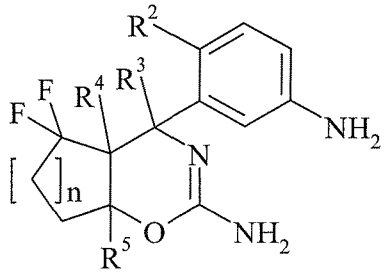
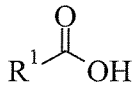
In a second aspect, there is provided a process for preparing a compound of formula I as defined herein, which process comprises reacting a compound of formula I' with a compound of formula XIV.



I'



XIV

wherein n, R^1, R^2, R^3, R^4, R^5 are as defined herein.

In a third aspect, there is provided a compound of formula I as defined herein, whenever prepared by a process as defined herein.

In a fourth aspect, there is provided a compound of formula I as defined herein for use as therapeutically active substance.

In a fifth aspect, there is provided a compound of formula I as defined herein for the use as therapeutically active substance for the therapeutic and/or prophylactic treatment of diseases and disorders characterized by elevated β-amyloid levels and/or β-amyloid oligomers and/or β-amyloid plaques and further deposits, particularly Alzheimer's disease.

In a sixth aspect, there is provided a pharmaceutical composition comprising a compound of formula I as defined herein and a pharmaceutically acceptable carrier and/or a pharmaceutically acceptable auxiliary substance.

In a seventh aspect, there is provided use of a compound of formula I as defined herein ~~for~~ in the manufacture of a medicament for the therapeutic and/or prophylactic treatment of ~~diseases and disorders characterized by elevated β-amyloid levels and/or β-amyloid oligomers and/or β-amyloid plaques and further deposits, particularly~~ Alzheimer's disease.

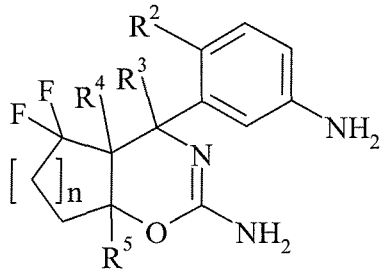
Detailed description of the invention

Object of the present invention is a compound of formula I and their pharmaceutically acceptable salts thereof, the preparation of the above mentioned compounds, medicaments containing them and their manufacture as well as the use of the above mentioned compounds in the therapeutic and/or prophylactic treatment of diseases and disorders which are associated with inhibition of BACE1 activity, such as Alzheimer's disease. Furthermore, the formation, or formation and deposition, of β-amyloid plaques in, on or around neurological tissue (e.g., the brain) are inhibited by the present compounds by inhibiting the Aβ production from APP or an APP fragment.

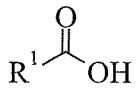
5-Cyano-pyridine-2-carboxylic acid [3-((4S,4aR,8aR)-2-amino-5,5-difluoro-4-methyl-4a,5,6,7,8,8a-hexahydro-4H-benzo[e][1,3]oxazin-4-yl)-4-fluoro-phenyl]-amide,
5-Chloro-thiophene-2-carboxylic acid [3-((4S,4aR,8aR)-2-amino-5,5-difluoro-4-methyl-4a,5,6,7,8,8a-hexahydro-4H-benzo[e][1,3]oxazin-4-yl)-4-fluoro-phenyl]-amide, and
5-(1,1-Difluoro-ethyl)-pyrazine-2-carboxylic acid [3-((4S,4aR,7aR)-2-amino-5,5-difluoro-4-methyl-4,4a,5,6,7,7a-hexahydro-cyclopenta[e][1,3]oxazin-4-yl)-4-fluoro-phenyl]-amide,

or a pharmaceutical acceptable salt thereof.

14. A process for preparing a compound of formula I as defined in any of claims 1 to 13, which process comprises reacting a compound of formula I' with a compound of formula XIV.



I'



XIV

wherein n, R^1, R^2, R^3, R^4, R^5 are as defined in any of claim 1 to 12.

15. A compound of formula I according to any of claims 1 to 13, whenever prepared by a process as defined in claim 14.

16. A compound of formula I according to any of claims 1 to 13 for use as therapeutically active substance.

17. A compound of formula I according to claims 1 to 13 for the use as therapeutically active substance for the therapeutic and/or prophylactic treatment of diseases and disorders characterized by elevated β-amyloid levels and/or β-amyloid oligomers and/or β-amyloid plaques and further deposits, particularly Alzheimer's disease.

18. A pharmaceutical composition comprising a compound of formula I according to any of claims 1 to 13 and a pharmaceutically acceptable carrier and/or a pharmaceutically acceptable auxiliary substance.

19. Use of a compound of formula I according to any of claims 1 to 13 ~~for~~ in the manufacture of a medicament for the therapeutic and/or prophylactic treatment of ~~diseases and disorders characterized by elevated β-amyloid levels and/or β-amyloid oligomers and/or β-amyloid plaques and further deposits, particularly~~ Alzheimer's disease.

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