proteins of the Notch receptor family, however, γ-secretase has loose substrate specificity and may cleave further membrane proteins unrelated to APP and Notch.

The γ-secretase activity is absolutely required for the production of Aβ peptides. This has been shown both by genetic means, i.e., ablation of the presenilin genes and by low-molecular-weight inhibitory compounds. Since according to the amyloid hypothesis for AD the production and deposition of Aβ is the ultimate cause for the disease, it is thought that selective and potent inhibitors of γ-secretase will be useful for the prevention and treatment of AD.

An alternative mode of treatment is the modulation of the γ-secretase activity which results in a selective reduction of the Aβ42 production. This will result in an increase of shorter Aβ isoforms, such as Aβ38, Aβ37 or others, which have reduced capability for aggregation and plaque formation, and are less neurotoxic. Compounds which show this effect on modulating γ-secretase activity include certain non-steroidal anti-inflammatory drugs (NSAIDs) and related analogues (Weggen et al. Nature, 414 (2001) 212-16).

Thus, the compounds of this disclosure~~invention~~ will be useful for the treatment or prevention of a disease associated with the deposition of β-amyloid in the brain, in particular Alzheimer's disease, and other diseases such as cerebral amyloid angiopathy, hereditary cerebral hemorrhage with amyloidosis, Dutch-type (HCHWA-D), multi-infarct dementia, dementia pugilistica and Down syndrome.

Numerous documents describe the current knowledge on γ-secretase modulation, for example the following publications:

Morihara et al, J. Neurochem., 83 (2002) 1009-12

Jantzen et al, J.Neuroscience, 22 (2002) 226-54

Takahashi et al, J. Biol. Chem., 278 (2003) 18644-70

Beher et al, J. Biol. Chem. 279 (2004) 43419-26

Lleo et al, Nature Med. 10 (2004) 1065-6

Kukar et al, Nature Med. 11 (2005) 545-50

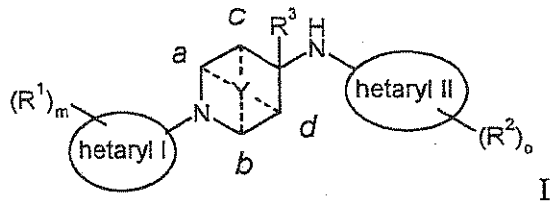
Perretto et al, J. Med. Chem. 48 (2005) 5705-20

Clarke et al, J. Biol. Chem. 281 (2006) 31279-89

Stock et al, Bioorg. Med. Chem. Lett. 16 (2006) 2219–2223

Narlawar et al, J. Med. Chem. 49 (2006) 7588-91

In a first aspect, there is provided a compound of formula



I

hetaryl I is a five or six membered heteroaryl group, containing 1 to 3 heteroatoms, selected from S or N;

hetaryl II is a six membered heteroaryl group, containing 1 to 3 heteroatoms, selected from S or N, or is a two membered ring system containing 1 to 4 heteroatoms selected from S, or N, wherein at least one ring is aromatic in nature;

R^1 is lower alkyl, lower alkoxy, lower alkyl substituted by halogen or halogen;

R^2 is lower alkyl, lower alkyl substituted by halogen, halogen, lower alkoxy, cycloalkyl substituted by lower alkyl or lower alkyl substituted by halogen, or is lower alkyl substituted by hydroxy, furyl, O-benzyl, or $-(CH_2)_p$-phenyl, optionally substituted by halogen, lower alkoxy, lower alkyl substituted by halogen, lower alkyl or by cyano;

R^3 is hydrogen or lower alkyl;

Y is $-(CH_2)_n$-, $-CH_2OCH_2$-, $-CH_2O$-, CH_2S-, $-CH_2SCH_2$- and is bonded to two of the ring carbon atoms, bonding being to either the ring carbon atoms *a* and *b* or the ring carbon atoms *c* and *d*;

p is 0 or 1;

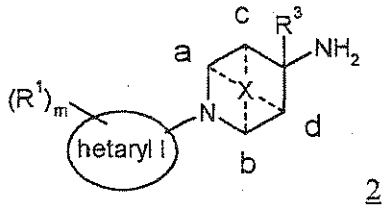
m is 0, 1 or 2; if m is 2 then R^1 may be the same or different;

n is 2 or 3;

o is 0, 1 or 2, if o is 2, then R^2 may be the same or different;

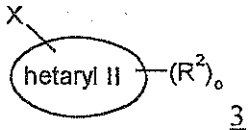
or a pharmaceutically active acid addition salts thereof.

In a second aspect, there is provided a process for preparing a compound of formula I as defined above, which process comprises a) reacting a compound of formula



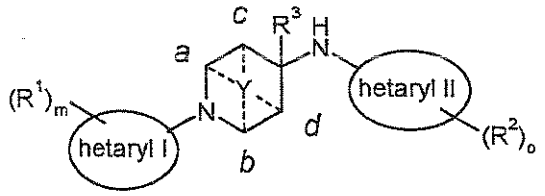
2

with a compound of formula



3

to a compound of formula



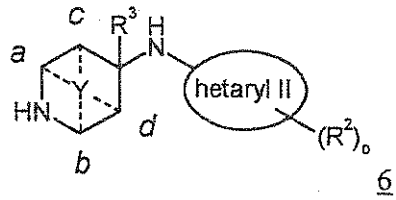
I

wherein X is halogen and the further groups have the meaning as described above and,

if desired, converting the compounds obtained into pharmaceutically acceptable acid addition salts;

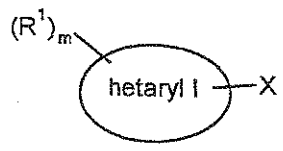
or

b) reacting a compound of formula



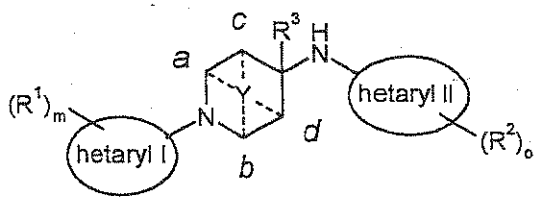
6

with a compound of formula



7

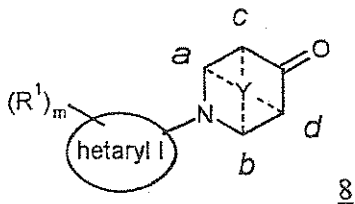
to a compound of formula



I

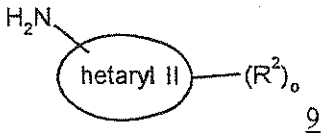
wherein X is halogen and the further groups have the meaning as described above, or

c) reacting a compound of formula



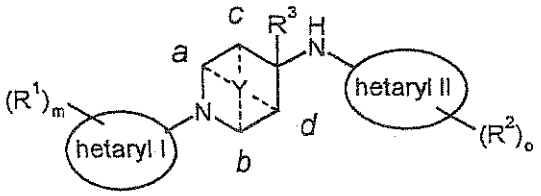
8

with a compound of formula



9

to a compound of formula



I

wherein the groups have the meaning as described above and R^3 is hydrogen, and,
if desired converting the compounds obtained into pharmaceutically acceptable acid addition salts.

In a third aspect, there is provided a compound as defined above, whenever prepared by a process as defined above.

In a fourth aspect, there is provided a medicament containing one or more compounds as defined above and pharmaceutically acceptable excipients.

In a fifth aspect, there is provided the use of a compound as defined above for the manufacture of medicaments for the treatment of Alzheimer's disease, cerebral amyloid angiopathy, hereditary cerebral hemorrhage with amyloidosis, Dutch-type (HCHWA-D), multi-infarct dementia, dementia pugilistica or Down syndrome.

In a sixth aspect, there is provided a compound as defined above for use as therapeutically active substance.

In a seventh aspect, there is provided a compound as defined above for the treatment of Alzheimer's disease, cerebral amyloid angiopathy, hereditary cerebral hemorrhage with amyloidosis, Dutch-type (HCHWA-D), multi-infarct dementia, dementia pugilistica or Down syndrome.

The following definitions for compounds of formula I are used: