macrophage cell proliferation could be of value in the treatment of cancer and autoimmune disease. Targeting specific cell types would be expected to lead to reduced side-effects. The way in which the esterase motif is linked to the p38 kinase inhibitor determines whether it is hydrolysed, and hence whether or not it accumulates in different cell types. Specifically, macrophages contain the human carboxylesterase hCE-1 whereas other cell types do not. In the general formula (I) of WO 2007/129040, when the nitrogen of the esterase motif R1CH(R2)NH- is not directly linked to a carbonyl (-C(=O)-), ie when Y is not a –C(=O), -C(=O)O- or -C(=O)NR3- radical, the ester will only be hydrolysed by hCE-1 and hence the inhibitors will only accumulate in macrophages. Herein, unless "monocyte" or "monocytes" is specified, the term macrophage or macrophages will be used to denote macrophages (including tumour associated macrophages) and/or monocytes.

WO 2009/060160 discloses a group of specific compounds falling within the general disclosures of WO 2007/129040, but not specifically identified or exemplified therein. The compounds display the macrophage selectivity property discussed above.

Summary

The present inventors have found that the compound tert-butyl N-[2-{4-[6-amino-5-(2,4-difluorobenzoyl)-2-oxopyridin-1(2H)-yl]-3,5-difluorophenyl}ethyl)-L-alaninate is surprisingly good at inhibiting p38 MAP kinase activity. Tests have shown that the IC50 value for ester TNF-α inhibition in human blood is significantly lower than would be expected given the IC50 values for ester TNF-α inhibition in human blood observed for related compounds. Further, tests carried out by the inventors have demonstrated that the bioavailability of the compound of the present disclosure is much higher than would have been predicted from structurally-similar, known compounds.

Accordingly, in one aspect of the present disclosure, there is provided a compound which is: tert-butyl N-[2-{4-[6-amino-5-(2,4-difluorobenzoyl)-2-oxopyridin-1(2H)-yl]-3,5-difluorophenyl}ethyl)-L-alaninate or a pharmaceutically acceptable salt, hydrate or solvate thereof.

In another aspect of the present disclosure, there is also provided a pharmaceutical composition comprising the compound together with one or more pharmaceutically acceptable carriers and/or excipients.

The present disclosure further provides a compound as defined above or a composition as defined above for use in a method of treatment of the human or animal body by therapy.

The present disclosure also provides a compound as defined above or a composition as defined above for use in the inhibition of the activity of a p38 MAP kinase enzyme *in vitro* or

in vivo. There is further provided a compound as defined above or a composition as defined above for use in the prevention or treatment of autoimmune or inflammatory disease. Also provided is a compound as defined above or a composition as defined above for use in the treatment of a cell proliferative disease.

The present disclosure further provides a method of inhibiting the activity of a p38 MAP kinase enzyme, which method comprises contacting the enzyme with an amount of a compound as defined above or a composition as defined above effective for such inhibition. Also provided is a method of treating or preventing autoimmune or inflammatory disease in a subject, which method comprises administering to said subject an effective amount of a compound as defined above or a composition as defined above. There is further provided a method of treating a cell proliferative disease in a subject, which method comprises administering to said subject an effective amount of a compound as defined above or a composition as defined above. Said treatment may comprise ameliorating or reducing the incidence of the cell proliferative disease.

The present disclosure also provides the use of a compound as defined above or a composition as defined above in the manufacture of a medicament for inhibiting the activity of a p38 MAP kinase enzyme. Further provided is the use of a compound as defined above or a composition as defined above in the manufacture of a medicament for the prevention or treatment of an autoimmune or inflammatory disease. Also provided is the use of a compound as defined above or a composition as defined above in the manufacture of a medicament for the treatment of a cell proliferative disease.

The present disclosure also provides an agent for inhibiting the activity of a p38 MAP kinase enzyme comprising a compound as defined above or a composition as defined above as active ingredient. The agent is typically for the prevention or treatment of autoimmune or inflammatory disease. It may alternatively be for the treatment of cell proliferative disease.

In a further aspect of the present disclosure, there is provided an acid which is: N-[2-{4-[6-amino-5-(2,4-difluorobenzoyl)-2-oxopyridin-1(2H)-yl]-3,5-difluorophenyl}ethyl)-L-alanine.

Detailed description of the invention

The invention provides a compound which is: tert-butyl N-[2-{4-[6-amino-5-(2,4-difluorobenzoyl)-2-oxopyridin-1(2H)-yl]-3,5-difluorophenyl}ethyl)-L-alaninate.

The compound of the invention may be prepared in the form of a salt, hydrate or solvate. The invention thus also provides a salt, hydrate or solvate of the compound. Typically, the salt is a pharmaceutically acceptable salt.

CLAIMS

1. A compound which is:

tert-butyl N-[2-{4-[6-amino-5-(2,4-difluorobenzoyl)-2-oxopyridin-1(2H)-yl]-3,5-difluorophenyl}ethyl)-L-alaninate, or a pharmaceutically acceptable salt, hydrate or solvate thereof.

2. A pharmaceutical composition comprising a compound according to claim 1 together with one or more pharmaceutically acceptable carriers and/or excipients.

3. An acid which is:

N-[2-{4-[6-amino-5-(2,4-difluorobenzoyl)-2-oxopyridin-1(2H)-yl]-3,5-difluorophenyl}ethyl)-L-alanine.