ring A may be attached to the requisite amide moiety (i.e. the –C(O)-N(R^1)- moiety) *via* either one of two possible bonds represented by the dotted lines, which bonds are linked to ring A at two different atoms (of that ring);

ring A is a 5-membered aromatic ring containing at least one heteroatom (preferably containing at least one nitrogen atom);

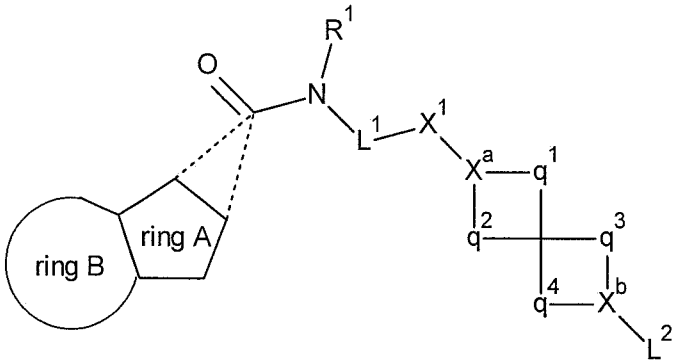
ring B is a 5- or 6-membered ring, which may be aromatic or non-aromatic, optionally containing one to four heteroatoms (preferably selected from nitrogen, oxygen and sulfur);

either ring A and/or ring B may be optionally substituted by one or more substituents selected from: halo, C_{1-6} alkyl (optionally substituted by one or more halo, e.g. fluoro atoms) and/or -OC_{1-6}alkyl (itself optionally substituted by one or more fluoro atoms),

or a pharmaceutically-acceptable salt thereof,

which compounds may also be referred to herein as "compounds of the invention".

In one aspect, the present disclosure relates to a compound of formula (IA) for use in the treatment of tuberculosis



(IA)

wherein

R^1 represents C_{1-6} alkyl or hydrogen;

L^1 represents a linker group -C(R^a)(R^b)-;

X^1 represents an optional linker group comprising at least one carbocyclic aromatic moiety optionally substituted by one or more substituents selected from fluoro, -OH, -OC_{1-6} alkyl optionally substituted by one or more fluoro atoms and C_{1-6} alkyl optionally substituted by one or more fluoro atoms;

R^a and R^b independently represent hydrogen or C_{1-6} alkyl optionally substituted by one or more fluoro atoms;

X^a represents $C(R^c)$ or N;
X^b represents $C(R^d)$, N, or when L^2 is not present, X^b represents O or C=O;

R^c and R^d independently represent H, F or $-OR^e$ wherein R^e represents H or C_{1-6} alkyl optionally substituted by one or more fluoro atoms, or, R^d and L^2 is linked together to form a 4- to 6-membered cyclic group i.e. a spiro-cycle, optionally containing one to three heteroatoms;

q^1 represents $-X^c-(CH_2)_{n1}-X^d-$;
n1 repesents 0, 1 or 2;
q^2 represents $-X^e-(CH_2)_{n2}-X^f-$;
n2 represents 0, 1 or 2, but wherein n1 and n2 do not both represent 0;

X^c, which is attached to X^a, is either not present, or, when X^a represents CH, then X^c represents -O-, -NH- or -S-;
X^d is either not present, or, when n1 represents 2 or when X^c is not present, X^a represents $C(R^c)$ and n1 represents 1, then X^d represents -O-, -NH- or -S-;
X^e and X^f independently are either not present, or independently represent -O-, -NH- or -S-, provided that the aforementioned heteroatoms are not directly attached to or α to another heteroatom;

q^3 represents $-X^g-(CH_2)_{n3}-X^h-$;
q^4 represents $-X^i-(CH_2)_{n4}-X^j-$;
n3 repesents 0, 1 or 2;
n4 represents 0, 1 or 2, but wherein n3 and n4 do not both represent 0;

X^g, X^h, X^i and X^j independently are either not present, or represent -O-, -NH- or -S-, provided that the aforementioned heteroatoms are not directly attached to or α to another heteroatom;

when X^b represents O or C=O, then L^2 is not present;

when X^b represents $C(R^d)$ or N, then L^2 may represent hydrogen, halo, $-OR^f$, $-C(O)-R^g$, C_{1-6} alkyl optionally substituted by one or more halo, e.g. fluoro atoms or an aromatic group optionally substituted by one or more substituents selected from halo, C_{1-6} alkyl optionally substituted by one or more substituents selected from fluoro, $-CF_3$ and/or $-SF_5$,
$-OC_{1-6}$alkyl optionally substituted by one or more fluoro atoms,
-O-phenyl optionally substituted by halo, C_{1-6}alkyl, C_{1-6}fluoroalkyl and/or $-OC_{1-6}$alkyl or
$-SF_5$); or, when attached to nitrogen, i.e. when X^b is N, L^2 represents $-S(O)_2$-C_{1-6}alkyl optionally substituted by one or more fluoro atoms e.g. forming $-S(O)_2CF_3$;

R^f represents hydrogen, C_{1-6} alkyl optionally substituted by one or more fluoro or an aromatic group optionally substituted by one or more substituents selected from halo, C_{1-6}alkyl optionally substituted by one or more fluoro atoms and $-OC_{1-6}$alkyl optionally substituted by one or more fluoro atoms;

R^g represents hydrogen or C_{1-6}alkyl optionally substituted by one or more substituents selected from fluoro, or $-OC_{1-3}$ alkyl optionally substuituted by one or more fluoro atoms or an aromatic group optionally substituted by one or more substituents selected from halo, C_{1-6} alkyl or $-OC_{1-6}$alkyl;

ring A is attached to the requisite amide moiety i.e. the $-C(O)-N(R^1)-$ moiety *via* either one of two possible bonds represented by the dotted lines, which bonds are linked to ring A at two different atoms of that ring;

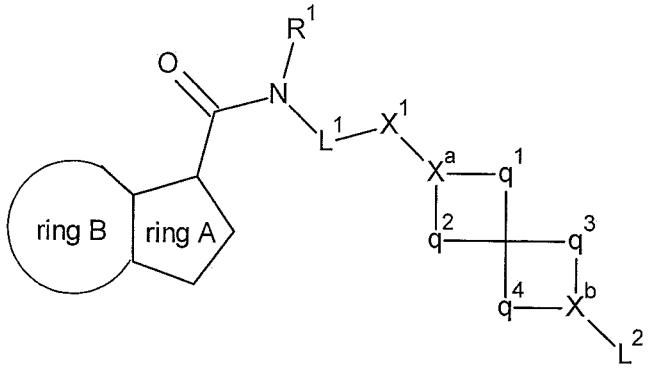
ring A is a 5-membered aromatic ring containing at least one heteroatom preferably containing at least one nitrogen atom;

ring B is a 5- or 6-membered ring, which may be aromatic or non-aromatic, optionally containing one to four heteroatoms preferably selected from nitrogen, oxygen and sulfur;

either ring A and/or ring B is optionally substituted by one or more substituents selected from: halo, C_{1-6} alkyl optionally substituted by one or more halo, e.g. fluoro atoms and/or $-OC_{1-6}$alkyl optionally substituted by one or more fluoro atoms,

or a pharmaceutically-acceptable salt thereof.

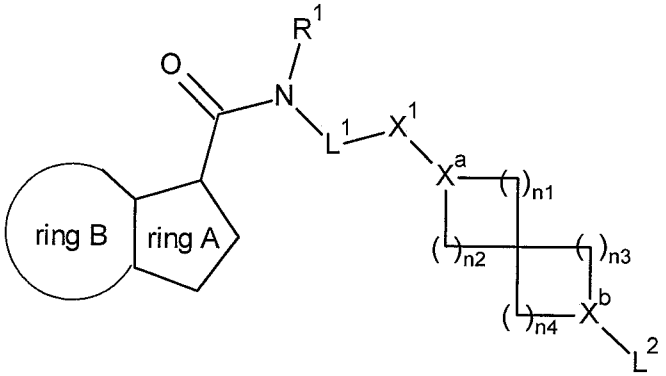
For instance, compounds of formula (IA) may as described above, may be such that the ring A is linked to the amide moiety *via* a specific ring atom, as depicted by compounds of formula (I) below:



(I)

This embodiment is essentially a graphical depiction of ring A being linked to the requisite amido moiety *via* a bond represented by one of the dotted lines in formula (IA).

In another aspect, the present disclosure relates to a compound of formula (IB) as depicted below:



(IB)

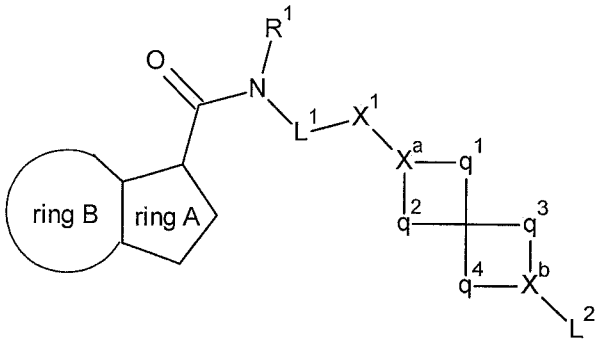
wherein

ring A, ring B, R^1, L^1, X^1, X^a, n1, n2, n3, n4, X^b and L^2 are as hereinbefore defined, and where, preferably:

n1, n2, n3 and n4 independently represent 1;

at least one of X^a and X^b represents N and the other represents CH or N.

In another aspect, the present disclosure relates to a compound of formula (I)



(I)

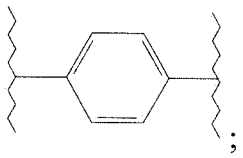
wherein

R^1 represents hydrogen;

L^1 represents $-CH_2-$;

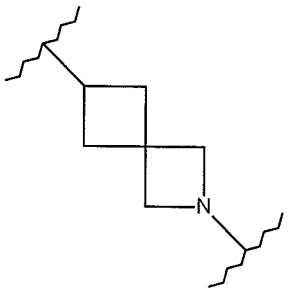
X^1 represents a carbocyclic aromatic linker group that is:

-phenylene- especially a 1,4-phenylene, e.g.:



;

the spiro-cyclic moiety, i.e. the combined X^a and X^b-containing ring is represented as follows:

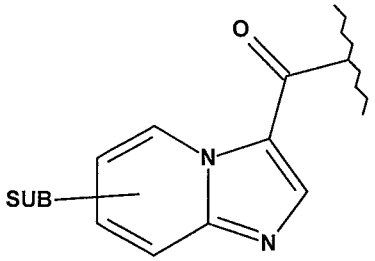


L^2 represents $-S(O)_2$-C_{1-6}alkyl optionally substituted by one or more fluoro atoms e.g. forming $-S(O)_2CF_3$;

ring A is a 5-membered aromatic ring containing at least one heteroatom, preferably containing at least one nitrogen atom;

ring B is a 5- or 6-membered ring, which is aromatic or non-aromatic, optionally containing one to four heteroatoms, preferably selected from nitrogen, oxygen and sulfur;

wherein the combined ring systems, i.e. Ring A-C(=O)- and Ring B are represented as follows:



optional substituents on ring A and ring B are halo, C_{1-3} alkyl and $-OC_{1-3}$ alkyl,

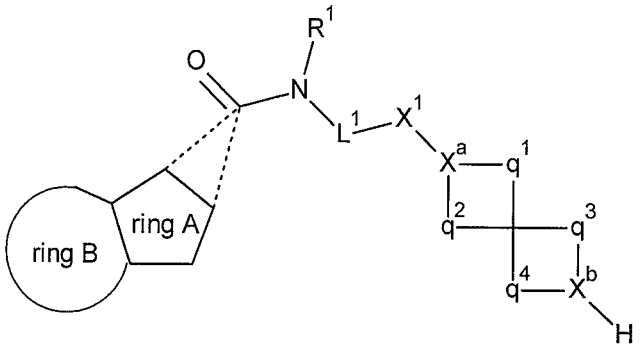
or a pharmaceutically-acceptable salt thereof.

Pharmaceutically-acceptable salts include acid addition salts and base addition salts. Such salts may be formed by conventional means, for example by reaction of a free acid or a free base form of a compound of formula I with one or more equivalents of an

In another aspect, the present disclosure relates to a product containing (a) a compound as defined herein, and (b) one or more other anti-tuberculosis agent, as a combined preparation for simultaneous, separate or sequential use in the treatment of tuberculosis.

In another aspect, the present disclosure relates to a process for the preparation of a compound of formula (IA) as defined herein, which process comprises:

(i) reaction of a compound of formula (II),



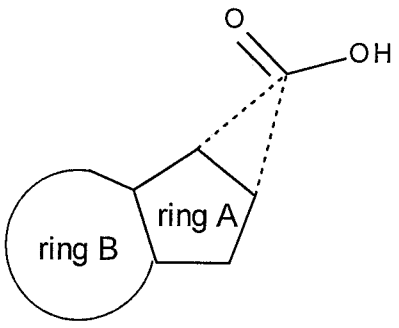
(II)

in which ring A, ring B, R^1, L^1, X^1, X^a, q^1, q^2, q^3, q^4 and X^b are as defined herein, with a compound of formula (III),

$$LG^1\text{-}L^2 \qquad \text{(III)}$$

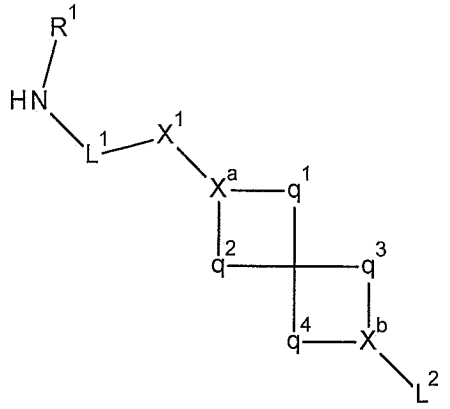
wherein L^2 is as defined herein but when L^2 is not hydrogen, halo or linked to O or S, and LG^1 is a suitable leaving group;

(ii) reaction of a compound of formula (IV),



(IV)

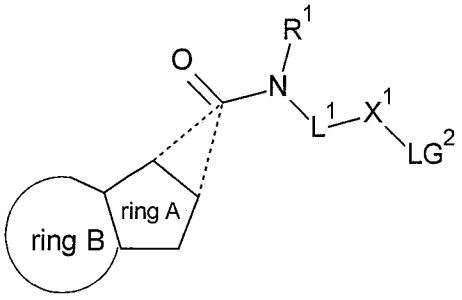
wherein ring A and ring B are as defined herein, or a suitable derivative thereof, such as a carboxylic acid ester derivative, with a compound of formula (V)



(V)

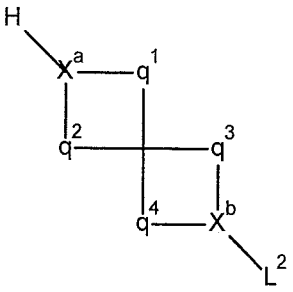
wherein R^1, L^1, X^1, X^a, q^1, q^2, q^3, q^4, X^b and L^2 are as hereinbefore defined, under amide coupling reaction conditions;

(iii) coupling of a compound of formula (VI),



(VI)

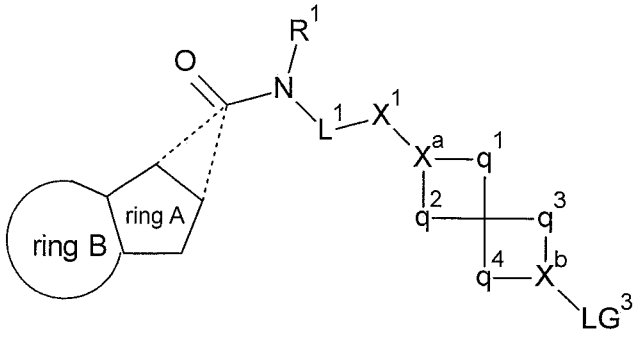
wherein ring A, ring B, R^1, L^1, and X^1 are as defined herein, and LG^2 represents a suitable leaving group, with a compound of formula (VI),



(VII)

wherein X^a, q^1, q^2, q^3, q^4, X^b and L^2 are as defined herein; or

(iv) coupling of a compound of formula (VIII),



(VIII)

wherein ring A, ring B, R^1, L^1, X^1, X^a, q^1, q^2, q^3, q^4 and X^b are as defined herein, and LG^3 represents a suitable leaving group as described above with respect to LG^2 and particularly represents chloro, bromo or iodo, with a compound of formula (IX),

$$LG^4\text{-}L^2 \qquad \text{(IX)}$$

wherein L^2 is as defined herein but when L^2 is not hydrogen, halo or linked to O or S, and LG^4 is a suitable group.

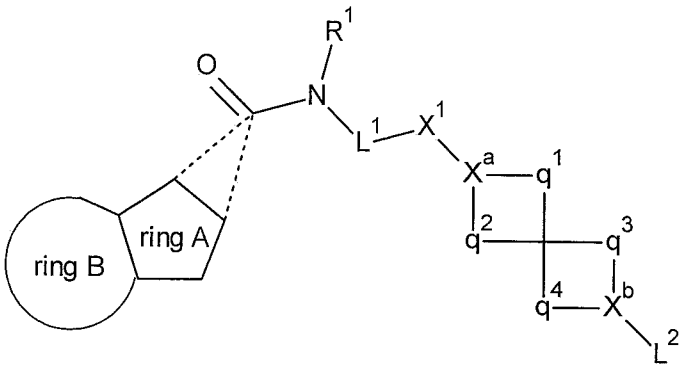
For the purposes of this invention solvates, prodrugs, N-oxides and stereoisomers of compounds of the invention are also included within the scope of the invention.

The term "prodrug" of a relevant compound of the invention includes any compound that, following oral or parenteral administration, is metabolised *in vivo* to form that compound in an experimentally-detectable amount, and within a predetermined time (e.g. within a dosing interval of between 6 and 24 hours (i.e. once to four times daily)). For the avoidance of doubt, the term "parenteral" administration includes all forms of administration other than oral administration.

Prodrugs of compounds of the invention may be prepared by modifying functional groups present on the compound in such a way that the modifications are cleaved, *in vivo* when such prodrug is administered to a mammalian subject. The modifications typically are achieved by synthesising the parent compound with a prodrug substituent. Prodrugs include compounds of the invention wherein a hydroxyl, amino, sulfhydryl, carboxy or carbonyl group in a compound of the invention is bonded to any group that may be cleaved *in vivo* to regenerate the free hydroxyl, amino, sulfhydryl, carboxy or carbonyl group, respectively.

CLAIMS

1. A compound of formula (IA) for use in the treatment of tuberculosis



(IA)

wherein

R^1 represents C_{1-6} alkyl or hydrogen;

L^1 represents a linker group $-C(R^a)(R^b)-$;

X^1 represents an optional linker group comprising at least one carbocyclic aromatic moiety optionally substituted by one or more substituents selected from fluoro, -OH, $-OC_{1-6}$ alkyl optionally substituted by one or more fluoro atoms or C_{1-6} alkyl optionally substituted by one or more fluoro atoms;

R^a and R^b independently represent hydrogen or C_{1-6} alkyl optionally substituted by one or more fluoro atoms;

X^a represents $C(R^c)$ or N;

X^b represents $C(R^d)$, N, or when L^2 is not present, X^b represents O or C=O;

R^c and R^d independently represent H, F or $-OR^e$ wherein R^e represents H or C_{1-6} alkyl optionally substituted by one or more fluoro atoms, or, R^d and L^2 is linked together to form a 4- to 6-membered cyclic group i.e. a spiro-cycle, optionally containing one to three heteroatoms;

q^1 represents $-X^c-(CH_2)_{n1}-X^d-$;

n1 repesents 0, 1 or 2;

q^2 represents $-X^e-(CH_2)_{n2}-X^f-$;

n2 represents 0, 1 or 2, but wherein n1 and n2 do not both represent 0;

X^c, which is attached to X^a, is either not present, or, when X^a represents CH, then X^c represents -O-, -NH- or -S-;
X^d is either not present, or, when n1 represents 2 or when X^c is not present, X^a represents $C(R^c)$ and n1 represents 1, then X^d represents -O-, -NH- or -S-;
X^e and X^f independently are either not present, or independently represent -O-, -NH- or -S-, provided that the aforementioned heteroatoms are not directly attached to or α to another heteroatom;

q^3 represents $-X^g-(CH_2)_{n3}-X^h-$;
q^4 represents $-X^i-(CH_2)_{n4}-X^j-$;
n3 repesents 0, 1 or 2;
n4 represents 0, 1 or 2, but wherein n3 and n4 do not both represent 0;

X^g, X^h, X^i and X^j independently are either not present, or represent -O-, -NH- or -S-, provided that the aforementioned heteroatoms are not directly attached to or α to another heteroatom;

when X^b represents O or C=O, then L^2 is not present;
when X^b represents $C(R^d)$ or N, then L^2 may represent hydrogen, halo, $-OR^f$, $-C(O)-R^g$, C_{1-6} alkyl optionally substituted by one or more halo, e.g. fluoro atoms or an aromatic group optionally substituted by one or more substituents selected from halo, C_{1-6} alkyl optionally substituted by one or more substituents selected from fluoro, $-CF_3$ and/or $-SF_5$,
$-OC_{1-6}$alkyl optionally substituted by one or more fluoro atoms,
-O-phenyl optionally substituted by halo, C_{1-6}alkyl, C_{1-6}fluoroalkyl and/or $-OC_{1-6}$alkyl or
$-SF_5$; or, when attached to nitrogen, i.e. when X^b is N, L^2 represents $-S(O)_2-C_{1-6}$alkyl optionally substituted by one or more fluoro atoms e.g. forming $-S(O)_2CF_3$;

R^f represents hydrogen, C_{1-6} alkyl optionally substituted by one or more fluoro or an aromatic group optionally substituted by one or more substituents selected from halo, C_{1-6}alkyl optionally substituted by one or more fluoro atoms and $-OC_{1-6}$alkyl optionally substituted by one or more fluoro atoms;

R^g represents hydrogen or C_{1-6}alkyl optionally substituted by one or more substituents selected from fluoro, or $-OC_{1-3}$ alkyl optionally substuituted by one or more fluoro atoms or an aromatic group optionally substituted by one or more substituents selected from halo, C_{1-6} alkyl or $-OC_{1-6}$alkyl;

ring A is attached to the requisite amide moiety i.e. the –C(O)-N(R^1)- moiety *via* either one of two possible bonds represented by the dotted lines, which bonds are linked to ring A at two different atoms of that ring;

ring A is a 5-membered aromatic ring containing at least one heteroatom preferably containing at least one nitrogen atom;

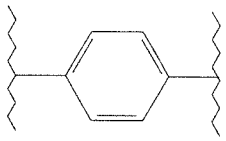
ring B is a 5- or 6-membered ring, which is aromatic or non-aromatic, optionally containing one to four heteroatoms preferably selected from nitrogen, oxygen and sulfur;

either ring A and/or ring B is optionally substituted by one or more substituents selected from: halo, C_{1-6} alkyl optionally substituted by one or more halo, e.g. fluoro atoms and/or -OC_{1-6}alkyl optionally substituted by one or more fluoro atoms,

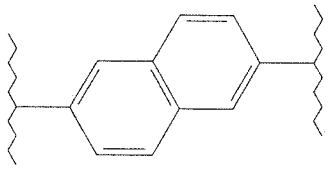
or a pharmaceutically-acceptable salt thereof.

2. A compound for use as claimed in Claim 1, wherein:
R^1 represents hydrogen;
R^a and R^b independently represent hydrogen; and/or
L^1 represents –CH_2-.

3. A compound for use as claimed in Claim 1 or Claim 2, wherein X^1 represents a carbocyclic aromatic linker group that is:
-phenylene- especially a 1,4-phenylene, e.g.:

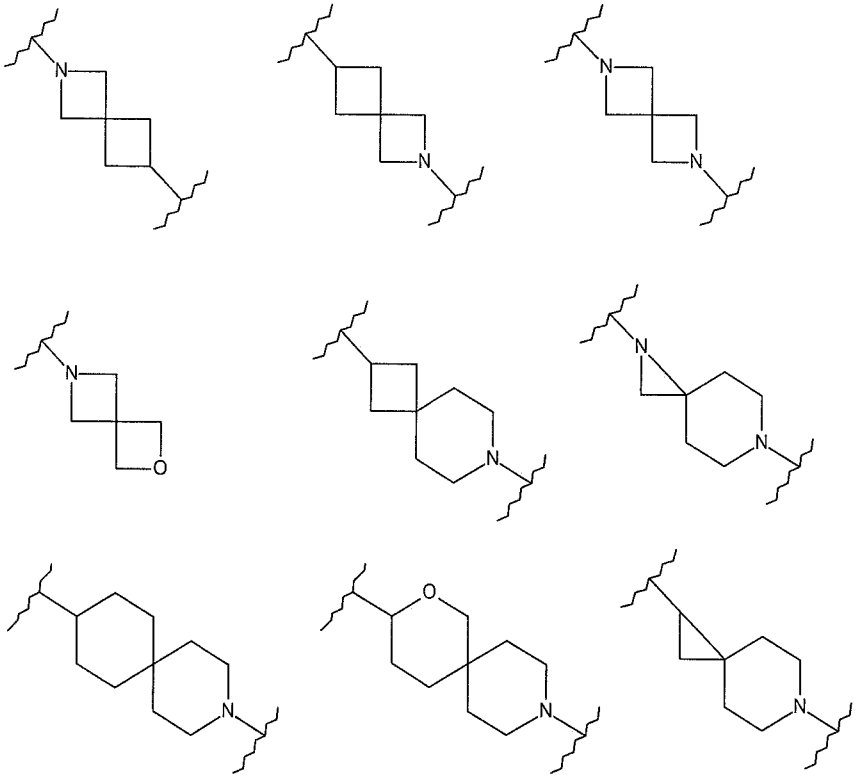


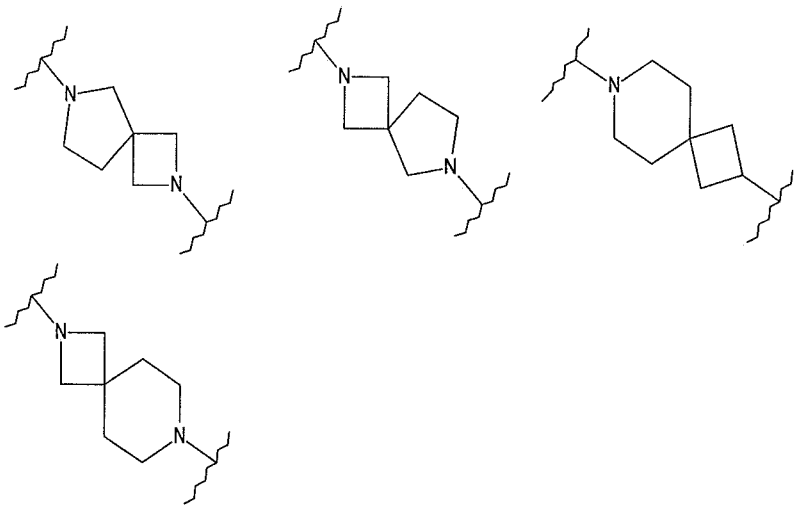
-naphthylene, e.g.:



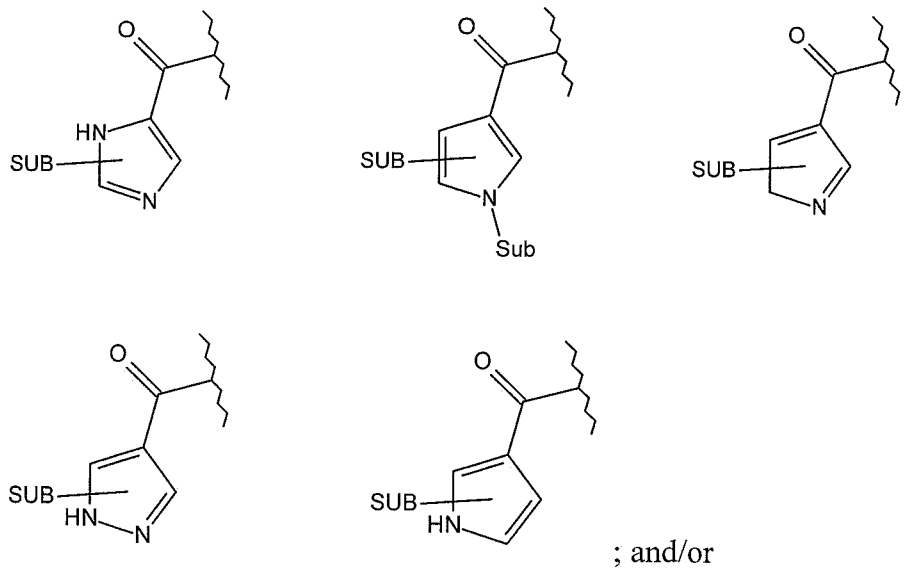
in which such linker groups are optionally substituted by one or more substituents selected from fluoro, CH_3, CF_3, $-OCH_3$ and $-OCF_3$.

4. A compound for use as claimed in any of the preceding claims, wherein the spiro-cyclic moiety, i.e. the combined X^a and X^b-containing ring is represented as follows:



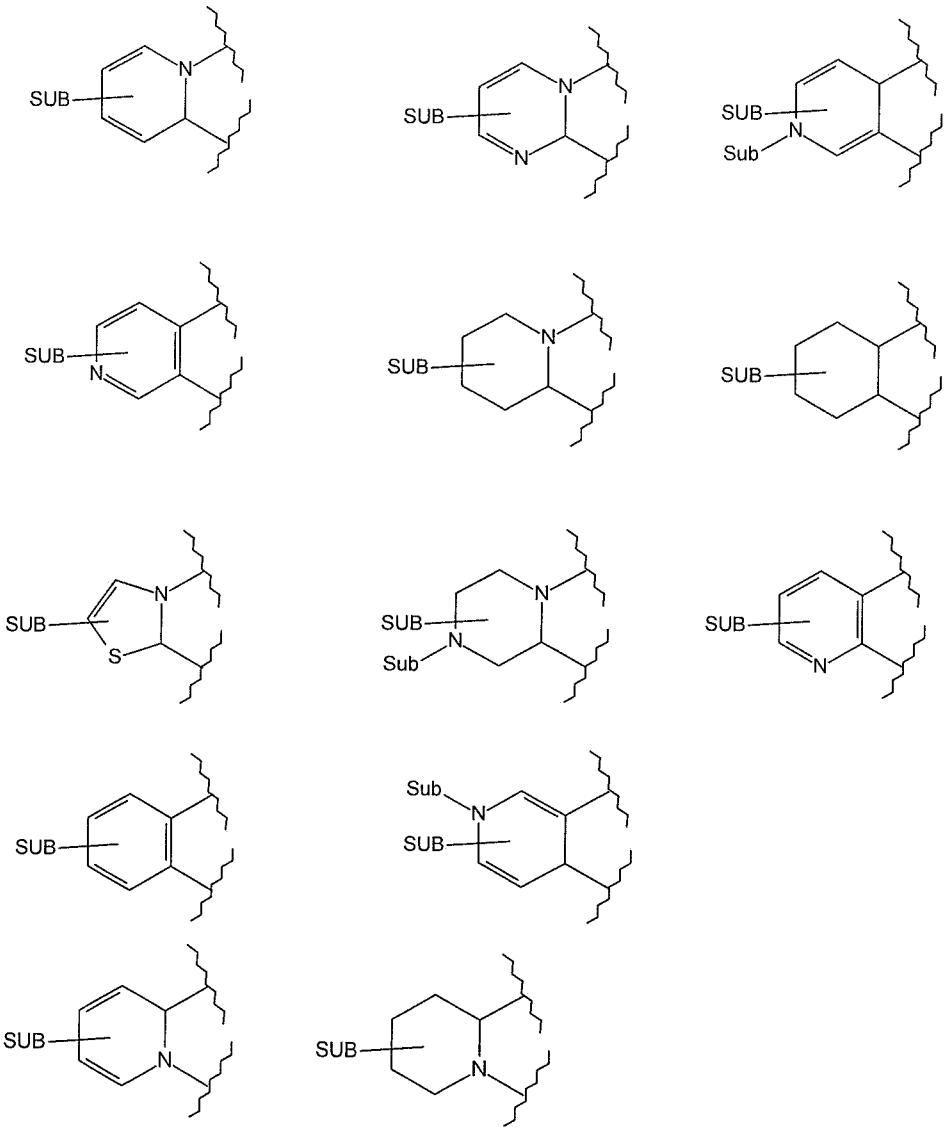


5. A compound for use as claimed in any of the preceding claims wherein: ring A-C(=O)- is represented as follows:



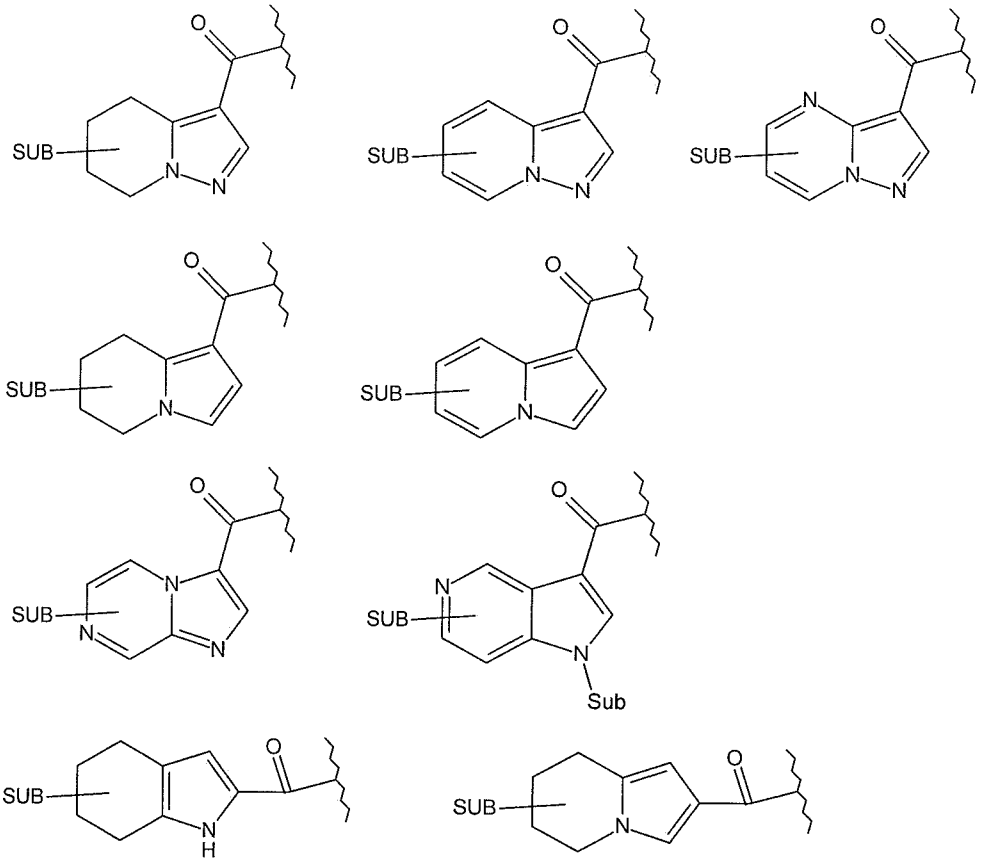
; and/or

ring B is represented as follows:



wherein "SUB" and "Sub" represent one or more possible substituents on the relevant atom e.g. carbon or nitrogen atom.

6. A compound for use as claimed in any one of the preceding claims, wherein the combined ring systems, i.e. Ring A-C(=O)- and Ring B is represented as follows:



where "SUB" represents one or more possible substituents on the bicycle i.e. on ring A and/or on ring B and "Sub" represents a possible optional substituent on the N atom of the bicycle and "NH" represents unsubstituted.

7. A compound for use as claimed in any one of the preceding claims, wherein:
X^a represents N or $C(R^c)$, e.g. CH;
X^b represents N, O, $C(R^c)$, e.g. CH, or C=O;
at least one of X^a and X^b represents N and the other represents $C(R^c)$, N or, in the case of X^b, O;
both X^a and X^b do not represent $C(R^c)$;
X^c is not present or represents –O-;
X^d is not present;
X^e is not present;
X^f is not present;
X^g, X^h, X^i and X^j independently are not present;
n1 represents 0, 1 or 2;
n2 represents 1 or 2;
n3 represents 1 or 2;

n4 represents 1 or 2;

q^1 represents $-CH_2-$, $-CH_2-CH_2-$, $-O-CH_2-$ or "-", i.e. in the latter case, n1 = 0, X^c is not present and X^d is not present;

q^2 represents $-CH_2-$ or $-CH_2-CH_2-$;

q^3 represents $-CH_2-$ or $-CH_2-CH_2-$; and/or

q^4 represents $-CH_2-$ or $-CH_2-CH_2-$.

8. A compound for use as claimed in any one of the preceding claims, wherein L^2 represents hydrogen, halo e.g. fluoro, $-OR^f$, $-C(O)R^g$, or an aromatic group optionally substituted by one or two e.g. one substituent(s) selected from $-OC_{1-6}$alkyl optionally substituted by one or more fluoro atoms or $-SF_5$, or, alternatively by halo, e.g. fluoro.

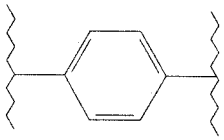
9. A compound for use as claimed in Claim 8, wherein R^f represents C_{1-6}alkyl or an aryl group optionally substituted by C_{1-3}alkyl optionally substituted by one or more fluoro atoms, so forming e.g. a $-CF_3$ group and/or R^g represents C_{1-3}alkyl optionally substituted by fluoro, or phenyl.

10. A compound of formula (IA) as defined in Claim 1 but wherein:

L^1 represents $-CH_2-$;

X^1 is not present or X^1 represents a carbocyclic aromatic linker group;

when X^1 represents a carbocyclic linker group it represents phenylene e.g. a 1,4-phenylene for instance:



at least one of X^a and X^b represents N and the other represents $C(R^c)$, N or ,in the case of X^b, O;

the X^a and X^b-containing spiro-cycle 3- to 6-membered ring attached to a 4- to 6-membered ring;

L^2 represents an aromatic group optionally substituted as defined herein, and/or, L^2 represents $-OR^f$ in which R^f represents an aryl group optionally substituted as defined herein;

when L^2 represents an optionally substituted aromatic group, L^2 is phenyl or a 5- or 6-membered heterocyclic group e.g. containing at least one nitrogen atom, so forming a pyridyl, thiazolyl or triazolyl ring; preferably the heterocyclic group is a pyridyl, where the optional substituents are as defined herein;

optional substituents on aromatic L^2 groups are selected from halo, C_{1-6} alkyl, $-CF_3$, $-OC_{1-6}$ alkyl and $-OCF_3$;

when R^f represents an aryl group, then it is preferably phenyl optionally substituted by C_{1-3} alkyl optionally substituted by fluoro;

ring A and ring B together represent a 8 or 9-membered bicyclic ring where ring A is a 5-membered ring and ring B is a 5 or 6-membered ring, in which both rings are preferably aromatic, containing at least one nitrogen atom, preferably the at least one nitogen atom is common to both rings);

optional substituents on ring A and ring B are halo, C_{1-3} alkyl and $-OC_{1-3}$ alkyl,

or a pharmaceutically-acceptable salt thereof.

11. A compound as claimed in Claim 10 wherein:

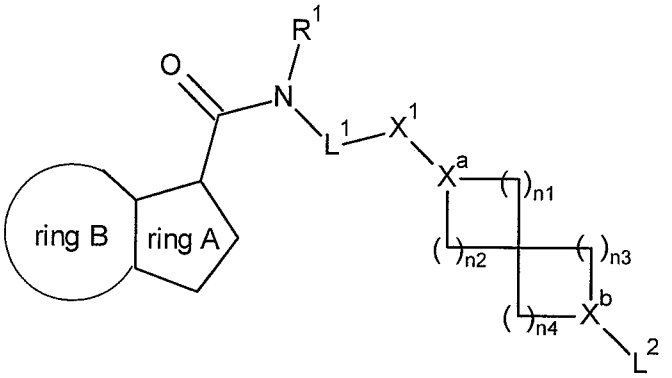
q^1 represents $-CH_2-$, $-CH_2-CH_2-$, $-O-CH_2-$ or "-", i.e. in the latter case, n1 = 0, X^c is not present and X^d is not present;

q^2 represents $-CH_2-$ or $-CH_2-CH_2-$;

q^3 represents $-CH_2-$ or $-CH_2-CH_2-$;

q^4 represents $-CH_2-$ or $-CH_2-CH_2-$.

12. A compound of formula (IB) as depicted below:



(IB)

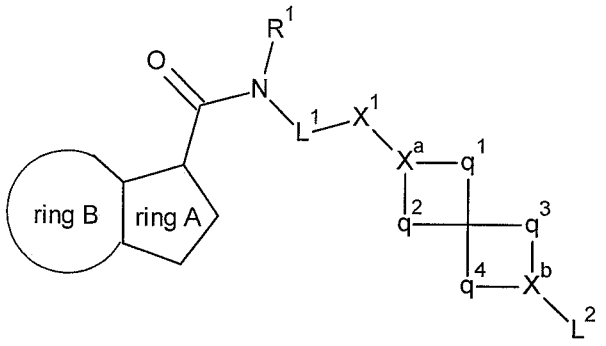
wherein

ring A, ring B, R^1, L^1, X^1, X^a, n1, n2, n3, n4, X^b and L^2 are as hereinbefore defined, and where, preferably:

n1, n2, n3 and n4 independently represent 1;

at least one of X^a and X^b represents N and the other represents CH or N.

13. A compound of formula (I)



(I)

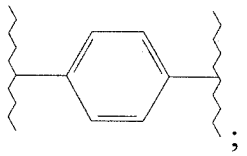
wherein

R^1 represents hydrogen;

L^1 represents $-CH_2-$;

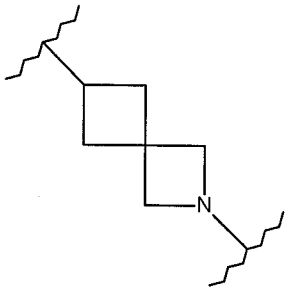
X^1 represents a carbocyclic aromatic linker group that is:

-phenylene-, especially a 1,4-phenylene, e.g.:



;

the spiro-cyclic moiety, i.e. the combined X^a and X^b-containing ring is represented as follows:

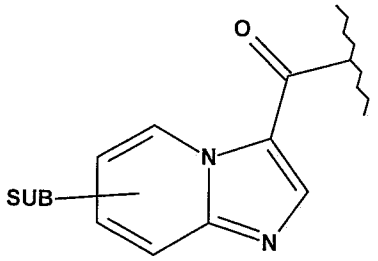


L^2 represents $-S(O)_2$-C_{1-6}alkyl optionally substituted by one or more fluoro atoms e.g. forming $-S(O)_2CF_3$;

ring A is a 5-membered aromatic ring containing at least one heteroatom, preferably containing at least one nitrogen atom;

ring B is a 5- or 6-membered ring, which is aromatic or non-aromatic, optionally containing one to four heteroatoms, preferably selected from nitrogen, oxygen and sulfur;

wherein the combined ring systems, i.e. Ring A-C(=O)- and Ring B are represented as follows:



optional substituents on ring A and ring B are halo, C_{1-3} alkyl and -OC_{1-3} alkyl,

or a pharmaceutically-acceptable salt thereof.

14. A compound as defined in any one of claims 10 to 13, for use as a pharmaceutical.

15. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and, as active ingredient, a therapeutically effective amount of a compound as defined in any one of claims 10-13.

16. Compound according to any one of claims 10-13 for use in the treatment of tuberculosis.

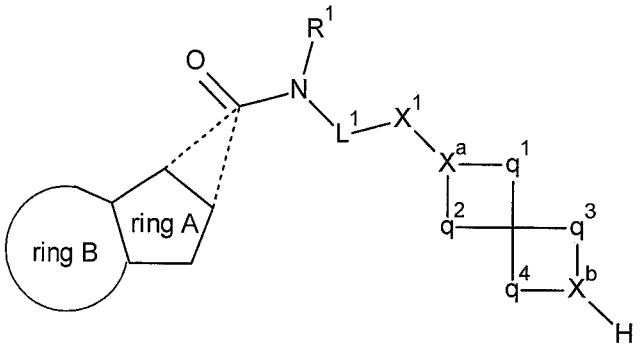
17. Use of a compound according to any one of claims 1 to 13 for the manufacture of a medicament for the treatment of tuberculosis.

18. A combination of (a) a compound according to any one of claims 1 to 13, and (b) one or more other anti-tuberculosis agent.

19. A product containing (a) a compound according to any one of claims 1 to 13, and (b) one or more other anti-tuberculosis agent, as a combined preparation for simultaneous, separate or sequential use in the treatment of tuberculosis.

20. A process for the preparation of a compound of formula (IA) as claimed in Claims 10-13, which process comprises:

(i) reaction of a compound of formula (II),



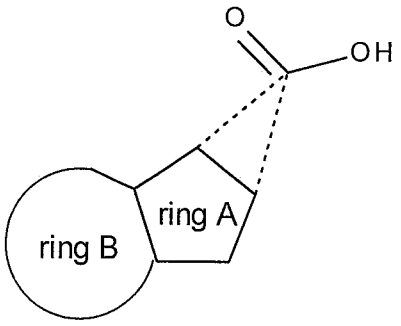
(II)

in which ring A, ring B, R^1, L^1, X^1, X^a, q^1, q^2, q^3, q^4 and X^b are as defined in Claim 1, with a compound of formula (III),

$$LG^1\text{-}L^2 \qquad \text{(III)}$$

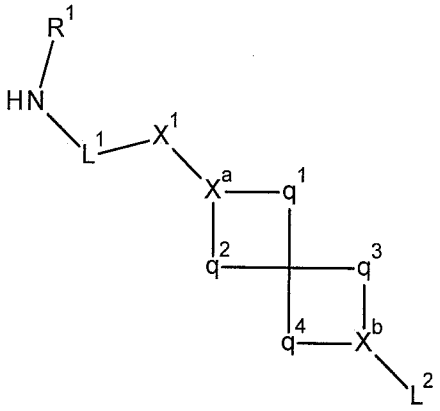
wherein L^2 is as defined in Claim 1 but when L^2 is not hydrogen, halo or linked to O or S, and LG^1 is a suitable leaving group;

(ii) reaction of a compound of formula (IV),



(IV)

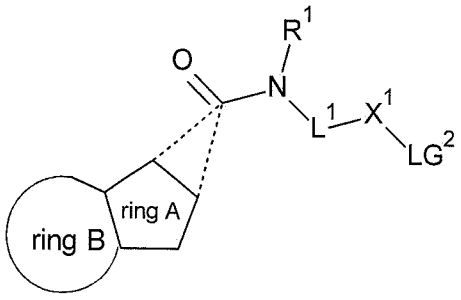
wherein ring A and ring B are as defined in Claim 1, or a suitable derivative thereof, such as a carboxylic acid ester derivative, with a compound of formula (V)



(V)

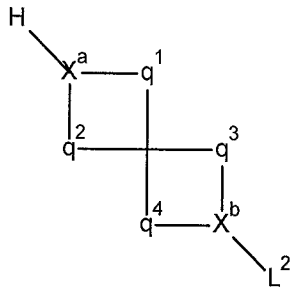
wherein R^1, L^1, X^1, X^a, q^1, q^2, q^3, q^4, X^b and L^2 are as hereinbefore defined, under amide coupling reaction conditions;

(iii) coupling of a compound of formula (VI),



(VI)

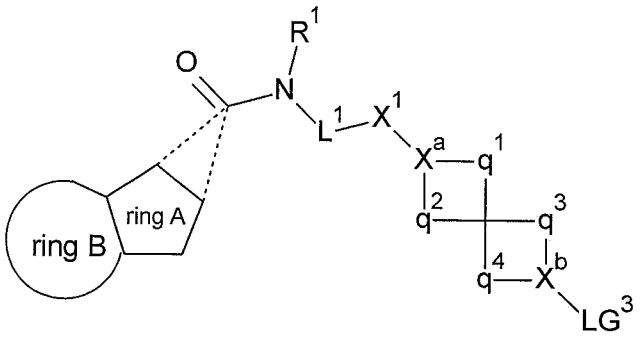
wherein ring A, ring B, R^1, L^1, and X^1 are as defined in Claim 1, and LG^2 represents a suitable leaving group, with a compound of formula (VI),



(VII)

wherein X^a, q^1, q^2, q^3, q^4, X^b and L^2 are as defined in Claim 1; or

(iv) coupling of a compound of formula (VIII),



(VIII)

wherein ring A, ring B, R^1, L^1, X^1, X^a, q^1, q^2, q^3, q^4 and X^b are as defined in Claim 1, and LG^3 represents a suitable leaving group as described above with respect to LG^2 and particularly represents chloro, bromo or iodo, with a compound of formula (IX),

$$LG^4\text{-}L^2 \qquad \text{(IX)}$$

wherein L^2 is as defined in Claim 1 but when L^2 is not hydrogen, halo or linked to O or S, and LG^4 is a suitable group.