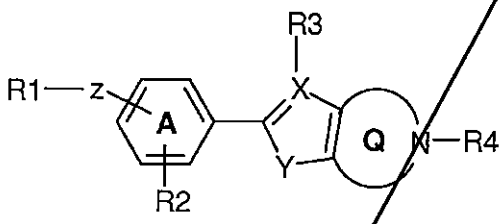
Claims

1. A fused heterocyclic derivative of the formula (**I**)



(I)

wherein

R1 is selected from

cyano,

(2-4C)alkenyl, (2-4C)alkynyl, (1-4C)alkyl, each optionally substituted with CN or one or more fluoro atoms,

(3-6C)cycloalkyl, (4-6C)cycloalkenyl or a (8-10C)bicyclic group, each optionally substituted with halogen or (1-4C)alkyl optionally substituted with one or more fluoro atoms,

phenyl, biphenyl, naphthyl, each optionally substituted with one or more substituents independently selected from halogen, cyano, (1-4C)alkyl optionally substituted with one or more fluoro atoms, (1-4C)alkoxy optionally substituted with one or more fluoro atoms, amino, dimethylamino, and (3-6C)cycloalkyl optionally substituted with phenyl which may be substituted with (1-4C)alkyl or halogen, and

phenyl substituted with phenoxy, benzyl, benzyloxy, phenylethyl or monocyclic heterocycle, each optionally substituted with (1-4C)alkyl,

Z is a linking group –W-(C_n-alkylene)-T- wherein

W is attached to R1 and selected from a bond, -O-, -CO-, -S-, -SO-, -SO_2-, -NH-, -CH=CH-, -C(CF_3)=CH-, -C≡C-, -CH_2-O-, -O-CO-, -CO-O-, -CO-NH-, -NH-CO- and trans-cyclopropylene;

n is an integer from 0 to 10; and

T is attached to the phenylene/pyridyl moiety and selected from a bond, -O-, -S-, -SO-, -SO_2-, -NH-, -CO-, -C=C-, -C≡C-, and trans-cyclopropylene;

R2 is H or one or more substituents independently selected from cyano, halogen, (1-4C)alkyl optionally substituted with one or more halogen atoms, or (1-4C)alkoxy optionally substituted with one or more halogen atoms;

ring structure A may contain one nitrogen atom;

X is selected from C or N; if X is C, R3 is selected from H and (1-4C)alkyl, otherwise R3 is not present;

Y is selected from NH, O and S;

structure **Q** is a 5-, 6- or 7- membered cyclic amine;

and

R4 is (1-4C)alkylene-R5 wherein one or more carbon atoms in the alkylene group may independently be substituted with one or more halogen atoms or with $(CH_2)_2$ to form a cyclopropyl moiety , or R4 is (3-6C)cycloalkylene-R5, $-CH_2$-(3-6C)cycloalkylene-R5, (3-6C)cycloalkylene-CH_2-R5 or -CO-CH_2-R5, wherein R5 is -OH, $-PO_3H_2$, $-OPO_3H_2$, -COOH, -COO(1-4C)alkyl or tetrazol-5-yl;

or a pharmaceutically acceptable salt, a solvate or hydrate thereof or one or more N-oxides thereof.

2. The compound of claim 1, wherein

R1 is selected from

(3-6C)cycloalkyl or a (8-10C)bicyclic group optionally substituted with halogen, (1-4C)alkyl, and

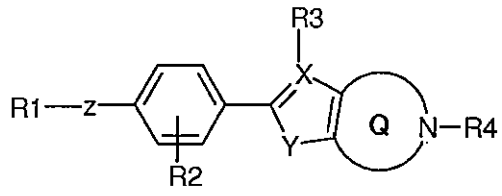
phenyl optionally substituted with one or more substituents independently selected from halogen, cyano, (1-4C)alkyl, (1-4C)alkoxy, trifluoromethyl and trifluoromethoxy;

W is selected from a bond, -O-, -CO-, -S-, -SO-, $-SO_2$-, -NH-, -CH=CH-, -C≡C-, and trans-cyclopropylene; and

n is an integer from 0 to 4; and

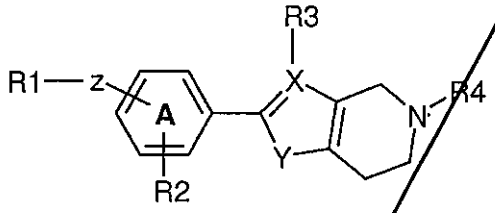
R2 is H or one or more substituents independently selected from halogen, (1-4C)alkyl optionally substituted with one or more fluoro atoms or (1-4C)alkoxy optionally substituted with one or more fluoro atoms.

3. The compound of claim 1 or 2, wherein the compound has the structure (**Ia**)



(Ia).

4. The compound of any one of claims 1 -3, wherein the compound has the structure (Ib)



(Ib).

5. The compound of any one of claims 1 -4, wherein Y is O.

6. The compound of any one of claims 1 -5, wherein R4 is selected from -$(CH_2)_2$-COOH, -$(CH_2)_3$-COOH, -CH_2-$CHCH_3$-COOH, -CH_2-$C(CH_3)_2$-COOH, -$CHCH_3$-CH_2-COOH, -CH_2-CF_2-COOH and 1,3-cyclobutylene-COOH.

7. The compound of any one of claims 1 -6, wherein R1 is optionally substituted phenyl.

8. The compound of claim 7, wherein the optional substituents are one or more substituents independently selected from halogen, cyano, (1-4C)alkyl, (1-4C)alkoxy, trifluoromethyl and trifluoromethoxy.

9. The compound of any one of claims 1-8, wherein Z is -CH_2O-.

10. The compound of any one of claims 1-9, wherein X is N.

11. The compound of claim 1, selected from 3-{2-[4-(2-Fluoro-benzyloxy)-phenyl]-6,7-dihydro-4H-furo[3,2-c]pyridine-5-yl}-propionic acid,

3-{2-[4-(4-Chloro-benzyloxy)-phenyl]-6,7-dihydro-4H-furo[3,2-c]pyridine-5-yl}-2-methyl-propionic acid,

3-{2-[4-Benzyloxy-phenyl]-6,7-dihydro-4H-furo[3,2-c]pyridine-5-yl}-butyric acid,

4-{2-[4-(2-Fluoro-benzyloxy)-phenyl]-6,7-dihydro-4H-furo[3,2-c]pyridine-5-yl}-butyric acid,

4-{2-[4-(2-Fluoro-benzyloxy)-2-fluoro-phenyl]-6,7-dihydro-4H-furo[3,2-c]pyridine-5-yl}-butyric acid,

3-{2-[4-(Benzyloxy)-phenyl)]-6,7-dihydro-*H*-oxazolo[4,5-c]pyridine-5-yl}-propionic acid,

4-{2-[4-(2,3-Difluoro-benzyloxy)-phenyl)]-6,7-dihydro-*H*-oxazolo[4,5-c]pyridine-5-yl}-butyric acid,

4-{2-[4-Benzyloxy-phenyl]-6,7-dihydro-*H*-oxazolo[4,5-c]pyridine-5-yl}-butyric acid,

4-{2-[4-(4-Trifluoromethyl-benzyloxy)-2-fluoro-phenyl]-6,7-dihydro-*H*-oxazolo[4,5-c]pyridine-5-yl}-butyric acid,

4-{2-[4-(2-Fluoro-benzyloxy)-2-methyl-phenyl]-6,7-dihydro-*H*-oxazolo[4,5-c]pyridine-5-yl}-butyric acid,

4-{2-[4-(3,4-Dichloro-benzyloxy)-2-fluoro-phenyl]-6,7-dihydro-*H*-oxazolo[4,5-c]pyridine-5-yl}-butyric acid,

4-{2-[4-(2-Fluoro-benzyloxy)-3-chloro-phenyl]-6,7-dihydro-*H*-oxazolo[4,5-c]pyridine-5-yl}-butyric acid,

4-{2-[4-(4-Chloro-benzyloxy)-3-fluoro-phenyl]-6,7-dihydro-*H*-oxazolo[4,5-c]pyridine-5-yl}-butyric acid,

3-[2-(4-Benzyloxy-phenyl)-6,7-dihydro-*H*-oxazolo[4,5-c]pyridine-5-yl]-2-methyl-propionic acid,

3-{2-[4-(4-Trifluoromethyl-benzyloxy)-phenyl]-6,7-dihydro-*H*-oxazolo[4,5-c]pyridine-5-yl}-2-methyl-propionic acid,

3-{2-[4-(4-Chloro-benzyloxy)-phenyl]-6,7-dihydro-*H*-oxazolo[4,5-c]pyridine-5-yl}-2-methyl-propionic acid,

3-{2-[4-(4-2,3-Difluoro-benzyloxy)-phenyl]-6,7-dihydro-*H*-oxazolo[4,5-c]pyridine-5-yl}-butyric acid,

3-{2-[4-(4-Trifluoromethyl-benzyloxy)-2-fluoro-phenyl]-6,7-dihydro-*H*-oxazolo[4,5-c]pyridine-5-yl}-2-methyl-propionic acid,

Cis and trans 3-{2-[4-(4-Trifluoromethoxybenzyloxy)-phenyl]-6,7-dihydro-*H*-

oxazolo[4,5-c]pyridine-5-yl}-cyclobutane carboxylic acid,
Cis and trans 3-{2-[4-(3,4-Difluorobenzyloxy)-phenyl]-6,7-dihydro-*H*-oxazolo[4,5-c]pyridine-5-yl}-cyclobutane carboxylic acid,
3-[2-(4-(2-Fluoro-benzyloxy)-phenyl)-6,7-dihydro-4H-thiazolo[5,4-c]pyridine-5-yl]-propionic acid,
4-{2-[4-(3,5-Difluoro-benzyloxy)-phenyl]-6,7-dihydro-4H-thiazolo-[4,5c]-pyridin-5-yl}–butyric acid,
2-{2-[4-(3,5-Difluoro-benzyloxy)-phenyl]-6,7-dihydro-*H*-oxazolo[4,5-c]pyridine-5-yl}-acetic acid,
2-{2-[4-(3,5-Difluoro-benzyloxy)-phenyl]-6,7-dihydro-*H*-oxazolo[4,5-c]pyridine-5-yl}-propionic acid,
3-{2-[4-(3,5-Difluoro-benzyloxy)-phenyl]-6,7-dihydro-4H-oxazolo[4,5-c]-pyridin-5-yl}-cyclopentane carboxylic acid,
4-{2-[4-(2,3-Difluoro-benzyloxy)-2-methyl-phenyl]-6,7-dihydro-4H-oxazolo-[4,5c]-pyridin-5-yl}-pentanoic acid,
4-{2-[4-(2,3-Difluoro-benzyloxy)-2-methyl-phenyl]-6,7-dihydro-4H-oxazolo[4,5-c]-pyridin-5-yl}-2-methyl-butyric acid,
4-{2-[4-(2,3-Difluoro-benzyloxy)-2-methyl-phenyl]-6,7-dihydro-4H-oxazolo-[4,5c]-pyridin-5-yl}-3-methyl-butyric acid,
3-{2-[4-(2-phenyl-cyclopropyl)-3-fluoro-phenyl]-6,7-dihydro-4H-oxazolo-[4,5-c]-pyridin-5-yl}-cyclobutane carboxylic acid,
4-(2-{4-[2-(3,5-Difluoro-phenyl)-vinyl]-phenyl}-6,7-dihydro-4H-oxazolo-[4,5c]-pyridin-5-yl)-butyric acid,
4-(2-{4-[2-(3,5-Difluoro-phenyl)-ethyl]-phenyl}-6,7-dihydro-4H-oxazolo[4,5c] pyridin-5-yl)-butyric acid,
or a pharmaceutically acceptable salt, a solvate or hydrate thereof or one or more N-oxides thereof.

12. The compound of any one of claims 1 to 11 for use in therapy.

13. The compound of any one of claims 1 to 11 for use in the treatment, alleviation or prevention of diseases and conditions in which any S1P receptor is involved or in

which modulation of the endogenous S1P signaling system via any S1P receptor is involved.

14. The compound of claim 13, wherein the disease is a CNS disorder, such as a neurodegenerative disorder, in particular selected from a cognitive disorder, Alzheimer's disease, (vascular) dementia, Nieman's Pick disease, and cognitive deficits in schizophrenia, obsessive-compulsive behavior, major depression, autism, multiple sclerosis and pain, and specifically a cognitive disorder, such as age-related cognitive decline.

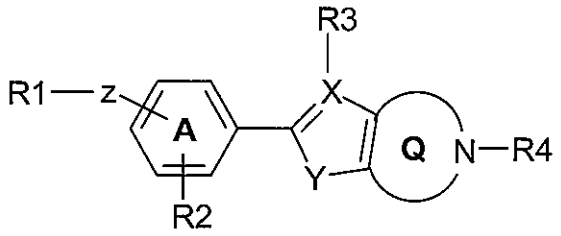
15. A pharmaceutical composition comprising the compound of any one of claims 1 to 11 and at least one pharmaceutically acceptable auxiliary.

16. Use of the compound of any one of claims 1 to 11 for the manufacture of a medicament for the treatment, alleviation or prevention of diseases and conditions in which any S1P receptor is involved or in which modulation of the endogenous S1P signaling system via any S1P receptor is involved.

17. The use of claim 16, wherein the disease is a CNS disorder, such as a neurodegenerative disorder, in particular selected from a cognitive disorder, Alzheimer's disease, (vascular) dementia, Nieman's Pick disease, and cognitive deficits in schizophrenia, obsessive-compulsive behavior, major depression, autism, multiple sclerosis and pain, and specifically a cognitive disorder, such as age-related cognitive decline.

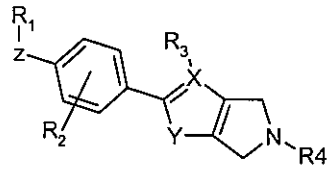
claims

1. A fused heterocyclic derivative of the formula (I)

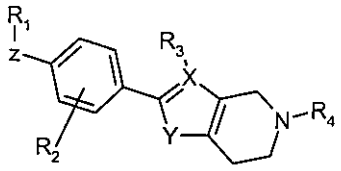


(I)

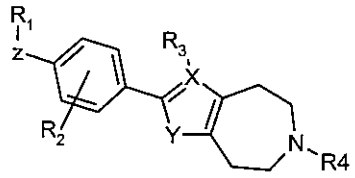
wherein formula (I) is selected from the formula's A, B, C, D and E:



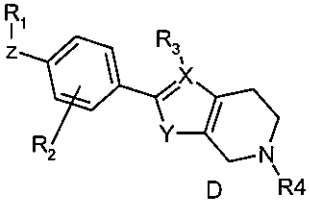
A



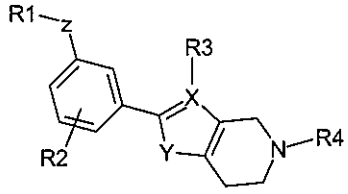
B



C



D



E

wherein
R1 is selected from

cyano,

(2-4C)alkenyl, (2-4C)alkynyl, (1-4C)alkyl, each optionally substituted with CN or one or more fluoro atoms,

(3-6C)cycloalkyl, (4-6C)cycloalkenyl or a (8-10C)bicyclic group, each optionally substituted with halogen or (1-4C)alkyl optionally substituted with one or more fluoro atoms,

phenyl, biphenyl, naphthyl, each optionally substituted with one or more substituents independently selected from halogen, cyano, (1-4C)alkyl

optionally substituted with one or more fluoro atoms, (1-4C)alkoxy optionally substituted with one or more fluoro atoms, amino, dimethylamino, and (3-6C)cycloalkyl optionally substituted with phenyl which may be substituted with (1-4C)alkyl or halogen, and

phenyl substituted with phenoxy, benzyl, benzyloxy, phenylethyl or monocyclic heterocycle, each optionally substituted with (1-4C)alkyl,

Z is a linking group –W-(C_n-alkylene)-T- wherein

W is attached to R1 and selected from a bond, -O-, -CO-, -S-, -SO-, -SO_2-, -NH-, -CH=CH-, -C(CF_3)=CH-, -C≡C-, -CH_2-O-, -O-CO-, -CO-O-, -CO-NH-, -NH-CO- and trans-cyclopropylene;

n is an integer from 0 to 10; and

T is attached to the phenylene/pyridyl moiety and selected from a bond, -O-, -S-, -SO-, -SO_2-, -NH-, -CO-, -C=C-, -C≡C-, and trans-cyclopropylene;

R2 is H or one or more substituents independently selected from cyano, halogen, (1-4C)alkyl optionally substituted with one or more halogen atoms, or (1-4C)alkoxy optionally substituted with one or more halogen atoms;

X is selected from C or N; if X is C, R3 is selected from H and (1-4C)alkyl, otherwise R3 is not present;

Y is selected from NH, O and S;

and

R4 is (1-4C)alkylene-R5 wherein one or more carbon atoms in the alkylene group may independently be substituted with one or more halogen atoms or with $(CH_2)_2$ to form a cyclopropyl moiety , or R4 is (3-6C)cycloalkylene-R5, -CH_2-(3-6C)cycloalkylene-R5, (3-6C)cycloalkylene-CH_2-R5 or -CO-CH_2-R5, wherein R5 is -OH, -PO_3H_2, -OPO_3H_2, -COOH, -COO(1-4C)alkyl or tetrazol-5-yl;

or a pharmaceutically acceptable salt, a solvate or hydrate thereof or one or more N-oxides thereof.

2. The compound of claim 1, wherein

R1 is selected from

(3-6C)cycloalkyl or a (8-10C)bicyclic group optionally substituted with halogen, (1-4C)alkyl, and

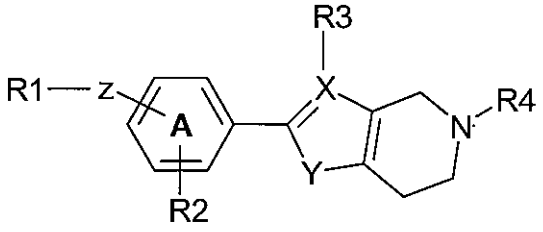
phenyl optionally substituted with one or more substituents independently selected from halogen, cyano, (1-4C)alkyl, (1-4C)alkoxy, trifluoromethyl and trifluoromethoxy;

W is selected from a bond, -O-, -CO-, -S-, -SO-, -SO_2-, -NH-, -CH=CH-, -C≡C-, and trans-cyclopropylene; and

n is an integer from 0 to 4; and

R2 is H or one or more substituents independently selected from halogen, (1-4C)alkyl optionally substituted with one or more fluoro atoms or (1-4C)alkoxy optionally substituted with one or more fluoro atoms.

3. The compound of claim 1 or 2, wherein the compound has the structure (**Ib**)



(**Ib**).

4. The compound of any one of claims 1-3, wherein Y is O.

5. The compound of any one of claims 1-4, wherein R4 is selected from -$(CH_2)_2$-COOH, -$(CH_2)_3$-COOH, -CH_2-$CHCH_3$-COOH, -CH_2-$C(CH_3)_2$-COOH, -$CHCH_3$-CH_2-COOH, -CH_2-CF_2-COOH and 1,3-cyclobutylene-COOH.

6. The compound of any one of claims 1-5, wherein R1 is phenyl optionally substituted with one or more substituents independently selected from halogen, cyano, (1-4C)alkyl optionally substituted with one or more fluoro atoms, (1-4C)alkoxy optionally substituted with one or more fluoro atoms, amino, dimethylamino, and (3-6C)cycloalkyl optionally substituted with phenyl which may be substituted with (1-4C)alkyl or halogen.

7. The compound of claim 6, wherein the optional substituents are one or more substituents independently selected from halogen, cyano, (1-4C)alkyl, (1-4C)alkoxy, trifluoromethyl and trifluoromethoxy.

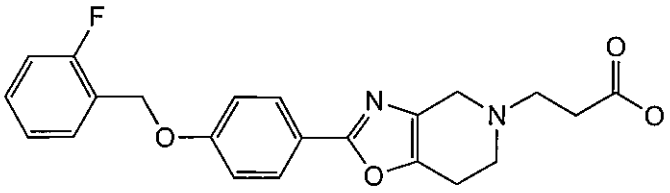
8. The compound of any one of claims 1-7, wherein Z is -CH_2O-.

9. The compound of any one of claims 1-8, wherein X is N.

10. The compound of claim 1, selected from
3-{2-[4-(2-Fluoro-benzyloxy)-phenyl]-6,7-dihydro-4H-furo[3,2-c]pyridine-5-yl}-propionic acid,
3-{2-[4-(4-Chloro-benzyloxy)-phenyl]-6,7-dihydro-4H-furo[3,2-c]pyridine-5-yl}-2-methyl-propionic acid,
3-{2-[4-Benzyloxy-phenyl]-6,7-dihydro-4H-furo[3,2-c]pyridine-5-yl}-butyric acid,
4-{2-[4-(2-Fluoro-benzyloxy)-phenyl]-6,7-dihydro-4H-furo[3,2-c]pyridine-5-yl}-butyric acid,
4-{2-[4-(2-Fluoro-benzyloxy)-2-fluoro-phenyl]-6,7-dihydro-4H-furo[3,2-c]pyridine-5-yl}-butyric acid,
3-{2-[4-(Benzyloxy)-phenyl)]-6,7-dihydro-*H*-oxazolo[4,5-c]pyridine-5-yl}-propionic acid,
4-{2-[4-(2,3-Difluoro-benzyloxy)-phenyl)]-6,7-dihydro-*H*-oxazolo[4,5-c]pyridine-5-yl}-butyric acid,
4-{2-[4-Benzyloxy-phenyl]-6,7-dihydro-*H*-oxazolo[4,5-c]pyridine-5-yl}-butyric acid,
4-{2-[4-(4-Trifluoromethyl-benzyloxy)-2-fluoro-phenyl]-6,7-dihydro-*H*-oxazolo[4,5-c]pyridine-5-yl}-butyric acid,
4-{2-[4-(2-Fluoro-benzyloxy)-2-methyl-phenyl]-6,7-dihydro-*H*-oxazolo[4,5-c]pyridine-5-yl}-butyric acid,
4-{2-[4-(3,4-Dichloro-benzyloxy)-2-fluoro-phenyl]-6,7-dihydro-*H*-oxazolo[4,5-c]pyridine-5-yl}-butyric acid,
4-{2-[4-(2-Fluoro-benzyloxy)-3-chloro-phenyl]-6,7-dihydro-*H*-oxazolo[4,5-c]pyridine-5-yl}-butyric acid,
4-{2-[4-(4-Chloro-benzyloxy)-3-fluoro-phenyl]-6,7-dihydro-*H*-oxazolo[4,5-c]pyridine-5-yl}-butyric acid,
3-[2-(4-Benzyloxy-phenyl)-6,7-dihydro-*H*-oxazolo[4,5-c]pyridine-5-yl]-2-methyl-propionic acid,
3-{2-[4-(4-Trifluoromethyl-benzyloxy)-phenyl]-6,7-dihydro-*H*-oxazolo[4,5-c]pyridine-5-yl}-2-methyl-propionic acid,
3-{2-[4-(4-Chloro-benzyloxy)-phenyl]-6,7-dihydro-*H*-oxazolo[4,5-c]pyridine-5-yl}-2-methyl-propionic acid,
3-{2-[4-(2,3-Difluoro-benzyloxy)-phenyl]-6,7-dihydro-*H*-oxazolo[4,5-c]pyridine-5-yl}-

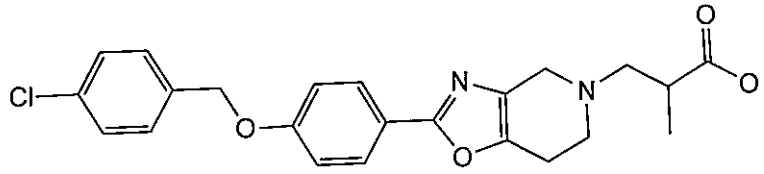
butyric acid,
3-{2-[4-(4-Trifluoromethyl-benzyloxy)-2-fluoro-phenyl]-6,7-dihydro-*H*-oxazolo[4,5-c]pyridine-5-yl}-2-methyl-propionic acid,
Cis and trans 3-{2-[4-(4-Trifluoromethoxybenzyloxy)-phenyl]-6,7-dihydro-*H*-oxazolo[4,5-c]pyridine-5-yl}-cyclobutane carboxylic acid,
Cis and trans 3-{2-[4-(3,4-Difluorobenzyloxy)-phenyl]-6,7-dihydro-*H*-oxazolo[4,5-c]pyridine-5-yl}-cyclobutane carboxylic acid,
3-[2-(4-(2-Fluoro-benzyloxy)-phenyl)-6,7-dihydro-4H-thiazolo[5,4-c]pyridine-5-yl]-propionic acid,
4-{2-[4-(3,5-Difluoro-benzyloxy)-phenyl]-6,7-dihydro-4H-thiazolo-[4,5c]-pyridin-5-yl}–butyric acid,
2-{2-[4-(3,5-Difluoro-benzyloxy)-phenyl]-6,7-dihydro-*H*-oxazolo[4,5-c]pyridine-5-yl}-acetic acid,
2-{2-[4-(3,5-Difluoro-benzyloxy)-phenyl]-6,7-dihydro-*H*-oxazolo[4,5-c]pyridine-5-yl}-propionic acid,
3-{2-[4-(3,5-Difluoro-benzyloxy)-phenyl]-6,7-dihydro-4H-oxazolo[4,5-c]-pyridin-5-yl}-cyclopentane carboxylic acid,
4-{2-[4-(2,3-Difluoro-benzyloxy)-2-methyl-phenyl]-6,7-dihydro-4H-oxazolo-[4,5c]-pyridin-5-yl}-pentanoic acid,
4-{2-[4-(2,3-Difluoro-benzyloxy)-2-methyl-phenyl]-6,7-dihydro-4H-oxazolo[4,5-c]-pyridin-5-yl}-2-methyl-butyric acid,
4-{2-[4-(2,3-Difluoro-benzyloxy)-2-methyl-phenyl]-6,7-dihydro-4H-oxazolo-[4,5c]-pyridin-5-yl}-3-methyl-butyric acid,
3-{2-[4-(2-phenyl-cyclopropyl)-3-fluoro-phenyl]-6,7-dihydro-4H-oxazolo-[4,5-c]-pyridin-5-yl}-cyclobutane carboxylic acid,
4-(2-{4-[2-(3,5-Difluoro-phenyl)-vinyl]-phenyl}-6,7-dihydro-4H-oxazolo-[4,5c]-pyridin-5-yl)-butyric acid,
4-(2-{4-[2-(3,5-Difluoro-phenyl)-ethyl]-phenyl}-6,7-dihydro-4H-oxazolo[4,5c] pyridin-5-yl)-butyric acid,
or a pharmaceutically acceptable salt, a solvate or hydrate thereof or one or more N-oxides thereof.

11. A compound of formula



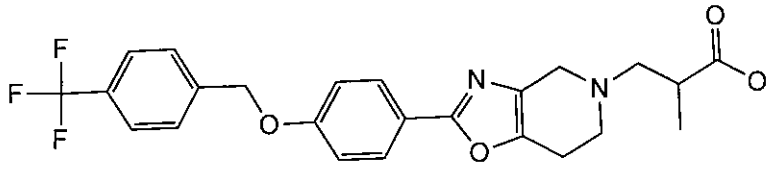
or a pharmaceutically acceptable salt thereof.

12. A compound of formula



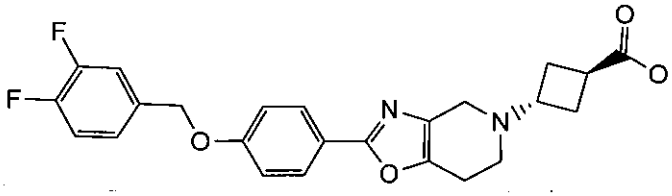
or a pharmaceutically acceptable salt thereof.

13. A compound of formula



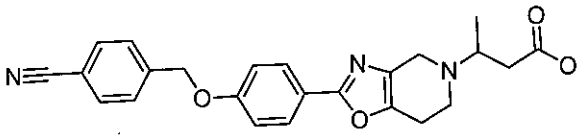
or a pharmaceutically acceptable salt thereof.

14. A compound of formula



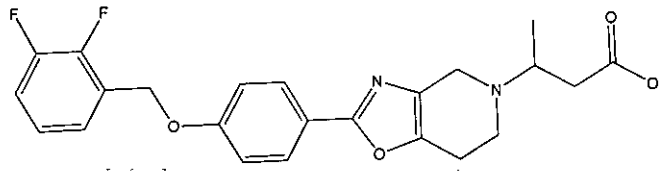
or a pharmaceutically acceptable salt thereof.

15. A compound of formula



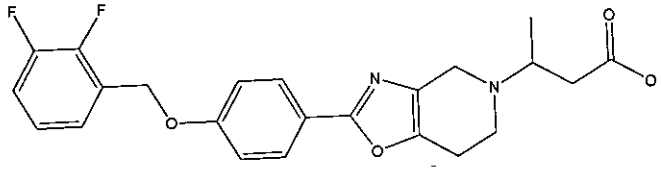
or a pharmaceutically acceptable salt thereof.

16. A compound of formula



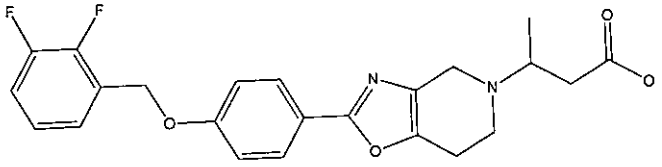
or a pharmaceutically acceptable salt thereof.

17. A compound which is the plus (+) enantiomer of formula



or a pharmaceutically acceptable salt thereof.

18. A compound which is the minus (-) enantiomer of formula



or a pharmaceutically acceptable salt thereof.

19. The compound of any one of claims 1 to 18 for use in therapy.

20. The compound of any one of claims 1 to 18 for use in the treatment, alleviation or prevention of a CNS disorder, such as a neurodegenerative disorder, in particular selected from a cognitive disorder, Alzheimer's disease, (vascular) dementia, Nieman's Pick disease, and cognitive deficits in schizophrenia, obsessive-compulsive behavior, major depression, autism, multiple sclerosis and pain, and specifically a cognitive disorder, such as age-related cognitive decline.

21. A pharmaceutical composition comprising the compound of any one of claims 1 to 18 and at least one pharmaceutically acceptable auxiliary.

22. Use of the compound of any one of claims 1 to 18 for the manufacture of a medicament for the treatment, alleviation or prevention of a CNS disorder, such as a neurodegenerative disorder, in particular selected from a cognitive disorder, Alzheimer's disease, (vascular) dementia, Nieman's Pick disease, and cognitive

deficits in schizophrenia, obsessive-compulsive behavior, major depression, autism, multiple sclerosis and pain, and specifically a cognitive disorder, such as age-related cognitive decline.