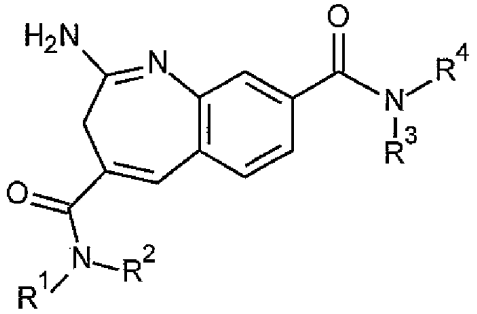
towards TLR8 and possess only low or even no activity towards TLR7. Thus, they are expected to possess advantageous properties compared to combined TLR7/8 agonists due to the more restricted expression pattern of TLR8 resulting in less servere side effects when administered systemically.

SUMMARY

The present disclosure relates to benzazepine-4-carboxamide compounds of the formula



I

wherein

R^1 is C_{3-7}-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

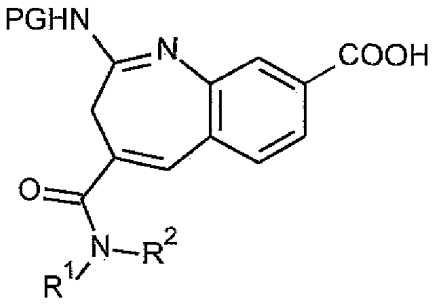
heteroaryl, said heteroaryl being a 5- or 6-membered aromatic ring containing one, two or three heteroatoms selected from N, O or S and being unsubstituted or substituted by one or

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-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 pharmaceutically acceptable salts thereof.

The disclosure is also concerned with processes for the manufacture of compounds of formula I. In another aspect, the disclosure relates to a process for the manufacture of a compound of formula I as defined above, which process comprises

a) coupling a compound of the formula II



II

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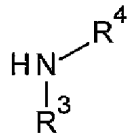
wherein R^1 and R^2 are as defined above and PG is a protecting group, with a compound of the formula III



III

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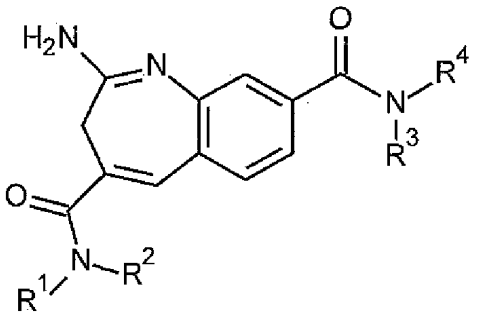
wherein R^3 and R^4 are as defined above, under basic conditions in the presence of a coupling agent and removing the protecting group PG under acidic conditions to obtain a compound of the formula I



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 for the treatment of diseases which can be mediated with TLR agonists, particularly 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.

The term "compound(s) of this invention" and "compound(s) of the present invention" refers to compounds of formula I and solvates or salts thereof (e.g., pharmaceutically acceptable salts).

The term "substituent" denotes an atom or a group of atoms replacing a hydrogen atom on the parent molecule.

The term "halogen" refers to fluoro, chloro, bromo and iodo, with fluoro, chloro and bromo being of particular interest. More particularly, halogen refers to fluoro.