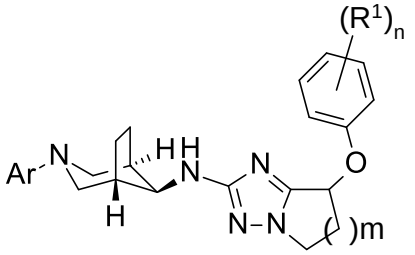
Chem., 286 (2011) 37181-86; Oehlich, Gijsen *et al.*, *J. Med. Chem.*, 54 (2011), 669 – 698; Li *et al.*, *Biochemistry*, 52 (2013), 3197 – 3216; Hall *et al.*, *Progress in Med. Chem.*, 53 (2014) 101-145; Bursavich *et al.*, *J. Med. Chem.*, 59 (2016); WO 2018/111926.

Therefore, modulating the γ-secretase activity is a promising therapeutic strategy for the treatment or prevention of diseases associated with the deposition of β-amyloid in the brain, such as Alzheimer's disease, cerebral amyloid angiopathy, cochlear synaptopathy, hearing loss, hereditary cerebral hemorrhage with amyloidosis-Dutch type (HCHWA-D), multi-infarct dementia, dementia pugilistica and Down syndrome.

There is a need for new compounds, formulations, treatments and therapies to treat diseases and disorders associated with the deposition of β-amyloid in the brain. It is, therefore, an object of this invention to provide compounds useful for the treatment or prevention or amelioration of such diseases and disorders with improved therapeutic properties.

Summary

A first object of the present disclosure is a compound of formula (I)



(I),

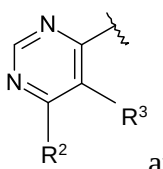
wherein

R^1 is halogen, lower alkyl, lower alkyl substituted by halogen, lower alkoxy, or lower alkoxy substituted by halogen,
and R^1 may be different if n = 2 or 3;

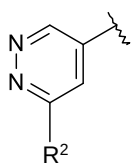
m is 1, 2 or 3;

n is 1, 2 or 3;

Ar is a six membered heteroaryl group, selected from



and



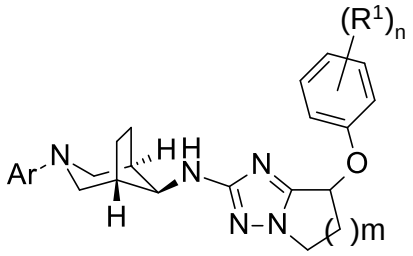
wherein

R^2 is hydrogen, halogen, lower alkyl, lower alkyl substituted by halogen, or lower alkoxy;

R^3 is hydrogen or halogen;

or a pharmaceutically acceptable salt thereof.

In one aspect, the present disclosure provides a compound of formula (I)



(I),

wherein

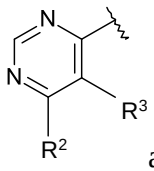
R^1 is halogen, C_{1-7} alkyl, C_{1-7} alkyl substituted by halogen, C_{1-7} alkoxy, or C_{1-7} alkoxy substituted by halogen,

and R^1 may be different if n = 2 or 3;

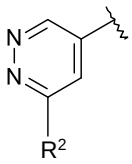
m is 1, 2 or 3;

n is 1, 2 or 3;

Ar is a six membered heteroaryl group, selected from



and



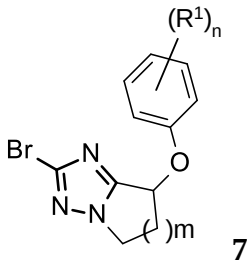
wherein

R^2 is hydrogen, halogen, C_{1-7} alkyl, C_{1-7} alkyl substituted by halogen, or C_{1-7} alkoxy;

R^3 is hydrogen or halogen;

or a pharmaceutically acceptable salt thereof.

In another aspect, the present disclosure provides a process for the preparation of a compound as described herein, or a pharmaceutically acceptable salt thereof, comprising reacting a compound **7**



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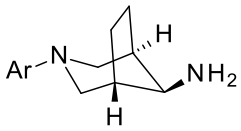
with an amine **8**



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wherein Ar, R^1, n and m are as defined above,

to form said compound of formula (I), and if desired, converting the compounds obtained into a pharmaceutically acceptable salt thereof.

A further object of the present disclosure is a compound of formula (I) as described herein, or a pharmaceutically acceptable salt thereof, when manufactured according to the process as described above.

In another aspect, the present disclosure provides a compound as described herein, or a pharmaceutically acceptable salt thereof, for use as therapeutically active substance.

In another aspect, the present disclosure provides a pharmaceutical composition comprising a compound as described herein, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient.

In another aspect, the present disclosure provides a compound as described herein, or a pharmaceutically acceptable salt thereof, for use in the therapeutic and/or prophylactic treatment of Alzheimer's disease, cerebral amyloid angiopathy, cochlear synaptopathy, hearing

loss, hereditary cerebral hemorrhage with amyloidosis-Dutch type (HCHWA-D), multi-infarct dementia, dementia pugilistica, or Down syndrome.

A further object of the present disclosure is the use of a compound of formula (I) as described herein, or a pharmaceutically acceptable salt thereof, for the therapeutic and/or prophylactic treatment of Alzheimer's disease, cerebral amyloid angiopathy, cochlear synaptopathy, hearing loss, hereditary cerebral hemorrhage with amyloidosis-Dutch type (HCHWA-D), multi-infarct dementia, dementia pugilistica, or Down syndrome.

In another aspect, the present disclosure provides the use of a compound as described herein, or a pharmaceutically acceptable salt thereof, in the preparation of a medicament for the therapeutic and/or prophylactic treatment of Alzheimer's disease, cerebral amyloid angiopathy, cochlear synaptopathy, hearing loss, hereditary cerebral hemorrhage with amyloidosis-Dutch type (HCHWA-D), multi-infarct dementia, dementia pugilistica, or Down syndrome.

A further object of the present disclosure is a method for the therapeutic and/or prophylactic treatment of Alzheimer's disease, cerebral amyloid angiopathy, cochlear synaptopathy, hearing loss, hereditary cerebral hemorrhage with amyloidosis-Dutch type (HCHWA-D), multi-infarct dementia, dementia pugilistica, or Down syndrome, which method comprises administering an effective amount of a compound of formula (I) as described herein, or a pharmaceutically acceptable salt thereof.

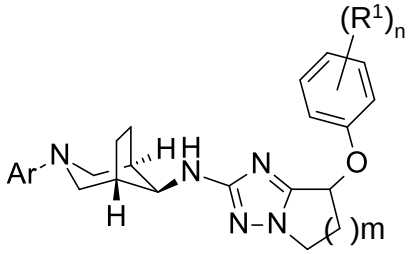
Detailed description of the invention

The following definitions of the general terms used in the present description apply irrespectively of whether the terms in question appear alone or in combination with other groups.

The term "lower alkyl", alone or in combination with other groups, refers to saturated straight- or branched-chain alkyl group, with single or multiple branching, wherein the alkyl group in general comprises 1 to 7 carbon atoms ("C_{1-7}-alkyl"), for example, methyl (Me), ethyl (Et), propyl, isopropyl (i-propyl), n-butyl, i-butyl (isobutyl), 2-butyl (sec-butyl), t-butyl (tert-butyl), isopentyl, 2-ethyl-propyl, 1,2-dimethyl-propyl and the like. Particular lower alkyl groups have 1 to 4 carbon atoms ("C_{1-4}-alkyl").

Claims

1. A compound of formula (I)



(I),

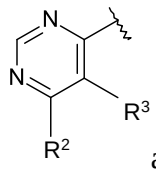
wherein

R^1 is halogen, C_{1-7} alkyl, C_{1-7} alkyl substituted by halogen, C_{1-7} alkoxy, or C_{1-7} alkoxy substituted by halogen,
and R^1 may be different if n = 2 or 3;

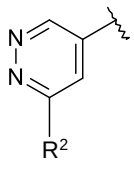
m is 1, 2 or 3;

n is 1, 2 or 3;

Ar is a six membered heteroaryl group, selected from



and



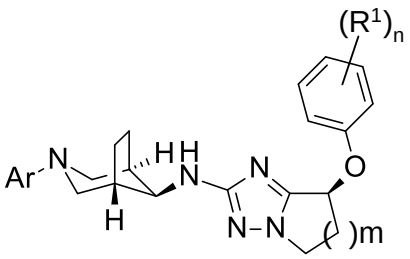
wherein

R^2 is hydrogen, halogen, C_{1-7} alkyl, C_{1-7} alkyl substituted by halogen, or C_{1-7} alkoxy;

R^3 is hydrogen or halogen;

or a pharmaceutically acceptable salt thereof.

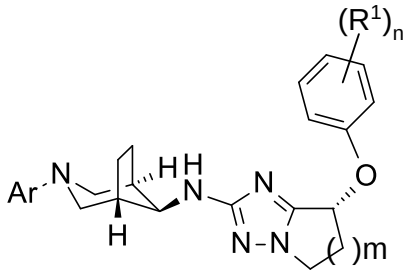
2. The compound of formula (I) according to claim 1, or a pharmaceutically acceptable salt thereof, wherein the compound of formula (I) is a compound of formula (Ia):



(Ia)

wherein R^1, m, n and Ar are as defined in claim 1.

3. The compound of formula (I) according to claim 1, or a pharmaceutically acceptable salt thereof, wherein the compound of formula (I) is a compound of formula (Ib):



(Ib)

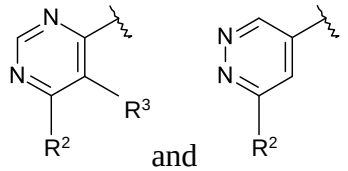
wherein R^1, m, n and Ar are as defined in claim 1.

4. The compound of formula (I) according to any one of claims 1 to 3, or a pharmaceutically acceptable salt thereof, wherein R^1 is halogen.

5. The compound of formula (I) according to any one of claims 1 to 4, or a pharmaceutically acceptable salt thereof, wherein R^1 is fluorine or chlorine.

6. The compound of formula (I) according to any one of claims 1 to 5, or a pharmaceutically acceptable salt thereof, wherein m is 1 or 2.

7. The compound of formula (I) according to any one of claims 1 to 6, or a pharmaceutically acceptable salt thereof, wherein Ar is a six membered heteroaryl group, selected from



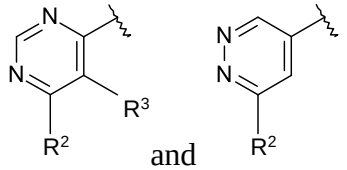
and

wherein

R^2 is C_{1-7} alkyl or C_{1-7} alkoxy;

R^3 is hydrogen.

8. The compound of formula (I) according to any one of claims 1 to 7, or a pharmaceutically acceptable salt thereof, wherein Ar is a six membered heteroaryl group, selected from



wherein

R^2 is methyl or methoxy;

R^3 is hydrogen.

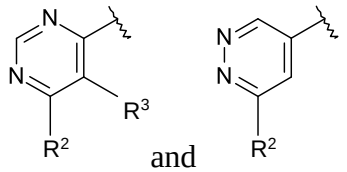
9. The compound of formula (I) according to any one of claims 1 to 3, or a pharmaceutically acceptable salt thereof, wherein:

R^1 is halogen;

m is 1 or 2;

n is 1, 2 or 3;

Ar is a six membered heteroaryl group, selected from



wherein

R^2 is C_{1-7} alkyl or C_{1-7} alkoxy;

R^3 is hydrogen.

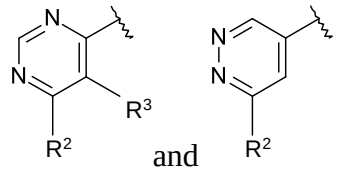
10. The compound of formula (I) according to any one of claims 1 to 3, or a pharmaceutically acceptable salt thereof, wherein:

R^1 is fluorine or chlorine,

m is 1 or 2;

n is 1, 2 or 3;

Ar is a six membered heteroaryl group, selected from



and

wherein

R^2 is methyl or methoxy;

R^3 is hydrogen.

11. A compound according to any one of claims 1 to 10, selected from:
(R)-7-(3,5-difluorophenoxy)-N-((1R,5S,8s)-3-(6-methoxypyridazin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-amine;
(S)-7-(3,5-difluorophenoxy)-N-((1R,5S,8s)-3-(6-methoxypyridazin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-amine;
(R)-7-(3-chloro-5-fluorophenoxy)-N-((1R,5S,8s)-3-(6-methoxypyridazin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-amine;
(S)-7-(3-chloro-5-fluorophenoxy)-N-((1R,5S,8s)-3-(6-methoxypyridazin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-amine;
(R)-N-((1R,5S,8s)-3-(6-methoxypyridazin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-7-(2,3,4-trifluorophenoxy)-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-amine;
(S)-N-((1R,5S,8s)-3-(6-methoxypyridazin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-7-(2,3,4-trifluorophenoxy)-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-amine;
(R)-8-(3-chloro-5-fluorophenoxy)-N-((1R,5S,8s)-3-(6-methoxypyridazin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amine;
(S)-8-(3-chloro-5-fluorophenoxy)-N-((1R,5S,8s)-3-(6-methoxypyridazin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amine;
(R)-8-(3,5-difluorophenoxy)-N-((1R,5S,8s)-3-(6-methoxypyridazin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amine;
(S)-8-(3,5-difluorophenoxy)-N-((1R,5S,8s)-3-(6-methoxypyridazin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amine;
(R)-N-((1R,5S,8s)-3-(6-methoxypyridazin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-8-(2,3,4-trifluorophenoxy)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amine;
(S)-N-((1R,5S,8s)-3-(6-methoxypyridazin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-8-(2,3,4-trifluorophenoxy)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amine;

(R)-8-(3-chloro-5-fluorophenoxy)-N-((1R,5S,8s)-3-(6-methylpyridazin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amine;
(S)-8-(3-chloro-5-fluorophenoxy)-N-((1R,5S,8s)-3-(6-methylpyridazin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amine;
(R)-8-(3,5-difluorophenoxy)-N-((1R,5S,8s)-3-(6-methylpyridazin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amine;
(S)-8-(3,5-difluorophenoxy)-N-((1R,5S,8s)-3-(6-methylpyridazin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amine;
(R)-N-((1R,5S,8s)-3-(6-methylpyridazin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-8-(2,3,4-trifluorophenoxy)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amine;
(S)-N-((1R,5S,8s)-3-(6-methylpyridazin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-8-(2,3,4-trifluorophenoxy)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amine;
(R)-8-(2,4-difluorophenoxy)-N-((1R,5S,8s)-3-(6-methoxypyridazin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amine;
(S)-8-(2,4-difluorophenoxy)-N-((1R,5S,8s)-3-(6-methoxypyridazin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amine;
(R)-8-(2,3-difluorophenoxy)-N-((1R,5S,8s)-3-(6-methoxypyridazin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amine;
(S)-8-(2,3-difluorophenoxy)-N-((1R,5S,8s)-3-(6-methoxypyridazin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amine;
(R)-8-(3-chlorophenoxy)-N-((1R,5S,8s)-3-(6-methoxypyridazin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amine;
(S)-8-(3-chlorophenoxy)-N-((1R,5S,8s)-3-(6-methoxypyridazin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amine;
(R)-8-(2-chlorophenoxy)-N-((1R,5S,8s)-3-(6-methoxypyridazin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amine;
(S)-8-(2-chlorophenoxy)-N-((1R,5S,8s)-3-(6-methoxypyridazin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amine;
(R)-7-(4-chlorophenoxy)-N-((1R,5S,8s)-3-(6-methylpyrimidin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-amine;
(S)-7-(4-chlorophenoxy)-N-((1R,5S,8s)-3-(6-methylpyrimidin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-amine;
(R)-7-(3-chlorophenoxy)-N-((1R,5S,8s)-3-(6-methylpyrimidin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-amine;

(S)-7-(3-chlorophenoxy)-N-((1R,5S,8s)-3-(6-methylpyrimidin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-amine;
(R)-8-(2-chlorophenoxy)-N-((1R,5S,8s)-3-(6-methylpyrimidin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amine;
(S)-8-(2-chlorophenoxy)-N-((1R,5S,8s)-3-(6-methylpyrimidin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amine;
(R)-8-(2,3-difluorophenoxy)-N-((1R,5S,8s)-3-(6-methylpyrimidin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amine;
(S)-8-(2,3-difluorophenoxy)-N-((1R,5S,8s)-3-(6-methylpyrimidin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amine;
(R)-7-(3,5-dichlorophenoxy)-N-((1R,5S,8s)-3-(6-methylpyrimidin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-amine;
(S)-7-(3,5-dichlorophenoxy)-N-((1R,5S,8s)-3-(6-methylpyrimidin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-amine;
(R)-8-(2,4-difluorophenoxy)-N-((1R,5S,8s)-3-(6-methylpyrimidin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amine;
(S)-8-(2,4-difluorophenoxy)-N-((1R,5S,8s)-3-(6-methylpyrimidin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amine;
(R)-7-(3,5-difluorophenoxy)-N-((1R,5S,8s)-3-(6-methylpyrimidin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-amine;
(S)-7-(3,5-difluorophenoxy)-N-((1R,5S,8s)-3-(6-methylpyrimidin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-amine;
(R)-8-(3-chlorophenoxy)-N-((1R,5S,8s)-3-(6-methylpyrimidin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amine;
(S)-8-(3-chlorophenoxy)-N-((1R,5S,8s)-3-(6-methylpyrimidin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amine;
(R)-8-(3,5-difluorophenoxy)-N-((1R,5S,8s)-3-(6-methylpyrimidin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amine;
(S)-8-(3,5-difluorophenoxy)-N-((1R,5S,8s)-3-(6-methylpyrimidin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amine;
(R)-8-(4-chlorophenoxy)-N-((1R,5S,8s)-3-(6-methylpyrimidin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amine;
(S)-8-(4-chlorophenoxy)-N-((1R,5S,8s)-3-(6-methylpyrimidin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amine;

(R)-7-(3-chloro-5-fluorophenoxy)-N-((1R,5S,8s)-3-(6-methylpyrimidin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-amine;

(S)-7-(3-chloro-5-fluorophenoxy)-N-((1R,5S,8s)-3-(6-methylpyrimidin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-amine;

(R)-8-(3,5-dichlorophenoxy)-N-((1R,5S,8s)-3-(6-methylpyrimidin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amine;

(S)-8-(3,5-dichlorophenoxy)-N-((1R,5S,8s)-3-(6-methylpyrimidin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amine;

(R)-N-((1R,5S,8s)-3-(6-methylpyrimidin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-7-(2,3,4-trifluorophenoxy)-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-amine;

(S)-N-((1R,5S,8s)-3-(6-methylpyrimidin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-7-(2,3,4-trifluorophenoxy)-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-amine;

(R)-8-(3,4-difluorophenoxy)-N-((1R,5S,8s)-3-(6-methylpyrimidin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amine;

(S)-8-(3,4-difluorophenoxy)-N-((1R,5S,8s)-3-(6-methylpyrimidin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amine;

(R)-8-(3-chloro-5-fluorophenoxy)-N-((1R,5S,8s)-3-(6-methylpyrimidin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amine;

(S)-8-(3-chloro-5-fluorophenoxy)-N-((1R,5S,8s)-3-(6-methylpyrimidin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amine;

(R)-N-((1R,5S,8s)-3-(6-methylpyrimidin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-8-(2,3,4-trifluorophenoxy)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amine;

(S)-N-((1R,5S,8s)-3-(6-methylpyrimidin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-8-(2,3,4-trifluorophenoxy)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amine;

(R)-9-(4-fluorophenoxy)-N-((1R,5S,8s)-3-(6-methylpyrimidin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-6,7,8,9-tetrahydro-5H-[1,2,4]triazolo[1,5-a]azepin-2-amine;

(S)-9-(4-fluorophenoxy)-N-((1R,5S,8s)-3-(6-methylpyrimidin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-6,7,8,9-tetrahydro-5H-[1,2,4]triazolo[1,5-a]azepin-2-amine;

(R)-N-((1R,5S,8s)-3-(6-methylpyrimidin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-9-(2,3,4-trifluorophenoxy)-6,7,8,9-tetrahydro-5H-[1,2,4]triazolo[1,5-a]azepin-2-amine;

(S)-N-((1R,5S,8s)-3-(6-methylpyrimidin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-9-(2,3,4-trifluorophenoxy)-6,7,8,9-tetrahydro-5H-[1,2,4]triazolo[1,5-a]azepin-2-amine;

(R)-9-(3-chloro-5-fluorophenoxy)-N-((1R,5S,8s)-3-(6-methylpyrimidin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-6,7,8,9-tetrahydro-5H-[1,2,4]triazolo[1,5-a]azepin-2-amine; (S)-9-(3-chloro-5-fluorophenoxy)-N-((1R,5S,8s)-3-(6-methylpyrimidin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-6,7,8,9-tetrahydro-5H-[1,2,4]triazolo[1,5-a]azepin-2-amine;

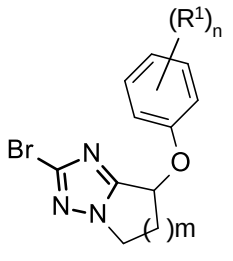
or a pharmaceutically acceptable salt thereof.

12. A compound according to any one of claims 1 to 11, selected from:
(R)-7-(3,5-difluorophenoxy)-N-((1R,5S,8s)-3-(6-methoxypyridazin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-amine;
(S)-7-(3,5-difluorophenoxy)-N-((1R,5S,8s)-3-(6-methoxypyridazin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-amine;
(R)-7-(3-chloro-5-fluorophenoxy)-N-((1R,5S,8s)-3-(6-methoxypyridazin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-amine;
(S)-7-(3-chloro-5-fluorophenoxy)-N-((1R,5S,8s)-3-(6-methoxypyridazin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-amine;
(R)-N-((1R,5S,8s)-3-(6-methoxypyridazin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-7-(2,3,4-trifluorophenoxy)-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-amine;
(S)-N-((1R,5S,8s)-3-(6-methoxypyridazin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-7-(2,3,4-trifluorophenoxy)-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-amine;
(R)-8-(3-chloro-5-fluorophenoxy)-N-((1R,5S,8s)-3-(6-methoxypyridazin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amine;
(S)-8-(3-chloro-5-fluorophenoxy)-N-((1R,5S,8s)-3-(6-methoxypyridazin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amine;
(R)-8-(3,5-difluorophenoxy)-N-((1R,5S,8s)-3-(6-methoxypyridazin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amine;
(S)-8-(3,5-difluorophenoxy)-N-((1R,5S,8s)-3-(6-methoxypyridazin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amine;
(R)-N-((1R,5S,8s)-3-(6-methoxypyridazin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-8-(2,3,4-trifluorophenoxy)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amine;
(S)-N-((1R,5S,8s)-3-(6-methoxypyridazin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-8-(2,3,4-trifluorophenoxy)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amine;
(R)-8-(3-chlorophenoxy)-N-((1R,5S,8s)-3-(6-methoxypyridazin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amine;

(S)-8-(3-chlorophenoxy)-N-((1R,5S,8s)-3-(6-methoxypyridazin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amine;
(R)-8-(4-chlorophenoxy)-N-((1R,5S,8s)-3-(6-methylpyrimidin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amine;
(S)-8-(4-chlorophenoxy)-N-((1R,5S,8s)-3-(6-methylpyrimidin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amine;
(R)-8-(3-chlorophenoxy)-N-((1R,5S,8s)-3-(6-methylpyrimidin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amine;
(S)-8-(3-chlorophenoxy)-N-((1R,5S,8s)-3-(6-methylpyrimidin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amine;
(R)-8-(3,5-dichlorophenoxy)-N-((1R,5S,8s)-3-(6-methylpyrimidin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amine;
(S)-8-(3,5-dichlorophenoxy)-N-((1R,5S,8s)-3-(6-methylpyrimidin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amine;
(R)-8-(3,5-difluorophenoxy)-N-((1R,5S,8s)-3-(6-methylpyrimidin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amine;
(S)-8-(3,5-difluorophenoxy)-N-((1R,5S,8s)-3-(6-methylpyrimidin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amine;
(R)-8-(3-chloro-5-fluorophenoxy)-N-((1R,5S,8s)-3-(6-methylpyrimidin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amine;
(S)-8-(3-chloro-5-fluorophenoxy)-N-((1R,5S,8s)-3-(6-methylpyrimidin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amine;
(R)-7-(3-chloro-5-fluorophenoxy)-N-((1R,5S,8s)-3-(6-methylpyrimidin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-amine;
(S)-7-(3-chloro-5-fluorophenoxy)-N-((1R,5S,8s)-3-(6-methylpyrimidin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-amine;
(R)-N-((1R,5S,8s)-3-(6-methylpyrimidin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-8-(2,3,4-trifluorophenoxy)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amine;
(S)-N-((1R,5S,8s)-3-(6-methylpyrimidin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-8-(2,3,4-trifluorophenoxy)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amine;
(R)-8-(3,4-difluorophenoxy)-N-((1R,5S,8s)-3-(6-methylpyrimidin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amine; and
(S)-8-(3,4-difluorophenoxy)-N-((1R,5S,8s)-3-(6-methylpyrimidin-4-yl)-3-azabicyclo[3.2.1]octan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amine;

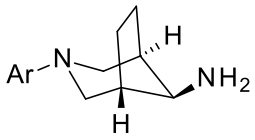
or a pharmaceutically acceptable salt thereof.

13. A process for the preparation of a compound according to any one of claims 1 to 12, or a pharmaceutically acceptable salt thereof, comprising reacting a compound **7**



7

with an amine **8**



8

wherein Ar, R^1, n and m are as defined in any one of claims 1 to 12,
to form said compound of formula (I), and if desired, converting the compounds obtained into a pharmaceutically acceptable salt thereof.

14. A compound according to any one of claims 1 to 12, or a pharmaceutically acceptable salt thereof, for use as therapeutically active substance.

15. A pharmaceutical composition comprising a compound according to any one of claims 1 to 12, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient.

16. A compound according to any one of claims 1 to 12, or a pharmaceutically acceptable salt thereof, for use in the therapeutic and/or prophylactic treatment of Alzheimer's disease, cerebral amyloid angiopathy, cochlear synaptopathy, hearing loss, hereditary cerebral hemorrhage with amyloidosis-Dutch type, multi-infarct dementia, dementia pugilistica, or Down syndrome.

17. The use of a compound according to any one of claims 1 to 12, or a pharmaceutically acceptable salt thereof, in the preparation of a medicament for the therapeutic and/or prophylactic treatment of Alzheimer's disease, cerebral amyloid angiopathy, cochlear synaptopathy, hearing loss, hereditary cerebral hemorrhage with

amyloidosis-Dutch type, multi-infarct dementia, dementia pugilistica, or Down syndrome.