Drug Derivatives

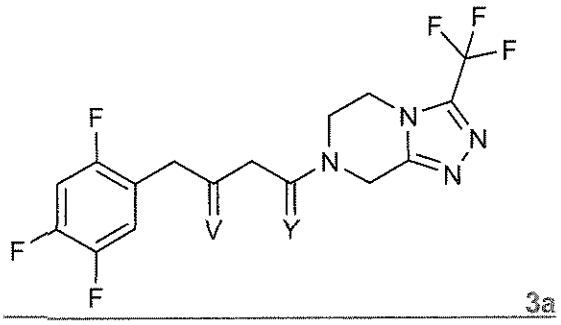
The present invention relates to derivatives of known active pharmaceutical compounds. These derivatives are differentiated from the parent active compound by virtue of being redox derivatives of the active compound. This means that one or more of the functional groups in the active compound has been converted to another group in one or more reactions which may be considered to represent a change of oxidation state. We refer to these compounds generally as redox derivatives.

Many known drugs are less stable than the ideal. For example, drug molecules containing carboxylic acids may undergo decarboxylation of the terminal acid. This represents a significant problem during manufacture of an active principal or during extended storage of the same in a pharmacy. Similarly, amides can be subject to hydrolysis to the carboxylic acid derivatives. The resulting decomposition products may have reduced activity and potentially increased toxicity when compared with the parent active.

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 longevity 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/or bioavailability relative to the parent active compound. It is thus an aim to provide reduced or oxidised derivatives having improved stability. Another aim of the present invention is to provide compounds having improved bioavailability. Ideally, the reduced or oxidised derivatives will have an extended shelf-life.

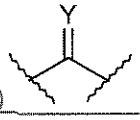
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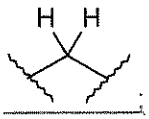
In one aspect, there is provided a compound according to formula 3 below:

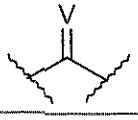


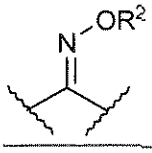
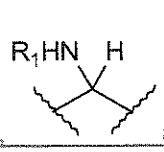
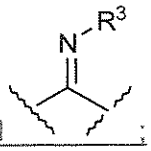
3a

wherein either:

A)  is:

;

 is independently selected from the group comprising:

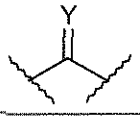
,  and ;

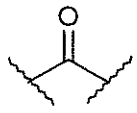
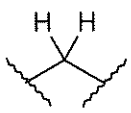
R^1 is independently at each occurrence H or Ac;

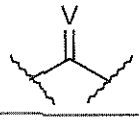
R^2 is independently at each occurrence C_1 alkyl, C_2 alkyl, C_3 alkyl or C_4 alkyl;

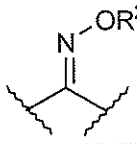
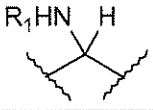
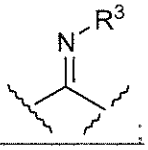
R^3 is independently at each occurrence H, C_1 alkyl, C_2 alkyl, C_3 alkyl or C_4 alkyl;

or

B)  is independently selected from the group comprising:

 and ;

 is independently selected from the group comprising:

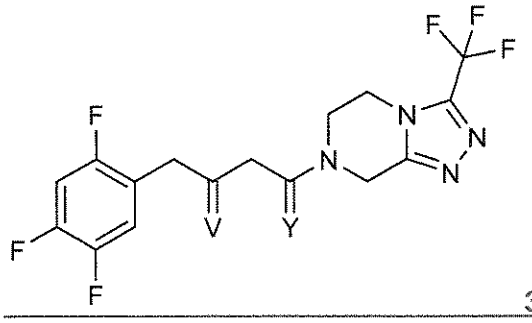


and

;

R^1 is Ac;

R^2 is independently at each occurrence C_1 alkyl, C_2 alkyl, C_3 alkyl or C_4 alkyl;

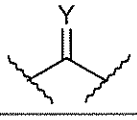
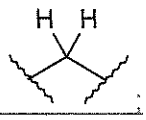
R^3 is independently at each occurrence H, C_1 alkyl, C_2 alkyl, C_3 alkyl or C_4 alkyl.

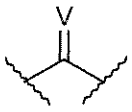
In another aspect, there is provided a compound of formula **3b** for use as a medicament:

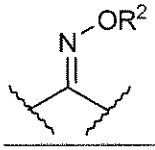
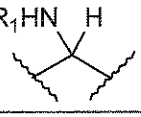
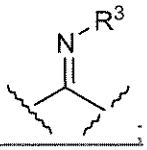


3b

wherein either:

A)  is ;

 is independently selected from the group comprising:

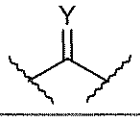


and

;

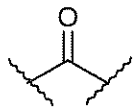
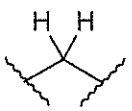
R^1 is independently at each occurrence H or Ac;

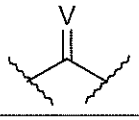
R^2 is independently at each occurrence H, C_1 alkyl, C_2 alkyl, C_3 alkyl or C_4 alkyl;

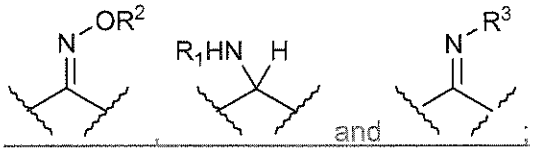
R^3 is independently at each occurrence H, C_1 alkyl, C_2 alkyl, C_3 alkyl or C_4 alkyl;

or

B)  is independently selected from the group comprising:


and

;


is independently selected from the group comprising:

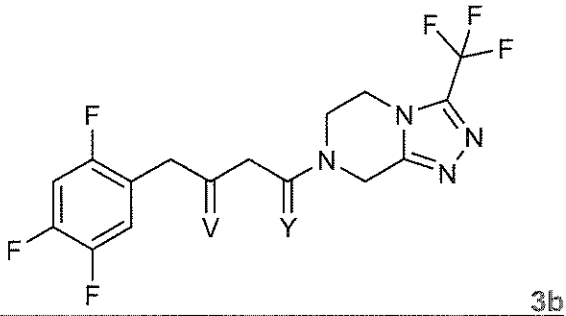


R^1 is Ac;

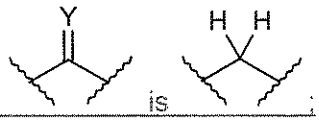
R^2 is independently at each occurrence H, C_1 alkyl, C_2 alkyl, C_3 alkyl or C_4 alkyl;

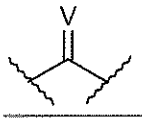
R^3 is independently at each occurrence H, C_1 alkyl, C_2 alkyl, C_3 alkyl or C_4 alkyl.

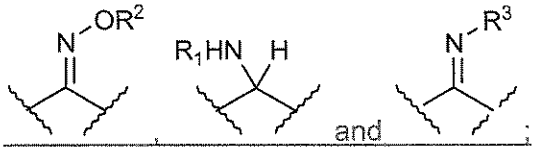
In another aspect, there is provided a pharmaceutical composition comprising one or more pharmaceutical excipients with a compound of formula **3b**:


3b

wherein either:

A)  is ;


is independently selected from the group comprising:

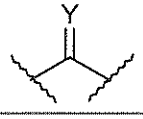


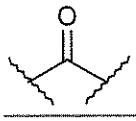
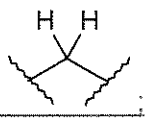
R^1 is independently at each occurrence H or Ac;

R^2 is independently at each occurrence H, C_1 alkyl, C_2 alkyl, C_3 alkyl or C_4 alkyl;

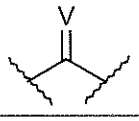
R^3 is independently at each occurrence H, C_1 alkyl, C_2 alkyl, C_3 alkyl or C_4 alkyl;

or

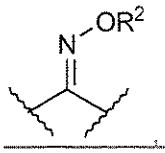
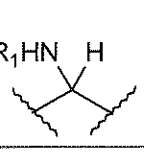
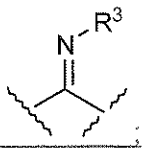
B)  is independently selected from the group comprising:

and ;



is independently selected from the group comprising:

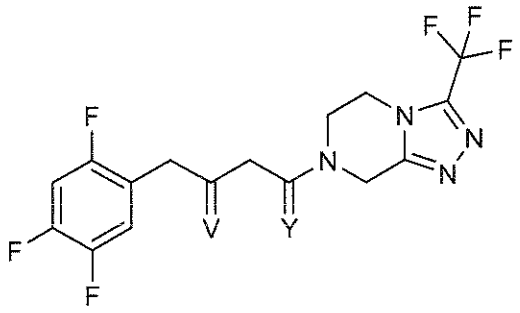
, and ;

R^1 is Ac;

R^2 is independently at each occurrence H, C_1 alkyl, C_2 alkyl, C_3 alkyl or C_4 alkyl;

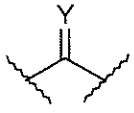
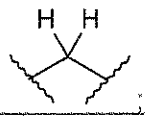
R^3 is independently at each occurrence H, C_1 alkyl, C_2 alkyl, C_3 alkyl or C_4 alkyl.

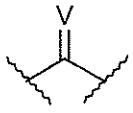
In yet another aspect, there is provided the compound of formula 3b, for use in the treatment of diabetes:



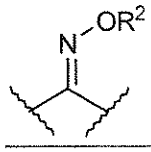
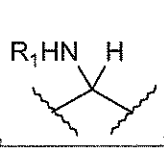
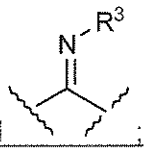
3b

wherein either:

A)  is ;



is independently selected from the group comprising:

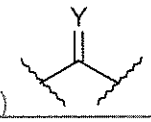
, and ;

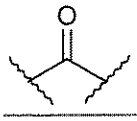
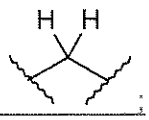
R^1 is independently at each occurrence H or Ac;

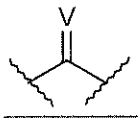
R^2 is independently at each occurrence H, C_1 alkyl, C_2 alkyl, C_3 alkyl or C_4 alkyl;

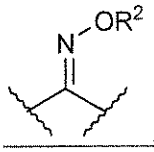
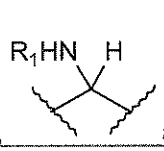
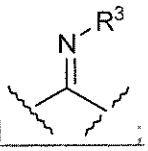
R^3 is independently at each occurrence H, C_1 alkyl, C_2 alkyl, C_3 alkyl or C_4 alkyl;

or

B)  is independently selected from the group comprising:

 and ;

 is independently selected from the group comprising:

  and ;

R^1 is Ac;

R^2 is independently at each occurrence H, C_1 alkyl, C_2 alkyl, C_3 alkyl or C_4 alkyl;

R^3 is independently at each occurrence H, C_1 alkyl, C_2 alkyl, C_3 alkyl or C_4 alkyl.

Description

The derivatives of the invention may be related to the original parent active pharmaceutical compound by only a single step transformation, or may be related via several synthetic steps including one or more changes of oxidation state. In certain cases, the functional group obtained after two or more transformations may be in the same oxidation state as the parent active compound (and we include these compounds in our definition of redox derivatives). In other cases, the oxidation state of the derivative of the invention may be regarded as being different from that of the parent compound.

In many cases, the compounds of the invention have inherent therapeutic activity on their own account. In some cases, this activity relative to the same target or targets of the parent compound is as good as or better than the activity which the parent compound has against the target or targets. However, the present invention also concerns such redox derivatives of