))-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)benzamide;
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl))-2-methoxy-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)benzamide;
4-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl))-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)-2-(phenoxymethyl)benzamide;
5-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl))-N-((3-nitro-4-((tetrahydro-2H-pyran-4-ylmethyl)amino)phenyl)sulfonyl)-1,1'-biphenyl-2-carboxamide;
5-(4-((4'-chloro-1,1'-biphenyl-2-yl)methyl)piperazin-1-yl))-N-((4-((3-dimethylamino)propyl)amino)-3-nitrophenyl)sulfonyl)-1,1'-biphenyl-2-carboxamide;}
N-([3-nitro-4-[(tetrahydro-2H-pyran-4-yl)methyl]amino]phenyl)sulfonyl)-2-phenoxy-4-(4-[(3-phenylpropanoyl)[(1S,2S,3S,5R)-2,6,6-trimethylbicyclo[3.1.1]hept-3-yl]amino]piperidin-1-yl)benzamide;

N-([4-[(3-morpholin-4-ylpropyl)amino]-3-nitrophenyl]sulfonyl)-2-phenoxy-4-(4-[(3-phenylpropanoyl)[(1S,2S,3S,5R)-2,6,6-trimethylbicyclo[3.1.1]hept-3-yl]amino]piperidin-1-yl)benzamide;

N-([3-nitro-4-[(tetrahydro-2H-pyran-4-yl)methyl]amino]phenyl)sulfonyl)-2-phenoxy-4-(4-[(3-phenylpropyl)[(1S,2S,3S,5R)-2,6,6-trimethylbicyclo[3.1.1]hept-3-yl]amino]piperidin-1-yl)benzamide;

N-([4-[(3-morpholin-4-ylpropyl)amino]-3-nitrophenyl]sulfonyl)-2-phenoxy-4-(4-[(3-phenylpropyl)[(1S,2S,3S,5R)-2,6,6-trimethylbicyclo[3.1.1]hept-3-yl]amino]piperidin-1-yl)benzamide;

4-(4-[(1R,5S)-8-methyl-8-azabicyclo[3.2.1]oct-3-yl]amino)benzyl)piperazin-1-yl]-N-([4-[(3-morpholin-4-ylpropyl)amino]-3-nitrophenyl]sulfonyl)-2-phenoxybenzamide;


4-[(2-azabicyclo[3.2.2]non-3-yl)benzyl]piperazin-1-yl]-2-phenoxy-N-([4-[(tetrahydro-2H-pyran-4-yl)methyl]amino]-3-(trifluoromethyl)sulfonyl]phenyl)sulfonyl)benzamide;

4-[(2-azabicyclo[3.2.2]non-3-yl)benzyl]piperazin-1-yl]-2-phenoxy-N-([4-[(tetrahydro-2H-pyran-4-yl)methyl]amino]phenyl)sulfonyl)benzamide;

4-[(2-azabicyclo[3.2.2]non-3-yl)benzyl]piperazin-1-yl]-N-([4-[(3-morpholin-4-ylpropyl)amino]-3-nitrophenyl]sulfonyl)-2-phenoxybenzamide;

4-[(4R,7S)-2,3,3a,4,7,7a-hexahydro-1H-4,7-methanoinden-5-yl]benzyl)piperazin-1-yl]-N-(3-nitro-4-[(tetrahydro-2H-pyran-4-yl)methyl]amino]phenyl)sulfonyl)-2-phenoxybenzamide;

4-[4-(2-{5-[(1R,5S)-8-azabicyclo[3.2.1]oct-8-ylmethyl]thien-2-yl}benzyldiene)piperidin-1-yl]-N-{3-nitro-4-[(tetrahydro-2H-pyran-4-ylmethyl)amino]phenyl}sulfonyl)-2-phenoxycyzbenzamide; and


13. A pharmaceutical composition comprising an excipient and a therapeutically effective amount of the compound or therapeutically acceptable salt of any one of claims 1-12.

14. Use of the compound or therapeutically acceptable salt of any one of claims 1-12 for treating bladder cancer, brain cancer, breast cancer, bone marrow cancer, cervical cancer, chronic lymphocytic leukemia, colorectal cancer, esophageal cancer, hepatocellular cancer, lymphoblastic leukemia, follicular lymphoma, a lymphoid malignancy of T cell or B cell origin, melanoma, myelogenous leukemia, myeloma, oral cancer, ovarian cancer, non small cell lung cancer, prostate cancer, small cell lung cancer or spleen cancer in a patient.

15. Use of the compound or therapeutically acceptable salt of any one of claims 1-12, and one additional therapeutic agent or more than one additional therapeutic agent, for treating bladder cancer, brain cancer, breast cancer, bone marrow cancer, cervical cancer, chronic lymphocytic leukemia, colorectal cancer, esophageal cancer, hepatocellular cancer, lymphoblastic leukemia, follicular lymphoma, a lymphoid malignancy of T cell or B cell origin, melanoma, myelogenous leukemia, myeloma, oral cancer, ovarian cancer, non small cell lung cancer, prostate cancer, small cell lung cancer or spleen cancer in a patient.

16. Use of the compound or therapeutically acceptable salt of any one of claims 1-12 for the manufacture of a medicament for treating bladder cancer, brain cancer, breast cancer, bone marrow cancer, cervical cancer, chronic lymphocytic leukemia, colorectal cancer, esophageal cancer, hepatocellular cancer, lymphoblastic leukemia, follicular lymphoma, a lymphoid malignancy of T cell or B cell origin, melanoma, myelogenous leukemia, myeloma,
oral cancer, ovarian cancer, non small cell lung cancer, prostate cancer, small cell lung cancer or spleen cancer in a patient.

17. Use of the compound or therapeutically acceptable salt of any one of claims 1-12, and one additional therapeutic agent or more than one additional therapeutic agent, for the manufacture of a medicament for treating bladder cancer, brain cancer, breast cancer, bone marrow cancer, cervical cancer, chronic lymphocytic leukemia, colorectal cancer, esophageal cancer, hepatocellular cancer, lymphoblastic leukemia, follicular lymphoma, a lymphoid malignancy of T cell or B cell origin, melanoma, myelogenous leukemia, myeloma, oral cancer, ovarian cancer, non small cell lung cancer, prostate cancer, small cell lung cancer or spleen cancer in a patient.