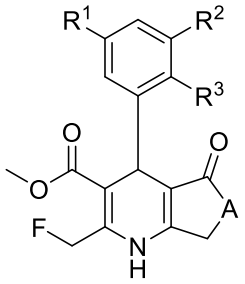
Claims

1. A compound according to formula (I) or a pharmaceutically acceptable salt or solvate thereof



(I)

wherein:

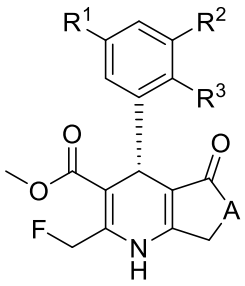
A is O or CH_2;

R^1 is H or F;

R^2 is H or F; and

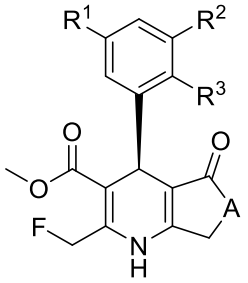
R^3 is $OCHF_2$, methyl, ethyl, or cyclopropyl each of which is optionally substituted with 1 to 3 F.

2. The compound according to claim 1 which is compound of formula (Ia) or a pharmaceutically acceptable salt or solvate thereof



(Ia).

3. The compound according to claim 1 which is a compound of formula (Ib) or a pharmaceutically acceptable salt or solvate thereof



(Ib).

4. The compound according to any one of claims 1-3 wherein A is O.

5. The compound according to claim 4 wherein R^2 is F.

6. The compound according to claim 4 wherein R^2 is H.

7. The compound according to claim 4 wherein R^3 is $OCHF_2$.

8. The compound according to claim 4 wherein R^3 is methyl, ethyl, or cyclopropyl each of which is substituted with 1 to 3 F.

9. The compound according to claim 4 wherein R^3 is CHF_2 or CF_3.

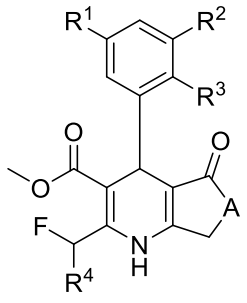
10. The compound according to claim 4 wherein R^3 is ethyl substituted with 1 or 2 F or cyclopropyl either unsubstituted or substituted with 2 F.

11. The compound according to any one of claims 1-3 where in A is CH_2.

12. The compound according to claim 11 wherein R^2 is F.

13. The compound according to claim 11 or claim 12 wherein R^3 is ethyl substituted with 1 to 3 F.

14. A compound according to formula (III) or a pharmaceutically acceptable salt or solvate thereof



(III)

wherein:

A is O or CH_2;

R^1 is H or F;

R^2 is H or F;

R^3 is $OCHF_2$, methyl, ethyl, or cyclopropyl each of which is optionally substituted with 1 to 3 F; and

R^4 is H or F.

15. The compound according to claim 14 wherein A is O.

16. The compound according to claim 15 wherein R^2 is F.

17. The compound according to claim 15 wherein R^2 is H.

18. The compound according to claim 15 wherein R^3 is $OCHF_2$.

19. The compound according to claim 15 wherein R^3 is methyl, ethyl, or cyclopropyl each of which is optionally substituted with 1 to 3 F.

20. The compound according to claim 15 wherein R^3 is CHF_2 or CF_3.

21. The compound according to claim 15 wherein R^3 is ethyl optionally substituted with 1 or 2 F or cyclopropyl either unsubstituted or substituted with 2 F.

22. The compound according to claim 15 wherein R^3 is ethyl.

23. The compound according to claim 15 wherein R^4 is F.

24. The compound according to claim 15 wherein R^4 is H.

25. The compound according to claim 14 where in A is CH_2.

26. The compound according to claim 23 wherein R^2 is F.

27. The compound according to claim 23 wherein R^3 is ethyl substituted with 1 to 3 F.

28. The compound according to claim 23 wherein R^4 is F.

29. The compound according to claim 23 wherein R^4 is H.

30. The compound according to claim 1 selected from the group consisting of:
methyl (R)-4-(2-((R)-2,2-difluorocyclopropyl)-3-fluorophenyl)-2-(fluoromethyl)-5-oxo-1,4,5,7-tetrahydrofuro[3,4-b]pyridine-3-carboxylate;
methyl (R)-4-(2-((S)-2,2-difluorocyclopropyl)-3-fluorophenyl)-2-(fluoromethyl)-5-oxo-1,4,5,7-tetrahydrofuro[3,4-b]pyridine-3-carboxylate;
(R)-4-(2-cyclopropyl-3-fluorophenyl)-2-(fluoromethyl)-5-oxo-1,4,5,7-tetrahydrofuro[3,4-b]pyridine-3-carboxylate;
Methyl (R)-4-(2-((R)-2,2-difluorocyclopropyl)-3,5-difluorophenyl)-2-(fluoromethyl)-5-oxo-1,4,5,7-tetrahydrofuro[3,4-b]pyridine-3-carboxylate;
Methyl (R)-4-(2-((S)-2,2-difluorocyclopropyl)-3,5-difluorophenyl)-2-(fluoromethyl)-5-oxo-1,4,5,7-tetrahydrofuro[3,4-b]pyridine-3-carboxylate;
methyl (R)-4-(3,5-difluoro-2-((R)-1-fluoroethyl)phenyl)-2-(fluoromethyl)-5-oxo-1,4,5,7-tetrahydrofuro[3,4-b]pyridine-3-carboxylate;

methyl (R)-4-(3,5-difluoro-2-((S)-1-fluoroethyl)phenyl)-2-(fluoromethyl)-5-oxo-1,4,5,7-tetrahydrofuro[3,4-b]pyridine-3-carboxylate;
methyl (R)-4-(2-((S)-1,2-difluoroethyl)-3-fluorophenyl)-2-(fluoromethyl)-5-oxo-1,4,5,7-tetrahydrofuro[3,4-b]pyridine-3-carboxylate;
methyl (R)-4-(3-fluoro-2-((R)-1-fluoroethyl)phenyl)-2-(fluoromethyl)-5-oxo-1,4,5,7-tetrahydrofuro[3,4-b]pyridine-3-carboxylate;
methyl (R)-4-(3-fluoro-2-((S)-1-fluoroethyl)phenyl)-2-(fluoromethyl)-5-oxo-1,4,5,7-tetrahydrofuro[3,4-b]pyridine-3-carboxylate;
methyl (R)-4-(2-(difluoromethoxy)phenyl)-2-(fluoromethyl)-5-oxo-1,4,5,7-tetrahydrofuro[3,4-b]pyridine-3-carboxylate;
methyl (R)-4-(3,5-difluoro-2-(trifluoromethyl)phenyl)-2-(fluoromethyl)-5-oxo-1,4,5,7-tetrahydrofuro[3,4-b]pyridine-3-carboxylate;
methyl (R)-4-(2-(2,2-difluoroethyl)-3-fluorophenyl)-2-(fluoromethyl)-5-oxo-1,4,5,7-tetrahydrofuro[3,4-b]pyridine-3-carboxylate;
methyl (R)-4-(2-(2,2-difluoroethyl)-3,5-difluorophenyl)-2-(fluoromethyl)-5-oxo-1,4,5,7-tetrahydrofuro [3,4-b]pyridine-3-carboxylate;
methyl (R)-4-(2-cyclopropyl-3,5-difluorophenyl)-2-(fluoromethyl)-5-oxo-1,4,5,7-tetrahydrofuro[3,4-b]pyridine-3-carboxylate;
methyl (R)-4-(2-(difluoromethyl)-3-fluorophenyl)-2-(fluoromethyl)-5-oxo-1,4,5,7-tetrahydrofuro[3,4-b]pyridine-3-carboxylate;
methyl (R)-4-(2-((R)-1,2-difluoroethyl)-3,5-difluorophenyl)-2-(fluoromethyl)-5-oxo-1,4,5,7-tetrahydrofuro[3,4-b]pyridine-3-carboxylate;
methyl (R)-4-(2-((S)-1,2-difluoroethyl)-3,5-difluorophenyl)-2-(fluoromethyl)-5-oxo-1,4,5,7-tetrahydrofuro[3,4-b]pyridine-3-carboxylate;
methyl (R)-4-(3-fluoro-2-(trifluoromethyl)phenyl)-2-(fluoromethyl)-5-oxo-1,4,5,7-tetrahydrofuro[3,4-b]pyridine -3-carboxylate;
methyl (R)-4-(2-(difluoromethyl)-3,5-difluorophenyl)-2-(fluoromethyl)-5-oxo-1,4,5,7-tetrahydrofuro[3,4-b]pyridine-3-carboxylate;
methyl (R)-4-(2-(difluoromethoxy)-3-fluorophenyl)-2-(fluoromethyl)-5-oxo-1,4,5,7-tetrahydrofuro[3,4-b]pyridine-3-carboxylate;
methyl 4-(2-(difluoromethoxy)-5-fluorophenyl)-2-(fluoromethyl)-5-oxo-1,4,5,7-tetrahydrofuro[3,4-b]pyridine-3-carboxylate;
methyl (R)-4-(2-cyclopropyl-5-fluorophenyl)-2-(fluoromethyl)-5-oxo-1,4,5,7-tetrahydrofuro[3,4-b]pyridine-3-carboxylate;

methyl (R)-4-(2-cyclopropylphenyl)-2-(fluoromethyl)-5-oxo-1,4,5,7-tetrahydrofuro[3,4-b]pyridine-3-carboxylate;
methyl (R)-4-(5-fluoro-2-(trifluoromethyl)phenyl)-2-(fluoromethyl)-5-oxo-1,4,5,7-tetrahydrofuro[3,4-b]pyridine-3-carboxylate;
methyl 4-(2-ethylphenyl)-2-(fluoromethyl)-5-oxo-1,4,5,7-tetrahydrofuro[3,4-b]pyridine-3-carboxylate; and
methyl (R)-2-(fluoromethyl)-5-oxo-4-(2-(trifluoromethyl)phenyl)-1,4,5,7-tetrahydrofuro[3,4-b]pyridine-3-carboxylate; or a pharmaceutically acceptable salt or solvate thereof.

31. The compound according to claim 1 selected from the group consisting of
ethyl (R)-4-(2-((R)-1,2-difluoroethyl)-3-fluorophenyl)-2-(fluoromethyl)-5-oxo-4,5,6,7-tetrahydro-1H-cyclopenta[b]pyridine-3-carboxylate;
methyl (R)-4-(2-((S)-1,2-difluoroethyl)-3-fluorophenyl)-2-(fluoromethyl)-5-oxo-4,5,6,7-tetrahydro-1H-cyclopenta[b]pyridine-3-carboxylate;
(R)-4-(3-fluoro-2-(2,2,2-trifluoroethyl)phenyl)-2-(fluoromethyl)-5-oxo-4,5,6,7-tetrahydro -1H-cyclopenta[b]pyridine-3-carboxylate;
methyl (R)-4-(2-cyclopropyl-3,5-difluorophenyl)-2-(fluoromethyl)-5-oxo-4,5,6,7-tetrahydro-1H-cyclopenta[b]pyridine-3-carboxylate;
methyl (R)-4-(2-(2,2-difluoroethyl)-3-fluorophenyl)-2-(fluoromethyl)-5-oxo-4,5,6,7-tetrahydro-1Hcyclopenta[b]pyridine-3-carboxylate;
methyl (R)-4-(3-fluoro-2-((R)-1-fluoroethyl)phenyl)-2-(fluoromethyl)-5-oxo-4,5,6,7-tetrahydro-1H-cyclopenta[b]pyridine-3-carboxylate;
methyl (R)-4-(3-fluoro-2-((S)-1-fluoroethyl)phenyl)-2-(fluoromethyl)-5-oxo-4,5,6,7-tetrahydro-1H-cyclopenta[b]pyridine-3-carboxylate;
methyl (R)-4-(2-cyclopropyl-3-fluorophenyl)-2-(fluoromethyl)-5-oxo-4,5,6,7-tetrahydro-1H-cyclopenta[b]pyridine-3-carboxylate;
methyl (S)-4-(3,5-difluoro-2-((S)-1-fluoroethyl)phenyl)-2-(fluoromethyl)-5-oxo-4,5,6,7-tetrahydro-1H-cyclopenta[b]pyridine-3-carboxylate; and
methyl (S)-4-(3,5-difluoro-2-((R)-1-fluoroethyl)phenyl)-2-(fluoromethyl)-5-oxo-4,5,6,7-tetrahydro-1H-cyclopenta[b]pyridine-3-carboxylate; or a pharmaceutically acceptable salt or solvate thereof.

32. The compound according to claim 14, wherein the compound is methyl 2-(difluoromethyl)-4-(3-fluoro-2-(1-fluoroethyl)phenyl)-5-oxo-1,4,5,7-tetrahydrofuro[3,4-b]pyridine-3-carboxylate or a pharmaceutically acceptable salt or solvate thereof.

33. A crystalline form of methyl (R)-4-(3-fluoro-2-((R)-1-fluoroethyl)phenyl)-2-(fluoromethyl)-5-oxo-1,4,5,7-tetrahydrofuro[3,4-b]pyridine-3-carboxylate.

34. The crystalline form according to claim 33, wherein the form is Form A.

35. The crystalline form according to claim 33, wherein the form is Form B.

36. The crystalline form according to claim 33, wherein the form is Form C.

37. A crystalline hydrated form of methyl (R)-4-(3-fluoro-2-((R)-1-fluoroethyl)phenyl)-2-(fluoromethyl)-5-oxo-1,4,5,7-tetrahydrofuro[3,4-b]pyridine-3-carboxylate.

38. The crystalline hydrated form according to claim 37, wherein the hydrated form is Hydrate A.

39. The crystalline hydrated form according to claim 37, wherein the hydrated form is Hydrate B.

40. A pharmaceutical composition comprising a compound according to any one of claims 1-32 and a pharmaceutically acceptable excipient.

41. Use of the compound according to any one of claims 1-32, or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for the treatment of schizophrenia, bipolar disorder, major depressive disorder, substance use disorder, ADHD, Phelan-McDermid Syndrome, autism spectrum disorder, multiple sclerosis, frontotemporal dementia, Alzheimer's disease, Brugada Syndrome, Short QT syndrome, or early repolarization syndrome, wherein an effective amount of the compound or a pharmaceutically acceptable salt thereof is to be administered to a patient in need of treatment thereof.

42. Use of the compound according to any one of claims 1-32, or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for the treatment of schizophrenia, bipolar disorder, major depressive disorder, substance use disorder, ADHD, Phelan-McDermid Syndrome, autism spectrum disorder, multiple sclerosis, frontotemporal dementia, Alzheimer's disease, Brugada Syndrome, Short QT syndrome, or early repolarization

syndrome, wherein the compound or a pharmaceutically acceptable salt thereof is to be administered to a patient in need of treatment thereof.

43. A compound according to any one of claims 1-32, or a pharmaceutically acceptable salt thereof for use in therapy, wherein the compound or a pharmaceutically acceptable salt thereof is to be administered to a patient in need of therapy thereof.