7B, and 8A and 8B, 2) cGMP specific, PDE 5A, 6A-C, and 9A, and 3) those that are dual substrate, PDE 1A-C, 2A, 3A and 3B, 10A, and 11A. The homology between the families, ranging from 20% to 45% suggests that it may be possible to develop selective inhibitors for each of these subtypes.

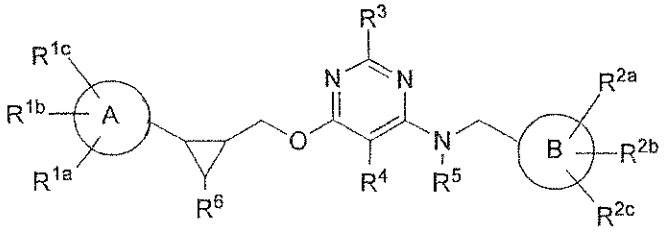
The identification of PDE10 was reported by three groups independently and was distinguished from other PDEs on the basis of its amino acid sequence, functional properties, and tissue distribution (Fujishige et al., J. Biol. Chem. (1999) 274:18438-18445; Loughney et al., Gene (1999) 234: 109-117; Soderling et al., PNAS, USA (1999) 96: 7071-7076). The PDE10 subtype at present consists of a sole member, PDE10A, having alternative splice variants at both the N-terminus (three variants) and C-terminus (two variants), but that does not affect the GAF domain in the N-terminus or the catalytic site in C-terminus. The N-terminus splice variants, PDE10A1 and PDE10A2, differ in that the A2 variant has a PKA phosphorylation site that upon activation, i.e. PKA phosphorylation in response to elevated cAMP levels, results in intracellular changes to the localization of the enzyme. PDE10A is unique relative to other PDE families also having the conserved GAF domain in that its ligand is cAMP, while for the other GAF-domain PDEs the ligand is cGMP (Kehler et al., Expert Opin. Ther. Patents (2007) 17(2): 147-158). PDE10A has limited but high expression in the brain and testes. The high expression in the brain and, in particular, the neurons of the striatum, unique to PDE10, suggests that inhibitors thereto may be well suited from treating neurological and psychiatric disorders and conditions.

Inhibition of PDE10 is believed to be useful in the treatment of schizophrenia and a wide variety of conditions or disorders that would benefit from increasing levels of cAMP and/or cGMP within neurons, including a variety neurological, psychotic, anxiety and/or movement disorders. Accordingly, agents that inhibit PDE10 and especially PDE10A would be desirable as therapeutics for neurological and psychiatric disorders.

SUMMARY ~~OF THE INVENTION~~

The present disclosure~~invention~~ is directed to pyrimidine compounds which are useful as therapeutic agents for the treatment of central nervous system disorders associated with phosphodiesterase 10 (PDE10). The present disclosure~~invention~~ also relates to the use of such compounds for treating neurological and psychiatric disorders, such as schizophrenia, psychosis or Huntington's disease, and those associated with striatal hypofunction or basal ganglia dysfunction.

In a first aspect, there is provided a compound of the formula I:



I

wherein:

A is selected from the group consisting of:

(1) pyridyl,
(2) quinolinyl,
(3) naphthyridinyl,
(4) thiazolyl,
(5) pyridazinyl,
(6) oxazolyl, and
(7) pyrazolyl,
(8) dihydropyrrolopyrazolyl,
(9) dihydrocyclopentapyridinyl,
(10) imidazopyridazinyl, and
(11) pyrazolopyrimidinyl;

B is selected from the group consisting of:

(1) thiazolyl,
(2) pyrazolyl,
(3) thiadiazolyl,
(4) isoxazolyl,
(5) isothiazolyl,
(6) pyridyl, and
(7) pyrimidinyl;

R^{1a}, R^{1b} and R^{1c} are independently selected from the group consisting of:

(1) hydrogen,

(2) halogen,

(3) hydroxyl,

(4) -(C=O)$_m$-O$_n$-C$_{1-6}$alkyl, where m is 0 or 1, n is 0 or 1 (wherein if m is 0 or n is 0, a bond is present) and where the alkyl is unsubstituted or substituted with one or more substituents selected from R^{13},

(5) -(C=O)$_m$-O$_n$-C$_{3-6}$cycloalkyl, where the cycloalkyl is unsubstituted or substituted with one or more substituents selected from R^{13},

(6) -(C=O)$_m$-C$_{2-4}$alkenyl, where the alkenyl is unsubstituted or substituted with one or more substituents selected from R^{13},

(7) -(C=O)$_m$-C$_{2-4}$alkynyl, where the alkynyl is unsubstituted or substituted with one or more substituents selected from R^{13},

(8) -(C=O)$_m$-O$_n$-phenyl or -(C=O)$_m$-O$_n$-naphthyl, where the phenyl or naphthyl is unsubstituted or substituted with one or more substituents selected from R^{13},

(9) -(C=O)$_m$-O$_n$-heteroaryl, where the heteraryl is unsubstituted or substituted with one or more substituents selected from R^{13},

(10) -(C=O)$_m$-N$R^{10}R^{11}$,

(11) -S(O)$_2$-N$R^{10}R^{11}$,

(12) -S(O)$_q$-R^{12}, where q is 0, 1 or 2 and where R^{12} is selected from the definitions of R^{10} and R^{11},

(13) -CO_2H,

(14) -CN, and

(15) -NO_2;

R^{2a}, R^{2b} and R^{2c} are independently selected from the group consisting of:

(1) hydrogen,

(2) halogen,

(3) hydroxyl,

(4) -(C=O)$_m$-O$_n$-C$_{1-6}$alkyl, where the alkyl is unsubstituted or substituted with one or more substituents selected from R^{13},

(5) -(C=O)$_m$-O$_n$-C$_{3-6}$cycloalkyl, where the cycloalkyl is unsubstituted or substituted with one or more substituents selected from R^{13},

(6) -(C=O)$_m$-C$_{2-4}$alkenyl, where the alkenyl is unsubstituted or substituted with one or more substituents selected from R^{13},

(7) -(C=O)$_m$-C$_{2-4}$alkynyl, where the alkynyl is unsubstituted or substituted with one or more substituents selected from R^{13},

(8) -(C=O)$_m$-O$_n$-phenyl or -(C=O)$_m$-O$_n$-naphthyl, where the phenyl or naphthyl is unsubstituted or substituted with one or more substituents selected from R^{13},

(9) -$(C=O)_m$-O_n-heterocyclyl, where the heterocyclyl is unsubstituted or substituted with one or more substituents selected from R^{13},

(10) -$(C=O)_m$-$NR^{10}R^{11}$,

(11) -$S(O)_2$-$NR^{10}R^{11}$,

(12) -$S(O)_q$-R^{12},

(13) -CO_2H,

(14) -CN, and

(15) -NO_2;

R^3 is selected from the group consisting of:

(1) CH_3,

(2) CF_3,

(3) CH_2F,

(4) CH_2CH_3,

(5) cyclopropyl,

(6) cyano,

(7) hydrogen,

(8) NH_2,

(9) $C(O)OR^5$,

(10) -O-C_{1-6}alkyl,

(11) -$(CO)NH_2$,

(12) C_{1-6}alkylOH,

(13) C(O) C_{1-6}alky, and

(14) halogen;

R^4 is selected from the group consisting of:

(1) hydrogen,

(2) halo,

(3) -C_{1-6}alkyl, and

(4) cyano,

R^5 is selected from the group consisting of:

(1) hydrogen, and

(2) C_{1-6}alkyl;

R^6 is selected from the group consisting of:

(1) hydrogen,

(2) C_{1-6}alkyl, and

(3) OC_{1-6}alkyl;

R^{10} and R^{11} are independently selected from the group consisting of:

(a) hydrogen,

(b) C_{1-6}alkyl, which is unsubstituted or substituted with R^{14},

(c) C_{3-6}alkenyl, which is unsubstituted or substituted with R^{14},

(d) C_{3-6}alkynyl, which is unsubstituted or substituted with R^{14},

(e) C_{3-6}cycloalkyl which is unsubstituted or substituted with R^{14},

(f) C_{1-6}alkoxyl, which is unsubstituted or substituted with R^{14},

(g) phenyl, which is unsubstituted or substituted with R^{14}, and

(h) heteroaryl, which is unsubstituted or substituted with R^{14},

R^{13} is selected from the group consisting of:

(1) halogen,

(2) hydroxyl,

(3) $-(C=O)_m-O_n-C_{1-6}$alkyl, where the alkyl is unsubstituted or substituted with one or more substituents selected from R^{14},

(4) $-O_n-(C_{1-3})$perfluoroalkyl,

(5) $-(C=O)_m-O_n-C_{3-6}$cycloalkyl, where the cycloalkyl is unsubstituted or substituted with one or more substituents selected from R^{14},

(6) $-(C=O)_m-C_{2-4}$alkenyl, where the alkenyl is unsubstituted or substituted with one or more substituents selected from R^{14},

(7) $-(C=O)_m-C_{2-4}$alkynyl, where the alkynyl is unsubstituted or substituted with one or more substituents selected from R^{14},

(8) $-(C=O)_m-O_n$-phenyl or $-(C=O)_m-O_n$-naphthyl, where the phenyl or naphthyl is unsubstituted or substituted with one or more substituents selected from R^{14},

(9) $-(C=O)_m-O_n$-heteroaryl, where the heteroaryl is unsubstituted or substituted with one or more substituents selected from R^{14},

(10) $-(C=O)_m-NR^{10}R^{11}$,

(11) $-S(O)_2-NR^{10}R^{11}$,

(12) $-S(O)_q-R^{12}$,

(13) $-CO_2H$,

(14) -CN, and

(15) $-NO_2$;

R^{14} is selected from the group consisting of:

(1) hydroxyl,

(2) halogen,
(3) C_{1-6}alkyl,
(4) -C_{3-6}cycloalkyl,
(5) -O-C_{1-6}alkyl,
(6) -O(C=O)-C_{1-6}alkyl,
(7) -NH-C_{1-6}alkyl,
(8) phenyl,
(9) heteroaryl,
(10) -CO_2H, and
(11) -CN;

or a pharmaceutically acceptable salt thereof.

In a second aspect, there is provided a compound which is selected from the group consisting of:

2-methyl-N-[(1-methyl-1H-pyrazol-4-yl)methyl]-6-[(2-pyridin-2-ylcyclopropyl)methoxy] pyrimidin-4-amine;

S,S-2-methyl-N-[(1-methyl-1H-pyrazol-4-yl)methyl]-6-[(2-pyridin-2-ylcyclopropyl)methoxy] pyrimidin-4-amine;

2-methyl-6-{[2-(5-methylpyridin-2-yl)cyclopropyl]methoxy}-N-[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]pyrimidin-4-amine;

2-methyl-6-{[(1S,2S)-2-(5-methylpyridin-2-yl)cyclopropyl]methoxy}-N-[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]pyrimidin-4-amine;

N-[(2,4-dimethyl-1,3-thiazol-5-yl)methyl]-2-methyl-6-[(2-pyridin-2-ylcyclopropyl)methoxy]pyrimidin-4-amine;

S,S-N-[(2,4-dimethyl-1,3-thiazol-5-yl)methyl]-2-methyl-6-[(2-pyridin-2-ylcyclopropyl)methoxy]pyrimidin-4-amine;

N-[(1,3-dimethyl-1H-pyrazol-5-yl)methyl]-2-methyl-6-[(2-quinolin-2-ylcyclopropyl)methoxy]pyrimidin-4-amine;

S,S-N-[(1,3-dimethyl-1H-pyrazol-5-yl)methyl]-2-methyl-6-[(2-quinolin-2-ylcyclopropyl)methoxy]pyrimidin-4-amine;

N-[(1,3-dimethyl-1H-pyrazol-5-yl)methyl]-2-methyl-6-{[2-(1,5-naphthyridin-2-yl)cyclopropyl]methoxy}pyrimidin-4-amine;

S,S-N-[(1,3-dimethyl-1H-pyrazol-5-yl)methyl]-2-methyl-6-{[2-(1,5-naphthyridin-2-yl)cyclopropyl]methoxy}pyrimidin-4-amine;

N-[(1,3-dimethyl-1H-pyrazol-5-yl)methyl]-2-methyl-6-{[2-(5-methylpyridin-2-yl)cyclopropyl]methoxy}pyrimidin-4-amine;

S,S-N-[(1,3-dimethyl-1H-pyrazol-5-yl)methyl]-2-methyl-6-{[2-(5-methylpyridin-2-yl)cyclopropyl]methoxy}pyrimidin-4-amine;

N-[(1,3-dimethyl-1H-pyrazol-5-yl)methyl]-6-{[2-(5-methoxypyridin-2-yl)cyclopropyl]methoxy}-2-methylpyrimidin-4-amine;

S,S-N-[(1,3-dimethyl-1H-pyrazol-5-yl)methyl]-6-{[2-(5-methoxypyridin-2-yl)cyclopropyl]methoxy}-2-methylpyrimidin-4-amine;

N-[(1,3-dimethyl-1H-pyrazol-5-yl)methyl]-2-methyl-6-[(-2-pyridin-2-ylcyclopropyl)methoxy]pyrimidin-4-amine;

S,S-N-[(1,3-dimethyl-1H-pyrazol-5-yl)methyl]-2-methyl-6-[(-2-pyridin-2-ylcyclopropyl)methoxy]pyrimidin-4-amine;

S,S-2-methyl-N-[(1-methyl-1H-pyrazol-4-yl)methyl]-6-[(2-quinolin-2-ylcyclopropyl)methoxy]pyrimidin-4-amine;

2-methyl-N-[(1-methyl-1H-pyrazol-4-yl)methyl]-6-[(2-quinolin-2-ylcyclopropyl)methoxy]pyrimidin-4-amine;

S,S-2-methyl-N-[(1-methyl-1H-pyrazol-4-yl)methyl]-6-[(2-quinolin-2-ylcyclopropyl)methoxy]pyrimidin-4-amine;

2-methyl-N-[(1-methyl-1H-pyrazol-4-yl)methyl]-6-{[2-(1,5-naphthyridin-2-yl)cyclopropyl]methoxy}pyrimidin-4-amine;

S,S-2-methyl-N-[(1-methyl-1H-pyrazol-4-yl)methyl]-6-{[2-(1,5-naphthyridin-2-yl)cyclopropyl]methoxy}pyrimidin-4-amine;

6-{[2-(5-methoxypyridin-2-yl)cyclopropyl]methoxy}-2-methyl-N-[(1-methyl-1H-pyrazol-4-yl)methyl]pyrimidin-4-amine;

S,S-6-{[2-(5-methoxypyridin-2-yl)cyclopropyl]methoxy}-2-methyl-N-[(1-methyl-1H-pyrazol-4-yl)methyl]pyrimidin-4-amine;

S,S-2-methyl-N-[(1-methyl-1H-pyrazol-4-yl)methyl]-6-{[-2-(5-methylpyridin-2-yl)cyclopropyl]methoxy}pyrimidin-4-amine;

2-methyl-N-[(1-methyl-1H-pyrazol-4-yl)methyl]-6-{[-2-(5-methylpyridin-2-yl)cyclopropyl]methoxy}pyrimidin-4-amine;

6-{[2-(3-methoxypyridin-2-yl)cyclopropyl]methoxy}-2-methyl-N-[(1-methyl-1H-pyrazol-4-yl)methyl]pyrimidin-4-amine;

6-{[2-(5-fluoropyridin-2-yl)cyclopropyl]methoxy}-2-methyl-N-[(1-methyl-1H-pyrazol-4-yl)methyl]pyrimidin-4-amine;

S,S-6-{[2-(5-fluoropyridin-2-yl)cyclopropyl]methoxy}-2-methyl-N-[(1-methyl-1H-pyrazol-4-yl)methyl]pyrimidin-4-amine;

6-({2-[5-(fluoromethyl)pyridin-2-yl]cyclopropyl}methoxy)-2-methyl-N-[(1-methyl-1H-pyrazol-4-yl)methyl]pyrimidin-4-amine;

6-({2-[5-(difluoromethyl)pyridin-2-yl]cyclopropyl}methoxy)-2-methyl-N-[(1-methyl-1H-pyrazol-4-yl)methyl]pyrimidin-4-amine;

2-methyl-N-[(1-methyl-1H-pyrazol-4-yl)methyl]-6-({2-[5-(trifluoromethyl)pyridin-2-yl]cyclopropyl}methoxy)pyrimidin-4-amine;

2-methyl-N-[(1-methyl-1H-pyrazol-4-yl)methyl]-6-{[2-(1,3-thiazol-4-yl)cyclopropyl]methoxy}pyrimidin-4-amine;

2-methyl-N-[(2-methyl-1,3-thiazol-5-yl)methyl]-6-[(2-quinolin-2-ylcyclopropyl)methoxy]pyrimidin-4-amine;

S,S-2-methyl-N-[(2-methyl-1,3-thiazol-5-yl)methyl]-6-[(2-quinolin-2-ylcyclopropyl)methoxy]pyrimidin-4-amine;

2-methyl-N-[(2-methyl-1,3-thiazol-5-yl)methyl]-6-{[2-(1,5-naphthyridin-2-yl)cyclopropyl]methoxy}pyrimidin-4-amine;

S,S-2-methyl-N-[(2-methyl-1,3-thiazol-5-yl)methyl]-6-{[2-(1,5-naphthyridin-2-yl)cyclopropyl]methoxy}pyrimidin-4-amine;

2-methyl-6-{[2-(5-methylpyridin-2-yl)cyclopropyl]methoxy}-N-[(2-methyl-1,3-thiazol-5-yl)methyl]pyrimidin-4-amine;

S,S-2-methyl-6-{[2-(5-methylpyridin-2-yl)cyclopropyl]methoxy}-N-[(2-methyl-1,3-thiazol-5-yl)methyl]pyrimidin-4-amine;

6-{[2-(5-methoxypyridin-2-yl)cyclopropyl]methoxy}-2-methyl-N-[(2-methyl-1,3-thiazol-5-yl)methyl]pyrimidin-4-amine;

S,S-6-{[2-(5-methoxypyridin-2-yl)cyclopropyl]methoxy}-2-methyl-N-[(2-methyl-1,3-thiazol-5-yl)methyl]pyrimidin-4-amine;

2-methyl-N-[(2-methyl-1,3-thiazol-5-yl)methyl]-6-[(2-pyridin-2-ylcyclopropyl)methoxy]pyrimidin-4-amine;

S,S-2-methyl-N-[(2-methyl-1,3-thiazol-5-yl)methyl]-6-[(2-pyridin-2-ylcyclopropyl)methoxy]pyrimidin-4-amine;

2-methyl-N-[(2-methyl-1,3-thiazol-5-yl)methyl]-6-[(2-pyridin-2-ylcyclopropyl)methoxy]pyrimidin-4-amine;

S,S-2-methyl-N-[(2-methyl-1,3-thiazol-5-yl)methyl]-6-[(2-pyridin-2-ylcyclopropyl)methoxy]pyrimidin-4-amine;

2-methyl-N-[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]-6-[(2-quinolin-2-ylcyclopropyl)methoxy]pyrimidin-4-amine;

S,S-2-methyl-N-[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]-6-[(2-quinolin-2-ylcyclopropyl)methoxy]pyrimidin-4-amine;

2-methyl-N-[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]-6-{[2-(1,5-naphthyridin-2-yl)cyclopropyl]methoxy}pyrimidin-4-amine;

S,S-2-methyl-N-[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]-6-{[2-(1,5-naphthyridin-2-yl)cyclopropyl]methoxy}pyrimidin-4-amine;

6-{[2-(5-methoxypyridin-2-yl)cyclopropyl]methoxy}-2-methyl-N-[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]pyrimidin-4-amine;

S,S-6-{[2-(5-methoxypyridin-2-yl)cyclopropyl]methoxy}-2-methyl-N-[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]pyrimidin-4-amine;

2-methyl-N-[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]-6-[(2-pyridin-2-ylcyclopropyl)methoxy]pyrimidin-4-amine;

S,S-2-methyl-N-[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]-6-[(2-pyridin-2-ylcyclopropyl)methoxy]pyrimidin-4-amine;

6-{[2-(5-fluoropyridin-2-yl)cyclopropyl]methoxy}-2-methyl-N-[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]pyrimidin-4-amine;

S,S-6-{[2-(5-fluoropyridin-2-yl)cyclopropyl]methoxy}-2-methyl-N-[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]pyrimidin-4-amine;

6-({2-[5-(fluoromethyl)pyridin-2-yl]cyclopropyl}methoxy)-2-methyl-N-[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]pyrimidin-4-amine;

6-({2-[5-(difluoromethyl)pyridin-2-yl]cyclopropyl}methoxy)-2-methyl-N-[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]pyrimidin-4-amine

2-methyl-6-{[2-(6-methylpyridazin-3-yl)cyclopropyl]methoxy}-N-[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]pyrimidin-4-amine;

S,S-2-methyl-N-[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]-6-{[2-(2-methyl-1,3-thiazol-4-yl)cyclopropyl]methoxy}pyrimidin-4-amine;

2-methyl-6-{[2-(2-methyl-1,3-oxazol-4-yl)cyclopropyl]methoxy}-N-[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]pyrimidin-4-amine;

2-methyl-6-{[2-(1-methyl-1H-pyrazol-3-yl)cyclopropyl]methoxy}-N-[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]pyrimidin-4-amine;

N -[(5-cyclopropyl-1,3,4-thiadiazol-2-yl)methyl]-2-methyl-6-[(2-pyridin-2-ylcyclopropyl)methoxy]pyrimidin-4-amine;

S,S-N -[(5-cyclopropyl-1,3,4-thiadiazol-2-yl)methyl]-2-methyl-6-[(2-pyridin-2-ylcyclopropyl)methoxy]pyrimidin-4-amine;

N -[(2,4-dimethyl-1,3-thiazol-5-yl)methyl]-6-[(2-pyridin-2-ylcyclopropyl)methoxy]pyrimidin-4-amine;

S,S-N -[(2,4-dimethyl-1,3-thiazol-5-yl)methyl]-6-[(2-pyridin-2-ylcyclopropyl)methoxy]pyrimidin-4-amine;

N -[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]-6-[(2-quinolin-2-ylcyclopropyl)methoxy]pyrimidin-4-amine;

S,S-N -[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]-6-[(2-quinolin-2-ylcyclopropyl)methoxy]pyrimidin-4-amine;

N-[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]-6-{[2-(1,5-naphthyridin-2-yl)cyclopropyl]methoxy}pyrimidin-4-amine;

S,S-N -[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]-6-{[2-(1,5-naphthyridin-2-yl)cyclopropyl]methoxy}pyrimidin-4-amine;

6-{[2-(5-methoxypyridin-2-yl)cyclopropyl]methoxy}-N-[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]pyrimidin-4-amine;

S,S-6-{[2-(5-methoxypyridin-2-yl)cyclopropyl]methoxy}-N-[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]pyrimidin-4-amine;

6-{[2-(5-methylpyridin-2-yl)cyclopropyl]methoxy}-N-[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]pyrimidin-4-amine;

S,S-6-{[2-(5-methylpyridin-2-yl)cyclopropyl]methoxy}-N-[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]pyrimidin-4-amine;

N-[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]-6-[(2-pyridin-2-ylcyclopropyl)methoxy]pyrimidin-4-amine;

S,S-N-[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]-6-[(2-pyridin-2-ylcyclopropyl)methoxy]pyrimidin-4-amine;

N-4-[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]-6-[(2-pyridin-2-ylcyclopropyl)methoxy]pyrimidine-2,4-diamine;

S,S-N-4-[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]-6-[(2-pyridin-2-ylcyclopropyl)methoxy]pyrimidine-2,4-diamine;

2-methoxy-N-[(1-methyl-1H-pyrazol-4-yl)methyl]-6-[(2-pyridin-2-ylcyclopropyl)methoxy]pyrimidin-4-amine;

S,S-2-methoxy-N-[(1-methyl-1H-pyrazol-4-yl)methyl]-6-[(2-pyridin-2-ylcyclopropyl)methoxy]pyrimidin-4-amine;

2,5-dimethyl-N-[(1-methyl-1H-pyrazol-4-yl)methyl]-6-[(2-pyridin-2-ylcyclopropyl)methoxy]pyrimidin-4-amine;

S,S-2,5-dimethyl-N-[(1-methyl-1H-pyrazol-4-yl)methyl]-6-[(2-pyridin-2-ylcyclopropyl)methoxy]pyrimidin-4-amine;

N-[(2,4-dimethyl-1,3-thiazol-5-yl)methyl]-2,5-dimethyl-6-[(2-pyridin-2-ylcyclopropyl)methoxy]pyrimidin-4-amine;

S,S-N-[(2,4-dimethyl-1,3-thiazol-5-yl)methyl]-2,5-dimethyl-6-[(2-pyridin-2-ylcyclopropyl)methoxy]pyrimidin-4-amine;

N-6-{[2-(5-methoxypyridin-2-yl)cyclopropyl]methoxy}-N-[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]-2-(trifluoromethyl)pyrimidin-4-amine;

S,S-N-6-{[2-(5-methoxypyridin-2-yl)cyclopropyl]methoxy}-N-[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]-2-(trifluoromethyl)pyrimidin-4-amine;

6-{[2-(5-methylpyridin-2-yl)cyclopropyl]methoxy}-N-[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]-2-(trifluoromethyl)pyrimidin-4-amine;

S,S-6-{[2-(5-methylpyridin-2-yl)cyclopropyl]methoxy}-N-[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]-2-(trifluoromethyl)pyrimidin-4-amine;

N-[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]-6-[(2-pyridin-2-ylcyclopropyl)methoxy]-2-(trifluoromethyl)pyrimidin-4-amine;

S,S-N-[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]-6-[(2-pyridin-2-ylcyclopropyl)methoxy]-2-(trifluoromethyl)pyrimidin-4-amine;

N-[(1-methyl-1H-pyrazol-4-yl)methyl]-6-[(2-pyridin-2-ylcyclopropyl)methoxy]-2-(trifluoromethyl)pyrimidin-4-amine;

S,S-N-[(1-methyl-1H-pyrazol-4-yl)methyl]-6-[(2-pyridin-2-ylcyclopropyl)methoxy]-2-(trifluoromethyl)pyrimidin-4-amine;

6-{[2-(5,6-dihydro-4H-pyrrolo[1,2-b]pyrazol-2-yl)cyclopropyl]methoxy}-2-methyl-N-[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]pyrimidin-4-amine;

6-{[(1S,2S)-2-(5,6-dihydro-4H-pyrrolo[1,2-b]pyrazol-2-yl)cyclopropyl]methoxy}-2-methyl-N-[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]pyrimidin-4-amine;

6-{[2-(5-methoxypyridin-2-yl)cyclopropyl]methoxy}-N-4-[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]pyrimidine-2,4-diamine;

S,S-6-{[(1S,2S)-2-(5-methoxypyridin-2-yl)cyclopropyl]methoxy}-N-4-[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]pyrimidine-2,4-diamine;

2-methyl-N-[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]-6-{[2-pyrazolo[1,5-a]pyrimidin-2-ylcyclopropyl]methoxy}pyrimidin-4-amine;

2-methyl-N-[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]-6-{[(1S,2S)-2-pyrazolo[1,5-a]pyrimidin-2-ylcyclopropyl]methoxy}pyrimidin-4-amine;

2-methyl-N-[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]-6-{[2-pyrazolo[1,5-a]pyrimidin-5-ylcyclopropyl]methoxy}pyrimidin-4-amine;

2-methyl-N-[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]-6-{[(1S,2S)-2-pyrazolo[1,5-a]pyrimidin-5-ylcyclopropyl]methoxy}pyrimidin-4-amine;

6-{[2-(5-bromopyridin-2-yl)cyclopropyl]methoxy}-2-methyl-N-[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]pyrimidin-4-amine;

S,S-6-{[(1S,2S)-2-(5-bromopyridin-2-yl)cyclopropyl]methoxy}-2-methyl-N-[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]pyrimidin-4-amine;

2-methyl-6-{[2-(2-methylimidazo[1,2-b]pyridazin-6-yl)cyclopropyl]methoxy}-N-[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]pyrimidin-4-amine;

2-methyl-6-{[(1S,2S)-2-(2-methylimidazo[1,2-b]pyridazin-6-yl)cyclopropyl]methoxy}-N-[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]pyrimidin-4-amine;

5-chloro-2-methyl-6-{[2-(5-methylpyridin-2-yl)cyclopropyl]methoxy}-N-[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]pyrimidin-4-amine;

S,S-5-chloro-2-methyl-6-{[(1S,2S)-2-(5-methylpyridin-2-yl)cyclopropyl]methoxy}-N-[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]pyrimidin-4-amine;

2-ethyl-N-[(1-methyl-1H-pyrazol-4-yl)methyl]-6-[(2-pyridin-2-ylcyclopropyl)methoxy]pyrimidin-4-amine;

N-[(2,4-dimethyl-1,3-thiazol-5-yl)methyl]-5-fluoro-2-methyl-6-[(2-pyridin-2-ylcyclopropyl)methoxy]pyrimidin-4-amine;

S,S-N-[(2,4-dimethyl-1,3-thiazol-5-yl)methyl]-5-fluoro-2-methyl-6-[(2-pyridin-2-ylcyclopropyl)methoxy]pyrimidin-4-amine;

N-[(2,4-dimethyl-1,3-thiazol-5-yl)methyl]-5-fluoro-2-methyl-6-[(2-pyridin-2-ylcyclopropyl)methoxy]pyrimidin-4-amine;

S,S-N-[(2,4-dimethyl-1,3-thiazol-5-yl)methyl]-5-fluoro-2-methyl-6-[(2-pyridin-2-ylcyclopropyl)methoxy]pyrimidin-4-amine;

5-fluoro-2-methyl-N-[(1-methyl-1H-pyrazol-4-yl)methyl]-6-[(-2-pyridin-2-ylcyclopropyl)methoxy]pyrimidin-4-amine;

S,S-5-fluoro-2-methyl-N-[(1-methyl-1H-pyrazol-4-yl)methyl]-6-[(-2-pyridin-2-ylcyclopropyl)methoxy]pyrimidin-4-amine;

5-fluoro-2-methyl-6-{[2-(5-methylpyridin-2-yl)cyclopropyl]methoxy}-N-[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]pyrimidin-4-amine;

S,S-5-fluoro-2-methyl-6-{[2-(5-methylpyridin-2-yl)cyclopropyl]methoxy}-N-[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]pyrimidin-4-amine;

2-(fluoromethyl)-N-[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]-6-[(2-pyridin-2-ylcyclopropyl)methoxy]pyrimidin-4-amine;

S,S-2-(fluoromethyl)-N-[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]-6-[(2-pyridin-2-ylcyclopropyl)methoxy]pyrimidin-4-amine;

N -[(2,4-dimethyl-1,3-thiazol-5-yl)methyl]-2-ethyl-6-[(2-pyridin-2-ylcyclopropyl)methoxy]pyrimidin-4-amine;

S,S-N -[(2,4-dimethyl-1,3-thiazol-5-yl)methyl]-2-ethyl-6-[(2-pyridin-2-ylcyclopropyl)methoxy]pyrimidin-4-amine;

2-ethyl-N-[(1-methyl-1H-pyrazol-4-yl)methyl]-6-[(2-pyridin-2-ylcyclopropyl)methoxy]pyrimidin-4-amine;

S,S-2-ethyl-N-[(1-methyl-1H-pyrazol-4-yl)methyl]-6-[(2-pyridin-2-ylcyclopropyl)methoxy]pyrimidin-4-amine;

2-cyclopropyl-N-[(2,4-dimethyl-1,3-thiazol-5-yl)methyl]-6-[(2-pyridin-2-ylcyclopropyl)methoxy]pyrimidin-4-amine;

S,S-2-cyclopropyl-N-[(2,4-dimethyl-1,3-thiazol-5-yl)methyl]-6-[(2-pyridin-2-ylcyclopropyl)methoxy]pyrimidin-4-amine;

2-cyclopropyl-N-[(1-methyl-1H-pyrazol-4-yl)methyl]-6-[(2-pyridin-2-ylcyclopropyl)methoxy]pyrimidin-4-amine;

S,S-2-cyclopropyl-N-[(1-methyl-1H-pyrazol-4-yl)methyl]-6-[(2-pyridin-2-ylcyclopropyl)methoxy]pyrimidin-4-amine;

5-fluoro-6-{[2-(5-methoxypyridin-2-yl)cyclopropyl]methoxy}-N-4-[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]pyrimidine-2,4-diamine;

5-fluoro-6-{[(1S,2S)-2-(5-methoxypyridin-2-yl)cyclopropyl]methoxy}-N-4-[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]pyrimidine-2,4-diamine;

5-fluoro-N-4-[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]-6-{[2-(1,5-naphthyridin-2-yl)cyclopropyl]methoxy}pyrimidine-2,4-diamine;

5-fluoro-N-4-[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]-6-{[(1S,2S)-2-(1,5-naphthyridin-2-yl)cyclopropyl]methoxy}pyrimidine-2,4-diamine;

5-fluoro-6-{[2-(5-methylpyridin-2-yl)cyclopropyl]methoxy}-N-4-[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]pyrimidine-2,4-diamine;

5-fluoro-6-{[(1S,2S)-2-(5-methylpyridin-2-yl)cyclopropyl]methoxy}-N-4-[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]pyrimidine-2,4-diamine;

5-fluoro-N-4-[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]-6-{[2-pyridin-2-ylcyclopropyl]methoxy}pyrimidine-2,4-diamine;

5-fluoro-N-4-[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]-6-{[(1S,2S)-2-pyridin-2-ylcyclopropyl]methoxy}pyrimidine-2,4-diamine;

5-fluoro-N-4-[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]-6-{[2-pyridin-2-ylcyclopropyl]methoxy}pyrimidine-2,4-diamine;

5-fluoro-N-4-[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]-6-{[(1S,2S)-2-pyridin-2-ylcyclopropyl]methoxy}pyrimidine-2,4-diamine;

N -4-(2,4-dimethoxybenzyl)-5-fluoro-6-{[2-pyridin-2-ylcyclopropyl]methoxy}pyrimidine-2,4-diamine;

N -4-(2,4-dimethoxybenzyl)-5-fluoro-6-{[(1S,2S)-2-pyridin-2-ylcyclopropyl]methoxy}pyrimidine-2,4-diamine;

6-{[2-(5-chloropyridin-2-yl)cyclopropyl]methoxy}-5-fluoro-N-4-[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]pyrimidine-2,4-diamine;

6-{[(1S,2S)-2-(5-chloropyridin-2-yl)cyclopropyl]methoxy}-5-fluoro-N-4-[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]pyrimidine-2,4-diamine;

5-fluoro-6-{[2-(5-fluoropyridin-2-yl)cyclopropyl]methoxy}-N-4-[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]pyrimidine-2,4-diamine;

5-fluoro-6-{[(1S,2S)-2-(5-fluoropyridin-2-yl)cyclopropyl]methoxy}-N-4-[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]pyrimidine-2,4-diamine;

5-chloro-6-{[2-(5-methylpyridin-2-yl)cyclopropyl]methoxy}-N-[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]pyrimidine-2,4-diamine;

5-chloro-6-{[(1S,2S)-2-(5-methylpyridin-2-yl)cyclopropyl]methoxy}-N-[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]pyrimidine-2,4-diamine;

6-{[2-(4,5-dimethylpyridin-2-yl)cyclopropyl]methoxy}-N-[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]pyrimidine-2,4-diamine;

6-{[(1S,2S)-2-(4,5-dimethylpyridin-2-yl)cyclopropyl]methoxy}-N-[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]pyrimidine-2,4-diamine;

6-((2-(5,6-dihydro-4H-pyrrolo[1,2-b]pyrazol-2-yl)cyclopropyl)methoxy)-5-fluoro-N4-((5-methyl-1,3,4-thiadiazol-2-yl)methyl)pyrimidine-2,4-diamine;

6-(((1S,2S)-2-(5,6-dihydro-4H-pyrrolo[1,2-b]pyrazol-2-yl)cyclopropyl)methoxy)-5-fluoro-N4-((5-methyl-1,3,4-thiadiazol-2-yl)methyl)pyrimidine-2,4-diamine;

5-fluoro-N4-((5-methyl-1,3,4-thiadiazol-2-yl)methyl)-6-((2-(6-methylpyridin-2-yl)cyclopropyl)methoxy)pyrimidine-2,4-diamine;

5-fluoro-N4-((5-methyl-1,3,4-thiadiazol-2-yl)methyl)-6-(((1S,2S)-2-(6-methylpyridin-2-yl)cyclopropyl)methoxy)pyrimidine-2,4-diamine;

6-((2-(6,7-dihydro-5H-cyclopenta[b]pyridin-2-yl)cyclopropyl)methoxy)-5-fluoro-N4-((5-methyl-1,3,4-thiadiazol-2-yl)methyl)pyrimidine-2,4-diamine;

S,S-6-(((1S,2S)-2-(6,7-dihydro-5H-cyclopenta[b]pyridin-2-yl)cyclopropyl)methoxy)-5-fluoro-N4-((5-methyl-1,3,4-thiadiazol-2-yl)methyl)pyrimidine-2,4-diamine;

6-((2-(6,7-dihydro-5H-cyclopenta[b]pyridin-2-yl)cyclopropyl)methoxy)-5-fluoro-N4-((5-methyl-1,3,4-thiadiazol-2-yl)methyl)pyrimidine-2,4-diamine;

S,S-6-(((1S,2S)-2-(6,7-dihydro-5H-cyclopenta[b]pyridin-2-yl)cyclopropyl)methoxy)-5-fluoro-N4-((5-methyl-1,3,4-thiadiazol-2-yl)methyl)pyrimidine-2,4-diamine;

6-((2-(6,7-dihydro-5H-cyclopenta[b]pyridin-2-yl)cyclopropyl)methoxy)-5-fluoro-N4-((5-methyl-1,3,4-thiadiazol-2-yl)methyl)pyrimidine-2,4-diamine;

S,S-6-(((1S,2S)-2-(6,7-dihydro-5H-cyclopenta[b]pyridin-2-yl)cyclopropyl)methoxy)-5-fluoro-N4-((5-methyl-1,3,4-thiadiazol-2-yl)methyl)pyrimidine-2,4-diamine;

6-((2-(6,7-dihydro-5H-cyclopenta[b]pyridin-2-yl)cyclopropyl)methoxy)-5-fluoro-N4-((5-methyl-1,3,4-thiadiazol-2-yl)methyl)pyrimidine-2,4-diamine;

S,S-6-(((1S,2S)-2-(6,7-dihydro-5H-cyclopenta[b]pyridin-2-yl)cyclopropyl)methoxy)-5-fluoro-N4-((5-methyl-1,3,4-thiadiazol-2-yl)methyl)pyrimidine-2,4-diamine;

6-((2-(6,7-dihydro-5H-cyclopenta[b]pyridin-2-yl)cyclopropyl)methoxy)-5-fluoro-N4-((5-methyl-1,3,4-thiadiazol-2-yl)methyl)pyrimidine-2,4-diamine;

S,S-6-(((1S,2S)-2-(6,7-dihydro-5H-cyclopenta[b]pyridin-2-yl)cyclopropyl)methoxy)-5-fluoro-N4-((5-methyl-1,3,4-thiadiazol-2-yl)methyl)pyrimidine-2,4-diamine;

5-bromo-N-((2,4-dimethylthiazol-5-yl)methyl)-2-methyl-6-((2-(pyridin-2-yl)cyclopropyl)methoxy)pyrimidin-4-amine;

4-((2,4-dimethylthiazol-5-yl)methylamino)-2-methyl-6-((2-(pyridin-2-yl)cyclopropyl)methoxy)pyrimidine-5-carbonitrile;

2-methyl-4-((1-methyl-1H-pyrazol-4-yl)methylamino)-6-((2-(pyridin-2-yl)cyclopropyl)methoxy)pyrimidine-5-carbonitrile;

4-((1-methyl-1H-pyrazol-4-yl)methylamino)-6-((2-(pyridin-2-yl)cyclopropyl)methoxy)-pyrimidine-2-carboxamide;

4-((1-methyl-1H-pyrazol-4-yl)methylamino)-6-((2-(pyridin-2-yl)cyclopropyl)methoxy)-pyrimidine-2-carbonitrile;

2-methyl-N-((5-methyl-1,3,4-thiadiazol-2-yl)methyl)-6-((2-(5-(thiazol-4-yl)pyridin-2-yl)cyclopropyl)methoxy)pyrimidin-4-amine;

6-{[2-(2,3'-bipyridin-6'-yl)cyclopropyl]methoxy}-2-methyl-N-[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]pyrimidin-4-amine;

2-methyl-N-[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]-6-({2-[5-(1,3-thiazol-5-yl)pyridin-2-yl]cyclopropyl}methoxy)pyrimidin-4-amine;

6-{[2-(3,4'-bipyridin-6-yl)cyclopropyl]methoxy}-2-methyl-N-[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]pyrimidin-4-amine;

2-methyl-N-[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]-6-({2-[5-(1,3-thiazol-2-yl)pyridin-2-yl]cyclopropyl}methoxy)pyrimidin-4-amine;

6-{[2-(3,3'-bipyridin-6-yl)cyclopropyl]methoxy}-2-methyl-N-[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]pyrimidin-4-amine;

2-methyl-N-[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]-6-{[2-(5-pyridazin-4-ylpyridin-2-yl)cyclopropyl]methoxy}pyrimidin-4-amine;

6-((2-(5-ethylpyridin-2-yl)cyclopropyl)methoxy)-2-methyl-N-((5-methyl-1,3,4-thiadiazol-2-yl)methyl)pyrimidin-4-amine;

6-{[2-(5-cyclopropylpyridin-2-yl)cyclopropyl]methoxy}-2-methyl-N-[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]pyrimidin-4-amine;

6-((2-(5-(1H-pyrazol-1-yl)pyridin-2-yl)cyclopropyl)methoxy)-2-methyl-N-((5-methyl-1,3,4-thiadiazol-2-yl)methyl)pyrimidin-4-amine;

6-(2-((2-methyl-6-((5-methyl-1,3,4-thiadiazol-2-yl)methylamino)pyrimidin-4-yloxy)methyl)cyclopropyl)nicotinonitrile;

2-methyl-N-((5-methylisoxazol-3-yl)methyl)-6-((2-(pyridin-2-yl)cyclopropyl)methoxy)-pyrimidin-4-amine;

N-[(2-fluoro-5-methylpyridin-3-yl)methyl]-2-methyl-6-[(2-pyridin-2-ylcyclopropyl)methoxy]pyrimidin-4-amine;

S,S-N-(isothiazol-5-ylmethyl)-2-methyl-6-[(2-pyridin-2-ylcyclopropyl)methoxy]pyrimidin-4-amine;

2-methyl-N-[(5-methylpyrazin-2-yl)methyl]-6-[(2-pyridin-2-ylcyclopropyl)methoxy]pyrimidin-4-amine;

2-methyl-6-[(2-pyridin-2-ylcyclopropyl)methoxy]-N-(pyrimidin-5-ylmethyl)pyrimidin-4-amine;

2-methyl-6-((2-(pyridin-2-yl)cyclopropyl)methoxy)-N-(pyridin-4-ylmethyl)pyrimidin-4-amine;

2-methyl-6-[(2-pyridin-2-ylcyclopropyl)methoxy]-N-(pyridin-3-ylmethyl)pyrimidin-4-amine;

2-methyl-N-((3-methylpyridin-4-yl)methyl)-6-((2-(pyridin-2-yl)cyclopropyl)methoxy)pyrimidin-4-amine;

6-(2-((2-methyl-6-((5-methyl-1,3,4-thiadiazol-2-yl)methylamino)pyrimidin-4-yloxy)methyl)cyclopropyl)pyridine;

2-amino-4-{[(1S,2S)-2-(5-methylpyridin-2-yl)cyclopropyl]methoxy}-6-{[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]amino}pyrimidine-5-carbonitrile;

2-amino-4-{[(1S,2S)-2-(5-methylpyridin-2-yl)cyclopropyl]methoxy}-6-{[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]amino}pyrimidine-5-carbonitrile; and

S,S-2-amino-4-{[(1S,2S)-2-(5-methylpyridin-2-yl)cyclopropyl]methoxy}-6-{[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]amino}pyrimidine-5-carbonitrile; and

2-amino-4-{[(1S,2S)-2-(5-methoxypyridin-2-yl)cyclopropyl]methoxy}-6-{[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]amino}pyrimidine-5-carbonitrile;

S,S-2-amino-4-{[(1S,2S)-2-(5-methoxypyridin-2-yl)cyclopropyl]methoxy}-6-{[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]amino}pyrimidine-5-carbonitrile;

N-methoxy-N-methyl-5-((2-methyl-6-(((1S,2S)-2-(5-methylpyridin-2-yl)cyclopropyl)methoxy)pyrimidin-4-ylamino)methyl)-1,3,4-thiadiazole-2-carboxamide;

1-(5-((2-methyl-6-(((1S,2S)-2-(5-methylpyridin-2-yl)cyclopropyl)methoxy)pyrimidin-4-ylamino)methyl)-1,3,4-thiadiazol-2-yl)ethanone;

1-(5-((2-methyl-6-(((1S,2S)-2-(5-methylpyridin-2-yl)cyclopropyl)methoxy)pyrimidin-4-ylamino)methyl)-1,3,4-thiadiazol-2-yl)ethanol;

4-((5-methyl-1,3,4-thiadiazol-2-yl)methylamino)-6-(((1R,2R)-2-(5-methylpyridin-2-yl)cyclopropyl)methoxy)pyrimidine-2-carboxylic acid;

ethyl 4-((5-methyl-1,3,4-thiadiazol-2-yl)methylamino)-6-(((1R,2R)-2-(5-methylpyridin-2-yl)cyclopropyl)methoxy)pyrimidine-2-carboxylate;

2-(5-((2-methyl-6-(((1S,2S)-2-(5-methylpyridin-2-yl)cyclopropyl)methoxy)pyrimidin-4-ylamino)methyl)-1,3,4-thiadiazol-2-yl)propan-2-ol;

2-(6-((1S,2S)-2-((2-methyl-6-((5-methyl-1,3,4-thiadiazol-2-yl)methylamino)pyrimidin-4-yloxy)methyl)cyclopropyl)pyridin-3-yl)propan-2-ol;

methyl 5-((2-methyl-6-(((1S,2S)-2-(5-methylpyridin-2-yl)cyclopropyl)methoxy)pyrimidin-4-ylamino)methyl)-1,3,4-thiadiazole-2-carboxylate;

5-((2-methyl-6-(((1S,2S)-2-(5-methylpyridin-2-yl)cyclopropyl)methoxy)pyrimidin-4-ylamino)methyl)-1,3,4-thiadiazole-2-carbonitrile;

5-((2-methyl-6-(((1S,2S)-2-(5-methylpyridin-2-yl)cyclopropyl)methoxy)pyrimidin-4-ylamino)methyl)-1,3,4-thiadiazole-2-carboxamide;

6-(((1S,3S)-2-tert-butoxy-3-(5-methylpyridin-2-yl)cyclopropyl)methoxy)-2-methyl-N-((5-methyl-1,3,4-thiadiazol-2-yl)methyl)pyrimidin-4-amine;

2-ethyl-N-((5-methyl-1,3,4-thiadiazol-2-yl)methyl)-6-(((1S,2S)-2-(5-methylpyridin-2-yl)cyclopropyl)methoxy)pyrimidin-4-amine;

2-(4-((5-methyl-1,3,4-thiadiazol-2-yl)methylamino)-6-(((1R,2R)-2-(5-methylpyridin-2-yl)cyclopropyl)methoxy)pyrimidin-2-yl)propan-2-ol;

N-((5-tert-butyl-1,3,4-thiadiazol-2-yl)methyl)-2-methyl-6-(((1S,2S)-2-(5-methylpyridin-2-yl)cyclopropyl)methoxy)pyrimidin-4-amine;

1-(4-((5-methyl-1,3,4-thiadiazol-2-yl)methylamino)-6-(((1R,2R)-2-(5-methylpyridin-2-yl)cyclopropyl)methoxy)pyrimidin-2-yl)ethanone;

2-methyl-N-((5-methyl-1,3,4-thiadiazol-2-yl)methyl)-6-(((1R,2R)-2-(5-methylpyridin-2-yl)cyclopropyl)methoxy)pyrimidin-4-amine;

1-(5-((2-methyl-6-(((1S,2S)-2-(5-methylpyridin-2-yl)cyclopropyl)methoxy)pyrimidin-4-ylamino)methyl)-1,3,4-thiadiazol-2-yl)ethanol;

2-chloro-N-((5-methyl-1,3,4-thiadiazol-2-yl)methyl)-6-(((1S,2S)-2-(5-methylpyridin-2-yl)cyclopropyl)methoxy)pyrimidin-4-amine;

or a pharmaceutically acceptable salt thereof.

In a third aspect, there is provided a compound which is 2-methyl-N-[(1-methyl-1H-pyrazol-4-yl)methyl]-6-[(2-pyridin-2-ylcyclopropyl)methoxy] pyrimidin-4-amine, or a pharmaceutically acceptable salt thereof.

In a fourth aspect, there is provided a compound which is 2-Methyl-6-{[(1S,2S)-2-(5-methylpyridin-2-yl)cyclopropyl]methoxy}-N-[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]pyrimidin-4-amine, or a pharmaceutically acceptable salt thereof.

In a fifth aspect, there is provided a compound which is S,S-N -[(1,3-dimethyl-1H-pyrazol-5-yl)methyl]-2-methyl-6-[(2-quinolin-2-ylcyclopropyl)methoxy]pyrimidin-4-amine, or a pharmaceutically acceptable salt thereof.

In a sixth aspect, there is provided a compound which is S,S-2-methyl-N-[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]-6-{[2-(1,5-naphthyridin-2-yl)cyclopropyl]methoxy}pyrimidin-4-amine, or a pharmaceutically acceptable salt thereof.

In a seventh aspect, there is provided a compound which is S,S-6-{[(1S,2S)-2-(5-methoxypyridin-2-yl)cyclopropyl]methoxy}-N-4-[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]pyrimidine-2,4-diamine, or a pharmaceutically acceptable salt thereof.

In an eighth aspect, there is provided a compound which is 2-ethyl-N-[(1-methyl-1H-pyrazol-4-yl)methyl]-6-[(2-pyridin-2-ylcyclopropyl)methoxy] pyrimidin-4-amine or a pharmaceutically acceptable salt thereof.

In a ninth aspect, there is provided a compound which is 5-fluoro-6-{[(1S,2S)-2-(5-methoxypyridin-2-yl)cyclopropyl]methoxy}-N-4-[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]pyrimidine-2,4-diamine or a pharmaceutically acceptable salt thereof.

In a tenth aspect, there is provided a compound which is 6-{[2-(3,3'-bipyridin-6-yl)cyclopropyl]methoxy}-2-methyl-N-[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]pyrimidin-4-amine or a pharmaceutically acceptable salt thereof.

In an eleventh aspect, there is provided a compound which is 6-{[2-(5-cyclopropylpyridin-2-yl)cyclopropyl]methoxy}-2-methyl-N-[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]pyrimidin-4-amine or a pharmaceutically acceptable salt thereof.

In a twelfth aspect, there is provided a compound which is 2-methyl-N-((5-methylisoxazol-3-yl)methyl)-6-((2-(pyridin-2-yl)cyclopropyl)methoxy)-pyrimidin-4-amine or a pharmaceutically acceptable salt thereof.

In a thirteenth aspect, there is provided a compound which is 2-amino-4-{[(1S,2S)-2-(5-methylpyridin-2-yl)cyclopropyl]methoxy}-6-{[(5-methyl-1,3,4-thiadiazol-2-yl)methyl]amino}pyrimidine-5-carbonitrile or a pharmaceutically acceptable salt thereof.

In a fourteenth aspect, there is provided a pharmaceutical composition which comprises a pharmaceutically acceptable carrier and a compound as defined above or a pharmaceutically acceptable salt thereof.

In a fifteenth aspect, there is provided a compound as defined above or a pharmaceutically acceptable salt thereof for use in medicine.

In a sixteenth aspect, there is provided the use of a compound as defined above, or a pharmaceutically acceptable salt thereof, for the manufacture of a medicament for the treatment of schizophrenia.

In a seventeenth aspect, there is provided a compound as defined above or a pharmaceutically acceptable salt thereof for use in treating a neurological or psychiatric disorder associated with PDE10 dysfunction in a mammalian patient.

In an eighteenth aspect, there is provided a compound as defined above or a pharmaceutically acceptable salt thereof for use in treating a neurological or psychiatric disorder associated with striatal hypofunction or basal ganglia dysfunction in a mammalian patient.

In a nineteenth aspect, there is provided a compound as defined above or a pharmaceutically acceptable salt thereof for use in treating schizophrenia in a mammalian patient.