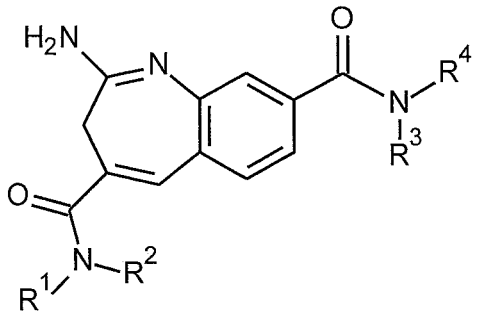


I

,

wherein R^1 to R^4 are as defined above, and, if desired, converting the compound obtained into a pharmaceutically acceptable salt.

In another aspect, the disclosure relates to pharmaceutical compositions comprising a compound of formula I as described above and a pharmaceutically acceptable carrier and/or adjuvant.

The disclosure also relates to use of compounds of formula I as therapeutic active substances for the treatment of diseases that can be mediated with TLR agonists, in particular TLR8 agonists. The disclosure thus relates to a method for the treatment of a disease that can be mediated with TLR agonists such as for example cancer and autoimmune or infectious diseases.

In another aspect, the disclosure relates to a compound of formula I as defined above for use as medicament.

In another aspect, the disclosure relates to a compound of formula I as defined above for use as a medicament for the treatment of diseases which can be mediated with TLR agonists.

In another aspect, the disclosure relates to use of a compound of formula I as defined above for the preparation of a medicament for the treatment of diseases selected from the group consisting of cancer, autoimmune diseases, inflammation, sepsis, allergy, asthma, graft rejection, graft-versus-host disease, immunodeficiencies, and infectious diseases.

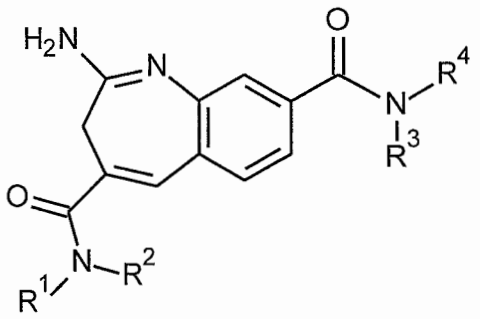
DETAILED DESCRIPTION OF THE INVENTION

Unless otherwise defined, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this invention belongs. Furthermore, the following definitions are set forth to illustrate and define the meaning and scope of the various terms used to describe the invention.

The nomenclature used in this application is based on IUPAC systematic nomenclature, unless indicated otherwise.

Claims

1. A compound of the formula



I

wherein

R^1 is C_{1-7}-alkyl or C_{3-7}-cycloalkyl,

R^2 is selected from the group consisting of C_{1-7}-alkyl, hydroxy-C_{1-7}-alkyl, C_{2-7}-alkenyl, C_{3-7}-alkinyl, amino-C_{1-7}-alkoxy-C_{1-7}-alkyl, amino-C_{1-7}-alkoxy-C_{1-7}-alkoxy-C_{1-7}-alkyl, halogen-C_{1-7}-alkyl, C_{3-7}-cycloalkyl-C_{1-7}-alkyl and phenyl-C_{1-7}-alkyl, wherein phenyl is unsubstituted or substituted by amino-C_{1-7}-alkyl;

R^3 is hydrogen;

R^4 is selected from the group consisting of

phenyl, said phenyl being unsubstituted or substituted by one or two groups selected from the group consisting of C_{1-7}-alkyl, halogen, halogen-C_{1-7}-alkyl, C_{1-7}-alkoxy, hydroxy-C_{1-7}-alkyl, amino-C_{1-7}-alkyl, C_{1-7}-alkyl-amino-C_{1-7}-alkyl, di-C_{1-7}-alkyl-amino-C_{1-7}-alkyl, amino-C_{2-7}-alkenyl, C_{1-7}-alkyl-amino-C_{2-7}-alkenyl, di-C_{1-7}-alkyl-amino-C_{2-7}-alkenyl, amino-C_{2-7}-alkinyl, C_{1-7}-alkyl-amino-C_{2-7}-alkinyl, di-C_{1-7}-alkyl-amino-C_{2-7}-alkinyl, benzyloxycarbonylamino-C_{1-7}-alkyl, amino-C_{1-7}-alkoxy, amino-C_{1-7}-alkoxy-C_{1-7}-alkoxy, amino-C_{1-7}-alkoxy-C_{1-7}-alkyl, amino-C_{1-7}-alkoxy-C_{1-7}-alkoxy-C_{1-7}-alkyl, C_{1-7}-alkylsulfonyl, heterocyclylcarbonyl and phenyl-C_{1-7}-alkyl, wherein phenyl is unsubstituted or substituted by C_{1-7}-alkoxy or amino-C_{1-7}-alkyl, or

heteroaryl, said heteroaryl being a 5- or 6-membered aromatic ring containing one, two or three heteroatoms selected from N, O or S and being unsubstituted or substituted by one or two groups selected from the group consisting of C_{1-7}-alkyl, halogen, halogen-C_{1-7}-alkyl, C_{1-7}-alkoxy, hydroxy-C_{1-7}-alkyl, amino-C_{1-7}-alkyl, C_{1-7}-alkyl-amino-C_{1-7}-alkyl, di-C_{1-7}-alkyl-amino-C_{1-7}-alkyl, amino-C_{2-7}-alkenyl, C_{1-7}-alkyl-amino-C_{2-7}-alkenyl, di-C_{1-7}-alkyl-amino-C_{2-7}-alkenyl, amino-C_{2-7}-alkinyl, C_{1-7}-alkyl-amino-C_{2-7}-alkinyl, di-C_{1-7}-alkyl-amino-C_{2-7}-alkinyl, benzyloxycarbonylamino-C_{1-7}-alkyl, amino-C_{1-7}-alkoxy, amino-C_{1-7}-alkoxy-

17. A compound of formula I according to claim 1, selected from the group consisting of

2-amino-*N8*-[3-(2-aminoethyl)phenyl]-*N4,N4*-dipropyl-*3H*-1-benzazepine-4,8-dicarboxamide,

2-amino-*N4*-isobutyl-*N8*-(m-tolyl)-*N4*-propyl-*3H*-1-benzazepine-4,8-dicarboxamide,

2-amino-*N8*-[3-(3-aminopropyl)phenyl]-*N4,N4*-dipropyl-3*H*-1-benzazepine-4,8-dicarboxamide,

benzyl-*N*-[[5-[[2-amino-4-(dipropylcarbamoyl)-*3H*-1-benzazepine-8-carbonyl]amino]-3-pyridyl]methyl]carbamate,

2-amino-*N8*-[5-(2-phenylethyl)-3-pyridyl]-*N4,N4*-dipropyl-*3H*-1-benzazepine-4,8-dicarboxamide,

2-amino-*N4*-(cyclopropylmethyl)-*N8*-(5-ethoxy-3-pyridyl)-*N4*-propyl-3H-1-benzazepine-4,8-dicarboxamide,

and pharmaceutically acceptable salts thereof.

18. A compound of formula I according to any one of claims 1 to 17 for use as medicament.

19. A compound of formula I according to any one of claims 1 to 17 for use as medicament for the treatment of diseases which can be mediated with TLR agonists.

20. A pharmaceutical composition comprising a compound of formula I according to any one of claims 1 to 17 and a pharmaceutically acceptable carrier and/or adjuvant.

21. The use of a compound of formula I according to any one of claims 1 to 17 for the preparation of a medicament for the treatment of diseases selected from the group consisting of cancer, autoimmune diseases, inflammation, sepsis, allergy, asthma, graft rejection, graft-versus-host disease, immunodeficiencies, and infectious diseases.

22. A process for the manufacture of a compound of formula I as defined in claim 1, which process comprises

a) coupling a compound of the formula II