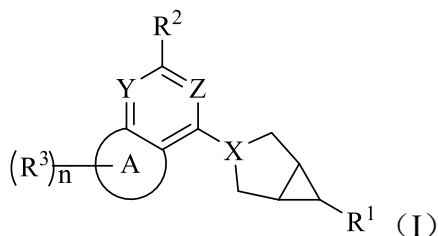


CLAIMS

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:

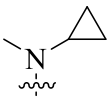
10 X, Y and Z are each independently -N-;

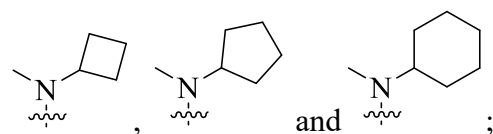
ring A is 4-7 membered cycloalkyl which is a saturated or partially saturated monocyclic non-aromatic cyclic alkyl containing 4-7 carbon atoms;

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, ,



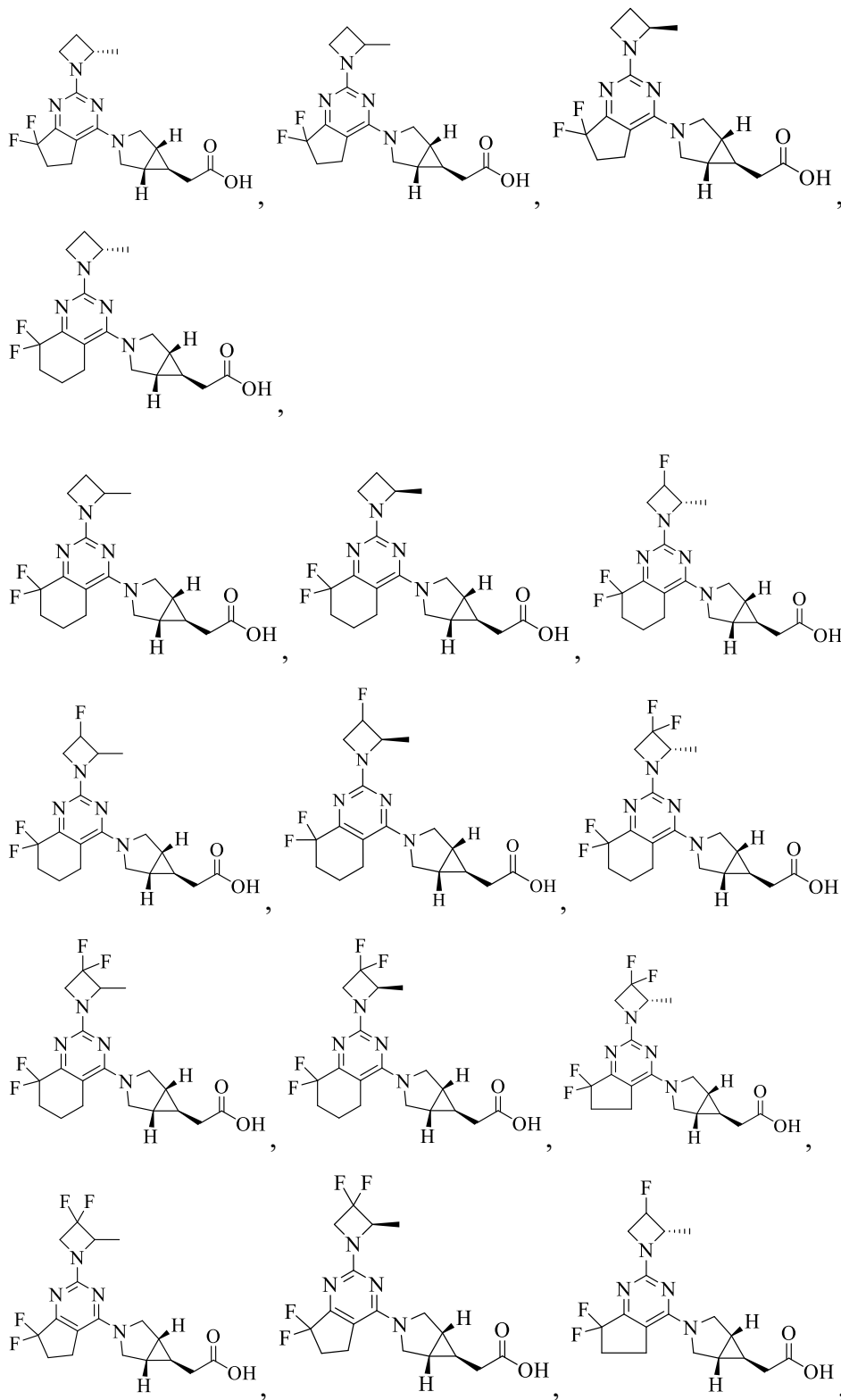
each R^3 is halogen;

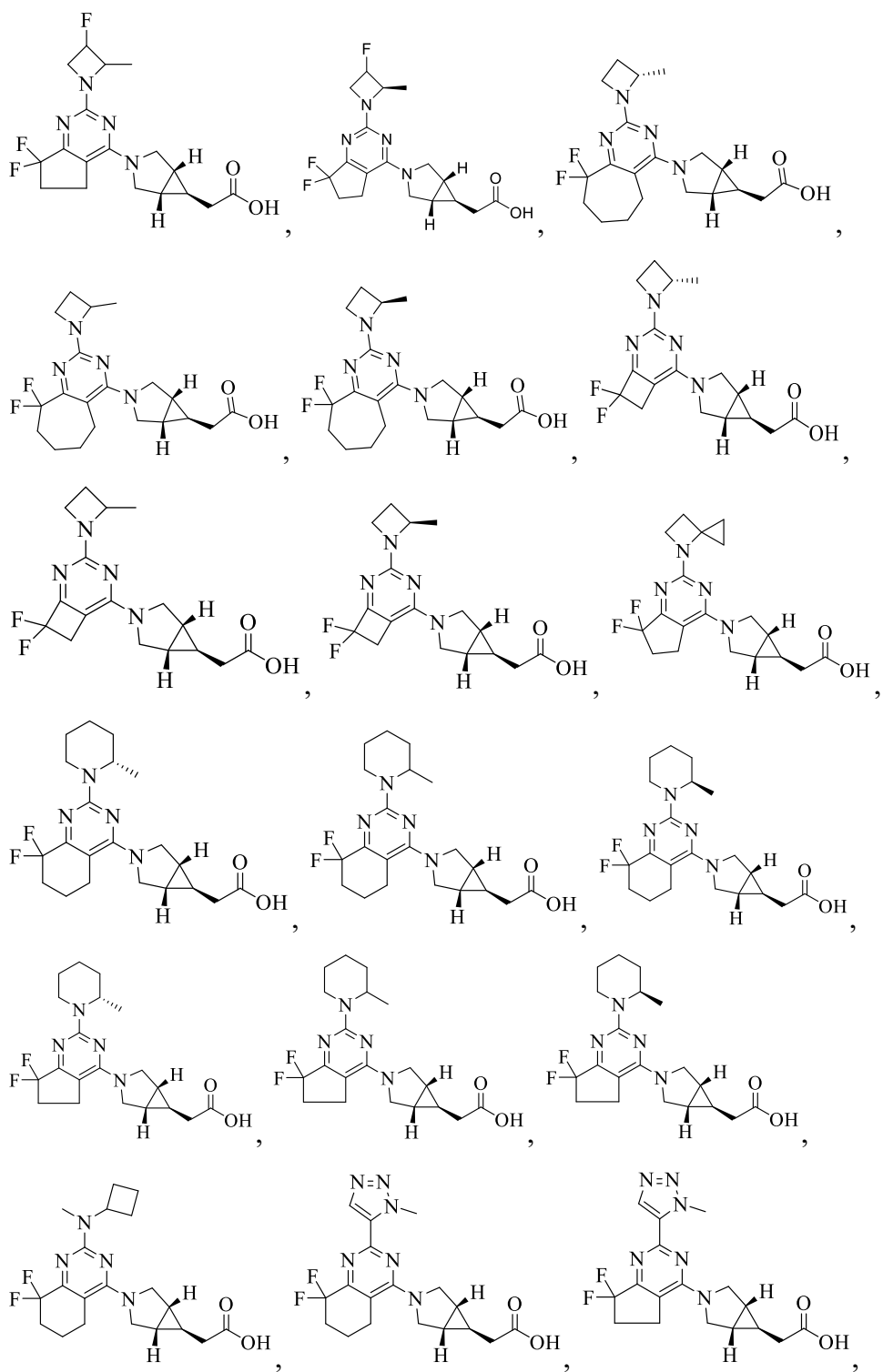
20 R^a is hydrogen;

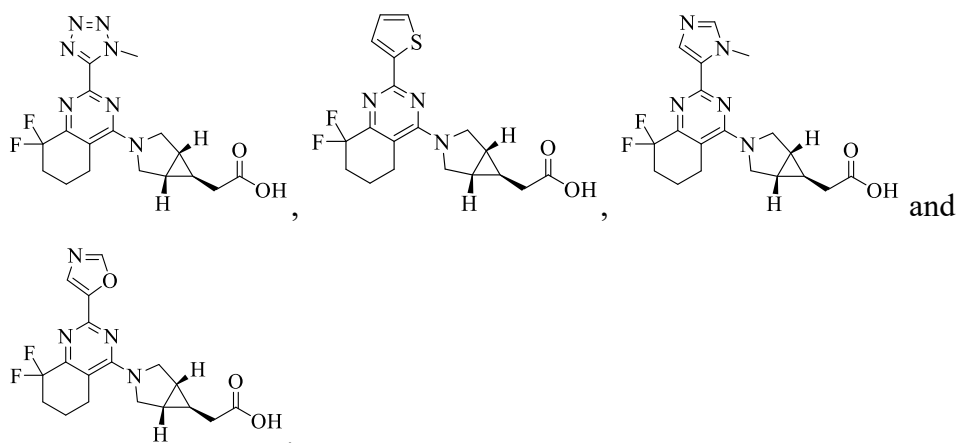
each of Q2 groups is independently selected from fluorine, chlorine, bromine, iodine, methyl, ethyl, propyl, isopropyl, butyl, isobutyl, sec-butyl and tert-butyl; and

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

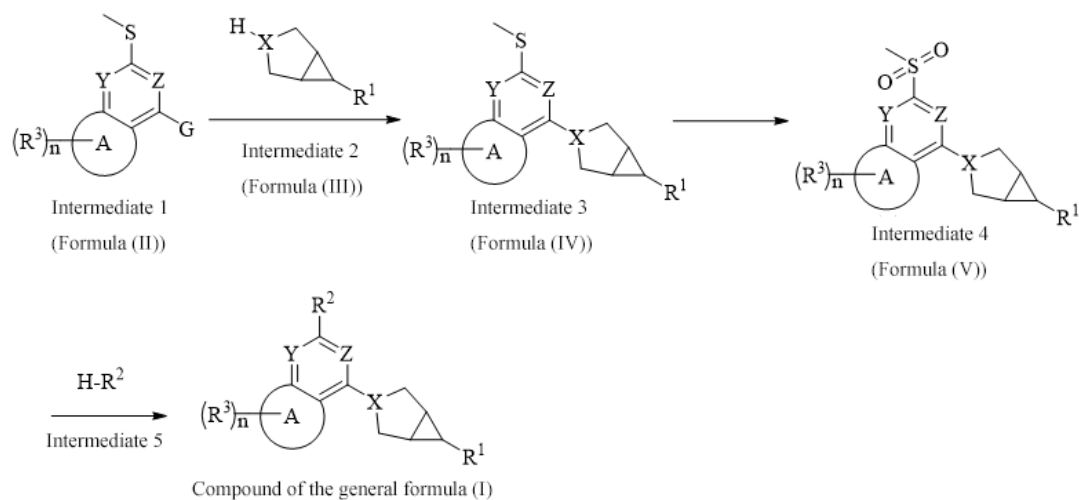
7. A compound, pharmaceutically acceptable salt, ester or stereoisomer thereof according to Claim 1, in which the compound is selected from:







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:



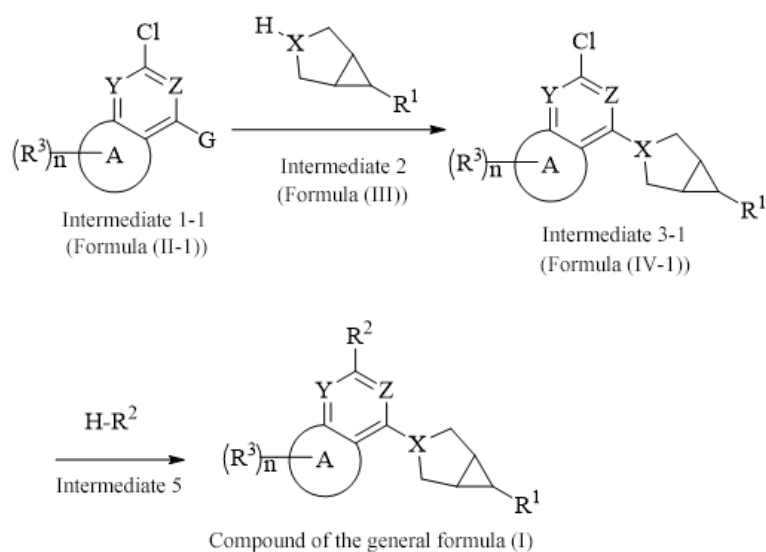
reacting the compound represented by formula (II) with the compound represented by formula (III) to obtain the compound represented by formula (IV);

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:

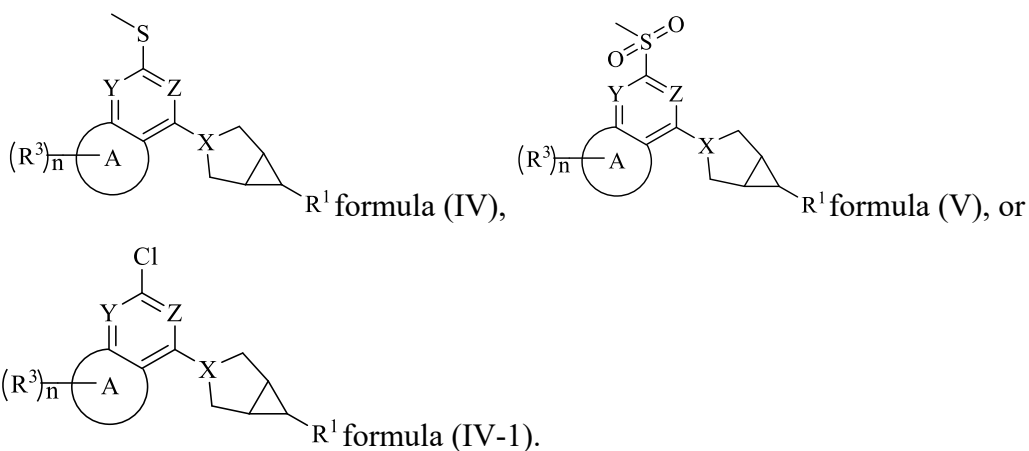


reacting the compound represented by formula (II-1) with the compound represented by formula (III) to obtain the compound represented by formula (IV-1); and

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

in which G is halogen; 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.

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:

