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Filla et al.

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[54] **5-HT<sub>1F</sub> AGONISTS**

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- [60] Provisional application No. 60/030,950 Nov. 15, 1996.
- [51] **Int. Cl.<sup>6</sup>** ..... **A61K 31/44**; C07D 471/04
- [52] **U.S. Cl.** ..... **514/300**; 544/58.4; 544/127; 546/113
- [58] **Field of Search** ..... 546/113; 514/300

[56] **References Cited**

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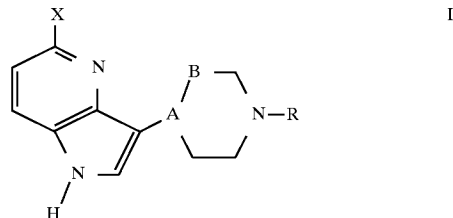
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[57] **ABSTRACT**

This invention provides 5-HT<sub>1F</sub> agonists of Formula I:



where A—B, X, and R are as defined in the specification. The invention also encompasses pharmaceutical formulations employing compounds of Formula I as well as methods of treating conditions associated with 5-HT<sub>1F</sub> activation employing these compounds or compositions. The invention also provides intermediates useful for the preparation of the compounds of Formula I.

**13 Claims, No Drawings**

5-HT<sub>1F</sub> AGONISTS

## CROSS-REFERENCE

This application claims the benefit of U.S. Provisional application Ser. No. 60/030,950, filed Nov. 15, 1996.

## BACKGROUND OF THE INVENTION

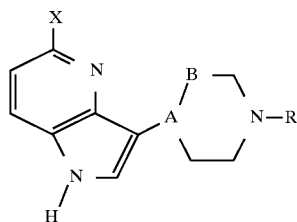
Serotonin (5-HT) exhibits diverse physiological activity mediated by at least seven receptor classes, the most heterogeneous of which appears to be 5-HT<sub>1</sub>. A human gene which expresses one of these 5-HT<sub>1</sub> receptor subtypes, named 5-HT<sub>1F</sub>, was isolated by Kao and coworkers (*Proc. Natl. Acad. Sci. USA*, 90, 408-412 (1993)). This 5-HT<sub>1F</sub> receptor exhibits a pharmacological profile distinct from any serotonergic receptor yet described.

Moskowitz has proposed that currently unknown triggers for pain stimulate trigeminal ganglia which innervate vasculature within the cephalic tissue, giving rise to release of vasoactive neuropeptides from axons on the vasculature. These released neuropeptides then activate a series of events, a consequence of which is pain. This neurogenic inflammation is blocked by sumatriptan and ergot alkaloids by mechanisms involving 5-HT receptors, believed to be closely related to the 5-HT<sub>1D</sub> subtype, located on the trigeminovascular fibers (*Neurology*, 43(suppl. 3), S16-S20 (1993)). It has been demonstrated that agonists of the 5-HT<sub>1F</sub> receptor inhibit peptide extravasation due to stimulation of the trigeminal ganglia (Audia and Nissen, U.S. Pat. No. 5,521,196).

Compounds which exhibit affinity for the 5-HT<sub>1F</sub> receptor provide a new approach for the treatment of diseases linked to abnormal serotonergic neurotransmission. Furthermore, compounds selective for the 5-HT<sub>1F</sub> receptor subtype are potentially useful for treating such diseases while causing fewer undesired side effects.

## SUMMARY OF THE INVENTION

The present invention provides 5-substituted-3-(piperidin-4-yl)- and 5-substituted-3-(1,2,3,6-tetrahydropyridin-4-yl)pyrrolo[3,2-b]pyridines of Formula I:



in which

A—B is —C=CH— or —CH—CH<sub>2</sub>—;

R is H, C<sub>1</sub>–C<sub>6</sub> alkyl, benzyl, or phenylethyl;

X is —NR<sup>1</sup>SO<sub>2</sub>R<sup>2</sup>, —NHC(Q)NR<sup>3</sup>R<sup>4</sup>, —NHC(O)OR<sup>5</sup>, or —NR<sup>1</sup>C(O)R<sup>6</sup> where:

Q is O, or S;

R<sup>1</sup> is H or C<sub>1</sub>–C<sub>4</sub> alkyl;

R<sup>2</sup> is C<sub>1</sub>–C<sub>4</sub> alkyl, phenyl or substituted phenyl;

R<sup>3</sup> and R<sup>4</sup> are independently selected from the group consisting of H, C<sub>1</sub>–C<sub>6</sub> alkyl, C<sub>3</sub>–C<sub>6</sub> alkenyl, C<sub>3</sub>–C<sub>8</sub> cycloalkyl, phenyl, substituted phenyl, phenyl (C<sub>1</sub>–C<sub>4</sub> alkylene), phenyl(C<sub>1</sub>–C<sub>4</sub> alkylene) substituted in the phenyl ring, ((C<sub>1</sub>–C<sub>4</sub> alkyl or C<sub>1</sub>–C<sub>4</sub>

alkoxycarbonyl substituted)C<sub>1</sub>–C<sub>4</sub> alkyl)phenyl, C<sub>1</sub>–C<sub>4</sub> alkyl α-substituted with C<sub>1</sub>–C<sub>4</sub> alkoxycarbonyl, heteroaryl; or

R<sup>3</sup> and R<sup>4</sup> taken together with the nitrogen atom to which they are attached form a pyrrolidine, piperidine, piperazine, 4-substituted piperazine, morpholine or thiomorpholine ring;

R<sup>5</sup> is C<sub>1</sub>–C<sub>6</sub> alkyl, C<sub>3</sub>–C<sub>6</sub> alkenyl, phenyl, substituted phenyl, C<sub>3</sub>–C<sub>8</sub> cycloalkyl, C<sub>1</sub>–C<sub>4</sub> alkyl ω-substituted with C<sub>1</sub>–C<sub>4</sub> alkoxy;

R<sup>6</sup> is C<sub>1</sub>–C<sub>10</sub> alkyl, substituted C<sub>1</sub>–C<sub>10</sub> alkyl, C<sub>2</sub>–C<sub>10</sub> alkenyl, C<sub>2</sub>–C<sub>10</sub>alkynyl, C<sub>3</sub>–C<sub>8</sub> cycloalkyl, phenyl, substituted phenyl, naphthyl, phenyl(C<sub>1</sub>–C<sub>4</sub> alkylene), phenyl(C<sub>1</sub>–C<sub>4</sub> alkylene) substituted on the phenyl ring, 2-phenylethylen-1-yl, diphenylmethyl, benzofused C<sub>4</sub>–C<sub>8</sub> cycloalkyl, C<sub>1</sub>–C<sub>4</sub> alkylene ω-substituted with C<sub>3</sub>–C<sub>6</sub> cycloalkyl, or a heterocycle; and pharmaceutically acceptable acid addition salts and solvates thereof.

This invention also provides a pharmaceutical formulation which comprises, in association with a pharmaceutically acceptable carrier, diluent or excipient, a compound of Formula I.

A further embodiment of this invention is a method for increasing activation of the 5-HT<sub>1F</sub> receptor for treating a variety of disorders which have been linked to decreased neurotransmission of serotonin in mammals. Included among these disorders are depression, migraine pain, bulimia, premenstrual syndrome or late luteal phase syndrome, alcoholism, tobacco abuse, panic disorder, anxiety, general pain, chronic pain, post-traumatic syndrome, memory loss, dementia of aging, social phobia, attention deficit hyperactivity disorder, disruptive behavior disorders, impulse control disorders, borderline personality disorder, obsessive compulsive disorder, chronic fatigue syndrome, premature ejaculation, erectile difficulty, anorexia nervosa, disorders of sleep, autism, mutism, allergic rhinitis, trichotillomania, trigeminal neuralgia, dental pain or temporomandibular joint dysfunction pain. The compounds of this invention are also useful as a prophylactic treatment for migraine. Any of these methods employ a compound of Formula I.

The use of a compound of Formula I for the activation of the 5-HT<sub>1F</sub> receptor, for the inhibition of peptide extravasation in general or due to stimulation of the trigeminal ganglia specifically, and for the treatment of any of the disorders described supra, are all embodiments of the present invention.

The present invention also includes intermediates useful for the preparation of compounds of Formula I.

## DETAILED DESCRIPTION OF THE INVENTION

The general chemical terms used in the formulae above have their usual meanings. For example, the term "alkyl" includes such groups as methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, sec-butyl, tert-butyl, pentyl, 2-pent-yl-, 3-pent-yl-, neopentyl, hexyl, heptyl, octyl and the like. The term "alkoxy" includes such groups as methoxy, ethoxy, isopropoxy, sec-butoxy, tert-butoxy, 2-pentoxy-, 3-hexyloxy, heptyloxy, octyloxy, and the like. The term "alkylthio" includes such groups as methylthio, ethylthio, isopropylthio, sec-butylthio, tert-butylthio, and the like. The term "alkenyl" includes vinyl, allyl, 1-buten-4-yl, 2-buten-4-yl, 1-penten-5-yl, 2-penten-5-yl, 3-penten-5-yl, 1-hexen-6-yl, 2-hexen-6-yl, 3-hexen-6-yl, 4-hexen-6-yl and the like. The term "alkynyl" includes acetylenyl, propynyl, 2-butyln-

4-yl, 1-butyn-4-yl, 1-pentyn-5-yl, 2-pentyn-5-yl and the like. The term “acyl” includes, for example, formyl, acetyl, propanoyl, butanoyl, and 2-methylpropanoyl. The term “cycloalkyl” includes such groups as cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl and cyclooctyl. The term “phenyl(C<sub>1</sub>-C<sub>4</sub> alkylene)” includes such groups as benzyl, phenethyl, phenpropyl and phenbutyl. The term “(C<sub>1</sub>-C<sub>4</sub> alkyl)sulfonyl” includes methanesulfonyl, ethanesulfonyl, propanesulfonyl, isopropanesulfonyl, butanesulfonyl and the like. The term “halo” includes fluoro, chloro, bromo and iodo.

The term “substituted alkyl” is taken to mean an alkyl moiety substituted with up to three substituents selected from the group consisting of hydroxy, C<sub>1</sub>-C<sub>4</sub> alkoxy, halo, aryloxy, C<sub>1</sub>-C<sub>4</sub> alkoxy, carbonyl and heteroaryloxy.

The term “substituted phenyl” or “phenyl(C<sub>1</sub>-C<sub>4</sub> alkylene) substituted in the phenyl ring” is taken to mean the phenyl moiety may be substituted with one substituent selected from the group consisting of halo, C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>1</sub>-C<sub>8</sub> alkoxy, C<sub>1</sub>-C<sub>4</sub> alkylthio, nitro, cyano, di(C<sub>1</sub>-C<sub>4</sub> alkyl)amino, trifluoromethyl, trifluoromethoxy, phenyl, C<sub>1</sub>-C<sub>4</sub> acyl, benzoyl or (C<sub>1</sub>-C<sub>4</sub> alkyl)sulfonyl, or two to three substituents independently selected from the group consisting of halo, nitro, C<sub>1</sub>-C<sub>4</sub> alkyl, or C<sub>1</sub>-C<sub>4</sub> alkoxy.

The term “heterocycle” is taken to mean stable aromatic and non-aromatic 5- and 6-membered rings containing carbon and from 1 to 3 heteroatoms selected from the group consisting of nitrogen, oxygen and sulfur, said rings being optionally monobenzofused. All of these rings may be substituted with up to three substituents independently selected from the group consisting of halo, C<sub>1</sub>-C<sub>4</sub> alkoxy, C<sub>1</sub>-C<sub>4</sub> alkyl, cyano, nitro, hydroxy, —S(O)<sub>n</sub>-(C<sub>1</sub>-C<sub>4</sub> alkyl) and —S(O)<sub>n</sub>-phenyl where n is 0, 1 or 2. Where tautomers are possible, all tautomeric forms are contemplated by the present invention. Non-aromatic rings include, for example, pyrrolidinyl, piperidinyl, piperazinyl, tetrahydrofuryl, oxazolidinyl, dioxanyl, pyranal, and the like. Benzofused non-aromatic rings include indolinyl, 1,2,3,4-tetrahydroquinolinyl, 1,2,3,4-tetrahydroisoquinolinyl and the like. Aromatic rings include furyl, thienyl, pyridinyl, pyridinyl-N-oxide, pyrrolyl, N-methylpyrrolyl, oxazolyl, isoxazolyl, pyrazolyl, imidazolyl, triazolyl, oxadiazolyl, thiadiazolyl, thiazolyl, pyrimidinyl, pyrazinyl, pyridazinyl, and the like. Benzofused aromatic rings include isoquinolinyl, isoquinolinyl-N-oxide, benzoxazolyl, benzthiazolyl, quinolinyl, quinolinyl-N-oxide, benzofuranyl, thionaphthyl, indolyl and the like.

The term “heteroaryl” is taken to mean an aromatic or benzofused aromatic heterocycle as defined in the previous paragraph. The term “substituted heteroaryl” is taken to mean an aromatic or benzofused aromatic heterocycle as defined in the previous paragraph substituted with up to three substituents independently selected from the group consisting of halo, C<sub>1</sub>-C<sub>4</sub> alkoxy, C<sub>1</sub>-C<sub>4</sub> alkyl, cyano, nitro, hydroxy, —S(O)<sub>n</sub>-(C<sub>1</sub>-C<sub>4</sub> alkyl) and —S(O)<sub>n</sub>-phenyl where n is 0, 1 or 2. Where tautomers are possible, all tautomeric forms are contemplated by the present invention. The term “heteroaryl(C<sub>1</sub>-C<sub>4</sub> alkyl)” is taken to mean a branched or linear alkyl chain of 1 to 4 carbon atoms substituted at some point with an aromatic or benzofused aromatic heterocycle moiety. The term “substituted heteroaryl(C<sub>1</sub>-C<sub>4</sub> alkyl)” is taken to mean a branched or linear alkyl chain of 1 to 4 carbon atoms substituted at some point with an aromatic or benzofused aromatic heterocycle moiety which is substituted with up to three substituents independently selected from the group consisting of halo, C<sub>1</sub>-C<sub>4</sub> alkoxy, C<sub>1</sub>-C<sub>4</sub> alkyl, cyano, nitro, hydroxy, —S(O)<sub>n</sub>-(C<sub>1</sub>-C<sub>4</sub> alkyl) and —S(O)<sub>n</sub>-phenyl where n is 0, 1 or 2.

The term “heteroaryloxy” is taken to mean a heteroaryl or substituted heteroaryl group, as defined in the previous paragraph, bonded to an oxygen atom.

The term “aryloxy” is taken to mean a phenyl or substituted phenyl group bonded to an oxygen atom.

The term “4-substituted piperazine” is taken to mean a piperazine ring substituted at the 4-position with a substituent selected from the group consisting of C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>4</sub> alkoxy substituted C<sub>1</sub>-C<sub>6</sub> alkyl, phenyl, substituted phenyl, phenyl(C<sub>1</sub>-C<sub>4</sub> alkylene), phenyl(C<sub>1</sub>-C<sub>4</sub> alkylene) substituted in the phenyl ring, heteroaryl, and heteroaryl (C<sub>1</sub>-C<sub>4</sub> alkylene).

The term “benzofused C<sub>4</sub>-C<sub>8</sub> cycloalkyl” is taken to mean a C<sub>4</sub>-C<sub>8</sub> cycloalkyl group fused to a phenyl ring. Examples of these groups include benzocyclobutyl, indanyl, 1,2,3,4-tetrahydronaphthyl, and the like.

While all of the compounds of this invention are useful as 5-HT<sub>1F</sub> agonists, certain classes are preferred. The following paragraphs describe such preferred classes.

- aa) R is hydrogen;
- ab) R is methyl;
- ac) X is —NR<sup>1</sup>SO<sub>2</sub>R<sup>2</sup>;
- ad) X is —NHC(Q)NR<sup>3</sup>R<sup>4</sup>;
- ae) X is —NHC(O)OR<sup>5</sup>;
- af) X is —NR<sup>1</sup>C(O)R<sup>6</sup>;
- ag) Q is O;
- ah) R<sup>1</sup> is H;
- ai) R<sup>2</sup> is phenyl;
- aj) R<sup>3</sup> is H;
- ak) R<sup>4</sup> is C<sub>1</sub>-C<sub>4</sub> alkyl;
- al) R<sup>4</sup> is methyl;
- am) R<sup>4</sup> is phenyl;
- an) R<sup>4</sup> is C<sub>3</sub>-C<sub>8</sub> alkenyl;
- ao) R<sup>4</sup> is allyl;
- ap) R<sup>4</sup> is phenyl monosubstituted with halo;
- aq) R<sup>4</sup> is 4-fluorophenyl;
- ar) R<sup>4</sup> is heteroaryl;
- as) R<sup>4</sup> is 4-pyridyl;
- at) R<sup>5</sup> is C<sub>1</sub>-C<sub>4</sub> alkyl;
- au) R<sup>5</sup> is methyl;
- av) R<sup>5</sup> is ethyl;
- aw) R<sup>5</sup> is propyl;
- ax) R<sup>6</sup> is C<sub>1</sub>-C<sub>10</sub> alkyl;
- ay) R<sup>6</sup> is C<sub>1</sub>-C<sub>4</sub> alkyl;
- az) R<sup>6</sup> is methyl;
- ba) R<sup>6</sup> is ethyl;
- bb) R<sup>6</sup> is propyl;
- bc) R<sup>6</sup> is C<sub>3</sub>-C<sub>6</sub> alkenyl;
- bd) R<sup>6</sup> is allyl;
- be) R<sup>6</sup> is C<sub>3</sub>-C<sub>6</sub> cycloalkyl;
- bf) R<sup>6</sup> is cyclopropyl;
- bg) R<sup>6</sup> is cyclobutyl;
- bd) R<sup>6</sup> is phenyl;
- be) R<sup>6</sup> is phenyl monosubstituted with halo;
- bf) R<sup>6</sup> is phenyl monosubstituted with fluoro;
- bg) R<sup>6</sup> is 4-fluorophenyl;
- bh) R<sup>6</sup> is phenyl monosubstituted with nitro;
- bi) R<sup>6</sup> is phenyl monosubstituted with cyano;
- bj) R<sup>6</sup> is 4-nitrophenyl;

- bk) R<sup>6</sup> is 4-cyanophenyl;  
 bl) R<sup>6</sup> is a heterocycle;  
 bm) R<sup>6</sup> is furyl optionally substituted with C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>1</sub>-C<sub>4</sub> alkoxy, or halo;  
 bn) R<sup>6</sup> is 3-furyl;  
 bo) R<sup>6</sup> is thienyl optionally substituted with halo, C<sub>1</sub>-C<sub>4</sub> alkyl or C<sub>1</sub>-C<sub>4</sub> alkoxy;  
 bp) R<sup>6</sup> is 3-thienyl;  
 bq) R<sup>6</sup> is pyridinyl optionally substituted with halo, C<sub>1</sub>-C<sub>4</sub> alkyl or C<sub>1</sub>-C<sub>4</sub> alkoxy;  
 br) R<sup>6</sup> is 4-pyridinyl;  
 bs) A—B is —C=CH—;  
 bt) A—B is —CH—CH<sub>2</sub>—;  
 bu) The compound is a free base;  
 bv) The compound is a salt;  
 bw) The compound is the hydrochloride salt;  
 bx) The compound is the fumarate salt.

It will be understood that the above classes may be combined to form additional preferred classes.

The compounds of the present invention may, depending upon their structure and manner of synthesis and isolation, exist as a pharmaceutically acceptable solvate. These solvates include water, methanol, and ethanol. Solvated forms of the compounds of the present invention represent a further embodiment of the present invention.

The compounds of this invention are useful in a method for increasing activation of the 5-HT<sub>1F</sub> receptor for treating a variety of disorders which have been linked to decreased neurotransmission of serotonin in mammals. It is preferred that the mammal to be treated by the administration of compounds of this invention is human.

Since the compounds of this invention are amines, they are basic in nature and accordingly react with any of a number of inorganic and organic acids to form pharmaceutically acceptable acid addition salts. It is preferable to convert the free amines to their pharmaceutically acceptable acid addition salts for ease of handling and administration. Acids commonly employed to form such salts are inorganic acids such as hydrochloric acid, hydrobromic acid, hydroiodic acid, sulfuric acid, phosphoric acid, and the like, and organic acids, such as p-toluenesulfonic acid, methanesulfonic acid, oxalic acid, p-bromophenylsulfonic acid, carbonic acid, succinic acid, citric acid, benzoic acid, acetic acid and the like. Examples of such pharmaceutically acceptable salts thus are the sulfate, pyrosulfate, bisulfate, sulfite, bisulfite, phosphate, monohydrogenphosphate, dihydrogenphosphate, metaphosphate, pyrophosphate, chloride, bromide, iodide, acetate, propionate, decanoate, caprylate, acrylate, formate, isobutyrate, caproate, heptanoate, propionate, oxalate, malonate, succinate, suberate, sebacate, fumarate, maleate, butyne-1,4-dioate, hexyne-1,6-dioate, benzoate, chlorobenzoate, methylbenzoate, dinitrobenzoate, hydroxybenzoate, methoxybenzoate, phthalate, sulfonate, xylenesulfonate, phenylacetate, phenylpropionate, phenylbutyrate, citrate, lactate, β-hydroxybutyrate, glycollate, tartrate, methanesulfonate, propanesulfonate, naphthalene-1-sulfonate, naphthalene-2-sulfonate, mandelate and the like. Preferred pharmaceutically acceptable salts are those formed with hydrochloric acid or fumaric acid.

The following group is illustrative of compounds contemplated within the scope of this invention:

- N-propyl-N'-(3-(1-(2-pentyl)-1,2,3,4-tetrahydropyridin-4-yl)pyrrolo[3,2-b]pyridin-5-yl)thiourea decanoate  
 N-butyl-N'-(3-(1-isopropylpiperidin-4-yl)pyrrolo[3,2-b]pyridin-5-yl)thiourea acrylate

- N-(2-methoxy)phenyl-N'-(3-(1-(sec-butyl)-1,2,3,4-tetrahydropyridin-4-yl)pyrrolo[3,2-b]pyridin-5-yl)thiourea formate  
 N-(4-propoxy)phenyl-N'-(3-(1-ethylpiperidin-4-yl)pyrrolo[3,2-b]pyridin-5-yl)thiourea isobutyrate  
 N-(2-butoxy)phenyl-N'-(3-(1-hexylpiperidin-4-yl)pyrrolo[3,2-b]pyridin-5-yl)thiourea fumarate  
 N-(2,3-dibromo)phenyl-N'-(3-(1-isopropylpiperidin-4-yl)pyrrolo[3,2-b]pyridin-5-yl)thiourea caproate  
 N-(2-bromo-3-iodo)phenyl-N'-(3-(1-(2-pentyl)piperidin-4-yl)pyrrolo[3,2-b]pyridin-5-yl)thiourea heptanoate  
 N-(3-phenpropyl)-N'-(3-(1-(sec-butyl)piperidin-4-yl)pyrrolo[3,2-b]pyridin-5-yl)thiourea propionate  
 N-(4-trifluoromethyl)phenyl-N'-(3-(1-neopentyl-1,2,3,4-tetrahydropyridin-4-yl)pyrrolo[3,2-b]pyridin-5-yl)thiourea oxalate  
 N-(4-phenyl)phenyl-N'-(3-(1-pentylpiperidin-4-yl)pyrrolo[3,2-b]pyridin-5-yl)thiourea malonate  
 N-hexyl-N'-(3-(1-propylpiperidin-4-yl)pyrrolo[3,2-b]pyridin-5-yl)urea succinate  
 N-(2-buten-4-yl)-N'-(3-(1-butylpiperidin-4-yl)pyrrolo[3,2-b]pyridin-5-yl)urea suberate  
 N-(3-hexen-6-yl)-N'-(3-(1-(3-pentyl)piperidin-4-yl)pyrrolo[3,2-b]pyridin-5-yl)urea sebacate  
 N-cyclopropyl-N'-(3-(1-hexyl-1,2,3,4-tetrahydropyridin-4-yl)pyrrolo[3,2-b]pyridin-5-yl)urea fumarate  
 N-cyclopentyl-N'-(3-(1-(3-pentyl)piperidin-4-yl)pyrrolo[3,2-b]pyridin-5-yl)urea maleate  
 N-cyclooctyl-N'-(3-(1-(tert-butyl)piperidin-4-yl)pyrrolo[3,2-b]pyridin-5-yl)urea malonate  
 N-(2-chloro)phenyl-N'-(3-(1-butylpiperidin-4-yl)pyrrolo[3,2-b]pyridin-5-yl)urea mandelate  
 N-(3-phenyl)phenyl-N'-(3-(1-propyl-1,2,3,4-tetrahydropyridin-4-yl)pyrrolo[3,2-b]pyridin-5-yl)urea butyne-1,4-dioate  
 N-(2-ethoxy)phenyl-N'-(3-(1-neopentylpiperidin-4-yl)pyrrolo[3,2-b]pyridin-5-yl)urea hexyne-1,6-dioate  
 N-(4-isopropoxy)phenyl-N'-(3-(1-isobutylpiperidin-4-yl)pyrrolo[3,2-b]pyridin-5-yl)urea benzoate  
 N-(2-formyl)phenyl-N'-(3-(1-(3-pentyl)piperidin-4-yl)pyrrolo[3,2-b]pyridin-5-yl)urea 4-chlorobenzoate  
 N-(3-propanoyl)phenyl-N'-(3-(1-pentylpiperidin-4-yl)pyrrolo[3,2-b]pyridin-5-yl)urea 2-methylbenzoate  
 N-(3-ethylthio)phenyl-N'-(3-(1-propylpiperidin-4-yl)pyrrolo[3,2-b]pyridin-5-yl)urea 2,4-dinitrobenzoate  
 N-(3-isopropylthio)phenyl-N'-(3-(1-isopropylpiperidin-4-yl)pyrrolo[3,2-b]pyridin-5-yl)urea 3-hydroxybenzoate  
 N-(2-methyl)phenyl-N'-(3-(1-propylpiperidin-4-yl)pyrrolo[3,2-b]pyridin-5-yl)urea 4-methoxybenzoate  
 N-(3-isopropyl)phenyl-N'-(3-(1-isopropylpiperidin-4-yl)pyrrolo[3,2-b]pyridin-5-yl)urea phthalate  
 N-(2-ethoxycarbonyl)phenyl-N'-(3-(1-(tert-butyl)piperidin-4-yl)pyrrolo[3,2-b]pyridin-5-yl)urea sulfonate  
 N-(2-butoxycarbonyl)phenyl-N'-(3-(1-propylpiperidin-4-yl)pyrrolo[3,2-b]pyridin-5-yl)urea  
 N-(3,4-difluoro)phenyl-N'-(3-(1-butylpiperidin-4-yl)pyrrolo[3,2-b]pyridin-5-yl)urea  
 N-(3-chloro-4-bromo)phenyl-N'-(3-(1-(3-pentyl)piperidin-4-yl)pyrrolo[3,2-b]pyridin-5-yl)urea  
 N-(3-phenpropyl)-N'-(3-(1-propylpiperidin-4-yl)pyrrolo[3,2-b]pyridin-5-yl)urea



N-ethyl-N-phenyl-N'-(3-(1-butylpiperidin-4-yl)pyrrolo[3,2-b]pyridin-5-yl)urea  
 N-isopropyl-N-phenyl-N'-(3-(1-(sec-butyl)piperidin-4-yl)pyrrolo[3,2-b]pyridin-5-yl)urea  
 N-ethyl-N-methyl-N'-(3-(1-(2-pentyl)piperidin-4-yl)pyrrolo[3,2-b]pyridin-5-yl)urea<sup>5</sup>  
 N-methyl-N-isopropyl-N'-(3-(1-neopentylpiperidin-4-yl)pyrrolo[3,2-b]pyridin-5-yl)urea  
 N,N-diisopropyl-N'-(3-(1-butylpiperidin-4-yl)pyrrolo[3,2-b]pyridin-5-yl)urea<sup>10</sup>  
 5-butoxycarbonylamino-3-(1-propyl-1,2,3,4-tetrahydropyridin-4-yl)pyrrolo[3,2-b]pyridine  
 5-(2-buten-4-yloxy)carbonylamino-3-(1,2,3,4-tetrahydropyridin-4-yl)pyrrolo[3,2-b]pyridine<sup>15</sup>  
 5-(2-penten-5-yloxy)carbonylamino-3-(1-(sec-butyl)piperidin-4-yl)pyrrolo[3,2-b]pyridine  
 5-(3-chlorophenoxy)carbonylamino-3-(1-hexylpiperidin-4-yl)pyrrolo[3,2-b]pyridine  
 5-(2-methoxyphenoxy)carbonylamino-3-(1-hexylpiperidin-4-yl)-2-pyrrolo[3,2-b]pyridine citrate<sup>20</sup>  
 5-(3-butoxyphenoxy)carbonylamino-3-(1-neopentylpiperidin-4-yl)pyrrolo[3,2-b]pyridine  
 5-cyclopropoxycarbonylamino-3-(1-(tert-butyl)piperidin-4-yl)pyrrolo[3,2-b]pyridine<sup>25</sup>  
 5-cyclohexyloxycarbonylamino-3-(1-isobutylpiperidin-4-yl)pyrrolo[3,2-b]pyridine  
 5-cyclooctyloxycarbonylamino-3-(1-isopropylpiperidin-4-yl)pyrrolo[3,2-b]pyridine<sup>30</sup>  
 5-(propoxyethoxy)carbonylamino-3-(1-ethylpiperidin-4-yl)pyrrolo[3,2-b]pyridine  
 5-(4-methoxybutoxy)carbonylamino(1-ethylpiperidin-4-yl)pyrrolo[3,2-b]pyridine  
 5-(propanoyl)amino-3-(1-neopentylpiperidin-4-yl)pyrrolo[3,2-b]pyridine mandelate<sup>35</sup>  
 5-(2-methylpropanoyl)amino-3-(1-(3-pentyl)piperidin-4-yl)pyrrolo[3,2-b]pyridine  
 5-(2-methyl-4-butyn-1-oyl)amino-3-(1-(tert-butyl)piperidin-4-yl)pyrrolo[3,2-b]pyridine<sup>40</sup>  
 5-(2-methylbutanoyl)-N-methylamino-3-(1-ethylpiperidin-4-yl)pyrrolo[3,2-b]pyridine phenylacetate  
 5-(hex-3-enoyl)amino-3-(1-propylpiperidin-4-yl)pyrrolo[3,2-b]pyridine<sup>45</sup>  
 5-(cyclohexaneacetyl)amino-3-(1-isopropylpiperidin-4-yl)pyrrolo[3,2-b]pyridine  
 5-(cycloheptylcarbonyl)amino-3-(1-butylpiperidin-4-yl)pyrrolo[3,2-b]pyridine phenylpropionate<sup>50</sup>  
 5-(4-phenylbutanoyl)amino-3-(1-isopropyl-1,2,3,4-tetrahydropyridin-4-yl)pyrrolo[3,2-b]pyridine phenylbutyrate  
 5-(5-phenoxypanoyl)amino-3-(1-neopentyl-1,2,3,4-tetrahydropyridin-4-yl)pyrrolo[3,2-b]pyridine citrate<sup>55</sup>  
 5-(5-methoxypanoyl)amino-3-(1-isopropylpiperidin-4-yl)pyrrolo[3,2-b]pyridine lactate  
 5-((3-propoxycarbonyl)propanoyl)amino-3-(1-isobutylpiperidin-4-yl)pyrrolo[3,2-b]pyridine<sup>60</sup>  
 5-((5-methoxycarbonyl)pentanoyl)amino-3-(1-isopropylpiperidin-4-yl)pyrrolo[3,2-b]pyridine β-hydroxybutyrate  
 5-(benzoyl-N-ethyl)amino-3-(1-ethylpiperidin-4-yl)pyrrolo[3,2-b]pyridine glycollate<sup>65</sup>  
 5-benzoylamino-3-(1-propylpiperidin-4-yl)pyrrolo[3,2-b]pyridine tartrate

5-benzoylamino-3-(1-isopropylpiperidin-4-yl)pyrrolo[3,2-b]pyridine  
 5-benzoylamino-3-(1-(tert-butyl)-1,2,3,4-tetrahydropyridin-4-yl)pyrrolo[3,2-b]pyridine hydrochloride  
 5-(4-fluorobenzoyl)amino-3-(1-ethyl-1,2,3,4-tetrahydropyridin-4-yl)pyrrolo[3,2-b]pyridine  
 5-(4-(formyl)benzoyl)amino-3-(1-(sec-butyl)piperidin-4-yl)pyrrolo[3,2-b]pyridine  
 5-(3-(butanoyl)benzoyl)amino-3-(1-methylpiperidin-4-yl)pyrrolo[3,2-b]pyridine  
 5-(2-(butanoyl)benzoyl)amino-3-(1-neopentylpiperidin-4-yl)pyrrolo[3,2-b]pyridine  
 5-(2-(benzoyl)benzoyl)amino-3-(1-pentylpiperidin-4-yl)pyrrolo[3,2-b]pyridine  
 5-(2-(methanesulfonyl)benzoyl)amino-3-(1-butylpiperidin-4-yl)pyrrolo[3,2-b]pyridine  
 5-(3-phenylbenzoyl)amino-3-(1-(tert-butyl)piperidin-4-yl)pyrrolo[3,2-b]pyridine  
 5-(2,3-dibromo)benzoyl-N-isopropylamino-3-(1-isopropylpiperidin-4-yl)pyrrolo[3,2-b]pyridine  
 5-(2-bromo-3-iodo)benzoylamino-3-(1-(2-pentyl)piperidin-4-yl)pyrrolo[3,2-b]pyridine  
 5-(2-thiophenecarbonyl)-N-butylamino-3-(1-ethylpiperidin-4-yl)pyrrolo[3,2-b]pyridine  
 5-(2-thiophenecarbonyl)amino-3-(1-isopropylpiperidin-4-yl)pyrrolo[3,2-b]pyridine  
 5-(2-thiophenecarbonyl)amino-3-(1-(tert-butyl)piperidin-4-yl)pyrrolo[3,2-b]pyridine  
 5-(2-thiophenecarbonyl)amino-3-(1-hexylpiperidin-4-yl)pyrrolo[3,2-b]pyridine  
 5-(3-thiophenecarbonyl)amino-3-(1-ethylpiperidin-4-yl)pyrrolo[3,2-b]pyridine  
 5-(2-furoyl)amino-3-(1-isopropyl-1,2,3,4-tetrahydropyridin-4-yl)pyrrolo[3,2-b]pyridine  
 5-(2-furoyl)amino-3-(1-butyl-1,2,3,4-tetrahydropyridin-4-yl)pyrrolo[3,2-b]pyridine  
 5-(2-furoyl)amino-3-(1-neopentylpiperidin-4-yl)pyrrolo[3,2-b]pyridine  
 5-(3-furoyl)amino-3-(1-butylpiperidin-4-yl)pyrrolo[3,2-b]pyridine  
 5-(2-pyridinecarbonyl)amino-3-(1-butylpiperidin-4-yl)pyrrolo[3,2-b]pyridine  
 5-(2-chloro-4-pyridinecarbonyl)amino-3-(1-methylpiperidin-4-yl)pyrrolo[3,2-b]pyridine  
 5-(3-pyrrolicarbonyl)amino-3-(1-methylpiperidin-4-yl)pyrrolo[3,2-b]pyridine  
 5-(2-oxazolecarbonyl)amino-3-(1-hexylpiperidin-4-yl)pyrrolo[3,2-b]pyridine  
 5-(2-methyl-4-oxazolecarbonyl)amino-3-(1-methylpiperidin-4-yl)pyrrolo[3,2-b]pyridine  
 5-(4-pyrazolecarbonyl)amino-3-(1-methylpiperidin-4-yl)pyrrolo[3,2-b]pyridine  
 5-(5-isoxazolecarbonyl)amino-3-(1-methylpiperidin-4-yl)pyrrolo[3,2-b]pyridine  
 5-(3-imidazolecarbonyl)amino-3-(1-methylpiperidin-4-yl)pyrrolo[3,2-b]pyridine  
 5-(2-methoxy-4-pyrimidinecarbonyl)amino-3-(1-methylpiperidin-4-yl)pyrrolo[3,2-b]pyridine  
 5-(2-quinolinecarbonyl)amino-3-(1-methylpiperidin-4-yl)pyrrolo[3,2-b]pyridine  
 5-(2-cyano-5-quinolinecarbonyl)amino-3-(1-methylpiperidin-4-yl)pyrrolo[3,2-b]pyridine

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