supra), it would appear that the known AT2R antagonists have so far found limited success in their (further) clinical development.

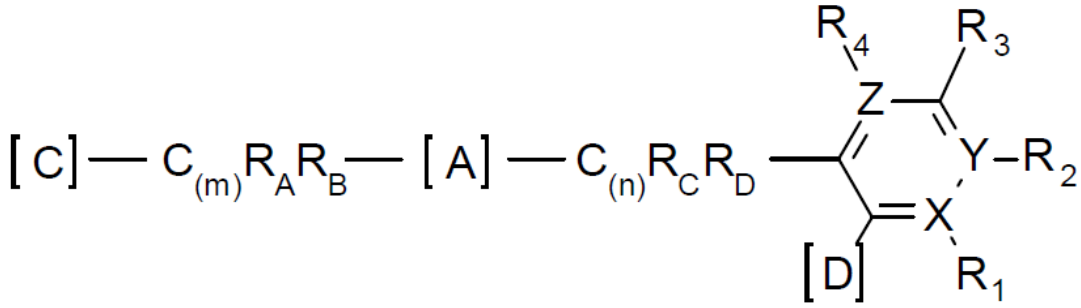
Rice et al., *Pain*, 2021, March, 1 describe the results of two multicentre, randomised, double-blind treatment Phase 2b studies on the analgesic efficacy and safety of EMA401 in patients with post-herpetic neuralgia and painful diabetic neuropathy. As mentioned by Rice et al.: ”*The primary outcome for both the studies was change in weekly mean of the 24-hour average pain score, using a numeric rating scale (NRS), from baseline to Week 12. Both the studies were prematurely terminated due to preclinical hepatotoxicity on long-term dosing, although not observed in these studies.*”. Rice et al. further state that “*[…] as the studies were terminated prematurely, no firm conclusion could be drawn but the consistent clinical improvement in pain intensity reduction across these two studies in two different populations is worth noting.*”

As will be clear from the above, there remains a constant need in the art for compounds that can be used in the prevention and/or treatment of pain, and in particular of chronic pain such as neuropathic pain. In the words of Rice et al.: “*Existing treatments for peripheral neuropathic pain (PNP) have modest efficacy and are often not well tolerated, and the development of improved treatments for these common chronic pain conditions is recognised as a significant unmet need*”.

In particular, there is a need for novel classes of molecules that can be used to target AT2R and/or to modulate the interaction(s) of AT2R with one or more of its ligands (such as Ang II) and that can be used in the prevention and/or treatment of various forms of chronic pain, such as the chronic pain states that are caused by and/or associated with damage to and/or disease of the somatosensory nervous system (and in particular damage to and/or disease of the peripheral nerves), the chronic pain states that are caused by and/or associated with hypersensitivity to pain in response to tissue damage and/or inflammation, and more generally the chronic pain states that are associated with AT2R-mediated signaling, Ang II-mediated activation of AT2R and/or Ang II-mediated activation signaling pathways involving p38 MAPK and/or p44/p42 MAPK.

Summary

In a first aspect of the present disclosure, there is provided a compound of Formula I:



(I)

in which:

[C] is a monocyclic or polycyclic aromatic ring system which (i) contains at least one aromatic ring and (ii) is linked to the remainder of the compound of Formula I via a carbon atom of the at least one aromatic ring, the at least one aromatic ring having at least one heteroatom each independently and suitably chosen from N, S and O;

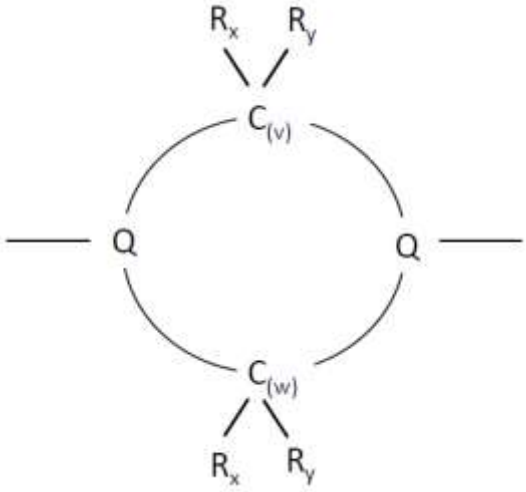
m is 1;

n is 0, and R_C and R_D are not present;

each of R_A and R_B is independently selected from the group consisting of hydrogen, methyl and/or trifluoromethyl, or R_A and R_B, together with the carbon atom to which they are bound, form a carbonyl (C=O) group;

[A] is:

(1) a ring system according to Scheme C:



(Scheme C)

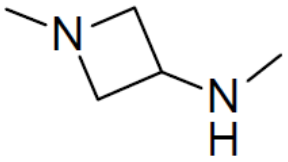
in which:

each Q is independently a carbon atom or a nitrogen atom;

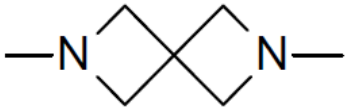
v is 1, 2, 3 or 4 and w is 1, 2, 3 or 4, such that the sum of (v+w) is 3, 4, 5, 6, 7 or 8 and such that the difference (v-w) is 1, 0 or -1;

each R_x that is present and each R_y that is present is independently selected from the group consisting of hydrogen, methyl, ethyl, F, CF_3 and isopropyl; or

(2) Formula XCIX or Formula C:



(XCIX)



(C)

in which Formula XCIX or Formula C may be unsubstituted or substituted with one or more substituents selected from the group consisting of methyl, ethyl, F, CF_3, and isopropyl;

[D] is selected from the group consisting of COOH, $CONHSO_2R$ or SO_2NHCOR, wherein R is -C_1-C_8 alkyl, CH_2(C_1-C_8 cycloalkyl), CH_2(heterocyclyl with 1-6 ring atoms), C_1-C_8 alkoxy or C_1-C_8 amine; tetrazole; and 4*H*-1,2,4-oxadiazol-5-one;

X and Y are each independently a nitrogen atom or a carbon atom, such that no more than one of X and Y is a nitrogen atom; and

Z is a nitrogen atom or a carbon atom, wherein X, Y and Z are chosen such that the resulting ring structure is an aromatic ring when X is a nitrogen atom, R_1 is not present;

when Y is a nitrogen atom, R_2 is not present; and when Z is a nitrogen atom, R_4 is not present; R_1, when present, is selected from the group consisting of H, F, Cl, Br, I, C_1-C_8

alkyl, C_3-C_4 cycloalkyl, CF_3, C_1-C_8 alkoxy, amine (-NH_2), C_1-C_2 substituted amine, and cyano;

R_2, when present, is selected from the group consisting of H, F, Cl, Br, I, C_1-C_8 alkyl, C_1-C_8 alkoxy, cycloalkyl, amine (-NH_2), and C_1-C_2 substituted amine;

R_3 is selected from the group consisting of H, F, Cl, Br, I, C_1-$_8$ alkyl, fluoro-substituted methyl, C_1-C_8 alkoxy, -O-CF_3, -O-$(CH_2)_2$-O-CH_3, -O-CH_2-CHF_2, C_3-C_6 cycloalkyl, -CH_2-(C_3-C_6 cycloalkyl), -O-CH_2-(C_3-C_6 cycloalkyl), -O-(C_3-C_6 cycloalkyl), -NH-(C_3-C_6 cycloalkyl), -N(C_1-C_3)-(C_3-C_6 cycloalkyl), -NH-heteroalkyl, -N(C_1-C_3)-heteroalkyl, 3-10 membered heterocyclyl, -CH_2-(heterocyclyl), -O-CH_2-(3-10 membered heterocyclyl), -O-(3-10 membered heterocyclyl), -NH-(3-membered heterocyclyl), -N(C_1-C_3)-(3-10 membered heterocyclyl), vinyl, methyl-substituted vinyl, allyl, methyl-substituted allyl, isobutenyl, methyl-substituted isobutenyl, and cyano, wherein a 3-10 membered heterocyclyl has 1-2 heteroatoms independently selected from N, O, and S; and

R_4, when present, is selected from the group consisting of H, F, Cl, Br, and I.

In another aspect of the present disclosure, there is provided a use of the compound as disclosed herein, or the pharmaceutical composition as disclosed herein, in the manufacture of a medicament for the prevention, treatment and/or management of pain, in particular chronic pain, such as neuropathic pain.

In another aspect of the present disclosure, there is provided a use of the compound as disclosed herein, or the pharmaceutical composition as disclosed herein, in the manufacture of a medicament for treating or preventing chronic pain.

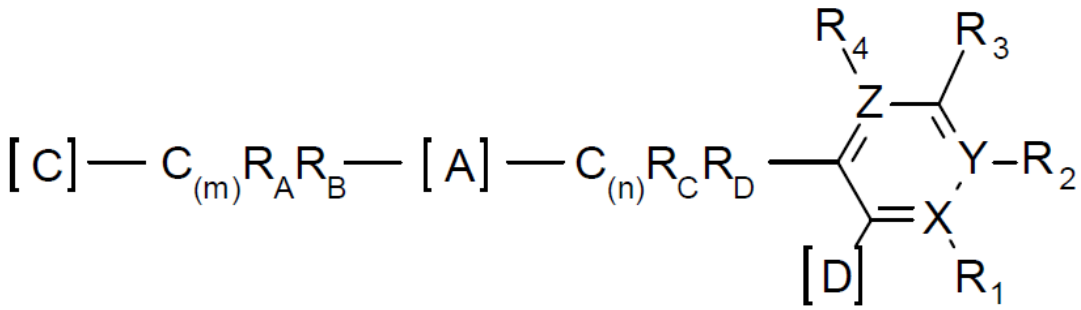
In a further aspect of the present disclosure, there is provided the compound as disclosed herein, or the pharmaceutical composition as disclosed herein, for use in therapy.

Description

The invention generally aims to meet this need by providing compounds that can interact with AT2R. In particular, the invention generally aims to provide compounds that can modulate (as defined herein) AT2R and AT2R-mediated signaling, such as the AT2R-mediated signaling that is associated with binding to AT2R of an AT2R ligand (such as a natural ligand of AT2R such as Ang II).

C L A I M S

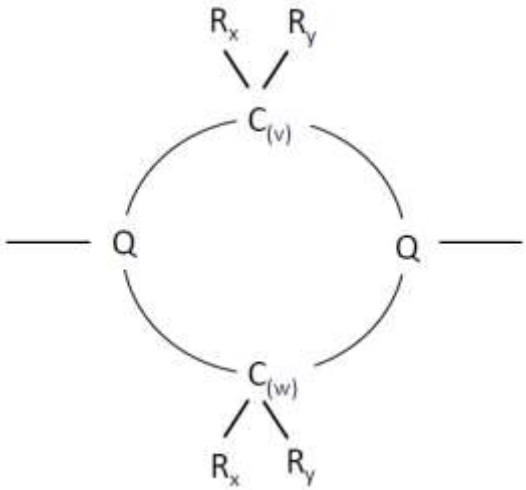
1. A compound of Formula I:



(I)

in which:

- [C] is a monocyclic or polycyclic aromatic ring system which (i) contains at least one aromatic ring and (ii) is linked to the remainder of the compound of Formula I via a carbon atom of the at least one aromatic ring, the at least one aromatic ring having at least one heteroatom each independently and suitably chosen from N, S and O;
- m is 1;
- n is 0, and R_C and R_D are not present;
- each of R_A and R_B is independently selected from the group consisting of hydrogen, methyl and/or trifluoromethyl, or R_A and R_B, together with the carbon atom to which they are bound, form a carbonyl (C=O) group;
- [A] is:
- (1) a ring system according to Scheme C:



(Scheme C)

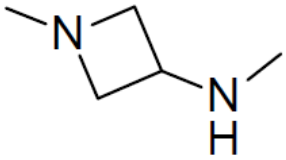
in which:

each Q is independently a carbon atom or a nitrogen atom;

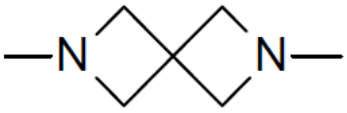
v is 1, 2, 3 or 4 and w is 1, 2, 3 or 4, such that the sum of (v+w) is 3, 4, 5, 6, 7 or 8 and such that the difference (v-w) is 1, 0 or -1;

each R_x that is present and each R_y that is present is independently selected from the group consisting of hydrogen, methyl, ethyl, F, CF_3 and isopropyl; or

(2) Formula XCIX or Formula C:



(XCIX)



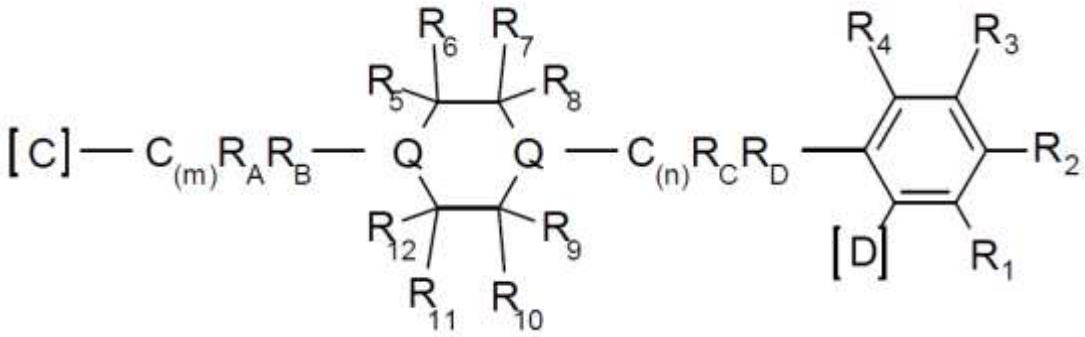
(C)

in which Formula XCIX or Formula C may be unsubstituted or substituted with one or more substituents selected from the group consisting of methyl, ethyl, F, CF_3, and isopropyl;

- [D] is selected from the group consisting of COOH, $CONHSO_2R$ or SO_2NHCOR, wherein R is -C_1-C_8 alkyl, CH_2(C_1-C_8 cycloalkyl), CH_2(heterocyclyl with 1-6 ring atoms), C_1-C_8 alkoxy or C_1-C_8 amine; tetrazole; and 4*H*-1,2,4-oxadiazol-5-one;
- X and Y are each independently a nitrogen atom or a carbon atom, such that no more than one of X and Y is a nitrogen atom; and
- Z is a nitrogen atom or a carbon atom, wherein X, Y and Z are chosen such that the resulting ring structure is an aromatic ring when X is a nitrogen atom, R_1 is not present;

- when Y is a nitrogen atom, R_2 is not present; and when Z is a nitrogen atom, R_4 is not present; R_1, when present, is selected from the group consisting of H, F, Cl, Br, I, C_1-C_8 alkyl, C_3-C_4 cycloalkyl, CF_3, C_1-C_8 alkoxy, amine (-NH_2), C_1-C_2 substituted amine, and cyano;
- R_2, when present, is selected from the group consisting of H, F, Cl, Br, I, C_1-C_8 alkyl, C_1-C_8 alkoxy, cycloalkyl, amine (-NH_2), and C_1-C_2 substituted amine;
- R_3 is selected from the group consisting of H, F, Cl, Br, I, C_{1-8} alkyl, fluoro-substituted methyl, C_1-C_8 alkoxy, -O-CF_3, -O-$(CH_2)_2$-O-CH_3, -O-CH_2-CHF_2, C_3-C_6 cycloalkyl, -CH_2-(C_3-C_6 cycloalkyl), -O-CH_2-(C_3-C_6 cycloalkyl), -O-(C_3-C_6 cycloalkyl), -NH-(C_3-C_6 cycloalkyl), -N(C_1-C_3)-(C_3-C_6 cycloalkyl), -NH-heteroalkyl, -N(C_1-C_3)-heteroalkyl, 3-10 membered heterocyclyl, -CH_2-(heterocyclyl), -O-CH_2-(3-10 membered heterocyclyl), -O-(3-10 membered heterocyclyl), -NH-(3-membered heterocyclyl), -N(C_1-C_3)-(3-10 membered heterocyclyl), vinyl, methyl-substituted vinyl, allyl, methyl-substituted allyl, isobutenyl, methyl-substituted isobutenyl, and cyano, wherein a 3-10 membered heterocyclyl has 1-2 heteroatoms independently selected from N, O, and S; and
- R_4, when present, is selected from the group consisting of H, F, Cl, Br, and I.

2. The compound of claim 1, which is a compound of Formula V:

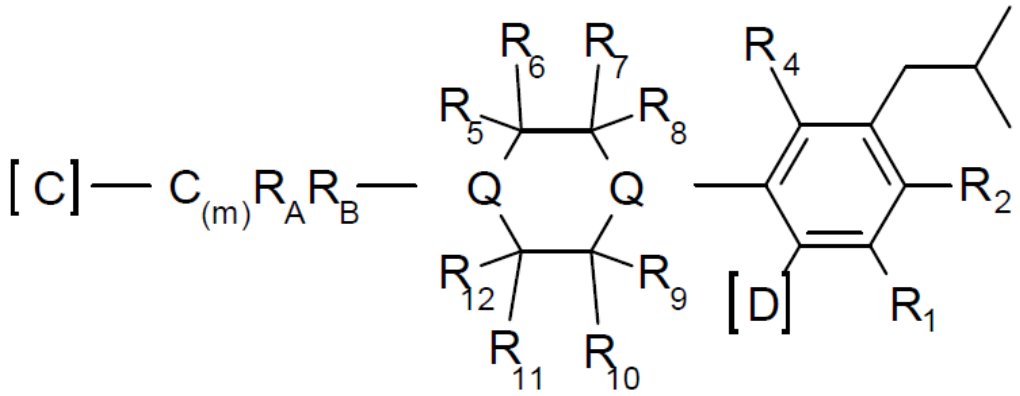


(V).

3. The compound of claim 1 or claim 2, wherein each Q is N.

4. The compound of any one of claims 1-3, wherein [C] is monocyclic.

5. The compound of any one of claims 1-4, which is a compound of Formula VI:



(VI).

6. The compound of any one of claims 1-5, wherein:

R_A is H;

R_B is H;

R_1 is selected from the group consisting of H, F, C_1-C_4 alkyl, C_3 cycloalkyl, and NH(C_1-C_2 alkyl);

R_2 is selected from the group consisting of H, F, C_1-C_4 alkyl, C_3 cycloalkyl, and C_1-C_4 alkoxy;

R_4 is H or F;

R_5 is H, methyl, ethyl, or isopropyl;

R_6 is H or methyl;

R_7 is H, methyl, or ethyl;

R_9 is H or methyl;

R_{11} is H or methyl;

R_8, R_{10}, and R_{12} are each H; and

D is tetrazole.

7. The compound of claim 1, selected from the group consisting of:

2-[[4-(1,3-benzothiazol-2-yl)piperazin-1-yl]methyl]benzoic acid;

2-[[4-(1,3-benzothiazol-2-yl)piperazin-1-yl]methyl]-N-ethylsulfonyl-benzamide;

2-[4-[[2-(2H-tetrazol-5-yl)phenyl]methyl]piperazin-1-yl]-1,3-benzothiazole;

2-[4-(1,3-benzothiazol-2-ylmethyl)piperazin-1-yl]-N-ethylsulfonyl-benzamide;

2-[[4-[2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1,3-benzothiazole;

2-[[1-[2-(2H-tetrazol-5-yl)phenyl]-4-piperidyl]methyl]-1,3-benzothiazole;
6-nitro-2-[4-[[2-(2H-tetrazol-5-yl)phenyl]methyl]piperazin-1-yl]-1,3-benzothiazole;
ethyl N-[2-[4-[(1-methylbenzimidazol-2-yl)methyl]piperazin-1-yl]-4-(trifluoromethyl)phenyl]sulfonylcarbamate;
butyl N-[2-[4-[(1-methylbenzimidazol-2-yl)methyl]piperazin-1-yl]-4-(trifluoromethyl)phenyl]sulfonylcarbamate;
1-butyl-3-[2-[4-[(1-methylbenzimidazol-2-yl)methyl]piperazin-1-yl]-4-(trifluoromethyl)phenyl]sulfonyl-urea;
butyl N-[4-methyl-2-[4-[(1-methylbenzimidazol-2-yl)methyl]piperazin-1-yl]phenyl]sulfonylcarbamate;
1-butyl-3-[4-methyl-2-[4-[(1-methylbenzimidazol-2-yl)methyl]piperazin-1-yl]phenyl]sulfonyl-urea;
N-ethylsulfonyl-2-[4-[(1-methylbenzimidazol-2-yl)methyl]piperazin-1-yl]benzamide;
N-ethylsulfonyl-4-isopropoxy-2-[4-[(1-methylbenzimidazol-2-yl)methyl]piperazin-1-yl]benzamide;
1-methyl-2-[[4-[2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]benzimidazole;
1-methyl-2-[[4-[5-methyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]benzimidazole;
1-methyl-2-[[4-[2-(2H-tetrazol-5-yl)-5-(trifluoromethyl)phenyl]piperazin-1-yl]methyl]benzimidazole;
1-methyl-2-[[4-[5-[(E)-prop-1-enyl]-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]benzimidazole;
1-methyl-2-[[4-[5-propyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]benzimidazole;
2-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1-methyl-benzimidazole;
1-methyl-2-[[4-[5-(2-methylprop-1-enyl)-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]benzimidazole
2-[[4-[5-methoxy-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1-methyl-benzimidazole
2-[[4-[5-ethoxy-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1-methyl-benzimidazole
2-[[4-[5-isopropoxy-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1-methyl-benzimidazole

2-[[1-[5-isopropoxy-2-(2H-tetrazol-5-yl)phenyl]-4-piperidyl]methyl]-1-methyl-benzimidazole

2-[[4-[2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-3H-quinazolin-4-one

2-[[4-[5-methyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-3H-quinazolin-4-one

2-[[4-[5-cyclopropyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-3H-quinazolin-4-one

2-[[4-[2-(2H-tetrazol-5-yl)-5-(trifluoromethyl)phenyl]piperazin-1-yl]methyl]-3H-quinazolin-4-one

2-[[4-[5-(2-methylprop-1-enyl)-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-3H-quinazolin-4-one

2-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-3H-quinazolin-4-one

2-[[4-[5-isopropoxy-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-3H-quinazolin-4-one

2-[4-(1,3-benzothiazol-2-ylmethyl)piperazin-1-yl]-4-ethyl-N-ethylsulfonyl-benzamide

2-[4-(1,3-benzothiazol-2-ylmethyl)piperazin-1-yl]-N-ethylsulfonyl-4-isopropyl-benzamide

2-[4-(1,3-benzothiazol-2-ylmethyl)piperazin-1-yl]-4-cyclopropyl-N-ethylsulfonyl-benzamide

2-[4-(1,3-benzothiazol-2-ylmethyl)piperazin-1-yl]-N-ethylsulfonyl-4-isobutyl-benzamide

2-[4-(1,3-benzothiazol-2-ylmethyl)piperazin-1-yl]-N-ethylsulfonyl-4-methoxy-benzamide

2-[4-(1,3-benzothiazol-2-ylmethyl)piperazin-1-yl]-4-ethoxy-N-ethylsulfonyl-benzamide

2-[[4-(1,3-benzothiazol-2-yl)piperazin-1-yl]methyl]-N-ethylsulfonyl-4-isopropoxy-benzamide

2-[4-(1,3-benzothiazol-2-ylmethyl)piperazin-1-yl]-N-ethylsulfonyl-4-isopropoxy-benzamide

2-[4-(1,3-benzothiazol-2-ylmethyl)piperazin-1-yl]-4-(cyclopropoxy)-N-ethylsulfonyl-benzamide

2-[4-(1,3-benzothiazol-2-ylmethyl)piperazin-1-yl]-N-ethylsulfonyl-4-propoxy-benzamide

2-[4-(1,3-benzothiazol-2-ylmethyl)piperazin-1-yl]-N-ethylsulfonyl-4-isobutoxy-benzamide

2-[4-(1,3-benzothiazol-2-ylmethyl)piperazin-1-yl]-4-(ethylamino)-N-ethylsulfonyl-benzamide

2-[[4-[5-ethyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1,3-benzothiazole

2-[[4-[5-isopropyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1,3-benzothiazole

2-[[4-[5-cyclopropyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1,3-benzothiazole

2-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1,3-benzothiazole

2-[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]-1,3-benzothiazole

2-[4-[[5-isopropoxy-2-(2H-tetrazol-5-yl)phenyl]methyl]piperazin-1-yl]-1,3-benzothiazole

2-[[4-[5-isopropoxy-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1,3-benzothiazole

2-[[4-[5-(cyclopropoxy)-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1,3-benzothiazole

2-[[4-[5-isobutoxy-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1,3-benzothiazole

2-[[4-[5-(cyclopropylmethoxy)-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1,3-benzothiazole

2-[[4-[5-(2,2-difluoroethoxy)-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1,3-benzothiazole

2-[[4-[5-(2-methoxyethoxy)-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1,3-benzothiazole

2-[[4-[5-(cyclopentoxy)-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1,3-benzothiazole

2-[[4-[5-(oxetan-3-ylmethoxy)-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1,3-benzothiazole

3-[4-(1,3-benzothiazol-2-ylmethyl)piperazin-1-yl]-N-ethyl-4-(2H-tetrazol-5-yl)aniline

3-[4-(1,3-benzothiazol-2-ylmethyl)piperazin-1-yl]-N-isopropyl-4-(2H-tetrazol-5-yl)aniline

3-[4-(1,3-benzothiazol-2-ylmethyl)piperazin-1-yl]-N-cyclopropyl-4-(2H-tetrazol-5-yl)aniline hydrochloride

3-[4-(1,3-benzothiazol-2-ylmethyl)piperazin-1-yl]-N-(cyclopropylmethyl)-4-(2H-tetrazol-5-yl)aniline

3-[4-(1,3-benzothiazol-2-ylmethyl)piperazin-1-yl]-N-(2-methoxyethyl)-4-(2H-tetrazol-5-yl)aniline

3-[4-(1,3-benzothiazol-2-ylmethyl)piperazin-1-yl]-N-cyclopentyl-4-(2H-tetrazol-5-yl)aniline

2-[[4-[5-(1-piperidyl)-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1,3-benzothiazole

2-[[4-[5-(4-methylpiperazin-1-yl)-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1,3-benzothiazole

4-[3-[4-(1,3-benzothiazol-2-ylmethyl)piperazin-1-yl]-4-(2H-tetrazol-5-yl)phenyl]morpholine

3-[4-(1,3-benzothiazol-2-ylmethyl)piperazin-1-yl]-N-(3-methoxycyclobutyl)-4-(2H-tetrazol-5-yl)aniline

6-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1-methyl-7H-pyrazolo[3,4-d]pyrimidin-4-one

2-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-7-methyl-pyrido[1,2-a]pyrimidin-4-one

2-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]oxazolo[4,5-b]pyridine

2-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-8-methyl-pyrido[1,2-a]pyrimidin-4-one

2-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-6-methyl-pyrido[1,2-a]pyrimidin-4-one

5-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1-methyl-pyrazolo[1,5-a]pyrimidin-7-one

7-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-3-methyl-thiazolo[3,2-a]pyrimidin-5-one

2-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]pyrido[1,2-a]pyrimidin-4-one

3-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1-methyl-quinolin-2-one

2-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-3-methyl-quinazolin-4-one

3-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1-methyl-quinoxalin-2-one

3-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]imidazo[1,2-a]pyridine

3-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1-methyl-indazole

3-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-5-methyl-isoxazole

1-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-4-[(1-methylimidazol-2-yl)methyl]piperazine

1-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-4-[(2-methylpyrazol-3-yl)methyl]piperazine

1-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-4-[[5-(trifluoromethyl)-2-pyridyl]methyl]piperazine

3-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-5-methyl-1,2,4-oxadiazole

4-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-2-methyl-thiazole

2-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]pyrimidine

5-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-3-methyl-isoxazole

3-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]pyridazine

3-[[4-[5-cyclopropyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]pyridazine

2-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole

2-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]pyrazine

1-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-4-[(4-methyl-1,2,4-triazol-3-yl)methyl]piperazine

6-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-2-methyl-1H-pyrimidin-4-one

5-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-3-methyl-1,2,4-oxadiazole

2-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]thiazole

2-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]oxazole

4-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-2-methyl-pyrimidine

2-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-6-methyl-1H-pyrimidin-4-one

4-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-3,5-dimethyl-isoxazole

5-cyclopropyl-3-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]isoxazole

5-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-2-methyl-pyrimidine

1-[(2,5-dimethylpyrazol-3-yl)methyl]-4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazine

1-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-4-[(3-methylimidazol-4-yl)methyl]piperazine

2-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-5-methyl-thiazole

6-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]pyridine-2-carbonitrile

3-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1,2,4-oxadiazole

1-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-4-[(1-methylimidazol-4-yl)methyl]piperazine

1-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-4-[(1-methylpyrazol-3-yl)methyl]piperazine

4-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-5-methyl-thiazole

3-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-5-methyl-pyridazine

3-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-6-methyl-pyridazine

1-[(2,3-dimethylimidazol-4-yl)methyl]-4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazine

3-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-6-methoxy-pyridazine

2-[[4-[3-fluoro-5-methoxy-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1,3-benzothiazole

2-[[4-[4-fluoro-5-methoxy-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1,3-benzothiazole

2-[[4-[3-fluoro-5-isopropoxy-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1,3-benzothiazole

2-[[4-[4-ethyl-5-isopropoxy-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1,3-benzothiazole

2-[[4-[3-ethyl-5-isopropoxy-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1,3-benzothiazole

2-[[4-[4-cyclopropyl-5-isopropoxy-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1,3-benzothiazole

2-[[4-[3-cyclopropyl-5-isopropoxy-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1,3-benzothiazole

2-[[4-[4-ethoxy-5-isopropoxy-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1,3-benzothiazole

2-[[4-[5-cyclopropyl-4-fluoro-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1,3-benzothiazole

2-[[4-[5-cyclopropyl-3-fluoro-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1,3-benzothiazole

2-[[4-[5-cyclopropyl-4-methyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1,3-benzothiazole

2-[[4-[5-cyclopropyl-3-methyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1,3-benzothiazole

2-[[4-[5-cyclopropyl-3-ethyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1,3-benzothiazole

2-[[4-[3,5-dicyclopropyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1,3-benzothiazole

4-[4-(1,3-benzothiazol-2-ylmethyl)piperazin-1-yl]-2-cyclopropyl-N-ethyl-5-(2H-tetrazol-5-yl)aniline

N-[4-[4-(1,3-benzothiazol-2-ylmethyl)piperazin-1-yl]-2-cyclopropyl-5-(2H-tetrazol-5-yl)phenyl]acetamide

2-[[4-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1,3-benzothiazole

2-[[4-[4-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1,3-benzothiazole

2-[[4-[5-isobutyl-4-methyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1,3-benzothiazole

2-[[4-[5-isobutyl-3-methyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1,3-benzothiazole

2-[[4-[3-ethyl-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1,3-benzothiazole

2-[[4-[3-cyclopropyl-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1,3-benzothiazole

4-[4-(1,3-benzothiazol-2-ylmethyl)piperazin-1-yl]-2-isobutyl-5-(2H-tetrazol-5-yl)aniline

4-[4-(1,3-benzothiazol-2-ylmethyl)piperazin-1-yl]-2-isobutyl-N-methyl-5-(2H-tetrazol-5-yl)aniline

4-[4-(1,3-benzothiazol-2-ylmethyl)piperazin-1-yl]-N-ethyl-2-isobutyl-5-(2H-tetrazol-5-yl)aniline

2-[[4-[5-ethyl-2-(2H-tetrazol-5-yl)-3-pyridyl]piperazin-1-yl]methyl]-1,3-benzothiazole

2-[[4-[6-ethyl-3-(2H-tetrazol-5-yl)-2-pyridyl]piperazin-1-yl]methyl]-1,3-benzothiazole

2-[[4-[5-cyclopropyl-2-(2H-tetrazol-5-yl)-3-pyridyl]piperazin-1-yl]methyl]-1,3-benzothiazole

2-[[4-[2-cyclopropyl-5-(2H-tetrazol-5-yl)-4-pyridyl]piperazin-1-yl]methyl]-1,3-benzothiazole

2-[[4-[6-cyclopropyl-3-(2H-tetrazol-5-yl)-2-pyridyl]piperazin-1-yl]methyl]-1,3-benzothiazole

2-[[4-[6-cyclopropyl-3-(2H-tetrazol-5-yl)pyrazin-2-yl]piperazin-1-yl]methyl]-1,3-benzothiazole

2-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)-3-pyridyl]piperazin-1-yl]methyl]-1,3-benzothiazole

2-[[4-[6-isobutyl-3-(2H-tetrazol-5-yl)-2-pyridyl]piperazin-1-yl]methyl]-1,3-benzothiazole

5-[4-(1,3-benzothiazol-2-ylmethyl)piperazin-1-yl]-N-(cyclopropylmethyl)-6-(2H-tetrazol-5-yl)pyridin-3-amine

2-[[4-[3-fluoro-5-methoxy-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-3H-quinazolin-4-one

2-[[4-[3-fluoro-5-isopropoxy-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-3H-quinazolin-4-one

2-[[4-[3-cyclopropyl-5-isopropoxy-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-3H-quinazolin-4-one

2-[[4-[4-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-3H-quinazolin-4-one

2-[[4-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-3H-quinazolin-4-one

3-[[4-[3-fluoro-5-methoxy-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]pyridazine

3-[[4-[3-fluoro-5-isopropoxy-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]pyridazine

3-[[4-[2-fluoro-3-isopropoxy-6-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]pyridazine

3-[[4-[4-ethyl-5-isopropoxy-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]pyridazine

3-[[4-[3-ethyl-5-isopropoxy-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]pyridazine

3-[[4-[4-cyclopropyl-5-isopropoxy-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]pyridazine

3-[[4-[3-cyclopropyl-5-isopropoxy-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]pyridazine

3-[[4-[4-ethoxy-5-isopropoxy-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]pyridazine

3-[[4-[4-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]pyridazine

3-[[4-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]pyridazine

3-[[4-[2-fluoro-3-isobutyl-6-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]pyridazine

3-[[4-[5-isobutyl-4-methyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]pyridazine

3-[[4-[5-isobutyl-3-methyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]pyridazine

3-[[4-[3-ethyl-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]pyridazine

3-[[4-[3-cyclopropyl-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]pyridazine

2-isobutyl-N-methyl-4-[4-(pyridazin-3-ylmethyl)piperazin-1-yl]-5-(2H-tetrazol-5-yl)aniline

5-isobutyl-N-methyl-3-[4-(pyridazin-3-ylmethyl)piperazin-1-yl]-2-(2H-tetrazol-5-yl)aniline

N-ethyl-2-isobutyl-4-[4-(pyridazin-3-ylmethyl)piperazin-1-yl]-5-(2H-tetrazol-5-yl)aniline

3-[[4-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-2-methyl-piperazin-1-yl]methyl]pyridazine

3-[[(2S)-4-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-2-methyl-piperazin-1-yl]methyl]pyridazine

3-[[(2R)-4-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-2-methyl-piperazin-1-yl]methyl]pyridazine

3-[[(2S)-4-[2-fluoro-3-isobutyl-6-(2H-tetrazol-5-yl)phenyl]-2-methyl-piperazin-1-yl]methyl]pyridazine

3-[[(2S)-4-[5-isobutyl-2-(2H-tetrazol-5-yl)-3-pyridyl]-2-methyl-piperazin-1-yl]methyl]pyridazine

3-[[2-ethyl-4-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]pyridazine

3-[[4-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-2-isopropyl-piperazin-1-yl]methyl]pyridazine

3-[[4-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-3-methyl-piperazin-1-yl]methyl]pyridazine

3-[[3-ethyl-4-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]pyridazine

3-[[4-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-2,2-dimethyl-piperazin-1-yl]methyl]pyridazine

3-[[4-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-2,5-dimethyl-piperazin-1-yl]methyl]pyridazine

3-[[4-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-2,6-dimethyl-piperazin-1-yl]methyl]pyridazine

3-[[(2R,6R)-4-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-2,6-dimethyl-piperazin-1-yl]methyl]pyridazine

3-[[(2S,6R)-4-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-2,6-dimethyl-piperazin-1-yl]methyl]pyridazine

3-[[(2S,6S)-4-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-2,6-dimethyl-piperazin-1-yl]methyl]pyridazine

3-[[4-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-2,3-dimethyl-piperazin-1-yl]methyl]pyridazine

2-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-5-(pyridazin-3-ylmethyl)-2,5-diazabicyclo[2.2.1]heptane

3-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-8-(pyridazin-3-ylmethyl)-3,8-diazabicyclo[3.2.1]octane

1-[(4-chloro-2-pyridyl)methyl]-4-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazine

1-[(5-chloro-2-pyridyl)methyl]-4-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazine

1-[(3-chloro-2-pyridyl)methyl]-4-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazine

1-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-4-[(5-methoxy-2-pyridyl)methyl]piperazine

1-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-4-[(5-fluoro-2-pyridyl)methyl]piperazine

1-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-4-[(3-fluoro-2-pyridyl)methyl]piperazine

1-[(3,5-dimethyl-2-pyridyl)methyl]-4-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazine

1-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-4-[(3-methoxy-2-pyridyl)methyl]piperazine

1-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-4-[(4-methoxy-2-pyridyl)methyl]piperazine

1-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-4-[(4-methoxy-3,5-dimethyl-2-pyridyl)methyl]piperazine

1-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-4-[(5-methyl-2-pyridyl)methyl]piperazine

1-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-4-[[4-(trifluoromethyl)-2-pyridyl]methyl]piperazine

1-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-4-[(3-methyl-2-pyridyl)methyl]piperazine

1-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-4-[(4-methyl-2-pyridyl)methyl]piperazine

1-[(5-chloro-3-fluoro-2-pyridyl)methyl]-4-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazine

1-[(3-chloro-5-fluoro-2-pyridyl)methyl]-4-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazine

1-[(4,5-dimethoxy-2-pyridyl)methyl]-4-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazine

1-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-4-[(4-methoxy-3-methyl-2-pyridyl)methyl]piperazine

6-[[4-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]pyridine-3-carbonitrile

1-[(4-chloro-5-fluoro-2-pyridyl)methyl]-4-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazine

1-[(3,5-difluoro-2-pyridyl)methyl]-4-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazine

3-[1-[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]ethyl]pyridazine

[4-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]-pyridazin-3-yl-methanone

1-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-4-[1-(2-pyridyl)ethyl]piperazine

[4-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]-(2-pyridyl)methanone

[(2S)-4-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-2-methyl-piperazin-1-yl]-(2-pyridyl)methanone

(2S)-4-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-2-methyl-1-(2-pyridylmethyl)piperazine

(2S)-4-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-2-methyl-1-[1-(2-pyridyl)ethyl]piperazine

2-[[4-[2-fluoro-3-isobutyl-6-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-5-methyl-thiazole

2-[[4-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-5-methyl-thiazole

2-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)-3-pyridyl]piperazin-1-yl]methyl]-5-methyl-thiazole

2-[[4-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-2-methyl-piperazin-1-yl]methyl]-5-methyl-thiazole

2-[[(2S)-4-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-2-methyl-piperazin-1-yl]methyl]-5-methyl-thiazole

2-[[4-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-2,6-dimethyl-piperazin-1-yl]methyl]-5-methyl-thiazole

2-[1-[4-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]ethyl]-5-methyl-thiazole

2-[1-[(2S)-4-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-2-methyl-piperazin-1-yl]ethyl]-5-methyl-thiazole

(2S)-4-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-1-[(4-methoxy-2-pyridyl)methyl]-2-methyl-piperazine

(2S)-4-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-2-methyl-1-[(3-methyl-2-pyridyl)methyl]piperazine

(2S)-4-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-2-methyl-1-[(4-methyl-2-pyridyl)methyl]piperazine

1-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-4-(pyridazin-3-ylmethyl)-1,4-diazepane

1-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-4-(pyridazin-3-ylmethyl)-1,4-diazepane

5-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-2-(pyridazin-3-ylmethyl)-1,3,3a,4,6,6a-hexahydropyrrolo[3,4-c]pyrrole

5-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-2-(pyridazin-3-ylmethyl)-1,3,3a,4,6,6a-hexahydropyrrolo[3,4-c]pyrrole

3-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-1-piperidyl]methyl]pyridazine

3-[[3-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]pyrrolidin-1-yl]methyl]pyridazine

1-(5-isobutyl-2-(2H-tetrazol-5-yl)phenyl)-N-(pyridazin-3-ylmethyl)azetidin-3-amine

2-((1-(3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl)piperidin-4-yl)methyl)pyridine

3-[[4-[[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]methyl]piperazin-1-yl]methyl]pyridazine

(5-isobutyl-2-(2H-tetrazol-5-yl)phenyl)(4-(pyridazin-3-ylmethyl)piperazin-1-yl)methanone

2-ethyl-3-[[1-[2-(2H-tetrazol-5-yl)phenyl]-4-piperidyl]methyl]quinazolin-4-one

2-[4-[(2-ethyl-4-oxo-quinazolin-3-yl)methyl]-1-piperidyl]-N-ethylsulfonyl-benzamide

2-ethyl-6-nitro-3-[[1-[2-(2H-tetrazol-5-yl)phenyl]-4-piperidyl]methyl]quinazolin-4-one

N-[2-ethyl-4-oxo-3-[[1-[2-(2H-tetrazol-5-yl)phenyl]-4-piperidyl]methyl]quinazolin-6-yl]-N-propyl-thiophene-2-carboxamide

N-[2-ethyl-4-oxo-3-[[1-[2-(2H-tetrazol-5-yl)phenyl]-4-piperidyl]methyl]quinazolin-6-yl]-N-(3-pyridylmethyl)thiophene-2-carboxamide

N-[2-ethyl-4-oxo-3-[[1-[2-(2H-tetrazol-5-yl)phenyl]-4-piperidyl]methyl]quinazolin-6-yl]benzamide

N-benzyl-N-[2-ethyl-4-oxo-3-[[1-[2-(2H-tetrazol-5-yl)phenyl]-4-piperidyl]methyl]quinazolin-6-yl]thiophene-2-carboxamide

N-[2-ethyl-4-oxo-3-[[1-[2-(2H-tetrazol-5-yl)phenyl]-4-piperidyl]methyl]quinazolin-6-yl]cyclopropanecarboxamide

N-[(2-chlorophenyl)methyl]-N-[2-ethyl-4-oxo-3-[[1-[2-(2H-tetrazol-5-yl)phenyl]-4-piperidyl]methyl]quinazolin-6-yl]thiophene-2-carboxamide

2-phenyl-3-[[1-[2-(1H-tetrazol-5-yl)phenyl]-4-piperidyl]methyl]quinazolin-4-one

3-[[(2S)-4-[5-(1,2-dideuterio-2-methyl-propyl)-3-f(luoro-2-(2H-tetrazol-5-yl)phenyl]-2-methyl-piperazin-1-yl]methyl]pyridazine

2,2,3,3,5,6,6-heptadeuterio-1-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-4-(pyridazin-3-ylmethyl)-5-(trideuteriomethyl)piperazine.

8. The compound of claim 7, selected from the group consisting of:

2-[[4-[5-cyclopropyl-3-fluoro-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1,3-benzothiazole;

3-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]imidazo[1,2-a]pyridine;

2-[[4-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1,3-benzothiazole;

2-[4-(1,3-benzothiazol-2-ylmethyl)piperazin-1-yl]-N-ethylsulfonyl-4-isopropyl-benzamide;

2-[[4-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-3H-quinazolin-4-one;

2-[[4-[3-cyclopropyl-5-isopropoxy-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1,3-benzothiazole;

2-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-5-methyl-thiazole;

2-[[4-[3,5-dicyclopropyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1,3-benzothiazole;

3-[[4-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-3-methyl-piperazin-1-yl]methyl]pyridazine;

3-[[4-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-2-methyl-piperazin-1-yl]methyl]pyridazine;

3-[[2-ethyl-4-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]pyridazine;

2-[[4-[3-ethyl-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1,3-benzothiazole;

2-[[4-[5-cyclopropyl-3-methyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1,3-benzothiazole;

3-[[4-[3-cyclopropyl-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]pyridazine;

3-[[4-[3-ethyl-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]pyridazine;

5-isobutyl-N-methyl-3-[4-(pyridazin-3-ylmethyl)piperazin-1-yl]-2-(2H-tetrazol-5-yl)aniline;

2-[[4-[3-cyclopropyl-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1,3-benzothiazole;

2-[[4-[5-isobutyl-3-methyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1,3-benzothiazole;

3-[[3-ethyl-4-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]pyridazine;

3-[[4-[5-isobutyl-3-methyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]pyridazine;

3-[[4-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-2,5-dimethyl-piperazin-1-yl]methyl]pyridazine;

3-[[4-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-2,2-dimethyl-piperazin-1-yl]methyl]pyridazine;

3-[1-[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]ethyl]pyridazine;

3-[[4-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-2,6-dimethyl-piperazin-1-yl]methyl]pyridazine;

3-[[4-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-2,3-dimethyl-piperazin-1-yl]methyl]pyridazine;

3-[[(2S)-4-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-2-methyl-piperazin-1-yl]methyl]pyridazine;

3-[[(2R)-4-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-2-methyl-piperazin-1-yl]methyl]pyridazine;

1-[(4-chloro-2-pyridyl)methyl]-4-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazine;

1-[(3-chloro-2-pyridyl)methyl]-4-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazine;

1-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-4-[(4-methoxy-2-pyridyl)methyl]piperazine;

1-[(3,5-dimethyl-2-pyridyl)methyl]-4-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazine;

[4-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]-pyridazin-3-yl-methanone;

2-[[4-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-5-methyl-thiazole;

2-[1-[4-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]ethyl]-5-methyl-thiazole;

2-[[4-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-2-methyl-piperazin-1-yl]methyl]-5-methyl-thiazole;

2-[[(2S)-4-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-2-methyl-piperazin-1-yl]methyl]-5-methyl-thiazole;

1-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-4-[(3-methyl-2-pyridyl)methyl]piperazine;

1-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-4-[(4-methyl-2-pyridyl)methyl]piperazine;

1-[(5-chloro-3-fluoro-2-pyridyl)methyl]-4-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazine;

2-[[4-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-2,6-dimethyl-piperazin-1-yl]methyl]-5-methyl-thiazole;

2-[1-[(2S)-4-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-2-methyl-piperazin-1-yl]ethyl]-5-methyl-thiazole;

3-[[(2S)-4-[2-fluoro-3-isobutyl-6-(2H-tetrazol-5-yl)phenyl]-2-methyl-piperazin-1-yl]methyl]pyridazine;

3-[[(2R,6R)-4-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-2,6-dimethyl-piperazin-1-yl]methyl]pyridazine;

3-[[(2S,6R)-4-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-2,6-dimethyl-piperazin-1-yl]methyl]pyridazine;

3-[[(2S,6S)-4-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-2,6-dimethyl-piperazin-1-yl]methyl]pyridazine;

(2S)-4-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-1-[(4-methoxy-2-pyridyl)methyl]-2-methyl-piperazine;

(2S)-4-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-2-methyl-1-[(3-methyl-2-pyridyl)methyl]piperazine;

(2S)-4-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-2-methyl-1-[(4-methyl-2-pyridyl)methyl]piperazine;

1-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-4-(pyridazin-3-ylmethyl)-1,4-diazepane;

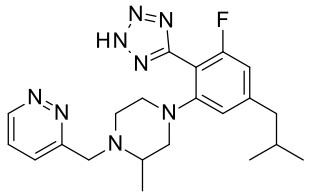
[4-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]-(2-pyridyl)methanone;

(2S)-4-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-2-methyl-1-(2-pyridylmethyl)piperazine; and

(2S)-4-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-2-methyl-1-[1-(2-pyridyl)ethyl]piperazine;

or a pharmaceutically acceptable salt thereof.

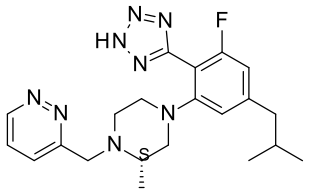
9. The compound of claim 7 or claim 8, which is:



;

or a pharmaceutically acceptable salt thereof.

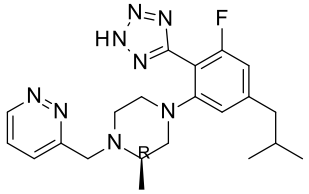
10. The compound of any one of claims 7-9, which is:



;

or a pharmaceutically acceptable salt thereof.

11. The compound of any one of claims 7-9, which is:



;

or a pharmaceutically acceptable salt thereof.

12. The compound of claim 7, selected from the group consisting of:

2-[[4-(1,3-benzothiazol-2-yl)piperazin-1-yl]methyl]benzoic acid;

2-[[4-(1,3-benzothiazol-2-yl)piperazin-1-yl]methyl]-N-ethylsulfonyl-benzamide;

2-[4-[[2-(2H-tetrazol-5-yl)phenyl]methyl]piperazin-1-yl]-1,3-benzothiazole;

2-[4-(1,3-benzothiazol-2-ylmethyl)piperazin-1-yl]-N-ethylsulfonyl-benzamide;

2-[[4-[2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1,3-benzothiazole;

2-[[1-[2-(2H-tetrazol-5-yl)phenyl]-4-piperidyl]methyl]-1,3-benzothiazole;

6-nitro-2-[4-[[2-(2H-tetrazol-5-yl)phenyl]methyl]piperazin-1-yl]-1,3-benzothiazole;

ethyl N-[2-[4-[(1-methylbenzimidazol-2-yl)methyl]piperazin-1-yl]-4-(trifluoromethyl)phenyl]sulfonylcarbamate;

butyl N-[2-[4-[(1-methylbenzimidazol-2-yl)methyl]piperazin-1-yl]-4-(trifluoromethyl)phenyl]sulfonylcarbamate;

1-butyl-3-[2-[4-[(1-methylbenzimidazol-2-yl)methyl]piperazin-1-yl]-4-(trifluoromethyl)phenyl]sulfonyl-urea;

butyl N-[4-methyl-2-[4-[(1-methylbenzimidazol-2-yl)methyl]piperazin-1-yl]phenyl]sulfonylcarbamate;

1-butyl-3-[4-methyl-2-[4-[(1-methylbenzimidazol-2-yl)methyl]piperazin-1-yl]phenyl]sulfonyl-urea;

N-ethylsulfonyl-2-[4-[(1-methylbenzimidazol-2-yl)methyl]piperazin-1-yl]benzamide;

N-ethylsulfonyl-4-isopropoxy-2-[4-[(1-methylbenzimidazol-2-yl)methyl]piperazin-1-yl]benzamide;

1-methyl-2-[[4-[2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]benzimidazole;

1-methyl-2-[[4-[5-methyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]benzimidazole;

1-methyl-2-[[4-[2-(2H-tetrazol-5-yl)-5-(trifluoromethyl)phenyl]piperazin-1-yl]methyl]benzimidazole;

1-methyl-2-[[4-[5-[(E)-prop-1-enyl]-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]benzimidazole;

1-methyl-2-[[4-[5-propyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]benzimidazole;

2-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1-methyl-benzimidazole;

1-methyl-2-[[4-[5-(2-methylprop-1-enyl)-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]benzimidazole;

2-[[4-[5-methoxy-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1-methyl-benzimidazole;

2-[[4-[5-ethoxy-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1-methyl-benzimidazole;

2-[[4-[5-isopropoxy-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1-methyl-benzimidazole;

2-[[1-[5-isopropoxy-2-(2H-tetrazol-5-yl)phenyl]-4-piperidyl]methyl]-1-methyl-benzimidazole;

2-[[4-[2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-3H-quinazolin-4-one;

2-[[4-[5-methyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-3H-quinazolin-4-one;

2-[[4-[5-cyclopropyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-3H-quinazolin-4-one;

2-[[4-[2-(2H-tetrazol-5-yl)-5-(trifluoromethyl)phenyl]piperazin-1-yl]methyl]-3H-quinazolin-4-one;

2-[[4-[5-(2-methylprop-1-enyl)-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-3H-quinazolin-4-one;

2-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-3H-quinazolin-4-one;

2-[[4-[5-isopropoxy-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-3H-quinazolin-4-one;

2-[4-(1,3-benzothiazol-2-ylmethyl)piperazin-1-yl]-4-ethyl-N-ethylsulfonyl-benzamide;

2-[4-(1,3-benzothiazol-2-ylmethyl)piperazin-1-yl]-4-cyclopropyl-N-ethylsulfonyl-benzamide;

2-[4-(1,3-benzothiazol-2-ylmethyl)piperazin-1-yl]-N-ethylsulfonyl-4-isobutyl-benzamide;

2-[4-(1,3-benzothiazol-2-ylmethyl)piperazin-1-yl]-N-ethylsulfonyl-4-methoxy-benzamide;

2-[4-(1,3-benzothiazol-2-ylmethyl)piperazin-1-yl]-4-ethoxy-N-ethylsulfonyl-benzamide;

2-[[4-(1,3-benzothiazol-2-yl)piperazin-1-yl]methyl]-N-ethylsulfonyl-4-isopropoxy-benzamide;

2-[4-(1,3-benzothiazol-2-ylmethyl)piperazin-1-yl]-N-ethylsulfonyl-4-isopropoxy-benzamide;

2-[4-(1,3-benzothiazol-2-ylmethyl)piperazin-1-yl]-4-(cyclopropoxy)-N-ethylsulfonyl-benzamide;

2-[4-(1,3-benzothiazol-2-ylmethyl)piperazin-1-yl]-N-ethylsulfonyl-4-propoxy-benzamide;

2-[4-(1,3-benzothiazol-2-ylmethyl)piperazin-1-yl]-N-ethylsulfonyl-4-isobutoxy-benzamide;

2-[4-(1,3-benzothiazol-2-ylmethyl)piperazin-1-yl]-4-(ethylamino)-N-ethylsulfonyl-benzamide;

2-[[4-[5-ethyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1,3-benzothiazole;

2-[[4-[5-isopropyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1,3-benzothiazole;

2-[[4-[5-cyclopropyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1,3-benzothiazole;

2-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1,3-benzothiazole;

2-[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]-1,3-benzothiazole;

2-[4-[[5-isopropoxy-2-(2H-tetrazol-5-yl)phenyl]methyl]piperazin-1-yl]-1,3-benzothiazole;

2-[[4-[5-isopropoxy-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1,3-benzothiazole;

2-[[4-[5-(cyclopropoxy)-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1,3-benzothiazole;

2-[[4-[5-isobutoxy-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1,3-benzothiazole;

2-[[4-[5-(cyclopropylmethoxy)-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1,3-benzothiazole;

2-[[4-[5-(2,2-difluoroethoxy)-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1,3-benzothiazole;

2-[[4-[5-(2-methoxyethoxy)-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1,3-benzothiazole;

2-[[4-[5-(cyclopentoxy)-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1,3-benzothiazole;

2-[[4-[5-(oxetan-3-ylmethoxy)-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1,3-benzothiazole;

3-[4-(1,3-benzothiazol-2-ylmethyl)piperazin-1-yl]-N-ethyl-4-(2H-tetrazol-5-yl)aniline;

3-[4-(1,3-benzothiazol-2-ylmethyl)piperazin-1-yl]-N-isopropyl-4-(2H-tetrazol-5-yl)aniline;

3-[4-(1,3-benzothiazol-2-ylmethyl)piperazin-1-yl]-N-cyclopropyl-4-(2H-tetrazol-5-yl)aniline hydrochloride;

3-[4-(1,3-benzothiazol-2-ylmethyl)piperazin-1-yl]-N-(cyclopropylmethyl)-4-(2H-tetrazol-5-yl)aniline;

3-[4-(1,3-benzothiazol-2-ylmethyl)piperazin-1-yl]-N-(2-methoxyethyl)-4-(2H-tetrazol-5-yl)aniline;

3-[4-(1,3-benzothiazol-2-ylmethyl)piperazin-1-yl]-N-cyclopentyl-4-(2H-tetrazol-5-yl)aniline;

2-[[4-[5-(1-piperidyl)-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1,3-benzothiazole;

2-[[4-[5-(4-methylpiperazin-1-yl)-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1,3-benzothiazole;

4-[3-[4-(1,3-benzothiazol-2-ylmethyl)piperazin-1-yl]-4-(2H-tetrazol-5-yl)phenyl]morpholine;

3-[4-(1,3-benzothiazol-2-ylmethyl)piperazin-1-yl]-N-(3-methoxycyclobutyl)-4-(2H-tetrazol-5-yl)aniline;

6-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1-methyl-7H-pyrazolo[3,4-d]pyrimidin-4-one;

2-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-7-methyl-pyrido[1,2-a]pyrimidin-4-one;

2-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]oxazolo[4,5-b]pyridine;

2-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-8-methyl-pyrido[1,2-a]pyrimidin-4-one;

2-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-6-methyl-pyrido[1,2-a]pyrimidin-4-one;

5-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1-methyl-pyrazolo[1,5-a]pyrimidin-7-one;

7-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-3-methyl-thiazolo[3,2-a]pyrimidin-5-one;

2-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]pyrido[1,2-a]pyrimidin-4-one;

3-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1-methyl-quinolin-2-one;

2-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-3-methyl-quinazolin-4-one;

3-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1-methyl-quinoxalin-2-one;

3-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1-methyl-indazole;

3-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-5-methyl-isoxazole;

1-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-4-[(1-methylimidazol-2-yl)methyl]piperazine;

1-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-4-[(2-methylpyrazol-3-yl)methyl]piperazine;

1-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-4-[[5-(trifluoromethyl)-2-pyridyl]methyl]piperazine;

3-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-5-methyl-1,2,4-oxadiazole;

4-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-2-methyl-thiazole;

2-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]pyrimidine;

5-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-3-methyl-isoxazole;

3-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]pyridazine;

3-[[4-[5-cyclopropyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]pyridazine;

2-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;

2-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]pyrazine;

1-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-4-[(4-methyl-1,2,4-triazol-3-yl)methyl]piperazine;

6-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-2-methyl-1H-pyrimidin-4-one;

5-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-3-methyl-1,2,4-oxadiazole;

2-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]thiazole;

2-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]oxazole;

4-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-2-methyl-pyrimidine;

2-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-6-methyl-1H-pyrimidin-4-one;

4-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-3,5-dimethyl-isoxazole;

5-cyclopropyl-3-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]isoxazole;

5-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-2-methyl-pyrimidine;

1-[(2,5-dimethylpyrazol-3-yl)methyl]-4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazine;

1-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-4-[(3-methylimidazol-4-yl)methyl]piperazine;

6-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]pyridine-2-carbonitrile;

3-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1,2,4-oxadiazole;

1-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-4-[(1-methylimidazol-4-yl)methyl]piperazine;

1-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-4-[(1-methylpyrazol-3-yl)methyl]piperazine;

4-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-5-methyl-thiazole;

3-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-5-methyl-pyridazine;

3-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-6-methyl-pyridazine;

1-[(2,3-dimethylimidazol-4-yl)methyl]-4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazine;

3-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-6-methoxy-pyridazine;

2-[[4-[3-fluoro-5-methoxy-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1,3-benzothiazole;

2-[[4-[4-fluoro-5-methoxy-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1,3-benzothiazole;

2-[[4-[3-fluoro-5-isopropoxy-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1,3-benzothiazole;

2-[[4-[4-ethyl-5-isopropoxy-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1,3-benzothiazole;

2-[[4-[3-ethyl-5-isopropoxy-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1,3-benzothiazole;

2-[[4-[4-cyclopropyl-5-isopropoxy-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1,3-benzothiazole;

2-[[4-[4-ethoxy-5-isopropoxy-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1,3-benzothiazole;

2-[[4-[5-cyclopropyl-4-fluoro-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1,3-benzothiazole;

2-[[4-[5-cyclopropyl-3-fluoro-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1,3-benzothiazole;

2-[[4-[5-cyclopropyl-4-methyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1,3-benzothiazole;

2-[[4-[5-cyclopropyl-3-ethyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1,3-benzothiazole;

4-[4-(1,3-benzothiazol-2-ylmethyl)piperazin-1-yl]-2-cyclopropyl-N-ethyl-5-(2H-tetrazol-5-yl)aniline;

N-[4-[4-(1,3-benzothiazol-2-ylmethyl)piperazin-1-yl]-2-cyclopropyl-5-(2H-tetrazol-5-yl)phenyl]acetamide;

2-[[4-[4-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1,3-benzothiazole;

2-[[4-[5-isobutyl-4-methyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-1,3-benzothiazole;

4-[4-(1,3-benzothiazol-2-ylmethyl)piperazin-1-yl]-2-isobutyl-5-(2H-tetrazol-5-yl)aniline;

4-[4-(1,3-benzothiazol-2-ylmethyl)piperazin-1-yl]-2-isobutyl-N-methyl-5-(2H-tetrazol-5-yl)aniline;

4-[4-(1,3-benzothiazol-2-ylmethyl)piperazin-1-yl]-N-ethyl-2-isobutyl-5-(2H-tetrazol-5-yl)aniline;

2-[[4-[5-ethyl-2-(2H-tetrazol-5-yl)-3-pyridyl]piperazin-1-yl]methyl]-1,3-benzothiazole;

2-[[4-[6-ethyl-3-(2H-tetrazol-5-yl)-2-pyridyl]piperazin-1-yl]methyl]-1,3-benzothiazole;

2-[[4-[5-cyclopropyl-2-(2H-tetrazol-5-yl)-3-pyridyl]piperazin-1-yl]methyl]-1,3-benzothiazole;

2-[[4-[2-cyclopropyl-5-(2H-tetrazol-5-yl)-4-pyridyl]piperazin-1-yl]methyl]-1,3-benzothiazole;

2-[[4-[6-cyclopropyl-3-(2H-tetrazol-5-yl)-2-pyridyl]piperazin-1-yl]methyl]-1,3-benzothiazole;

2-[[4-[6-cyclopropyl-3-(2H-tetrazol-5-yl)pyrazin-2-yl]piperazin-1-yl]methyl]-1,3-benzothiazole;

2-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)-3-pyridyl]piperazin-1-yl]methyl]-1,3-benzothiazole;

2-[[4-[6-isobutyl-3-(2H-tetrazol-5-yl)-2-pyridyl]piperazin-1-yl]methyl]-1,3-benzothiazole;

5-[4-(1,3-benzothiazol-2-ylmethyl)piperazin-1-yl]-N-(cyclopropylmethyl)-6-(2H-tetrazol-5-yl)pyridin-3-amine;

2-[[4-[3-fluoro-5-methoxy-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-3H-quinazolin-4-one;

2-[[4-[3-fluoro-5-isopropoxy-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-3H-quinazolin-4-one;

2-[[4-[3-cyclopropyl-5-isopropoxy-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-3H-quinazolin-4-one;

2-[[4-[4-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-3H-quinazolin-4-one;

3-[[4-[3-fluoro-5-methoxy-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]pyridazine;

3-[[4-[3-fluoro-5-isopropoxy-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]pyridazine;

3-[[4-[2-fluoro-3-isopropoxy-6-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]pyridazine;

3-[[4-[4-ethyl-5-isopropoxy-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]pyridazine;

3-[[4-[3-ethyl-5-isopropoxy-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]pyridazine;

3-[[4-[4-cyclopropyl-5-isopropoxy-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]pyridazine;

3-[[4-[3-cyclopropyl-5-isopropoxy-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]pyridazine;

3-[[4-[4-ethoxy-5-isopropoxy-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]pyridazine;

3-[[4-[4-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]pyridazine;

3-[[4-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]pyridazine;

3-[[4-[2-fluoro-3-isobutyl-6-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]pyridazine;

3-[[4-[5-isobutyl-4-methyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]pyridazine;

2-isobutyl-N-methyl-4-[4-(pyridazin-3-ylmethyl)piperazin-1-yl]-5-(2H-tetrazol-5-yl)aniline;

N-ethyl-2-isobutyl-4-[4-(pyridazin-3-ylmethyl)piperazin-1-yl]-5-(2H-tetrazol-5-yl)aniline;

3-[[(2S)-4-[5-isobutyl-2-(2H-tetrazol-5-yl)-3-pyridyl]-2-methyl-piperazin-1-yl]methyl]pyridazine;

3-[[4-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-2-isopropyl-piperazin-1-yl]methyl]pyridazine;

2-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-5-(pyridazin-3-ylmethyl)-2,5-diazabicyclo[2.2.1]heptane;

3-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-8-(pyridazin-3-ylmethyl)-3,8-diazabicyclo[3.2.1]octane;

1-[(5-chloro-2-pyridyl)methyl]-4-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazine;

1-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-4-[(5-methoxy-2-pyridyl)methyl]piperazine;

1-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-4-[(5-fluoro-2-pyridyl)methyl]piperazine;

1-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-4-[(3-fluoro-2-pyridyl)methyl]piperazine;

1-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-4-[(3-methoxy-2-pyridyl)methyl]piperazine;

1-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-4-[(4-methoxy-3,5-dimethyl-2-pyridyl)methyl]piperazine;

1-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-4-[(5-methyl-2-pyridyl)methyl]piperazine;

1-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-4-[[4-(trifluoromethyl)-2-pyridyl]methyl]piperazine;

1-[(3-chloro-5-fluoro-2-pyridyl)methyl]-4-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazine;

1-[(4,5-dimethoxy-2-pyridyl)methyl]-4-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazine;

1-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-4-[(4-methoxy-3-methyl-2-pyridyl)methyl]piperazine;

6-[[4-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]pyridine-3-carbonitrile;

1-[(4-chloro-5-fluoro-2-pyridyl)methyl]-4-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazine;

1-[(3,5-difluoro-2-pyridyl)methyl]-4-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]piperazine;

1-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-4-[1-(2-pyridyl)ethyl]piperazine;

[(2S)-4-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-2-methyl-piperazin-1-yl]-(2-pyridyl)methanone;

2-[[4-[2-fluoro-3-isobutyl-6-(2H-tetrazol-5-yl)phenyl]piperazin-1-yl]methyl]-5-methyl-thiazole;

2-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)-3-pyridyl]piperazin-1-yl]methyl]-5-methyl-thiazole;

1-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-4-(pyridazin-3-ylmethyl)-1,4-diazepane;

5-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-2-(pyridazin-3-ylmethyl)-1,3,3a,4,6,6a-hexahydropyrrolo[3,4-c]pyrrole;

5-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-2-(pyridazin-3-ylmethyl)-1,3,3a,4,6,6a-hexahydropyrrolo[3,4-c]pyrrole;

3-[[4-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-1-piperidyl]methyl]pyridazine;

3-[[3-[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]pyrrolidin-1-yl]methyl]pyridazine;

1-(5-isobutyl-2-(2H-tetrazol-5-yl)phenyl)-N-(pyridazin-3-ylmethyl)azetidin-3-amine;

2-((1-(3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl)piperidin-4-yl)methyl)pyridine;

3-[[4-[[5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]methyl]piperazin-1-yl]methyl]pyridazine;

(5-isobutyl-2-(2H-tetrazol-5-yl)phenyl)(4-(pyridazin-3-ylmethyl)piperazin-1-yl)methanone;

2-ethyl-3-[[1-[2-(2H-tetrazol-5-yl)phenyl]-4-piperidyl]methyl]quinazolin-4-one;

2-[4-[(2-ethyl-4-oxo-quinazolin-3-yl)methyl]-1-piperidyl]-N-ethylsulfonyl-benzamide;

2-ethyl-6-nitro-3-[[1-[2-(2H-tetrazol-5-yl)phenyl]-4-piperidyl]methyl]quinazolin-4-one;

N-[2-ethyl-4-oxo-3-[[1-[2-(2H-tetrazol-5-yl)phenyl]-4-piperidyl]methyl]quinazolin-6-yl]-N-propyl-thiophene-2-carboxamide;

N-[2-ethyl-4-oxo-3-[[1-[2-(2H-tetrazol-5-yl)phenyl]-4-piperidyl]methyl]quinazolin-6-yl]-N-(3-pyridylmethyl)thiophene-2-carboxamide;

N-[2-ethyl-4-oxo-3-[[1-[2-(2H-tetrazol-5-yl)phenyl]-4-piperidyl]methyl]quinazolin-6-yl]benzamide;

N-benzyl-N-[2-ethyl-4-oxo-3-[[1-[2-(2H-tetrazol-5-yl)phenyl]-4-piperidyl]methyl]quinazolin-6-yl]thiophene-2-carboxamide;

N-[2-ethyl-4-oxo-3-[[1-[2-(2H-tetrazol-5-yl)phenyl]-4-piperidyl]methyl]quinazolin-6-yl]cyclopropanecarboxamide;

N-[(2-chlorophenyl)methyl]-N-[2-ethyl-4-oxo-3-[[1-[2-(2H-tetrazol-5-yl)phenyl]-4-piperidyl]methyl]quinazolin-6-yl]thiophene-2-carboxamide;

2-phenyl-3-[[1-[2-(1H-tetrazol-5-yl)phenyl]-4-piperidyl]methyl]quinazolin-4-one;

3-[[(2S)-4-[5-(1,2-dideuterio-2-methyl-propyl)-3-f(luoro-2-(2H-tetrazol-5-yl)phenyl]-2-methyl-piperazin-1-yl]methyl]pyridazine; and

2,2,3,3,5,6,6-heptadeuterio-1-[3-fluoro-5-isobutyl-2-(2H-tetrazol-5-yl)phenyl]-4-(pyridazin-3-ylmethyl)-5-(trideuteriomethyl)piperazine;

or a pharmaceutically acceptable salt thereof.

13. A pharmaceutical composition comprising the compound of any one of claims 1-12, and optionally a pharmaceutically acceptable carrier.

14. Use of the compound of any one of claims 1-12, or the pharmaceutical composition of claim 13, in the manufacture of a medicament for the prevention, treatment and/or management of pain, in particular chronic pain, such as neuropathic pain.

15. The use of claim 14, wherein the pain is diabetic peripheral neuropathic pain.

16. Use of the compound of any one of claims 1-12, or the pharmaceutical composition of claim 13, in the manufacture of a medicament for treating or preventing chronic pain.

17. The use of claim 16, wherein the pain is diabetic peripheral neuropathic pain.

18. The compound of any one of claims 1-12, or the pharmaceutical composition of claim 13, for use in therapy.