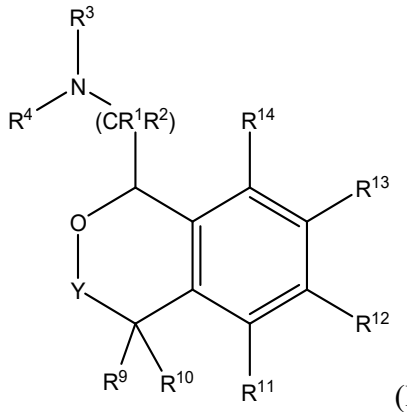
CLAIMS

1. A compound of formula (I):



(I),

or a pharmaceutically acceptable salt thereof,

wherein:

Y is $-C(R^5R^6)-$;

R^1, R^2, R^3 and R^4 are chosen independently from H, aliphatic (C_1-C_8)hydrocarbon and (C_3-C_6)cycloalkyl, wherein the aliphatic (C_1-C_8)hydrocarbon is optionally substituted with one or more of halogen, hydroxyl, (C_1-C_6)alkoxy, amino, (C_1-C_6)alkylamino and di(C_1-C_6)alkylamino;

or, taken together, R^1 and R^2 may form (C_3-C_6)cycloalkyl;

R^5 and R^6 are both H;

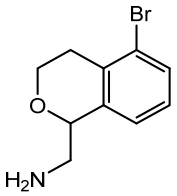
R^9 and R^{10} are chosen independently from H, halogen, hydroxyl, (C_1-C_6)alkyl, (C_1-C_6)haloalkyl and (C_1-C_6)alkoxy;

R^{11}, R^{12}, R^{13}, and R^{14} are chosen independently from H, halogen, cyano, aliphatic (C_1-C_8)hydrocarbon, (C_3-C_6)cycloalkyl, (C_1-C_6)haloalkyl, aminocarbonyl, (C_1-C_6)alkylaminocarbonyl, di(C_1-C_6)alkylaminocarbonyl, (C_1-C_6)acyl, (C_1-C_6)haloalkoxy, hydroxy(C_1-C_6)alkyl, carboxy, (C_1-C_6)alkoxycarbonyl, acetoxy, nitro, amino, (C_1-C_6)alkylamino, di(C_1-C_6)alkylamino, and aminosulfonyl;

or, taken together, any adjacent pair of R^{11}, R^{12}, R^{13}, and R^{14} may form a fused difluoro-1,3-dioxole, 2,3-dihydrofuran optionally mono- or bisubstituted with fluorine, or 2,5-dihydrofuran optionally mono- or bi-substituted with fluorine,

with the provisos that:

at least one of R^9, R^{10} R^{11}, R^{12}, R^{13}, and R^{14} is other than hydrogen;

and the compound is not 

.

2. The compound according to claim 1, or a pharmaceutically acceptable salt thereof, wherein R^1 is hydrogen and R^2 is hydrogen or methyl.

3. The compound according to claim 1 or 2, or a pharmaceutically acceptable salt thereof, wherein R^3 is hydrogen and R^4 is hydrogen or methyl.

4. The compound according to any one of claims 1-3, or a pharmaceutically acceptable salt thereof, wherein R^{11}, R^{12}, R^{13}, and R^{14} are chosen independently from hydrogen, fluoro, chloro, methyl and cyano.

5. The compound according to any one of claims 1-4, or a pharmaceutically acceptable salt thereof, wherein R^9 and R^{10} are chosen independently from H, fluoro, and methyl.

6. The compound according to any one of claims 1-5, or a pharmaceutically acceptable salt thereof, wherein R^{11}, R^{12}, R^{13}, and R^{14} are H.

7. The compound according to any one of claims 1-5, or a pharmaceutically acceptable salt thereof, wherein one of R^{11}, R^{12}, R^{13}, and R^{14} is fluoro, chloro, methyl or cyano and the remaining three are H.

8. The compound according to any one of claims 1-5, or a pharmaceutically acceptable salt thereof, wherein two of R^{11}, R^{12}, R^{13}, and R^{14} are fluoro, chloro, methyl or cyano and the remaining two are H.

9. The compound according to claim 7, or a pharmaceutically acceptable salt thereof, wherein R^{12} and R^{13} are H, one of R^{11} and R^{14} is chosen from fluoro, chloro, methyl and cyano, and the other of R^{11} and R^{14} is H.

10. The compound according to claim 8, or a pharmaceutically acceptable salt thereof, wherein R^{12} and R^{13} are H, and R^{11} and R^{14} are chosen from fluoro, chloro, methyl and cyano.

11. The compound according to claim 1, or a pharmaceutically acceptable salt thereof, wherein R^1 is hydrogen; R^2 is hydrogen or methyl; R^3 is hydrogen; R^4 is hydrogen or methyl; R^5, R^6, R^9 and R^{10} are hydrogen.

12. A compound according to claim 11, or a pharmaceutically acceptable salt thereof, wherein R^{12} and R^{13} are H, one of R^{11} and R^{14} is chosen from fluoro, chloro, methyl and cyano, and the other of R^{11} and R^{14} is H.

13. The compound according to claim 11, or a pharmaceutically acceptable salt thereof, wherein R^{12} and R^{13} are H, and R^{11} and R^{14} are chosen from fluoro, chloro, methyl and cyano.

14. The compound according to claim 12, or a pharmaceutically acceptable salt thereof, wherein R^{14} is chosen from fluoro, chloro, methyl and cyano.

15. The compound according to claim 1, or a pharmaceutically acceptable salt thereof, wherein R^1 is hydrogen; R^2 is hydrogen or methyl; R^3 is hydrogen; R^4 is hydrogen or methyl; R^9 and R^{10} are hydrogen; and R^{14} is chosen from fluoro, chloro, methyl and cyano, and R^{11}, R^{12} and R^{13} are H.

16. The compound according to claim 1, or a pharmaceutically acceptable salt thereof, wherein R^3 is hydrogen or methyl; R^1, R^2, R^4, R^{11}, and R^{14} are hydrogen; R^9 and R^{10} are hydrogen; one of R^{12} and R^{13} is chosen from fluoro, chloro, methyl and cyano, and the other of R^{12} and R^{13} is hydrogen.

17. The compound according to claim 1, or a pharmaceutically acceptable salt thereof, wherein R^3 is hydrogen or methyl; R^1, R^2, R^4, R^{11}, and R^{14} are hydrogen; one or both of R^9 and R^{10} is chosen from methyl and fluoro; and R^{12} and R^{13} are hydrogen.

18. The compound according to claim 1, or a pharmaceutically acceptable salt thereof, wherein R^3 is methyl; R^1, R^2, and $R^4$are hydrogen; R^9, R^{10} and R^{11} are hydrogen, and one of R^{12}, R^{13} or R^{14} is chosen from fluoro, chloro, methyl and cyano, and the remaining two are H.

19. The compound according to claim 1, or a pharmaceutically acceptable salt thereof, wherein R^3 is methyl; R^1, R^2, R^4, R^9 and R^{10} are hydrogen; R^{11} and R^{14} are fluoro; and R^{12} and R^{13} are H.

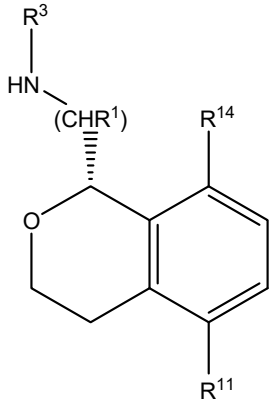
20. The compound according to claim 17, or a pharmaceutically acceptable salt thereof, wherein R^3 is methyl.

21. The compound according to claim 1, or a pharmaceutically acceptable salt thereof, wherein R^1 and R^3 are hydrogen or methyl; R^2, R^4, R^9, R^{10}, R^{13}, and R^{14} are hydrogen and one of R^{11} and R^{12} is fluoro and the other is hydrogen.

22. The compound according to claim 1, or a pharmaceutically acceptable salt thereof, wherein R^1 and R^3 are hydrogen or methyl; R^2, R^4, and R^9 are hydrogen; R^{10} is hydrogen or methyl; R^{11} is hydrogen or fluorine; R^{12} and R^{13} are hydrogen; and R^{14} is chosen from hydrogen, fluoro, chloro, methyl and cyano.

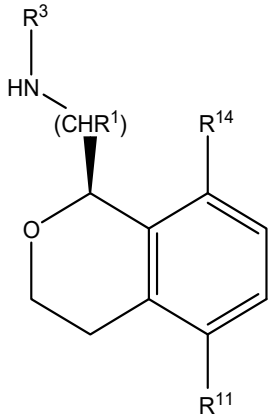
23. The compound according to claim 22, or a pharmaceutically acceptable salt thereof, wherein R^{10} is hydrogen.

24. The compound according to claim 23, or a pharmaceutically acceptable salt thereof, wherein C(1) of the isochroman is of absolute configuration:



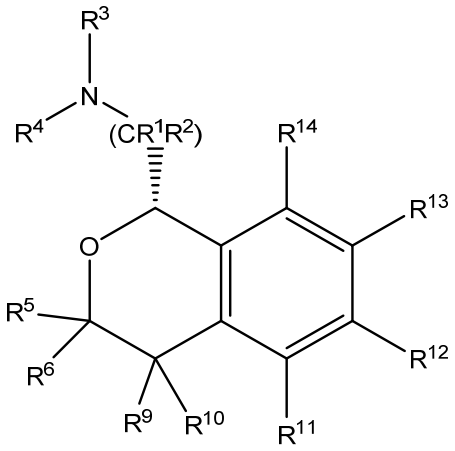
or a pharmaceutically acceptable salt thereof.

25. The compound according to claim 23, wherein C(1) of the isochroman is of absolute configuration:



or a pharmaceutically acceptable salt thereof.

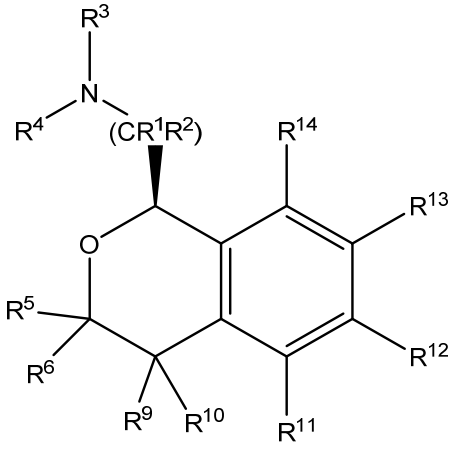
26. The compound according to claim 1, of formula **IIa**:



IIa

or a pharmaceutically acceptable salt thereof.

27. The compound according to claim 1, of formula **IIb**:



IIb

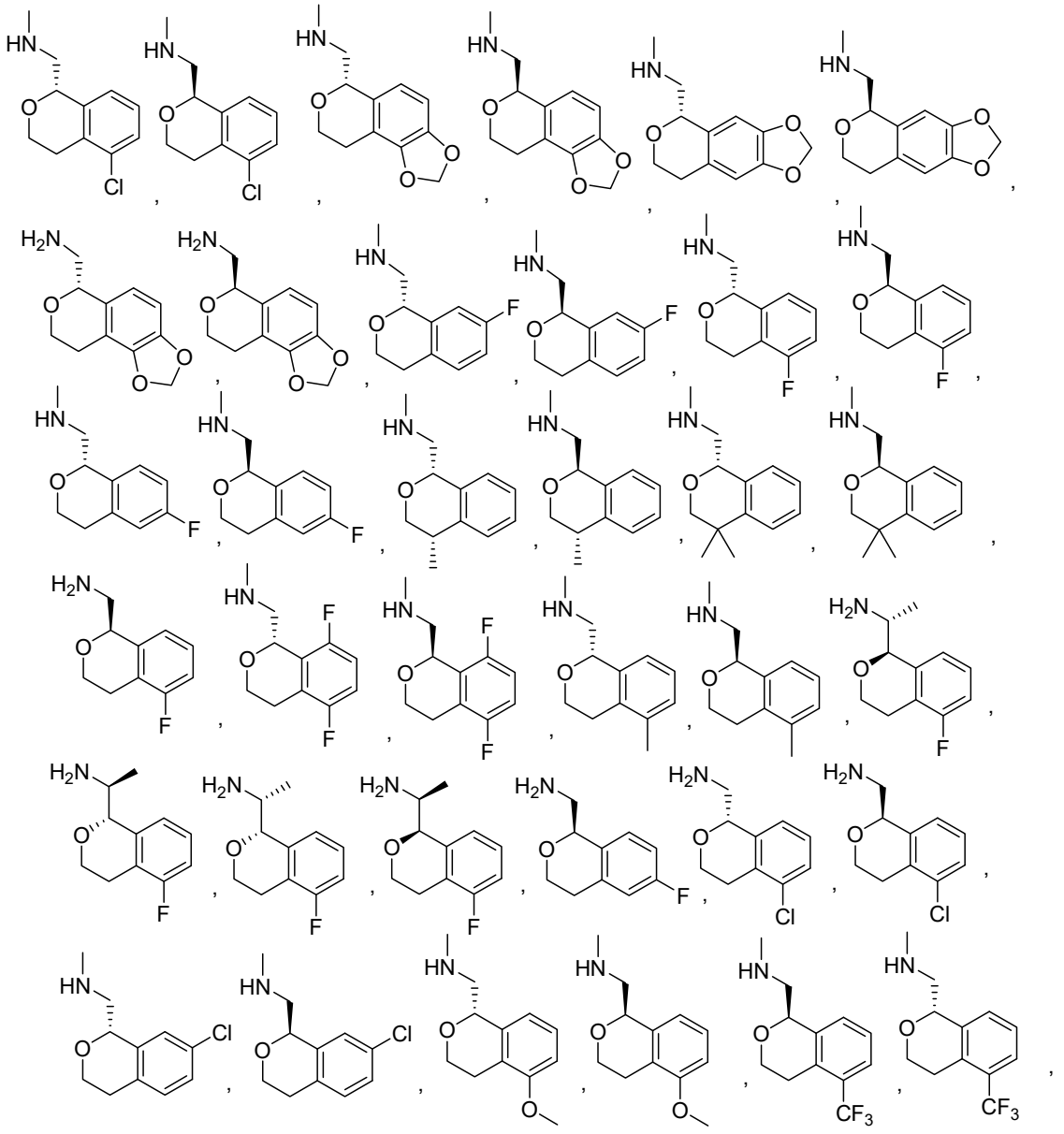
or a pharmaceutically acceptable salt thereof.

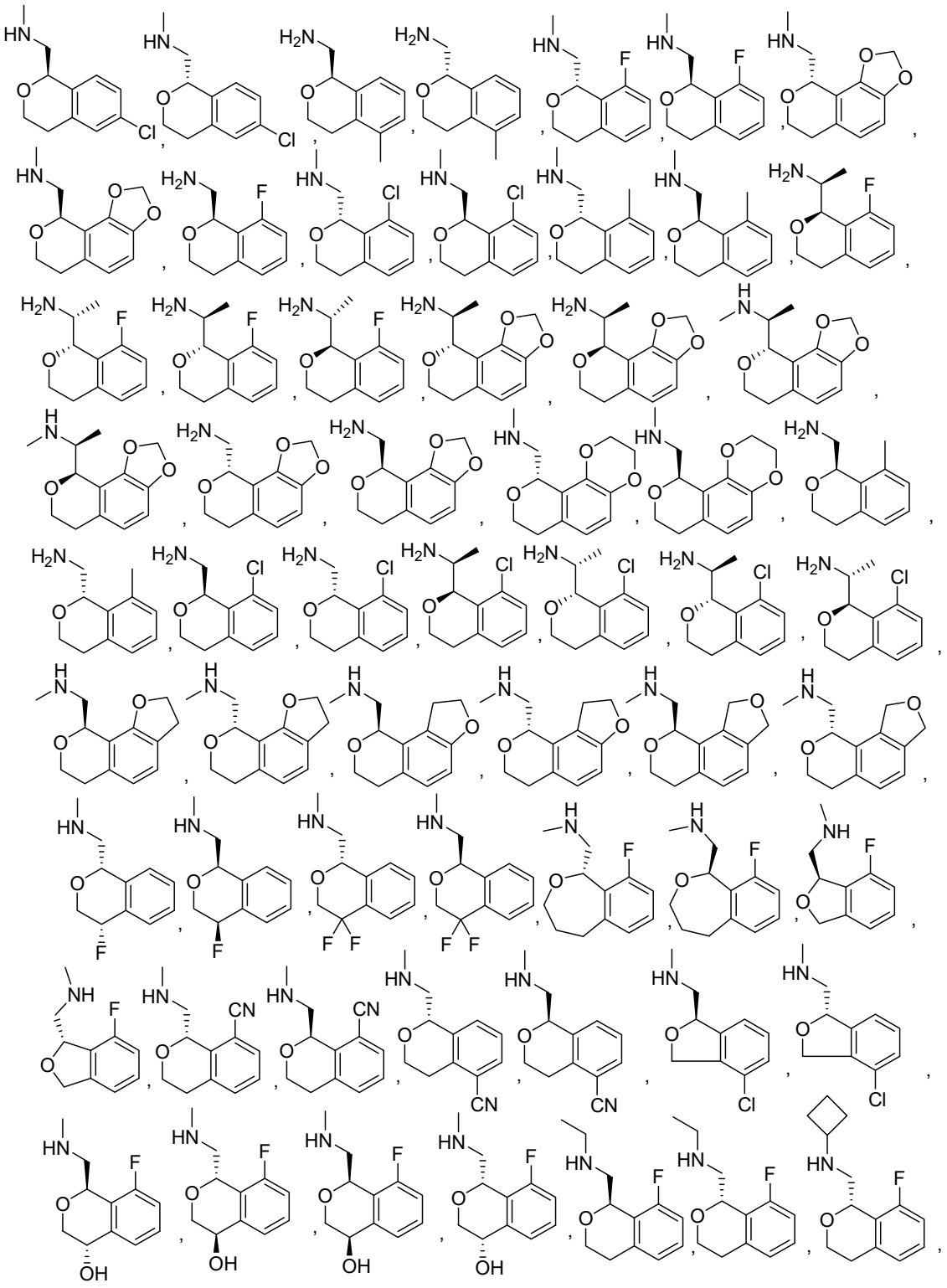
28. The compound according to claim 1, or a pharmaceutically acceptable salt thereof, wherein R^1 is hydrogen; R^2 is hydrogen or methyl; R^3 is hydrogen; and R^4 is hydrogen or methyl.

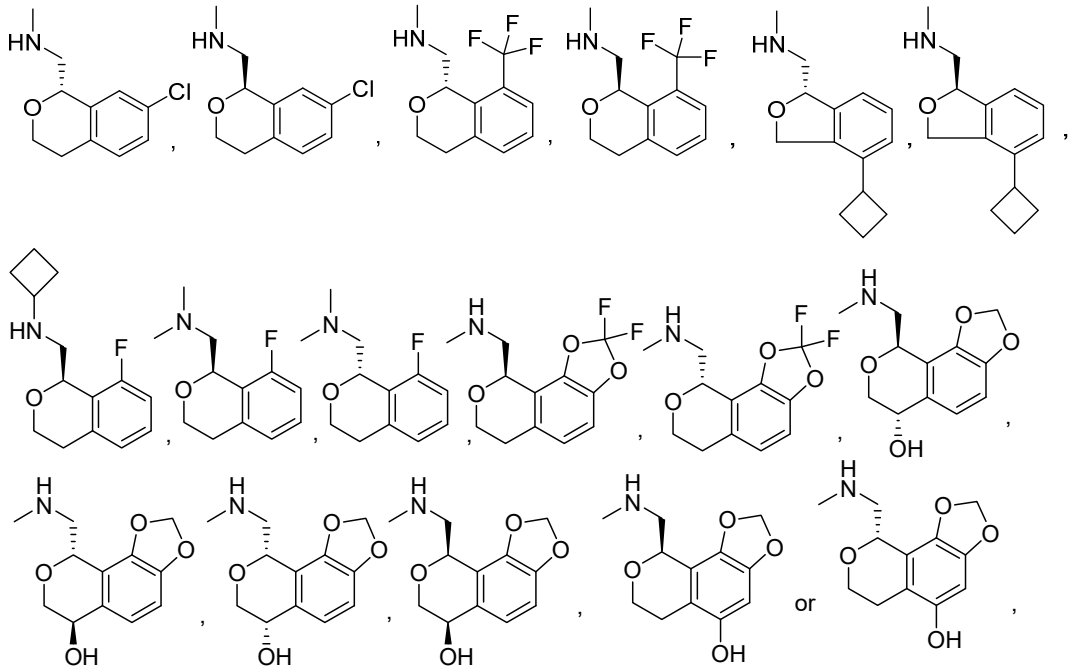
29. The compound according to claim 28, or a pharmaceutically acceptable salt thereof, wherein R^4 is hydrogen; and R^9 and R^{10} are each independently hydrogen, methyl or fluoro.

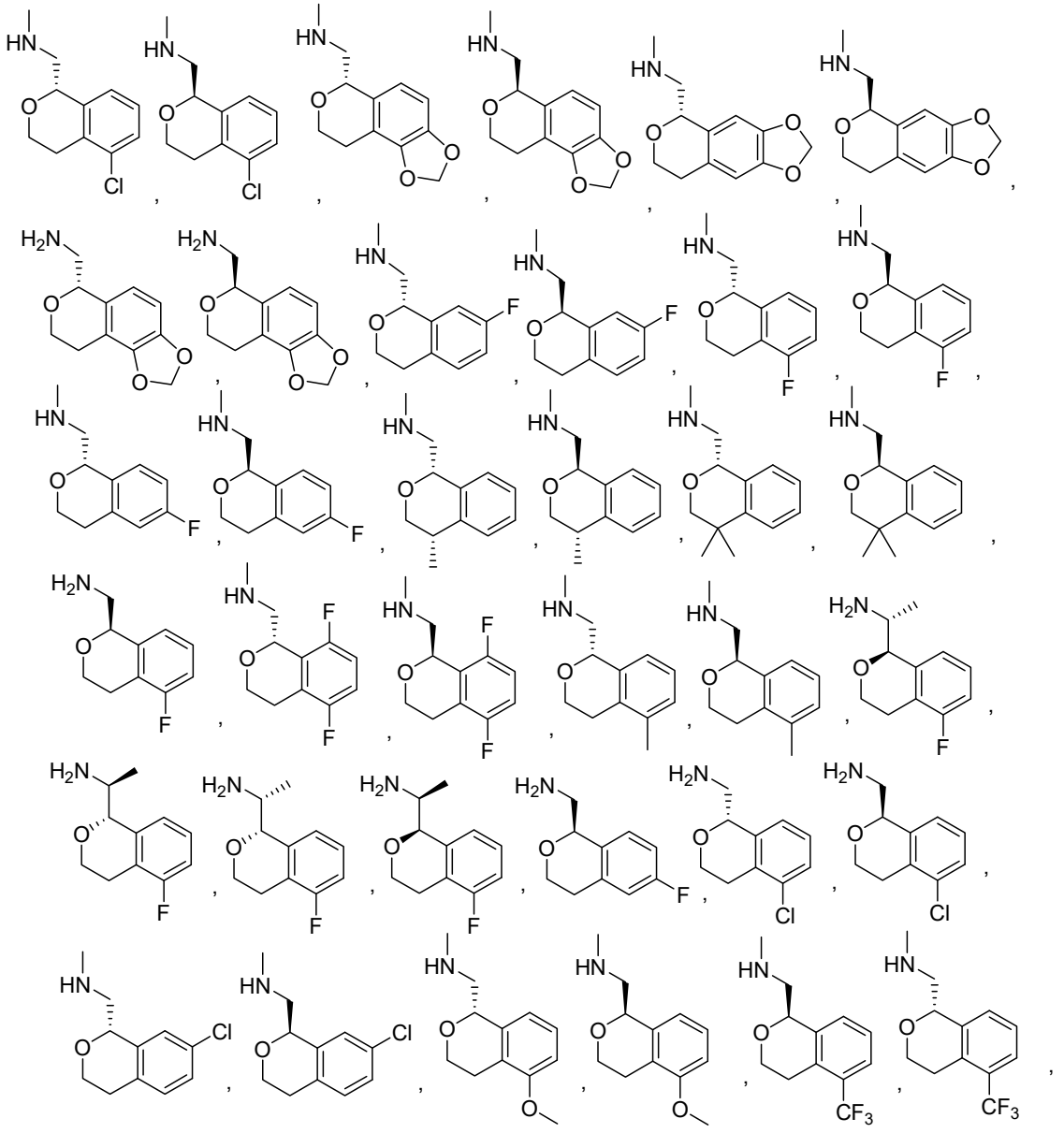
30. The compound according to claim 1, or a pharmaceutically acceptable salt thereof, wherein any adjacent pair of R^{11}, R^{12}, R^{13}, and R^{14} may form a fused difluoro-1,3-dioxole ring.

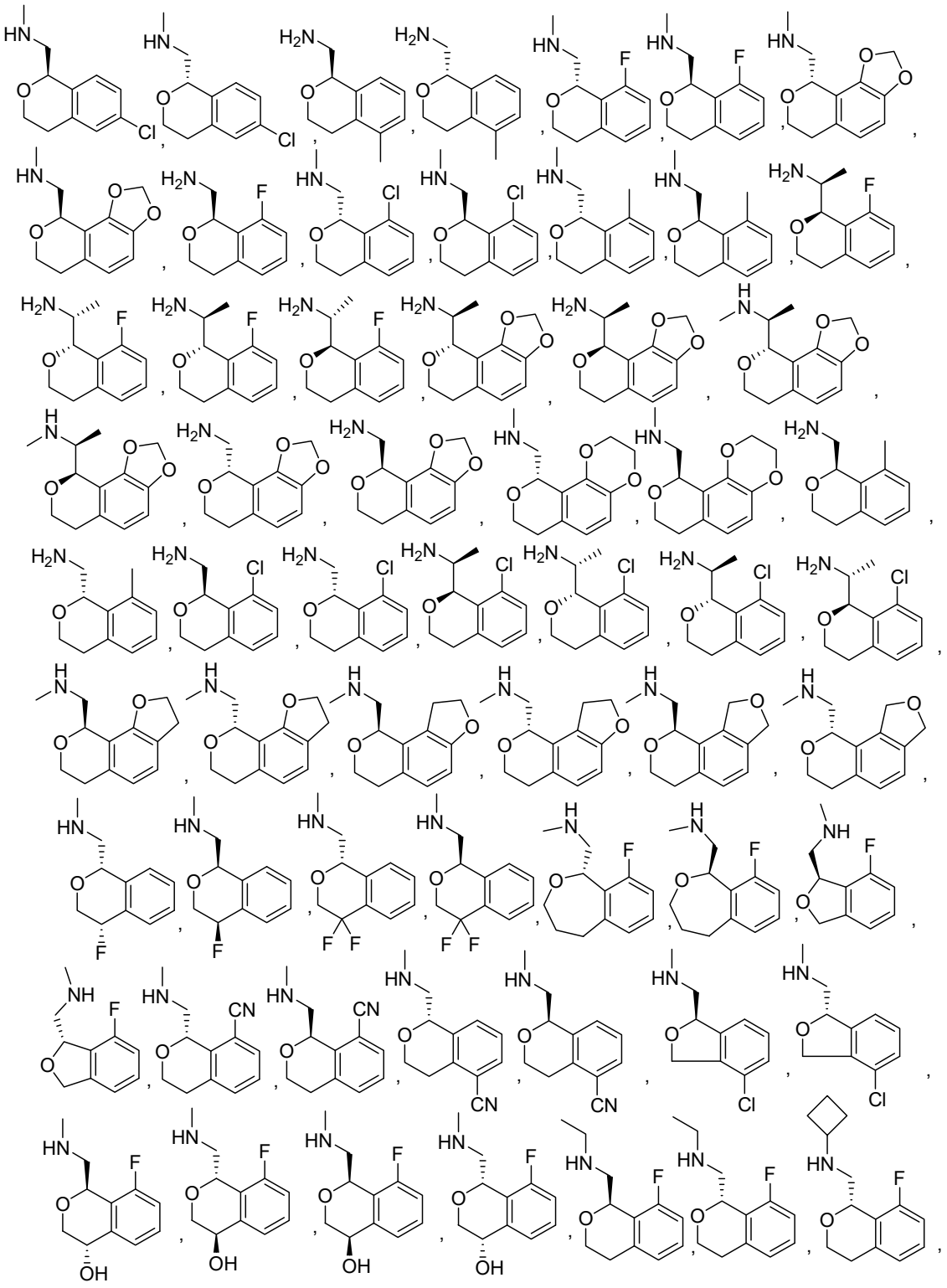
31. A compound selected from the following:

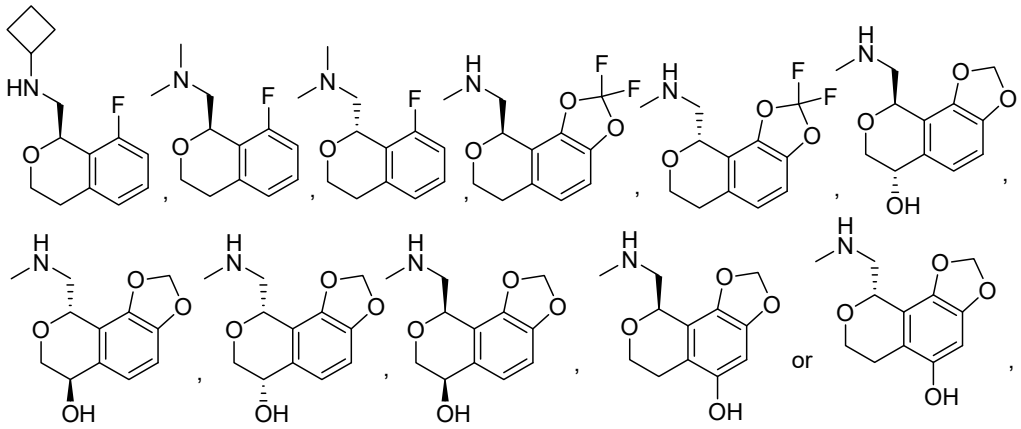






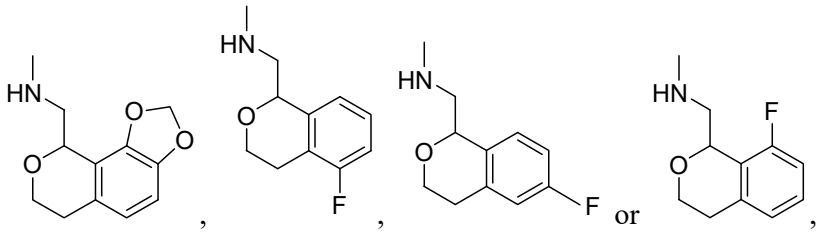






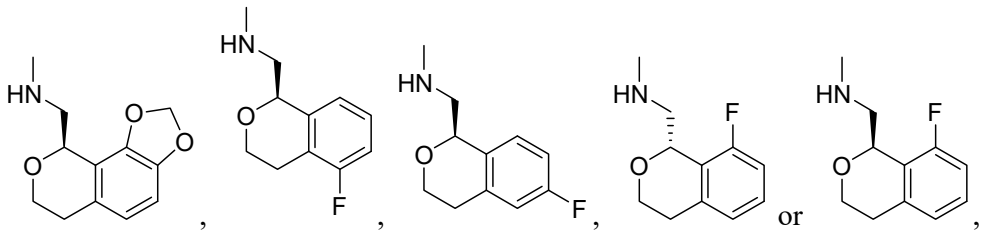
or a pharmaceutically acceptable salt thereof.

33. A compound selected from the following:



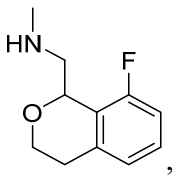
or a pharmaceutically acceptable salt thereof.

34. The compound according to claim 33, wherein said compound is:



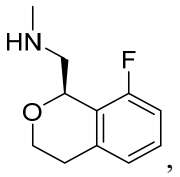
or a pharmaceutically acceptable salt thereof.

35. The compound:



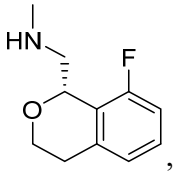
or a pharmaceutically acceptable salt or stereoisomer thereof.

36. The compound:



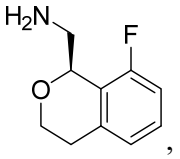
or a pharmaceutically acceptable salt thereof.

37. The compound:



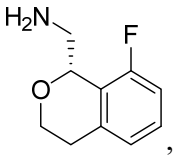
or a pharmaceutically acceptable salt thereof.

38. The compound:



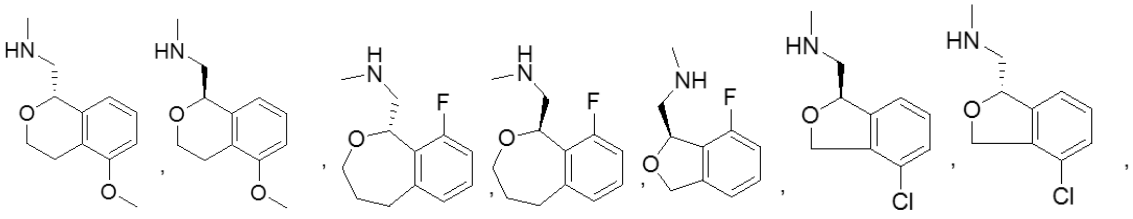
or a pharmaceutically acceptable salt thereof.

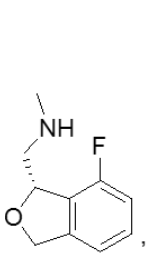
39. The compound:



or a pharmaceutically acceptable salt thereof.

40. A compound selected from:





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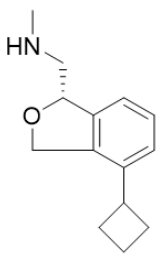
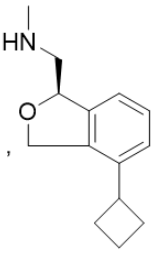


or


,

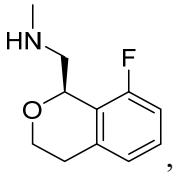
or a pharmaceutically acceptable salt thereof.

41. The compound according to any one of claims 1-40, or a pharmaceutically acceptable salt thereof, wherein said compound is greater than 90% enantiomerically pure.

42. The compound according to any one of claims 1-41, or a pharmaceutically acceptable salt thereof, wherein said compound is greater than 95% enantiomerically pure.

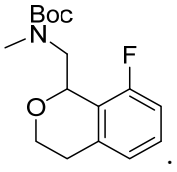
43. A composition, comprising the compound, or a pharmaceutically acceptable salt thereof, according to any one of claims 1-42, and a pharmaceutically acceptable carrier, adjuvant, or vehicle.

44. A process for preparing (R)-1-(8-fluoroisochroman-1-yl)-N-methylmethanamine, having structure:



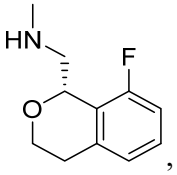
,

or a pharmaceutically acceptable salt thereof, comprising deprotecting tert-butyl ((8-fluoroisochroman-1-yl)methyl)((methyl)carbamate, having the structure:



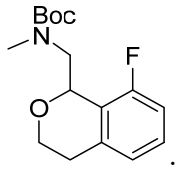
.

45. A process for preparing (S)-1-(8-fluoroisochroman-1-yl)-N-methylmethanamine, having structure:



,

or a pharmaceutically acceptable salt thereof, comprising deprotecting tert-butyl ((8-fluoroisochroman-1-yl)methyl)((methyl)carbamate, having the structure:



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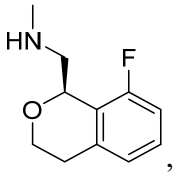
46. The process of any one of claims 44 or 45, further comprising separating (S)-1-(8-fluoroisochroman-1-yl)-N-methylmethanamine and (R)-1-(8-fluoroisochroman-1-yl)-N-methylmethanamine.

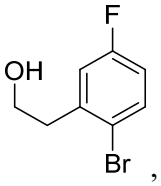
47. A process for preparing (R)-1-(8-fluoroisochroman-1-yl)-N-methylmethanamine, having the structure:



,

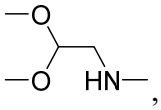
or a pharmaceutically acceptable salt thereof, comprising:

a) reacting 2-(2-bromo-5-fluorophenyl) ethanol, having the structure:



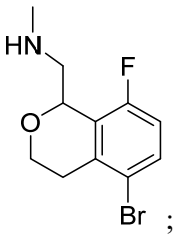
,

with 2,2-dimethoxy-*N*-methylethanamine, having the structure:



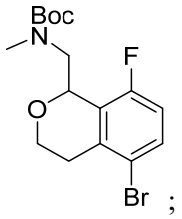
,

in the presence of an acid to provide 1-(5-bromo-8-fluoroisochroman-1-yl)-*N*-methylmethanamine, having the structure:



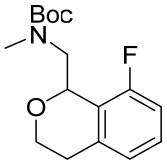
;

b) protecting 1-(5-bromo-8-fluoroisochroman-1-yl)-*N*-methylmethanamine to provide *tert*-butyl (5-bromo-8-fluoroisochroman-1-yl)methyl)(methyl)carbamate, having the structure:



;

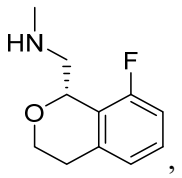
c) converting *tert*-butyl ((5-bromo-8-fluoroisochroman-1-yl)methyl)(methyl)carbamate to *tert*-butyl ((8-fluoroisochroman-1-yl)methyl)(methyl)carbamate having the structure:



; and

d) deprotecting *tert*-butyl ((8-fluoroisochroman-1-yl)methyl)(methyl)carbamate to provide (R)-1-(8-fluoroisochroman-1-yl)-N-methylmethanamine, or a pharmaceutically acceptable salt thereof.

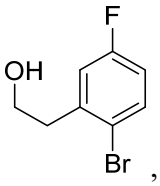
48. A process for preparing (S)-1-(8-fluoroisochroman-1-yl)-N-methylmethanamine, having the structure:



,

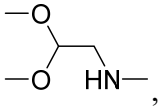
or a pharmaceutically acceptable salt thereof, comprising:

a) reacting 2-(2-bromo-5-fluorophenyl) ethanol, having the structure:



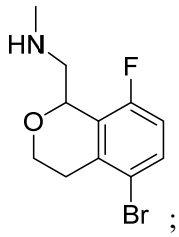
,

with 2,2-dimethoxy-*N*-methylethanamine, having the structure:



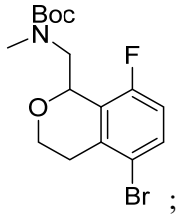
,

in the presence of an acid to provide 1-(5-bromo-8-fluoroisochroman-1-yl)-*N*-methylmethanamine, having the structure:



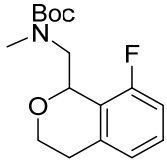
;

b) protecting 1-(5-bromo-8-fluoroisochroman-1-yl)-*N*-methylmethanamine to provide *tert*-butyl (5-bromo-8-fluoroisochroman-1-yl)methyl)(methyl)carbamate, having the structure:



;

c) converting *tert*-butyl ((5-bromo-8-fluoroisochroman-1-yl)methyl)(methyl)carbamate to *tert*-butyl ((8-fluoroisochroman-1-yl)methyl)(methyl)carbamate having the structure:



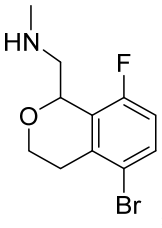
; and

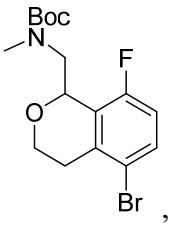
d) deprotecting *tert*-butyl ((8-fluoroisochroman-1-yl)methyl)(methyl)carbamate to provide (S)-1-(8-fluoroisochroman-1-yl)-N-methylmethanamine, or a pharmaceutically acceptable salt thereof.

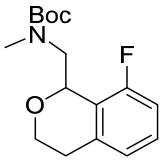
49. A compound, which is (R)-1-(8-fluoroisochroman-1-yl)-N-methylmethanamine, or a pharmaceutically acceptable salt thereof, obtainable by the process of any one of claims 44, 46 or 47.

50. A compound, which is (S)-1-(8-fluoroisochroman-1-yl)-N-methylmethanamine, or a pharmaceutically acceptable salt thereof, obtainable by the process of any one of claims 45, 46 or 48.

51. A compound selected from:



,


, and


.

52. Use of the compound, or a pharmaceutically acceptable salt thereof, according to any one of claims 1-40, in the manufacture of a medicament for the treatment of a neurological or psychiatric disease or neuropsychiatric and behavior symptoms in a neurological disease or disorder;

wherein the neurological or psychiatric disease or disorder is bipolar disorder, pain, schizophrenia, or other psychotic diseases, obsessive compulsive disorder, addiction, social disorder, attention deficit hyperactivity disorder, an anxiety disorder, a movement disorder, epilepsy, autism, cognitive disease or disorder, Alzheimer's disease, Parkinson's disease, Alzheimer's Disease with agitation, Alzheimer's Disease with aggression, or Alzheimer's Disease with agitation aggression.

53. The use according to claim 52, wherein the neurological or psychiatric disease or disorder is a movement disorder or epilepsy.

54. The use according to claim 52, wherein said neurological or psychiatric disease or disorder is bipolar disorder, anxiety, Alzheimer's Disease with agitation, Alzheimer's Disease with aggression, or Alzheimer's Disease with agitation aggression.

55. The use according to claim 52, wherein said neurological disease or disorder is selected from Alzheimer's disease and Parkinson's disease.