It is therefore an aim of the present invention to provide reduced or oxidised derivatives of active compounds which are able to demonstrate similar to or better than the parent active compound. It is also an aim of the present invention to provide compounds which have an IC50 value comparable to or better than that of the parent active. Ideally, these reduced or oxidised derivatives will have good stability and bioavailability relative to the parent active compound. It is thus an aim to provide reduced or oxidised derivatives having improved stability. Ideally, the reduced or oxidised derivatives will have an extended shelf-life. It is thus an aim of the present invention to provide further compounds having improved bioavailability.

This invention provides compounds that achieve one or more of the above aims. The compounds may be active in their own right or may metabolise or react in aqueous media to yield a parent active compound.

Summary

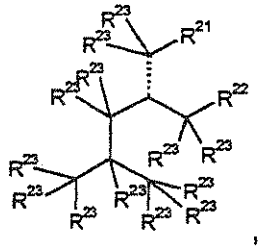
In one aspect, there is provided a method of preparing an oxidised or reduced pharmaceutical active derivative, comprising:

(i) obtaining a parent pharmaceutical active;

(ii) oxidising the parent pharmaceutical active to provide an oxidised pharmaceutical active derivative which is in an oxidation state one or more oxidation states higher than the parent pharmaceutical active; or reducing the parent pharmaceutical active to provide a reduced pharmaceutical active derivative which is in an oxidation state one or more oxidation states lower than the parent pharmaceutical active; and

(iii) isolating the oxidised or reduced pharmaceutical active derivative;

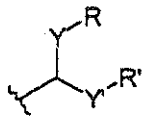
wherein the oxidised or reduced pharmaceutical active derivative is a compound of formula III:



wherein:

each R^{23} is independently selected from the group comprising: -H, -Cl, -F and C_{1-3} alkyl;

R^{21} is –NRR'; and

R^{22} is selected from the group comprising: –CR"O, -CR"=NOR"', -N(=NR")R", CR"R"OR" and 

;

wherein:

-Y- is selected from the group comprising: =N-, -O- and -S-;

-Y'- is selected from the group comprising: -O- and -S-;

each R, R' and R" is independently selected from the group comprising: -H and C_{1-4} alkyl; or each R" is independently selected from the group comprising: -H and C_{1-4} alkyl, and R and R' join to form a 5 to 8 membered ring together with the atom(s) to which they are bonded; and

R"' is selected from the group comprising: H, C_{1-4} alkyl and $-(CR''''R'''')_n$-aryl; wherein R"" is selected from the group comprising: H and aryl and wherein n is from 1 to 4;

or

wherein R^{21} is –N= and R^{22} is –CR"= and R^{21} and R^{22} join to form a 5 membered ring together with the atoms to which they are bonded; or

wherein R^{21} is –NR"- and R^{22} is –C(O)- and R^{21} and R^{22} join to form a 5 membered ring together with the atoms to which they are bonded.

Detailed Description

According to a first aspect, the present invention provides a method of preparing an oxidised or reduced pharmaceutical active derivative, comprising:

(i) obtaining a parent pharmaceutical active;

(ii) oxidising the parent pharmaceutical active to provide an oxidised pharmaceutical active derivative which is in an oxidation state one or more oxidation states higher than the parent pharmaceutical active; or reducing the parent pharmaceutical active to provide a reduced

pharmaceutical active derivative which is in an oxidation state one or more oxidation states lower than the parent pharmaceutical active; and

(iii) isolating the oxidised or reduced pharmaceutical active derivative.

The term derivative in this context means a compound that is identical to a target active compound (which may be an approved drug compound or a known active structural compound of the same class as an approved drug compound) in terms of its structure except that one or more functional groups in the compound have been oxidised or reduced.

This approach is novel and the finding of activity for compounds of the invention is contrary to normal expectations in the pharmaceutical industry. Whilst, it is may be conventional in the industry to aim to provide prodrugs of certain compounds, the industry has been very wary of modifying active compounds to any significant degree. In addition, there is a concern in the industry that compounds such as aldehydes could be

CLAIMS:

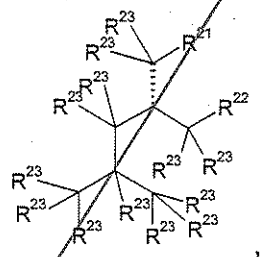
1. A method of preparing an oxidised or reduced pharmaceutical active derivative, comprising:

i obtaining a parent pharmaceutical active;

ii oxidising the parent pharmaceutical active to provide an oxidised pharmaceutical active derivative which is in an oxidation state one or more oxidation states higher than the parent pharmaceutical active; or reducing the parent pharmaceutical active to provide a reduced pharmaceutical active derivative which is in an oxidation state one or more oxidation states lower than the parent pharmaceutical active; and

iii isolating the oxidised or reduced pharmaceutical active derivative;.

wherein the oxidised or reduced pharmaceutical active derivative is a compound of formula III:



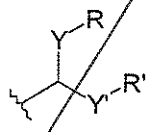
,

wherein:

each R^{23} is independently selected from the group comprising: -H, -Cl, -F and C_{1-3} alkyl;

R^{21} is –NRR'; and

R^{22} is selected from the group comprising: –CR"O, -CR"=NOR'", -N(=NR")R",



CR"R"OR" and ;

wherein:

-Y- is selected from the group comprising: =N-, -O- and -S-;

-Y'- is selected from the group comprising: -O- and -S-;

each R, R' and R" is independently selected from the group comprising: -H and C_{1-4} alkyl; or each R" is independently selected from the group comprising: -H and C_{1-4} alkyl, and R and R' join to form a 5 to 8 membered ring together with the atom(s) to which they are bonded; and

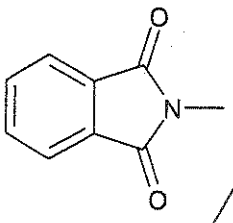
R''' is selected from the group comprising: H, C_{1-4} alkyl and $-(CR'''R'''')_n$-aryl; wherein R'''' is selected from the group comprising: H and aryl and wherein n is from 1 to 4;

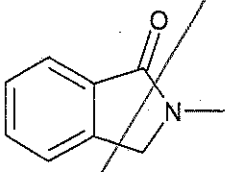
or

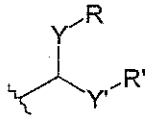
wherein R^{21} is –N= and R^{22} is –CR''= and R^{21} and R^{22} join to form a 5 membered ring together with the atoms to which they are bonded; or

wherein R^{21} is –NR''- and R^{22} is –C(O)- and R^{21} and R^{22} join to form a 5 membered ring together with the atoms to which they are bonded.

2. The method of claim 1, wherein R^{21} is $-NH_2$.

3. The method of claim 1, wherein R^{21} is .

4. The method of claim 1, wherein R^{21} is .

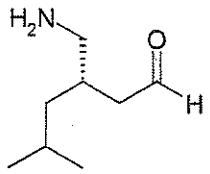
5. The method of any preceding claim, wherein R^{22} is –CHO, –CH=NOH, CH_2OH or .

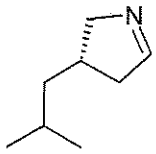
6. The method of claim 1, wherein R^{21} is –N= and R^{22} is –CR''= and R^{21} and R^{22} join to form a 5 membered ring together with the atoms to which they are bonded.

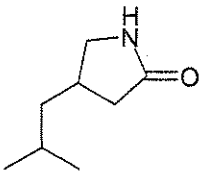
7. The method of claim 6, wherein R'' is H.

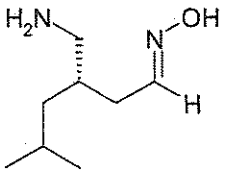
8. The method of any preceding claim, wherein each R^{23} is H.

9. The method of claim 1, wherein the compound of formula III is selected from the group comprising:

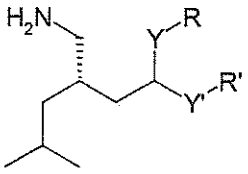




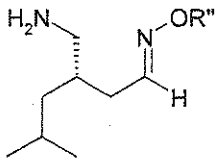




and



10. The method of claim 1, wherein the compound of formula III is:



CLAIMS:

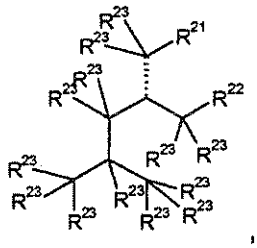
1. A method of preparing an oxidised or reduced pharmaceutical active derivative, comprising:

(i) obtaining a parent pharmaceutical active;

(ii) oxidising the parent pharmaceutical active to provide an oxidised pharmaceutical active derivative which is in an oxidation state one or more oxidation states higher than the parent pharmaceutical active; or reducing the parent pharmaceutical active to provide a reduced pharmaceutical active derivative which is in an oxidation state one or more oxidation states lower than the parent pharmaceutical active; and

(iii) isolating the oxidised or reduced pharmaceutical active derivative;

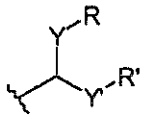
wherein the oxidised or reduced pharmaceutical active derivative is a compound of formula III:



wherein:

each R^{23} is independently selected from the group comprising: -H, -Cl, -F and C_{1-3} alkyl;

R^{21} is –NRR'; and

R^{22} is selected from the group comprising: –CR"O, -CR"=NOR"', -N(=NR")R", CR"R"OR" and  ;

wherein:

-Y- is selected from the group comprising: =N-, -O- and -S-;

-Y'- is selected from the group comprising: -O- and -S-;

each R, R' and R" is independently selected from the group comprising: -H and C_{1-4} alkyl; or each R" is independently selected from the group comprising: -H and C_{1-4} alkyl, and R and R' join to form a 5 to 8 membered ring together with the atom(s) to which they are bonded; and

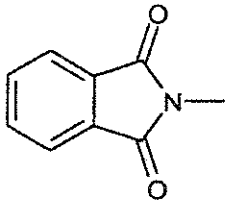
R''' is selected from the group comprising: H, C_{1-4} alkyl and $-(CR''''R'''')_n$-aryl; wherein R'''' is selected from the group comprising: H and aryl and wherein n is from 1 to 4;

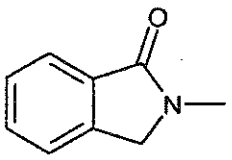
or

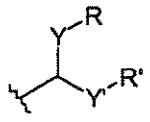
wherein R^{21} is –N= and R^{22} is –CR''= and R^{21} and R^{22} join to form a 5 membered ring together with the atoms to which they are bonded; or

wherein R^{21} is –NR''- and R^{22} is –C(O)- and R^{21} and R^{22} join to form a 5 membered ring together with the atoms to which they are bonded.

2. The method of claim 1, wherein R^{21} is $-NH_2$.

3. The method of claim 1, wherein R^{21} is .

4. The method of claim 1, wherein R^{21} is .

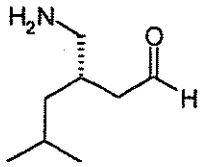
5. The method of any preceding claim, wherein R^{22} is –CHO, –CH=NOH or .

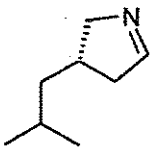
6. The method of claim 1, wherein R^{21} is –N= and R^{22} is –CR''= and R^{21} and R^{22} join to form a 5 membered ring together with the atoms to which they are bonded.

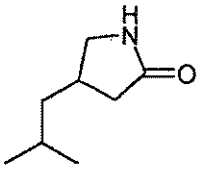
7. The method of claim 6, wherein R'' is H.

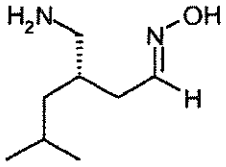
8. The method of any preceding claim, wherein each R^{23} is H.

9. The method of claim 1, wherein the compound of formula III is selected from the group comprising:

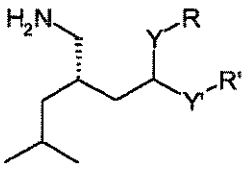








and



10. The method of claim 1, wherein the compound of formula III is:

