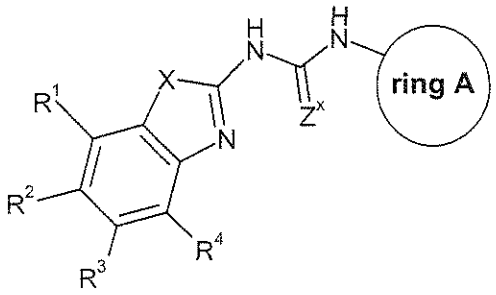
SUMMARY OF THE INVENTION

There is now provided, in one aspect, a compound of formula (I) for use in the treatment of a bacterial infection (e.g. a mycobacterial infection), wherein the compound of formula (I) represents:



(I)

wherein

R^1, R^2, R^3 and R^4 each independently represent hydrogen, halo, -CN, R^{t1}, -O-R^{t2}, -C(O)N(R^{t3})(R^{t4}), -SO_2R^{t5}, -N(H)SO_2R^{t6}, -N(R^{t7})(R^{t8}) or an aryl or heterocyclic group (which latter two groups are themselves optionally substituted by one or more substituents selected from halo and C_{1-6} alkyl);

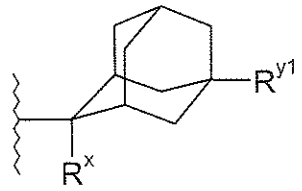
R^{t1}, R^{t2}, R^{t3}, R^{t4}, R^{t5}, R^{t6}, R^{t7} and R^{t8} independently represent hydrogen or C_{1-6} alkyl optionally substituted by one or more halo atoms, or, R^{t3} and R^{t4} and/or R^{t7} and R^{t8} may be linked together with the nitrogen atom to which they are attached to form a 3- to 7-membered ring, optionally containing one to three (e.g. one) further heteroatom(s) and optionally contain one to three double bonds;

Z^x represents O or S;

X represents S or O;

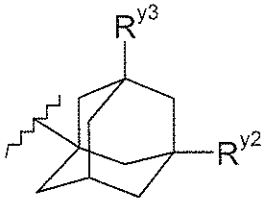
ring A represents either:

(i)



; or

(ii)



;

R^x represents hydrogen or C_{1-6} alkyl optionally substituted by one or more subsitutents selected from fluoro, -CN, $-OR^{x1}$, $-C(O)R^{x2}$ and $-C(O)NR^{x3}$;

R^{x1}, R^{x2} and R^{x3} independently represent hydrogen or C_{1-6} alkyl;

R^{y1}, R^{y2} and R^{y3} independently represent hydrogen, halo (e.g. fluoro), C_{1-6} alkyl, $-OR^{y4}$, $-C(O)-R^{y5}$ or $-CH_2-OR^{y6}$;

R^{y4}, R^{y5} and R^{y6} independently represent hydrogen or C_{1-6} alkyl;

or a pharmaceutically acceptable salt (e.g. acid addition salt) thereof.

The above-mentioned compounds of formula (I) (or salts thereof) may be referred to herein as "compounds of the invention". Such compounds are indicated as being useful in the treatment of a bacterial infection. However, some compounds mentioned above may also be useful as medicaments, and some compounds may be novel.

Hence, in another aspect ~~further embodiment of the invention~~, there is a compound of formula I, for use as a pharmaceutical, as defined herein, but in which:
R^1, R^2, R^3 and R^4 each independently represent hydrogen, fluoro or C_{1-6} alkyl (optionally substituted by one or more halo subsituents). Such compounds may also be contained/comprised in pharmaceutical formulations/compositons. In another aspect, there is a pharmaceutical composition comprising a compound as defined herein and a pharmaceutically acceptable carrier.

In a further embodiment of the ~~invention~~disclosure, there is provided novel compounds *per se*. In this respect, there is provided a compound of formula I, as defined herein, but in which:
R^1, R^2, R^3 and R^4 each independently represent hydrogen, fluoro or C_{1-6} alkyl optionally substituted by one or more halo subsituents (but which alkyl group is preferably substituted with one or more halo atoms);
for instance, in which:
one or two of R^1 to R^4 represents fluoro, and the remaining represent hydrogen;
one of R^1 to R^4 represents $-CF_3$, and the remaining represent hydrogen.

In another aspect, there is a compound of formula I, as defined herein, but in which: R^1, R^2, R^3 and R^4 each independently represent hydrogen, fluoro or C_{1-6} alkyl optionally substituted by one or more halo subsituents (but preferably unsubstituted); for instance, in which:
one or two of R^1 to R^4 represents fluoro, and the remaining represent hydrogen;
one of R^1 to R^4 represents $-CF_3$, and the remaining represent hydrogen,
provided that the following compounds of formula I are excluded:
those in which X represents S, Z^x represents O, R^1 and R^4 represent H, R^2 represents $-CH_3$, ring A represents ring (ii) in which R^{y2} and R^{y3} both represent hydrogen, and R^3 represents hydrogen or $-CH_3$.

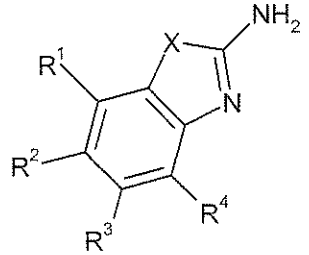
Insofar as the embodiment of the ~~invention~~ disclosure in which novel compounds *per se* are concerned, the following compounds are preferably excluded from the scope, compounds of formula I in which X represents S, Z^x represents O, R^1 and R^4 represent H, R^2 represents $-CH_3$, ring A represents ring (ii) in which R^{y2} and R^{y3} both represent hydrogen, and R^3 represents hydrogen or $-CH_3$.

The above mentioned embodiments of the disclosure ~~invention~~ (for use as a pharmaceutical and the novel *per se* compounds) may be combined with other preferred features of the disclosure~~invention~~, for instance those described hereinafter.

In another aspect, there is a combination for use in the treatment of a bacterial infection, wherein the combination comprises: (i) a compound as defined herein; and (ii) another therapeutic agent for use in the treatment of a bacterial infection.

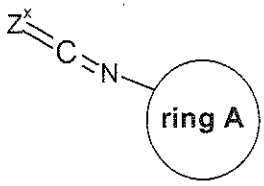
In another aspect, there is a process for preparing a composition as defined herein, wherein a therapeutically active amount of a compound as defined herein is intimately mixed with a pharmaceutically acceptable carrier.

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



(II)

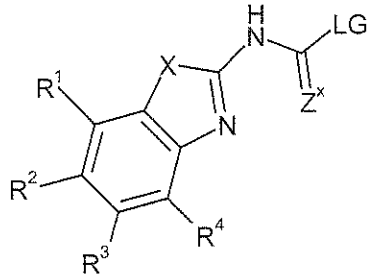
wherein X, R^1, R^2, R^3 and R^4 are as defined herein, with a compound of formula (III),



(III)

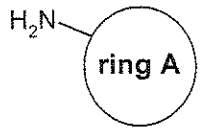
wherein ring A and Z^x are as defined herein;

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



(IV)

wherein LG represents a suitable leaving group, and R^1, R^2, R^3, R^4, X and Z^x are as defined herein, with a compound of formula (V),



(V)

wherein ring A is as defined herein.

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.

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)).

5. A compound of formula I for use as a pharmaceutical, wherein the compound is as claimed in any one of the preceding claims, but in which R^1, R^2, R^3 and R^4 each independently represent hydrogen, fluoro or C_{1-6} alkyl substituted by one or more halo subsituents.

6. A pharmaceutical composition comprising a compound as defined in claim 5 and a pharmaceutically acceptable carrier.

7. A compound of formula I, as defined herein in any one of the preceding claims, but in which:
R^1, R^2, R^3 and R^4 each independently represent hydrogen, fluoro or C_{1-6} alkyl optionally substituted by one or more halo subsituents (but preferably unsubstituted); for instance, in which:
one or two of R^1 to R^4 represents fluoro, and the remaining represent hydrogen;
one of R^1 to R^4 represents $-CF_3$, and the remaining represent hydrogen,
provided that the following compounds of formula I are excluded:
those in which X represents S, Z^x represents O, R^1 and R^4 represent H, R^2 represents $-CH_3$, ring A represents ring (ii) in which R^{y2} and R^{y3} both represent hydrogen, and R^3 represents hydrogen or $-CH_3$.

8. A combination for use in the treatment of a bacterial infection, wherein the combination comprises: (i) a compound as defined in any one of claims 1 to 7; and (ii) another therapeutic agent for use in the treatment of a bacterial infection.

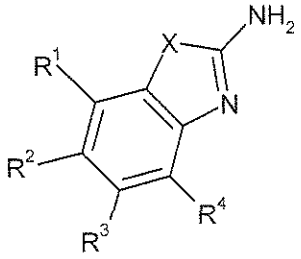
9. A compound for use as claimed in any one of claims 1 to 4, or a combination for use as claimed in claim 8, wherein the bacterial infection is a mycobacterial infection.

10. A compound for use or a combination for use as claimed in claim 9, wherein the mycobacterial infection is *Mycobacterium tuberculosis*.

11. A process for preparing a composition as claimed in claim 6, wherein a therapeutically active amount of a compound as claimed in claim 5 is intimately mixed with a pharmaceutically acceptable carrier.

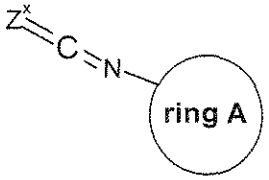
12. A process for the preparation of a compound as defined in ~~any one of claims 1 to 4 or~~ claim 7, which process comprises:

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



(II)

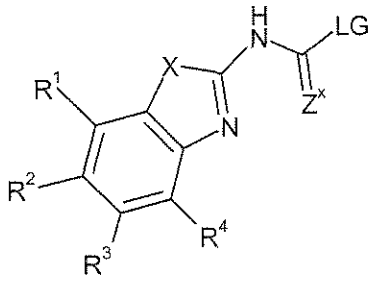
wherein X, R^1, R^2, R^3 and R^4 are as defined in claim ~~1~~7, with a compound of formula (III),



(III)

wherein ring A and Z^x are as defined in claim ~~1~~7;

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



(IV)

wherein LG represents a suitable leaving group, and R^1, R^2, R^3, R^4, X and Z^x are as defined in claim ~~1~~7, with a compound of formula (V),



(V)

wherein ring A is as defined in claim ~~1~~7.