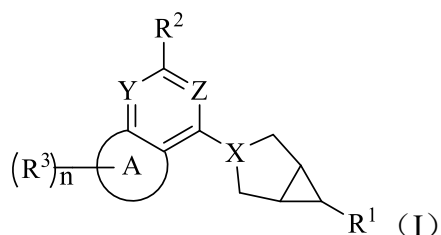


WHAT IS CLAIMED IS:

1. A compound represented by general formula (I), a pharmaceutically acceptable salt, an ester or a stereoisomer thereof:



wherein,

X, Y, and Z are each independently selected from $-CR^4-$ and $-N-$,

ring A is selected from 3-14 membered cycloalkyl, 3-14 membered heterocyclic group, 6-12 membered aryl and 5-12 membered heteroaryl;

R^1 is selected from hydrogen, halogen, nitro group, cyano group, $-(L)_m-C(O)OR^a$, $-(L)_m-CONR^aR^b$, $-(L)_m-CONHSO_2R^a$, $-(L)_m-SO_2R^a$, $-(L)_m-SO_2NHCOR^a$, $-(L)_m-OR^a$, $-(L)_m-SR^a$, $-(L)_m-NR^aR^b$, $-(L)_m-C(O)R^a$, $-(L)_m-OC(O)R^a$, $-(L)_m-OC(O)OR^a$, $-(L)_m-OC(O)NR^aR^b$, $-(L)_m-NR^aC(O)R^b$, $-(L)_m-NR^aC(O)OR^b$, $-(L)_m-OS(O)R^a$, $-(L)_m-OS(O)OR^a$, $-(L)_m-OS(O)NR^aR^b$, $-(L)_m-S(O)NR^aR^b$, $-(L)_m-NR^aS(O)R^b$, $-(L)_m-OS(O)_2R^a$, $-(L)_m-S(O)_2NR^aR^b$, $-(L)_m-NR^aS(O)_2R^b$; and the following groups optionally substituted with one or more Q1 groups: $-(L)_m-C_{1-6}$ alkyl, $-(L)_m-C_{1-6}$ alkoxy, $-(L)_m-C_{3-12}$ cycloalkyl, $-(L)_m-C_{3-12}$ heterocyclyl, $-(L)_m-C_{6-12}$ aryl and $-(L)_m-C_{5-12}$ heteroaryl;

L is selected from C_{1-6} alkylene and halo C_{1-6} alkylene;

R^2 is selected from the following groups optionally substituted by one or more Q2 groups: 3-12 membered heterocyclic group, 3-12 membered cycloalkyl group, 5-12 membered heteroaryl, 6-12 membered aryl, 5-12 membered spirocyclic group, 5-12 membered spiro heterocyclic group, 5-12 membered bridged group, 5-12 membered bridged heterocyclic group, $N(C_{1-6} \text{ alkyl})_2$, $N(C_{1-6} \text{ alkyl})(C_{3-8} \text{ cycloalkyl})$, $NH(C_{1-6} \text{ alkyl})$ and $NH(C_{3-8} \text{ cycloalkyl})$;

each R^3 is independently selected from hydrogen, halogen, nitro group, cyano group, amino group, hydroxyl, carboxy; and the following groups optionally substituted with one or more Q3 groups: C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkylamino, $di(C_{1-6} \text{ alkyl})$ amino, halo C_{1-6} alkyl, hydroxy C_{1-6} alkyl, amino C_{1-6} alkyl, halo C_{1-6} alkoxy, 3-12 membered cycloalkyl group, 3-12 membered heterocyclic group, 6-12 membered aryl and 5-12 membered heteroaryl;

each R^4 is independently selected from hydrogen, cyano group, and the following groups optionally substituted with one or more Q4 groups: C_{1-6} alkyl, $-C(O)R^a$, $-C(O)OR^a$, $-C(O)NR^aR^b$,

$-S(O)R^a$, $-S(O)OR^a$, $-S(O)NR^aR^b$, $-S(O)_2R^a$, $-S(O)_2OR^a$, $-S(O)_2NR^aR^b$, 3-12 membered cycloalkyl, 3-12 membered heterocyclic group, 6-12 membered aryl and 5-12 membered heteroaryl;

each of R^a and R^b is independently selected from hydrogen, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkylamino, di(C_{1-6} alkyl)amino, halo C_{1-6} alkyl, hydroxy C_{1-6} alkyl, amino C_{1-6} alkyl and halo C_{1-6} alkoxy;

each of Q1, Q2, Q3 and Q4 groups is independently selected from hydroxyl, amino group, halogen, nitro group, cyano group, carboxy, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkylamino, di(C_{1-6} alkyl)amino, halo C_{1-6} alkyl, hydroxy C_{1-6} alkyl, amino C_{1-6} alkyl, halo C_{1-6} alkoxy, 3-10 membered cycloalkyl group, 3-10 membered heterocyclic group, 6-10 membered aryl and 5-10 membered heteroaryl; and

m and n are each independently an integer from 0 to 8.

2. The compound, the pharmaceutically acceptable salt, the ester or the stereoisomer thereof according to claim 1,

wherein,

X, Y, and Z are each independently selected from $-CR^4-$ and $-N-$;

ring A is selected from 3-12 membered cycloalkyl, 3-12 membered heterocyclic group, 6-10 membered aryl and 5-10 membered heteroaryl;

R^1 is selected from hydrogen, halogen, nitro group, cyano group, $-(L)_m-C(O)OR^a$, $-(L)_m-CONR^aR^b$, $-(L)_m-CONHSO_2R^a$, $-(L)_m-SO_2R^a$, $-(L)_m-SO_2NHCOR^a$, $-(L)_m-OR^a$, $-(L)_m-SR^a$, $-(L)_m-NR^aR^b$, $-(L)_m-C(O)R^a$, $-(L)_m-OC(O)R^a$, $-(L)_m-OC(O)OR^a$, $-(L)_m-OC(O)NR^aR^b$, $-(L)_m-NR^aC(O)R^b$, $-(L)_m-NR^aC(O)OR^b$, $-(L)_m-OS(O)R^a$, $-(L)_m-OS(O)OR^a$, $-(L)_m-OS(O)NR^aR^b$, $-(L)_m-S(O)NR^aR^b$, $-(L)_m-NR^aS(O)R^b$, $-(L)_m-OS(O)_2R^a$, $-(L)_m-S(O)_2NR^aR^b$, $-(L)_m-NR^aS(O)_2R^b$; and the following groups optionally substituted with one or more Q1 groups: $-(L)_m-C_{1-6}$ alkyl, $-(L)_m-C_{1-6}$ alkoxy, $-(L)_m-C_{3-10}$ cycloalkyl, $-(L)_m-C_{3-10}$ heterocyclyl, $-(L)_m-C_{6-10}$ aryl and $-(L)_m-C_{5-10}$ heteroaryl;

L is selected from C_{1-6} alkylene and halo C_{1-6} alkylene;

R^2 is selected from the following groups optionally substituted by one or more Q2 groups: 3-8 membered heterocyclic group, 3-8 membered cycloalkyl group, 5-10 membered heteroaryl, 6-10 membered aryl, 5-10 membered spirocyclic group, 5-10 membered spiro heterocyclic group, 5-10 membered bridged group, 5-10 membered bridged heterocyclic group, $N(C_{1-6} \text{ alkyl})_2$, $N(C_{1-6} \text{ alkyl})(C_{3-8} \text{ cycloalkyl})$, $NH(C_{1-6} \text{ alkyl})$ and $NH(C_{3-8} \text{ cycloalkyl})$;

each R^3 is independently selected from hydrogen, halogen, nitro group, cyano group, amino group, hydroxyl, carboxy; and the following groups optionally substituted with one or more Q3 groups: C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkylamino, di(C_{1-6} alkyl)amino, halo C_{1-6} alkyl, hydroxy C_{1-6} alkyl, amino C_{1-6} alkyl, halo C_{1-6} alkoxy, 3-10 membered cycloalkyl group, 3-10 membered heterocyclic group, 6-10 membered aryl and 5-10 membered heteroaryl;

each R^4 is independently selected from hydrogen, cyano group, and the following groups optionally substituted with one or more Q4 groups: C_{1-6} alkyl, $-C(O)R^a$, $-C(O)OR^a$, $-C(O)NR^aR^b$, $-S(O)R^a$, $-S(O)OR^a$, $-S(O)NR^aR^b$, $-S(O)_2R^a$, $-S(O)_2OR^a$, and $-S(O)_2NR^aR^b$;

each of R^a and R^b is independently selected from hydrogen, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkylamino, di(C_{1-6} alkyl)amino, halo C_{1-6} alkyl, hydroxy C_{1-6} alkyl, amino C_{1-6} alkyl and halo C_{1-6} alkoxy;

each of Q1, Q2, Q3 and Q4 groups is independently selected from hydroxyl, amino group, halogen, nitro group, cyano group, carboxy, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkylamino, di(C_{1-6} alkyl)amino, halo C_{1-6} alkyl, hydroxy C_{1-6} alkyl, amino C_{1-6} alkyl, and halo C_{1-6} alkoxy; and

m and n are each independently an integer from 0 to 6.

3. The compound, the pharmaceutically acceptable salt, the ester or the stereoisomer thereof according to claim 2,

wherein,

X, Y, and Z are each independently selected from $-CR^4-$ and $-N-$;

ring A is selected from 3-10 membered cycloalkyl, 3-10 membered heterocyclic group, 6-10 membered aryl and 5-10 membered heteroaryl;

R^1 is selected from hydrogen, halogen, nitro group, cyano group, $-(L)_m-C(O)OR^a$, $-(L)_m-CONR^aR^b$, $-(L)_m-CONHSO_2R^a$, $-(L)_m-SO_2R^a$, $-(L)_m-SO_2NHCOR^a$, $-(L)_m-OR^a$, $-(L)_m-NR^aR^b$, $-(L)_m-C(O)R^a$, $-(L)_m-OC(O)R^a$, $-(L)_m-NR^aC(O)R^b$, $-(L)_m-NR^aC(O)OR^b$, $-(L)_m-OS(O)_2R^a$, $-(L)_m-S(O)_2NR^aR^b$, $-(L)_m-NR^aS(O)_2R^b$, and the following groups optionally substituted with one or more Q1 groups: $-(L)_m-C_{1-4}$ alkyl and $-(L)_m-C_{1-4}$ alkoxy;

L is selected from C_{1-4} alkylene and halo C_{1-4} alkylene;

R^2 is selected from the following groups optionally substituted by one or more Q2 groups: 3-8 membered heterocyclic group, 3-8 membered cycloalkyl group, 5-10 membered heteroaryl, 6-10 membered aryl, 5-10 membered spirocyclic group, 5-10 membered spiro heterocyclic group, $N(C_{1-4}$

alkyl)₂, N(C₁₋₄ alkyl)(C₃₋₆ cycloalkyl), NH(C₁₋₄ alkyl) and NH(C₃₋₆ cycloalkyl);

each R³ is independently selected from hydrogen, halogen, nitro group, cyano group, amino group, hydroxyl, carboxy, and the following groups optionally substituted with one or more Q3 groups: C₁₋₄ alkyl, C₁₋₄ alkoxy, C₁₋₄ alkylamino, di(C₁₋₄ alkyl)amino, halo C₁₋₄ alkyl, hydroxy C₁₋₄ alkyl, amino C₁₋₄ alkyl, and halo C₁₋₄ alkoxy;

each R⁴ is independently selected from hydrogen, cyano group, and the following groups optionally substituted with one or more Q4 groups: C₁₋₄ alkyl, -C(O)R^a, -C(O)OR^a, -C(O)NR^aR^b, -S(O)₂R^a, -S(O)₂OR^a, and -S(O)₂NR^aR^b;

each of R^a and R^b is independently selected from hydrogen, C₁₋₄ alkyl, C₁₋₄ alkoxy, C₁₋₄ alkylamino, di(C₁₋₄ alkyl)amino, halo C₁₋₄ alkyl, hydroxy C₁₋₄ alkyl, amino C₁₋₄ alkyl and halo C₁₋₄ alkoxy;

each of Q1, Q2, Q3, and Q4 groups is independently selected from hydroxyl, amino group, halogen, nitro group, cyano group, carboxy, C₁₋₄ alkyl, C₁₋₄ alkoxy, C₁₋₄ alkylamino, di(C₁₋₄ alkyl)amino, halo C₁₋₄ alkyl, hydroxy C₁₋₄ alkyl, amino C₁₋₄ alkyl, and halo C₁₋₄ alkoxy; and

m and n are each independently an integer from 0 to 6.

4. The compound, the pharmaceutically acceptable salt, the ester or the stereoisomer thereof according to claim 3,

wherein,

X, Y, and Z are each independently selected from -CR⁴- and -N-;

ring A is selected from 3-10 membered cycloalkyl and 3-10 membered heterocyclic group;

R¹ is selected from -(L)_m-C(O)OR^a, -(L)_m-CONR^aR^b, -(L)_m-CONHSO₂R^a, -(L)_m-SO₂R^a, -(L)_m-SO₂NHCOR^a, -(L)_m-OR^a, -(L)_m-NR^aR^b, -(L)_m-C(O)R^a, -(L)_m-OC(O)R^a, -(L)_m-NR^aC(O)R^b, -(L)_m-NR^aC(O)OR^b, -(L)_m-OS(O)₂R^a, -(L)_m-S(O)₂NR^aR^b, -(L)_m-NR^aS(O)₂R^b, and the following groups optionally substituted with 1-4 Q1 groups: -(L)_m-C₁₋₄ alkyl and -(L)_m-C₁₋₄ alkoxy;

L is selected from C₁₋₃ alkylene and halo C₁₋₃ alkylene;

R² is selected from the following groups optionally substituted by 1-4 Q2 groups: 3-6 membered heterocyclic group, 3-6 membered cycloalkyl group, 5-10 membered heteroaryl, 6-10 membered aryl, 5-8 membered spirocyclic group, 5-8 membered spiro heterocyclic group, and N(C₁₋₄ alkyl)(C₃₋₆ cycloalkyl);

each R³ is independently selected from hydrogen, halogen, nitro group, cyano group, amino

group, hydroxyl, carboxy, and the following groups optionally substituted with 1-4 Q3 groups: C₁₋₄ alkyl, C₁₋₄ alkoxy, C₁₋₄ alkylamino, di(C₁₋₄ alkyl)amino, halo C₁₋₄ alkyl, hydroxy C₁₋₄ alkyl, amino C₁₋₄ alkyl, and halo C₁₋₄ alkoxy;

each R⁴ is independently selected from hydrogen, and the following groups optionally substituted with 1-4 Q4 groups: C₁₋₄ alkyl, -C(O)R^a, -C(O)OR^a, -C(O)NR^aR^b, -S(O)₂R^a, and -S(O)₂NR^aR^b;

each of R^a and R^b is independently selected from hydrogen, C₁₋₄ alkyl, C₁₋₄ alkoxy, C₁₋₄ alkylamino, di(C₁₋₄ alkyl)amino, halo C₁₋₄ alkyl, hydroxy C₁₋₄ alkyl, amino C₁₋₄ alkyl and halo C₁₋₄ alkoxy;

each of Q1, Q2, Q3, and Q4 groups is independently selected from hydroxyl, amino group, halogen, nitro group, cyano group, carboxy, C₁₋₄ alkyl, C₁₋₄ alkoxy, C₁₋₄ alkylamino, di(C₁₋₄ alkyl)amino, halo C₁₋₄ alkyl, hydroxy C₁₋₄ alkyl, amino C₁₋₄ alkyl, and halo C₁₋₄ alkoxy; and

m and n are each independently an integer from 0 to 4.

5. The compound, the pharmaceutically acceptable salt, the ester or the stereoisomer thereof according to claim 4,

wherein,

X, Y, and Z are each independently selected from -CR⁴- and -N-;

ring A is selected from 4-8 membered cycloalkyl and 4-8 membered heterocyclic group;

R¹ is selected from -(L)_m-C(O)OR^a, -(L)_m-CONR^aR^b, -(L)_m-SO₂R^a, -(L)_m-OR^a, -(L)_m-NR^aR^b, -(L)_m-C(O)R^a, -(L)_m-OC(O)R^a, -(L)_m-NR^aC(O)R^b, -(L)_m-S(O)₂NR^aR^b, -(L)_m-NR^aS(O)₂R^b, and the following groups optionally substituted with 1-3 Q1 groups: -(L)_m-C₁₋₄ alkyl and -(L)_m-C₁₋₄ alkoxy;

L is C₁₋₃ alkylene;

R² is selected from the following groups optionally substituted by 1-4 Q2 groups: 3-6 membered heterocyclic group, 5-8 membered spiro heterocyclic group, 5-8 membered heteroaryl, and N(C₁₋₄ alkyl)(C₃₋₆ cycloalkyl);

each R³ is independently selected from hydrogen, halogen, nitro group, cyano group, amino group, hydroxyl and carboxy;

each R⁴ is independently selected from hydrogen and C₁₋₄ alkyl;

each of R^a and R^b is independently selected from hydrogen and C₁₋₄ alkyl;

each of Q1 and Q2 groups is independently selected from hydroxyl, amino group, halogen,

nitro group, cyano group, carboxy; C₁₋₄ alkyl, C₁₋₄ alkoxy, C₁₋₄ alkylamino, di(C₁₋₄ alkyl)amino, haloC₁₋₄ alkyl, hydroxy C₁₋₄ alkyl, amino C₁₋₄ alkyl, and halo C₁₋₄ alkoxy; and

m and n are each independently an integer from 0 to 3.

6. The compound, the pharmaceutically acceptable salt, the ester or the stereoisomer thereof according to claim 5,

wherein,

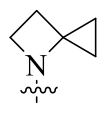
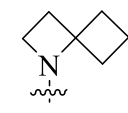
X, Y and Z are each independently -N-;

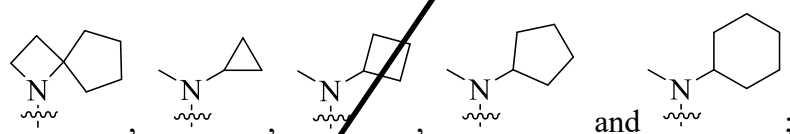
ring A is 4-7 membered cycloalkyl;

R¹ is selected from -(L)_m-C(O)OR^a, -(L)_m-CONR^aR^b, -(L)_m-SO₂R^a, -(L)_m-OR^a, -(L)_m-NR^aR^b, -(L)_m-C(O)R^a, and the following groups optionally substituted with 1-3 Q1 groups: -(L)_m-C₁₋₄ alkyl and -(L)_m-C₁₋₄ alkoxy;

L is methylene;

R² is selected from the following groups optionally substituted by 1-3 Q2 groups: oxetanyl, azetidiny, tetrahydrofuranyl, tetrahydrothienyl, pyrrolidinyl, imidazolidinyl, oxazolidinyl, thiazolidinyl, piperidinyl, piperazinyl, morpholinyl, furyl, pyranal, pyrrolyl, thienyl, thiazolyl, isothiazolyl, thiadiazolyl, imidazolyl, pyrazolyl, oxazolyl, isoxazolyl, oxadiazolyl, triazolyl,

tetrazolyl, pyridyl, pyrimidinyl, pyrazinyl, pyridazinyl, triazinyl, tetrazinyl, , ,



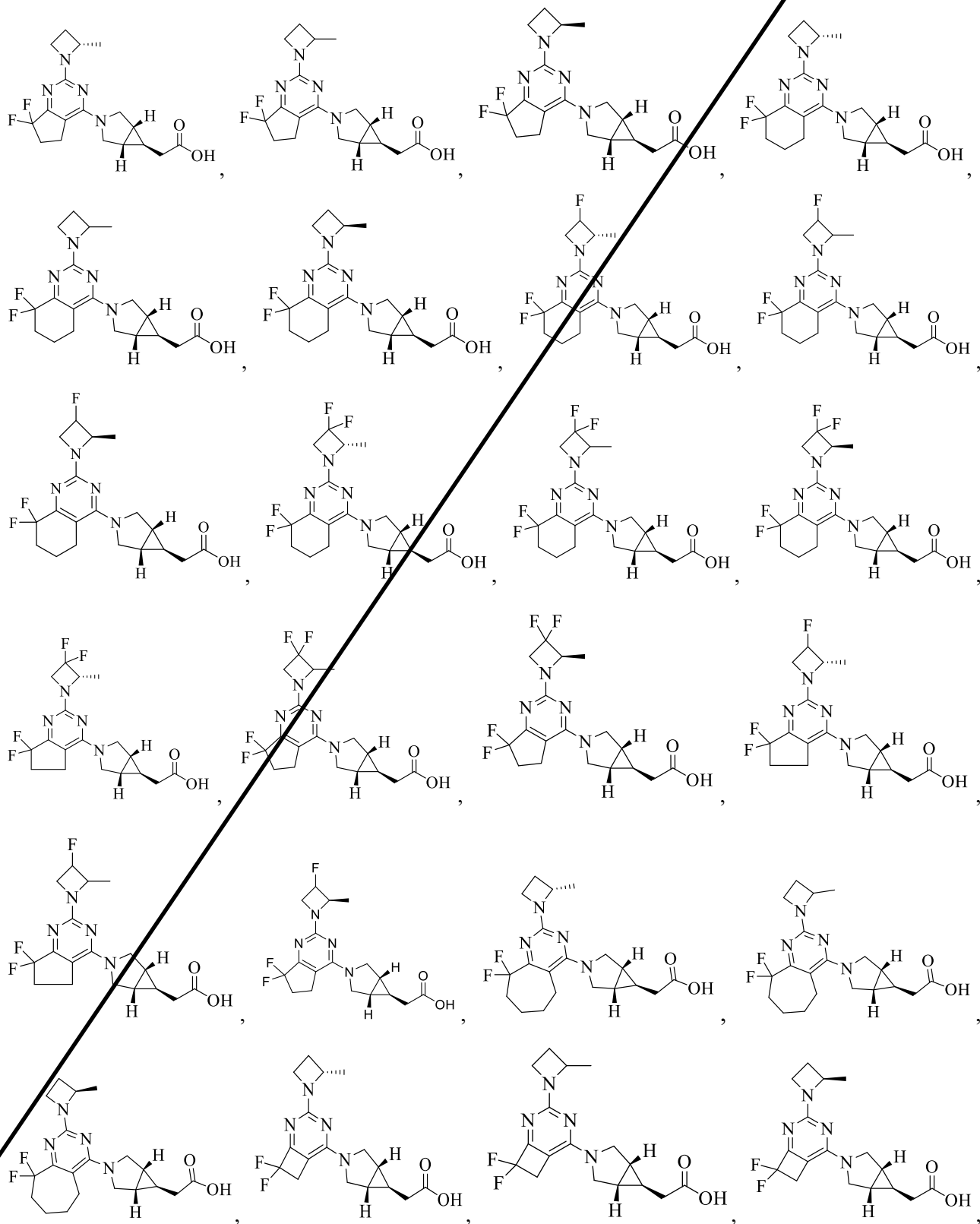
each R³ is independently selected from hydrogen, halogen, nitro group, cyano group, amino group, hydroxyl and carboxy;

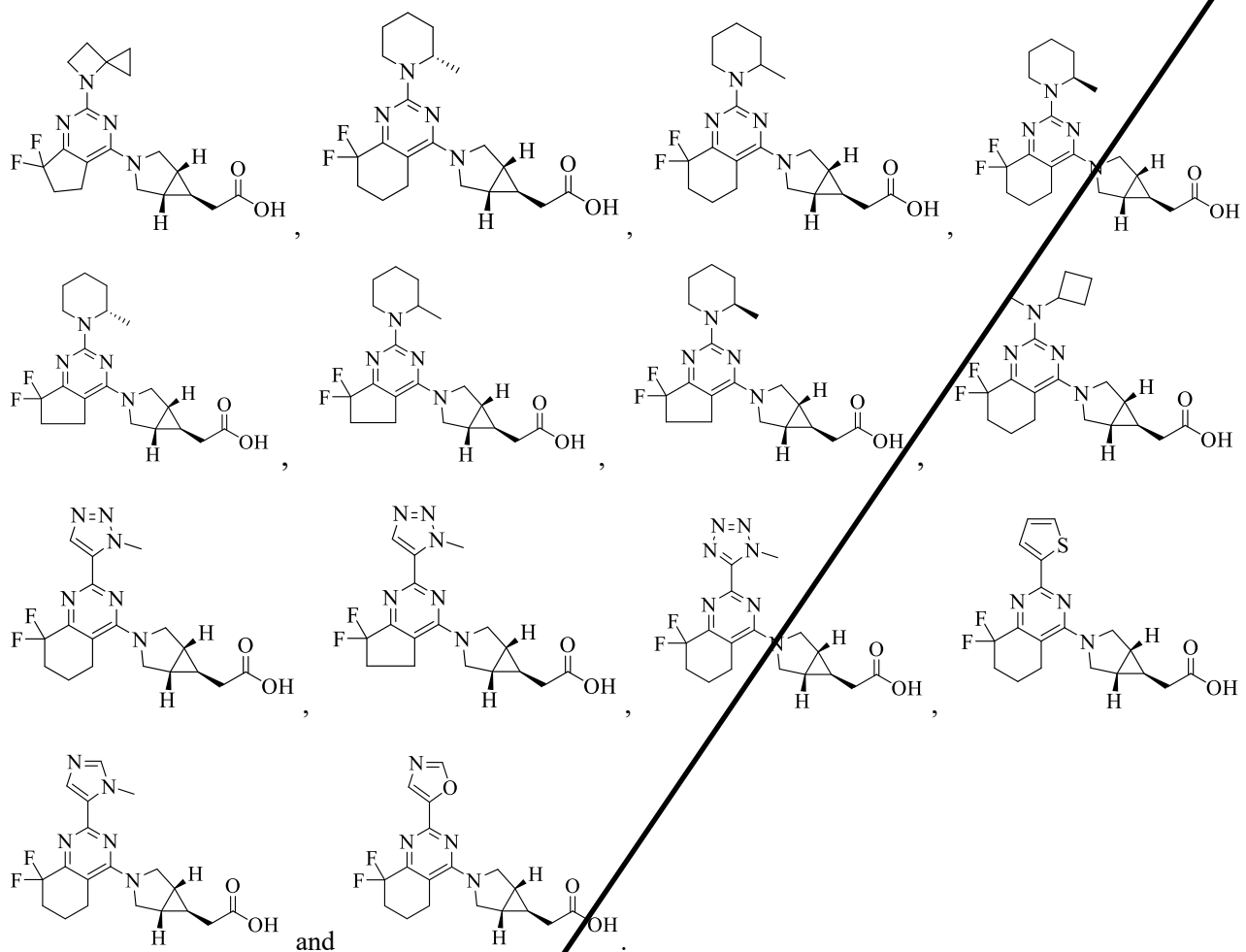
each of R^a and R^b is independently selected from hydrogen, methyl, ethyl, propyl, isopropyl, butyl, isobutyl, sec-butyl, and tert-butyl;

each of Q1 and Q2 groups is independently selected from hydroxyl, amino group, fluorine, chlorine, bromine, iodine, nitro group, cyano group, carboxy, methyl, ethyl, propyl, isopropyl, butyl, isobutyl, sec-butyl, tert-butyl, methoxy, ethoxy, propoxy, methylamino, dimethylamino, trifluoromethyl and trifluoromethoxy; and

m and n are each independently 0, 1, 2 or 3.

7. The compound, the pharmaceutically acceptable salt, the ester or the stereoisomer thereof according to claim 1, the compound is selected from:





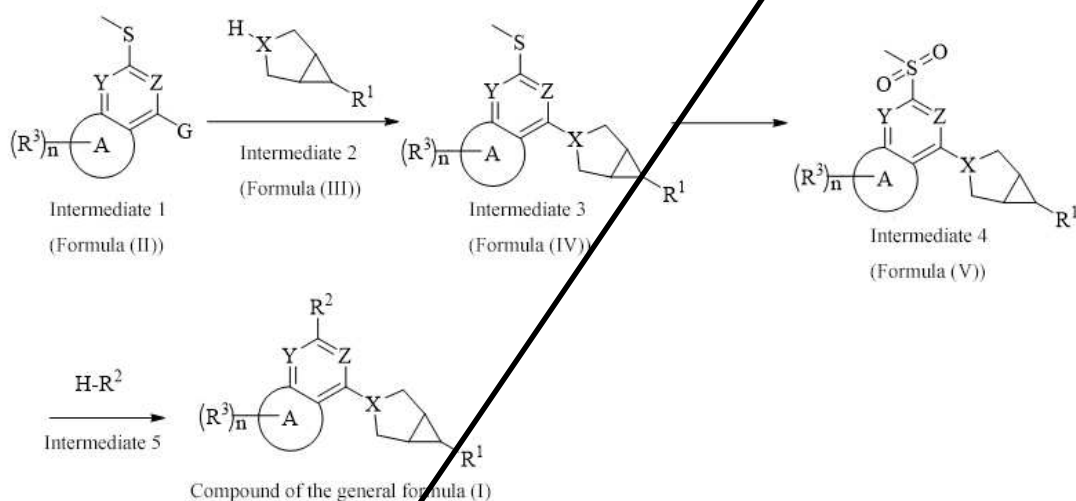
8. A pharmaceutical formulation comprising the compound, the pharmaceutically acceptable salt, the ester or the stereoisomer thereof according to any one of claims 1-7, and one or more pharmaceutically acceptable carriers and/or diluents, wherein the pharmaceutical formulation is in any dosage form that is clinically or pharmaceutically acceptable.

9. A pharmaceutical composition comprising the compound, the pharmaceutically acceptable salt, the ester or the stereoisomer thereof according to any one of claims 1-7, one or more second therapeutic agents; and optionally one or more pharmaceutically acceptable carriers and/or diluents.

10. Use of the compound, the pharmaceutically acceptable salt, the ester or the stereoisomer thereof according to any one of claims 1-7, the pharmaceutical formulation according to claim 8, or the pharmaceutical composition according to claim 9 in the manufacture of a medicament for the treatment and/or prevention of KHK-mediated diseases and related conditions.

11. Use according to claim 10, wherein the KHK-mediated diseases and related conditions are selected from endocrine disorders, urinary diseases, metabolic diseases, non-alcoholic steatohepatitis, liver cirrhosis, fatty liver, hepatitis, liver failure, hereditary fructose intolerance, non-alcoholic fatty liver disease, hepatobiliary diseases, fibrotic diseases, cardiovascular and cerebrovascular diseases, immune inflammatory diseases, central nervous system diseases, gastrointestinal diseases, and excessive proliferative diseases such as cancer.

12. A method for preparing the compound, the pharmaceutically acceptable salt, the ester or the stereoisomer thereof according to any one of claims 1-7, comprising steps of:



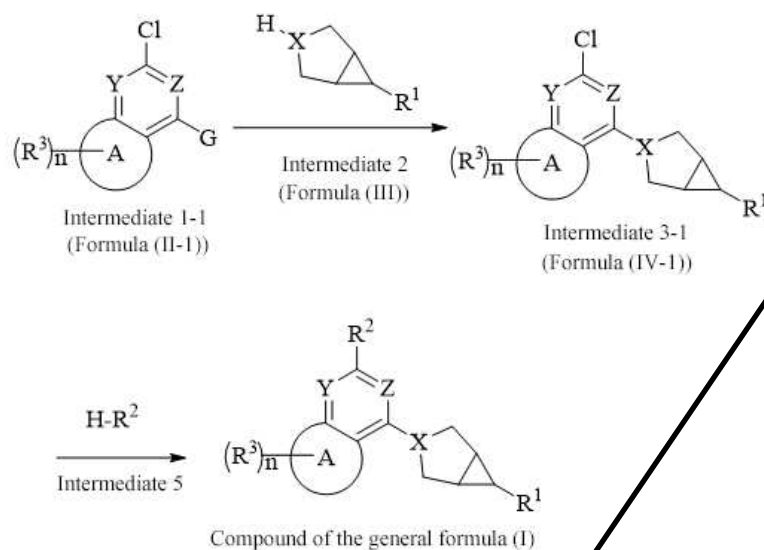
reacting the compound represented by formula (II) with the compound represented by formula (III) to obtain the compound represented by formula (IV);

subjecting the thio group in the compound represented by formula (IV) to functional group conversion reaction to obtain the compound represented by formula (V); and

reacting the compound represented by formula (V) to obtain the compound represented by the general formula (I);

wherein G is halogen; and R^1 , R^2 , R^3 , X , Y , Z , n and ring A are as defined in any one of claims 1-7.

13. The method for preparing the compound, the pharmaceutically acceptable salt, the ester or the stereoisomer thereof according to any one of claims 1-7, comprising steps of:

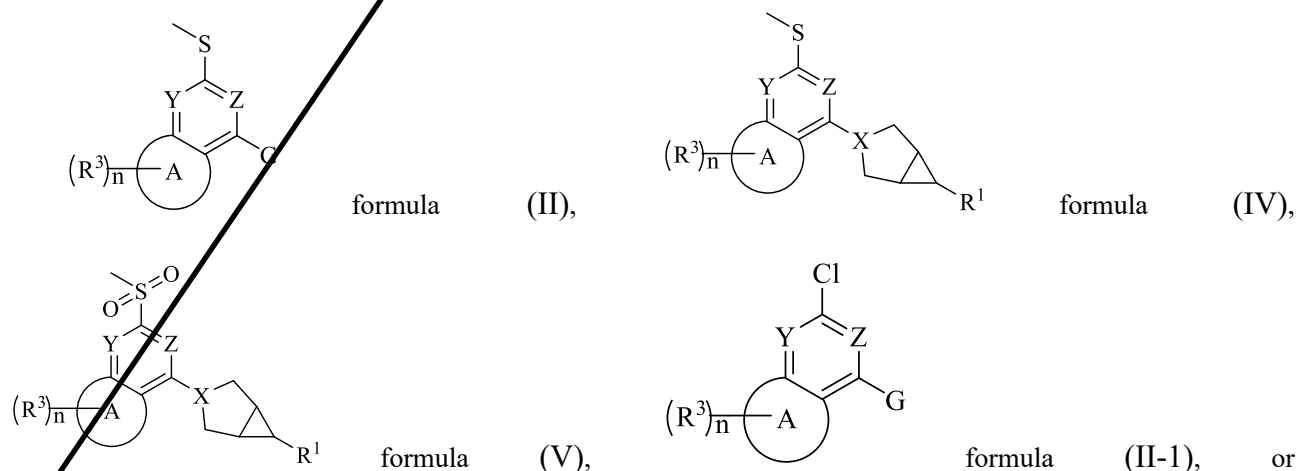


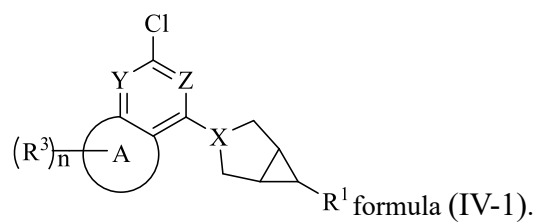
reacting the compound represented by formula (II-1) with the compound represented by formula (III) to obtain the compound represented by formula (IV-1); and

reacting the compound represented by formula (IV-1) to obtain the compound represented by the general formula (I);

wherein G is halogen; and R^1 , R^2 , R^3 , X, Y, Z, n and ring A are as defined in any one of claims 1-7.

14. An intermediate for preparing the compound represented by the general formula (I), the intermediate having a structure of:

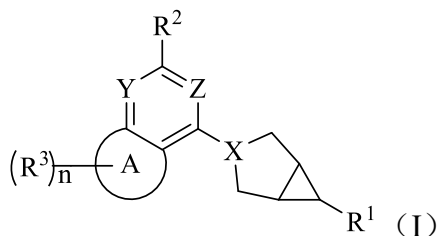




wherein G is halogen; and R^1 , R^3 , X, Y, Z, n and ring A are as defined in any one of claims 1-7.

CLAIMS

1. A compound represented by general formula (I), a pharmaceutically acceptable salt, an ester or a stereoisomer thereof:



5 in which,

X, Y and Z are each -N-;

ring A is selected from 3-7 membered cycloalkyl which is a saturated or partially saturated monocyclic non-aromatic cyclic alkyl containing 3-7 carbon atoms;

R¹ is -(L)_m-C(O)OR^a

10 L is methylene;

R² is selected from the following groups optionally substituted by 1-4 Q2 groups: 3-12 membered heterocyclic group containing at least one heteroatom which is nitrogen atom, 5-12 membered heteroaryl, N(C₁₋₆ alkyl)(C₃₋₈ cycloalkyl) and NH(C₃₋₈ cycloalkyl);

15 each R³ is independently selected from hydrogen, halogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, halo C₁₋₆ alkyl and halo C₁₋₆ alkoxy;

each of R^a is hydrogen;

each of Q2 groups is independently selected from halogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, halo C₁₋₆ alkyl and halo C₁₋₆ alkoxy; and

20 m and n are each independently an integer from 0 to 3.

2. A compound, pharmaceutically acceptable salt, ester or stereoisomer thereof according to Claim 1 in which:

X, Y and Z are each -N-;

ring A is selected from 3-7 membered cycloalkyl which is a saturated or partially saturated monocyclic non-aromatic cyclic alkyl containing 3-7 carbon atoms;

R^1 is $-(L)_m-C(O)OR^a$;

L is methylene;

- 5 R^2 is selected from the following groups optionally substituted by 1-3 Q2 groups: 3-8 membered heterocyclic group containing at least one heteroatom which is nitrogen atom, 5-10 membered heteroaryl, $N(C_{1-6} \text{ alkyl})(C_{3-6} \text{ cycloalkyl})$ and $NH(C_{3-6} \text{ cycloalkyl})$;

- 10 each R^3 is independently selected from hydrogen, halogen, C_{1-6} alkyl, C_{1-6} alkoxy, halo C_{1-6} alkyl and halo C_{1-6} alkoxy;

each of R^a is hydrogen;

each of Q2 groups is independently selected from halogen, C_{1-6} alkyl, C_{1-6} alkoxy, halo C_{1-6} alkyl and halo C_{1-6} alkoxy; and

m and n are each independently an integer from 1 to 3.

- 15 3. A compound, pharmaceutically acceptable salt, ester or stereoisomer thereof according to Claim 2, in which:

X, Y and Z are each -N-;

ring A is selected from 3-7 membered cycloalkyl which is a saturated or partially saturated monocyclic non-aromatic cyclic alkyl containing 3-7 carbon atoms;

- 20 R^1 is $-(L)_m-C(O)OR^a$;

L is methylene;

R^2 is selected from the following groups optionally substituted by 1-3 Q2 groups: 3-8 membered heterocyclic group containing at least one heteroatom which is nitrogen atom, 5-10 membered heteroaryl and $N(C_{1-4} \text{ alkyl})(C_{3-6} \text{ cycloalkyl})$;

- 25 each R^3 is independently selected from halogen, C_{1-4} alkyl, C_{1-4} alkoxy, halo C_{1-4} alkyl and halo C_{1-4} alkoxy;

R^a is hydrogen;

each of Q2 groups is independently selected from halogen, C₁₋₄ alkyl, C₁₋₄ alkoxy, halo C₁₋₄ alkyl and halo C₁₋₄ alkoxy; and

m and n are each independently an integer from 1 to 3.

4. A compound, pharmaceutically acceptable salt, ester or stereoisomer thereof according to Claim 3, in which:

X, Y and Z are each -N-;

ring A is selected from 3-7 membered cycloalkyl which is a saturated or partially saturated monocyclic non-aromatic cyclic alkyl containing 3-7 carbon atoms;

R¹ is -(L)_m-C(O)OR^a;

10 L is methylene;

R² is selected from the following groups optionally substituted by 1-3 Q2 groups: 3-6 membered heterocyclic group containing at least one heteroatom which is nitrogen atom, 5-10 membered heteroaryl and N(C₁₋₄ alkyl)(C₃₋₆ cycloalkyl);

each R³ is halogen;

15 R^a is hydrogen;

each of Q2 groups is independently selected from halogen, C₁₋₄ alkyl and halo C₁₋₄ alkyl; and

m and n are each independently an integer from 1 to 3.

5. A compound, pharmaceutically acceptable salt, ester or stereoisomer thereof according to Claim 4, in which:

X, Y and Z are each -N-;

ring A is selected from 4-7 membered cycloalkyl which is a saturated or partially saturated monocyclic non-aromatic cyclic alkyl containing 4-7 carbon atoms;

R¹ is -(L)_m-C(O)OR^a;

25 L is methylene;

R^2 is selected from the following groups optionally substituted by 1-3 Q2 groups: 3-6 membered heterocyclic group containing at least one heteroatom which is nitrogen atom, 5-8 membered heteroaryl and $N(C_{1-4} \text{ alkyl})(C_{3-6} \text{ cycloalkyl})$;

each R^3 is halogen;

5 R^a is hydrogen;

each of Q2 groups is independently selected from halogen and C_{1-4} alkyl; and

m and n are each independently an integer from 1 to 3.

6. A compound, pharmaceutically acceptable salt, ester or stereoisomer thereof according to Claim 5, in which:

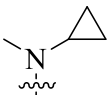
10 X, Y and Z are each independently -N-;

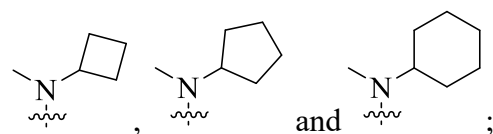
ring A is 4-7 membered cycloalkyl which is a saturated or partially saturated monocyclic non-aromatic cyclic alkyl containing 4-7 carbon atoms;

R^1 is $-(L)_m-C(O)OR^a$;

L is methylene;

15 R^2 is selected from the following groups optionally substituted by 1-3 Q2 groups: azetidiny, pyrrolidinyl, imidazolidinyl, oxazolidinyl, thiazolidinyl, piperidinyl,

piperazinyl, morpholinyl, thienyl, imidazolyl, oxazolyl, triazolyl, tetrazolyl, ,



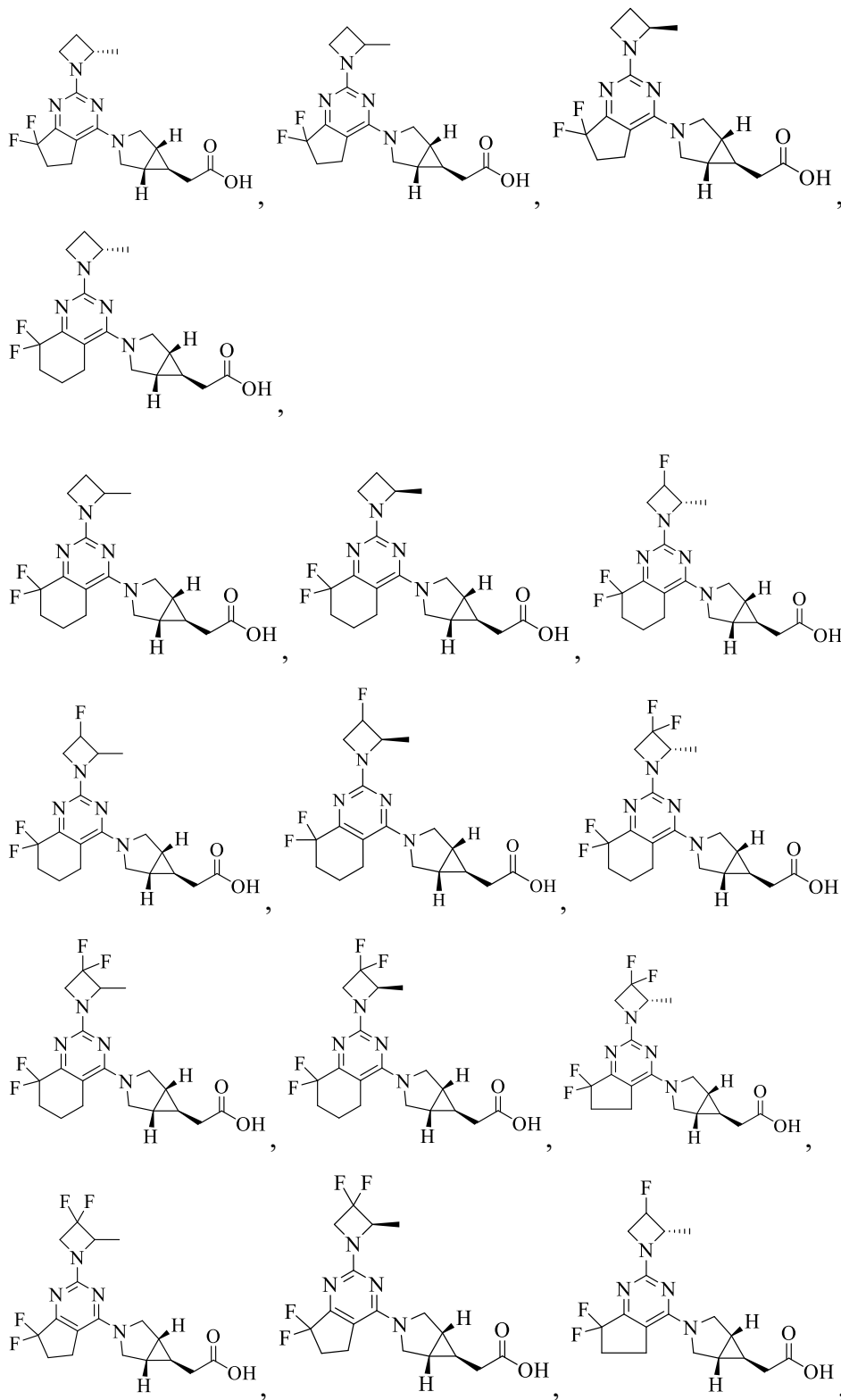
each R^3 is halogen;

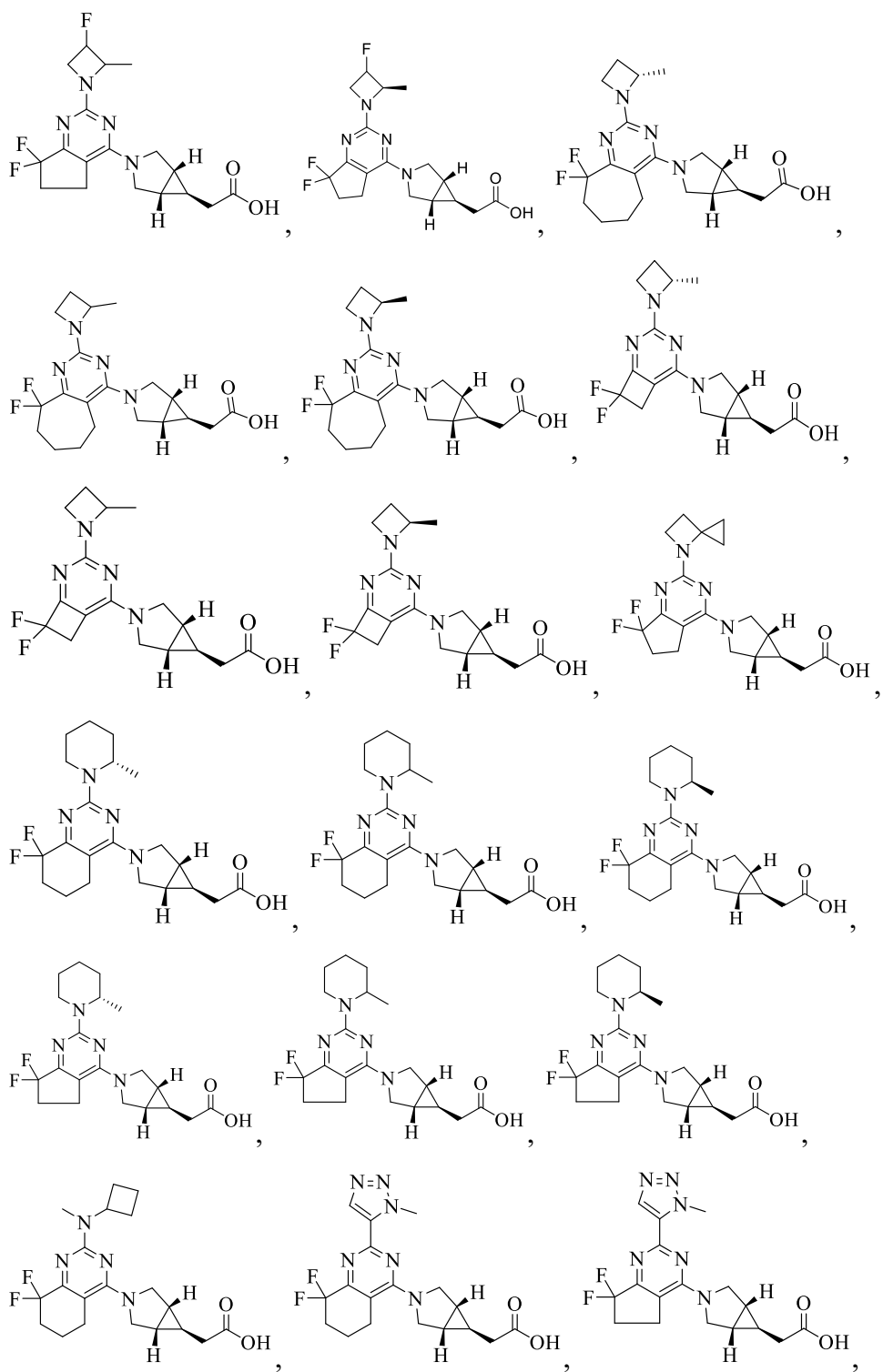
20 R^a is hydrogen;

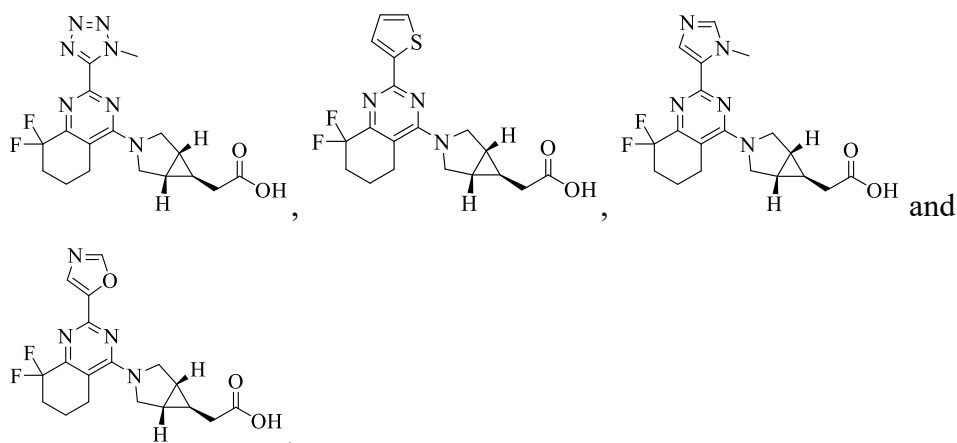
each of Q2 groups is independently selected from fluorine, chlorine, bromine, iodine, methyl, ethyl, propyl, isopropyl, butyl, isobutyl, sec-butyl and tert-butyl; and

m and n are each independently 1, 2 or 3.

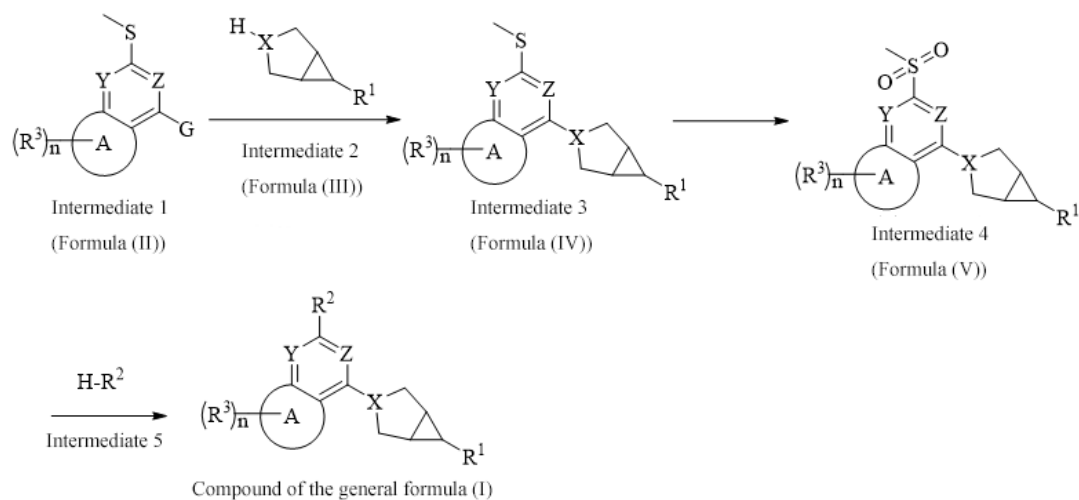
7. A compound, pharmaceutically acceptable salt, ester or stereoisomer thereof according to Claim 1, in which the compound is selected from:







8. A pharmaceutical formulation comprising a compound, pharmaceutically acceptable salt, ester or stereoisomer thereof according to any preceding claim and one or more
- 5 pharmaceutically acceptable carriers and/or diluents, in which the pharmaceutical formulation is in any dosage form that is clinically or pharmaceutically acceptable.
9. A pharmaceutical composition comprising a compound, pharmaceutically acceptable salt, ester or the stereoisomer thereof according to any of Claims 1 to 7, one or more second therapeutic agents; and optionally one or more pharmaceutically acceptable carriers and/or
- 10 diluents.
10. Use of a compound, pharmaceutically acceptable salt, ester or stereoisomer thereof according to any one Claims 1 to 7, a pharmaceutical formulation according to Claim 8, or a pharmaceutical composition according to Claim 9 in the manufacture of a medicament for the treatment and/or prevention of a KHK-mediated disease, in which the KHK-mediated disease
- 15 is selected from endocrine disorders, urinary diseases, metabolic diseases, non-alcoholic steatohepatitis, liver cirrhosis, fatty liver, hepatitis, liver failure, hereditary fructose intolerance, non-alcoholic fatty liver disease, hepatobiliary diseases, fibrotic diseases, cardiovascular and cerebrovascular diseases, immune inflammatory diseases, central nervous system diseases, gastrointestinal diseases and excessive proliferative diseases such as cancer.
- 20 11. A method for preparing a compound, pharmaceutically acceptable salt, ester or stereoisomer thereof according to any of Claims 1 to 7, comprising the steps of:



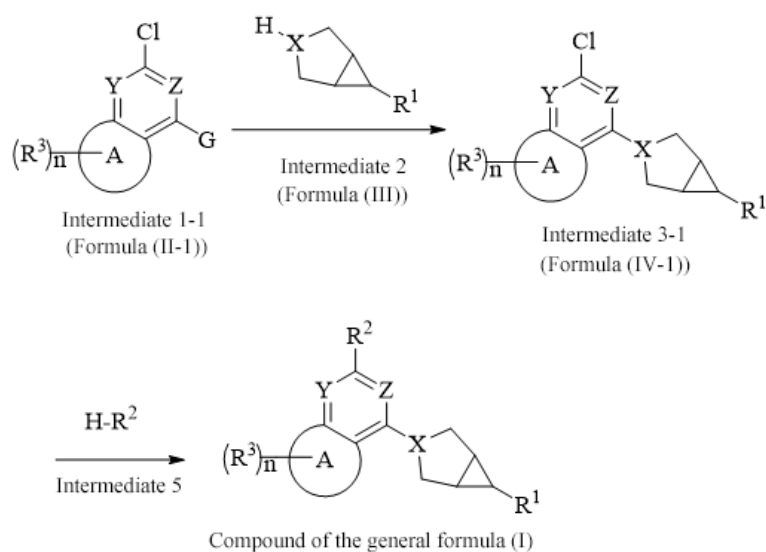
reacting the compound represented by formula (II) with the compound represented by formula (III) to obtain the compound represented by formula (IV);

subjecting the thio group in the compound represented by formula (IV) to functional group conversion reaction to obtain the compound represented by formula (V); and

reacting the compound represented by formula (V) to obtain the compound represented by the general formula (I);

in which G is halogen; R^1 is selected from $-(L)_m-C(O)OR^a$ where R^a is independently selected from hydrogen and C_{1-4} alkyl; and R^2 , R^3 , X, Y, Z, m, n and ring A are as defined in any of Claims 1 to 7.

12. A method for preparing the compound, pharmaceutically acceptable salt, ester or stereoisomer thereof according to any of Claims 1 to 7, comprising steps of:

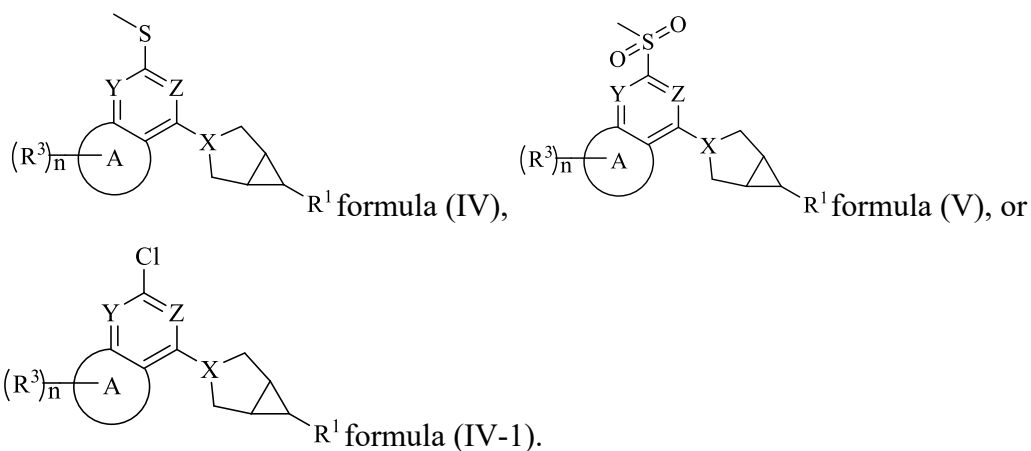


reacting the compound represented by formula (II-1) with the compound represented by formula (III) to obtain the compound represented by formula (IV-1); and

reacting the compound represented by formula (IV-1) to obtain the compound represented by the general formula (I);

in which G is halogen; R¹ is selected from -(L)_m-C(O)OR^a where R^a is independently selected from hydrogen and C₁₋₄ alkyl; and R², R³, X, Y, Z, m, n and ring A are as defined in any of Claims 1 to 7.

13. An intermediate for preparing a compound represented by the general formula (I), the intermediate having a structure of:



in which R^1 is selected from $-(L)_m-C(O)OR^a$ where R^a is independently selected from hydrogen and C_{1-4} alkyl; and R^3 , X, Y, Z, n and ring A are as defined in any of Claims 1 to 7.

14. A compound having the structure:

