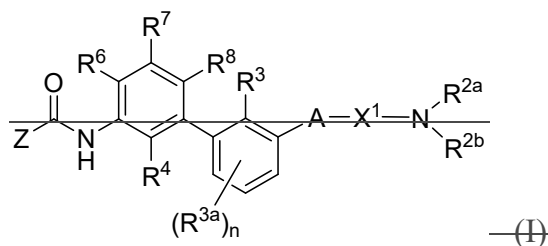


WHAT IS CLAIMED IS:

1. — A compound of Formula (I):



or a pharmaceutically acceptable salt, prodrug or bioisostere thereof, wherein:

A is a 5- to 10-membered heteroaryl group which is unsubstituted or substituted with from one to five members independently selected from the group consisting of halogen, C₁₋₃ alkyl,

C₁₋₃ haloalkyl, C₁₋₃ alkoxy, C₁₋₃ haloalkoxy, OH, and CN;

X¹ is C₁₋₃ alkylene, which is unsubstituted or substituted with one or two members independently selected from the group consisting of C₁₋₂ alkyl and CO₂H;

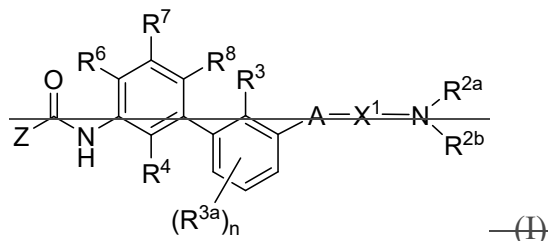
R^{2a} and R^{2b} are each independently selected from the group consisting of H, C₁₋₈ alkyl, C₁₋₈ haloalkyl, Y, X²-CO₂R^a, X²-OR^a, X²-NR^aR^b, X²-C(O)NR^aR^b, X²-SO₂R^a, X²-SO₂NR^aR^b, X²-SO₃R^a and X²-Y wherein each X² is C₁₋₆ alkylene and any C₁₋₈ alkyl or C₁₋₆ alkylene, is unsubstituted or substituted with one or two members independently selected from the group consisting of OH, SO₂NH₂, C(O)NH₂, C(O)NHOH, PO₃H₂, CO₂C₁₋₈ alkyl and CO₂H, and each Y is selected from the group consisting of C₃₋₆ cycloalkyl, C₄₋₈ heterocyclyl and 5- to 6-membered heteroaryl, each of which is unsubstituted or substituted with one to four substituents independently selected from the group consisting of oxo, OH, C₁₋₄ alkyl, C₁₋₄ haloalkyl, C₁₋₄ hydroxyalkyl, C₁₋₄ alkoxy, C₁₋₄ haloalkoxy, C₁₋₄ hydroxyalkoxy, SO₂NH₂, C(O)NH₂, C(O)NHOH, PO₃H₂, CO₂C₁₋₈ alkyl, SO₃H and CO₂H;

or R^{2a} and R^{2b} are combined to form a 4- to 9-membered ring or spirocyclic ring, having from zero to two additional heteroatom ring vertices selected from O, N or S; wherein the ring formed by combining R^{2a} and R^{2b}, is unsubstituted or substituted with 1 to 4 substituents independently selected from the group consisting of

~~26 oxo, C₁₋₈ alkyl, C₁₋₈ haloalkyl, C₁₋₈ hydroxyalkyl, X³-CO₂R^a, X³-OR^a,
 27 X³-NR^aR^b,
 28 X³-C(O)NR^aR^b, X³-SO₂R^a, X³-SO₂NR^aR^b, X³-N(R^b)SO₂R^a, and X³-SO₃R^a;
 29 wherein X³ is a bond or C₁₋₆-alkylene;
 30 R³ and R⁴ are each independently selected from the group consisting of H, F, Cl, CN, CH₃,
 31 OCH₃, CH₂CH₃ and CF₃;
 32 the subscript n is 0, 1, 2 or 3;
 33 each R^{3a} is independently selected from the group consisting of H, F, Cl, C₁₋₃ alkyl, C₁₋₃
 34 alkoxy, C₁₋₃ haloalkyl, C₁₋₃ haloalkoxy, C₂₋₃ alkenyl and CN;
 35 R⁶, R⁷ and R⁸ are each independently selected from the group consisting of H, F, Cl, CN,
 36 CH₃, OCH₃, CH₂CH₃ and CF₃;
 37 Z is selected from the group consisting of:
 38 i) a monocyclic, bicyclic, or spirocyclic non-aromatic heterocyclic ring,
 39 optionally substituted with one or two oxo groups and optionally substituted with up
 40 to four R^a and/or R^b; and
 41 ii) a monocyclic 5- or 6-membered heteroaryl ring, optionally substituted with
 42 one to three R^e;
 43 each R^a is independently selected from the group consisting of H, C₁₋₆ alkyl, C₃₋₆ cycloalkyl,
 44 C₁₋₆ haloalkyl, C₁₋₆ hydroxyalkyl, C₁₋₆ alkylene-CO₂H, and C₁₋₆ alkylene-SO₃H;
 45 each R^b is independently selected from the group consisting of H, C₁₋₆ alkyl, C₃₋₆ cycloalkyl,
 46 C₁₋₆ haloalkyl, C₁₋₆ hydroxyalkyl, C₁₋₆ alkylene-CO₂H, and C₁₋₆ alkylene-SO₃H, each
 47 of which is unsubstituted or substituted with one or two members independently
 48 selected from OH, SO₂NH₂, C(O)NH₂, C(O)NHOH, PO₃H₂, CO₂C₁₋₈ alkyl and CO₂H;
 49 and R^a and R^b, when attached to the same nitrogen atom, are optionally combined to form a
 50 4- to 8-membered ring or spirocyclic ring, which is unsubstituted or substituted with
 51 halogen, OH, SO₂NH₂, C(O)NH₂, C(O)NHOH, PO₃H₂, CO₂C₁₋₈ alkyl or CO₂H;
 52 each R^e is independently selected from the group consisting of H, halogen, CN, C₁₋₆ alkyl,
 53 C₁₋₆ haloalkyl, Y⁺, X⁴-CO₂R^a, O-X⁴-CO₂R^a, X⁴-OR^a, X⁴-NR^aR^b, X⁴-C(O)NR^aR^b,
 54 O-X⁴-C(O)NR^aR^b, X⁴-SO₂R^a, X⁴-SO₂NR^aR^b, X⁴-SO₃R^a, and N(R^a)-X⁴-CO₂R^a;
 55 wherein each X⁴ is a bond or C₁₋₆-alkylene, and each Y⁺ is selected from the group~~

consisting of C₃₋₆-cycloalkyl and C₄₋₈-heterocyclyl; and optionally two R^e on adjacent ring vertices are combined to form a fused 5- or 6- membered heterocyclic ring.

2. — A compound of Formula (I):



or a pharmaceutically acceptable salt, prodrug or bioisostere thereof, wherein:

A is a 5- to 10- membered heteroaryl group which is unsubstituted or substituted with from one to five members independently selected from the group consisting of halogen, C₁₋₃-alkyl,

C₁₋₃-haloalkyl, C₁₋₃-alkoxy, C₁₋₃-haloalkoxy and CN;

X¹ is C₁₋₃-alkylene, which is unsubstituted or substituted with one or two members independently selected from the group consisting of C₁₋₂-alkyl and CO₂H;

R^{2a} and R^{2b} are each independently selected from the group consisting of H, C₁₋₈-alkyl, C₁₋₈-

haloalkyl, Y, X²-CO₂R^a, X²-OR^a, X²-NR^aR^b, X²-C(O)NR^aR^b, X²-SO₂R^a,

X²-SO₂NR^aR^b, X²-SO₃R^a and X²-Y wherein each X² is C₁₋₆-alkylene and any C₁₋₈-

alkyl or C₁₋₆-alkylene, is unsubstituted or substituted with one or two members

independently selected from the group consisting of OH, SO₂NH₂, C(O)NH₂,

C(O)NHOH, PO₃H₂, CO₂C₁₋₈-alkyl and CO₂H, and each Y is selected from the group

consisting of C₃₋₆-cycloalkyl, C₄₋₈-heterocyclyl and 5- to 6- membered heteroaryl, each

of which is unsubstituted or substituted with one to four substituents independently

selected from the group consisting of oxo, OH, C₁₋₄-alkyl, C₁₋₄-haloalkyl, C₁₋₄-

hydroxyalkyl, C₁₋₄-alkoxy, C₁₋₄-haloalkoxy, C₁₋₄-hydroxyalkoxy, SO₂NH₂, C(O)NH₂,

C(O)NHOH, PO₃H₂, CO₂C₁₋₈-alkyl, SO₃H and CO₂H;

or R^{2a} and R^{2b} are combined to form a 4- to 9- membered ring or spirocyclic ring, having from zero to two additional heteroatom ring vertices selected from O, N or S;

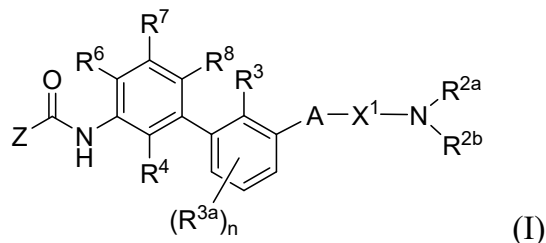
wherein the ring formed by combining R^{2a} and R^{2b}, is unsubstituted or substituted

with 1 to 4 substituents independently selected from the group consisting of

~~25 oxo, C₁₋₈ alkyl, C₁₋₈ haloalkyl, C₁₋₈ hydroxyalkyl, X³-CO₂R^a, X³-OR^a,
 26 X³-NR^aR^b,
 27 X³-C(O)NR^aR^b, X³-SO₂R^a, X³-SO₂NR^aR^b, X³-N(R^b)SO₂R^a, and X³-SO₃R^a;
 28 wherein X³ is a bond or C₁₋₆-alkylene;
 29 R³ and R⁴ are each independently selected from the group consisting of F, Cl, CN, CH₃,
 30 OCH₃, CH₂CH₃ and CF₃;
 31 the subscript n is 0, 1, 2 or 3;
 32 each R^{3a} is independently selected from the group consisting of H, F, Cl, C₁₋₃ alkyl, C₁₋₃
 33 alkoxy, C₁₋₃ haloalkyl, C₁₋₃ haloalkoxy, C₂₋₃ alkenyl and CN;
 34 R⁶, R⁷ and R⁸ are each independently selected from the group consisting of H, F, Cl, CN,
 35 CH₃, OCH₃, CH₂CH₃ and CF₃;
 36 Z is selected from the group consisting of:
 37 i) a monocyclic, bicyclic, or spirocyclic non-aromatic heterocyclic ring,
 38 optionally substituted with one or two oxo groups and optionally substituted with up
 39 to four R^a and/or R^b; and
 40 ii) a monocyclic 5- or 6-membered heteroaryl ring, optionally substituted with
 41 one to three R^e;
 42 each R^a is independently selected from the group consisting of H, C₁₋₆ alkyl, C₃₋₆ cycloalkyl,
 43 C₁₋₆ haloalkyl, C₁₋₆ hydroxyalkyl, C₁₋₆ alkylene-CO₂H, and C₁₋₆ alkylene-SO₃H;
 44 each R^b is independently selected from the group consisting of H, C₁₋₆ alkyl, C₃₋₆ cycloalkyl,
 45 C₁₋₆ haloalkyl, C₁₋₆ hydroxyalkyl, C₁₋₆ alkylene-CO₂H, and C₁₋₆ alkylene-SO₃H, each
 46 of which is unsubstituted or substituted with one or two members independently
 47 selected from OH, SO₂NH₂, C(O)NH₂, C(O)NHOH, PO₃H₂, CO₂C₁₋₈ alkyl and CO₂H;
 48 and R^a and R^b, when attached to the same nitrogen atom, are optionally combined to form a
 49 4- to 8-membered ring or spirocyclic ring, which is unsubstituted or substituted with
 50 halogen, OH, SO₂NH₂, C(O)NH₂, C(O)NHOH, PO₃H₂, CO₂C₁₋₈ alkyl or CO₂H;
 51 each R^e is independently selected from the group consisting of H, halogen, CN, C₁₋₆ alkyl,
 52 C₁₋₆ haloalkyl, Y⁺, X⁴-CO₂R^a, O-X⁴-CO₂R^a, X⁴-OR^a, X⁴-NR^aR^b, X⁴-C(O)NR^aR^b,
 53 O-X⁴-C(O)NR^aR^b, X⁴-SO₂R^a, X⁴-SO₂NR^aR^b, X⁴-SO₃R^a, and N(R^a)-X⁴-CO₂R^a;
 54 wherein each X⁴ is a bond or C₁₋₆-alkylene, and each Y⁺ is selected from the group~~

consisting of C₃₋₆ cycloalkyl and C₄₋₈ heterocyclyl; and optionally two R^e on adjacent ring vertices are combined to form a fused 5- or 6-membered heterocyclic ring.

31. A compound of Formula (I):



or a pharmaceutically acceptable salt, or a stereoisomer, prodrug or bioisostere thereof, wherein:

A is a 5- to 10-membered heteroaryl group which is unsubstituted or substituted with from one to five members independently selected from the group consisting of halogen, C₁₋₃ alkyl, C₁₋₃ haloalkyl, C₁₋₃ alkoxy, C₁₋₃ haloalkoxy and CN;

X¹ is C₁₋₃ alkylene, which is unsubstituted or substituted with one or two members independently selected from the group consisting of C₁₋₂ alkyl and CO₂H;

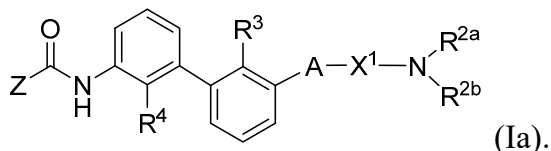
R^{2a} and R^{2b} are each independently selected from the group consisting of H, C₁₋₈ alkyl, C₁₋₈ haloalkyl, -Y, -X²-CO₂R^a, -X²-OR^a, -X²-NR^aR^b, -X²-C(O)NR^aR^b, -X²-SO₂R^a, -X²-SO₂NR^aR^b, -X²-SO₃R^a and -X²-Y₁ wherein each X² is C₁₋₆ alkylene, and any C₁₋₈ alkyl or C₁₋₆ alkylene, is unsubstituted or substituted with one or two members independently selected from the group consisting of OH, SO₂NH₂, C(O)NH₂, C(O)NHOH, PO₃H₂, CO₂-C₁₋₈ alkyl and CO₂H, and each Y is selected from the group consisting of C₃₋₆ cycloalkyl, C₄₋₈ heterocyclyl and 5- to 6-membered heteroaryl, each of which is unsubstituted or substituted with one to four substituents independently selected from the group consisting of oxo, OH, C₁₋₄ alkyl, C₁₋₄ haloalkyl, C₁₋₄ hydroxyalkyl, C₁₋₄ alkoxy, C₁₋₄ haloalkoxy, C₁₋₄ hydroxyalkoxy, SO₂NH₂, C(O)NH₂, C(O)NHOH, PO₃H₂, CO₂-C₁₋₈ alkyl, SO₃H and CO₂H;

or R^{2a} and R^{2b} are combined to form a 4- to 9-membered ring or spirocyclic ring, having from zero to two additional heteroatom ring vertices selected from O, N or S;

wherein the ring formed by combining R^{2a} and R^{2b}, is unsubstituted or substituted with 1 to 4 substituents independently selected from the group consisting of oxo, C₁₋₈ alkyl, C₁₋₈ haloalkyl, C₁₋₈ hydroxyalkyl, -X³-CO₂R^a, -X³-OR^a, -X³-NR^aR^b,

25 $-X^3-C(O)NR^aR^b$, $-X^3-SO_2R^a$, $-X^3-SO_2NR^aR^b$, and $-X^3-SO_3R^a$; wherein X^3 is a bond
 26 or C_{1-6} alkylene;
 27 R^3 and R^4 are each independently selected from the group consisting of F, Cl, CN, CH_3 , OCH_3 ,
 28 CH_2CH_3 and CF_3 ;
 29 the subscript n is 0, 1, 2 or 3;
 30 each R^{3a} is independently selected from the group consisting of H, F, Cl, C_{1-3} alkyl, C_{1-3} alkoxy,
 31 C_{1-3} haloalkyl, C_{1-3} haloalkoxy, C_{2-3} alkenyl and CN;
 32 R^6 , R^7 and R^8 are each independently selected from the group consisting of H, F, Cl, CN, CH_3 ,
 33 OCH_3 , CH_2CH_3 and CF_3 ;
 34 Z is selected from the group consisting of:
 35 i) a monocyclic, bicyclic, or spirocyclic non-aromatic heterocyclic ring, optionally
 36 substituted with one or two oxo groups and optionally substituted with up to four R^a
 37 and/or R^b ; and
 38 ii) a monocyclic 5- or 6-membered heteroaryl ring, optionally substituted with one to
 39 three R^c ;
 40 each R^a is independently selected from the group consisting of H, C_{1-6} alkyl, C_{3-6} cycloalkyl, C_{1-6}
 41 haloalkyl, C_{1-6} hydroxyalkyl, C_{1-6} alkylene- CO_2H , and C_{1-6} alkylene- SO_3H ;
 42 each R^b is independently selected from the group consisting of H, C_{1-6} alkyl, C_{3-6} cycloalkyl, C_{1-6}
 43 haloalkyl, C_{1-6} hydroxyalkyl, C_{1-6} alkylene- CO_2H , and C_{1-6} alkylene- SO_3H , each of which
 44 is unsubstituted or substituted with one or two members independently selected from OH,
 45 SO_2NH_2 , $C(O)NH_2$, $C(O)NHOH$, PO_3H_2 , CO_2C_{1-8} alkyl and CO_2H ;
 46 and R^a and R^b , when attached to the same nitrogen atom, are optionally combined to form a 4- to
 47 8-membered ring or spirocyclic ring, which is unsubstituted or substituted with halogen,
 48 OH, SO_2NH_2 , $C(O)NH_2$, $C(O)NHOH$, PO_3H_2 , CO_2C_{1-8} alkyl or CO_2H ;
 49 each R^c is independently selected from the group consisting of H, halogen, CN, C_{1-6} alkyl, C_{1-6}
 50 haloalkyl, $-Y^1$, $-X^4-CO_2R^a$, $-O-X^4-CO_2R^a$, $-X^4-OR^a$, $-X^4-NR^aR^b$, $-X^4-C(O)NR^aR^b$,
 51 $-O-X^4-C(O)NR^aR^b$, $-X^4-SO_2R^a$, $-X^4-SO_2NR^aR^b$, $-X^4-SO_3R^a$, and $-N(R^a)-X^4-CO_2R^a$,
 52 wherein each X^4 is a bond or C_{1-6} alkylene, and each Y^1 is selected from the group
 53 consisting of C_{3-6} cycloalkyl and C_{4-8} heterocyclyl; and optionally two R^c on adjacent ring
 54 vertices are combined to form a fused 5- or 6-membered heterocyclic ring.

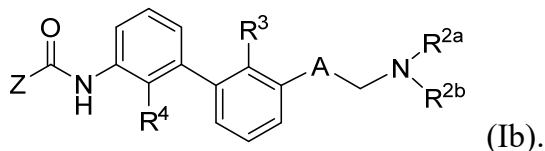
1 42. The compound of claim ~~1~~ or claim ~~3~~, or a pharmaceutically acceptable
2 salt thereof, having formula (Ia):



1 35. The compound of any one of claims ~~1~~ to ~~4~~ 2, or a pharmaceutically
2 acceptable salt thereof, wherein A is a 5- or 6-membered heteroaryl group which is
3 unsubstituted or substituted with from one to three members independently selected from the
4 group consisting of halogen, C₁₋₃ alkyl, C₁₋₃ haloalkyl, C₁₋₃ alkoxy, ~~OH~~, and CN.

1 64. The compound of any one of claims ~~1~~ to ~~4~~ 2, or a pharmaceutically
2 acceptable salt thereof, wherein A is a 6-membered heteroaryl group which is unsubstituted
3 or substituted with from one to three members independently selected from the group
4 consisting of halogen, C₁₋₃ alkyl, C₁₋₃ haloalkyl, C₁₋₃ alkoxy, ~~OH~~, and CN.

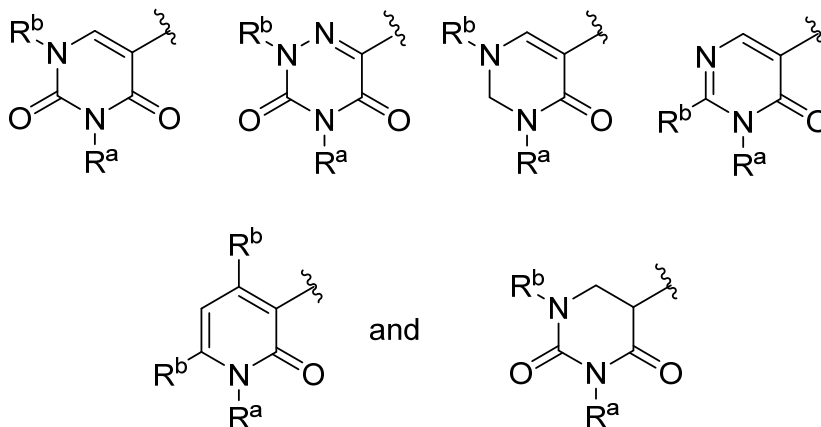
1 75. The compound of any one of claims ~~1~~ to ~~46~~ a pharmaceutically
2 acceptable salt thereof, having formula (Ib):



1 86. The compound of any one of claims ~~1~~ to ~~75~~, or a pharmaceutically
2 acceptable salt thereof, wherein A is unsubstituted or substituted with one or two members
3 independently selected from the group consisting of ~~CF₃, OH, Et, CN~~, OCH₃ and F.

1 97. The compound of any one of claims ~~1~~ to ~~57~~, or a pharmaceutically
2 acceptable salt thereof, wherein A is a 6-membered heteroaryl selected from the group
3 consisting of pyridine, pyrimidine, pyrazine and 1,2,4-triazine, each of which is unsubstituted
4 or substituted with one or two members independently selected from the group consisting of
5 ~~CF₃, OH, Et, CN~~, OCH₃ and F.

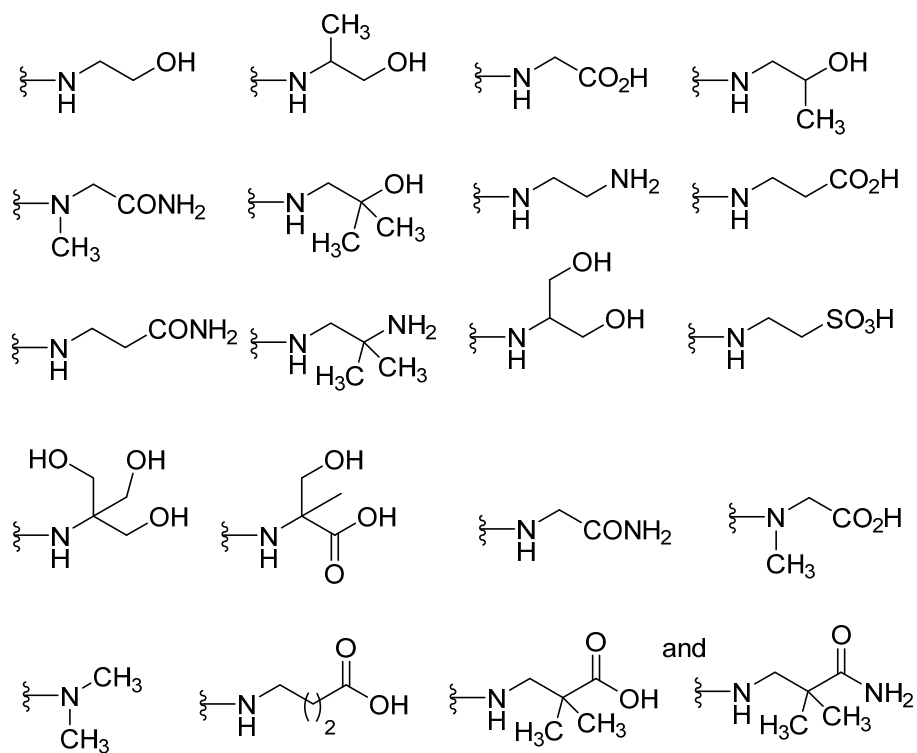
108. The compound of any one of claims **1** to **75**, or a pharmaceutically acceptable salt thereof, wherein Z is a non-aromatic heterocyclic ring having a formula selected from the group consisting of:



109. The compound of any one of claims **1** to **75**, or a pharmaceutically acceptable salt thereof, wherein Z is a monocyclic 5- or 6-membered heteroaryl ring, optionally substituted with one to three R^c; and said heterocyclic ring is selected from the group consisting of pyridinyl, pyrimidinyl, pyrazinyl, oxazolyl, thiazolyl, and pyrazolyl.

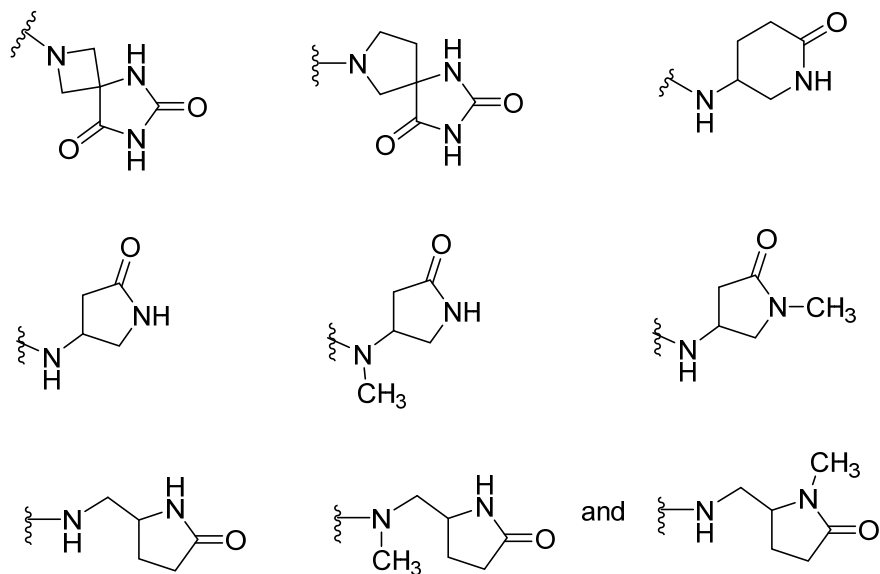
110. The compound of any one of claims **1** to **75**, or a pharmaceutically acceptable salt thereof, wherein Z is a non-aromatic heterocyclic ring selected from the group consisting of piperidinyl, morpholinyl, tetrahydropyranyl, and tetrahydrofuranyl, each of which is optionally substituted with up to four R^a and/or R^b.

111. The compound of any one of claims **1** to **109**, or a pharmaceutically acceptable salt thereof, wherein -N(R^{2a})(R^{2b}) is selected from the group consisting of:



3

1 **1412.** The compound of any one of claims **1** to **119**, or a pharmaceutically
 2 acceptable salt thereof, wherein $-N(R^{2a})(R^{2b})$ is selected from the group consisting of:



3

1 **1614.** The compound of any one of claims **1** to **1513**, or a pharmaceutically
2 acceptable salt thereof, wherein the compound is an optically pure or enriched stereoisomer.

1 **1715.** The compound of any one of claims **1** to **1513**, or a pharmaceutically
2 acceptable salt thereof, wherein Y is selected from the group consisting of C₃₋₆ cycloalkyl
3 and C₄₋₈ heterocyclyl, each of which is unsubstituted or substituted with one to four
4 substituents independently selected from the group consisting of oxo, OH, C₁₋₄ alkyl, C₁₋₄
5 haloalkyl, C₁₋₄ hydroxyalkyl, C₁₋₄ alkoxy, C₁₋₄ haloalkoxy, C₁₋₄ hydroxyalkoxy, SO₂NH₂,
6 C(O)NH₂, C(O)NHOH, PO₃H₂, CO₂C₁₋₈ alkyl, SO₃H and CO₂H.

1 **1816.** The compound of claim **1**, or a pharmaceutically acceptable salt
2 thereof, wherein Z is a 5- or 6-membered non-aromatic heterocyclic ring, optionally
3 substituted with one or two oxo groups and optionally substituted with R^a and/or R^b.

1 **1917.** The compound of claim **1**, or a pharmaceutically acceptable salt
2 thereof, wherein Z is a monocyclic 5- or 6-membered heteroaryl ring, optionally substituted
3 with one to three R^c.

1 **2018.** The compound of claim **1**, or a pharmaceutically acceptable salt
2 thereof, wherein Z is a 5- or 6-membered monocyclic non-aromatic heterocyclic ring,

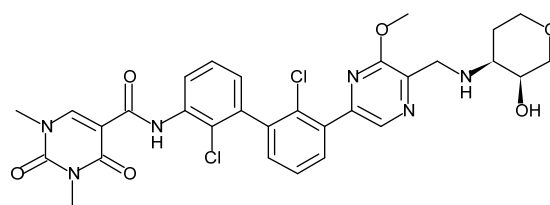
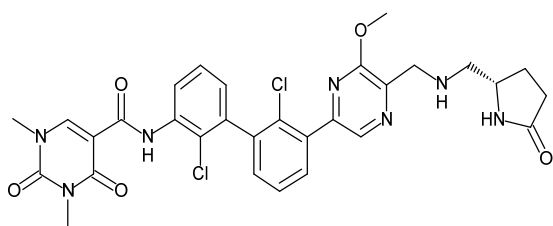
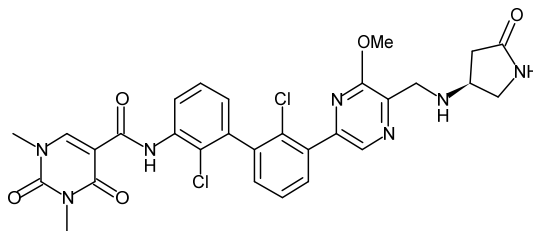
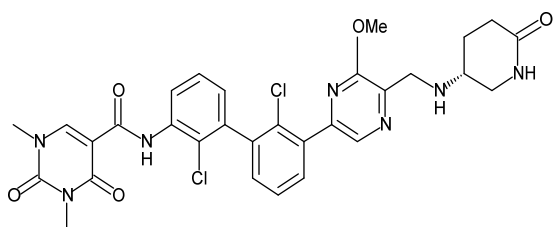
3 optionally substituted with one or two oxo groups and optionally substituted with R^a and/or
4 R^b; and each of R⁶, R⁷ and R⁸ is H.

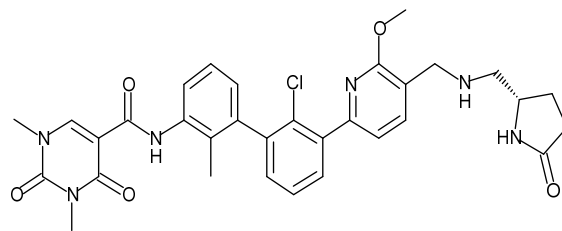
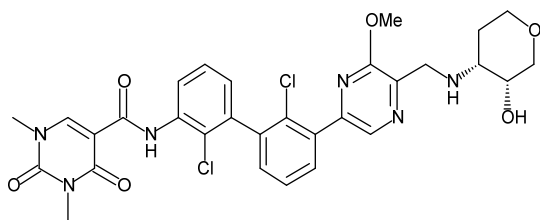
1 **2119.** The compound of claim 1, or a pharmaceutically acceptable salt
2 thereof, wherein Z is a monocyclic 5- or 6-membered heteroaryl ring, optionally substituted
3 with one to three R^c; and each of R⁶, R⁷ and R⁸ is H.

1 **2220.** The compound of claim 1, or a pharmaceutically acceptable salt
2 thereof, wherein Z is a 5- or 6-membered non-aromatic heterocyclic ring selected from the
3 group consisting of piperidinyl, morpholinyl, tetrahydropyranyl, and tetrahydrofuranyl,
4 optionally substituted with one or two oxo groups and optionally substituted with R^a and/or
5 R^b.

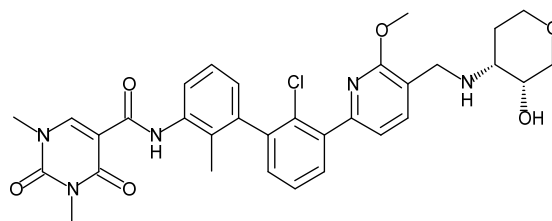
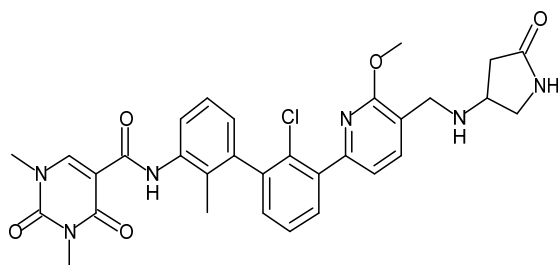
1 **2321.** The compound of claim 1, or a pharmaceutically acceptable salt
2 thereof, wherein Z is a monocyclic 5- or 6-membered heteroaryl ring selected from the group
3 consisting of pyridinyl, pyrimidinyl, pyrazinyl, oxazolyl, thiazolyl, and pyrazolyl, each of
4 which is optionally substituted with one to three R^c.

1 **2422.** The compound of claim 1, wherein said compound is selected from the
2 group consisting of compounds in Table 1

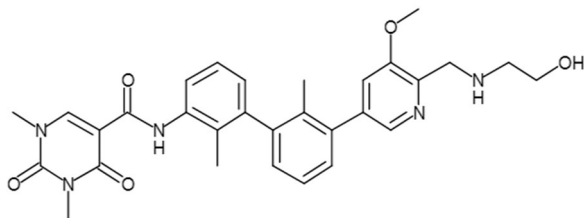




5



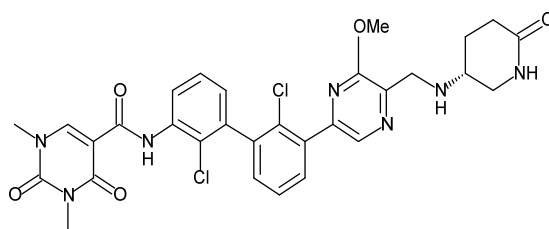
6



7 and

8 or a pharmaceutically acceptable salt thereof.

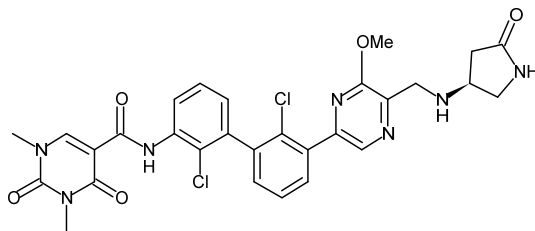
1 23. The compound of claim 1, having the formula



2

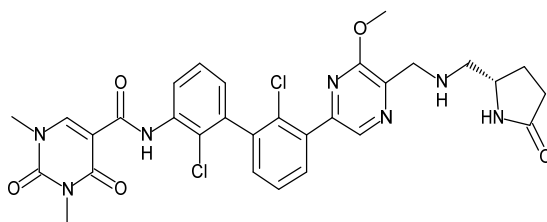
3 or a pharmaceutically acceptable salt thereof.

4 24. The compound of claim 1, having the formula



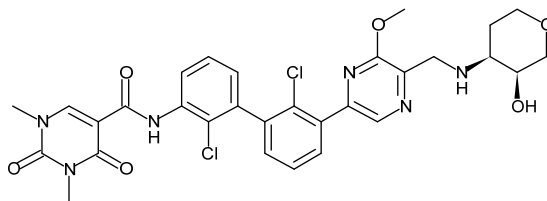
or a pharmaceutically acceptable salt thereof.

25. The compound of claim 1, having the formula



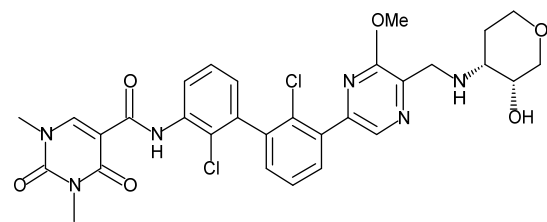
or a pharmaceutically acceptable salt thereof.

26. The compound of claim 1, having the formula



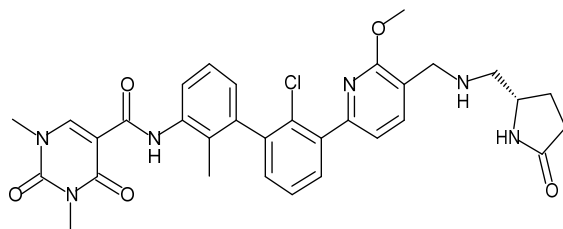
or a pharmaceutically acceptable salt thereof.

27. The compound of claim 1, having the formula



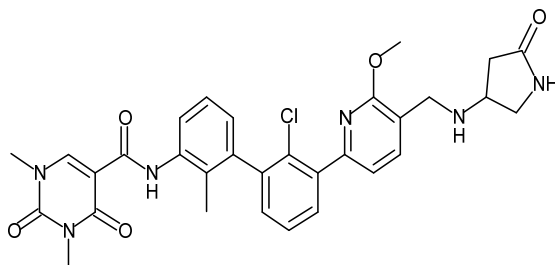
or a pharmaceutically acceptable salt thereof.

28. The compound of claim 1, having the formula



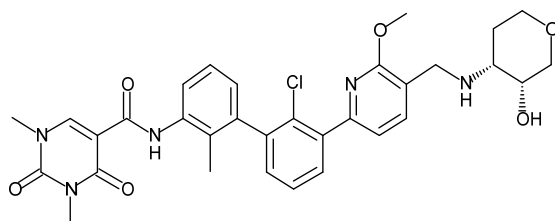
or a pharmaceutically acceptable salt thereof.

29. The compound of claim 1, having the formula



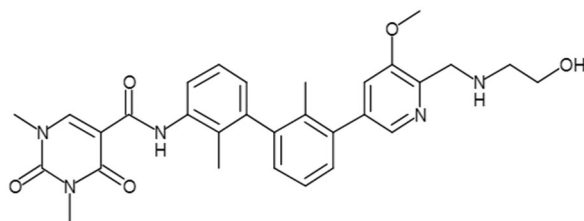
or a pharmaceutically acceptable salt thereof.

30. The compound of claim 1, having the formula



or a pharmaceutically acceptable salt thereof.

31. The compound of claim 1, having the formula



or a pharmaceutically acceptable salt thereof.

28 **2532.** A pharmaceutical composition comprising a compound of any one of
29 claims **1** to **2431**, or a pharmaceutically acceptable salt thereof, and a pharmaceutically
30 acceptable excipient.

1 **2633.** The pharmaceutical composition of claim **2532**, further comprising one
2 or more additional therapeutic agents.

1 **2734.** The pharmaceutical composition of claim **2633**, wherein the one or
2 more additional therapeutic agent is selected from the group consisting of an antimicrobial
3 agent, an antiviral agent, a cytotoxic agent, a gene expression modulatory agent, a
4 chemotherapeutic agent, an anti-cancer agent, an anti-angiogenic agent, an
5 immunotherapeutic agent, an anti-hormonal agent, an anti-fibrotic agent, radiotherapy, a
6 radiotherapeutic agent, an anti-neoplastic agent, and an anti-proliferation agent.

1 ~~**2835.** A method of modulating an immune response mediated by the PD-1~~
2 ~~signaling pathway in a subject, comprising administering to the subject a therapeutically~~
3 ~~effective amount~~ Use of a compound of any one of claims **1** to **2431**, or a pharmaceutically
4 acceptable salt thereof or a composition of any one of claims **25-32** to **2734**, in the
5 preparation of a medicament for modulating an immune response mediated by the PD-1
6 signaling pathway in a subject.

1 ~~**2936.** A method of enhancing, stimulating, modulating and/or increasing the~~
2 ~~immune response in a subject in need thereof, comprising administering to the subject a~~
3 ~~therapeutically effective amount~~ Use of a compound of any one of claims **1** to **2431**, or a
4 pharmaceutically acceptable salt thereof or a composition of any one of claims **25-32** to
5 **2734**, in the preparation of a medicament for enhancing, stimulating, modulating and/or
6 increasing the immune response in a subject in need thereof.

1 ~~**3037.** A method of inhibiting growth, proliferation, or metastasis of cancer~~
2 ~~cells in a subject in need thereof, comprising administering to the subject a therapeutically~~
3 ~~effective amount~~ Use of a compound of any one of claims **1** to **2431**, or a pharmaceutically
4 acceptable salt thereof or a composition of any one of claims **25-32** to **2734**, in the

5 preparation of a medicament for inhibiting growth, proliferation, or metastasis of cancer cells
6 in a subject in need thereof.

1 ~~3138.~~ A method of treating a subject suffering from or susceptible to a
2 ~~disease or disorder mediated by the PD-1 signaling pathway, comprising administering to the~~
3 ~~subject a therapeutically effective amount~~ Use of a compound of any one of claims 1 to
4 ~~2431,~~ or a pharmaceutically acceptable salt thereof or a composition of any one of claims 25
5 ~~32 to 2734,~~ in the preparation of a medicament for treating a subject suffering from or
6 susceptible to a disease or disorder mediated by the PD-1 signaling pathway.

1 ~~3239.~~ The ~~method-use~~ of any one of claims ~~28-35~~ to ~~3138,~~ wherein the
2 subject suffers from a disease or disorder selected from the group consisting of an infectious
3 disease, a bacterial infectious disease, a viral infectious disease a fungal infectious disease, a
4 solid tumor, a hematological malignancy, an immune disorder, an inflammatory disease, and
5 cancer.

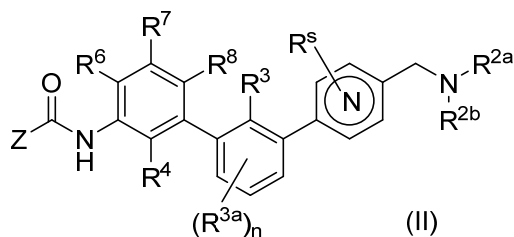
1 ~~3340.~~ The method of claim ~~3138,~~ wherein the disease or disorder is selected
2 from the group consisting of melanoma, glioblastoma, esophagus tumor, nasopharyngeal
3 carcinoma, uveal melanoma, lymphoma, lymphocytic lymphoma, primary CNS lymphoma,
4 T-cell lymphoma, diffuse large B-cell lymphoma, primary mediastinal large B-cell
5 lymphoma, prostate cancer, castration-resistant prostate cancer, chronic myelocytic
6 leukemia, Kaposi's sarcoma fibrosarcoma, liposarcoma, chondrosarcoma, osteogenic
7 sarcoma, angiosarcoma, lymphangiosarcoma, synovioma, , meningioma, leiomyosarcoma,
8 rhabdomyosarcoma, sarcoma of soft tissue, sarcoma, sepsis, biliary tumor, basal cell
9 carcinoma, thymus neoplasm, cancer of the thyroid gland, cancer of the parathyroid gland,
10 uterine cancer, cancer of the adrenal gland, liver infection, Merkel cell carcinoma, nerve
11 tumor, follicle center lymphoma, colon cancer, Hodgkin's disease, non-Hodgkin's lymphoma,
12 leukemia, chronic or acute leukemias including acute myeloid leukemia, chronic myeloid
13 leukemia, acute lymphoblastic leukemia, chronic lymphocytic leukemia, multiple myeloma,
14 ovary tumor, myelodysplastic syndrome, cutaneous or intraocular malignant melanoma, renal
15 cell carcinoma, small-cell lung cancer, lung cancer, mesothelioma, breast cancer, squamous

non-small cell lung cancer (SCLC), non-squamous NSCLC, colorectal cancer, ovarian cancer, gastric cancer, hepatocellular carcinoma, pancreatic carcinoma, pancreatic cancer, Pancreatic ductal adenocarcinoma, squamous cell carcinoma of the head and neck, cancer of the head or neck, gastrointestinal tract, stomach cancer, HIV, Hepatitis A, Hepatitis B, Hepatitis C, Hepatitis D, herpes viruses, papillomaviruses, influenza, bone cancer, skin cancer, rectal cancer, cancer of the anal region, testicular cancer, carcinoma of the fallopian tubes, carcinoma of the endometrium, carcinoma of the cervix, carcinoma of the vagina, carcinoma of the vulva, cancer of the esophagus, cancer of the small intestine, cancer of the endocrine system, cancer of the urethra, cancer of the penis, cancer of the bladder, cancer of the kidney, cancer of the ureter, carcinoma of the renal pelvis, neoplasm of the central nervous system (CNS), tumor angiogenesis, spinal axis tumor, brain stem glioma, pituitary adenoma, epidermoid cancer, abestosis, carcinoma, adenocarcinoma, papillary carcinoma, cystadenocarcinoma, bronchogenic carcinoma, renal cell carcinoma, transitional cell carcinoma, choriocarcinoma, seminoma, embryonal carcinoma, wilm's tumor, pleomorphic adenoma, liver cell papilloma, renal tubular adenoma, cystadenoma, papilloma, adenoma, leiomyoma, rhabdomyoma, hemangioma, lymphangioma, osteoma, chondroma, lipoma and fibroma.

3441. The ~~method-use~~ of any one of claims ~~28-35~~ to **3340**, further comprising ~~administering to the subject~~ a therapeutically effective amount of one or more additional therapeutic agents to be administered to the subject.

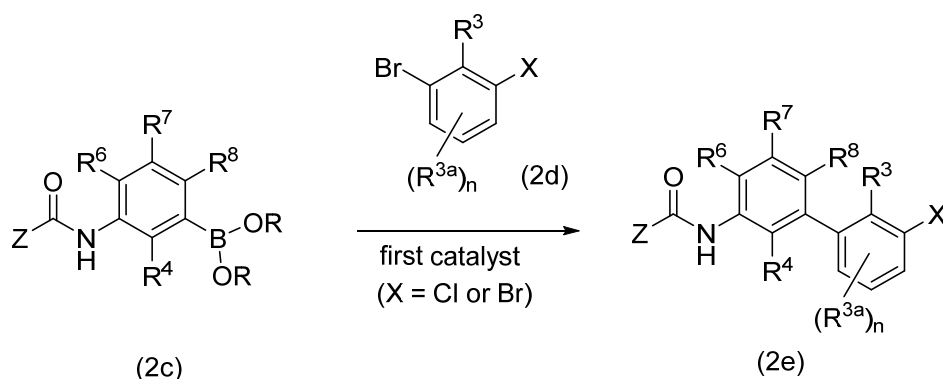
3542. The ~~method-use~~ of claim **3441**, wherein the one or more additional therapeutic agents is selected from the group consisting of an antimicrobial agent, an antiviral agent, a cytotoxic agent, a gene expression modulatory agent, a chemotherapeutic agent, an anti-cancer agent, an anti-angiogenic agent, an immunotherapeutic agent, an anti-hormonal agent, an anti-fibrotic agent, radiotherapy, a radiotherapeutic agent, an anti-neoplastic agent, and an anti-proliferation agent.

3643. A process for preparing a compound of formula (II),

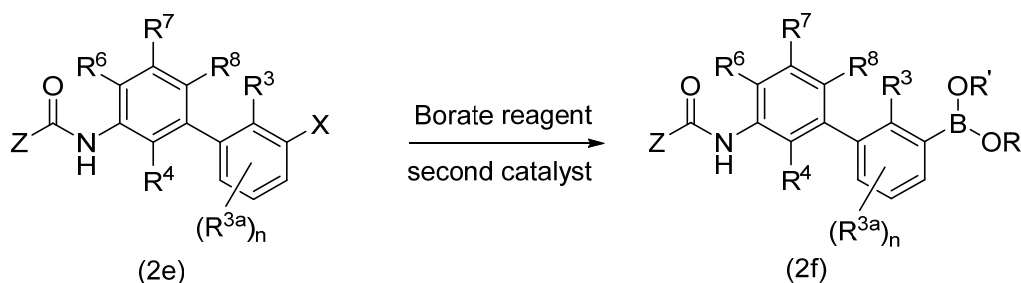


the process comprising:

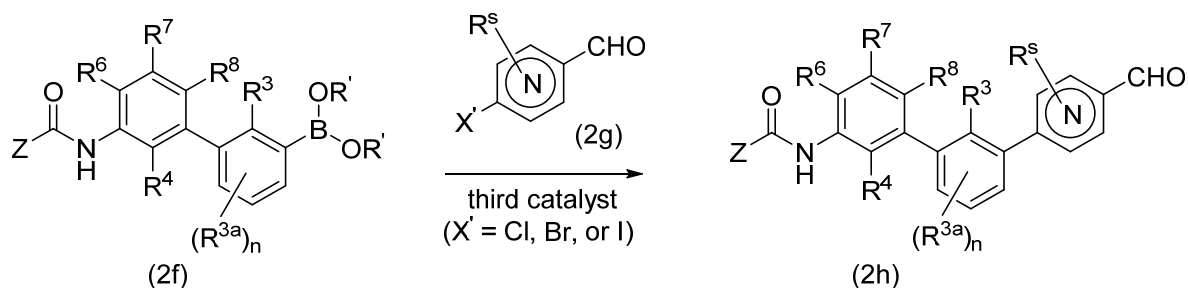
(a) contacting a compound having formula (2c) with a compound having formula (2d) and a first catalyst, under Suzuki-type conditions to produce a compound having formula (2e);



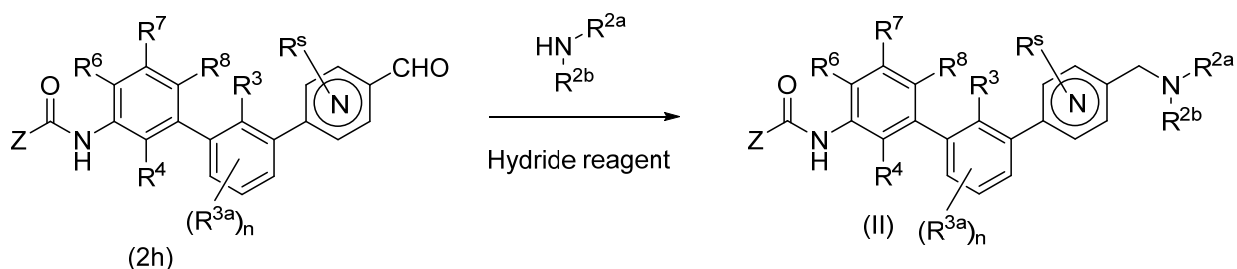
(b) converting the compound having formula (2e) to a compound having formula (2f) with a borate reagent and a second catalyst;



(c) contacting a compound having formula (2f) with a compound having formula (2g) and a third catalyst, under Suzuki-type conditions to produce a compound having formula (2h);



(d) reductively aminating the compound having formula (2h) with $\text{HN(R}^{2a}\text{)(R}^{2b}\text{)}$ and a hydride reagent to provide the compound having formula (II),



wherein in the above formulae (2c), (2d), (2e), (2f), (2h), and (II), each of Z, R^{2a} , R^{2b} , R^3 , R^{3a} , subscript n, R^4 , R^5 , R^6 , R^7 , R^8 , have the meanings provided in claim 1;

R and R' are each independently selected from the group consisting of H and $\text{C}_1\text{-C}_6$ alkyl;

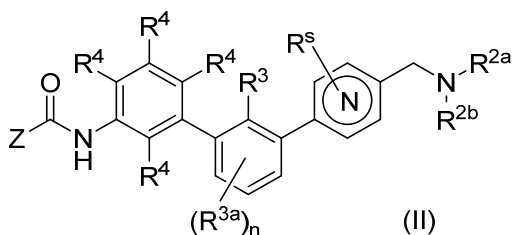
X is a member selected from the group consisting of Br and Cl;

X' is a member selected from the group consisting of I, Br and Cl;

the ring bearing R^s is a six-membered nitrogen heteroaryl ring selected from the group consisting of pyridine, pyrimidine and pyrazine, and R^s is 0, 1, 2 or 3 substituents

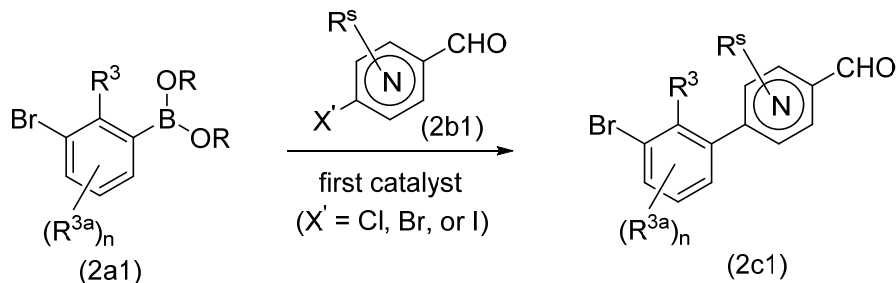
independently selected from the group consisting of halogen, C_{1-3} alkyl, C_{1-3} haloalkyl, C_{1-3} alkoxy, C_{1-3} haloalkoxy, OH, and CN.

3744. A process for preparing a compound of formula (II),

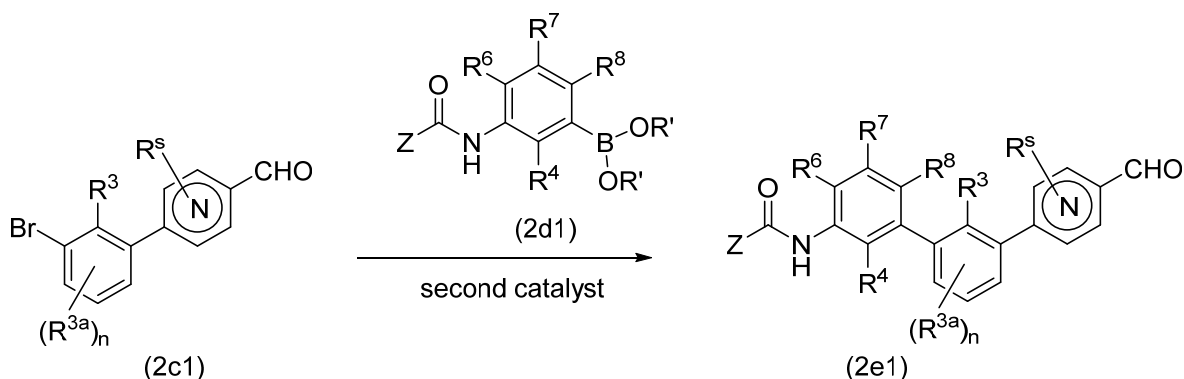


the process comprising:

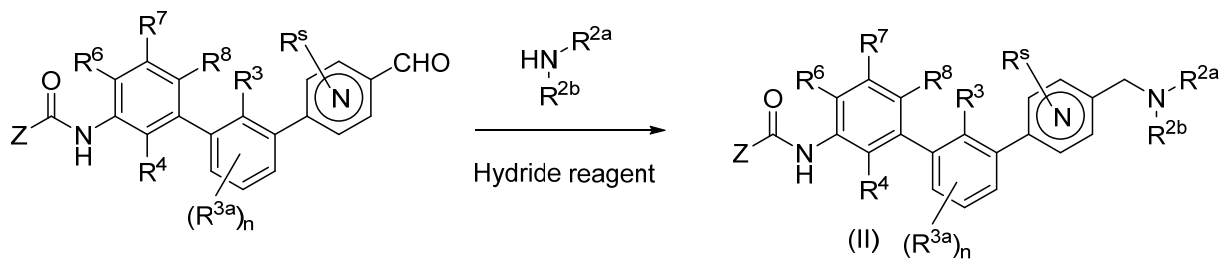
(a) contacting a compound having formula (2a1) with a compound having formula (2b1) and a first catalyst, under Suzuki-type conditions to produce a compound having formula (2c1);



(b) contacting a compound having formula (2c1) with a compound having formula (2d1) and a second catalyst, under Suzuki-type conditions to produce a compound having formula (2e1);



(c) reductively aminating the compound having formula (2e1) with $\text{HN(R}^{2a}\text{)(R}^{2b}\text{)}$ and a hydride reagent to provide the compound having formula (II),



(2h)

wherein in the above formulae (2a1), (2b1), (2c1), (2d1), (2e1), and (II), each of Z, R^{2a} , R^{2b} , R^3 , R^{3a} , subscript n, R^4 , R^5 , R^6 , R^7 , R^8 , have the meanings provided in claim 1;

R and R' are each independently selected from the group consisting of H and $\text{C}_1\text{-C}_6$ alkyl;

19 X' is a member selected from the group consisting of I, Br and Cl;
20 the ring bearing R^s is a six-membered nitrogen heteroaryl ring selected from the group
21 consisting of pyridine, pyrimidine and pyrazine, and R^s is 0, 1, 2 or 3 substituents
22 independently selected from the group consisting of halogen, C₁₋₃ alkyl, C₁₋₃ haloalkyl, C₁₋₃
23 alkoxy, C₁₋₃ haloalkoxy, OH, and CN.