

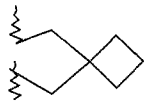
wherein

R^1 is phenyl, optionally substituted by one or two substituents, selected from ^3H , halogen, ~~lower C_{1-7} -alkyl~~, di-methyl-amino, $NHC(O)$ -~~lower C_{1-7} -alkyl~~, $C(O)O$ -~~lower C_{1-7} -alkyl~~, ~~lower C_{1-7} -alkoxy~~, $OC(^3H)_3$, $O^{11}CH_3$, $OCH_2CH_2^{18}F$, ~~lower C_{1-7} -alkoxy~~ substituted by halogen, hydroxy, ~~lower C_{1-7} -alkyl~~ substituted by hydroxy, S -~~lower C_{1-7} -alkyl~~, or by a heterocyclyl group; or is benzo[d][1,3]dioxol-5-yl, 2,3-dihydrobenzo[b][1,4]dioxin-6-yl, indolin-2-one, or is heteroaryl, selected from the group consisting of thiophenyl, benzofuranyl, benzothiophenyl, pyrazinyl, or benzothiazolyl;

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

R^3 is ~~lower C_{1-7} -alkyl~~, $C(^3H)_3$, $^{11}CH_3$, ~~lower C_{1-7} -alkyl~~ substituted by halogen, $-(CH_2)_2-O$ -~~lower C_{1-7} -alkyl~~ substituted by halogen or cycloalkyl; or

R^2 and R^3 form together with the N-atom to which they are attach a ring containing $-CH_2CH_2CHRCH_2CH_2-$, $-CH_2CH_2CH_2CH_2-$, $-CH_2CH_2CH_2-$, $-CH_2CH_2-NR-CH_2CH_2-$,

$-CH_2CH_2-O-CH_2CH_2-$, $-CH_2CH_2CHRCH_2-$, $-CH_2CHRCH_2-$ or  ;

R is hydrogen, halogen, ~~lower C_{1-7} -alkyl~~ substituted by halogen or ~~lower C_{1-7} -alkoxy~~; or a pharmaceutically acceptable acid addition salt, a racemic mixture or its corresponding enantiomer and/or optical isomers thereof.

In another aspect, there is provided a compound of formula I as defined herein for use in binding and imaging tau aggregates, beta-amyloid aggregates or alpha-synuclein aggregates.

In another aspect, there is provided a compound of formula I as defined herein for use in binding and imaging tau aggregates in Alzheimer patients.

In another aspect, there is provided a compound of formula I as defined herein for use in a tau-binding study.

In another aspect, there is provided a compound of formula I as defined herein for use in diagnostic imaging of tau-aggregates in the brain of a mammal.

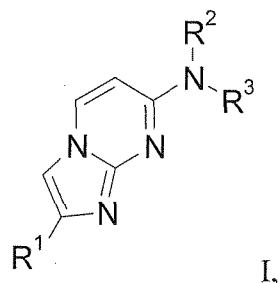
In another aspect, there is provided a pharmaceutical composition comprising a compound of formula I as defined herein and a pharmaceutical acceptable carrier.

The present invention also relates to a method of imaging tau-aggregate deposits, comprising

- introducing into a mammal a detectable quantity of a composition
- allowing sufficient time for the compound of formula I to be associated with tau-aggregate deposits, and
- detecting the compound associated with one or more tau-aggregate deposits.

Claims

1. A compound of formula



wherein

- 5 R^1 is phenyl, optionally substituted by one or two substituents, selected from ^3H , halogen, ~~lower C₁₋₇-alkyl~~, di-methyl-amino, $NHC(O)-\text{lower C}_{1-7}\text{-alkyl}$, $C(O)O-\text{lower C}_{1-7}\text{-alkyl}$, ~~lower C₁₋₇-alkoxy~~, $OC(^3H)_3$, $O^{11}CH_3$, $OCH_2CH_2^{18}F$, ~~lower C₁₋₇-alkoxy~~ substituted by halogen, hydroxy, ~~lower C₁₋₇-alkyl~~ substituted by hydroxy, $S-\text{lower C}_{1-7}\text{-alkyl}$, or by a heterocyclyl group; or is
- 10 benzo[d][1,3]dioxol-5-yl, 2,3-dihydrobenzo[b][1,4]dioxin-6-yl, indolin-2-one, or is heteroaryl, selected from the group consisting of thiophenyl, benzofuranyl, benzothiophenyl, pyrazinyl, or benzothiazolyl;

R^2 is hydrogen, ~~lower C₁₋₇-alkyl~~ or ~~lower C₁₋₇-alkyl~~ substituted by halogen;

- 15 R^3 is ~~lower C₁₋₇-alkyl~~, $C(^3H)_3$, $^{11}CH_3$, ~~lower C₁₋₇-alkyl~~ substituted by halogen, $-(CH_2)_2-O-\text{lower C}_{1-7}\text{-alkyl}$ substituted by halogen or cycloalkyl; or

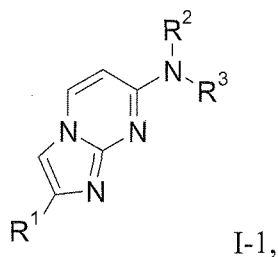
R^2 and R^3 form together with the N-atom to which they are attach a ring containing $-\text{CH}_2\text{CH}_2\text{CHRCH}_2\text{CH}_2-$, $-\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2-$, $-\text{CH}_2\text{CH}_2\text{CH}_2-$, $-\text{CH}_2\text{CH}_2-\text{NR}-\text{CH}_2\text{CH}_2-$,



R is hydrogen, halogen, ~~lower C₁₋₇-alkyl~~ substituted by halogen or ~~lower C₁₋₇-alkoxy~~;

- 20 or a pharmaceutically acceptable acid addition salt, a racemic mixture or its corresponding enantiomer and/or optical isomers thereof.

2. A compound of formula I-1 according to claim 1



wherein

R¹ is phenyl, optionally substituted by one or two substituents, selected from ³H, halogen, lower C₁₋₇-alkyl, di-methyl-amino, NHC(O)-lower C₁₋₇-alkyl, C(O)O-lower C₁₋₇-alkyl, lower C₁₋₇-alkoxy, OC(³H)₃, O¹¹CH₃, OCH₂CH₂¹⁸F, lower C₁₋₇-alkoxy substituted by halogen, hydroxy, lower C₁₋₇-alkyl substituted by hydroxy, S-lower C₁₋₇-alkyl, or by a heterocyclyl group;

R² is hydrogen, lower C₁₋₇-alkyl or lower C₁₋₇-alkyl substituted by halogen;

R³ is lower C₁₋₇-alkyl, C(³H)₃, ¹¹CH₃, lower C₁₋₇-alkyl substituted by halogen, -(CH₂)₂-O-lower C₁₋₇-alkyl substituted by halogen or cycloalkyl; or

R² and R³ form together with the N-atom to which they are attached a ring containing
-CH₂CH₂CHRCH₂CH₂-, -CH₂CH₂CH₂CH₂-, -CH₂CH₂CH₂-, -CH₂CH₂-NR-CH₂CH₂-,



R is hydrogen, halogen, lower C₁₋₇-alkyl substituted by halogen or lower C₁₋₇-alkoxy;

or a pharmaceutically acceptable acid addition salt, a racemic mixture or its corresponding enantiomer and/or optical isomers thereof.

3. A compound of formula I-1 according to any one of claims 1 or 2, wherein the compounds are

N-methyl-2-phenylimidazo[1,2-a]pyrimidin-7-amine

7-(4-fluoropiperidin-1-yl)-2-phenylimidazo[1,2-a]pyrimidine

7-(4-fluoropiperidin-1-yl)-2-(4-methoxyphenyl)imidazo[1,2-a]pyrimidine

2-(4-chlorophenyl)-7-(4-fluoropiperidin-1-yl)imidazo[1,2-a]pyrimidine

7-(4-fluoropiperidin-1-yl)-2-(3-methoxyphenyl)imidazo[1,2-a]pyrimidine

2-(4-fluorophenyl)-7-(4-fluoropiperidin-1-yl)imidazo[1,2-a]pyrimidine

wherein

R¹ is benzo[d][1,3]dioxol-5-yl, 2,3-dihydrobenzo[b][1,4]dioxin-6-yl or indolin-2-one;

R² is hydrogen, ~~lower C₁₋₇~~-alkyl or ~~lower C₁₋₇~~-alkyl substituted by halogen;

R³ is ~~lower C₁₋₇~~-alkyl, C(³H)₃, ¹¹CH₃, ~~lower C₁₋₇~~-alkyl substituted by halogen, -(CH₂)₂-O-
5 ~~lower C₁₋₇~~-alkyl substituted by halogen or cycloalkyl; or

R² and R³ form together with the N-atom to which they are attach a ring containing
-CH₂CH₂CHRCH₂CH₂-, -CH₂CH₂CH₂CH₂-, -CH₂CH₂CH₂-, -CH₂CH₂-NR-CH₂CH₂-,



R is hydrogen, halogen, ~~lower C₁₋₇~~-alkyl substituted by halogen or ~~lower C₁₋₇~~-alkoxy;

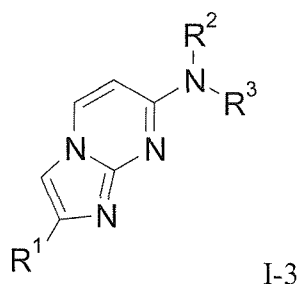
10 or a pharmaceutically acceptable acid addition salt, a racemic mixture or its
corresponding enantiomer and/or optical isomers thereof.

5. A compound of formula I-2 according to any one of claims 1 or 4, wherein the compounds
are

- 15 2-(1,3-benzodioxol-5-yl)-7-(4-fluoropiperidin-1-yl)imidazo[1,2-a]pyrimidine
2-(2,3-dihydro-1,4-benzodioxin-6-yl)-7-(4-fluoropiperidin-1-yl)imidazo[1,2-a]pyrimidine
2-(1,3-benzodioxol-5-yl)-N,N-dimethylimidazo[1,2-a]pyrimidin-7-amine
2-(2,3-dihydro-1,4-benzodioxin-6-yl)-N,N-dimethylimidazo[1,2-a]pyrimidin-7-amine
2-(1,3-benzodioxol-5-yl)-7-[4-(2-fluoroethyl)piperidin-1-yl]imidazo[1,2-a]pyrimidine
20 2-(2,3-dihydro-1,4-benzodioxin-6-yl)-7-[4-(2-fluoroethyl)piperidin-1-yl]imidazo[1,2-
a]pyrimidine
2-(1,3-benzodioxol-5-yl)-N-methylimidazo[1,2-a]pyrimidin-7-amine
2-(1,3-benzodioxol-5-yl)-N-(2-fluoroethyl)-N-methylimidazo[1,2-a]pyrimidin-7-amine or
5-(7-(methylamino)imidazo[1,2-a]pyrimidin-2-yl)indolin-2-one.

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6. A compound of formula I-3 according to claim 1



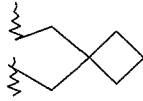
wherein

R^1 is heteroaryl, selected from the group consisting of thiophenyl, benzofuranyl, benzothiophenyl pyrazinyl or benzothiazolyl;

5 R^2 is hydrogen or lower C_{1-7} -alkyl;

R^3 is lower C_{1-7} -alkyl, $C(H)_3$, lower C_{1-7} -alkyl substituted by halogen, $-(CH_2)_2-O$ -lower C_{1-7} -alkyl substituted by halogen or cycloalkyl; or

R^2 and R^3 form together with the N-atom to which they are attached a ring containing
 $-CH_2CH_2CHRCH_2CH_2-$, $-CH_2CH_2CH_2CH_2-$, $-CH_2CH_2CH_2-$, $-CH_2CH_2-NR-CH_2CH_2-$,

10 $-CH_2CH_2-O-CH_2CH_2-$, $-CH_2CH_2CHRCH_2-$, $-CH_2CHRCH_2-$ or  ;

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

or a pharmaceutically acceptable acid addition salt, a racemic mixture or its corresponding enantiomer and/or optical isomers thereof.

15 7. A compound of formula I-3 according to any one of claims 1 and 6, which compounds are

7-(4-fluoropiperidin-1-yl)-2-thiophen-3-ylimidazo[1,2-a]pyrimidine

2-(1-benzofuran-2-yl)-7-(4-fluoropiperidin-1-yl)imidazo[1,2-a]pyrimidine

2-(1-benzothiophen-2-yl)-7-(4-fluoropiperidin-1-yl)imidazo[1,2-a]pyrimidine

2-[7-(4-fluoropiperidin-1-yl)imidazo[1,2-a]pyrimidin-2-yl]-1,3-benzothiazole

20 N,N-dimethyl-2-thiophen-3-ylimidazo[1,2-a]pyrimidin-7-amine or

7-(4-fluoropiperidin-1-yl)-2-(pyrazin-2-yl)imidazo[1,2-a]pyrimidine.

8. A compound of formula I according to any one of claims 1 – 7 for use in binding and imaging tau aggregates, beta-amyloid aggregates or alpha-synuclein aggregates.