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

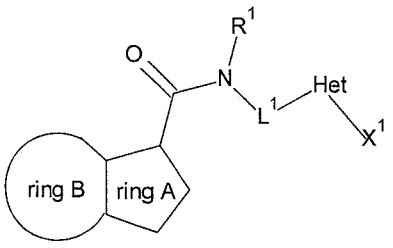
ring B is a 5- or 6-membered ring, which may be aromatic or non-aromatic, optionally containing one to four heteroatoms (preferably selected from nitrogen, oxygen and sulfur);

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 be referred to herein as "compounds of the invention" or "compounds of the disclosure".

In one aspect, there is provided a compound of formula (I) for use in the treatment of tuberculosis



(I)

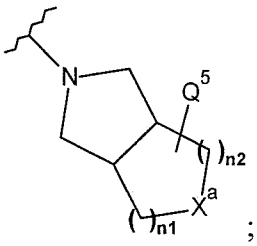
wherein
R^1 represents C_{1-6} alkyl or hydrogen;
L^1 represents a linker group -C(R^a)(R^b)- or is not present;
Het represents a linker group comprising at least one heteraromatic group optionally substituted by one or more substituents selected from fluoro, -O-R^c and C_{1-6} alkyl, wherein the C_{1-6} alkyl moiety is optionally substituted by one or more fluoro atoms;

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

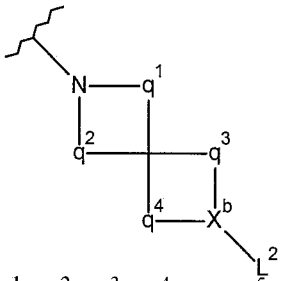
X^1 represents -N(R^2)(R^3);
R^2 and R^3:

(i) independently represent hydrogen or C_{1-6} alkyl optionally substituted by one or more substituents selected from Q^1 and =O;

(ii) independently represent aryl or heteroaryl, each of which is optionally substituted by one or more substituents selected from Q^2;
(iii) independently represent cycloalkyl or heterocycloalkyl, each of which is optionally substituted by one or more substituents selected from Q^3 and =O;
or
(iv) can be linked together to form:
a. a 3- to 8-membered ring optionally containing one to three heteroatoms (e.g. nitrogen, oxygen and/or sulfur), and which ring is substituted by one or more substituents selected from Q^4;
b. a "fused" bicyclic ring of the following type:



;
c. a "spiro" ring of the following type:



Q^1, Q^2, Q^3, Q^4 and Q^5 each independently represent one or more substituents selected from halo, C_{1-6} alkyl optionally substituted by one or more halo, e.g. fluoro, atoms, -OC_{1-6} alkyl optionally substituted by one or more halo, e.g. fluoro, atoms, aryl 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, and heteroaryl 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;

n1 and n2 independently represent 0 or 1;

X^a represents -$C(R^{a1})(R^{b1})$- or -$N(R^{c1})$-;
each R^{a1} and R^{b1} independently represents fluoro, hydrogen or C_{1-6} alkyl;
R^{c1} represents hydrogen or C_{1-6} alkyl;

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

R^d represents H, F or -OR^e wherein R^e represents H or C_{1-6} alkyl optionally substituted by one or more fluoro atoms;
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 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 $C(R^c)$ or when 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 $C(R^d)$ (e.g. CH) or N, then L^2 represents 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, wherein said aromatic group is 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 $-SF_5$;

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 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 optionally substituted by one or more fluoro atoms,

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 appropriate acid or base, optionally in a solvent, or in a medium in which the salt is insoluble, followed by removal of said solvent, or said medium, using standard techniques (e.g. *in vacuo*, by freeze-drying or by filtration). Salts may also be prepared by exchanging a counter-ion of a compound of the invention in the form of a salt with another counter-ion, for example using a suitable ion exchange resin.

The pharmaceutically acceptable acid addition salts as mentioned hereinabove are meant to comprise the therapeutically active non-toxic acid addition salt forms that the compounds of formula (I) are able to form. These pharmaceutically acceptable acid addition salts can conveniently be obtained by treating the base form with such appropriate acid. Appropriate acids comprise, for example, inorganic acids such as hydrohalic acids, e.g. hydrochloric or hydrobromic acid, sulfuric, nitric, phosphoric and the like acids; or organic acids such as, for example, acetic, propanoic, hydroxyacetic, lactic, pyruvic, oxalic (*i.e.* ethanedioic), malonic, succinic (*i.e.* butanedioic acid), maleic, fumaric, malic, tartaric, citric, methanesulfonic, ethanesulfonic, benzenesulfonic, *p*-toluenesulfonic, cyclamic, salicylic, *p*-aminosalicylic, pamoic and the like acids.

In another aspect, there is provided a compound as defined herein, for use as a pharmaceutical.

In another aspect, there is provided a pharmaceutical composition comprising a pharmaceutically acceptable carrier and, as active ingredient, a therapeutically effective amount of a compound as defined herein.

In another aspect, there is provided a compound as defined herein for use in the treatment of tuberculosis.

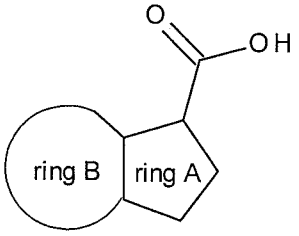
In another aspect, there is provided a use of a compound as defined herein for the manufacture of a medicament for the treatment of tuberculosis.

In another aspect, there is provided a combination of (a) a compound as defined herein, and (b) one or more other anti-tuberculosis agent.

In another aspect, there is provided 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 a bacterial infection.

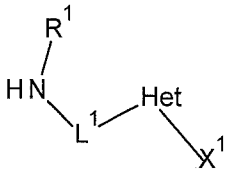
In another aspect, there is provided a process for the preparation of a compound of formula (I) as defined herein, which process comprises:

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



(II)

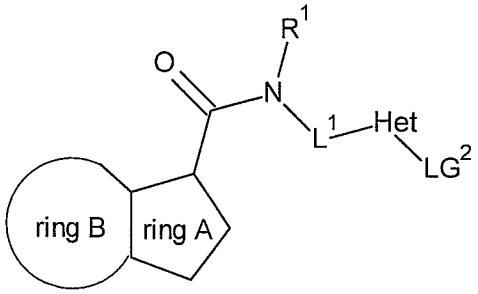
wherein ring A and ring B are as defined herein, or a suitable derivative thereof, with a compound of formula (III)



(III)

wherein Het, R^1, L^1 and X^1 are as defined herein;

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



(IV)

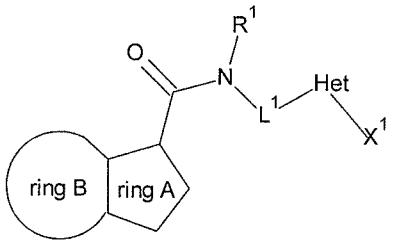
wherein ring A, ring B, R^1, L^1, and Het are as defined herein, and LG^2 represents a suitable leaving group, with a compound of formula (V),

$$X^1\text{-}H \qquad (V)$$

wherein X^1 is as defined herein.

CLAIMS

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



(I)

wherein

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

L^1 represents a linker group $-C(R^a)(R^b)-$ or is not present;

Het represents a linker group comprising at least one heteraromatic group optionally substituted by one or more substituents selected from fluoro, $-O-R^c$ and C_{1-6} alkyl, wherein the C_{1-6} alkyl moiety is optionally substituted by one or more fluoro atoms;

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

X^1 represents $-N(R^2)(R^3)$;

R^2 and R^3:

(i) independently represent hydrogen or C_{1-6} alkyl optionally substituted by one or more substituents selected from Q^1 and =O;

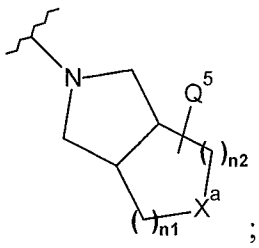
(ii) independently represent aryl or heteroaryl, each of which is optionally substituted by one or more substituents selected from Q^2;

(iii) independently represent cycloalkyl or heterocycloalkyl, each of which is optionally substituted by one or more substituents selected from Q^3 and =O; or

(iv) can be linked together to form:

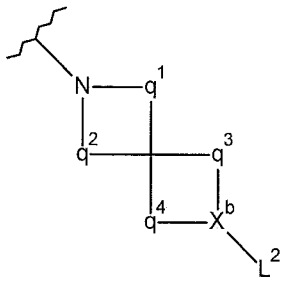
a. a 3- to 8-membered ring optionally containing one to three heteroatoms (e.g. nitrogen, oxygen and/or sulfur), and which ring is substituted by one or more substituents selected from Q^4;

b. a "fused" bicyclic ring of the following type:



;

c. a "spiro" ring of the following type:



Q^1, Q^2, Q^3, Q^4 and Q^5 each independently represent one or more substituents selected from halo, C_{1-6} alkyl optionally substituted by one or more halo, e.g. fluoro, atoms, -OC_{1-6} alkyl optionally substituted by one or more halo, e.g. fluoro, atoms, aryl 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, and heteroaryl 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;

n1 and n2 independently represent 0 or 1;

X^a represents -$C(R^{a1})(R^{b1})$- or -$N(R^{c1})$-;
each R^{a1} and R^{b1} independently represents fluoro, hydrogen or C_{1-6} alkyl;
R^{c1} represents hydrogen or C_{1-6} alkyl;

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

R^d represents H, F or -OR^e, wherein R^e represents H or C_{1-6} alkyl optionally substituted by one or more fluoro atoms;

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 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 $C(R^c)$ or when 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 $C(R^d)$ (e.g. CH) or N, then L^2 represents 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, wherein said aromatic group is 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 $-SF_5$;

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

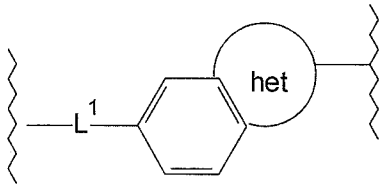
ring B is a 5- or 6-membered ring, which may be aromatic or non-aromatic, optionally containing one to four heteroatoms preferably selected from nitrogen, oxygen or sulfur;

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 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; and/or
R^a and R^b independently represent hydrogen.

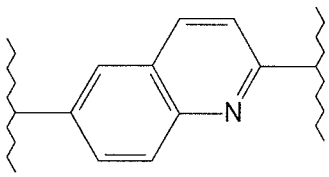
3. A compound for use as claimed in Claim 1 or Claim 2, wherein when the heteroaromatic linker group (Het) is a bicyclic heteroaromatic group linked to L^1, or the amido moiety when L^1 is not present, via a carbocyclic aromatic moiety, forms e.g.:

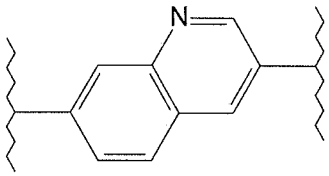


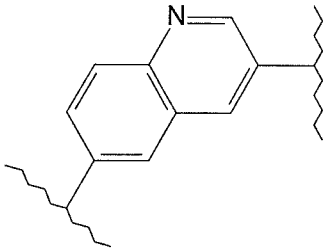
in which "het" in the above instance is a heteroaromatic 5- or 6-membered ring.

4. A compound for use as claimed in Claim 3, wherein the linker group is a fused bicyclic ring system comprising a phenyl and/or a 5- or 6-membered monocyclic heteroaryl group for instance forming a 9- or 10-membered heteroaromatic group, which consists of two separate rings fused with each other, in which each ring is 5- or 6-membered so forming a 6,6- or 6,5- or fused bicyclic ring, hence including groups such as those described below:

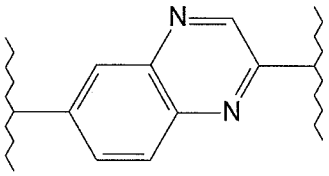
-quinolylene such as 2-quinolylene or 3-quinolylene, e.g.:







-quinoxalinyl such as 2-quinolylene, e.g.:



5. A compound for use as claimed in any of the preceding claims, wherein when X^1 represents $-N(R^2)(R^3)$, then:

(i) R^2 and R^3 independently represent C_{1-3} alkyl, e.g. methyl or ethyl, optionally substituted by one or more e.g. one substituent(s) selected from Q^1;

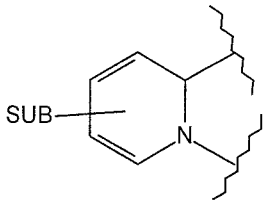
(ii) R^2 and R^3 are linked together to form:

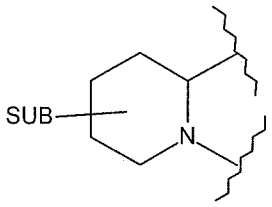
a. a 4- to 6-membered ring optionally containing one further heteroatom, e.g. forming a piperidinyl, piperazinyl or azetidinyl ring, which is optionally and preferablysubstituted by Q^4;

b. a fused bicyclic ring in which X^a represents $-CH_2-$ and which is optionally substituted e.g. at the X^a position by one or more e.g. one Q^5 substituent(s);

c. a spiro ring system, in which X^b represents CH and L^2 is present and as defined herein.

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

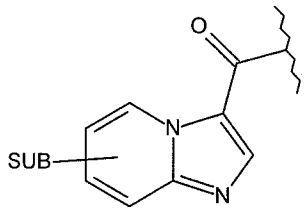


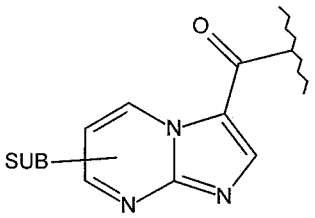


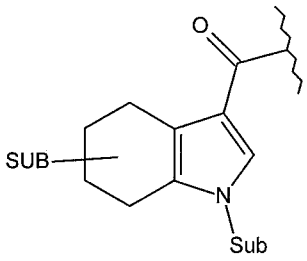
,

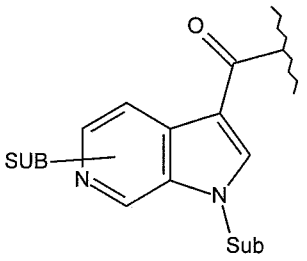
wherein "SUB" and "Sub" represent one or more possible substituents on the relevant atom e.g. carbon or nitrogen atom.

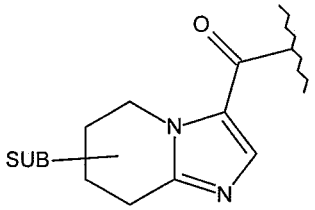
7. A compound for use as claimed in any one of the preceding claims, wherein the combined ring systems, i.e. Ring A-C(=O)- and Ring B represent as follows:

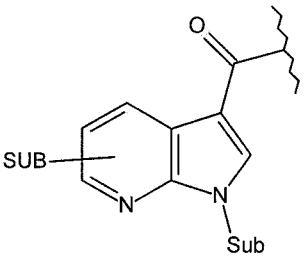


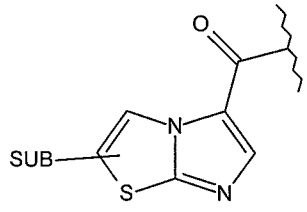


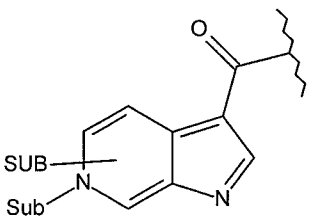


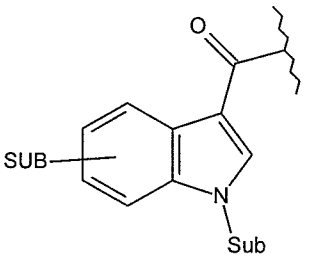


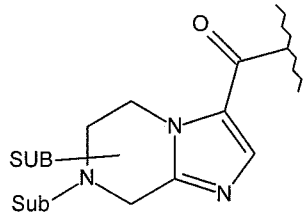


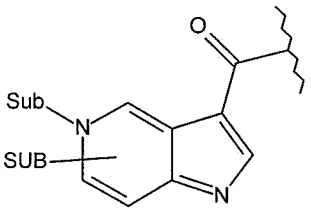


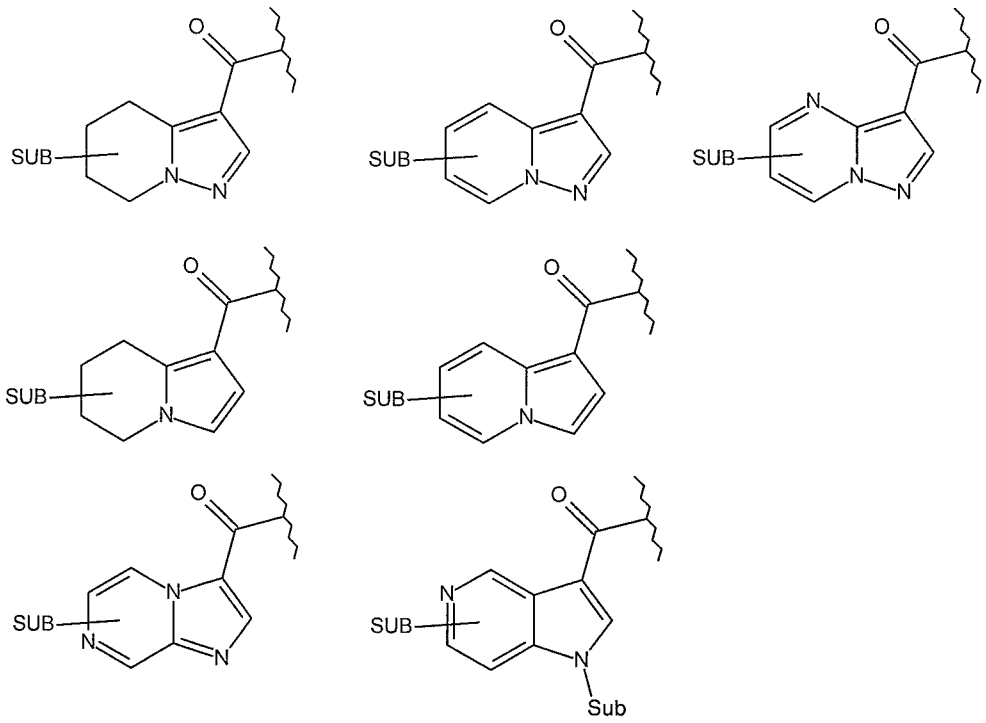










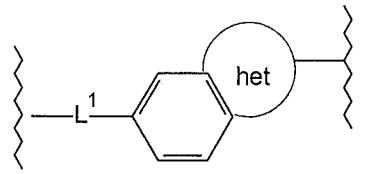


where "SUB" represents one or more possible substituents on the bicycle i.e. on ring A and/or on ring B and "Sub" represents a possible optional substituent on the N atom of the bicycle while "NH" represents unsubstituted.

8. A compound for use as claimed in any of the preceding claims, wherein:
   Q^1 represents aryl, e.g. phenyl, optionally substituted by $-OC_{1-3}$alkyl optionally substituted by one or more fluoro atoms, so forming e.g. a $-OCF_3$ group;
   Q^4 represents aryl, e.g. phenyl, optionally substituted by $-OC_{1-3}$alkyl optionally substituted by one or more fluoro atoms, so forming e.g. a $-OCF_3$ group;
   Q^5 represents halo e.g. fluoro;
   X^c, X^d, X^e and X^f are independently not present;
   n1 and n2 independently represent 1;
   X^g, X^h, X^i and X^j are independently not present;
   n3 and n4 independently represent 1; and/or
   L^2 represents an aromatic group, e.g. aryl or phenyl, optionally substituted by one or more e.g. one substituent(s) selected from $-OC_{1-3}$alkyl optionally substituted by one or more fluoro atoms, so forming e.g. a $-OCF_3$ group.

9. A compound of formula (I) as defined in Claim 1 but wherein:
   L^1 represents $-CH_2-$;

Het represents a bicyclic heteroaromatic group linked to L^1 or the amido moiety when L^1 is not present, via a carbocyclic aromatic moiety, forming e.g.:



in which "het" in the above instance is a heteroaromatic 5- or 6-membered ring;
when X^1 represents $-N(R^2)(R^3)$, then:

(i) R^2 and R^3 independently represent C_{1-3} alkyl, e.g. methyl or ethyl, optionally substituted by one or more e.g. one substituent(s) selected from Q^1, or when both R^2 and R^3 represent alkyl, then at least one is substituted by Q^1 in which Q^1 represents an optionally substituted aryl group as defined herein;

(ii) R^2 and R^3 are linked together to form:

a. a 4- to 6-membered ring optionally containing one further heteroatom, e.g. forming a piperidinyl, piperazinyl or azetidinyl ring, which is substituted by one or two substituents selected from Q^4, whereby at least one Q^4 substituent is present that represents an optionally substituted aryl group as defined herein;

b. a fused bicyclic ring in which X^a represents $-CH_2-$ and which is optionally substituted e.g. at the X^a position by one or more e.g. one Q^5 substituent(s);

c. a spiro ring system, in which X^b represents CH and L^2 is present and as defined herein;

L^2 represents an aromatic group, e.g. aryl or phenyl, optionally substituted by one or more e.g. one substituent(s) selected from $-OC_{1-3}$alkyl optionally substituted by one or more fluoro atoms, so forming e.g. a $-OCF_3$ group;
ring A and ring B together represent a 8 or 9-membered bicyclic ring containing at least one nitrogen atom, wherein ring A is a 5-membered aromatic ring and ring B is a 5 or 6-membered aromatic ring, and wherein 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; and
other integers are as defined herein.

10. A compound as claimed in claim 9 wherein:

when Q^1 represents aryl, then it is an optionally substituted as defined herein, e.g. by one or more substituents selected from -OC_{1-3}alkyl optionally substituted by one or more fluoro atoms, so forming e.g. a -OCF_3 group;

when Q^4 represents aryl, then it is an optionally substituted phenyl as defined herein, e.g. by one or more substituents selected from -OC_{1-3}alkyl optionally substituted by one or more fluoro atoms, so forming e.g. a -OCF_3 group;

when Q^4 represents a non-aromatic substituent, then it may represent fluoro;

Q^5 represents halo (e.g. fluoro);

X^c, X^d, X^e and X^f are independently not present;

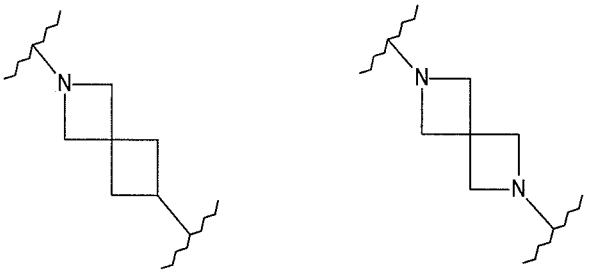
n1 and n2 independently represent 1;

X^g, X^h, X^i and X^j are independently not present;

n3 and n4 independently represent 1.

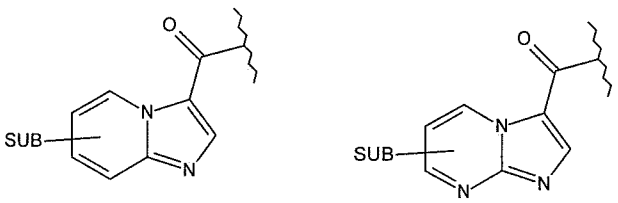
11. A compound as claimed in claim 9 or claim 10 wherein:

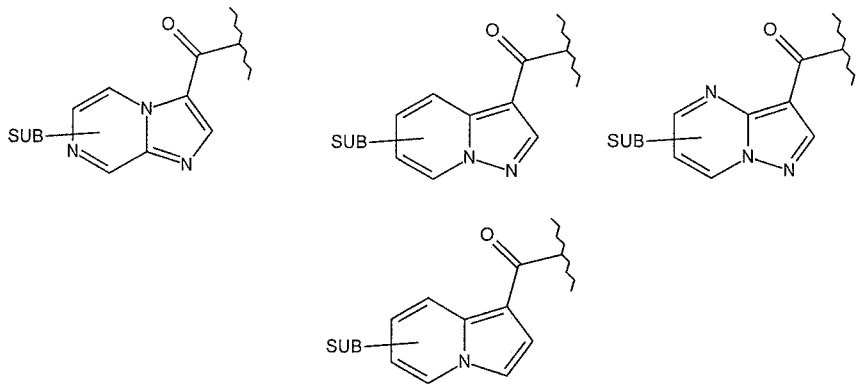
the X^b-containing rings are represented as defined herein or more particularly as follows:



or any one of the above-mentioned representations; and/or

the ring A-C(=O)- and ring B bicycles are represented as defined herein or more particularly as follows:





or any one of the above-mentioned representations.

12. A compound as defined in any of claims 9 to 11, for use as a pharmaceutical.

13. 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 9-11.

14. Compound according to any one of claims 9-11 for use in the treatment of tuberculosis.

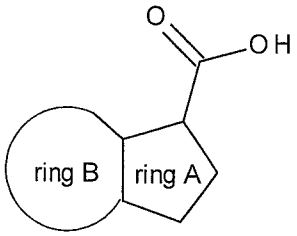
15. Use of a compound as defined in any one of claims 1 to 11 for the manufacture of a medicament for the treatment of tuberculosis.

16. A combination of (a) a compound as defined in any one of claims 1 to 11, and (b) one or more other anti-tuberculosis agent.

17. A product containing (a) a compound as defined in any one of claims 1 to 11, and (b) one or more other anti-tuberculosis agent, as a combined preparation for simultaneous, separate or sequential use in the treatment of a bacterial infection.

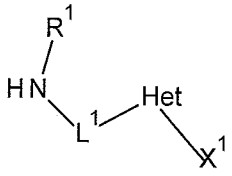
18. A process for the preparation of a compound of formula (I) as claimed in Claims 9-11, which process comprises:

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



(II)

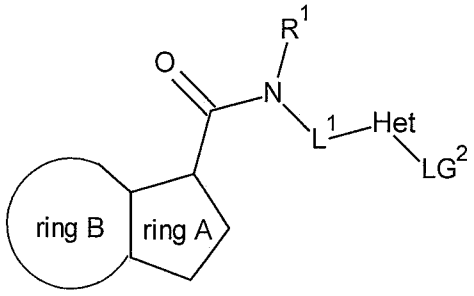
wherein ring A and ring B are as defined in Claim 1, or a suitable derivative thereof, with a compound of formula (III)



(III)

wherein Het, R^1, L^1 and X^1 are as defined in Claim 1;

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



(IV)

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

X^1-H (V)

wherein X^1 is as defined in Claim 1.