- Amyotrophic lateral
- Ischemia due to stroke

Other diseases:

- Inflammation in the CNS for instance following encephalitis, primary angiitis, meningitis

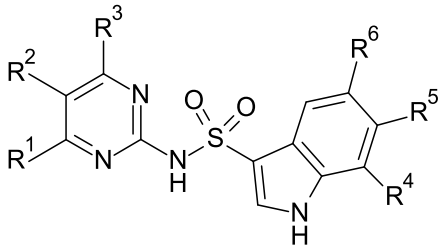
The compounds of formula I bind to and modulates GPR17 activity.

The compounds of formula I are therefore particularly useful in the treatment of diseases related to GPR17 antagonism.

The compounds of formula I are particularly useful in the treatment or prophylaxis of multiple sclerosis (MS), conditions related to direct damage to myelin sheaths such as carbon monoxide poisoning or virus induced demyelination, primary demyelinating disorders such as acute and multiphasic disseminated encephalomyelitis, and other CNS disorders associated with myelin loss such as Alzheimer's disease, schizophrenia, Parkinson's disease and Huntington's disease.

Summary

In one aspect, the present disclosure provides compounds of formula I



I

wherein

R^1 is alkoxy or haloalkoxy;

R^2 is halo, alkyl, alkoxy, haloalkyl, haloalkoxy, cyanoalkyl, cyanoalkoxy or cyclopropyl optional substituted with up to two substituents independently selected from cyano and halo;

R^3 is H, alkoxy or haloalkoxy;

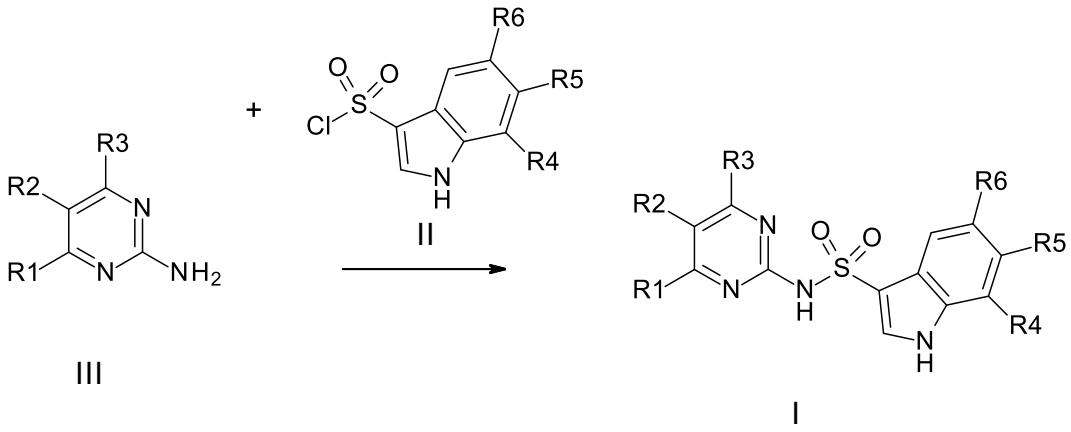
R^5 is H, halo, alkyl, or haloalkyl;

R^6 is H or halo;

R^4 is a C-linked aryl or a C-linked heteroaryl, wherein the C-linked aryl or C-linked heteroaryl is optionally substituted by one or more substituents independently selected from alkyl, halo, and haloalkyl;

and pharmaceutically acceptable salts.

In another aspect, the present disclosure provides a process to prepare a compound as described herein comprising the reacting a compound of formula III with a compound of formula II in the presence of a base selected from N-ethyldiisopropylamine, pyridine, potassium phosphate or sodium hydride, to provide a compound of formula I,



wherein R^1, R^2, R^3, R^3, R^4, R^5 and R^6 are as described above.

In another aspect, the present disclosure provides a compound as described herein for use as therapeutically active substance.

In another aspect, the present disclosure provides a compound as described herein for use in the treatment of a disease modulated by GPR17.

In another aspect, the present disclosure provides a pharmaceutical composition comprising a compound as described herein and a therapeutically inert carrier.

In another aspect, the present disclosure provides the use of a compound as described herein in the preparation of a medicament for the treatment or prophylaxis of multiple sclerosis.

In another aspect, the present disclosure provides the use of a compound as described herein in the preparation of a medicament for the treatment or prophylaxis of conditions resulting from direct damage to myelin sheaths (including but not limited central pontine and extra-pontine myelinolysis, carbon monoxide poisoning, nutritional deficiency, and virus-induced demyelination), demyelinating disorders (including but not limited to multiple sclerosis, acute and multiphasic disseminated encephalomyelitis, neuromyelitis optica spectrum disorders, and leukodystrophies), CNS disorders associated with myelin loss (including but not limited to Alzheimer's disease, schizophrenia, Parkinson's disease, Huntington's disease, Amyotrophic lateral sclerosis, and Ischemia due to stroke), and inflammation in the CNS for instance following encephalitis, primary angiitis, meningitis and obesity.

In another aspect, the present disclosure provides a compound as described herein for use in the treatment or prophylaxis of conditions resulting from direct damage to myelin sheaths (including but not limited central pontine and extra-pontine myelinolysis, carbon monoxide poisoning, nutritional deficiency, and virus-induced demyelination), demyelinating disorders (including but not limited to multiple sclerosis, acute and multiphasic disseminated encephalomyelitis, neuromyelitis optica spectrum disorders, and leukodystrophies), CNS disorders associated with myelin loss (including but not limited to Alzheimer's disease, schizophrenia, Parkinson's disease, Huntington's disease, Amyotrophic lateral sclerosis, and Ischemia due to stroke), and inflammation in the CNS for instance following encephalitis, primary angiitis, meningitis and obesity.

In another aspect, the present disclosure provides a compound as described herein for use in the treatment or prophylaxis of multiple sclerosis.

In another aspect, the present disclosure provides a compound as described herein, when manufactured according to a process as described herein.

The term “alkyl” denotes a monovalent linear or branched saturated hydrocarbon group of 1 to 6 carbon atoms. In some embodiments, if not otherwise described, alkyl comprises 1 to 6 carbon atoms (C_{1-6}-alkyl), or 1 to 4 carbon atoms (C_{1-4}-alkyl). Examples of C_{1-6}-alkyl include methyl, ethyl, propyl, isopropyl, n-butyl, iso-butyl, sec-butyl, tert-butyl and pentyl. Particular alkyl group is methyl. When an alkyl residue having a specific number of carbons is named, all geometric isomers having that number of carbons may be encompassed. Thus, for example, "butyl" can include n-butyl, sec-butyl, isobutyl and t-butyl, and "propyl" can include n-propyl and isopropyl. Particular example of alkyl is methyl.

The term “alkoxy” denotes a group of the formula -O-R’, wherein R’ is a C_{1-6}-alkyl group. Examples of C_{1-6}-alkoxy groups include methoxy, ethoxy, n-propoxy, isopropoxy, n-butoxy, isobutoxy and tert-butoxy. Particular example is methoxy.

The term “aryl”, alone or in combination with other groups, denotes a monovalent cyclic aromatic hydrocarbon moiety consisting of a mono- or bicyclic aromatic ring. Preferred aryl is phenyl. Aryl may be unsubstituted or substituted as described herein. Particular example of aryl is phenyl.

The term “halogen”, “halide” and “halo” are used interchangeably herein and denote fluoro, chloro, bromo or iodo. Particular halogens are fluoro, chloro and bromo.

The term “haloalkyl” denotes a C_{1-6}-alkyl group wherein at least one of the hydrogen atoms of the C_{1-6}-alkyl group has been replaced by the same or different halogen atoms. Particular examples are difluoroethyl and diflouromethyl.

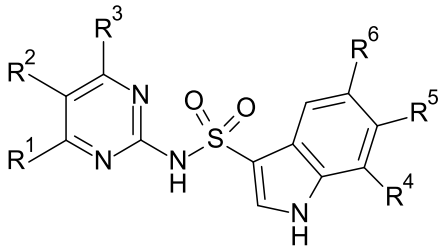
The term “haloalkoxy” denotes a C_{1-6}-alkoxy group wherein at least one of the hydrogen atoms of the C_{1-6}-alkoxy group has been replaced by the same or different halogen atoms. Particular examples fluoroethoxy, difluoroethoxy, and difluoromethoxy.

The term “cyano” denotes a -C≡N group.

“Cyanoalkyl" means a moiety of the formula -R'-R", where R' is alkyl as defined herein and R" is cyano or nitrile. An example of cyanoalkyl is cyanoethyl.

Claims

1. Compounds of formula I



I

wherein

R^1 is alkoxy or haloalkoxy;

R^2 is halo, alkyl, alkoxy, haloalkyl, haloalkoxy, cyanoalkyl, cyanoalkoxy or cyclopropyl optional substituted with up to two substituents independently selected from cyano and halo;

R^3 is H, alkoxy or haloalkoxy;

R^5 is H, halo, alkyl, or haloalkyl;

R^6 is H or halo;

R^4 is a C-linked aryl or a C-linked heteroaryl, wherein the C-linked aryl or C-linked heteroaryl is optionally substituted by one or more substituents independently selected from alkyl, halo, and haloalkyl;

and pharmaceutically acceptable salts.

2. A compound according to claim 1, wherein R^1 is alkoxy.

3. A compound according to claim 1 or claim 2, wherein R^2 is halo, alkyl, haloalkyl, haloalkoxy, cyanoalkyl, cyanoalkoxy or cyclopropyl substituted with cyano.

4. A compound according to any of claims 1 to 3, wherein R^2 is alkyl, haloalkyl or haloalkoxy.

5. A compound according to any of claims 1 to 4, wherein R^3 is H or alkoxy.

6. A compound according to any of claims 1 to 5, wherein R^5 is alkyl, H, or halo.

7. A compound according to any of claims 1 to 6, wherein R^5 is H or halo.

8. A compound according to any of claims 1 to 7 wherein R^6 is H.

9. A compound according to any of claims 1 to 8, wherein R^4 is a C-linked aryl or a C-linked heteroaryl, wherein the C-linked aryl or C-linked heteroaryl is optionally substituted by one or more substituents independently selected from alkyl and halo.

10. A compound according to any of claims 1 to 9, wherein R^4 is selected from

i. a C-linked 6-member aryl;

ii. a C-linked 6-member heteroaryl comprising 1 to 2 nitrogen heteroatoms optionally substituted with alkyl or halo;

iii. a C-linked 5-member heteroaryl comprising 1-3 heteroatoms independently selected from N, S and O, optionally substituted with 1 to 2 substituents independently selected from alkyl and halo; and

iv. a C-linked 8-membered bicyclic heteroaryl system comprising 2 N heteroatoms.

11. A compound according to claim 1, wherein

R^1 is alkoxy;

R^2 is halo, alkyl, haloalkyl, haloalkoxy, cyanoalkyl, cyanoalkoxy or cyclopropyl substituted with cyano;

R^3 is H or alkoxy;

R^5 is H, halo, alkyl, or haloalkyl;

R^6 is H or halo;

R^4 is a C-linked aryl or a C-linked heteroaryl, wherein the C-linked aryl or C-linked heteroaryl is optionally substituted by one or more substituents independently selected from alkyl and halo;

and pharmaceutically acceptable salts.

12. A compound according to claim 1, wherein

R^1 is alkoxy;

R^2 is halo, alkyl, haloalkyl, haloalkoxy, cyanoalkyl, cyanoalkoxy or cyclopropyl substituted with cyano;

R^3 is H or alkoxy;

R^5 is H, halo, alkyl, or haloalkyl;

R^6 is H or halo;

R^4 is selected from

i. a C-linked 6-member aryl;

ii. a C-linked 6-member heteroaryl comprising 1 to 2 nitrogen heteroatoms optionally substituted with alkyl or halo;

iii. a C-linked 5-member heteroaryl comprising 1-3 heteroatoms independently selected from N, S and O, optionally substituted with 1 to 2 substituents independently selected from alkyl and halo; and

iv. a C-linked 8-membered bicyclic heteroaryl system comprising 2 N heteroatoms;

and pharmaceutically acceptable salts

13. A compound according to any of claims 1 to 12, selected from

6-chloro-N-[5-(2,2-difluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-(2-pyrimidyl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2,2-difluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-oxazol-2-yl-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2,2-difluoroethyl)-4,6-dimethoxy-pyrimidin-2-yl]-7-(2-pyrimidyl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2,2-difluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-pyridazin-3-yl-1H-indole-3-sulfonamide;

N-[5-(2,2-difluoroethyl)-4,6-dimethoxy-pyrimidin-2-yl]-7-(1-methylimidazol-2-yl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2,2-difluoroethyl)-4,6-dimethoxy-pyrimidin-2-yl]-7-pyridazin-3-yl-1H-indole-3-sulfonamide;

N-[5-(2,2-difluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-(1-methylimidazol-2-yl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2,2-difluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-(1-methylimidazol-2-yl)-1H-indole-3-sulfonamide;

N-[5-(2,2-difluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-6-fluoro-7-(1-methylimidazol-2-yl)-1H-indole-3-sulfonamide;

N-[5-(2,2-difluoroethyl)-4,6-dimethoxy-pyrimidin-2-yl]-6-fluoro-7-(1-methylimidazol-2-yl)-1H-indole-3-sulfonamide;

N-[5-(2,2-difluoroethyl)-4,6-dimethoxy-pyrimidin-2-yl]-7-pyridazin-3-yl-1H-indole-3-sulfonamide;

N-[5-(2,2-difluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-pyridazin-3-yl-1H-indole-3-sulfonamide;

N-[5-(2,2-difluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-(4-methylpyridazin-3-yl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2,2-difluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-oxazol-4-yl-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2,2-difluoroethyl)-4,6-dimethoxy-pyrimidin-2-yl]-7-pyrazin-2-yl-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2,2-difluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-pyrazin-2-yl-1H-indole-3-sulfonamide;

N-[5-(2,2-difluoroethyl)-4,6-dimethoxy-pyrimidin-2-yl]-7-(2-pyrimidyl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2,2-difluoroethyl)-4,6-dimethoxy-pyrimidin-2-yl]-7-(2-pyridyl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2,2-difluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-(2-pyridyl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(difluoromethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-pyrazin-2-yl-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2-fluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-pyrazin-2-yl-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2-fluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-(2-pyrimidyl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(difluoromethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-(2-pyrimidyl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2-cyanocyclopropyl)-4,6-dimethoxy-pyrimidin-2-yl]-7-(2-pyrimidyl)-1H-indole-3-sulfonamide;

N-[5-(2,2-difluoroethyl)-4,6-dimethoxy-pyrimidin-2-yl]-7-pyrazin-2-yl-1H-indole-3-sulfonamide;

N-[5-(2,2-difluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-6-fluoro-7-(2-pyrimidyl)-1H-indole-3-sulfonamide;

N-[5-(2,2-difluoroethyl)-4,6-dimethoxy-pyrimidin-2-yl]-6-fluoro-7-(2-pyrimidyl)-1H-indole-3-sulfonamide;

6-fluoro-N-[5-(2-fluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-(2-pyrimidyl)-1H-indole-3-sulfonamide;

N-[5-(difluoromethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-6-fluoro-7-(2-pyrimidyl)-1H-indole-3-sulfonamide;

N-[5-(2,2-difluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-pyrazin-2-yl-1H-indole-3-sulfonamide;

N-[5-(2,2-difluoroethyl)-4,6-dimethoxy-pyrimidin-2-yl]-6-fluoro-7-pyrazin-2-yl-1H-indole-3-sulfonamide;

6-fluoro-N-[5-(2-fluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-pyrazin-2-yl-1H-indole-3-sulfonamide;

N-[5-(2,2-difluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-6-fluoro-7-pyrazin-2-yl-1H-indole-3-sulfonamide;

N-[5-(difluoromethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-6-fluoro-7-pyrazin-2-yl-1H-indole-3-sulfonamide;

6-bromo-N-[5-(2,2-difluoroethyl)-4,6-dimethoxy-pyrimidin-2-yl]-7-(2-pyrimidyl)-1H-indole-3-sulfonamide;

6-bromo-N-[5-(difluoromethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-(2-pyrimidyl)-1H-indole-3-sulfonamide;

6-bromo-N-[5-(2-fluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-(2-pyrimidyl)-1H-indole-3-sulfonamide;

6-bromo-N-[5-(2,2-difluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-(2-pyrimidyl)-1H-indole-3-sulfonamide;

6-bromo-N-[5-(2,2-difluoroethyl)-4,6-dimethoxy-pyrimidin-2-yl]-7-pyrazin-2-yl-1H-indole-3-sulfonamide;

6-bromo-N-[5-(difluoromethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-pyrazin-2-yl-1H-indole-3-sulfonamide;

6-bromo-N-[5-(2,2-difluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-pyrazin-2-yl-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2,2-difluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-(5-fluoropyrazin-2-yl)-1H-indole-3-sulfonamide;

6-bromo-N-[5-(2,2-difluoroethyl)-4,6-dimethoxy-pyrimidin-2-yl]-7-pyridazin-3-yl-1H-indole-3-sulfonamide;

6-(difluoromethyl)-N-[5-(2-fluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-(2-pyrimidyl)-1H-indole-3-sulfonamide;

N-[5-(2,2-difluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-6-fluoro-7-(1H-imidazol-2-yl)-1H-indole-3-sulfonamide; and

pharmaceutically acceptable salts thereof.

14. A compound according to any one of claims 1 to 12 selected from

6-chloro-N-[5-(2,2-difluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-(1,5-dimethylimidazol-4-yl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2,2-difluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-(1-methylimidazol-4-yl)-1H-indole-3-sulfonamide;

N-[5-(2,2-difluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-6-methyl-7-(2-pyrimidyl)-1H-indole-3-sulfonamide;

N-[5-(2,2-difluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-6-(difluoromethyl)-7-(2-pyrimidyl)-1H-indole-3-sulfonamide;

N-[5-(difluoromethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-6-(difluoromethyl)-7-(2-pyrimidyl)-1H-indole-3-sulfonamide;

N-[5-(2,2-difluoroethyl)-4,6-dimethoxy-pyrimidin-2-yl]-6-(difluoromethyl)-7-(2-pyrimidyl)-1H-indole-3-sulfonamide;

N-[5-(2,2-difluoroethyl)-4,6-dimethoxy-pyrimidin-2-yl]-6-methyl-7-(2-pyrimidyl)-1H-indole-3-sulfonamide;

N-[5-(2,2-difluoroethyl)-4,6-dimethoxy-pyrimidin-2-yl]-7-(3-methylpyrazin-2-yl)-1H-indole-3-sulfonamide;

N-[5-(2,2-difluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-(3-methylpyrazin-2-yl)-1H-indole-3-sulfonamide;

N-[5-(difluoromethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-6-methyl-7-(2-pyrimidyl)-1H-indole-3-sulfonamide;

N-[5-(2-fluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-6-methyl-7-(2-pyrimidyl)-1H-indole-3-sulfonamide;

N-[5-(2,2-difluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-6-methyl-7-pyridazin-3-yl-1H-indole-3-sulfonamide;

N-[5-(2,2-difluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-6-methyl-7-pyrazin-2-yl-1H-indole-3-sulfonamide;

N-[5-(difluoromethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-6-methyl-7-pyrazin-2-yl-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2,2-difluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-5-fluoro-7-(2-pyrimidyl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2,2-difluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-(1-methylpyrazol-3-yl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2,2-difluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-(2-methylpyrimidin-4-yl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2,2-difluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-(6-methylpyridazin-3-yl)-1H-indole-3-sulfonamide;

6-chloro-7-(3-chloropyrazin-2-yl)-N-[5-(difluoromethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-1H-indole-3-sulfonamide;

6-chloro-7-(3-chloropyrazin-2-yl)-N-[5-(2,2-difluoroethyl)-4,6-dimethoxy-pyrimidin-2-yl]-1H-indole-3-sulfonamide;

6-chloro-7-(3-chloropyrazin-2-yl)-N-[5-(2,2-difluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-1H-indole-3-sulfonamide;

6-chloro-N-[5-(difluoromethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-(1-methylpyrazol-3-yl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2-fluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-(1-methylpyrazol-3-yl)-1H-indole-3-sulfonamide;

6-bromo-N-[5-(2,2-difluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-(1-methylpyrazol-4-yl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2,2-difluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-phenyl-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2,2-difluoroethyl)-4,6-dimethoxy-pyrimidin-2-yl]-7-phenyl-1H-indole-3-sulfonamide;

N-[5-(2,2-difluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-(2-pyrimidyl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2,2-difluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-(3-methylpyrazin-2-yl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2,2-difluoroethyl)-4,6-dimethoxy-pyrimidin-2-yl]-7-(3-methylpyrazin-2-yl)-1H-indole-3-sulfonamide;

N-(5-bromo-4,6-dimethoxy-pyrimidin-2-yl)-6-chloro-7-(2-pyrimidyl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2,2-difluoroethyl)-4,6-dimethoxy-pyrimidin-2-yl]-7-(4-pyrimidyl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2,2-difluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-(4-pyrimidyl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(cyanomethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-(2-pyrimidyl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2-cyanoethyl)-4,6-dimethoxy-pyrimidin-2-yl]-7-(2-pyrimidyl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2-fluoroethoxy)-4-methoxy-pyrimidin-2-yl]-7-(2-pyrimidyl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(difluoromethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-(3-methylpyrazin-2-yl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2,2-difluoroethyl)-4,6-dimethoxy-pyrimidin-2-yl]-7-(5-methylpyrazin-2-yl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(difluoromethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-(5-methylpyrazin-2-yl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2,2-difluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-(5-methylpyrazin-2-yl)-1H-indole-3-sulfonamide;

6-chloro-N-(4,6-dimethoxy-5-methyl-pyrimidin-2-yl)-7-(2-pyrimidyl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2,2-difluoroethyl)-4,6-dimethoxy-pyrimidin-2-yl]-7-(6-methylpyrazin-2-yl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(difluoromethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-(6-methylpyrazin-2-yl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2,2-difluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-(6-methylpyrazin-2-yl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2,2-difluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-(5-pyrimidyl)-1H-indole-3-sulfonamide;

6-chloro-7-(5-chloropyrazin-2-yl)-N-[5-(2,2-difluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-1H-indole-3-sulfonamide;

6-chloro-7-(5-chloropyrazin-2-yl)-N-[5-(2,2-difluoroethyl)-4,6-dimethoxy-pyrimidin-2-yl]-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2,2-difluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-(6-methyl-2-pyridyl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2,2-difluoroethyl)-4,6-dimethoxy-pyrimidin-2-yl]-7-(6-methyl-2-pyridyl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(difluoromethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-(6-methyl-2-pyridyl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2,2-difluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-pyridazin-4-yl-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2,2-difluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-(6-methylpyrimidin-4-yl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2,2-difluoroethyl)-4,6-dimethoxy-pyrimidin-2-yl]-7-(3-fluoropyrazin-2-yl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2,2-difluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-(3-fluoropyrazin-2-yl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(difluoromethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-(3-fluoropyrazin-2-yl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2,2-difluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-(3-methyl-2-pyridyl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2,2-difluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-(1-methyltriazol-4-yl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2,2-difluoroethyl)-4,6-dimethoxy-pyrimidin-2-yl]-7-(3-methyl-2-pyridyl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(difluoromethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-(3-methyl-2-pyridyl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2,2-difluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-(1-methyl-1,2,4-triazol-3-yl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2,2-difluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-(5-fluoropyrimidin-2-yl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2,2-difluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-(2-methyltriazol-4-yl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(difluoromethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-(2-methyltriazol-4-yl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2,2-difluoroethyl)-4,6-dimethoxy-pyrimidin-2-yl]-7-(2-methyltriazol-4-yl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2-fluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-(2-methyltriazol-4-yl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2,2-difluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-(1,3,4-oxadiazol-2-yl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2,2-difluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-(1-methylpyrazol-4-yl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2-fluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-(1-methylpyrazol-4-yl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(difluoromethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-(1-methylpyrazol-4-yl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2,2-difluoroethyl)-4,6-dimethoxy-pyrimidin-2-yl]-7-(1-methylpyrazol-4-yl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2,2-difluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-thiazol-4-yl-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2,2-difluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-oxazol-5-yl-1H-indole-3-sulfonamide;

6-chloro-N-[5-(difluoromethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-oxazol-5-yl-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2,2-difluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-isoxazol-4-yl-1H-indole-3-sulfonamide;

6-chloro-N-[5-(difluoromethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-isoxazol-4-yl-1H-indole-3-sulfonamide;

6-chloro-N-[5-(difluoromethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-thiazol-4-yl-1H-indole-3-sulfonamide;

N-[5-(2,2-difluoroethyl)-4,6-dimethoxy-pyrimidin-2-yl]-7-(6,7-dihydro-5H-pyrrol[1,2-c]imidazol-3-yl)-1H-indole-3-sulfonamide; and

pharmaceutically acceptable salts thereof.

15. A compound according to any one of claims 1 to 13, selected from

6-chloro-N-[5-(2,2-difluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-(2-pyrimidyl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2,2-difluoroethyl)-4,6-dimethoxy-pyrimidin-2-yl]-7-(2-pyrimidyl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2,2-difluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-pyridazin-3-yl-1H-indole-3-sulfonamide;

N-[5-(2,2-difluoroethyl)-4,6-dimethoxy-pyrimidin-2-yl]-7-(1-methylimidazol-2-yl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2,2-difluoroethyl)-4,6-dimethoxy-pyrimidin-2-yl]-7-pyridazin-3-yl-1H-indole-3-sulfonamide;

N-[5-(2,2-difluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-(1-methylimidazol-2-yl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2,2-difluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-(1-methylimidazol-2-yl)-1H-indole-3-sulfonamide;

N-[5-(2,2-difluoroethyl)-4,6-dimethoxy-pyrimidin-2-yl]-6-fluoro-7-(1-methylimidazol-2-yl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2,2-difluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-oxazol-4-yl-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2,2-difluoroethyl)-4,6-dimethoxy-pyrimidin-2-yl]-7-pyrazin-2-yl-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2,2-difluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-pyrazin-2-yl-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2,2-difluoroethyl)-4,6-dimethoxy-pyrimidin-2-yl]-7-(2-pyridyl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2,2-difluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-(2-pyridyl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(difluoromethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-pyrazin-2-yl-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2-fluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-pyrazin-2-yl-1H-indole-3-sulfonamide;

6-chloro-N-[5-(difluoromethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-(2-pyrimidyl)-1H-indole-3-sulfonamide;

6-bromo-N-[5-(2,2-difluoroethyl)-4,6-dimethoxy-pyrimidin-2-yl]-7-(2-pyrimidyl)-1H-indole-3-sulfonamide;

6-bromo-N-[5-(difluoromethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-(2-pyrimidyl)-1H-indole-3-sulfonamide;

6-bromo-N-[5-(2,2-difluoroethyl)-4,6-dimethoxy-pyrimidin-2-yl]-7-pyrazin-2-yl-1H-indole-3-sulfonamide;

6-bromo-N-[5-(difluoromethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-pyrazin-2-yl-1H-indole-3-sulfonamide;

6-bromo-N-[5-(2,2-difluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-pyrazin-2-yl-1H-indole-3-sulfonamide; and

pharmaceutically acceptable salts thereof.

16. A compound according to claim 1 to 12, or claim 14 selected from

6-chloro-N-[5-(2,2-difluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-(1,5-dimethylimidazol-4-yl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2,2-difluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-(1-methylimidazol-4-yl)-1H-indole-3-sulfonamide;

N-[5-(2,2-difluoroethyl)-4,6-dimethoxy-pyrimidin-2-yl]-6-methyl-7-(2-pyrimidyl)-1H-indole-3-sulfonamide;

N-[5-(2,2-difluoroethyl)-4,6-dimethoxy-pyrimidin-2-yl]-7-(3-methylpyrazin-2-yl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2,2-difluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-(1-methylpyrazol-3-yl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2,2-difluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-(2-methylpyrimidin-4-yl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2,2-difluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-(6-methylpyridazin-3-yl)-1H-indole-3-sulfonamide;

6-chloro-7-(3-chloropyrazin-2-yl)-N-[5-(difluoromethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-1H-indole-3-sulfonamide;

6-chloro-7-(3-chloropyrazin-2-yl)-N-[5-(2,2-difluoroethyl)-4,6-dimethoxy-pyrimidin-2-yl]-1H-indole-3-sulfonamide;

6-chloro-N-[5-(difluoromethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-(1-methylpyrazol-3-yl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2-fluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-(1-methylpyrazol-3-yl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2,2-difluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-(3-methylpyrazin-2-yl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2,2-difluoroethyl)-4,6-dimethoxy-pyrimidin-2-yl]-7-(3-methylpyrazin-2-yl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2,2-difluoroethyl)-4,6-dimethoxy-pyrimidin-2-yl]-7-(4-pyrimidyl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2,2-difluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-(4-pyrimidyl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(difluoromethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-(3-methylpyrazin-2-yl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2,2-difluoroethyl)-4,6-dimethoxy-pyrimidin-2-yl]-7-(5-methylpyrazin-2-yl)-1H-indole-3-sulfonamide;

6-chloro-N-(4,6-dimethoxy-5-methyl-pyrimidin-2-yl)-7-(2-pyrimidyl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2,2-difluoroethyl)-4,6-dimethoxy-pyrimidin-2-yl]-7-(6-methylpyrazin-2-yl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(difluoromethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-(6-methylpyrazin-2-yl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2,2-difluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-(6-methylpyrazin-2-yl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2,2-difluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-(5-pyrimidyl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2,2-difluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-(6-methyl-2-pyridyl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2,2-difluoroethyl)-4,6-dimethoxy-pyrimidin-2-yl]-7-(6-methyl-2-pyridyl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(difluoromethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-(6-methyl-2-pyridyl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2,2-difluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-pyridazin-4-yl-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2,2-difluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-(6-methylpyrimidin-4-yl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2,2-difluoroethyl)-4,6-dimethoxy-pyrimidin-2-yl]-7-(3-fluoropyrazin-2-yl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2,2-difluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-(3-fluoropyrazin-2-yl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(difluoromethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-(3-fluoropyrazin-2-yl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2,2-difluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-(3-methyl-2-pyridyl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2,2-difluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-(1-methyltriazol-4-yl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2,2-difluoroethyl)-4,6-dimethoxy-pyrimidin-2-yl]-7-(3-methyl-2-pyridyl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2,2-difluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-(2-methyltriazol-4-yl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2,2-difluoroethyl)-4,6-dimethoxy-pyrimidin-2-yl]-7-(2-methyltriazol-4-yl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2-fluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-(2-methyltriazol-4-yl)-1H-indole-3-sulfonamide;

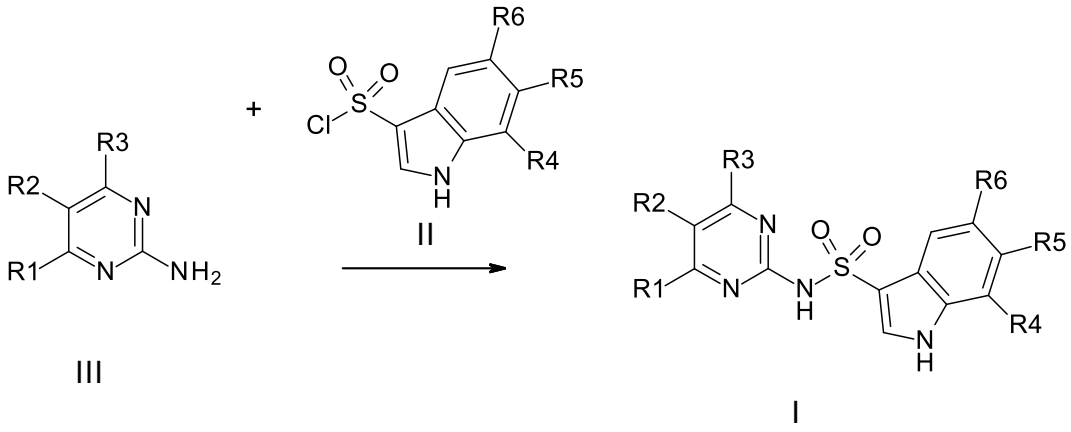
6-chloro-N-[5-(2,2-difluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-(1,3,4-oxadiazol-2-yl)-1H-indole-3-sulfonamide;

6-chloro-N-[5-(2,2-difluoroethoxy)-4,6-dimethoxy-pyrimidin-2-yl]-7-thiazol-4-yl-1H-indole-3-sulfonamide;

N-[5-(2,2-difluoroethyl)-4,6-dimethoxy-pyrimidin-2-yl]-7-(6,7-dihydro-5H-pyrrol[1,2-c]imidazol-3-yl)-1H-indole-3-sulfonamide;

and pharmaceutically acceptable salts thereof.

17. A process to prepare a compound according to any one of claims 1 to 16 comprising the reacting a compound of formula III with a compound of formula II in the presence of a base selected from N-ethyldiisopropylamine, pyridine, potassium phosphate or sodium hydride, to provide a compound of formula I,



wherein R^1, R^2, R^3, R^3, R^4, R^5 and R^6 are as described above.

18. A compound according to any one of claims 1 to 16 for use as therapeutically active substance.

19. A compound according to any one of claims 1 to 16 for use in the treatment of a disease modulated by GPR17.

20. A pharmaceutical composition comprising a compound according to any one of claims 1 to 16 and a therapeutically inert carrier.

21. The use of a compound according to any one of claims 1 to 16 in the preparation of a medicament for the treatment or prophylaxis of multiple sclerosis.

22. The use of a compound according to any one of claims 1 to 16 in the preparation of a medicament for the treatment or prophylaxis of conditions resulting from direct damage to myelin sheaths (including but not limited central pontine and extra-pontine myelinolysis, carbon monoxide poisoning, nutritional deficiency, and virus-induced demyelination), demyelinating disorders (including but not limited to multiple sclerosis, acute and multiphasic disseminated encephalomyelitis, neuromyelitis optica spectrum disorders, and leukodystrophies), CNS disorders associated with myelin loss (including but not limited to Alzheimer's disease, schizophrenia, Parkinson's disease, Huntington's disease, Amyotrophic lateral sclerosis, and Ischemia due to stroke), and inflammation in the CNS for instance following encephalitis, primary angiitis, meningitis and obesity.

23. A compound according to any one of claims 1 to 16 for use in the treatment or prophylaxis of conditions resulting from direct damage to myelin sheaths (including but not limited central pontine and extra-pontine myelinolysis, carbon monoxide poisoning, nutritional deficiency, and virus-induced demyelination), demyelinating disorders (including but not limited to multiple sclerosis, acute and multiphasic disseminated encephalomyelitis, neuromyelitis optica spectrum disorders, and leukodystrophies), CNS disorders associated with myelin loss (including but not limited to Alzheimer's disease, schizophrenia, Parkinson's disease, Huntington's disease, Amyotrophic lateral sclerosis, and Ischemia due to stroke), and inflammation in the CNS for instance following encephalitis, primary angiitis, meningitis and obesity.

24. A compound according to any one of claims 1 to 16 for use in the treatment or prophylaxis of multiple sclerosis.

25. A compound according to any one of claims 1 to 16, when manufactured according to a process of claim 18.

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