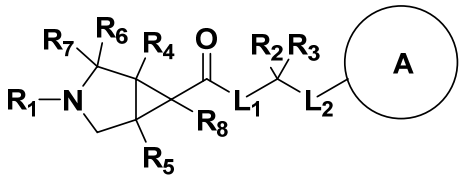
CLAIMS

1. A compound of Formula (I), or a stereoisomer, an *N*-oxide, a hydrate, a solvate, a metabolite, a pharmaceutically acceptable salt, a polymorph, or a prodrug thereof:



(I)

wherein R_1 is selected from -H and a C_{1-6} alkyl;

L_1 is selected from -NH- and -O-;

R_2 and R_3 are each independently selected from -H, a C_{1-6} alkyl, and a C_{3-6} cycloalkyl, wherein R_2 and R_3 are not both -H; or R_2 and R_3 together form a 3- to 6-membered saturated cyclic group comprising 0 to 1 group selected from -O-, -NR_9-, -SO-, and -SO_2-;

R_4, R_5, R_6, R_7, and R_8 are each independently selected from -H, a C_{1-6} alkyl, a C_{1-6} alkoxy, a C_{1-6} alkoxy C_{1-6} alkyl, a -$(CH_2)_m$-C_{3-10} carbocyclyl, a -$(CH_2)_m$-(3- to 10-membered heterocyclyl), a -$(CH_2)_m$-O-C_{3-10} carbocyclyl, a -$(CH_2)_m$-O-(3- to 10-membered heterocyclyl), phenyl, and a 5- to 6-membered heteroaryl, the heterocyclyl or the heteroaryl contains 1 to 4 heteroatoms selected from N, O, and S, and the alkyl, the alkoxy, the carbocyclyl, the phenyl, the heteroaryl, or the heterocyclyl in R_4, R_5, R_6, R_7, and R_8 is each independently optionally further substituted with 0 to 4 substituents selected from -H, -F, -Cl, -Br, -I, hydroxy, sulfydryl, cyano, amino, a C_{1-4} alkyl, and a C_{1-4} alkoxy;

R_9 is selected from -H, a C_{1-6} alkyl, a C_{1-4} alkoxy C_{1-6} alkyl, a halogen, hydroxy, cyano, and a C_{3-6} cycloalkyl;

A is selected from a C_{6-14} aryl, a 5- to 14-membered heteroaryl, a 5- to 14-membered heterocyclyl, and a 5- to 14-membered cycloalkyl, and the aryl, the heteroaryl, the heterocyclyl, and the cycloalkyl in A are optionally further substituted with 1 to 4 R_{10}, wherein the heteroaryl or the heterocyclyl contains 1 to 4 heteroatoms selected from N, O, and S;

when L_2 is selected from a single bond, -$(CR_aR_b)_n$-, and -$(CR_aR_b)_nO$-, R_{10} is independently selected from -H, -F, -Cl, -Br, -I, hydroxy, cyano, amino, a C_{1-6} alkyl, a C_{1-4} alkoxy C_{1-6} alkyl, a C_{3-6} cycloalkyl, and -SR_{11}, and at least one R_{10} is -SR_{11}, wherein R_{11} is each independently selected from -H, a C_{1-6} alkyl, a C_{1-4} alkoxy C_{1-6} alkyl, a -$(CH_2)_n$-C_{2-6} alkenyl, a -$(CH_2)_n$-C_{2-6} alkynyl, a -$(CH_2)_n$-C_{3-10} carbocyclyl, a -$(CH_2)_n$-(3- to 10-membered heterocyclyl), a C_{6-10} aryl, and a 5- to 6-membered heteroaryl, the heterocyclyl and the heteroaryl contain 1 to 4 heteroatoms selected from N, O, and S, the alkyl, and the alkoxy, the aryl, the heteroaryl, the carbocyclyl, or the heterocyclyl is each independently optionally further substituted with 0 to 4 substituents selected from -H, a halogen, hydroxy, cyano, a C_{1-4} alkyl, and a C_{1-4} alkoxy;

when L_2 is selected from -$(CR_aR_b)_nS$-, R_{10} is independently selected from -H, -F, -Cl, -Br, -I, hydroxy, cyano, amino, a C_{1-4} alkyl, a C_{1-4} alkoxy, a C_{1-4} alkoxy C_{1-6} alkyl, a -$(CH_2)_n$-C_{2-6} alkenyl, a -$(CH_2)_n$-C_{2-6} alkynyl, a -$(CH_2)_n$-C_{3-10} carbocyclyl, a -$(CH_2)_n$-(3- to 10-membered heterocyclyl), a -O-$(CH_2)_n$-C_{3-10} carbocyclyl or -O-$(CH_2)_n$-(3- to 10-membered heterocyclyl), and -SR_{11}, wherein R_{11} is each independently selected from -H, a C_{1-6} alkyl, a C_{1-4} alkoxy C_{1-6} alkyl, a -$(CH_2)_n$-C_{2-6} alkenyl, a -$(CH_2)_n$-C_{2-6} alkynyl, a -$(CH_2)_n$-C_{3-10} carbocyclyl, a -$(CH_2)_n$-(3- to 10-membered heterocyclyl), a C_{6-10} aryl, and a 5- to 6-membered heteroaryl, the heterocyclyl or the heteroaryl contains 1 to 4 heteroatoms selected from N, O, and S, and the alkyl, the alkoxy, the aryl, the heteroaryl, the carbocyclyl, or the heterocyclyl is each independently optionally further substituted with 0 to 4 substituents selected from H, a halogen, hydroxy, cyano, a C_{1-4} alkyl, and a C_{1-4} alkoxy;

R_a and R_b are each independently selected from -H and a C_{1-6} alkyl;

m is independently selected from 0, 1, 2, and 3 at each occurrence;

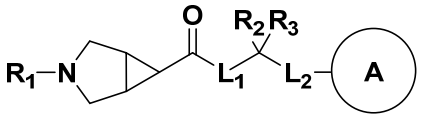
n is independently selected from 0, 1, 2, and 3 at each occurrence;~~.~~

~~2. The compound, or the stereoisomer, the *N*-oxide, the hydrate, the solvate, the metabolite, the pharmaceutically acceptable salt, the polymorph, or the prodrug thereof according to claim 1, wherein~~preferably, wherein:

L_1 is -NH-;

R_1 is -H~~.~~;

preferably, ~~3. The compound, or the stereoisomer, the *N*-oxide, the hydrate, the solvate, the metabolite, the pharmaceutically acceptable salt, the polymorph, or the prodrug thereof according to claim 1,~~ wherein the Formula (I) compound ~~–~~has structural features of Formula (VI):



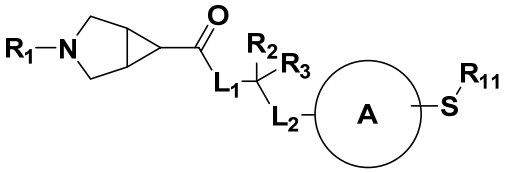
(VI)

L_1 is selected from -NH- and -O-;

L_2 is selected from a single bond and $-(CR_aR_b)_n-$ or $-(CR_aR_b)_nO-$, wherein R_a and R_b are independently selected from -H and a C_{1-6} alkyl;

n is independently selected from 0, 1, 2, and 3 at each occurrence.

4~~2~~. The compound, or the stereoisomer, the *N*-oxide, the hydrate, the solvate, the metabolite, the pharmaceutically acceptable salt, the polymorph, or the prodrug thereof according to claim 1, wherein the compound has structural features of Formula (II):



(II)

L_1 is selected from -NH- and -O-;

L_2 is selected from a single bond, $-(CR_aR_b)_n-$, and $-(CR_aR_b)_nO-$, wherein R_a and R_b are each independently selected from -H and a C_{1-6} alkyl;

n is independently selected from 0, 1, 2, and 3 at each occurrence~~;~~.

preferably~~5. The compound, or the stereoisomer, the *N*-oxide, the hydrate, the solvate, the metabolite, the pharmaceutically acceptable salt, the polymorph, or the prodrug thereof according to claim 4~~, ~~wherein~~in Formula (II):

R_1 is -H;

L_1 is -NH-;

L_2 is selected from a single bond, -CH_2-, -CH_2CH_2-, -$CH_2CH_2CH_2$-, -CH_2O-, and -CH_2CH_2O-; ~~.~~

preferably, in Formula (II):

~~6. The compound, or the stereoisomer, the *N*-oxide, the hydrate, the solvate, the metabolite, the pharmaceutically acceptable salt, the polymorph, or the prodrug thereof according to claim 4, wherein~~

R_2 and R_3 are each independently selected from a C_{1-6} alkyl and a C_{3-6} cycloalkyl; or

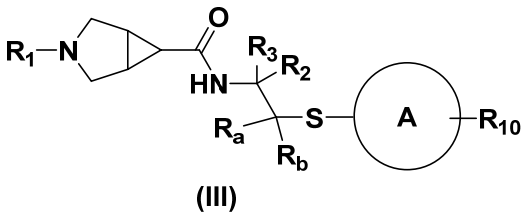
R_2 and R_3 together form a 3- to 6-membered saturated cyclic group comprising 0 to 1 group selected from -O-, -SO-, and -SO_2-; ~~.~~

preferably, in Formula (II):~~7. The compound, or the stereoisomer, the *N*-oxide, the hydrate, the solvate, the metabolite, the pharmaceutically acceptable salt, the polymorph, or the prodrug thereof according to claim 4, wherein~~

R_{11} is each independently selected from -H, a C_{1-6} alkyl, a C_{1-4} alkoxy C_{1-6} alkyl, a -$(CH_2)_n$-alkenyl, a -$(CH_2)_n$-alkynyl, a -$(CH_2)_n$-C_{3-10} carbocyclyl, a -$(CH_2)_n$-(3- to 10-membered heterocyclyl), a C_{6-10} aryl, and a 5- to 6-membered heteroaryl, the heterocyclyl or the heteroaryl contains 1 to 4 heteroatoms selected from N, O, and S, and the alkyl, the alkoxy, the aryl, the heteroaryl, the carbocyclyl, or the heterocyclyl is independently optionally further substituted with 0 to 4 substituents selected from -H, a halogen, hydroxy, cyano, a C_{1-4} alkyl, and a C_{1-4} alkoxy~~.~~; preferably,

~~8. The compound, or the stereoisomer, the *N*-oxide, the hydrate, the solvate, the metabolite, the pharmaceutically acceptable salt, the polymorph, or the prodrug thereof according to claim 7, wherein~~ R_{11} is each independently selected from methyl, ethyl, isopropyl, trifluoromethyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, phenyl, imidazolyl, pyrrolyl, furyl, thiophenyl, and pyridyl.

39. The compound, or the stereoisomer, the *N*-oxide, the hydrate, the solvate, the metabolite, the pharmaceutically acceptable salt, the polymorph, or the prodrug thereof according to claim 1, wherein the compound has structural features of Formula (III):



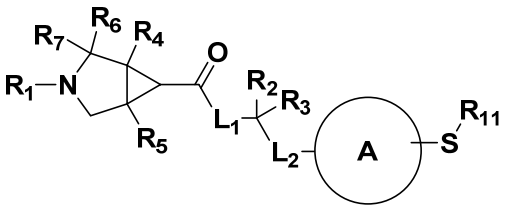
(III)

R_{10} is each independently selected from -H, -F, -Cl, -Br, -I, hydroxy, cyano, amino, a C_{1-4} alkyl, a C_{1-4} alkoxy, a C_{1-4} alkoxy C_{1-6} alkyl, a -$(CH_2)_n$-alkenyl, a -$(CH_2)_n$-alkynyl, a -O-$(CH_2)_n$-C_{3-10} carbocyclyl, a -O-$(CH_2)_n$-(3- to 10-membered heterocyclyl), a -O-$(CH_2)_n$-C_{3-10} carbocyclyl, a -O-$(CH_2)_n$-(3- to 10-membered heterocyclyl), and -SR_{11}, wherein R_{11} is each independently selected from -H, a C_{1-6} alkyl, a C_{1-4} alkoxy C_{1-6} alkyl, a -$(CH_2)_n$-alkenyl, a -$(CH_2)_n$-alkynyl, a -$(CH_2)_n$-C_{3-10} carbocyclyl, a -$(CH_2)_n$-(3- to 10-membered heterocyclyl), a C_{6-10} aryl, and a 5- to 6-membered heteroaryl, the heterocyclyl or the heteroaryl contains 1 to 4 heteroatoms selected from N, O, and S, and the alkyl, the alkoxy, the aryl, the heteroaryl, the carbocyclyl, or the heterocyclyl is each independently optionally further substituted with 0 to 4 substituents selected from -H, a halogen, hydroxy, cyano, a C_{1-4} alkyl, and a C_{1-4} alkoxy;

R_a and R_b are each independently selected from -H and a C_{1-6} alkyl;

preferably, in Formula (III):10. The compound, or the stereoisomer, the *N*-oxide, the hydrate, the solvate, the metabolite, the pharmaceutically acceptable salt, the polymorph, or the prodrug thereof according to claim 9, wherein R_{10} is each independently selected from -H, -F, -Cl, -Br, -I, hydroxy, cyano, amino, methyl, ethyl, isopropyl, trifluoromethyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclobutoxy, tetrahydrofuranyl, and -SR_{11}, wherein R_{11} is each independently selected from methyl, ethyl, isopropyl, trifluoromethyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, phenyl, imidazolyl, pyrrolyl, furyl, thienyl, and pyridyl; R_a and R_b are each independently selected from -H, methyl, ethyl, and isopropyl.

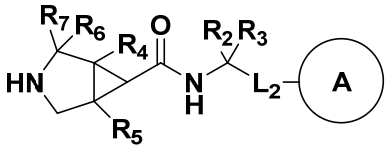
411. The compound, or the stereoisomer, the *N*-oxide, the hydrate, the solvate, the metabolite, the pharmaceutically acceptable salt, the polymorph, or the prodrug thereof according to claim 1, wherein the compound has structural features of Formula (IV):



(IV)

R_4 is selected from a C_{1-6} alkyl, a C_{1-6} alkoxy, a C_{1-6} alkoxy C_{1-6} alkyl, a $-(CH_2)_m-C_{3-10}$ carbocyclyl, a $-(CH_2)_m-$(3- to 10-membered heterocyclyl), a $-(CH_2)_m-O-C_{3-10}$ carbocyclyl, a $-(CH_2)_m-O-$(3- to 10-membered heterocyclyl), phenyl, and a 5- to 6-membered heteroaryl, the heterocyclyl or the heteroaryl contains 1 to 4 heteroatoms selected from N, O, and S, and the alkyl, the alkoxy, the carbocyclyl, the phenyl, the heteroaryl, or the heterocyclyl in R_4 is each independently optionally further substituted with 0 to 4 substituents selected from -H, -F, -Cl, -Br, -I, hydroxy, sulfydryl, cyano, amino, a C_{1-4} alkyl, and a C_{1-4} alkoxy.

512. The compound, or the stereoisomer, the *N*-oxide, the hydrate, the solvate, the metabolite, the pharmaceutically acceptable salt, the polymorph, or the prodrug thereof according to claim 1, wherein the compound has structural features of Formula (V):



(V)

R_2 and R_3 are each independently selected from a C_{1-6} alkyl and a C_{3-6} cycloalkyl, wherein R_2 and R_3 are not both -H; or R_2 and R_3 together form a 3- to 6-membered saturated cycloalkyl;

R_4, R_5, R_6, and R_7 are each independently selected from -H, a C_{1-6} alkyl, a C_{1-6} alkoxy, and a C_{1-6} alkoxy C_{1-6} alkyl, and the alkyl and the alkoxy in R_4, R_5, R_6, and R_7 are each independently optionally further substituted with 0 to 4 substituents selected from -H, -F, -Cl, -Br, -I, hydroxy, sulfydryl, cyano, amino, a C_{1-4} alkyl, and a C_{1-4} alkoxy;

A is selected from a C_{6-14} aryl, a 5- to 14-membered heteroaryl, a 5- to 14-membered heterocyclyl, and a 5- to 14-membered cycloalkyl, and the aryl, the heteroaryl, the heterocyclyl, and the cycloalkyl in A are optionally further substituted with 1 to 4 R_{10}, wherein the heteroaryl or the heterocyclyl contains 1 to 4 N atoms;

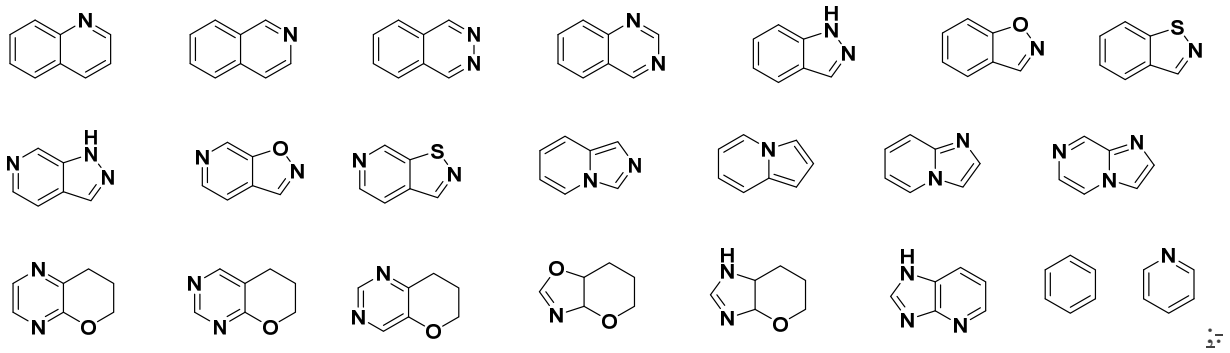
when L_2 is selected from a single bond, R_{10} is independently selected from -H, -F, -Cl, -Br, -I, hydroxy, cyano, amino, a C_{1-6} alkyl, a C_{1-4} alkoxy C_{1-6} alkyl, a C_{3-6} cycloalkyl, and $-SR_{11}$, and at least one R_{10} is $-SR_{11}$, wherein R_{11} is each independently selected from -H, a C_{1-6} alkyl, a C_{1-4} alkoxy C_{1-6} alkyl, a $-(CH_2)_n-C_{3-10}$ carbocyclyl, a $-(CH_2)_n-$(3- to 10-membered heterocyclyl), and a 5- to 6-membered heteroaryl, the heterocyclyl or the heteroaryl contains 1 to 4 heteroatoms selected from O, S, and N, and the alkyl, the alkoxy, the carbocyclyl, or the heterocyclyl is each independently optionally further substituted with 0 to 4 substituents selected from -H, a halogen, hydroxy, cyano, a C_{1-4} alkyl, and a C_{1-4} alkoxy;

when L_2 is selected from $-(CR_aR_b)_nS-$, R_{10} is each independently selected from -H, -F, -Cl, -Br, -I, hydroxy, cyano, amino, a C_{1-4} alkyl, a C_{1-4} alkoxy, and a C_{1-4} alkoxy C_{1-6} alkyl, the alkyl and the alkoxy are each independently optionally further substituted with 0 to 4 substituents selected from H, a halogen, hydroxy, cyano, a C_{1-4} alkyl, and a C_{1-4} alkoxy;

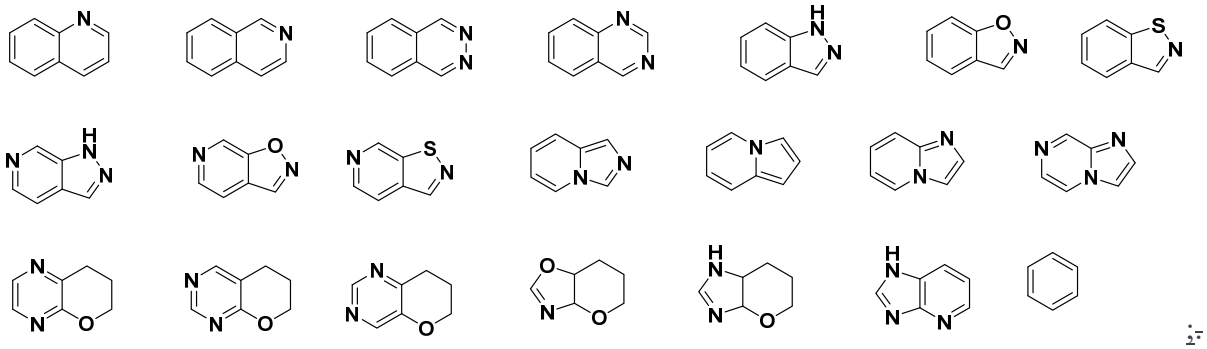
R_a and R_b are each independently selected from -H and a C_{1-6} alkyl;

n is independently selected from 0, 1, 2, and 3 at each occurrence;~~.~~

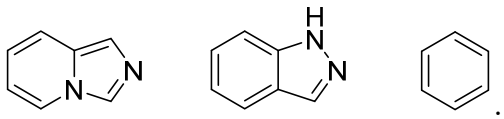
preferably~~13. The compound, or the stereoisomer, the *N*-oxide, the hydrate, the solvate, the metabolite, the pharmaceutically acceptable salt, the polymorph, or the prodrug thereof according to claim 1~~, wherein A is selected from the following structures:



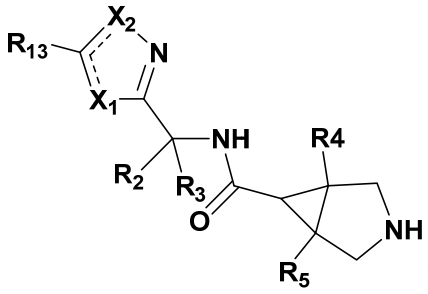
~~14. The compound, or the stereoisomer, the *N*-oxide, the hydrate, the solvate, the metabolite, the pharmaceutically acceptable salt, the polymorph, or the prodrug thereof according to claim 1~~preferably, wherein A is selected from one of the following structures:



preferably, ~~15. The compound, or the stereoisomer, the *N*-oxide, the hydrate, the solvate, the metabolite, the pharmaceutically acceptable salt, the polymorph, or the prodrug thereof according to claim 1,~~ wherein A is selected from the following structures:



~~16~~6. A compound of Formula (a) or a stereoisomer, an *N*-oxide, a hydrate, a solvate, a metabolite, a pharmaceutically acceptable salt, a polymorph, or a prodrug thereof,



Formula (a)

wherein

--- represents a single or double bond, provided that one and only one of two --- represents a double bond;

X_1 is CR_{13} or NR_{12};

X_2 is CR_{13} or NR_{12};

alternatively, X_1 and a substituent thereof together with an adjacent carbon atom and a substituent R_{13} thereof form a benzene ring or a 5- to 6-membered heteroaromatic ring, and the benzene ring or the 5- to 6-membered heteroaromatic ring is optionally substituted with 1 to 4 R_{13};

R_{13} is each independently selected from -H, a halogen, cyano, -$(CH_2)_n$-NR'R", a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, -$(CH_2)_n$-OR, a -$(CH_2)_n$-C_{2-6} alkenyl, a -$(CH_2)_n$-C_{2-6} alkynyl, a -$(CH_2)_n$-C_{3-10} carbocyclyl, a -$(CH_2)_n$-(3- to 10-membered heterocyclyl), a -$(CH_2)_n$-C_{6-10} aryl, a -$(CH_2)_n$-5- to 6-membered heteroaryl, and -SR_{11};

R_{12} is selected from H, a C_{1-6} alkyl, and a halogenated C_{1-6} alkyl;

R_{11} is selected from -H, a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, a -$(CH_2)_n$-C_{2-6} alkenyl, a -$(CH_2)_n$-C_{2-6} alkynyl, a -$(CH_2)_n$-C_{3-10} carbocyclyl, a -$(CH_2)_n$-(3- to 10-membered heterocyclyl), a -$(CH_2)_n$-C_{6-10} aryl, and a -$(CH_2)_n$-5- to 6-membered heteroaryl;

R' and R" are each selected from hydrogen, a C_{1-6} alkyl, and a halogenated C_{1-6} alkyl, or R' and R" together with a nitrogen atom attached thereto form a 3- to 10-membered heterocyclyl;

R is selected from hydrogen, a C_{1-6} alkyl, and a halogenated C_{1-6} alkyl;

R_2 and R_3 are each independently selected from H, a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, and -$(CH_2)_n$-OR;

R_4 and R_5 are each independently selected from H, a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, and -$(CH_2)_n$-OR;

n is 0, 1, 2, or 3,

provided that at least one R_{13} is an -SR_{11} substituent;~~.~~

preferably~~17. The compound of Formula (a) or the stereoisomer, the *N*-oxide, the hydrate, the solvate, the metabolite, the pharmaceutically acceptable salt, the polymorph, or the prodrug thereof according to claim 16~~, wherein

X_2 is CR_{13};

X_1 and the substituent thereof together with the adjacent carbon atom and the substituent R_{13} thereof form a benzene ring or a 5- to 6-membered heteroaromatic ring, and the benzene ring or the 5- to 6-membered heteroaromatic ring is substituted with 1 to 4 R_{13};

R_{13} is each independently selected from -H, halogen, cyano, -$(CH_2)_n$-NR'R", a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, -$(CH_2)_n$-OR, a -$(CH_2)_n$-C_{2-6} alkenyl, a -$(CH_2)_n$-C_{2-6} alkynyl, a -$(CH_2)_n$-C_{3-10} carbocyclyl, a -$(CH_2)_n$-(3- to 10-membered heterocyclyl), a -$(CH_2)_n$-C_{6-10} aryl, a -$(CH_2)_n$-5- to 6-membered heteroaryl, and -SR_{11};

R_{11} is selected from -H, a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, a -$(CH_2)_n$-C_{2-6} alkenyl, a -$(CH_2)_n$-C_{2-6} alkynyl, a -$(CH_2)_n$-C_{3-10} carbocyclyl, a -$(CH_2)_n$-(3- to 10-membered heterocyclyl), a -$(CH_2)_n$-C_{6-10} aryl, and a -$(CH_2)_n$-5- to 6-membered heteroaryl;

R' and R" are each selected from hydrogen, a C_{1-6} alkyl, and a halogenated C_{1-6} alkyl, or R' and R" together with a nitrogen atom attached thereto form a 3- to 10-membered heterocyclyl;

R is selected from hydrogen, a C_{1-6} alkyl, and a halogenated C_{1-6} alkyl;

R_2 and R_3 are each independently selected from H, a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, and -$(CH_2)_n$-OR;

R_4 and R_5 are each independently selected from H, a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, and -$(CH_2)_n$-OR;

n is 0, 1, 2, or 3,

provided that at least one R_{13} is an -SR_{11} substituent;~~.~~

preferably~~18. The compound of Formula (a) or the stereoisomer, the *N*-oxide, the hydrate, the solvate, the metabolite, the pharmaceutically acceptable salt, the polymorph, or the prodrug thereof according to claim 16~~, wherein:

X_2 is NR_{12};

X_1 and the substituent thereof together with the adjacent carbon atom and the substituent R_{13} thereof form a benzene ring or a 5- to 6-membered heteroaromatic ring, and the benzene ring or the 5- to 6-membered heteroaromatic ring is substituted with 1 to 4 R_{13};

R_{13} is each independently selected from -H, a halogen, cyano, -$(CH_2)_n$-NR'R", a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, -$(CH_2)_n$-OR, a -$(CH_2)_n$-C_{2-6} alkenyl, a -$(CH_2)_n$-C_{2-6} alkynyl, a -$(CH_2)_n$-C_{3-10} carbocyclyl, a -$(CH_2)_n$-(3- to 10-membered heterocyclyl), a -$(CH_2)_n$-C_{6-10} aryl, a -$(CH_2)_n$-5- to 6-membered heteroaryl, and -SR_{11};

R_{11} is selected from -H, a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, -$(CH_2)_n$-C_{2-6} alkenyl, a -$(CH_2)_n$-C_{2-6} alkynyl, a -$(CH_2)_n$-C_{3-10} carbocyclyl, a -$(CH_2)_n$-(3- to 10-membered heterocyclyl), a -$(CH_2)_n$-C_{6-10} aryl, and a -$(CH_2)_n$-5- to 6-membered heteroaryl;

R' and R" are each selected from hydrogen, a C_{1-6} alkyl, and a halogenated C_{1-6} alkyl, or R' and R" together with a nitrogen atom attached thereto form a 3- to 10-membered heterocyclyl;

R is selected from hydrogen, a C_{1-6} alkyl, and a halogenated C_{1-6} alkyl;

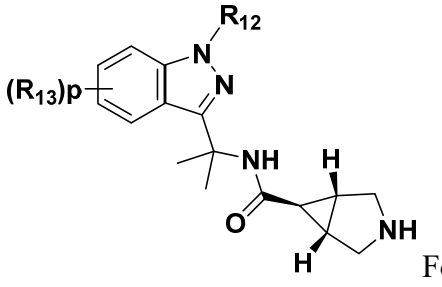
R_2 and R_3 are each independently selected from H, a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, and -$(CH_2)_n$-OR;

R_4 and R_5 are each independently selected from H, a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, and -$(CH_2)_n$-OR;

n is 0, 1, 2, or 3,

provided that at least one R_{13} is -SR_{11}.

~~19~~7. A compound of Formula (b) or a stereoisomer, an *N*-oxide, a hydrate, a solvate, a metabolite, a pharmaceutically acceptable salt, a polymorph, or a prodrug thereof,



Formula (b)

wherein

R_{13} is each independently selected from H, a halogen, cyano, -$(CH_2)_n$-NR'R", a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, -$(CH_2)_n$-OR, a -$(CH_2)_n$-C_{2-6} alkenyl, a -$(CH_2)_n$-C_{2-6} alkynyl, a -$(CH_2)_n$-C_{3-}

$_{10}$ carbocyclyl, a -$(CH_2)_n$-(3- to 10-membered heterocyclyl), a -$(CH_2)_n$-C_{6-10} aryl, a -$(CH_2)_n$-5- to 6-membered heteroaryl, and -SR_{11}, and at least one R_{13} is -SR_{11};

R_{12} is selected from H, a C_{1-6} alkyl, and a halogenated C_{1-6} alkyl;

R_{11} is selected from H, a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, -$(CH_2)_n$-C_{2-6} alkenyl, a -$(CH_2)_n$-C_{2-6} alkynyl, a -$(CH_2)_n$-C_{3-10} carbocyclyl, a -$(CH_2)_n$-(3- to 10-membered heterocyclyl), a -$(CH_2)_n$-C_{6-10} aryl, and a -$(CH_2)_n$-5- to 6-membered heteroaryl;

R is selected from hydrogen, a C_{1-6} alkyl, and a halogenated C_{1-6} alkyl;

R' and R" are each selected from hydrogen, a C_{1-6} alkyl, and a halogenated C_{1-6} alkyl, or R' and R" together with a nitrogen atom attached thereto form a 3- to 10-membered heterocyclyl;

n is 0, 1, 2, or 3;

p is 1, 2, 3, or 4;~~.~~

preferably~~20. The compound of Formula (b) or the stereoisomer, the *N*-oxide, the hydrate, the solvate, the metabolite, the pharmaceutically acceptable salt, the polymorph, or the prodrug thereof according to claim 19~~, wherein

p is 1, 2, or 3;

R_{13} is each independently selected from H, a halogen, a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, a -$(CH_2)_n$-C_{3-10} carbocyclyl, and -SR_{11}, and at least one R_{13} is -SR_{11};

R_{11} is selected from a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, and a -$(CH_2)_n$-C_{3-6} carbocyclyl;

R_{12} is selected from H, a C_{1-6} alkyl, or a halogenated C_{1-6} alkyl;

n is 0 or 1~~.~~;

preferably, ~~21. The compound of Formula (b) or the stereoisomer, the *N*-oxide, the hydrate, the solvate, the metabolite, the pharmaceutically acceptable salt, the polymorph, or the prodrug thereof according to claim 19,~~ wherein:

p is 1 or 2;

R_{13} is each independently selected from H, a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, and -SR_{11}, and at least one R_{13} is -SR_{11};

R_{11} is selected from a C_{1-4} alkyl and a -$(CH_2)_n$-C_{3-4} carbocyclyl;

R_{12} is selected from H, a C_{1-4} alkyl, and a halogenated C_{1-4} alkyl;

n is 0 or 1;~~.~~

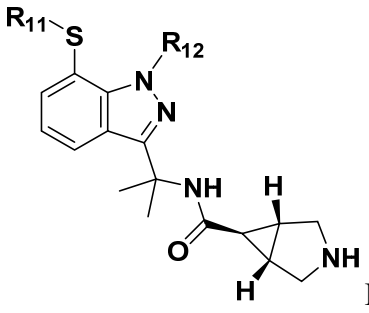
preferably~~22. The compound of Formula (b) or the stereoisomer, the *N*-oxide, the hydrate, the solvate, the metabolite, the pharmaceutically acceptable salt, the polymorph, or the prodrug thereof according to claim 19~~, wherein:

P is 1;

R_{13} is -SMe;

R_{12} is H or a C_{1-4} alkyl.

~~23~~8. A compound of Formula (b-1) or a stereoisomer, an *N*-oxide, a hydrate, a solvate, a metabolite, a pharmaceutically acceptable salt, a polymorph, or a prodrug thereof,



Formula (b-1)

wherein:

R_{11} is selected from H, a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, -$(CH_2)_n$-C_{2-6} alkenyl, a -$(CH_2)_n$-C_{2-6} alkynyl, a -$(CH_2)_n$-C_{3-10} carbocyclyl, a -$(CH_2)_n$-(3- to 10-membered heterocyclyl), a -$(CH_2)_n$-C_{6-10} aryl, and a -$(CH_2)_n$-5- to 6-membered heteroaryl;

R_{12} is selected from H, a C_{1-6} alkyl, and a halogenated C_{1-6} alkyl; and

n is 0, 1, 2, or 3~~.~~;

preferably, ~~24. The compound of Formula (b-1) or the stereoisomer, the *N*-oxide, the hydrate, the solvate, the metabolite, the pharmaceutically acceptable salt, the polymorph, or the prodrug thereof according to claim 23,~~ wherein:

R_{11} is selected from a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, and a $-(CH_2)_n-C_{3-6}$ carbocyclyl;

R_{12} is selected from H, a C_{1-6} alkyl, and a halogenated C_{1-6} alkyl; and

n is 0 or 1;~~.~~

preferably, ~~25. The compound of Formula (b-1) or the stereoisomer, the *N*-oxide, the hydrate, the solvate, the metabolite, the pharmaceutically acceptable salt, the polymorph, or the prodrug thereof according to claim 23,~~ wherein:

R_{11} is selected from a C_{1-4} alkyl and a $-(CH_2)_n-C_{3-4}$ carbocyclyl;

R_{12} is selected from H, a C_{1-4} alkyl, and a halogenated C_{1-4} alkyl;

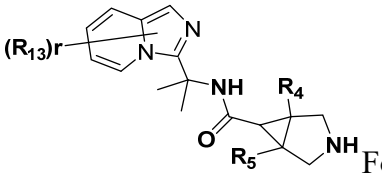
n is 0 or 1;~~.~~

preferably, ~~26. The compound of Formula (b-1) or the stereoisomer, the *N*-oxide, the hydrate, the solvate, the metabolite, the pharmaceutically acceptable salt, the polymorph, or the prodrug thereof according to claim 23,~~ wherein:

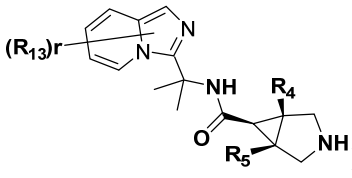
R_{11} is methyl;

R_{12} is H or a C_{1-4} alkyl.

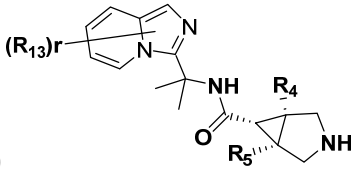
~~27~~9. A compound of Formula (c) or a stereoisomer thereof of Formula (c-1) or Formula (c-2), an *N*-oxide, a hydrate, a solvate, a metabolite, a pharmaceutically acceptable salt, a polymorph, or a prodrug thereof,



Formula (c)



Formula (c-1)



Formula (c-2)

wherein

R_{13} is each independently selected from H, a halogen, cyano, -$(CH_2)_n$-NR'R", a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, -$(CH_2)_n$-OR, a -$(CH_2)_n$-C_{2-6} alkenyl, a -$(CH_2)_n$-C_{2-6} alkynyl, a -$(CH_2)_n$-C_{3-10} carbocyclyl, a -$(CH_2)_n$-(3- to 10-membered heterocyclyl), a -$(CH_2)_n$-C_{6-10} aryl, a -$(CH_2)_n$-5- to 6-membered heteroaryl, and -SR_{11}, and at least one R_{13} is -SR_{11};

R_{11} is selected from H, a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, -$(CH_2)_n$-C_{2-6} alkenyl, a -$(CH_2)_n$-C_{2-6} alkynyl, a -$(CH_2)_n$-C_{3-10} carbocyclyl, a -$(CH_2)_n$-(3- to 10-membered heterocyclyl), a -$(CH_2)_n$-C_{6-10} aryl, and a -$(CH_2)_n$-5- to 6-membered heteroaryl;

R_4 and R_5 are each independently selected from H, a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, and -$(CH_2)_n$-OR;

R' and R" are each selected from hydrogen, a C_{1-6} alkyl, and a halogenated C_{1-6} alkyl, or R' and R" together with a nitrogen atom attached thereto form a 3- to 10-membered heterocyclyl;

R is selected from hydrogen, a C_{1-6} alkyl, and a halogenated C_{1-6} alkyl;

n is 0, 1, 2, or 3;

r is 1, 2, 3, 4, or 5;

preferably, ~~28. The compound of Formula (c) or the stereoisomer thereof of Formula (c-1) or Formula (c-2), the *N*-oxide, the hydrate, the solvate, the metabolite, the pharmaceutically acceptable salt, the polymorph, or the prodrug thereof according to claim 27,~~ wherein

r is 1, 2 or 3;

R_{13} is each independently selected from H, a halogen, a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, a -$(CH_2)_n$-C_{3-10} carbocyclyl, and -SR_{11}, and at least one R_{13} is -SR_{11};

R_{11} is selected from a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, and a -$(CH_2)_n$-C_{3-6} carbocyclyl;

R_4 and R_5 are each independently selected from H and a C_{1-6} alkyl;

n is 0 or 1;

preferably, 29. The compound of Formula (c) or the stereoisomer thereof of Formula (c-1) or Formula (c-2), the *N*-oxide, the hydrate, the solvate, the metabolite, the pharmaceutically acceptable salt, the polymorph, or the prodrug thereof according to claim 27, wherein

r is 1 or 2;

R_{13} is each independently selected from H, a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, and $-SR_{11}$, and at least one R_{13} is $-SR_{11}$;

R_{11} is selected from a C_{1-4} alkyl and a $-(CH_2)_n-C_{3-4}$ carbocyclyl;

R_4 and R_5 are each independently selected from H and a C_{1-6} alkyl;

n is 0 or 1;

preferably, 30. The compound of Formula (c) or the stereoisomer thereof of Formula (c-1) or Formula (c-2), the *N*-oxide, the hydrate, the solvate, the metabolite, the pharmaceutically acceptable salt, the polymorph, or the prodrug thereof according to claim 27, wherein

r is 2;

one of R_{13} is -SMe, and another one is selected from H and a C_{1-4} alkyl;

R_4 and R_5 are each independently selected from H and a C_{1-4} alkyl;

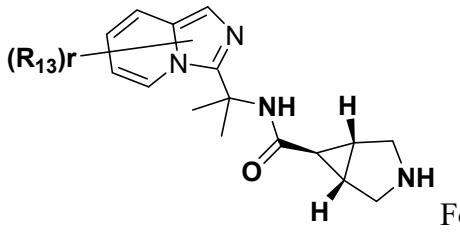
preferably, 31. The compound of Formula (c) or the stereoisomer thereof of Formula (c-1) or Formula (c-2), the *N*-oxide, the hydrate, the solvate, the metabolite, the pharmaceutically acceptable salt, the polymorph, or the prodrug thereof according to claim 27, wherein

r is 1;

R_{13} is -SMe;

R_4 and R_5 are each independently selected from H and a C_{1-4} alkyl.

~~32~~10. A compound of Formula (d) or a stereoisomer, an *N*-oxide, a hydrate, a solvate, a metabolite, a pharmaceutically acceptable salt, a polymorph, or a prodrug thereof,



Formula (d)

wherein

R_{13} is each independently selected from H, a halogen, cyano, -$(CH_2)_n$-NR'R", a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, -$(CH_2)_n$-OR, a -$(CH_2)_n$-C_{2-6} alkenyl, a -$(CH_2)_n$-C_{2-6} alkynyl, a -$(CH_2)_n$-C_{3-10} carbocyclyl, a -$(CH_2)_n$-(3- to 10-membered heterocyclyl), a -$(CH_2)_n$-C_{6-10} aryl, a -$(CH_2)_n$-5- to 6-membered heteroaryl, and -SR_{11}, and at least one R_{13} is -SR_{11};

R_{11} is selected from H, a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, -$(CH_2)_n$-C_{2-6} alkenyl, a -$(CH_2)_n$-C_{2-6} alkynyl, a -$(CH_2)_n$-C_{3-10} carbocyclyl, a -$(CH_2)_n$-(3- to 10-membered heterocyclyl), a -$(CH_2)_n$-C_{6-10} aryl, and a -$(CH_2)_n$-5- to 6-membered heteroaryl;

R' and R" are each selected from hydrogen, a C_{1-6} alkyl, and a halogenated C_{1-6} alkyl, or R' and R" together with a nitrogen atom attached thereto form a 3- to 10-membered heterocyclyl;

R is selected from hydrogen, a C_{1-6} alkyl, and a halogenated C_{1-6} alkyl;

n is 0, 1, 2, or 3;

r is 1, 2, 3, 4, or 5~~;~~.

preferably, ~~33. The compound of Formula (d) or the stereoisomer, the *N*-oxide, the hydrate, the solvate, the metabolite, the pharmaceutically acceptable salt, the polymorph, or the prodrug thereof according to claim 32,~~ wherein

r is 1, 2 or 3;

R_{13} is each independently selected from H, a halogen, a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, a -$(CH_2)_n$-C_{3-10} carbocyclyl, and -SR_{11}, and at least one R_{13} is -SR_{11};

R_{11} is selected from a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, and a -$(CH_2)_n$-C_{3-6} carbocyclyl;

n is 0 or 1;

preferably, ~~34. The compound of Formula (d) or the stereoisomer, the *N*-oxide, the hydrate, the solvate, the metabolite, the pharmaceutically acceptable salt, the polymorph, or the prodrug thereof according to claim 32,~~ wherein

r is 1 or 2;

R_{13} is each independently selected from H, a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, and $-SR_{11}$, and at least one R_{13} is $-SR_{11}$;

R_{11} is selected from a C_{1-4} alkyl and a $-(CH_2)_n-C_{3-4}$ carbocyclyl;

n is 0 or 1;

preferably, ~~35. The compound of Formula (d) or the stereoisomer, the *N*-oxide, the hydrate, the solvate, the metabolite, the pharmaceutically acceptable salt, the polymorph, or the prodrug thereof according to claim 32,~~ wherein

r is 2;

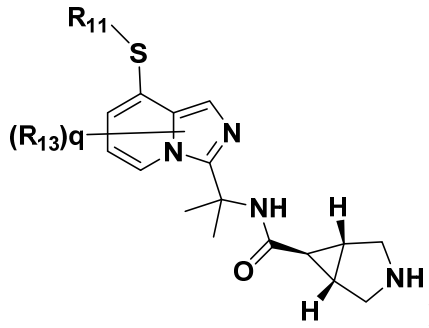
one of R_{13} is -SMe and another one is selected from H and a C_{1-4} alkyl;

preferably, ~~36. The compound of Formula (d) or the stereoisomer, the *N*-oxide, the hydrate, the solvate, the metabolite, the pharmaceutically acceptable salt, the polymorph, or the prodrug thereof according to claim 32,~~ wherein

r is 1;

R_{13} is -SMe.

~~37~~11. A compound of Formula (d-1) or a stereoisomer, an *N*-oxide, a hydrate, a solvate, a metabolite, a pharmaceutically acceptable salt, a polymorph, or a prodrug thereof,



Formula (d-1)

wherein

R_{11} is selected from H, a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, -$(CH_2)_n$-C_{2-6} alkenyl, a -$(CH_2)_n$-C_{2-6} alkynyl, a -$(CH_2)_n$-C_{3-10} carbocyclyl, a -$(CH_2)_n$-(3- to 10-membered heterocyclyl), a -$(CH_2)_n$-C_{6-10} aryl, and a -$(CH_2)_n$-5- to 6-membered heteroaryl;

R_{13} is each independently selected from H, a halogen, cyano, -$(CH_2)_n$-NR'R", a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, -$(CH_2)_n$-OR, a -$(CH_2)_n$-C_{2-6} alkenyl, a -$(CH_2)_n$-C_{2-6} alkynyl, a -$(CH_2)_n$-C_{3-10} carbocyclyl, a -$(CH_2)_n$-(3- to 10-membered heterocyclyl), a -$(CH_2)_n$-C_{6-10} aryl, a -$(CH_2)_n$-5- to 6-membered heteroaryl, and -SR_{11};

R' and R" are each selected from hydrogen, a C_{1-6} alkyl, and a halogenated C_{1-6} alkyl, or R' and R" together with a nitrogen atom attached thereto form a 3- to 10-membered heterocyclyl;

R is selected from hydrogen, a C_{1-6} alkyl, and a halogenated C_{1-6} alkyl;

n is 0, 1, 2, or 3;

q is 0, 1, 2, 3, or 4;~~.~~

preferably~~38. The compound of Formula (d-1) or the stereoisomer, the *N*-oxide, the hydrate, the solvate, the metabolite, the pharmaceutically acceptable salt, the polymorph, or the prodrug thereof according to claim 37~~, wherein

q is 0, 1 or 2;

R_{13} is each independently selected from H, a halogen, a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, a -$(CH_2)_n$-C_{3-10} carbocyclyl, and -SR_{11};

R_{11} is selected from a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, and a -$(CH_2)_n$-C_{3-6} carbocyclyl;

n is 0 or 1; ~~.~~

preferably, ~~39. The compound of Formula (d-1) or the stereoisomer, the *N*-oxide, the hydrate, the solvate, the metabolite, the pharmaceutically acceptable salt, the polymorph, or the prodrug thereof according to claim 37,~~ wherein

q is 0 or 1;

R_{11} is selected from a C_{1-4} alkyl and a $-(CH_2)_n-C_{3-4}$ carbocyclyl;

R_{13} is selected from H, a C_{1-4} alkyl, and a halogenated C_{1-4} alkyl;

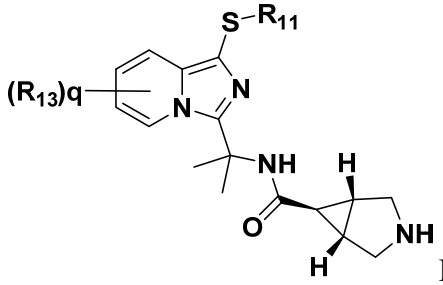
n is 0 or 1; ~~.~~

preferably, ~~40. The compound of Formula (d-1) or the stereoisomer, the *N*-oxide, the hydrate, the solvate, the metabolite, the pharmaceutically acceptable salt, the polymorph, or the prodrug thereof according to claim 37,~~ wherein

q is 0;

R_{11} is a C_{1-4} alkyl.

~~41~~12. A compound of Formula (d-2) or a stereoisomer, an *N*-oxide, a hydrate, a solvate, a metabolite, a pharmaceutically acceptable salt, a polymorph, or a prodrug thereof,



Formula (d-2)

wherein

R_{11} is selected from H, a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, $-(CH_2)_n-C_{2-6}$ alkenyl, a $-(CH_2)_n-C_{2-6}$ alkynyl, a $-(CH_2)_n-C_{3-10}$ carbocyclyl, a $-(CH_2)_n-$(3- to 10-membered heterocyclyl), a $-(CH_2)_n-C_{6-10}$ aryl, and a $-(CH_2)_n-$5- to 6-membered heteroaryl;

R_{13} is each independently selected from H, a halogen, cyano, -$(CH_2)_n$-NR'R", a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, -$(CH_2)_n$-OR, a -$(CH_2)_n$-C_{2-6} alkenyl, a -$(CH_2)_n$-C_{2-6} alkynyl, a -$(CH_2)_n$-C_{3-10} carbocyclyl, a -$(CH_2)_n$-(3- to 10-membered heterocyclyl), a -$(CH_2)_n$-C_{6-10} aryl, a -$(CH_2)_n$-5- to 6-membered heteroaryl, and -SR_{11};

R' and R" are each selected from hydrogen, a C_{1-6} alkyl, and a halogenated C_{1-6} alkyl, or R' and R" together with a nitrogen atom attached thereto form a 3- to 10-membered heterocyclyl;

R is selected from hydrogen, a C_{1-6} alkyl, and a halogenated C_{1-6} alkyl;

n is 0, 1, 2, or 3;

q is 0, 1, 2, 3, or 4;~~.~~

preferably, ~~42. The compound of Formula (d-2) or the stereoisomer, the *N*-oxide, the hydrate, the solvate, the metabolite, the pharmaceutically acceptable salt, the polymorph, or the prodrug thereof according to claim 41,~~ wherein

q is 0, 1, or 2;

R_{11} is selected from a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, and a -$(CH_2)_n$-C_{3-6} carbocyclyl;

R_{13} is each independently selected from H, a halogen, a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, a -$(CH_2)_n$-C_{3-10} carbocyclyl, and -SR_{11};

n is 0 or 1;~~.~~

preferably, ~~43. The compound of Formula (d-2) or the stereoisomer, the *N*-oxide, the hydrate, the solvate, the metabolite, the pharmaceutically acceptable salt, the polymorph, or the prodrug thereof according to claim 41,~~ wherein

q is 0 or 1;

R_{11} is selected from a C_{1-4} alkyl, a halogenated C_{1-4} alkyl, and a -$(CH_2)_n$-C_{3-4} carbocyclyl;

R_{13} is each independently selected from H, a C_{1-6} alkyl, and a halogenated C_{1-6} alkyl;

n is 0 or 1;~~.~~

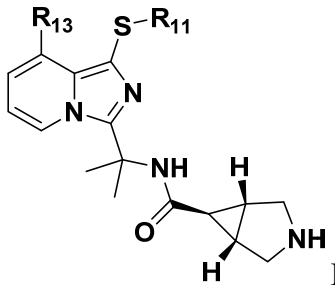
preferably, ~~44. The compound of Formula (d-2) or the stereoisomer, the *N*-oxide, the hydrate, the solvate, the metabolite, the pharmaceutically acceptable salt, the polymorph, or the prodrug thereof according to claim 41,~~ wherein

q is 1;

R_{11} is methyl;

R_{13} is H or a C_{1-4} alkyl.

~~45~~13. A compound of Formula (d-3) or a stereoisomer, an *N*-oxide, a hydrate, a solvate, a metabolite, a pharmaceutically acceptable salt, a polymorph, or a prodrug thereof,



Formula (d-3)

wherein

R_{11} is selected from H, a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, -$(CH_2)_n$-C_{2-6} alkenyl, a -$(CH_2)_n$-C_{2-6} alkynyl, a -$(CH_2)_n$-C_{3-10} carbocyclyl, a -$(CH_2)_n$-(3- to 10-membered heterocyclyl), a -$(CH_2)_n$-C_{6-10} aryl, and a -$(CH_2)_n$-5- to 6-membered heteroaryl;

R_{13} is each independently selected from H, a halogen, cyano, -$(CH_2)_n$-NR'R", a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, -$(CH_2)_n$-OR, a -$(CH_2)_n$-C_{2-6} alkenyl, a -$(CH_2)_n$-C_{2-6} alkynyl, a -$(CH_2)_n$-C_{3-10} carbocyclyl, a -$(CH_2)_n$-(3- to 10-membered heterocyclyl), a -$(CH_2)_n$-C_{6-10} aryl, a -$(CH_2)_n$-5- to 6-membered heteroaryl, and -SR_{11};

R' and R" are each selected from hydrogen, a C_{1-6} alkyl, and a halogenated C_{1-6} alkyl, or R' and R" together with a nitrogen atom attached thereto form a 3- to 10-membered heterocyclyl;

R is selected from hydrogen, a C_{1-6} alkyl, and a halogenated C_{1-6} alkyl;

n is 0, 1, 2, or 3~~;~~.

preferably, ~~46. The compound of Formula (d-3) or the stereoisomer, the *N*-oxide, the hydrate, the solvate, the metabolite, the pharmaceutically acceptable salt, the polymorph, or the prodrug thereof according to claim 45,~~ wherein

R_{11} is selected from a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, and a $-(CH_2)_n-C_{3-6}$ carbocyclyl;

R_{13} is each independently selected from H, a halogen, a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, a $-(CH_2)_n-C_{3-10}$ carbocyclyl, and $-SR_{11}$;

n is 0 or 1;~~,~~

preferably, ~~47. The compound of Formula (d-3) or the stereoisomer, the *N*-oxide, the hydrate, the solvate, the metabolite, the pharmaceutically acceptable salt, the polymorph, or the prodrug thereof according to claim 45,~~ wherein

R_{11} is selected from a C_{1-4} alkyl, a halogenated C_{1-4} alkyl, and a $-(CH_2)_n-C_{3-4}$ carbocyclyl;

R_{13} is each independently selected from H, a C_{1-4} alkyl, and a halogenated C_{1-4} alkyl;

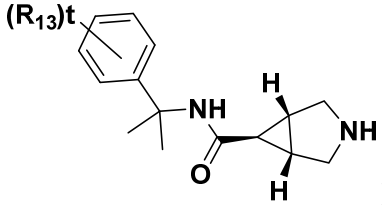
n is 0 or 1;~~,~~

preferably, ~~48. The compound of Formula (d-3) or the stereoisomer, the *N*-oxide, the hydrate, the solvate, the metabolite, the pharmaceutically acceptable salt, the polymorph, or the prodrug thereof according to claim 45,~~ wherein

R_{11} is methyl;

R_{13} is H or a C_{1-4} alkyl.

~~49~~14. A compound of Formula (e) or a stereoisomer, an *N*-oxide, a hydrate, a solvate, a metabolite, a pharmaceutically acceptable salt, a polymorph, or a prodrug thereof,



Formula (e)

wherein

R_{13} is each independently selected from H, a halogen, cyano, -$(CH_2)_n$-NR'R", a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, -$(CH_2)_n$-OR, a -$(CH_2)_n$-C_{3-10} cycloaryl, and -SR_{11}, and at least one R_{13} is -SR_{11};

R_{11} is selected from H, a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, -$(CH_2)_n$-OR, -$(CH_2)_n$-C_{2-6} alkenyl, a -$(CH_2)_n$-C_{2-6} alkynyl, a -$(CH_2)_n$-C_{3-10} carbocyclyl, a -$(CH_2)_n$-(3- to 10-membered heterocyclyl), a -$(CH_2)_n$-C_{6-10} aryl, and a -$(CH_2)_n$-5- to 6-membered heteroaryl;

R' and R" are each selected from hydrogen, a C_{1-6} alkyl, and a halogenated C_{1-6} alkyl, or R' and R" together with a nitrogen atom attached thereto form a 3- to 10-membered heterocyclyl;

R is selected from hydrogen, a C_{1-6} alkyl, and a halogenated C_{1-6} alkyl;

n is 0, 1, 2, or 3;

t is 1, 2, 3, 4, or 5;

preferably, ~~50. The compound of Formula (e) or the stereoisomer, the *N*-oxide, the hydrate, the solvate, the metabolite, the pharmaceutically acceptable salt, the polymorph, or the prodrug thereof according to claim 49,~~ wherein

t is 1, 2, or 3;

R_{13} is each independently selected from H, a halogen, a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, a -$(CH_2)_n$-C_{3-10} carbocyclyl, and -SR_{11}, and at least one R_{13} is -SR_{11};

R_{11} is selected from a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, and a -$(CH_2)_n$-C_{3-6} carbocyclyl;

n is 0 or 1;

preferably, ~~51. The compound of Formula (e) or the stereoisomer, the *N*-oxide, the hydrate, the solvate, the metabolite, the pharmaceutically acceptable salt, the polymorph, or the prodrug thereof according to claim 49,~~ wherein

t is 1 or 2;

R_{13} is each independently selected from H, a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, and -SR_{11}, and at least one R_{13} is -SR_{11};

R_{11} is selected from a C_{1-4} alkyl and a -$(CH_2)_n$-C_{3-4} carbocyclyl;

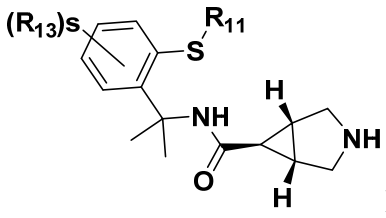
n is 0 or 1;~~.~~

preferably, ~~52. The compound of Formula (e) or the stereoisomer, the *N*-oxide, the hydrate, the solvate, the metabolite, the pharmaceutically acceptable salt, the polymorph, or the prodrug thereof according to claim 49,~~ wherein

t is 1;

R_{11} is a C_{1-4} alkyl.

~~53~~15. A compound of Formula (e-1) or a stereoisomer, an *N*-oxide, a hydrate, a solvate, a metabolite, a pharmaceutically acceptable salt, a polymorph, or a prodrug thereof,



Formula (e-1)

wherein

R_{13} is each independently selected from H, a halogen, cyano, -$(CH_2)_n$-NR'R", a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, -$(CH_2)_n$-OR, a -$(CH_2)_n$-C_{3-10} cycloaryl, and -SR_{11};

R_{11} is selected from H, a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, -$(CH_2)_n$-OR, -$(CH_2)_n$-C_{2-6} alkenyl, a -$(CH_2)_n$-C_{2-6} alkynyl, a -$(CH_2)_n$-C_{3-10} carbocyclyl, a -$(CH_2)_n$-(3- to 10-membered heterocyclyl), a -$(CH_2)_n$-C_{6-10} aryl, and a -$(CH_2)_n$-5- to 6-membered heteroaryl;

R' and R" are each selected from hydrogen, a C_{1-6} alkyl, and a halogenated C_{1-6} alkyl, or R' and R" together with a nitrogen atom attached thereto form a 3- to 10-membered heterocyclyl;

R is selected from hydrogen, a C_{1-6} alkyl, and a halogenated C_{1-6} alkyl;

n is 0, 1, 2, or 3;

s is 0, 1, 2, 3, or 4;

preferably, ~~54. The compound of Formula (e-1) or the stereoisomer, the *N*-oxide, the hydrate, the solvate, the metabolite, the pharmaceutically acceptable salt, the polymorph, or the prodrug thereof according to claim 53,~~ wherein

s is 0, 1, or 2;

R_{13} is each independently selected from H, a halogen, a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, a $-(CH_2)_n-C_{3-10}$ carbocyclyl, and $-SR_{11}$;

R_{11} is selected from a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, and a $-(CH_2)_n-C_{3-6}$ carbocyclyl;

n is 0 or 1;

preferably, ~~55. The compound of Formula (e-1) or the stereoisomer, the *N*-oxide, the hydrate, the solvate, the metabolite, the pharmaceutically acceptable salt, the polymorph, or the prodrug thereof according to claim 53,~~ wherein

s is 0 or 1;

R_{13} is each independently selected from H, a C_{1-6} alkyl, a halogenated C_{1-6} alkyl, a $-(CH_2)_n-C_{3-10}$ carbocyclyl, and $-SR_{11}$;

R_{11} is selected from a C_{1-4} alkyl and a $-(CH_2)_n-C_{3-4}$ carbocyclyl;

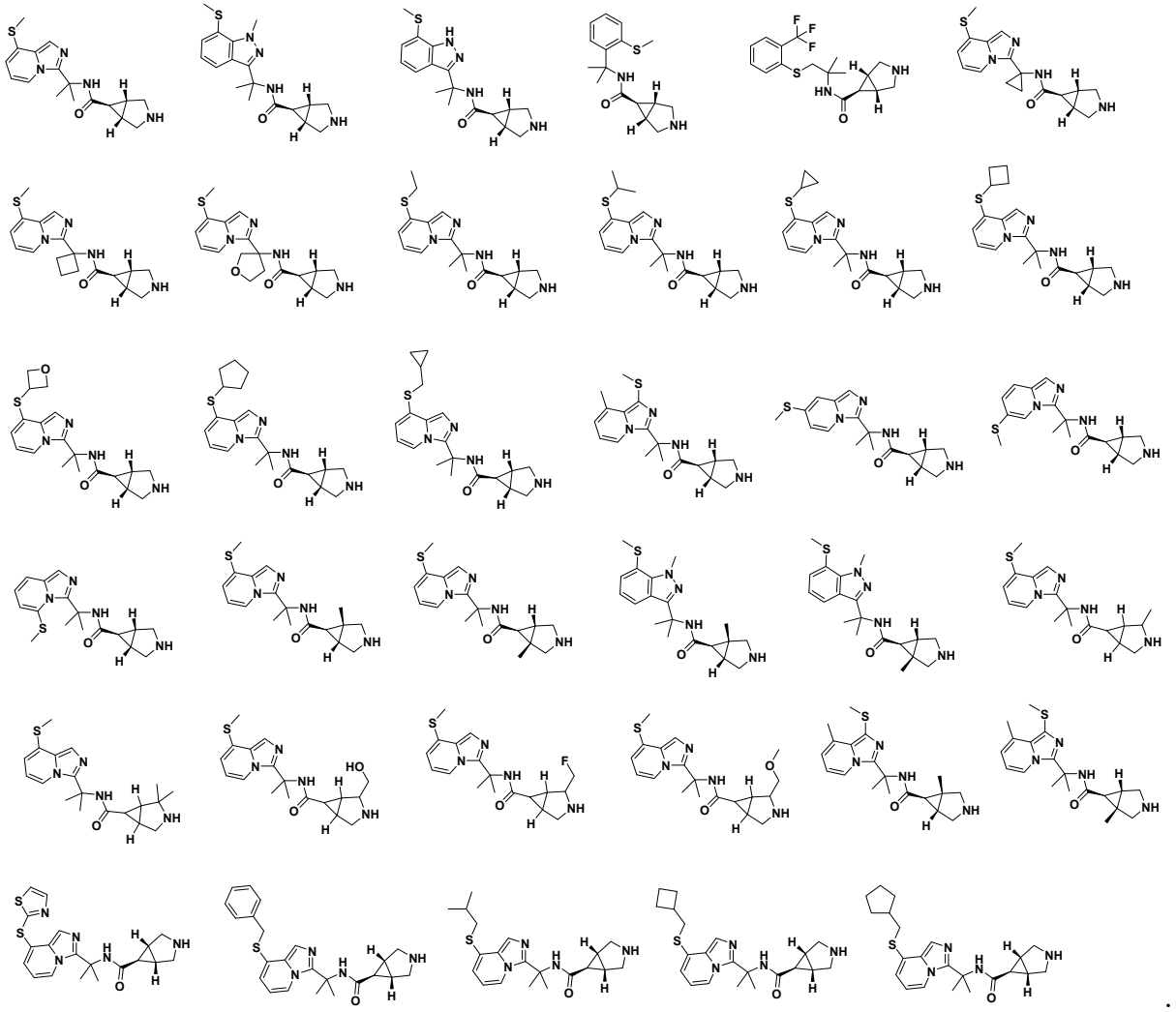
n is 0 or 1;

preferably, ~~56. The compound of Formula (e-1) or the stereoisomer, the *N*-oxide, the hydrate, the solvate, the metabolite, the pharmaceutically acceptable salt, the polymorph, or the prodrug thereof according to claim 53,~~ wherein

s is 0;

R_{11} is a C_{1-4} alkyl.

~~57~~16. The compound, or the stereoisomer, the *N*-oxide, the hydrate, the solvate, the metabolite, the pharmaceutically acceptable salt, the polymorph, or the prodrug thereof according to claim 1, selected from the following structures:



.

17~~58~~. The compound, or the stereoisomer, the *N*-oxide, the hydrate, the solvate, the metabolite, the pharmaceutically acceptable salt, the polymorph, or the prodrug thereof according to any one of claims 1 to ~~57~~16, wherein the pharmaceutically acceptable salt is selected from a hydrochloride, a hydrobromide, a sulfate, a nitrate, a phosphate, an acetate, a maleate, a succinate, a mandelate, a fumarate, a malonate, a malate, a 2-hydroxypropionate, an oxalate, a glycolate, a salicylate, a glucuronate, a galacturonate, a citrate, a tartrate, an aspartate, a glutamate, a benzoate, a cinnamate,

a *p*-toluenesulfonate, a benzenesulfonate, a mesylate, an ethanesulfonate, and a trifluoromethanesulfonate, or combinations thereof.

~~59~~18. A pharmaceutical composition, characterized by containing a therapeutically effective dose of the compound or the stereoisomer, the *N*-oxide, the hydrate, the solvate, the metabolite, the pharmaceutically acceptable salt, the polymorph, or the prodrug thereof according to any one of claims 1 to ~~58~~17, and a pharmaceutically acceptable carrier or excipient.

~~60~~19. ~~An application~~Use of the compound or the stereoisomer, the *N*-oxide, the hydrate, the solvate, the metabolite, the pharmaceutically acceptable salt, the polymorph, or the prodrug thereof according to any one of claims 1 to ~~58~~ 17 or the pharmaceutical composition according to claim ~~59~~ 18 in the preparation of a drug for treatment and/or prevention of a disease or a symptom affected by SSTR4 activation; preferably, for treatment and/or prevention of pain; preferably, the pain is neuralgia; preferably, the pain is back pain, chronic back pain, trigeminal neuralgia, type I complex regional pain syndrome, type II complex regional pain syndrome, irritable bowel syndrome symptoms, diabetic neuropathy, osteoarthritis-caused pain, tumor pain, or fibromyalgia.~~.~~

~~61. An application of the compound or the stereoisomer, the *N*-oxide, the hydrate, the solvate, the metabolite, the pharmaceutically acceptable salt, the polymorph, or the prodrug thereof according to any one of claims 1 to 58 or the pharmaceutical composition according to claim 59 in the preparation of a drug for treatment and/or prevention of pain.~~

~~62. The application according to claim 61, wherein the pain is neuralgia.~~

~~63. The application according to claim 61, wherein the pain is back pain, chronic back pain, trigeminal neuralgia, type I complex regional pain syndrome, type II complex regional pain syndrome, irritable bowel syndrome symptoms, diabetic neuropathy, osteoarthritis-caused pain, tumor pain, or fibromyalgia.~~

64. The compound or the stereoisomer, the *N*-oxide, the hydrate, the solvate, the metabolite, the pharmaceutically acceptable salt, the polymorph, or the prodrug thereof according to any one of claims 1 to 58 or the pharmaceutical composition according to claim 59, used to treat and/or prevent a disease or a symptom affected by SSTR4 activation.

65. The compound or the stereoisomer, the *N*-oxide, the hydrate, the solvate, the metabolite, the pharmaceutically acceptable salt, the polymorph, or the prodrug thereof according to any one of claims 1 to 58 or the pharmaceutical composition according to claim 59, used to treat and/or prevent pain.

66. The compound or the stereoisomer, the *N*-oxide, the hydrate, the solvate, the metabolite, the pharmaceutically acceptable salt, the polymorph, or the prodrug thereof according to claim 65 or the pharmaceutical composition according to claim 65, wherein the pain is neuralgia.

67. The compound or the stereoisomer, the *N*-oxide, the hydrate, the solvate, the metabolite, the pharmaceutically acceptable salt, the polymorph, or the prodrug thereof according to claim 65 or the pharmaceutical composition according to claim 65, wherein the pain is back pain, chronic back pain, trigeminal neuralgia, type I complex regional pain syndrome, type II complex regional pain syndrome, irritable bowel syndrome, diabetic neuropathy, osteoarthritis-caused pain, tumor pain, or muscle fiber pain.

68. A method for treating a disease or a symptom affected by SSTR4 activation, comprising administering the compound or the stereoisomer, the *N*-oxide, the hydrate, the solvate, the metabolite, the pharmaceutically acceptable salt, the polymorph, or the prodrug thereof according to any one of claims 1 to 58 or the pharmaceutical composition according to claim 59.

69. A method for treating pain, comprising administering the compound or the stereoisomer, the *N*-oxide, the hydrate, the solvate, the metabolite, the pharmaceutically acceptable salt, the polymorph, or the prodrug thereof according to any one of claims 1 to 58 or the pharmaceutical composition according to claim 59.

~~70. The method according to claim 69, wherein the pain is neuralgia.~~

~~71. The method according to claim 69, wherein the pain is back pain, chronic back pain, trigeminal neuralgia, type I complex regional pain syndrome, type II complex regional pain syndrome, irritable bowel syndrome, diabetic neuropathy, osteoarthritis-caused pain, tumor pain, or muscle fiber pain.~~