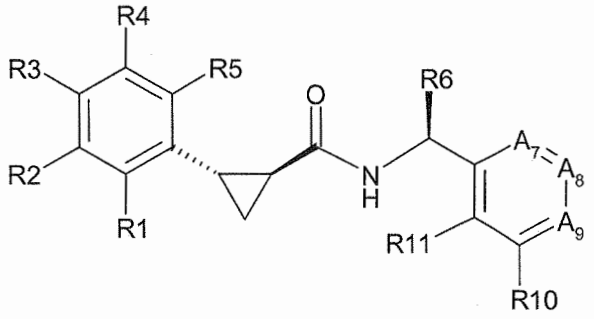
CLAIMS

1. A compound according to formula [I]



[I]

wherein R1, R2, R3, R4 and R5 are selected independently of each other from H, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}alkoxy, cyano and halogen, wherein said C_{1-6}alkyl, C_{2-6}alkenyl and C_{2-6}alkynyl is optionally substituted with one or more substituents independently selected from chlorine and fluorine;

R6 is hydroxymethyl;

A7 is C-R7, A8 is N and A9 is C-R9;

R7, R10 and R11 all represent H;

R9 is selected from methyl, C_{1-4}alkoxy or cyano, wherein said methyl is optionally substituted with one or more fluorine;

and pharmaceutically acceptable salts thereof.

2. The compound according to claim 1, wherein four or more of R1, R2, R3, R4 and R5 are H.

3. The compound according to any of claims 1-2 having a diastereomeric excess of at least 80%.

4. The compound according to claim 1 selected from

21: *(1S,2S)-2-Phenyl-cyclopropanecarboxylic acid [(R)-2-hydroxy-1-(6-propoxy-pyridin-3-yl)-ethyl]-amide;*

22: *(1S,2S)-2-Phenyl-cyclopropanecarboxylic acid [(R)-2-hydroxy-1-(6-trifluoromethyl-pyridin-3-yl)-ethyl]-amide;*

24: *(1S,2S)-2-Phenyl-cyclopropanecarboxylic acid [(R)-2-hydroxy-1-(6-methoxy-pyridin-3-yl)-ethyl]-amide;*

25: *(1S,2S)-2-Phenyl-cyclopropanecarboxylic acid [(R)-2-hydroxy-1-(6-methyl-pyridin-3-yl)-ethyl]-amide;*

26: *(1S,2S)-2-Phenyl-cyclopropanecarboxylic acid [(R)-2-hydroxy-1-(6-isopropoxy-pyridin-3-yl)-ethyl]-amide;*

27: *(1S,2S)-2-(3-Fluoro-phenyl)-cyclopropanecarboxylic acid [(R)-1-(6-ethoxy-pyridin-3-yl)-2-hydroxy-ethyl]-amide;*

28: *(1S,2S)-2-(4-Fluoro-phenyl)-cyclopropanecarboxylic acid [(R)-1-(6-ethoxy-pyridin-3-yl)-2-hydroxy-ethyl]-amide;*

29: *(1S,2S)-2-(3-Fluoro-phenyl)-cyclopropanecarboxylic acid [(R)-2-hydroxy-1-(6-propoxy-pyridin-3-yl)-ethyl]-amide;*

30: *(1S,2S)-2-(4-Fluoro-phenyl)-cyclopropanecarboxylic acid [(R)-2-hydroxy-1-(6-propoxy-pyridin-3-yl)-ethyl]-amide;*

31: *(1S,2S)-2-Phenyl-cyclopropanecarboxylic acid [(R)-1-(6-(2,2,2-d_3)-ethoxy-pyridin-3-yl)-2-hydroxy-ethyl]-amide;*

32: *(1S,2S)-2-(3-Fluoro-phenyl)-cyclopropanecarboxylic acid [(R)-1-(6-(1,1-d_2)-ethoxy-pyridin-3-yl)-2-hydroxy-ethyl]-amide;*

33: *(1S,2S)-2-Phenyl-cyclopropanecarboxylic acid [(R)-1-(6-ethoxy-pyridin-3-yl)-2-hydroxy-ethyl]-amide;*

34: *(1S,2S)-2-(4-Fluoro-phenyl)-cyclopropanecarboxylic acid [(R)-1-(6-(1,1,2,2,2-d_5)-ethoxy-pyridin-3-yl)-2-hydroxy-ethyl]-amide;*

35: *(1S,2S)-2-(4-Fluoro-phenyl)-cyclopropanecarboxylic acid [(R)-1-(6-(2,2,2-d_3)-ethoxy-pyridin-3-yl)-2-hydroxy-ethyl]-amide;*

36: *(1S,2S)-2-Phenyl-cyclopropanecarboxylic acid [(R)-1-(6-(1,1-d_2)-ethoxy-pyridin-3-yl)-2-hydroxy-ethyl]-amide;*

37: *(1S,2S)-2-(4-Fluoro-phenyl)-cyclopropanecarboxylic acid [(R)-1-(6-(1,1-d_2)-ethoxy-pyridin-3-yl)-2-hydroxy-ethyl]-amide;*

38: *(1S,2S)-2-Phenyl-cyclopropanecarboxylic acid [(R)-1-(6-(1,1,2,2,2-d_5)-ethoxy-pyridin-3-yl)-2-hydroxy-ethyl]-amide;*

39: *(1S,2S)-2-(3-Fluoro-phenyl)-cyclopropanecarboxylic acid [(R)-1-(6-(2,2,2-d_3)-ethoxy-pyridin-3-yl)-2-hydroxy-ethyl]-amide;*

40: *(1S,2S)-2-Phenyl-cyclopropanecarboxylic acid [(R)-1-(6-cyclobutoxy-pyridin-3-yl)-2-hydroxy-ethyl]-amide;*

41: *(1S,2S)-2-(3-Fluoro-phenyl)-cyclopropanecarboxylic acid [(R)-1-(6-cyclobutoxy-pyridin-3-yl)-2-hydroxy-ethyl]-amide;*

42: *(1S,2S)-2-(4-Fluoro-phenyl)-cyclopropanecarboxylic acid [(R)-1-(6-cyclobutoxy-pyridin-3-yl)-2-hydroxy-ethyl]-amide;*
and pharmaceutically acceptable salts of any of these compounds.

5. The compound according to claim 1, which is
21: *(1S,2S)-2-Phenyl-cyclopropanecarboxylic acid [(R)-2-hydroxy-1-(6-propoxy-pyridin-3-yl)-ethyl]-amide;*
and pharmaceutically acceptable salts thereof.

6. The compound according to claim 1, which is
27: *(1S,2S)-2-(3-Fluoro-phenyl)-cyclopropanecarboxylic acid [(R)-1-(6-ethoxy-pyridin-3-yl)-2-hydroxy-ethyl]-amide;*
and pharmaceutically acceptable salts thereof.

7. The compound according to claim 1, which is
28: *(1S,2S)-2-(4-Fluoro-phenyl)-cyclopropanecarboxylic acid [(R)-1-(6-ethoxy-pyridin-3-yl)-2-hydroxy-ethyl]-amide;*
and pharmaceutically acceptable salts thereof.

8. The compound according to claim 1, which is
30: *(1S,2S)-2-(4-Fluoro-phenyl)-cyclopropanecarboxylic acid [(R)-2-hydroxy-1-(6-propoxy-pyridin-3-yl)-ethyl]-amide;*
and pharmaceutically acceptable salts thereof.

9. The compound according to claim 1, which is
33: *(1S,2S)-2-Phenyl-cyclopropanecarboxylic acid [(R)-1-(6-ethoxy-pyridin-3-yl)-2-hydroxy-ethyl]-amide;*
and pharmaceutically acceptable salts thereof.

10. The compound according to claim 1, which is
35: *(1S,2S)-2-(4-Fluoro-phenyl)-cyclopropanecarboxylic acid [(R)-1-(6-(2,2,2-d_3)-ethoxy-pyridin-3-yl)-2-hydroxy-ethyl]-amide:*
and pharmaceutically acceptable salts thereof.

11. A compound according to any of claims 1-10, for use as a medicament.

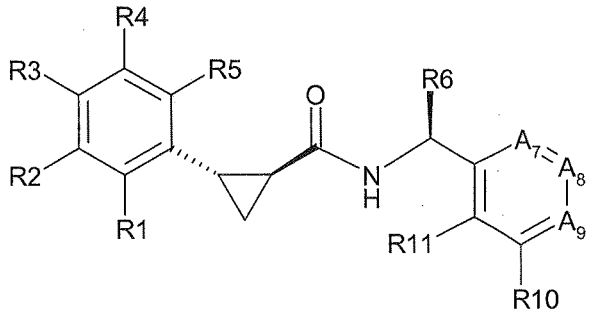
12. Use of a compound according to any of claims 1-10, in the manufacture of a medicament for the treatment of a disease or disorder selected from Psychosis; Schizophrenia; cognitive disorders; cognitive impairment associated with schizophrenia; Attention Deficit Hyperactivity Disorder (ADHD); autism spectrum disorders, Alzheimer's disease (AD); mild cognitive impairment (MCI); age associated memory impairment (AAMI); senile dementia; AIDS dementia; Pick's disease; dementia associated with Lewy bodies; dementia associated with Down's syndrome; Huntington's Disease; Parkinson's disease (PD); obsessive-compulsive disorder (OCD); traumatic brain injury; epilepsy; post-traumatic stress; Wernicke-Korsakoff syndrome (WKS); post-traumatic amnesia; cognitive deficits associated with depression; diabetes, weight control, inflammatory disorders, reduced angiogenesis; amyotrophic lateral sclerosis and pain.

13. A pharmaceutical composition comprising a compound according to any of claims 1-10, and one or more pharmaceutically acceptable carrier or excipient.

14. A kit comprising a compound according to any of claims 1-10, together with a second compound selected from the list consisting of acetylcholinesterase inhibitors; glutamate receptor antagonists; dopamine transport inhibitors; noradrenalin transport inhibitors; D2 antagonists; D2 partial agonists; PDE10 antagonists; 5-HT2A antagonists; 5-HT6 antagonists; KCNQ antagonists; lithium; sodium channel blockers and GABA signaling enhancers.

CLAIMS

1. A compound according to formula [I]



[I]

wherein R1, R2, R3, R4 and R5 are selected independently of each other from H, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}alkoxy, cyano and halogen, wherein said C_{1-6}alkyl, C_{2-6}alkenyl and C_{2-6}alkynyl is optionally substituted with one or more substituents independently selected from chlorine and fluorine;

R6 is hydroxymethyl;

A7 is C-R7, A8 is N and A9 is C-R9;

R7, R9, R10 and R11 are selected independently of each other from H, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}alkoxy, cyano, NR12R13, C_{1-6}alkylsulfonyl and halogen, wherein said C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl or C_{1-6}alkoxy is optionally substituted with one or more substituents selected from chlorine, fluorine, C_{1-6}alkoxy, cyano and NR12R13;

R12 and R13 independently represent hydrogen, C_{1-6}alkyl, C_{2-6}alkenyl and C_{2-6}alkynyl;

and pharmaceutically acceptable salts thereof.

2. The compound according to claim 1, wherein four or more of R1, R2, R3, R4 and R5 are H.

3. The compound according to any of claims 1-2, wherein R7, R9, R10 and R11 are selected independently of each other from H, C_{1-4}alkyl, C_{1-4}alkoxy, cyano, $-N(CH_3)_2$, methylsulfonyl, fluorine and chlorine, wherein said C_{1-4}alkyl or C_{1-4}alkoxy is optionally substituted with one or more substituents selected from fluorine, C_{1-4}alkoxy and cyano.

4. The compound according to any of claims 1-2, wherein R7, R8, R9, R10 and R11 are selected independently from H, C_{1-4}alkyl, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{1-4}alkoxy, cyano and halogen, wherein said C_{1-4}alkyl, C_{2-4}alkenyl, C_{2-4}alkynyl or C_{1-4}alkoxy is optionally substituted with one or more substituents selected from fluorine and C_{1-4}alkoxy.

5. The compound according to claim 1, wherein one or more of the hydrogen atoms are represented by deuterium.

6. The compound according to claim 5, wherein at least about 85% of the compound has a deuterium atom at each position designated as deuterium, and any atom not designated as deuterium is present at about its natural isotopic abundance.

7. The compound according to any of claims 1-2 having a diastereomeric excess of at least 80% such as at least 85%, such as at least 90%, such as at least 95%.

8. The compound according to claim 1 selected from

21: *(1S,2S)-2-Phenyl-cyclopropanecarboxylic acid [(R)-2-hydroxy-1-(6-propoxy-pyridin-3-yl)-ethyl]-amide;*

22: *(1S,2S)-2-Phenyl-cyclopropanecarboxylic acid [(R)-2-hydroxy-1-(6-trifluoromethyl-pyridin-3-yl)-ethyl]-amide;*

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36: *(1S,2S)-2-Phenyl-cyclopropanecarboxylic acid [(R)-1-(6-(1,1-d_2)-ethoxy-pyridin-3-yl)-2-hydroxy-ethyl]-amide;*

37: *(1S,2S)-2-(4-Fluoro-phenyl)-cyclopropanecarboxylic acid [(R)-1-(6-(1,1-d_2)-ethoxy-pyridin-3-yl)-2-hydroxy-ethyl]-amide;*

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40: *(1S,2S)-2-Phenyl-cyclopropanecarboxylic acid [(R)-1-(6-cyclobutoxy-pyridin-3-yl)-2-hydroxy-ethyl]-amide;*

41: *(1S,2S)-2-(3-Fluoro-phenyl)-cyclopropanecarboxylic acid [(R)-1-(6-cyclobutoxy-pyridin-3-yl)-2-hydroxy-ethyl]-amide;*

42: *(1S,2S)-2-(4-Fluoro-phenyl)-cyclopropanecarboxylic acid [(R)-1-(6-cyclobutoxy-pyridin-3-yl)-2-hydroxy-ethyl]-amide;*

and pharmaceutically acceptable salts of any of these compounds.

9. A compound according to any of claims 1 or 8, for use as a medicament.

10. Use of a compound according to any of claims 1 or 8, in the manufacture of a medicament for the treatment of a disease or disorder selected from Psychosis; Schizophrenia; cognitive disorders; cognitive impairment associated with schizophrenia; Attention Deficit Hyperactivity Disorder (ADHD); autism spectrum disorders, Alzheimer's disease (AD); mild cognitive impairment (MCI); age associated memory impairment (AAMI); senile dementia; AIDS dementia; Pick's disease; dementia associated with Lewy bodies; dementia associated with Down's syndrome; Huntington's Disease; Parkinson's disease (PD); obsessive-compulsive disorder (OCD); traumatic brain injury; epilepsy; post-traumatic stress; Wernicke-Korsakoff syndrome (WKS); post-traumatic amnesia; cognitive deficits associated with depression; diabetes, weight control, inflammatory disorders, reduced angiogenesis; amyotrophic lateral sclerosis and pain.

12. A pharmaceutical composition comprising a compound according to any of claims 1 or 8, and one or more pharmaceutically acceptable carrier or excipient.

13. A kit comprising a compound according to any of claims 1 or 8, together with a second compound selected from the list consisting of acetylcholinesterase inhibitors; glutamate receptor antagonists; dopamine transport inhibitors; noradrenalin transport inhibitors;

D2 antagonists; D2 partial agonists; PDE10 antagonists; 5-HT2A antagonists; 5-HT6 antagonists; KCNQ antagonists; lithium; sodium channel blockers and GABA signaling enhancers.

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