The present invention provides certain new compounds that are PAMs of the D1 receptor and, as such, are useful in treatment of the disorders discussed above. The new compounds of the present invention may provide an alternative treatment for the such disorders. The present invention further provides a cocrystalline form of certain new compounds.

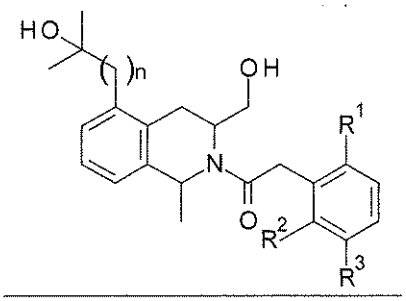
European Patent Application Publication No. EP 330360 discloses certain isoquinoline compounds as agonists of the opioid Kappa-receptor and useful as analgesics.

U.S. Patent No. 5236934 discloses certain 1,2,3,4-tetrahydroisoquinoline compounds as inhibitors of the angiotensin II receptor and useful in treating CNS disorders including cognitive dysfunction.

U.S. Patent Application Publication No. US 2006/0287359 discloses certain tetrahydroisoquinoline compounds as estrogen receptor antagonists and useful in treating estrogen related diseases including breast cancer.

Summary

In a first aspect of the present disclosure, there is provided a compound of the formula



wherein

n is 0, 1 or 2;

R^1 is halogen;

R^2 is halogen, H, CN, C1 – C3 alkoxy or C1 – C3 alkyl; and

R^3 is H, halogen, C1 – C3 alkoxy or C1 – C3 alkyl.

In a second aspect of the present disclosure, there is provided a composition comprising 2-(2,6-dichlorophenyl)-1-[(1S,3R)-3-(hydroxymethyl)-5-(3-hydroxy-3-methylbutyl)-1-methyl-3,4-dihydroisoquinolin-2(1*H*)-yl]ethanone and 4-hydroxybenzoic acid.

In a third aspect of the present disclosure, there is provided a cocrystalline form of the composition as described herein.

In a fourth aspect of the present disclosure, there is provided a pharmaceutical composition comprising 2-(2,6-dichlorophenyl)-1-[(1S,3R)-3-(hydroxymethyl)-5-(3-hydroxy-3-methylbutyl)-1-methyl-3,4-dihydroisoquinolin-2(1*H*)-yl]ethanone and 4-hydroxybenzoic acid, and a pharmaceutically acceptable carrier, diluent or excipient.

In a fifth aspect of the present disclosure, there is provided a pharmaceutical composition comprising a compound as described herein, and a pharmaceutically acceptable carrier, diluent or excipient.

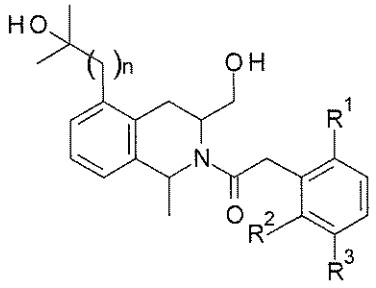
In a sixth aspect of the present disclosure, there is provided a compound as described herein for use in therapy.

In a seventh aspect of the present disclosure, there is provided a compound as described herein for use in the treatment of Parkinson's disease.

In an eighth aspect of the present disclosure, there is provided a compound as described herein for use in the treatment of schizophrenia.

Description

The present invention provides a compound of formula I



I

wherein

n is 0, 1 or 2;

R^1 is halogen;

R^2 is halogen, H, CN, C1 – C3 alkoxy or C1 – C3 alkyl; and

R^3 is H, halogen, C1 – C3 alkoxy or C1 – C3 alkyl.

The present invention further provides a compound of formula Ia

carrier, diluent or excipient.

11. A pharmaceutical composition comprising a compound according to any one of claims 1 to 6, and a pharmaceutically acceptable carrier, diluent or excipient.

~~12. A method of treating Parkinson's disease comprising administrating to a patient in need thereof an effective amount of a compound according to any one of claims 1 to 6.~~

~~13. A method of treating schizophrenia comprising administrating to a patient in need thereof an effective amount of a compound according to any one of claims 1 to 6.~~

~~14~~12. A compound as claimed in any one of claims 1 to 6 for use in therapy.

~~15~~13. A compound as claimed in any one of claims 1 to 6 for use in the treatment of Parkinson's disease.

~~16~~14. A compound as claimed in any one of claims 1 to 6 for use in the treatment of schizophrenia.