Body weight may also be affected by orexin-mediated regulation of appetite and metabolism (T. Sakurai et al., *Cell*, 1998, 92(4), 573-585; T. Sakurai, *Reg. Pept.*, 1999, 85(1), 25-30). Some effects of orexin on metabolism and appetite may be mediated in the gut, where, as mentioned, orexins alter gastric motility and gastric acid secretion. Orexin receptor antagonists therefore are likely to be useful in treatment of overweight or obesity and conditions related to overweight or obesity, such as insulin resistance, type II diabetes, hyperlipidemia, gallstones, angina, hypertension, breathlessness, tachycardia, infertility, sleep apnea, back and joint pain, varicose veins and osteoarthritis. Conversely, orexin receptor agonists are likely to be useful in treatment of underweight and related conditions such as hypotension, bradycardia, ammenorrhea and related infertility, and eating disorders such as anorexia and bulimia.

Intracerebroventricularly administered orexins have been shown to increase mean arterial pressure and heart rate in freely moving (awake) animals (Samson et al., *Brain Res.* 1999, 831, 248-253; Shirasaka et al., *Am. J. Physiol.* 1999, 277, R1780-R1785) and in urethane-anesthetized animals (Chen et al., *Am. J. Physiol.* 2000, 278, R692-R697), with similar results. Orexin receptor agonists may therefore be candidates for treatment of hypotension, bradycardia and heart failure related thereto, while orexin receptor antagonists may be useful for treatment of hypertension, tachycardia and other arrhythmias, angina pectoris and acute heart failure.

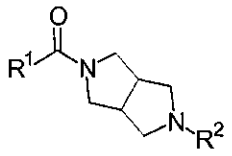
From the foregoing discussion, it can be seen that the identification of orexin receptor modulators, in one embodiment modulators of the orexin-2 receptor, will be of great advantage in the development of therapeutic agents for the treatment of a wide variety of disorders that are mediated through these receptor systems.

Citation of a reference herein shall not be construed as an admission that such reference is prior art to the present invention. All publications referred to herein are incorporated by reference in their entireties.

Various small-molecule orexin receptor modulators have been reported e.g., N-aroyl cyclic amine derivatives (International Publication No. WO2003002561, January 9, 3003), ethylene diamine derivatives (International

independent and dependent claims appended hereto, which are incorporated by reference herein.

In one general aspect, the invention is directed to a chemical entity of Formula (I):



Formula (I)

wherein:

R^1 is a member selected from the group consisting of:

A) phenyl substituted or unsubstituted with one or two R^a members, and substituted in the *ortho* position with R^b;

R^a is independently selected from the group consisting of: -H, halo, -C_{1-4}alkyl, -C_{1-4}alkoxy, and -NO_2, wherein two adjacent R^a members may come together to form a six membered aromatic ring;

R^b is a member selected from the group consisting of:

a) halo, -C_{1-4}alkoxy, -C_{1-4}alkyl,-CF_3, -OCF_3, or -CN;

b) 5-membered heteroaryl ring containing one oxygen or one sulfur members;

c) 5-6 membered heteroaryl ring containing one, two or three nitrogen members, optionally containing one oxygen member, substituted or unsubstituted with halo or -C_{1-4}alkyl; and

d) phenyl substituted or unsubstituted with halo, -CH_3, or -CF_3;

B) pyridine substituted or unsubstituted with one or two R^c members and substituted with R^d, wherein R^d is positioned adjacent to the point of attachment by R^1;

R^c is C_{1-4}alkyl;

R^d is a member selected from the group consisting of:

a) 5-6 membered heteroaryl ring selected from the group consisting of: 1H-1,2,3-triazol-1-yl, 2H-1,2,3-triazol-2-yl, 1H-pyrazol-5-yl, 3-methyl-1,2,4-oxadiazol-5-yl, pyridinyl, 3-methyl-pyridin-2-yl; 1-(tetrahydro-2H-pyran-2-yl)-1H-pyrazol-5-yl), phenyl, and pyrimidin-2-yl; and

Formula (II), and pharmaceutically active metabolites of compounds of Formula (I) or Formula (II).

In another aspect, the invention is directed to a method of treating a subject suffering from or diagnosed with a disease, disorder, or medical condition mediated by orexin receptor activity, comprising administering to the subject in need of such treatment an effective amount of at least one chemical entity selected from compounds of Formula (I) or Formula (II), pharmaceutically acceptable salts of compounds of Formula (I) or Formula (II), pharmaceutically acceptable prodrugs of compounds of Formula (I) or Formula (II), and pharmaceutically active metabolites of compounds of Formula (I) or Formula (II). Additional embodiments of methods of treatment are set forth in the detailed description.

In another aspect, method of studying isotopically labeled compounds in metabolic studies (preferably with ^{14}C), reaction kinetic studies (with, for example ^{2}H or ^{3}H), detection or imaging techniques [such as positron emission tomography (PET) or single-photon emission computed tomography (SPECT)] including drug or substrate tissue distribution assays, or in radioactive treatment of patients. For example, an ^{18}F or ^{11}C labeled compound may be particularly preferred for PET or an I^{123} for SPECT studies.

An object of the present invention is to overcome or ameliorate at least one of the disadvantages of the conventional methodologies and/or prior art, or to provide a useful alternative thereto. Additional embodiments, features, and advantages of the invention will be apparent from the following detailed description and through practice of the invention.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 is a Powder X-Ray Diffraction of an exemplied compound X

DETAILED DESCRIPTION

The invention may be more fully appreciated by reference to the following description, including the following glossary of terms and the concluding examples. For the sake of brevity, the disclosures of the

publications, including patents, cited in this specification are herein incorporated by reference.

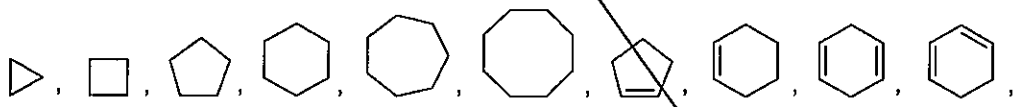
As used herein, the terms "including", "containing" and "comprising" are used herein in their open, non-limiting sense.

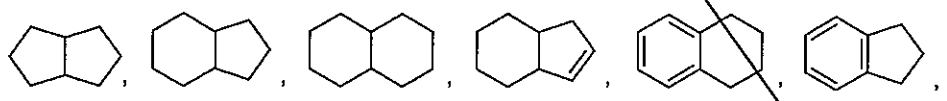
The term "alkyl" refers to a straight- or branched-chain alkyl group having from 1 to 12 carbon atoms in the chain. Examples of alkyl groups include methyl (Me, which also may be structurally depicted by the symbol, "/"), ethyl (Et), n-propyl, isopropyl, butyl, isobutyl, sec-butyl, tert-butyl (tBu), pentyl, isopentyl, tert-pentyl, hexyl, isohexyl, and groups that in light of the ordinary skill in the art and the teachings provided herein would be considered equivalent to any one of the foregoing examples.

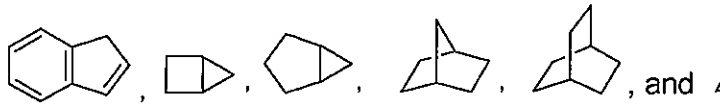
The term "alkoxy" includes a straight chain or branched alkyl group with a terminal oxygen linking the alkyl group to the rest of the molecule. Alkoxy includes methoxy, ethoxy, propoxy, isopropoxy, butoxy, t-butoxy, pentoxy and so on. "Aminoalkyl", "thioalkyl", and "sulfonylalkyl" are analogous to alkoxy, replacing the terminal oxygen atom of alkoxy with, respectively, NH (or NR), S, and SO_2.

The term "cyano" refers to the group -CN.

The term "cycloalkyl" refers to a saturated or partially saturated, monocyclic, fused polycyclic, or spiro polycyclic carbocycle having from 3 to 12 ring atoms per carbocycle. Illustrative examples of cycloalkyl groups include the following entities, in the form of properly bonded moieties:

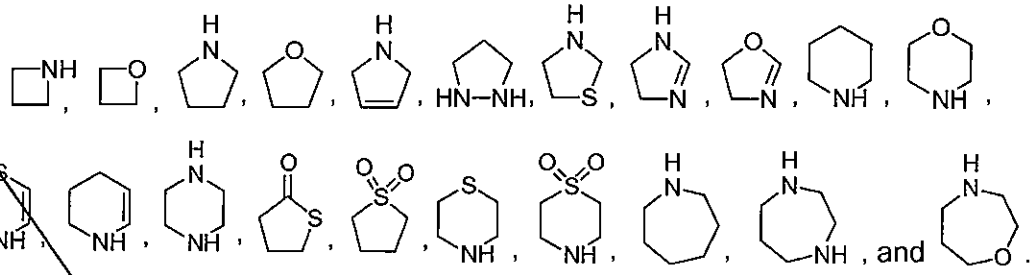




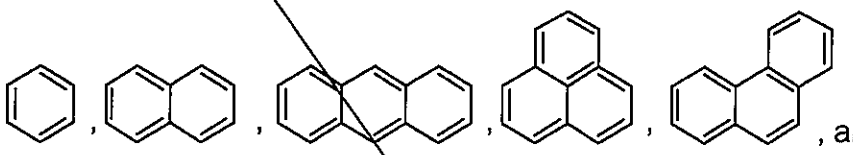

, and

A "heterocycloalkyl" refers to a monocyclic ring structure that is saturated or partially saturated and has from 4 to 7 ring atoms per ring structure selected from carbon atoms and up to two heteroatoms selected from nitrogen, oxygen, and sulfur. The ring structure may optionally contain up to two oxo

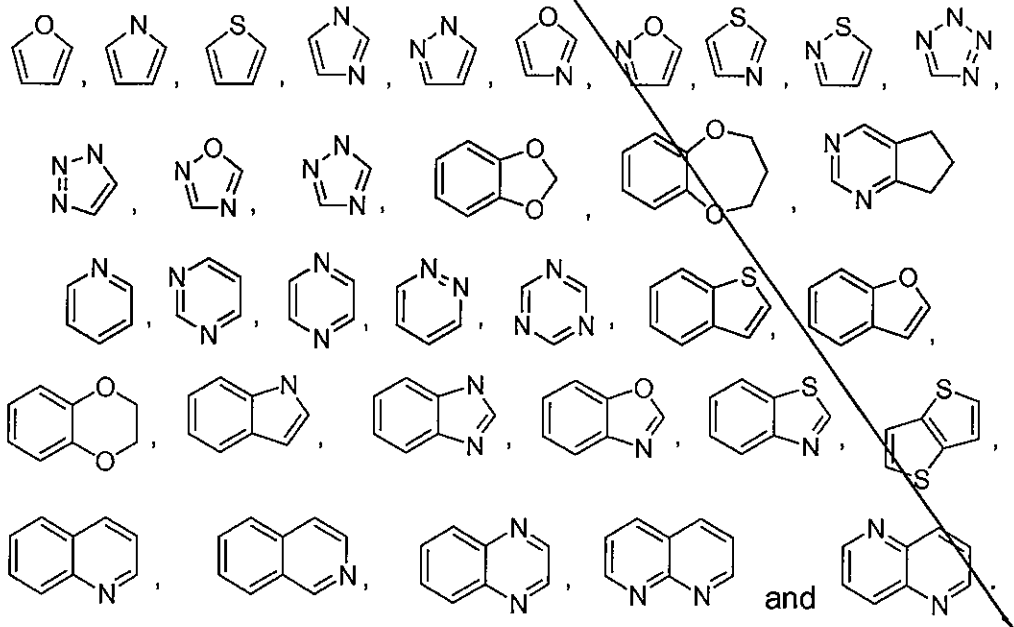
groups on sulfur ring members. Illustrative entities, in the form of properly bonded moieties, include:



The term "aryl" refers to a monocyclic, or fused or spiro polycyclic, aromatic carbocycle (ring structure having ring atoms that are all carbon) having from 3 to 12 ring atoms per ring. (Carbon atoms in aryl groups are sp^2 hybridized.) Illustrative examples of aryl groups include the following moieties:



The term "heteroaryl" refers to a monocyclic, fused bicyclic, or fused polycyclic aromatic heterocycle (ring structure having ring atoms selected from carbon atoms and up to four heteroatoms selected from nitrogen, oxygen, and sulfur) having from 3 to 12 ring atoms per heterocycle. Illustrative examples of heteroaryl groups include the following entities, in the form of properly bonded moieties:



Those skilled in the art will recognize that the species of heteroaryl,

groups, and accordingly react with a number of inorganic or organic bases, and inorganic and organic acids, to form a pharmaceutically acceptable salt.

bases, and inorganic and organic acids, to form a pharmaceutically acceptable salt.

Examples of pharmaceutically acceptable salts include sulfates, pyrosulfates, bisulfates, sulfites, bisulfites, phosphates, monohydrogen-phosphates, dihydrogenphosphates, metaphosphates, pyrophosphates, chlorides, bromides, iodides, acetates, propionates, decanoates, caprylates, acrylates, formates, isobutyrates, caproates, heptanoates, propiolates, oxalates, malonates, succinates, suberates, sebacates, fumarates, maleates, butyne-1,4-dioates, hexyne-1,6-dioates, benzoates, chlorobenzoates, methylbenzoates, dinitrobenzoates, hydroxybenzoates, methoxybenzoates, phthalates, sulfonates, xylenesulfonates, phenylacetates, phenylpropionates, phenylbutyrates, citrates, lactates, γ-hydroxybutyrates, glycolates, tartrates, methane-sulfonates, propanesulfonates, naphthalene-1-sulfonates, naphthalene-2-sulfonates, and mandelates.

When the compound of Formula (I) or Formula (II) contains a basic nitrogen, the desired pharmaceutically acceptable salt may be prepared by any suitable method available in the art, for example, treatment of the free base with an inorganic acid, such as hydrochloric acid, hydrobromic acid, sulfuric acid, sulfamic acid, nitric acid, boric acid, phosphoric acid, and the like, or with an organic acid, such as acetic acid, phenylacetic acid, propionic acid, stearic acid, lactic acid, ascorbic acid, maleic acid, hydroxymaleic acid, isethionic acid, succinic acid, valeric acid, fumaric acid, malonic acid, pyruvic acid, oxalic acid, glycolic acid, salicylic acid, oleic acid, palmitic acid, lauric acid, a pyranosidyl acid, such as glucuronic acid or galacturonic acid, an alpha-hydroxy acid, such as mandelic acid, citric acid, or tartaric acid, an amino acid, such as aspartic acid, glutaric acidor glutamic acid, an aromatic acid, such as benzoic acid, 2-acetoxybenzoic acid, naphthoic acid, or cinnamic acid, a sulfonic acid, such as laurylsulfonic acid, p-toluenesulfonic acid, methanesulfonic acid, ethanesulfonic acid, any compatible mixture of acids such as those given as examples herein, and any other acid and mixture thereof that are regarded as equivalents or acceptable substitutes in light of the ordinary level of skill in this technology.

Delivery forms of the pharmaceutical compositions containing one or more dosage units of the active agents may be prepared using suitable pharmaceutical excipients and compounding techniques known or that become available to those skilled in the art. The compositions may be administered in the inventive methods by a suitable route of delivery, e.g., oral, parenteral, rectal, topical, or ocular routes, or by inhalation.

The preparation may be in the form of tablets, capsules, sachets, dragees, powders, granules, lozenges, powders for reconstitution, liquid preparations, or suppositories. Preferably, the compositions are formulated for intravenous infusion, topical administration, or oral administration.

For oral administration, the compounds of the invention can be provided in the form of tablets or capsules, or as a solution, emulsion, or suspension. To prepare the oral compositions, the compounds may be formulated to yield a dosage of, e.g., from about 0.05 to about 100 mg/kg daily, or from about 0.05 to about 35 mg/kg daily, or from about 0.1 to about 10 mg/kg daily. For example, a total daily dosage of about 5 mg to 5 g daily may be accomplished by dosing once, twice, three, or four times per day.

Oral tablets may include a compound according to the invention mixed with pharmaceutically acceptable excipients such as inert diluents, disintegrating agents, binding agents, lubricating agents, sweetening agents, flavoring agents, coloring agents and preservative agents. Suitable inert fillers include sodium and calcium carbonate, sodium and calcium phosphate, lactose, starch, sugar, glucose, methyl cellulose, magnesium stearate, mannitol, sorbitol, and the like. Exemplary liquid oral excipients include ethanol, glycerol, water, and the like. Starch, polyvinyl-pyrrolidone (PVP), sodium starch glycolate, microcrystalline cellulose, and alginic acid are suitable disintegrating agents. Binding agents may include starch and gelatin. The lubricating agent, if present, may be magnesium stearate, stearic acid or talc. If desired, the tablets may be coated with a material such as glyceryl monostearate or glyceryl distearate to delay absorption in the gastrointestinal tract, or may be coated with an enteric coating.

Capsules for oral administration include hard and soft gelatin capsules. To prepare hard gelatin capsules, compounds of the invention may be mixed

with a solid, semi-solid, or liquid diluent. Soft gelatin capsules may be prepared by mixing the compound of the invention with water, an oil such as peanut oil or olive oil, liquid paraffin, a mixture of mono and di-glycerides of short chain fatty acids, polyethylene glycol 400, or propylene glycol.

Liquids for oral administration may be in the form of suspensions, solutions, emulsions or syrups or may be lyophilized or presented as a dry product for reconstitution with water or other suitable vehicle before use. Such liquid compositions may optionally contain: pharmaceutically-acceptable excipients such as suspending agents (for example, sorbitol, methyl cellulose, sodium alginate, gelatin, hydroxyethylcellulose, carboxymethylcellulose, aluminum stearate gel and the like); non-aqueous vehicles, e.g., oil (for example, almond oil or fractionated coconut oil), propylene glycol, ethyl alcohol, or water; preservatives (for example, methyl or propyl p-hydroxybenzoate or sorbic acid); wetting agents such as lecithin; and, if desired, flavoring or coloring agents.

The active agents of this invention may also be administered by non-oral routes. For example, the compositions may be formulated for rectal administration as a suppository. For parenteral use, including intravenous, intramuscular, intraperitoneal, or subcutaneous routes, the compounds of the invention may be provided in sterile aqueous solutions or suspensions, buffered to an appropriate pH and isotonicity or in parenterally acceptable oil. Suitable aqueous vehicles include Ringer's solution and isotonic sodium chloride. Such forms will be presented in unit-dose form such as ampules or disposable injection devices, in multi-dose forms such as vials from which the appropriate dose may be withdrawn, or in a solid form or pre-concentrate that can be used to prepare an injectable formulation. Illustrative infusion doses may range from about 1 to 1000 µg/kg/minute of compound, admixed with a pharmaceutical carrier over a period ranging from several minutes to several days.

For topical administration, the compounds may be mixed with a pharmaceutical carrier at a concentration of about 0.1% to about 10% of drug to vehicle. Another mode of administering the compounds of the invention may utilize a patch formulation to affect transdermal delivery.

that only one X member can be N), with commercially available HET compounds of formula (V), where

HET is a 5-6 membered heteroaryl ring containing one to three nitrogen members, in the presence of copper(I)iodide, Cs_2CO_3 and N,N'-dimethylcyclohexane-1,2-diamine; in a solvent such as DMF or dioxane, at temperatures ranging from 60 °C to 100 °C (using conventional or microwave heating). One skilled in the art will recognize that 1,2,3-triazole can exist in two tautomeric forms defined as 2H-[1,2,3]triazole and 1H-[1,2,3]triazole thus accounting for the formation of two regioisomers.

Alternatively, compounds of formula (VIb) are prepared by the reaction of halobenzonitrile compounds of formula (VII) with HET, where HET is a 5-membered heteroaryl ring selected from the group consisting of triazole or pyrazole, in a solvent such as DMF and the like, in the presence of an inorganic base such as K_2CO_3 and the like, at temperatures ranging from 100 °C to 130 °C. Subsequent hydrolysis of the nitrile using a base such as aqueous NaOH and the like, in a solvent such as methanol provides compounds of formula (VIb).

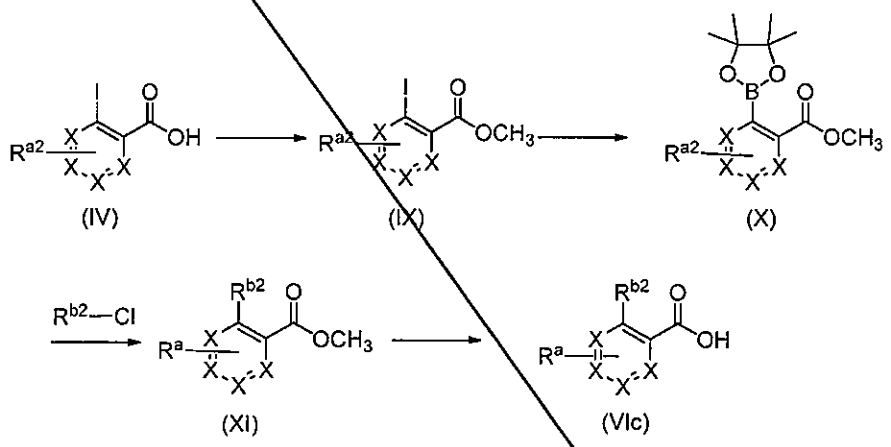
Compounds of formula (VIb) are also prepared by the reaction of halobenzonitrile compounds of formula (VII) with HET-$Sn(alkyl)_3$, where HET-$Sn(alkyl)_3$ is a commercially available or synthetically accessible trialkyltinheteroaryl compound, in a solvent such as DME, in the presence of a palladium catalyst such as $Pd(PPh_3)_4$, in the presence or absence of a catalytic amount of copper iodide, at temperatures ranging from 100 °C to 160 °C, using conventional or microwave heating. Subsequent hydrolysis of the nitrile using a base such as aqueous NaOH and the like, in a solvent such as methanol provides compounds of formula (VIb).

Compounds of formula (VIb) are also prepared by the reaction of halobenzonitrile compounds of formula (VII) with HET-boronic acid, where HET-boronic acid is a commercially available or synthetically accessible heteroarylboronic acid, in a solvent such as DME, in the presence of a base such as $NaHCO_3$, a palladium catalyst such as $Pd(PPh_3)_4$, at temperatures ranging from 80 °C to the reflux temperature of the solvent. Subsequent

hydrolysis using a base such as aqueous NaOH and the like, in a solvent such as methanol provides compounds of formula (VIb).

Compounds of formula (I), where R^{b2} is -I, are further elaborated to compounds of formula (I), where R^{b2} is HET, where HET is a 5-6 membered heteroaryl ring containg one to three nitrogen atoms optionally containing one oxygen member. Reaction of compounds of formula (I), where R^{b2} is -I, with HET-Sn(alkyl)$_3$, where HET-Sn(alkyl)$_3$ is a commercially available or synthetically accessible trialkyltinheteroaryl compound, in a solvent such as DME, in the presence of a palladium catalyst such as $Pd(PPh_3)_4$, in the presence or absence of a catalytic amount of copper iodide, at temperatures ranging from 100 °C to 160 °C, using conventional or microwave heating, provides compounds of formula (I).

SCHEME B

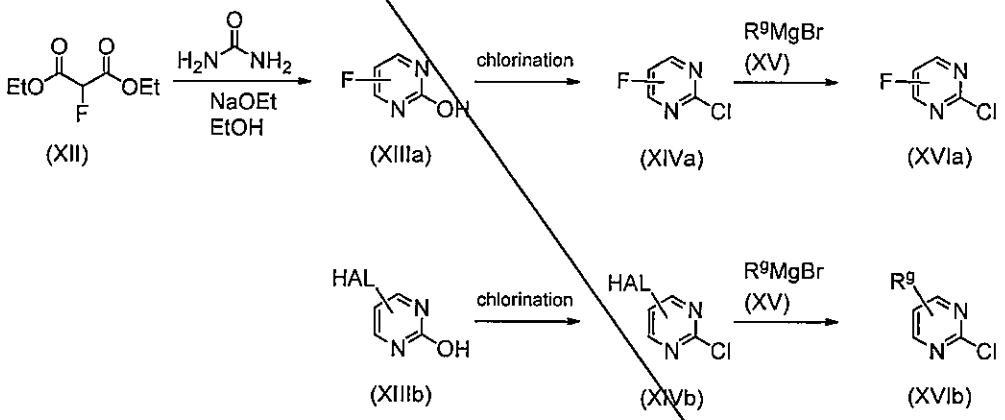


According to Scheme B, compounds of formula (VIc) are obtained from compounds of formula (IV), by first converting a commercially available or synthetically accessible compound of formula (IV), where R^{a2} is -H, halo, -C_{1-4}alkyl, -C_{1-4}alkoxy, -CF_3, or -NO_2, and where X is C or N (with the proviso that only one X may be N) to one of formula (IX) under esterification conditions, for example by treating an alcohol solution of a compound of formula (IV) with an acid. In a preferred method the compound of formula (IV) is dissolved in a solvent such as MeOH and treated with H_2SO_4 to afford a compound of formula (IX). A compound of formula (X) is obtained by reacting a suitable compound of formula (IX) with pinacol borane in the presence of a phosphine and a palladium catalyst, in the presence of an amine base, in a solvent such as THF, at temperatures ranging from room temperature to 70 °C. In a preferred

method the phosphine is tri(o-tolyl)phosphine, the palladium catalyst is $Pd(OAc)_2$ and the amine base is triethylamine.

A compound of formula (VIc) is obtained by reacting a compound of formula (X) with a compound R^{b2}-Cl, where R^{b2}-Cl is a suitable commercially available or synthetically accessible 6-membered chloro-substituted heteroaryl compound, in the presence of a palladium catalyst, a base such as Na_2CO_3, and the like, in a solvent such as 2-methyl-tetrahydrofuran (2-methyl-THF), and the like, at temperatures ranging from room temperature to 80 °C. In a preferred method the palladium catalyst is $PdCl_2$(dppf)-dcm adduct , the base is Na_2CO_3 and the solvent is 2-methyl-THF. A compound of formula (VIc) is obtained from a compound of formula (XI) via ester hydrolysis. In a preferred method of hydrolysis, a compound of formula (XI) in methyl-THF is treated with aqueous NaOH to afford a compound of formula (VIc).

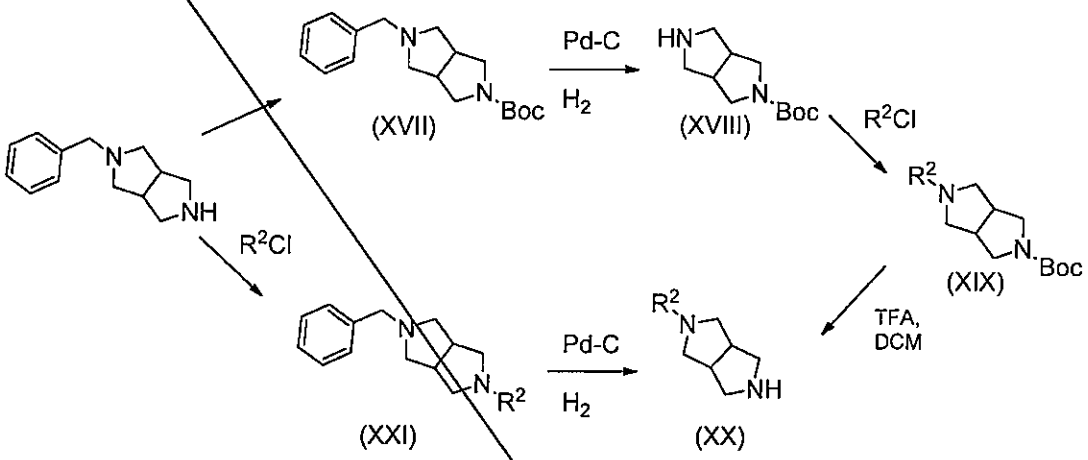
SCHEME C



According to SCHEME C, substituted heteroaryl compounds R^2Cl of formula (XIVa) and (XVIb) are prepared from commercially available or synthetically accessible compounds of formula (XIIIa) or (XIIIb). Pyrimidols of formula (XIIIa) or formula (XIIIb) are commercially available or are prepared by reacting substituted alkyl malonates of formula (XII), where R^e is halo, with urea in the presence of a base such as sodium ethoxide and the like; in a suitable solvent such as ethanol, at temperatures between room temperature and the reflux temperature of the solvent. Chlorination of commercially available pyrimidinols of formula (XIIIb) or synthetically accessible compounds of formula (XIIIa) using a chlorinating agent such as oxalyl chloride and the like; in a solvent such as CH_2Cl_2, in the presence of a base such as N,N-dimethylaniline

and the like; at temperatures ranging between room temperature and the reflux temperature of the solvent provides chloropyrimidines of formula (XIVa) or (XIVb). Additionally, chloropyrimidines of formula (XIVa) or (XIVb) are further elaborated. Chloropyrimidines of formula (XIVa) or (XIVb) are reacted with Grignard reagents (R^9MgBr) of formula (XV); in the presence of a catalytic amount of $Fe(acac)_3$, in a solvent such as Et_2O at 0 °C, provides alkyl chloropyrimidines of formula (XVIa) or (XVIb).

SCHEME D

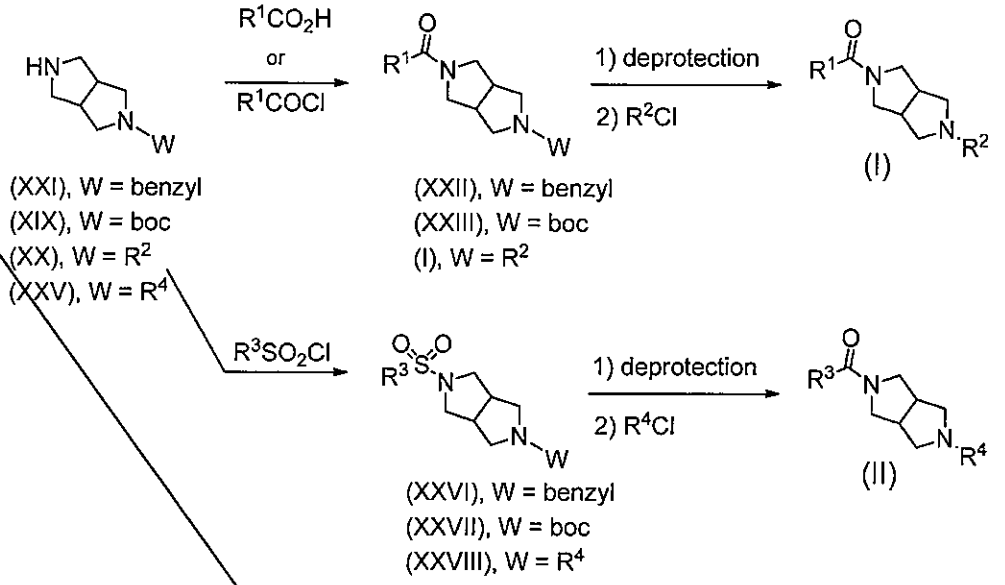


According to Scheme D, compounds of formula (XX) are obtained from synthetically accessible or commercially available 2-benzyl-octahydro-pyrrolo[3,4-c]pyrrole by first protecting the secondary nitrogen of 2-benzyl-octahydro-pyrrolo[3,4-c]pyrrole as a carbamate. In a preferred embodiment the carbamate is the *tert*-butylcarbamate (boc) which is introduced by treating 2-benzyl-octahydro-pyrrolo[3,4-c]pyrrole with di-*tert*-butyl-dicarbonate, in a solvent such as DCM, affording compound (XVII). Compound (XVIII) is obtained from treating compound (XVII) with hydrogen gas, in the presence of a catalyst. In a particularly preferred embodiment the catalyst is Pd on carbon, in a solvent such as MeOH in the presence of AcOH. A compound of formula (XIX) is obtained by treating compound (XVIII) with a compound of formula R^2Cl, where R^2 is as defined in formula (I). Commercially available or synthetically accessible appropriately heteroaryl compounds of formula R^2Cl are reacted with compound (XVIII) in the presence of a suitably selected tertiary organic or inorganic base such as Cs_2CO_3, Na_2CO_3, TEA, and the like;

in a solvent such as DMF, dichloromethane, THF, n-butanol, and the like; at a temperature between room temperature and the reflux temperature of the solvent, using conventional or microwave heating, to afford compounds of formula (XIX). In a preferred embodiment the base is Cs_2CO_3 and the solvent is DMF. Removal of the *tert*-butylcarbamate (boc) in compounds of formula (XIX) is accomplished by using methods known to one skilled in the art, such as, HCl, TFA, or *p*-toluenesulfonic acid, in a solvent such as CH_3OH, dioxane, or CH_2Cl_2. In a preferred embodiment, a compound of formula (XIX) is treated with TFA in DCM or HCl to afford a compound of formula (XX).

Compounds of formula (XX) are also obtained from 2-benzyl-octahydro-pyrrolo[3,4-c]pyrrole. Referring to Scheme D, 2-benzyl-octahydro-pyrrolo[3,4-c]pyrrole is treated with R^2Cl, where R^2 is as defined in a compound of formula (I). Commercially available or synthetically accessible suitably substituted heteroaryl compounds of formula R^2Cl are reacted with compound 2-benzyl-octahydro-pyrrolo[3,4-c]pyrrole in the presence of a tertiary organic or inorganic base such as Cs_2CO_3, Na_2CO_3, TEA, and the like; in a solvent such as DMF, dichloromethane, THF, and the like; at a temperature between room temperature and the reflux temperature of the solvent to afford a compound of formula (XXI). In a preferred embodiment the base is Cs_2CO_3 and the solvent is DMF. A compound of formula (XX) is obtained by treating a compound of formula (XXI) with hydrogen gas, in the presence of a catalyst, in a solvent such as AcOH. In a preferred embodiment the catalyst is Pd on carbon.

SCHEME E



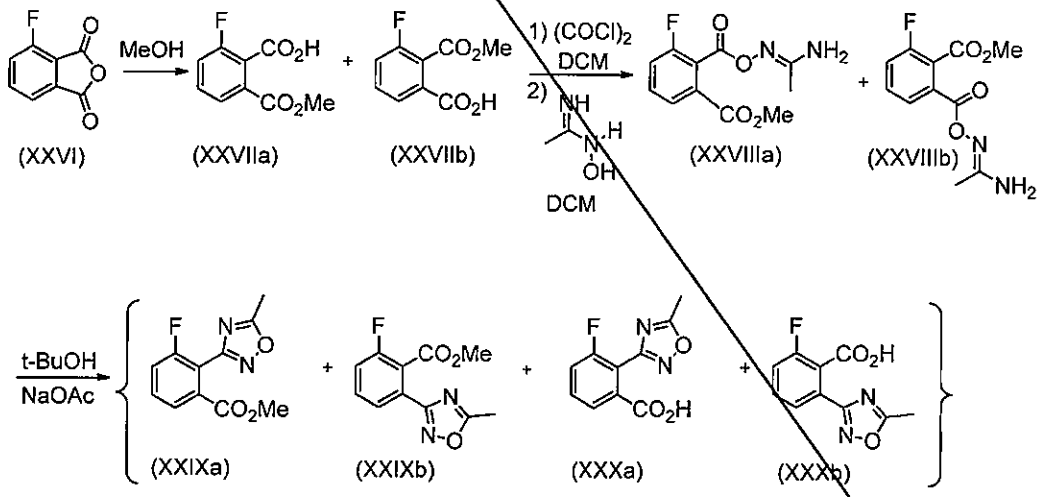
Referring to Scheme E, a compound of formula (I) is obtained from a compound of formula (XIX), (XX), or (XXI) by reacting a compound of formula (XIX), (XX), or (XXI) with a compound of formula R^1CO_2H under amide formation conditions. Compounds of formula R^1CO_2H, where R^1 is as defined in formula (I), are commercially available, as described, or synthetically accessible appropriately substituted aryl or heteroaryl carboxylic acids. In a preferred embodiment a compound of formula (XIX), (XX), or (XXI), either as a free base or as an acid salt, is reacted with a compound of formula R^1CO_2H, in the presence of a dehydrating agent such as HOBt/EDAC, CDI, HATU, HOAT; a suitably selected base such as DIPEA, TEA, and the like; in an organic solvent or mixture thereof, such as toluene, acetonitrile, ethyl acetate, DMF, THF, methylene chloride, and the like; to afford a compound of formula (XXII), (XXIII) or (I). In a particularly preferred embodiment the dehydrating agent is HATU, and the base is DIPEA.

In an alternative embodiment, a compound of formula R^1CO_2H (as described above) may be first converted to a compound of formula R^1COCl, or compound of formula R^1COCl is a commercially available substituted aryl sulfonyl chloride. In a preferred embodiment, a compound of formula R^1CO_2H is treated with thionyl chloride in a solvent such as toluene to afford a compound of formula R^1COCl. A compound of formula (I) is obtained by treating a compound of formula R^1COCl with a compound of formula (XIX), (XX), or (XXI), a suitably selected tertiary organic base such as TEA, and the

like, in a solvent such as dichloromethane, THF, and the like, at a temperature between room temperature and the reflux temperature of the solvent. A compound of formula (II) is obtained by treating a compound of formula R^1SO_2Cl with a compound of formula (XIX), (XXI), or (XXV), where R^4 is (5-trifluoromethyl)-pyridin-2-yl, (5-trifluoromethyl)-pyrimidin-2-yl, 4,6-dimethylpyrimidin-2-yl, or quinoxalin-2-yl; a suitably selected tertiary organic base such as TEA, and the like, in a solvent such as dichloromethane, THF, and the like, at a temperature between room temperature and the reflux temperature of the solvent.

Referring to Scheme E, one skilled in the art will recognize that the sequence of transformations shown in Schemes D and E may be reordered such that amide bond formation may be the initial reaction to give compounds of formulae (XXII) and (XXIII). Removal of the N-benzyl group from a compound of formulae (XXII) or removal of the carbamate from a compound of formula (XXIII) followed by the reaction with a compound R^2Cl, where R^2Cl is as described above gives a compound of formula (I).

SCHEME F

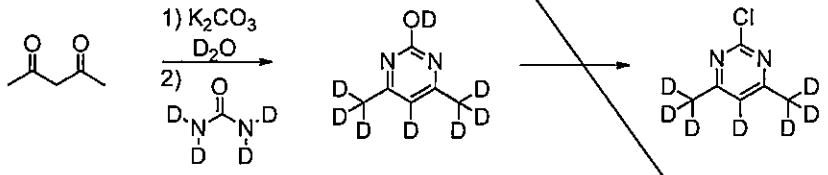


3-Fluoro-2-(3-methyl-1,2,4-oxadiazol-5-yl)benzoic acid and 2-fluoro-6-(3-methyl-1,2,4-oxadiazol-5-yl)benzoic acid are prepared according to SCHEME H. 3-Fluorophthalic anhydride was dissolved in a solvent such as MeOH, at temperatures ranging from room temperature to the reflux temperature of the solvent, to provide acid-esters (XXVIIa) and (XXIIb). Conversion of the acid to the acid chloride is accomplished under standard chlorination conditions. In a preferred method the acid is heated with oxalyl

chloride in a solvent such as DCM. Subsequent reaction of the acid chloride with N-hydroxyacetamide in a solvent such as CH_2Cl_2 provides a mixture of esters (XXVIIIa) and (XXVIIIb). Finally, esters (XXVIIIa) and (XXVIIIb) are converted to a mixtue of esters (XXIXa) and (XXIXb) and acids (XXXa) and (XXXb) by treatment with a base, preferably sodium acetate, in the presence of a solvent, preferably t-BuOH.

Alternately, acid (XXXa) is prepared by first converting 2-fluoro-6-iodobenzoic acid to the acid chloride by reaction with a chlorinating agent such as oxalyl chloride, in a solvent such as DCM, with a catalytic amount of DMF, at a temperature of 0 °C. Subsequent reaction of the acid chloride with N-hydroxyacetamide in a solvent such as CH_2Cl_2 provides (Z)-N'-((2-fluoro-6-iodobenzoyl)oxy)acetimidamide. 5-(2-Fluoro-6-iodophenyl)-3-methyl-1,2,4-oxadiazole is prepared by reacting (Z)-N'-((2-fluoro-6-iodobenzoyl)oxy)acetimidamide with sodium acetate, in a solvent such as tert-butanol, at temperatures ranging from 100 °C to 110 °C. 3-Fluoro-2-(3-methyl-1,2,4-oxadiazol-5-yl)benzoic acid (XXXa) is prepared by reacting 5-(2-fluoro-6-iodophenyl)-3-methyl-1,2,4-oxadiazole with a grignard reagent such as i-PrMgCl, in a suitable solvent such as THF and the like, at a temperature of -78 °C. Subsequent addition of CO_2 gas, at a temperature of -78 °C provides 3-fluoro-2-(3-methyl-1,2,4-oxadiazol-5-yl)benzoic acid (XXXa).

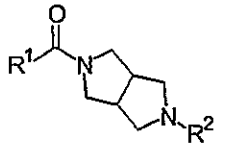
SCHEME H



Deuterated pyrimidine compounds of formula (XXXII) are prepared according to Scheme H. Acetylacetone is reacted with an inorganic base such as K_2CO_3 in deuterated water, at temperatures ranging from 100 °C to 120 °C to provide 1,1,1,3,3,3,5,5-octadeuteriopentane-2,4-dione. 1,1,1,3,3,3,5,5-Octadeuteriopentane-2,4-dione is subsequently reacted with deuterated urea, in a solvent such as deuterated ethanol, 35% wt. DCl in D_2O, at temperatures ranging from 90 °C to 100 °C to provide deuterated pyrimidinols of formula

What is claimed is:

1. A chemical entity that is a compound of Formula (I):



Formula (I)

wherein:

R^1 is a member selected from the group consisting of:

A) phenyl substituted or unsubstituted with one or two R^a members and substituted in the *ortho* position with R^b;

R^a is independently selected from the group consisting of: -H, halo, -C_{1-4}alkyl, -C_{1-4}alkoxy, and -NO_2, wherein two adjacent R^a members may come together to form a six membered aromatic ring;

R^b is a member selected from the group consisting of:

a) halo, -C_{1-4}alkoxy, -C_{1-4}alkyl,-CF_3, -OCF_3, or -CN;

b) 5-membered heteroaryl ring containing one oxygen or one sulfur members;

c) 5-6 membered heteroaryl ring containing one, two or three nitrogen members, optionally containing one oxygen member, substituted or unsubstituted with halo or -C_{1-4}alkyl; and

d) phenyl substituted or unsubstituted with halo, -CH_3, or -CF_3;

B) pyridine substituted or unsubstituted with one or two R^c members and substituted with R^d, wherein R^d is positioned adjacent to the point of attachment by R^1;

R^c is C_{1-4}alkyl;

R^d is a member selected from the group consisting of:

a) 5-6 membered heteroaryl ring selected from the group consisting of: 1H-1,2,3-triazol-1-yl, 2H-1,2,3-triazol-2-yl, 1H-pyrazol-5-yl, 3-methyl-1,2,4-oxadiazol-5-yl, pyridinyl, 3-methyl-pyridin-2-yl; 1-(tetrahydro-2H-pyran-2-yl)-1H-pyrazol-5-yl), phenyl, and pyrimidin-2-yl; and

b) -CF_3, -Br, and -C_{1-4}alkoxy;

C) 5-membered heteroaryl ring selected from the group consisting of: 2-methyl-1,3-thiazol-yl, 1H-pyrazol-5-yl, oxazole, isoxazolyl, thiophen-2-yl, and furan-2-yl, each substituted with phenyl substituted or unsubstituted with -F; and

D) 5-13 membered aryl or heteroaryl ring selected from the group consisting of: 3-methylfuran-2-yl, 9H-fluorene, quinoline, cinnoline; 3-(1H-pyrrol-1-yl)thiophen-2-yl, 8-[1,2,3]-triazol-2-yl-naphthalen-1-yl, 2,3-dihydro-1,4-benzodioxin-5-yl, 1H-indol-7-yl, 4-fluoronaphthalen-1-yl, and naphthalen-1-yl;

R^2 is a member selected from the group consisting of:

A) 6-membered heteroaryl ring containing two nitrogen members substituted with one or more members independently selected from the group consisting of: halo, -C_{1-4}alkyl, -CD_3, -D, -C_{1-4}alkoxy, cyclopropyl, morpholin-2-yl, -CO_2C_{1-4}alkyl, -CO_2H, -CH_2OH, -$C(O)N(C_{1-4}alkyl)_2$, -CF_3, -CN, -OH, -NO_2, -$N(C_{1-4}alkyl)_2$, phenyl, furan-2-yl, thiophen-2-yl, 1H-pyrazol-4-yl, and pyrrolidin-1-yl;

B) pyridine substituted with one or two members independently selected from the group consisting of: halo, -C_{1-4}alkyl, -C_{1-4}alkoxy, and -CF_3;

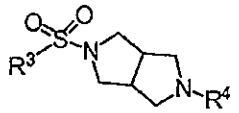
C) 9-membered heteroaryl ring selected from the group consisting of benzooxazol-2-yl, 6-fluoro-1,3-benzothiazole, 1,3-benzothiazole, 6-methoxy-1,3-benzothiazole, 6-methyl-1,3-benzothiazole, 6-chloro-benzothiazol-2-yl, and 4-methyl-6,7-dihydro-5H-cyclopenta[d]pyrimidine;

D) 10-membered heteroaryl ring selected from the group consisting of quinoxalin-2-yl, 3-methylquinoxalin-2-yl, 6,7-difluoroquinoxalin-2-yl, 3-(trifluoromethyl)quinoxaline, quinoline, 4-methylquinoline, and 6-fluoroquinazolin-2-yl; and

E) 4-methyl-1,3,5-triazin-2-yl or 2-methylpyrimidin-4(3H)-one;

and pharmaceutically acceptable salts of compounds of Formula (I).

2. A chemical entity selected from compounds of Formula (II):



(II)

wherein

R^3 is phenyl substituted or unsubstituted with a member independently selected from the group consisting of: -C_{1-4}alkoxy, and phenyl; and

R^4 is a member selected from the group consisting of (5-trifluoromethyl)-pyridin-2-yl, (5-trifluoromethyl)-pyrimidin-2-yl, 4,6-dimethylpyrimidin-2-yl, and quinoxalin-2-yl;

and pharmaceutically acceptable salts of compounds of Formula (II).

3. A chemical entity defined in claim 1, wherein R^1 is phenyl, where R^a is a member independently selected from the group consisting of -F, -I, -Cl, -OCH_3, -OCH_2CH_3, -CH_3, -$CH(CH_3)_2$, -$C(CH_3)_3$ and -NO_2.

4. A chemical entity defined in claim 1, wherein R^1 is phenyl wherein R^b is a member selected from the group consisting of -Br, -F, -I, -C_{1-4}alkyl, -OCH_3, -OCH_2CH_3, -CN, -CF_3, and -OCF_3.

5. A chemical entity defined in claim 1, wherein R^1 is phenyl, where R^a is selected from the group consisting of -H, -F, -Cl, -CH_3, -$C(CH_3)_3$, -OCH_3, and -OCH_2CH_3, and R^b is selected from the group consisting of -Br, -F, -I, -C_{1-4}alkyl, -OCH_3, -OCH_2CH_3, -CN, -CF_3, and -OCF_3.

6. A chemical entity defined in claim 1, wherein R^1 is phenyl, where R^b is 2-thiophen-2-yl or 2-furan-2-yl.

7. A chemical entity defined in claim 1, wherein R^1 is phenyl, where R^b is selected from the group consisting of phenyl, 3-chlorophenyl, 4-fluorophenyl, 3-fluorophenyl, 4-methylphenyl, and 4-trifluoromethylphenyl.

8. A chemical entity defined in claim 1, wherein R^1 is phenyl, where

R^b is a member selected from the group consisting of 1H-pyrrol-1-yl, 1H-pyrazol-1-yl, 1H-pyrazol-5-yl, 1H-imidazol-2-yl, 1-methyl-1H-imidazol-2-yl, 1H-1,2,3-triazol-1-yl, 2H-1,2,3-triazol-2-yl, 2H-1,2,3-triazol-1-yl, 1H-1,2,4-triazol-5-yl, 2H-1,2,4-triazol-1-yl, 2H-1,2,4-triazol-3-yl, 4H-1,2,4-triazol-3-yl, 4H-1,2,4-triazol-4-yl, 1-methyl-1H-1,2,4-triazol-3-yl, 1-methyl-1H-1,2,4-triazol-5-yl and 1-(tetrahydro-2H-pyran-2-yl)-1H-pyrazol-5-yl.

9. A chemical entity defined in claim 1, wherein R^1 is phenyl, where R^b is a member selected from the group consisting of pyridin-2-yl, 3-chloropyridin-2-yl, 3-fluoropyridin-2-yl, 3-methylpyridin-2-yl, 4-methylpyridin-2-yl, 5-methylpyridin-2-yl, 6-methylpyridin-2-yl, 2-pyridin-3-yl, and 2-pyrimidin-2-yl.

10. A chemical entity defined in claim 1, wherein R^1 is phenyl, where R^b is a member selected from the group consisting of 3-methyl-1,2,4-oxadiazol-5-yl and oxazol-2-yl.

11. A chemical entity defined in claim 1, wherein R^1 is phenyl, where R^a is halo, $-C_{1-4}$alkyl, or $-C_{1-4}$alkoxy, and R^b is triazole or pyrimidine substituted or unsubstituted with halo or $-C_{1-4}$alkyl.

12. A chemical entity defined in claim 1, wherein R^1 is (1-methylethyl)-2-(2H-1,2,3-triazol-2-yl)phenyl, 2-(1H-1,2,3-triazol-1-yl)phenyl, 2-(2H-1,2,3-triazol-2-yl)phenyl, 2-fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl, 2-methyl-6-(2H-1,2,3-triazol-2-yl)phenyl, 3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl, 3-fluoro-2-(1H-1,2,3-triazol-1-yl)phenyl, 3-methoxy-2-(1H-1,2,3-triazol-1-yl)phenyl, 3-methoxy-2-(2H-1,2,3-triazol-2-yl)phenyl, 3-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl, 3-methyl-2-(1H-1,2,3-triazol-1-yl)phenyl, 4-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl, 4-methoxy-2-(2H-1,2,3-triazol-2-yl)phenyl, 4-methoxy-2-(1H-1,2,3-triazol-2-yl)phenyl, 4,5-dimethoxy-2-[1,2,3]triazol-1-yl-phenyl, 4,5-dimethoxy-2-[1,2,3]triazol-2-yl-phenyl, 5-[1,2,3]triazol-2-yl-benzo[1,3]dioxol-4-yl, 5-chloro-2-(2H-1,2,3-triazol-2-yl)phenyl, 5-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl, 5-iodo-2-(2H-1,2,3-triazol-2-yl)phenyl, 5-methoxy-2-(2H-1,2,3-triazol-2-yl)phenyl, 5-methyl-2-(2H-1,2,3-

triazol-2-yl)phenyl, 1-[1,2,3]triazol-2-yl-naphthalen-2-yl, 2-(1H-1,2,4-triazol-1-yl)phenyl, 2-(1H-1,2,4-triazol-5-yl)phenyl, 2-(1-methyl-1H-1,2,4-triazol-5-yl)phenyl, 2-(1-methyl-1H-1,2,4-triazol-3-yl)phenyl, 2-(4H-1,2,4-triazol-3-yl)phenyl, 2-(4H-1,2,4-triazol-4-yl)phenyl, 2-(3-methyl-1,2,4-oxadiazol-5-yl)phenyl, 3-fluoro-2-(3-methyl-1,2,4-oxadiazol-5-yl)phenyl, 2-fluoro-6-(3-methyl-1,2,4-oxadiazol-5-yl)phenyl, 4,5-difluoro-2-(4H-1,2,4-triazol-4-yl)phenyl), 2-fluoro-6-pyrimidin-2-ylphenyl, 2-(pyrimidin-2-yl)pyridin-3-yl, 3-fluoro-2-pyrimidin-2-ylphenyl, 4-fluoro-2-(pyrimidin-2-yl)phenyl, 4-methoxy-2-(pyrimidin-2-yl)phenyl, 5-fluoro-2-pyrimidin-2-ylphenyl, and 5-methyl-2-pyrimidin-2-ylphenyl.

13. A chemical entity defined in claim 1, wherein R^1 is pyridine, where R^d is a member selected from the group consisting of $-CF_3$, -Br, and $-OCH_2CH_2CH_3$.

14. A chemical entity defined in claim 1, wherein R^1 is pyridine, where R^d is a member selected from the group consisting of 1H-pyrazol-5-yl, 2H-1,2,3-triazol-1-yl, 2H-1,2,3-triazol-2-yl, 4H-1,2,3-triazol-1-yl, 1-(tetrahydro-2H-pyran-2-yl)-1H-pyrazol-5-yl, 3-methylpyridin-2-yl, and 3-methyl-1,2,4-oxadiazol-5-yl.

15. A chemical entity defined in claim 1, wherein R^1 is pyridine, where R^d is a member selected from the group consisting of 1H-pyrazol-5-yl, 2H-1,2,3-triazol-1-yl, and 2H-1,2,3-triazol-2-yl.

16. A chemical entity defined in claim 1, wherein R^1 is 1-phenyl-1H-pyrazol-5-yl, 3-phenylthiophen-2-yl, 3-phenylfuran-2-yl, 5-phenyl-1,3-oxazol-4-yl, 5-phenylisoxazol-4-yl, 5-(2-fluorophenyl)-2-methyl-1,3-thiazol-4-yl, 2-methyl-5-phenyl-thiazol-4-yl, or 5-(4-fluorophenyl)-2-methyl-1,3-thiazol-4-yl.

17. A chemical entity defined in claim 1, wherein R^1 is selected from the group consisting of 3-methylfuran-2-yl, 9H-fluorene, quinoline, cinnoline; 3-(1H-pyrrol-1-yl)thiophen-2-yl, 8-[1,2,3]-triazol-2-yl-naphthalen-1-yl, 2,3-dihydro-1,4-

benzodioxin-5-yl, 1H-indol-7-yl, 4-fluoronaphthalen-1-yl, and naphthalen-1-yl and R^2 is selected from the group consisting of 4,6-dimethylpyrimidin-2-yl, 4-phenyl-pyrimidin-2-yl, quinoxaline, and 4-methoxypyrimidin-2-yl.

18. A chemical entity defined in claim 1, wherein R^2 is pyrimidine substituted with one or more members independently selected from the group consisting of -F, -Cl, -D, $-CD_3$, $-CH_3$, ethyl, isopropyl, propyl, tert-butyl, $-CF_3$, $-OCH_3$, $-N(CH_3)_2$, -CN, -OH, $-CH_2OH$, $-NO_2$, $-CO_2CH_3$, $-CO_2H$, $-C(O)N(CH_3)_2$, phenyl, furan-2-yl, thiophen-2-yl, 1H-pyrazol-4-yl, cyclopropyl, pyrrolidin-1-yl, and morpholin-4-yl.

19. A chemical entity defined in claim 1, wherein R^2 is 4,6-dimethylpyrimidin-2-yl, 4,5-dimethylpyrimidin-2-yl,4,6-dimethoxypyrimidin-2-yl,4-phenyl-pyrimidin-2-yl, 4-furan-2-ylpyrimidin-2-yl, 4-methylpyrimidin-2-yl, 4-methoxypyrimidin-2-yl, 4-thiophen-2-ylpyrimidin-2-yl, N,N,6-trimethyl-pyrimidin-4-amine, 4-(trifluoromethyl)pyrimidin-2-yl, 4,5,6-trimethylpyrimidin-2-yl, 4-(trifluoromethyl)pyrimidine-5-carboxylate, 4-(trifluoromethyl)pyrimidine-5-carboxylic acid, 5-nitro-pyrimidin-2-yl, 6-methylpyrimidine-4-carboxylic acid, N,N-dimethyl-4-(triflouoromethyl)pyrimidine-5-carboxamide, N,N,6-trimethylpyrimidine-carboxamide, 6-methylpyrimidine-4-carbonitrile, 4,6-bis(trifluoromethyl)pyrimidin-2-yl, 6-methyl-pyrimidin-4-ol, 4-(furan-2-yl)-6-methylpyrimidin-2-yl, 5-fluoro-4-methylpyrimidin-2-yl, 5-fluoropyrimidin-2-yl, 4-methoxy-6-methylpyrimidin-2-yl, 4-ethyl-6-methylpyrimidin-2-yl, 4-isopropyl-6-methylpyrimidin-2-yl, 4-tertbutyl-6-methylpyrimidin-2-yl, 4-cyclopropyl-6-methylpyrimidin-2-yl, 4-methyl-6-morpholin-4-ylpyrimidin-2-yl, 5-chloro-4-methylpyrimidin-2-yl, 5-chloro-4,6-dimethylpyrimidin-2-yl, 5-fluoro-4,6-dimethylpyrimidin-2-yl, 5-trifluoromethylpyrimidin-2-yl, 4,6-bis[(^{2}H3)methyl](^{2}H)pyrimidin-2-yl, and 5-ethyl-4,6-dimethylpyrimidin-2-yl.

20. A chemical entity defined in claim 1, wherein R^2 is pyrimidine substituted with one or more members independently selected from the group consisting of -Cl, -F, $-CH_3$, $-CF_3$, $-N(CH_3)_2$, -D, and $-CD_3$.

21. A chemical entity defined in claim 1, wherein R^2 is 4,6-dimethylpyrimidin-2-yl, 4,5-dimethylpyrimidin-2-yl,4,6-dimethoxypyrimidin-2-yl, 4-methylpyrimidin-2-yl, 4-methoxypyrimidin-2-yl, N,N,6-trimethyl-pyrimidin-4-amine, 4-(trifluoromethyl)pyrimidin-2-yl, 4,5,6-trimethylpyrimidin-2-yl, 4,6-bis(trifluoromethyl)pyrimidin-2-yl, 6-methyl-pyrimidin-4-ol, 5-fluoro-4-methylpyrimidin-2-yl, 5-fluoropyrimidin-2-yl, 4-methoxy-6-methylpyrimidin-2-yl, 5-chloro-4-methylpyrimidin-2-yl, 5-chloro-4,6-dimethylpyrimidin-2-yl, 5-fluoro-4,6-dimethylpyrimidin-2-yl, 5-trifluoromethylpyrimidin-2-yl, and 4,6-bis[(^{2}H3)methyl](^{2}H)pyrimidin-2-yl.

22. A chemical entity defined in claim 1, wherein R^2 is pyrazine or triazine substituted with one or more $-CH_3$.

23. A chemical entity defined in claim 1, wherein R^2 is pyridine substituted with one or more members independently selected from the group consisting of -F, $-OCH_3$, $-OCH_2CH_3$, $-CH_3$, and $-CF_3$.

24. A chemical entity defined in claim 1, wherein R^2 is a member selected from the group consisting of benzooxazol-2-yl, 2-methylpyrimidin-4(3H)-one and 4-methyl-6,7-dihydro-5H-cyclopenta[d]pyrimidine and R^1 is phenyl, substituted in the *ortho* position with R^b, where R^b is 2H-1,2,3-triazol-2-yl, 2H-1,2,3-triazol-1-yl, 3-methyl-1,2,4-oxadiazol-5-yl or 2-pyrimidin-2-yl.

25. A chemical entity defined in claim 1, wherein R^2 is a member selected from the group consisting of quinoxalin-2-yl, 3-methylquinoxalin-2-yl, 6,7-difluoroquinoxalin-2-yl, 3-(trifluoromethyl)quinoxaline, 4-methylquinoline, and 6-fluoroquinazolin-2-yl and R^1 is phenyl substituted in the *ortho* position with R^b, where R^b is 2H-1,2,3-triazol-2-yl, 2H-1,2,3-triazol-1-yl, 3-methyl-1,2,4-oxadiazol-5-yl or 2-pyrimidin-2-yl.

26. A chemical entity defined in claim 2, wherein R^3 is biphenyl or 2-methoxyphenyl and R^4 is (5-trifluoromethyl)-pyridin-2-yl, (5-trifluoromethyl)-pyrimidin-2-yl, 4,6-dimethylpyrimidin-2-yl, or quinoxalin-2-yl.

27. A chemical entity defined in claim 1, wherein R^1 is a member selected from the group consisting of 2-(1H-1,2,3-triazol-1-yl)phenyl, 2-(2H-1,2,3-triazol-2-yl)phenyl, 2-fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl, 2-methyl-6-(2H-1,2,3-triazol-2-yl)phenyl, 3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl, 3-fluoro-2-(1H-1,2,3-triazol-1-yl)phenyl, 3-methoxy-2-(1H-1,2,3-triazol-1-yl)phenyl, 3-methoxy-2-(2H-1,2,3-triazol-2-yl)phenyl, 3-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl, 3-methyl-2-(1H-1,2,3-triazol-1-yl)phenyl, 4-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl, 4-methoxy-2-(2H-1,2,3-triazol-2-yl)phenyl, 4-methoxy-2-(1H-1,2,3-triazol-2-yl)phenyl, 4,5-dimethoxy-2-[1,2,3]triazol-1-yl-phenyl, 4,5-dimethoxy-2-[1,2,3]triazol-2-yl-phenyl, 5-chloro-2-(2H-1,2,3-triazol-2-yl)phenyl, 5-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl, 5-methoxy-2-(2H-1,2,3-triazol-2-yl)phenyl, 5-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl, 2-(1H-1,2,4-triazol-1-yl)phenyl, 2-(1H-1,2,4-triazol-5-yl)phenyl, 2-(1-methyl-1H-1,2,4-triazol-5-yl)phenyl, 2-(1-methyl-1H-1,2,4-triazol-3-yl)phenyl, 2-(4H-1,2,4-triazol-3-yl)phenyl, 2-(4H-1,2,4-triazol-4-yl)phenyl, 2-(3-methyl-1,2,4-oxadiazol-5-yl)phenyl, 3-fluoro-2-(3-methyl-1,2,4-oxadiazol-5-yl)phenyl, 2-fluoro-6-(3-methyl-1,2,4-oxadiazol-5-yl)phenyl, 4,5-difluoro-2-(4H-1,2,4-triazol-4-yl)phenyl), 2-fluoro-6-pyrimidin-2-ylphenyl, 2-(pyrimidin-2-yl)pyridin-3-yl, 3-fluoro-2-pyrimidin-2-ylphenyl, 4-fluoro-2-(pyrimidin-2-yl)phenyl, 4-methoxy-2-(pyrimidin-2-yl)phenyl, 5-fluoro-2-pyrimidin-2-ylphenyl, and 5-methyl-2-pyrimidin-2-ylphenyl and R^2 is a member selected from the group consisting of 4,6-dimethylpyrimidin-2-yl, 4,5-dimethylpyrimidin-2-yl,4,6-dimethoxypyrimidin-2-yl, 4-methylpyrimidin-2-yl, 4-methoxypyrimidin-2-yl, N,N,6-trimethyl-pyrimidin-4-amine, 4-(trifluoromethyl)pyrimidin-2-yl, 4,5,6-trimethylpyrimidin-2-yl, 4,6-bis(trifluoromethyl)pyrimidin-2-yl, 6-methyl-pyrimidin-4-ol, 5-fluoro-4-methylpyrimidin-2-yl, 5-fluoropyrimidin-2-yl, 4-methoxy-6-methylpyrimidin-2-yl, 5-chloro-4-methylpyrimidin-2-yl, 5-chloro-4,6-dimethylpyrimidin-2-yl, 5-fluoro-4,6-dimethylpyrimidin-2-yl, 5-trifluoromethylpyrimidin-2-yl, and 4,6-bis[(^{2}H3)methyl](^{2}H)pyrimidin-2-yl.

28. A chemical entity defined in claim 1, wherein R^1 is a member selected from the group consisting of 3-fluoro-2-(3-methyl-1,2,4-oxadiazol-5-yl)phenyl, 6-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl, 4-methoxy-2-(2H-1,2,3-triazol-2-yl)phenyl, and 3-[1,2,3]triazol-2-yl-pyridin-2-yl and R^2 is a member selected from the group consisting of 4,6-dimethylpyrimidin-2-yl, 5-fluoro-4,6-dimethylpyrimidin-2-yl, and 5-fluoro-4-methylpyrimidin-2-yl.

29. A chemical entity selected from the group consisting of:
4-[5-{[2-Fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-6-methoxy-N,N-dimethylpyrimidin-2-amine;
N,N-Dimethyl-6-[5-{[2-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-2-(trifluoromethyl)pyrimidin-4-amine;
6-[5-{[2-Fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-N,N-dimethyl-2-(trifluoromethyl)pyrimidin-4-amine;
4-[5-{[5-Fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-6-methoxy-N,N-dimethylpyrimidin-2-amine;
4-Methoxy-N,N-dimethyl-6-[5-{[2-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}hexahydropyrrolo-[3,4-c]pyrrol-2(1H)-yl]pyrimidin-2-amine;
6-[5-{[4-Fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-N,N-dimethyl-2-(trifluoromethyl)pyrimidin-4-amine;
4-[5-{[4-Fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-6-methoxy-N,N-dimethylpyrimidin-2-amine;
2-(4,6-Dimethylpyrimidin-2-yl)-5-{[3-(1H-pyrrol-1-yl)thiophen-2-yl]carbonyl}octahydro-pyrrolo[3,4-c]pyrrole;
6-[5-{[5-Fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-N,N-dimethyl-2-(trifluoromethyl)pyrimidin-4-amine;
2-(4,6-Dimethylpyrimidin-2-yl)-5-[(1-phenyl-1H-pyrazol-5-yl)carbonyl]octahydropyrrolo[3,4-c]pyrrole;
8-{[5-(4,6-Dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]carbonyl}-quinoline;
2-(4,6-Dimethylpyrimidin-2-yl)-5-[(3-phenylthiophen-2-yl)carbonyl]octahydropyrrolo[3,4-c]pyrrole;

2-(4,6-Dimethylpyrimidin-2-yl)-5-[(3-phenylfuran-2-yl)carbonyl]octahydropyrrolo[3,4-c]pyrrole;
2-(4,6-Dimethylpyrimidin-2-yl)-5-{[2-(1H-1,2,4-triazol-5-yl)phenyl]carbonyl} octahydro-pyrrolo[3,4-c]pyrrole;
2-(4,6-Dimethylpyrimidin-2-yl)-5-{[3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl} octahydropyrrolo[3,4-c]pyrrole;
2-{5-[(2,4-Dimethoxyphenyl)carbonyl]hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl}-6-fluoro-1,3-benzothiazole;
2-{5-[(2,4-Dimethoxyphenyl)carbonyl]hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl}-1,3-benzothiazole;
2-[5-{[2-(1H-Pyrazol-1-yl)phenyl]carbonyl}hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]quinoxaline;
2-{5-[(2-Thiophen-2-ylphenyl)carbonyl]hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl}quinoxaline;
2-{5-[(2-Methylnaphthalen-1-yl)carbonyl]hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl}quinoxaline;
2-(2,3-Dihydro-1,4-benzodioxin-5-ylcarbonyl)-5-(4-phenylpyrimidin-2-yl)octahydropyrrolo[3,4-c]pyrrole;
2-(4-Phenylpyrimidin-2-yl)-5-[(2-thiophen-2-ylphenyl)carbonyl]octahydro-pyrrolo[3,4-c]pyrrole;
2-(4-Phenylpyrimidin-2-yl)-5-{[2-(1H-pyrazol-1-yl)phenyl]carbonyl}octahydro-pyrrolo[3,4-c]pyrrole;
2-(4-Phenylpyrimidin-2-yl)-5-{[2-(1H-pyrrol-1-yl)phenyl]carbonyl}octahydro-pyrrolo[3,4-c]pyrrole;
2-[(2-Methylnaphthalen-1-yl)carbonyl]-5-(4-phenylpyrimidin-2-yl)octahydropyrrolo[3,4-c]pyrrole;
2-(5-Quinoxalin-2-yl-hexahydro-pyrrolo[3,4-c]pyrrole;-2-carbonyl)-benzonitrile;
2-[5-{[2-(1H-Pyrrol-1-yl)phenyl]carbonyl}hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]quinoxaline;
2-{5-[(4'-Fluorobiphenyl-2-yl)carbonyl]hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl}quinoxaline;
2-{5-[(3'-Fluorobiphenyl-2-yl)carbonyl]hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl}quinoxaline;

2-{5-[(2-Methylphenyl)carbonyl]hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl}quinoxaline;
2-(Biphenyl-2-ylcarbonyl)-5-(4-furan-2-ylpyrimidin-2-yl)octahydropyrrolo[3,4-c]pyrrole;
2-(4-Methylpyrimidin-2-yl)-5-[(2-thiophen-2-ylphenyl)carbonyl]octahydropyrrolo[3,4-c]pyrrole;
2-{5-[(2-Thiophen-2-ylphenyl)carbonyl]hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl}quinoline;
2-(4-Furan-2-ylpyrimidin-2-yl)-5-[(2-thiophen-2-ylphenyl)carbonyl]octahydropyrrolo[3,4-c]pyrrole;
2-{5-[(2-Ethylphenyl)carbonyl]hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl}quinoxaline;
2-[5-(1H-Indol-7-ylcarbonyl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]quinoxaline;
2-[(2-Thiophen-2-ylphenyl)carbonyl]-5-(4-thiophen-2-ylpyrimidin-2-yl)octahydropyrrolo[3,4-c]pyrrole;
2-(Biphenyl-2-ylcarbonyl)-5-(4-thiophen-2-ylpyrimidin-2-yl)octahydropyrrolo[3,4-c]pyrrole;
[5-(4,6-Dimethyl-pyrimidin-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-[2-(1-methyl-1H-imidazol-2-yl)-phenyl]-methanone;
2-[(2-Bromophenyl)carbonyl]-5-(4-phenylpyrimidin-2-yl)octahydropyrrolo[3,4-c]pyrrole;
2-{5-[(3'-Chlorobiphenyl-2-yl)carbonyl]hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl}quinoxaline;
2-{5-[(2-Bromophenyl)carbonyl]hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl}quinoxaline;
2-(4,6-Dimethylpyrimidin-2-yl)-5-[(2-thiophen-2-ylphenyl)carbonyl]octahydropyrrolo[3,4-c]pyrrole;
2-(Biphenyl-2-ylcarbonyl)-5-(4,6-dimethylpyrimidin-2-yl)octahydropyrrolo[3,4-c]pyrrole;
2-(4-Methoxypyrimidin-2-yl)-5-[(2-thiophen-2-ylphenyl)carbonyl]octahydropyrrolo[3,4-c]pyrrole;
6-Fluoro-2-{5-[(2-thiophen-2-ylphenyl)carbonyl]hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl}-1,3-benzothiazole

2-(4,6-Dimethylpyrimidin-2-yl)-5-[(2-methylnaphthalen-1-yl)carbonyl]octahydro-pyrrolo[3,4-c]pyrrole;
2-[(3'-Fluorobiphenyl-2-yl)carbonyl]-5-(4-methylpyrimidin-2-yl)octahydro-pyrrolo[3,4-c]pyrrole;
2-(4-Methoxypyrimidin-2-yl)-5-[(2-methylnaphthalen-1-yl)carbonyl]octahydro-pyrrolo[3,4-c]pyrrole;
2-[(2-Methylnaphthalen-1-yl)carbonyl]-5-(4-methylpyrimidin-2-yl)octahydro-pyrrolo[3,4-c]pyrrole;
2-[(3'-Fluorobiphenyl-2-yl)carbonyl]-5-(4-methoxypyrimidin-2-yl)octahydro-pyrrolo[3,4-c]pyrrole;
2-(4,6-Dimethylpyrimidin-2-yl)-5-[(3'-fluorobiphenyl-2-yl)carbonyl]octahydro-pyrrolo[3,4-c]pyrrole;
[5-(4,6-Dimethyl-pyrimidin-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-(2-fluoro-phenyl)-methanone;
2-(4-Methoxypyrimidin-2-yl)-5-[(4'-methylbiphenyl-2-yl)carbonyl]octahydro-pyrrolo[3,4-c]pyrrole;
2-[(3'-Chlorobiphenyl-2-yl)carbonyl]-5-(4-methoxypyrimidin-2-yl)octahydro-pyrrolo[3,4-c]pyrrole;
2-[(2-Ethoxynaphthalen-1-yl)carbonyl]-5-(4-methoxypyrimidin-2-yl)octahydropyrrolo[3,4-c]pyrrole;
2-[(4-Fluoronaphthalen-1-yl)carbonyl]-5-(4-methoxypyrimidin-2-yl)octahydro-pyrrolo[3,4-c]pyrrole;
2-(4-Methoxypyrimidin-2-yl)-5-(naphthalen-1-ylcarbonyl)octahydropyrrolo[3,4-c]pyrrole;
2-[(2-Ethoxyphenyl)carbonyl]-5-(4-methoxypyrimidin-2-yl)octahydropyrrolo[3,4-c]pyrrole;
2-[(2-Methoxynaphthalen-1-yl)carbonyl]-5-(4-methoxypyrimidin-2-yl)octahydropyrrolo[3,4-c]pyrrole;
2-(Biphenyl-2-ylcarbonyl)-5-[4-(1H-pyrazol-4-yl)pyrimidin-2-yl]octahydro-pyrrolo[3,4-c]pyrrole;
2-[4-(1H-Pyrazol-4-yl)pyrimidin-2-yl]-5-[(2-thiophen-2-ylphenyl)carbonyl]octahydro-pyrrolo[3,4-c]pyrrole;

2-(3,6-Dimethylpyrazin-2-yl)-5-[(2-thiophen-2-ylphenyl)carbonyl]octahydro-pyrrolo[3,4-c]pyrrole;
2-(Biphenyl-2-ylcarbonyl)-5-(3,5-dimethylpyrazin-2-yl)octahydropyrrolo[3,4-c]pyrrole;
2-Methyl-3-{5-[(2-thiophen-2-ylphenyl)carbonyl]hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl}quinoxaline;
2-[5-(Biphenyl-2-ylcarbonyl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-3-methylquinoxaline;
2-(4,6-Dimethylpyrimidin-2-yl)-5-{[2-(1H-pyrazol-1-yl)phenyl]carbonyl}octahydro-pyrrolo[3,4-c]pyrrole;
2-(4,6-Dimethoxypyrimidin-2-yl)-5-[(2-fluoro-6-pyrimidin-2-ylphenyl)carbonyl]octahydropyrrolo[3,4-c]pyrrole;
2-(4,6-Dimethylpyrimidin-2-yl)-5-[(2-pyridin-2-ylphenyl)carbonyl]octahydro-pyrrolo[3,4-c]pyrrole;
2-(4,6-Dimethoxypyrimidin-2-yl)-5-[(2-pyridin-2-ylphenyl)carbonyl]octahydro-pyrrolo[3,4-c]pyrrole;
2-(4,6-Dimethoxypyrimidin-2-yl)-5-[(5-fluoro-2-pyrimidin-2-ylphenyl)carbonyl]octahydropyrrolo[3,4-c]pyrrole;
2-(4,6-Dimethoxypyrimidin-2-yl)-5-{[5-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}octahydropyrrolo[3,4-c]pyrrole;
2-(4,6-Dimethylpyrimidin-2-yl)-5-[(2-fluoro-6-pyrimidin-2-ylphenyl)carbonyl]octahydropyrrolo[3,4-c]pyrrole;
2-(4,6-Dimethylpyrimidin-2-yl)-5-[(5-fluoro-2-pyrimidin-2-ylphenyl)carbonyl]octahydropyrrolo[3,4-c]pyrrole;
2-(4,6-Dimethylpyrimidin-2-yl)-5-{[5-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}octahydropyrrolo[3,4-c]pyrrole;
2-(4,6-Dimethylpyrimidin-2-yl)-5-[(2-ethylphenyl)carbonyl]octahydropyrrolo[3,4-c]pyrrole;
2-(4,6-Dimethylpyrimidin-2-yl)-5-[(2-ethoxynaphthalen-1-yl)carbonyl]octahydro-pyrrolo[3,4-c]pyrrole;
2-(4,6-Dimethoxypyrimidin-2-yl)-5-{[2-(1H-pyrazol-1-yl)phenyl]carbonyl}octahydro-pyrrolo[3,4-c]pyrrole;

2-(4,6-Dimethylpyrimidin-2-yl)-5-[(5-phenyl-1,3-oxazol-4-yl)carbonyl]octahydro-pyrrolo[3,4-c]pyrrole;

2-(4,6-Dimethylpyrimidin-2-yl)-5-[(5-phenylisoxazol-4-yl)carbonyl]octahydro-pyrrolo[3,4-c]pyrrole;

[5-(2-Isopropyl-6-methyl-pyrimidin-4-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone;

2-[(2-Bromophenyl)carbonyl]-5-(4,6-dimethylpyrimidin-2-yl)octahydropyrrolo[3,4-c]pyrrole;

2-(4,6-Dimethylpyrimidin-2-yl)-5-{[2-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl} octahydropyrrolo[3,4-c]pyrrole;

2-(4,6-Dimethoxypyrimidin-2-yl)-5-{[2-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl} octahydropyrrolo[3,4-c]pyrrole;

2-[5-{[2-(4H-1,2,4-Triazol-3-yl)phenyl]carbonyl}hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]quinoxaline;

2-[5-{[2-(4H-1,2,4-Triazol-3-yl)phenyl]carbonyl}hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-1,3-benzoxazole;

2-(4-Methylpyrimidin-2-yl)-5-{[2-(4H-1,2,4-triazol-3-yl)phenyl]carbonyl}octahydro-pyrrolo[3,4-c]pyrrole;

2-(4,6-Dimethylpyrimidin-2-yl)-5-[(2-ethoxyphenyl)carbonyl]octahydropyrrolo[3,4-c]pyrrole;

2-(4,6-Dimethylpyrimidin-2-yl)-5-{[4-fluoro-2-(trifluoromethyl)phenyl]carbonyl} octahydropyrrolo[3,4-c]pyrrole;

2-(4,6-Dimethylpyrimidin-2-yl)-5-[(4-fluoronaphthalen-1-yl)carbonyl]octahydro-pyrrolo[3,4-c]pyrrole;

2-(4,6-Dimethylpyrimidin-2-yl)-5-{[2-(1-methylethyl)phenyl]carbonyl}octahydro-pyrrolo[3,4-c]pyrrole;

2-(4,6-Dimethylpyrimidin-2-yl)-5-[(3-methoxy-2-methylphenyl)carbonyl]octahydro-pyrrolo[3,4-c]pyrrole;

2-(4,6-Dimethylpyrimidin-2-yl)-5-(naphthalen-1-ylcarbonyl)octahydropyrrolo[3,4-c]pyrrole;

2-[5-{[2-(4H-1,2,4-Triazol-3-yl)phenyl]carbonyl}hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-3-(trifluoromethyl)quinoxaline;

2-Methyl-3-[5-{[2-(4H-1,2,4-triazol-3-yl)phenyl]carbonyl}hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]quinoxaline;

2-[6-Methyl-2-(trifluoromethyl)pyrimidin-4-yl]-5-{[2-(4H-1,2,4-triazol-3-yl)phenyl]carbonyl}octahydropyrrolo[3,4-c]pyrrole;

2-[6-Methyl-2-(trifluoromethyl)pyrimidin-4-yl]-5-{[2-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}octahydropyrrolo[3,4-c]pyrrole;

2-{[2-Fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}-5-[6-methyl-2-(trifluoromethyl)pyrimidin-4-yl]octahydropyrrolo[3,4-c]pyrrole;

2-{[4-Fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}-5-[6-methyl-2-(trifluoromethyl)pyrimidin-4-yl]octahydropyrrolo[3,4-c]pyrrole;

2-(6-Methylpyrazin-2-yl)-5-{[5-methyl-2-(2H-1,2,3-triazol-2 yl)phenyl]carbonyl} octahydropyrrolo[3,4-c]pyrrole;

2-(3,6-Dimethylpyrazin-2-yl)-5-{[2-fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl} octahydropyrrolo[3,4-c]pyrrole;

2-(4,6-Dimethylpyrimidin-2-yl)-5-[(5-methyl-2-pyrimidin-2-ylphenyl)carbonyl] octahydropyrrolo[3,4-c]pyrrole;

2-(3,6-Dimethylpyrazin-2-yl)-5-[(5-methyl-2-pyrimidin-2-ylphenyl)carbonyl] octahydropyrrolo[3,4-c]pyrrole;

2-(3,6-Dimethylpyrazin-2-yl)-5-{[4-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl} octahydropyrrolo[3,4-c]pyrrole;

2-(4,6-Dimethylpyrimidin-2-yl)-5-{[5-iodo-2-(2H-1,2,3-triazol-2-yl)phenyl] carbonyl}octahydropyrrolo[3,4-c]pyrrole;

4-[5-{[2-Fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-N,N-dimethyl-6-(trifluoromethyl)pyrimidin-2-amine;

2-(4,6-Dimethylpyrimidin-2-yl)-5-{[2-fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl] carbonyl}octahydropyrrolo[3,4-c]pyrrole;

N,N-Dimethyl-4-{5-[(5-methyl-2-pyrimidin-2-ylphenyl)carbonyl]hexahydropyrrolo [3,4-c]pyrrol-2(1H)-yl}-6-(trifluoromethyl)pyrimidin-2-amine;

4-{5-[(5-Fluoro-2-pyrimidin-2-ylphenyl)carbonyl]hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl}-N,N-dimethyl-6-(trifluoromethyl)pyrimidin-2-amine;

4-[5-{[5-Fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-N,N-dimethyl-6-(trifluoromethyl)pyrimidin-2-amine;

4-[5-{[4-Fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-N,N-dimethyl-6-(trifluoromethyl)pyrimidin-2-amine;
2-[(5-Methyl-2-pyrimidin-2-ylphenyl)carbonyl]-5-[6-methyl-2-(trifluoromethyl) pyrimidin-4-yl]octahydropyrrolo[3,4-c]pyrrole;
2-[(5-Fluoro-2-pyrimidin-2-ylphenyl)carbonyl]-5-(4-phenylpyrimidin-2-yl)octahydropyrrolo[3,4-c]pyrrole;
2-{[5-Fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}-5-[6-methyl-2-(trifluoromethyl)pyrimidin-4-yl]octahydropyrrolo[3,4-c]pyrrole;
[5-(2,6-Dimethyl-pyrimidin-4-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-(5-fluoro-2-[1,2,3]triazol-2-yl-phenyl)-methanone;
4-{5-[(2-Fluoro-6-pyrimidin-2-ylphenyl)carbonyl]hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl}-N,N-dimethyl-6-(trifluoromethyl)pyrimidin-2-amine
2-[(2-Fluoro-6-pyrimidin-2-ylphenyl)carbonyl]-5-[6-methyl-2-(trifluoromethyl) pyrimidin-4-yl]octahydropyrrolo[3,4-c]pyrrole;
2-(4,6-Dimethylpyrimidin-2-yl)-5-{[4-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl] carbonyl}octahydropyrrolo[3,4-c]pyrrole;
N,N,6-Trimethyl-2-[5-{[2-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}hexahydro pyrrolo[3,4-c]pyrrol-2(1H)-yl]pyrimidin-4-amine;
N,N,4-Trimethyl-6-[5-{[2-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}hexahydro pyrrolo[3,4-c]pyrrol-2(1H)-yl]pyrimidin-2-amine;
N,N-Dimethyl-4-[5-{[2-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}hexahydropyrrolo [3,4-c]pyrrol-2(1H)-yl]-6-(trifluoromethyl)pyrimidin-2-amine;
2-(2,6-Dimethylpyrimidin-4-yl)-5-{[2-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl} octahydropyrrolo[3,4-c]pyrrole;
[5-(3,6-Dimethyl-pyrazin-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-(5-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;
2-[5-{[5-Fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-N,N,6-trimethylpyrimidin-4-amine;
2-(5-Methoxypyridin-2-yl)-5-[(2-thiophen-2-ylphenyl)carbonyl]octahydropyrrolo [3,4-c]pyrrole;
2-[(2-Ethoxynaphthalen-1-yl)carbonyl]-5-(4-phenylpyrimidin-2-yl)octahydro pyrrolo[3,4-c]pyrrole;

2-{[5-Methyl-2-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}-5-(4-phenylpyrimidin-2-yl)octahydropyrrolo[3,4-c]pyrrole;

(4-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[5-(4,6-dimethyl-pyrimidin-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-methanone;

2-(4,6-Dimethoxypyrimidin-2-yl)-5-{[5-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl] carbonyl}octahydropyrrolo[3,4-c]pyrrole;

2-(4,6-Dimethylpyrimidin-2-yl)-5-{[5-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl] carbonyl}octahydropyrrolo[3,4-c]pyrrole;

2-(4-Phenylpyrimidin-2-yl)-5-{[2-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}octahydro pyrrolo[3,4-c]pyrrole;

2-(4,6-Dimethylpyrimidin-2-yl)-5-{[5-(2-fluorophenyl)-2-methyl-1,3-thiazol-4-yl]carbonyl}octahydropyrrolo[3,4-c]pyrrole;

2-[(2-Thiophen-2-ylphenyl)carbonyl]-5-[6-(trifluoromethyl)pyridin-2-yl]octahydro pyrrolo[3,4-c]pyrrole;

2-(6-Methylpyridin-2-yl)-5-[(2-thiophen-2-ylphenyl)carbonyl]octahydropyrrolo[3,4-c]pyrrole;

2-(4-Methylpyrimidin-2-yl)-5-{[2-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}octahydro pyrrolo[3,4-c]pyrrole;

2-(4-Methylpyridin-2-yl)-5-[(2-thiophen-2-ylphenyl)carbonyl]octahydropyrrolo[3,4-c]pyrrole;

2-(6-Methoxypyridin-2-yl)-5-[(2-thiophen-2-ylphenyl)carbonyl]octahydro pyrrolo[3,4-c]pyrrole;

2-(4,6-Dimethoxypyrimidin-2-yl)-5-[(2-thiophen-2-ylphenyl)carbonyl]octahydro pyrrolo[3,4-c]pyrrole;

2-{5-[(2-Thiophen-2-ylphenyl)carbonyl]hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl}-1,3-benzoxazole;

2-[(2-Thiophen-2-ylphenyl)carbonyl]-5-[3-(trifluoromethyl)pyridin-2-yl]octahydro pyrrolo[3,4-c]pyrrole;

[5-(4-Phenyl-pyrimidin-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-[2-(4H-[1,2,4]triazol-3-yl)-phenyl]-methanone;

2-(4,6-Dimethoxypyrimidin-2-yl)-5-{[5-(2-fluorophenyl)-2-methyl-1,3-thiazol-4-yl]carbonyl}octahydropyrrolo[3,4-c]pyrrole;

2-(4-Thiophen-2-ylpyrimidin-2-yl)-5-{[2-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl} octahydropyrrolo[3,4-c]pyrrole;

2-[5-{[2-(2H-1,2,3-Triazol-2-yl)phenyl]carbonyl}hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-1,3-benzoxazole;

2-{5-[(2-Ethoxynaphthalen-1-yl)carbonyl]hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl}quinoxaline;

2-{5-[(5-Fluoro-2-pyrimidin-2-ylphenyl)carbonyl]hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl}quinoxaline;

2-(6-Ethoxypyridin-2-yl)-5-{[2-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}octahydro pyrrolo[3,4-c]pyrrole;

2-[(5-Fluoro-2-pyrimidin-2-ylphenyl)carbonyl]-5-[4-(trifluoromethyl)pyrimidin-2-yl]octahydropyrrolo[3,4-c]pyrrole;

2-[5-{[2-(2H-1,2,3-Triazol-2-yl)phenyl]carbonyl}hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]quinoxaline

2-[(5-Fluoro-2-pyrimidin-2-ylphenyl)carbonyl]-5-(4-methoxypyrimidin-2-yl)octahydropyrrolo[3,4-c]pyrrole;

2-(4-Furan-2-ylpyrimidin-2-yl)-5-{[2-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl} octahydropyrrolo[3,4-c]pyrrole;

2-(5-Fluoropyridin-2-yl)-5-{[2-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}octahydro pyrrolo[3,4-c]pyrrole;

2-{[2-(2H-1,2,3-Triazol-2-yl)phenyl]carbonyl}-5-[4-(trifluoromethyl)pyrimidin-2-yl]octahydropyrrolo[3,4-c]pyrrole;

2-(4-Methoxypyrimidin-2-yl)-5-{[2-(1H-1,2,4-triazol-5-yl)phenyl]carbonyl} octahydropyrrolo[3,4-c]pyrrole;

2-(3,6-Dimethylpyrazin-2-yl)-5-{[2-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}octa hydropyrrolo[3,4-c]pyrrole;

2-(4-Methoxypyrimidin-2-yl)-5-{[2-(2H-1, 2,3-triazol-2-yl)phenyl]carbonyl}octa hydropyrrolo[3,4-c]pyrrole;

2-{[5-Chloro-2-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}-5-(4,6-dimethylpyrimidin-2-yl)octahydropyrrolo[3,4-c]pyrrole;

2-{[4-Fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}-5-(6-methylpyrazin-2-yl)octahydropyrrolo[3,4-c]pyrrole;

2-{[4-Fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}-5-(4-methoxypyrimidin-2-yl)octahydropyrrolo[3,4-c]pyrrole;

2-(4,6-Dimethoxypyrimidin-2-yl)-5-{[4-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}octahydropyrrolo[3,4-c]pyrrole;

[5-(4,6-Dimethyl-pyrimidin-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-(5-methoxy-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

(2-Fluoro-6-[1,2,3]triazol-2-yl-phenyl)-[5-(4-methoxy-pyrimidin-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-methanone;

6-Chloro-2-{5-[(2,4-dimethoxyphenyl)carbonyl]hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl}-1,3-benzothiazole;

2-(Biphenyl-2-ylcarbonyl)-5-(4-phenylpyrimidin-2-yl)octahydropyrrolo[3,4-c]pyrrole;

2-{5-[(2,6-Dimethoxyphenyl)carbonyl]hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl}quinoxaline;

2-[(2,6-Dimethoxyphenyl)carbonyl]-5-(4-phenylpyrimidin-2-yl)octahydropyrrolo[3,4-c]pyrrole;

2-[(2,4-Dimethoxyphenyl)carbonyl]-5-(4-phenylpyrimidin-2-yl)octahydropyrrolo[3,4-c]pyrrole;

2-[5-(Biphenyl-2-ylcarbonyl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]quinoxaline;

2-[5-(Biphenyl-2-ylcarbonyl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-1,3-benzothiazole;

2-{5-[(2,4-Dimethoxyphenyl)carbonyl]hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl}-4-methylquinoline;

2-{5-[(2,4-Dimethoxyphenyl)carbonyl]hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl}-6-methoxy-1,3-benzothiazole;

2-{5-[(2,4-Dimethoxyphenyl)carbonyl]hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl}-6-methyl-1,3-benzothiazole;

2-(Biphenyl-2-ylcarbonyl)-5-(6-methylpyridin-2-yl)octahydropyrrolo[3,4-c]pyrrole;

2-(Biphenyl-2-ylcarbonyl)-5-(4-methylpyrimidin-2-yl)octahydropyrrolo[3,4-c]pyrrole;

2-[5-(Biphenyl-2-ylcarbonyl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]quinoline;

2-[5-(Biphenyl-2-ylcarbonyl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-6-fluoro-1,3-benzothiazole;
2-(Biphenyl-2-ylcarbonyl)-5-(4-methoxypyrimidin-2-yl)octahydropyrrolo[3,4-c]pyrrole;
2-[5-(Biphenyl-2-ylcarbonyl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-4-methylquinoline;
(2,4-Dimethoxy-phenyl)-[5-(4-methoxy-pyrimidin-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-methanone;
(5-Benzooxazol-2-yl-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl)-(2-methoxy-phenyl)-methanone;
(2-Pyridin-3-yl-phenyl)-(5-quinoxalin-2-yl-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl)-methanone;
[5-(4,6-Dimethyl-pyrimidin-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-[2-(1H-imidazol-2-yl)-phenyl]-methanone;
(5-Benzooxazol-2-yl-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl)-(2,4-dimethoxy-phenyl)-methanone;
(5-Benzooxazol-2-yl-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl)-biphenyl-2-yl-methanone;
(2,4-Dimethoxy-phenyl)-[5-(6-methyl-pyridin-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-methanone;
(2,4-Dimethoxy-phenyl)-[5-(4-methyl-pyrimidin-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-methanone;
Biphenyl-2-yl-[5-(6-methoxy-benzothiazol-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-methanone;
Biphenyl-2-yl-[5-(6-methyl-benzothiazol-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-methanone;
[5-(6-Chloro-benzothiazol-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-(2,6-dimethoxy-phenyl)-methanone;
Biphenyl-2-yl-[5-(6-chloro-benzothiazol-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-methanone;
(2,4-Dimethoxy-phenyl)-(5-quinoxalin-2-yl-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl)-methanone;

(5-Benzooxazol-2-yl-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl)-(2,6-dimethoxy-phenyl)-methanone;
(4'-Methyl-biphenyl-2-yl)-(5-quinoxalin-2-yl-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl)-methanone;
(5-Quinoxalin-2-yl-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl)-(4'-trifluoromethyl-biphenyl-2-yl)-methanone;
(4'-Methyl-biphenyl-2-yl)-[5-(4-phenyl-pyrimidin-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-methanone;
[5-(4-Phenyl-pyrimidin-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-(4'-trifluoromethyl-biphenyl-2-yl)-methanone;
(4-Methoxy-2-methyl-phenyl)-(5-quinoxalin-2-yl-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl)-methanone;
(3'-Chloro-biphenyl-2-yl)-[5-(4-phenyl-pyrimidin-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-methanone;
(2-Methoxy-phenyl)-[5-(4-methoxy-pyrimidin-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-methanone;
(2-Methoxy-phenyl)-[5-(4-methyl-pyrimidin-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-methanone;
[5-(4,6-Dimethyl-pyrimidin-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-(2-methoxy-phenyl)-methanone;
2-[5-(4,6-Dimethyl-pyrimidin-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrole;-2-carbonyl]-benzonitrile;
Cinnolin-4-yl-[5-(4,6-dimethyl-pyrimidin-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-methanone;
(5-Fluoro-2-pyrimidin-2-yl-phenyl)-[5-(6-methyl-2-trifluoromethyl-pyrimidin-4-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-methanone;
[5-(4,6-Dimethyl-pyrimidin-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-(2-[1,2,3]triazol-1-yl-phenyl)-methanone;
[5-(4,6-Dimethyl-pyrimidin-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-(2-[1,2,4]triazol-1-yl-phenyl)-methanone;
[5-(4,6-Dimethoxy-pyrimidin-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-(3-phenyl-pyridin-2-yl)-methanone;

[5-(4,6-Dimethyl-pyrimidin-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-(3-phenyl-pyridin-2-yl)-methanone;
[5-(6-Methyl-2-propyl-pyrimidin-4-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone;
[5-(2-Methyl-pyrimidin-4-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone;
[5-(6-Methyl-pyrazin-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone;
[5-(3,6-Dimethyl-pyrazin-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-(5-fluoro-2-pyrimidin-2-yl-phenyl)-methanone;
[5-(3,6-Dimethyl-pyrazin-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-[2-(2H-[1,2,4]triazol-3-yl)-phenyl]-methanone;
[5-(2-Pyrrolidin-1-yl-6-trifluoromethyl-pyrimidin-4-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone;
2-(2,6-Dimethylpyrimidin-4-yl)-5-{[5-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}octahydropyrrolo[3,4-c]pyrrole;
[5-(4,6-Dimethyl-pyrimidin-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-(2-nitro-6-[1,2,3]triazol-2-yl-phenyl)-methanone;
[5-(4,6-Dimethyl-pyrimidin-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-(2-furan-2-yl-phenyl)-methanone;
[5-(4,6-Dimethyl-pyrimidin-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-(2-methyl-5-phenyl-thiazol-4-yl)-methanone;
2-[(2,3-Dimethylphenyl)carbonyl]-5-(4,6-dimethylpyrimidin-2-yl)octahydropyrrolo[3,4-c]pyrrole;
2-(4,6-Dimethylpyrimidin-2-yl)-5-[(3-fluoro-2-methylphenyl)carbonyl]octahydropyrrolo[3,4-c]pyrrole;
2-(4,6-Dimethylpyrimidin-2-yl)-5-{[5-fluoro-2-(trifluoromethyl)phenyl]carbonyl}octahydropyrrolo[3,4-c]pyrrole;
2-[(4-Chloro-2-methoxyphenyl)carbonyl]-5-(4,6-dimethylpyrimidin-2-yl)octahydropyrrolo[3,4-c]pyrrole;
2-[(5-Chloro-2-methylphenyl)carbonyl]-5-(4,6-dimethylpyrimidin-2-yl)octahydropyrrolo[3,4-c]pyrrole;

2-[(2,5-Dimethylphenyl)carbonyl]-5-(4,6-dimethylpyrimidin-2-yl)octahydropyrrolo[3,4-c]pyrrole;
2-[(2,6-Dimethylphenyl)carbonyl]-5-(4,6-dimethylpyrimidin-2-yl)octahydropyrrolo[3,4-c]pyrrole;
2-(4,6-Dimethylpyrimidin-2-yl)-5-[(5-fluoro-2-methylphenyl)carbonyl]octahydropyrrolo[3,4-c]pyrrole;
2-[(2,4-Dimethylphenyl)carbonyl]-5-(4,6-dimethylpyrimidin-2-yl)octahydropyrrolo[3,4-c]pyrrole;
2-[(2,5-Diethoxyphenyl)carbonyl]-5-(4,6-dimethylpyrimidin-2-yl)octahydropyrrolo[3,4-c]pyrrole;
2-[(2,6-Diethoxyphenyl)carbonyl]-5-(4,6-dimethylpyrimidin-2-yl)octahydropyrrolo[3,4-c]pyrrole;
2-[(2-Chloro-6-methylphenyl)carbonyl]-5-(4,6-dimethylpyrimidin-2-yl)octahydropyrrolo[3,4-c]pyrrole;
(5-(4,6-Dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(4-fluoro-2-(pyrimidin-2-yl)phenyl)methanone;
(5-(4,6-dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(3-fluoro-2-iodophenyl)methanone;
2-(4,6-Dimethylpyrimidin-2-yl)-5-{[2-(trifluoromethyl)pyridin-3-yl]carbonyl}octahydropyrrolo[3,4-c]pyrrole;
2-Bromopyridin-3-yl)(5-(4,6-dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)methanone;
(5-(4,6-Dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(2-(pyrimidin-2-yl)pyridin-3-yl)methanone;
(5-(4,6-Dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(2-(1-(tetrahydro-2H-pyran-2-yl)-1H-pyrazol-5-yl)pyridin-3-yl)methanone;
(2-(1H-Pyrazol-5-yl)pyridin-3-yl)(5-(4,6-dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)methanone;
(2-(2H-1,2,3-Triazol-2-yl)pyridin-3-yl)(5-(4,6-dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)methanone;
(3-Fluoro-2-(pyrimidin-2-yl)phenyl)(5-(4,5,6-trimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)methanone;

(3-Fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)(5-(4,5,6-trimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)methanone;
(5-Methoxy-2-(2H-1,2,3-triazol-2-yl)phenyl)(5-(4,5,6-trimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)methanone;
(3-Fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)(5-(6-fluoroquinazolin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)methanone;
(3-Fluoro-2-(pyrimidin-2-yl)phenyl)(5-(6-fluoroquinazolin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)methanone;
(5-(6,7-Difluoroquinoxalin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone;
(5-(6,7-Difluoroquinoxalin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(5-methoxy-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone;
(5-(6,7-Difluoroquinoxalin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(2-fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl)methanone;
(2-Bromo-3-fluorophenyl)(5-(6-fluoroquinazolin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)methanone;
(5-(4,6-dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(4-fluoro-2-(5-methylpyridin-2-yl)phenyl)methanone;
(2-Bromopyridin-3-yl)(5-(4,5,6-trimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)methanone;
(2-(1-(Tetrahydro-2H-pyran-2-yl)-1H-pyrazol-5-yl)pyridin-3-yl)(5-(4,5,6-trimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)methanone;
(2-(1H-Pyrazol-5-yl)pyridin-3-yl)(5-(4,5,6-trimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)methanone;
6-[5-{[2-Fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-2-methylpyrimidin-4(3H)-one;
2-(2,6-Dimethylpyrimidin-4-yl)-5-{[5-(4-fluorophenyl)-2-methyl-1,3-thiazol-4-yl]carbonyl}octahydropyrrolo[3,4-c]pyrrole;
2-(4,6-Dimethylpyrimidin-2-yl)-5-{[5-(4-fluorophenyl)-2-methyl-1,3-thiazol-4-yl]carbonyl}octahydropyrrolo[3,4-c]pyrrole;
6-[5-{[5-(4-Fluorophenyl)-2-methyl-1,3-thiazol-4-yl]carbonyl}hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-2-methylpyrimidin-4(3H)-one;

6-{5-[(5-Fluoro-2-pyrimidin-2-ylphenyl)carbonyl]hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl}-2-methylpyrimidin-4(3H)-one;

(5-(4,6-Dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(4-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone;

(5-(4,6-Dimethoxypyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(2-fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl)methanone;

(5-(4,6-Dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(2-methyl-6-(2H-1,2,3-triazol-2-yl)phenyl)methanone;

(5-(4,6-Dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(3-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone;

(2-Fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl)(5-(5-nitropyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)methanone;

Methyl 2-(5-(2-fluoro-6-(2H-1,2,3-triazol-2-yl)benzoyl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)-4-(trifluoromethyl)pyrimidine-5-carboxylate;

2-(5-(2-Fluoro-6-(2H-1,2,3-triazol-2-yl)benzoyl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)-4-(trifluoromethyl)pyrimidine-5-carboxylic acid;

(2-(4H-1,2,4-Triazol-4-yl)phenyl)(5-(4,6-dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)methanone;

2-(5-(2-Fluoro-6-(2H-1,2,3-triazol-2-yl)benzoyl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)-6-methylpyrimidine-4-carboxylic acid;

(4,5-Difluoro-2-(4H-1,2,4-triazol-4-yl)phenyl)(5-(4,6-dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)methanone;

(5-(4,6-Dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(3-methyl-2-(1H-1,2,3-triazol-1-yl)phenyl)methanone;

2-(5-(2-Fluoro-6-(2H-1,2,3-triazol-2-yl)benzoyl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)-N,N,6-trimethylpyrimidine-4-carboxamide;

2-(5-(2-Fluoro-6-(2H-1,2,3-triazol-2-yl)benzoyl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)-N,N-dimethyl-4-(trifluoromethyl)pyrimidine-5-carboxamide;

(5-(4,6-Dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(mesityl)methanone;

(2,3-Difluorophenyl)(5-(4,6-dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)methanone;

(5-(4,6-Dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(4-methoxy-2-(pyrimidin-2-yl)phenyl)methanone;
(2,3-Dimethoxyphenyl)(5-(4,6-dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)methanone;
(5-(4,6-Dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(2-(trifluoromethoxy)phenyl)methanone;
[5-(4,6-Dimethyl-pyrimidin-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-(6-methyl-2-[1,2,3]triazol-2-yl-pyridin-3-yl)-methanone;
(5-(4,6-Dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(2-methoxy-4-methylphenyl)methanone;
(5-(4,6-Dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(4-methoxy-2-methylphenyl)methanone;
(2,6-Difluorophenyl)(5-(4,6-dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)methanone;
2-[5-{[2-Fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-6-methylpyrimidine-4-carbonitrile;
2-[4,6-Bis(trifluoromethyl)pyrimidin-2-yl]-5-{[2-fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}octahydropyrrolo[3,4-c]pyrrole;
2-[5-{[2-Fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-6-methylpyrimidin-4-ol;
(2-Fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl)(5-(4-(furan-2-yl)-6-methylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)methanone;
2-(4,6-Dimethylpyrimidin-2-yl)-5-[(3-fluoro-2-pyrimidin-2-ylphenyl)carbonyl]octahydropyrrolo[3,4-c]pyrrole;
2-(4,6-Dimethylpyrimidin-2-yl)-5-{[3-fluoro-2-(1H-pyrazol-5-yl)phenyl]carbonyl}octahydropyrrolo[3,4-c]pyrrole;
2-(4,6-Dimethylpyrimidin-2-yl)-5-{[3-methoxy-2-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}octahydropyrrolo[3,4-c]pyrrole;
2-(4,6-Dimethylpyrimidin-2-yl)-5-{[3-methoxy-2-(1H-1,2,3-triazol-1-yl)phenyl]carbonyl}octahydropyrrolo[3,4-c]pyrrole;
2-(4,6-Dimethylpyrimidin-2-yl)-5-{[3-fluoro-2-(1H-1,2,3-triazol-1-yl)phenyl]carbonyl}octahydropyrrolo[3,4-c]pyrrole;

2-(4,6-Dimethylpyrimidin-2-yl)-5-{[4-methoxy-2-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}octahydropyrrolo[3,4-c]pyrrole;
2-(4,6-Dimethylpyrimidin-2-yl)-5-{[4-methoxy-2-(1H-1,2,3-triazol-2-yl)phenyl]carbonyl}octahydropyrrolo[3,4-c]pyrrole;
2-(5-Fluoro-4-methylpyrimidin-2-yl)-5-{[2-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}octahydropyrrolo[3,4-c]pyrrole;
2-(2-Chloro-5-fluoropyrimidin-4-yl)-5-{[2-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}octahydropyrrolo[3,4-c]pyrrole;
2-(5-Fluoropyrimidin-2-yl)-5-{[2-fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}octahydropyrrolo[3,4-c]pyrrole;
2-(5-Fluoro-4-methylpyrimidin-2-yl)-5-{[2-fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}octahydropyrrolo[3,4-c]pyrrole;
2-{[2-Fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}-5-(4,5,6-trimethylpyrimidin-2-yl)octahydropyrrolo[3,4-c]pyrrole;
2-(4,5-Dimethylpyrimidin-2-yl)-5-{[2-fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}octahydropyrrolo[3,4-c]pyrrole;
2-{[2-Fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}-5-(4-methoxy-6-methylpyrimidin-2-yl)octahydropyrrolo[3,4-c]pyrrole;
2-(4-Ethyl-6-methylpyrimidin-2-yl)-5-{[2-fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}octahydropyrrolo[3,4-c]pyrrole;
2-{[2-Fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}-5-[4-methyl-6-(1-methylethyl)pyrimidin-2-yl]octahydropyrrolo[3,4-c]pyrrole;
2-[4-Methyl-6-(1-methylethyl)pyrimidin-2-yl]-5-{[2-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}octahydropyrrolo[3,4-c]pyrrole;
2-{[5-(1-Methylethyl)-2-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}-5-[4-methyl-6-(1-methylethyl)pyrimidin-2-yl]octahydropyrrolo[3,4-c]pyrrole;
2-(4-tert-Butyl-6-methylpyrimidin-2-yl)-5-{[2-fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}octahydropyrrolo[3,4-c]pyrrole;
2-(4-Cyclopropyl-6-methylpyrimidin-2-yl)-5-{[2-fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}octahydropyrrolo[3,4-c]pyrrole;
2-{[2-Fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}-5-(4-methyl-1,3,5-triazin-2-yl)octahydropyrrolo[3,4-c]pyrrole;

2-{[2-Fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}-5-(4-methyl-6-morpholin-4-ylpyrimidin-2-yl)octahydropyrrolo[3,4-c]pyrrole;
2-{[2-(4H-1,2,4-Triazol-3-yl)phenyl]carbonyl}-5-(4,5,6-trimethylpyrimidin-2-yl)octahydropyrrolo[3,4-c]pyrrole;
2-(4,6-Dimethylpyrimidin-2-yl)-5-{[2-(3-methyl-1,2,4-oxadiazol-5-yl)phenyl]carbonyl}octahydropyrrolo[3,4-c]pyrrole;
2-(4,6-Dimethylpyrimidin-2-yl)-5-{[2-(1-methyl-1H-1,2,4-triazol-5-yl)phenyl]carbonyl}octahydropyrrolo[3,4-c]pyrrole;
2-(4,6-Dimethylpyrimidin-2-yl)-5-{[2-(1-methyl-1H-1,2,4-triazol-3-yl)phenyl]carbonyl}octahydropyrrolo[3,4-c]pyrrole;
2-{[2-(3-Methyl-1,2,4-oxadiazol-5-yl)phenyl]carbonyl}-5-(4,5,6-trimethylpyrimidin-2-yl)octahydropyrrolo[3,4-c]pyrrole;
2-(5-Fluoro-4-methylpyrimidin-2-yl)-5-{[2-(3-methyl-1,2,4-oxadiazol-5-yl)phenyl]carbonyl}octahydropyrrolo[3,4-c]pyrrole;
2-{[2-(1-Methyl-1H-1,2,4-triazol-3-yl)phenyl]carbonyl}-5-(4,5,6-trimethylpyrimidin-2-yl)octahydropyrrolo[3,4-c]pyrrole;
2-(5-Fluoro-4-methylpyrimidin-2-yl)-5-{[2-(1-methyl-1H-1,2,4-triazol-3-yl)phenyl]carbonyl}octahydropyrrolo[3,4-c]pyrrole;
2-[5-{[2-Fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-4-methyl-6,7-dihydro-5H-cyclopenta[d]pyrimidine;
2-(4,6-Dimethylpyrimidin-2-yl)-5-{[3-fluoro-2-(3-methyl-1,2,4-oxadiazol-5-yl)phenyl]carbonyl}octahydropyrrolo[3,4-c]pyrrole;
2-(4,6-Dimethylpyrimidin-2-yl)-5-{[2-fluoro-6-(3-methyl-1,2,4-oxadiazol-5-yl)phenyl]carbonyl}octahydropyrrolo[3,4-c]pyrrole;
2-(5-Chloro-4-methylpyrimidin-2-yl)-5-{[2-fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}octahydropyrrolo[3,4-c]pyrrole;
2-(5-Chloro-4,6-dimethylpyrimidin-2-yl)-5-{[2-fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}octahydropyrrolo[3,4-c]pyrrole;
2-(5-Chloro-4,6-dimethylpyrimidin-2-yl)-5-{[2-(3-methyl-1,2,4-oxadiazol-5-yl)phenyl]carbonyl}octahydropyrrolo[3,4-c]pyrrole;
4-Methyl-2-[5-{[2-(3-methyl-1,2,4-oxadiazol-5-yl)phenyl]carbonyl}hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-6,7-dihydro-5H-cyclopenta[d]pyrimidine;

2-(5-Chloro-4,6-dimethylpyrimidin-2-yl)-5-{[2-(1-methyl-1H-1,2,4-triazol-3-yl)phenyl]carbonyl}octahydropyrrolo[3,4-c]pyrrole;
2-(5-Chloro-4-methylpyrimidin-2-yl)-5-{[2-(1-methyl-1H-1,2,4-triazol-3-yl)phenyl]carbonyl}octahydropyrrolo[3,4-c]pyrrole;
2-(5-Ethyl-4,6-dimethylpyrimidin-2-yl)-5-{[2-(1-methyl-1H-1,2,4-triazol-3-yl)phenyl]carbonyl}octahydropyrrolo[3,4-c]pyrrole;
2-{[3-(2H-1,2,3-Triazol-2-yl)pyridin-2-yl]carbonyl}-5-(4,5,6-trimethylpyrimidin-2-yl)octahydropyrrolo[3,4-c]pyrrole;
2-(5-Chloro-4,6-dimethylpyrimidin-2-yl)-5-{[3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl]carbonyl}octahydropyrrolo[3,4-c]pyrrole;
2-(5-Fluoro-4,6-dimethylpyrimidin-2-yl)-5-{[3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl]carbonyl}octahydropyrrolo[3,4-c]pyrrole;
2-(4,6-Dimethylpyrimidin-2-yl)-5-(9H-fluoren-4-ylcarbonyl)octahydropyrrolo[3,4-c]pyrrole;
[5-(4,6-Dimethyl-pyrimidin-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-(5-[1,2,3]triazol-2-yl-benzo[1,3]dioxol-4-yl)-methanone;
[5-(4,6-Dimethyl-pyrimidin-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-(8-[1,2,3]triazol-2-yl-naphthalen-1-yl)-methanone;
[5-(4,6-Dimethyl-pyrimidin-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-(4-[1,2,3]triazol-1-yl-pyridin-3-yl)-methanone;
(5-tert-Butyl-2-methoxy-phenyl)-[5-(4,6-dimethyl-pyrimidin-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-methanone;
[5-(4,6-Dimethyl-pyrimidin-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-(1-[1,2,3]triazol-2-yl-naphthalen-2-yl)-methanone;
[5-(4,6-Dimethyl-pyrimidin-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-(3-[1,2,3]triazol-2-yl-pyridin-2-yl)-methanone;
(2-Bromo-4,5-dimethoxy-phenyl)-[5-(4,6-dimethyl-pyrimidin-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-methanone;
(3,4-Dihydro-2H-benzo[b][1,4]dioxepin-6-yl)-[5-(4,6-dimethyl-pyrimidin-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-methanone;
(5-(4,6-Dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(4-fluoro-2-(6-methylpyridin-2-yl)phenyl)methanone;

[5-(4,6-Dimethyl-pyrimidin-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-(6-methyl-2-[1,2,3]triazol-1-yl-pyridin-3-yl)-methanone;
(1-Bromo-naphthalen-2-yl)-[5-(4,6-dimethyl-pyrimidin-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-methanone;
[5-(4,6-Dimethyl-pyrimidin-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-(3-methoxy-naphthalen-2-yl)-methanone;
[5-(4,6-Dimethyl-pyrimidin-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-(8-[1,2,3]triazol-2-yl-naphthalen-1-yl)-methanone;
[5-(4,6-Dimethyl-pyrimidin-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-(1-methoxy-naphthalen-2-yl)-methanone;
(4,5-Dimethoxy-2-[1,2,3]triazol-1-yl-phenyl)-[5-(4,6-dimethyl-pyrimidin-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-methanone;
(4,5-Dimethoxy-2-[1,2,3]triazol-2-yl-phenyl)-[5-(4,6-dimethyl-pyrimidin-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-methanone;
(5-(4,6-Dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(4-fluoro-2-(4-methylpyridin-2-yl)phenyl)methanone;
(5-(4,6-Dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(3-propoxypyridin-2-yl)methanone;
(3-Propoxypyridin-2-yl)(5-(5-(trifluoromethyl)pyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)methanone;
(5-(4,6-Dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(4-fluoro-2-(3-fluoropyridin-2-yl)phenyl)methanone;
(3-Propoxypyridin-2-yl)(5-(quinoxalin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)methanone;
2-(5-([1,1'-Biphenyl]-2-ylsulfonyl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)quinoxaline;
2-[(2,6-Dimethoxyphenyl)carbonyl]-5-[5-(trifluoromethyl)pyridin-2-yl]octahydropyrrolo[3,4-c]pyrrole;
(2,6-Dimethoxyphenyl)(5-(5-(trifluoromethyl)pyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)methanone;
(2,6-Dimethoxyphenyl)(5-(4,6-dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)methanone;

(5-(4,6-Dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(3-methylfuran-2-yl)methanone;
2-[(3-Methylfuran-2-yl)carbonyl]-5-[5-(trifluoromethyl)pyridin-2-yl]octahydropyrrolo[3,4-c]pyrrole;
(3-Methylfuran-2-yl)(5-(5-(trifluoromethyl)pyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)methanone;
(3-Methylfuran-2-yl)(5-(quinoxalin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)methanone;
2-([1,1'-Biphenyl]-2-ylsulfonyl)-5-(5-(trifluoromethyl)pyridin-2-yl)octahydropyrrolo[3,4-c]pyrrole;
2-([1,1'-Biphenyl]-2-ylsulfonyl)-5-(5-(trifluoromethyl)pyrimidin-2-yl)octahydropyrrolo[3,4-c]pyrrole;
2-([1,1'-Biphenyl]-2-ylsulfonyl)-5-(4,6-dimethylpyrimidin-2-yl)octahydropyrrolo[3,4-c]pyrrole;
2-(4,6-Dimethylpyrimidin-2-yl)-5-((2-methoxyphenyl)sulfonyl)octahydropyrrolo[3,4-c]pyrrole;
2-((2-Methoxyphenyl)sulfonyl)-5-(5-(trifluoromethyl)pyrimidin-2-yl)octahydropyrrolo[3,4-c]pyrrole;
2-((2-Methoxyphenyl)sulfonyl)-5-(5-(trifluoromethyl)pyridin-2-yl)octahydropyrrolo[3,4-c]pyrrole;
2-(5-((2-Methoxyphenyl)sulfonyl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)quinoxaline;
(3,6'-Dimethyl-[2,3'-bipyridin]-2'-yl)(5-(quinoxalin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)methanone;
(3,6'-Dimethyl-[2,3'-bipyridin]-2'-yl)(5-(5-(trifluoromethyl)pyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)methanone;
(3,6'-Dimethyl-[2,3'-bipyridin]-2'-yl)(5-(5-(trifluoromethyl)pyridin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)methanone;
(5-(4,6-Dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(4-fluoro-2-(pyridin-2-yl)phenyl)methanone;
(5-(4,6-Dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(3-fluoro-2-(pyridin-2-yl)phenyl)methanone;

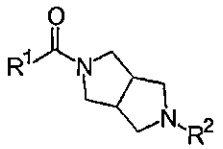
[2,3'-Bipyridin]-2'-yl(5-(4,6-dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)methanone;
(5-(4,6-Dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(4-fluoro-2-(oxazol-2-yl)phenyl)methanone;
(5-(4,6-Dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(3-fluoro-2-(6-methylpyridin-2-yl)phenyl)methanone;
(5-(4,6-Dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(3-fluoro-2-(3-methylpyridin-2-yl)phenyl)methanone;
(2-(3-Chloropyridin-2-yl)-3-fluorophenyl)(5-(4,6-dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)methanone;
(5-(4,6-Dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(3-fluoro-2-(4-methylpyridin-2-yl)phenyl)methanone;
(5-(4,6-Dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(3-fluoro-2-(5-methylpyridin-2-yl)phenyl)methanone;
(5-(4,6-Dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(3-fluoro-2-(3-fluoropyridin-2-yl)phenyl)methanone;
(5-(4,6-Dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(3-fluoro-2-(oxazol-2-yl)phenyl)methanone;
2-(5-Fluoro-4-methylpyrimidin-2-yl)-5-{[4-methoxy-2-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}octahydropyrrolo[3,4-c]pyrrole;
2-(5-Chloro-4-methylpyrimidin-2-yl)-5-{[4-methoxy-2-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}octahydropyrrolo[3,4-c]pyrrole;
2-(5-Fluoro-4,6-dimethylpyrimidin-2-yl)-5-{[4-methoxy-2-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}octahydropyrrolo[3,4-c]pyrrole;
2-(4,5-Dimethylpyrimidin-2-yl)-5-{[4-methoxy-2-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}octahydropyrrolo[3,4-c]pyrrole;
2-[(3-Propoxypyridin-2-yl)carbonyl]-5-[5-(trifluoromethyl)pyridin-2-yl]octahydropyrrolo[3,4-c]pyrrole;
2-{4,6-Bis[(2H3)methyl](2H)pyrimidin-2-yl}-5-{[2-fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}octahydropyrrolo[3,4-c]pyrrole;
2-{4,6-Bis[(2H3)methyl](2H)pyrimidin-2-yl}-5-{[3-fluoro-2-(3-methyl-1,2,4-oxadiazol-5-yl)phenyl]carbonyl}octahydropyrrolo[3,4-c]pyrrole;

2-{4,6-Bis[(2H3)methyl](2H)pyrimidin-2-yl}-5-{[4-methoxy-2-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}octahydropyrrolo[3,4-c]pyrrole;
2-(5-Ethyl-4,6-dimethylpyrimidin-2-yl)-5-{[3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl]carbonyl}octahydropyrrolo[3,4-c]pyrrole;
2-(4,6-Dimethylpyrimidin-2-yl)-5-{[3-(3-methyl-1,2,4-oxadiazol-5-yl)pyridin-2-yl]carbonyl}octahydropyrrolo[3,4-c]pyrrole;
(5-(6,7-Difluoroquinoxalin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(3-fluoro-2-(pyrimidin-2-yl)phenyl)methanone;
(5-(6,7-Difluoroquinoxalin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(3-fluoro-2-(pyrimidin-2-yl)phenyl)methanone;
(5-(6,7-Difluoroquinoxalin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(4-methoxy-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone;
(5-(6-(Dimethylamino)pyrimidin-4-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(4-methoxy-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone;
(5-(6-(Dimethylamino)-2-methylpyrimidin-4-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(4-methoxy-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone;
(5-(6-(Dimethylamino)-2-methylpyrimidin-4-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(3-fluoro-2-(pyrimidin-2-yl)phenyl)methanone;
(5-(6-(Dimethylamino)pyrimidin-4-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(3-fluoro-2-(pyrimidin-2-yl)phenyl)methanone;
(3-Fluoro-2-(pyrimidin-2-yl)phenyl)(5-(5-fluoro-4,6-dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)methanone;
(5-(5-Chloro-4,6-dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(3-fluoro-2-(pyrimidin-2-yl)phenyl)methanone;
(5-(5-Chloro-4-methylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(3-fluoro-2-(pyrimidin-2-yl)phenyl)methanone;
(3-Fluoro-2-(pyrimidin-2-yl)phenyl)(5-(5-fluoro-4-methylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)methanone;
(5-(4,5-Dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(3-fluoro-2-(pyrimidin-2-yl)phenyl)methanone;
(5-(4,6-Dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(5-fluoro-2-(6-methylpyridin-2-yl)phenyl)methanone;

(5-(4,6-Dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(5-fluoro-2-(4-methylpyridin-2-yl)phenyl)methanone;
(5-(4,6-Dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(5-fluoro-2-(5-methylpyridin-2-yl)phenyl)methanone;
(5-(4,6-Dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(5-fluoro-2-(3-fluoropyridin-2-yl)phenyl)methanone;
(5-(4,6-Dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(5-fluoro-2-(pyridin-2-yl)phenyl)methanone;
(5-(4,6-Dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(4-fluoro-2-(oxazol-2-yl)phenyl)methanone;
(5-(4,6-Dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(6-fluoro-2-(6-methylpyridin-2-yl)phenyl)methanone;
(5-(4,6-Dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(6-fluoro-2-(4-methylpyridin-2-yl)phenyl)methanone;
(5-(4,6-Dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(6-fluoro-2-(5-methylpyridin-2-yl)phenyl)methanone;
(5-(4,6-Dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(6-fluoro-2-(3-fluoropyridin-2-yl)phenyl)methanone;
(5-(4,6-Dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(6-fluoro-2-(pyridin-2-yl)phenyl)methanone;
(5-(4,6-Dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(6-fluoro-2-(oxazol-2-yl)phenyl)methanone;
(3,6'-Dimethyl-[2,3'-bipyridin]-2'-yl)(5-(quinoxalin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)methanone; and
[5-(4,6-Dimethyl-pyrimidin-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-(2-fluoro-6-[1,2,3]triazol-2-yl-phenyl)-methanone•HCl•1.65H2O.

30. A pharmaceutical composition for treating a disease, disorder or medical condition mediated by orexin activity comprising:

(a) an effective amount of at least one chemical entity selected from compounds of Formula (I):



Formula (I)

wherein:

R^1 is a member selected from the group consisting of:

A) phenyl substituted or unsubstituted with one or two R^a members and substituted in the *ortho* position with R^b;

R^a is independently selected from the group consisting of: -H, halo, -C_{1-4}alkyl, -C_{1-4}alkoxy, and -NO_2, wherein two adjacent R^a members may come together to form a six membered aromatic ring;

R^b is a member selected from the group consisting of:

a) halo, -C_{1-4}alkoxy, -C_{1-4}alkyl,-CF_3, -OCF_3, or -CN;

b) 5-membered heteroaryl ring containing one oxygen or one sulfur members;

c) 5-6 membered heteroaryl ring containing one, two or three nitrogen members, optionally containing one oxygen member, substituted or unsubstituted with halo or -C_{1-4}alkyl; and

d) phenyl substituted or unsubstituted with halo, -CH_3, or -CF_3;

B) pyridine substituted or unsubstituted with one or two R^c members and substituted with R^d, wherein R^d is positioned adjacent to the point of attachment by R^1;

R^c is C_{1-4}alkyl;

R^d is a member selected from the group consisting of:

a) 5-6 membered heteroaryl ring selected from the group consisting of: 1H-1,2,3-triazol-1-yl, 2H-1,2,3-triazol-2-yl, 1H-pyrazol-5-yl, 3-methyl-1,2,4-oxadiazol-5-yl, pyridinyl, 3-methyl-pyridin-2-yl; 1-(tetrahydro-2H-pyran-2-yl)-1H-pyrazol-5-yl), phenyl, and pyrimidin-2-yl; and

b) -CF_3, -Br, and -C_{1-4}alkoxy;

C) 5-membered heteroaryl ring selected from the group consisting of: 2-methyl-1,3-thiazol-yl, 1H-pyrazol-5-yl, oxazole, isoxazolyl, thiophen-

2-yl, and furan-2-yl, each substituted with phenyl substituted or unsubstituted with -F; and

D) 5-13 membered aryl or heteroaryl ring selected from the group consisting of: 3-methylfuran-2-yl, 9H-fluorene, quinoline, cinnoline; 3-(1H-pyrrol-1-yl)thiophen-2-yl, 8-[1,2,3]-triazol-2-yl-naphthalen-1-yl, 2,3-dihydro-1,4-benzodioxin-5-yl, 1H-indol-7-yl, 4-fluoronaphthalen-1-yl, and naphthalen-1-yl;

R^2 is a member selected from the group consisting of:

A) 6-membered heteroaryl ring containing two nitrogen members substituted with one or more members independently selected from the group consisting of: halo, -C_{1-4}alkyl, -CD_3, -D, -C_{1-4}alkoxy, cyclopropyl, morpholin-2-yl, -CO_2C_{1-4}alkyl, -CO_2H, -CH_2OH, -$C(O)N(C_{1-4}alkyl)_2$, -CF_3, -CN, -OH, -NO_2, -$N(C_{1-4}alkyl)_2$, phenyl, furan-2-yl, thiophen-2-yl, 1H-pyrazol-4-yl, and pyrrolidin-1-yl;

B) pyridine substituted with one or two members independently selected from the group consisting of halo, -C_{1-4}alkyl, -C_{1-4}alkoxy, and -CF_3;

C) 9-membered heteroaryl ring selected from the group consisting of: benzooxazol-2-yl, 2-methylpyrimidin-4(3H)-one, 6-fluoro-1,3-benzothiazole, 1,3-benzothiazole, 6-methoxy-1,3-benzothiazole, 6-methyl-1,3-benzothiazole, 6-chloro-benzothiazol-2-yl, and 4-methyl-6,7-dihydro-5H-cyclopenta[d]pyrimidine;

D) 10-membered heteroaryl ring selected from the group consisting of: quinoxalin-2-yl, 3-methylquinoxalin-2-yl, 6,7-difluoroquinoxalin-2-yl, 3-(trifluoromethyl)quinoxaline, quinoline, 4-methylquinoline, and 6-fluoroquinazolin-2-yl; and

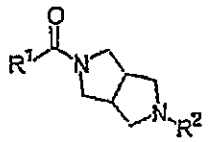
E) 4-methyl-1,3,5-triazin-2-yl;

and pharmaceutically acceptable salts of compounds of Formula (I); and

(b) at least one pharmaceutically acceptable excipient.

31. A pharmaceutical composition comprising and effective amount of at least one chemical entity of claim 29, and at least one pharmaceutically acceptable excipient.

32. At least one chemical entity selected from compounds of Formula(I) :



Formula (I)

wherein:

R^1 is a member selected from the group consisting of:

A) phenyl substituted or unsubstituted with one or two R^a members and substituted in the *ortho* position with R^b;

R^a is independently selected from the group consisting of: -H, halo, -C_{1-4}alkyl, -C_{1-4}alkoxy, and -NO_2, wherein two adjacent R^a members may come together to form a six membered aromatic ring;

R^b is a member selected from the group consisting of:

a) halo, -C_{1-4}alkoxy, -C_{1-4}alkyl,-CF_3, -OCF_3, or -CN;

b) 5-membered heteroaryl ring containing one oxygen or one sulfur members;

c) 5-6 membered heteroaryl ring containing one, two or three nitrogen members, optionally containing one oxygen member, substituted or unsubstituted with halo or -C_{1-4}alkyl; and

d) phenyl substituted or unsubstituted with halo, -CH_3, or -CF_3;

B) pyridine substituted or unsubstituted with one or two R^c members and substituted with R^d, wherein R^d is positioned adjacent to the point of attachment by R^1;

R^c is C_{1-4}alkyl;

R^d is a member selected from the group consisting of:

a) 5-6 membered heteroaryl ring selected from the group consisting of: 1H-1,2,3-triazol-1-yl, 2H-1,2,3-triazol-2-yl, 1H-pyrazol-5-yl, 3-methyl-1,2,4-oxadiazol-5-yl, pyridinyl, 3-methyl-

pyridin-2-yl; 1-(tetrahydro-2H-pyran-2-yl)-1H-pyrazol-5-yl), phenyl, and pyrimidin-2-yl; and

b) $-CF_3$, -Br, and $-C_{1-4}$alkoxy;

C) 5-membered heteroaryl ring selected from the group consisting of: 2-methyl-1,3-thiazol-yl, 1H-pyrazol-5-yl, oxazole, isoxazolyl, thiophen-2-yl, and furan-2-yl, each substituted with phenyl substituted or unsubstituted with -F; and

D) 5-13 membered aryl or heteroaryl ring selected from the group consisting of: 3-methylfuran-2-yl, 9H-fluorene, quinoline, cinnoline; 3-(1H-pyrrol-1-yl)thiophen-2-yl, 8-[1,2,3]-triazol-2-yl-naphthalen-1-yl, 2,3-dihydro-1,4-benzodioxin-5-yl, 1H-indol-7-yl, 4-fluoronaphthalen-1-yl, and naphthalen-1-yl;

R^2 is a member selected from the group consisting of:

A) 6-membered heteroaryl ring containing two nitrogen members substituted with one or more members independently selected from the group consisting of: halo, $-C_{1-4}$alkyl, $-CD_3$, -D, $-C_{1-4}$alkoxy, cyclopropyl, morpholin-2-yl, $-CO_2C_{1-4}$alkyl, $-CO_2H$, $-CH_2OH$, $-C(O)N(C_{1-4}alkyl)_2$, $-CF_3$, -CN, -OH, $-NO_2$, $-N(C_{1-4}alkyl)_2$, phenyl, furan-2-yl, thiophen-2-yl, 1H-pyrazol-4-yl, and pyrrolidin-1-yl;

B) pyridine substituted with one or two members independently selected from the group consisting of: halo, $-C_{1-4}$alkyl, $-C_{1-4}$alkoxy, and $-CF_3$;

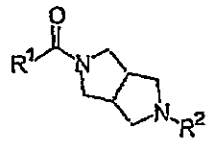
C) 9-membered heteroaryl ring selected from the group consisting of: benzooxazol-2-yl, 2-methylpyrimidin-4(3H)-one, 6-fluoro-1,3-benzothiazole, 1,3-benzothiazole, 6-methoxy-1,3-benzothiazole, 6-methyl-1,3-benzothiazole, 6-chloro-benzothiazol-2-yl, and 4-methyl-6,7-dihydro-5H-cyclopenta[d]pyrimidine;

D) 10-membered heteroaryl ring selected from the group consisting of: quinoxalin-2-yl, 3-methylquinoxalin-2-yl, 6,7-difluoroquinoxalin-2-yl, 3-(trifluoromethyl)quinoxaline, quinoline, 4-methylquinoline, and 6-fluoroquinazolin-2-yl; and

E) 4-methyl-1,3,5-triazin-2-yl;

and pharmaceutically acceptable salts of compounds of Formula (I), and at least one pharmaceutically acceptable excipient for use in the treatment of a disease, disorder, or medical condition mediated by orexin receptor activity..

33. At least one chemical entity selected from compounds of Formula(I) :



Formula (I)

wherein:

R^1 is a member selected from the group consisting of:

A) phenyl substituted or unsubstituted with one or two R^a members and substituted in the *ortho* position with R^b;

R^a is independently selected from the group consisting of: -H, halo, -C_{1-4}alkyl, -C_{1-4}alkoxy, and -NO_2, wherein two adjacent R^a members may come together to form a six membered aromatic ring;

R^b is a member selected from the group consisting of:

a) halo, -C_{1-4}alkoxy, -C_{1-4}alkyl,-CF_3, -OCF_3, or -CN;

b) 5-membered heteroaryl ring containing one oxygen or one sulfur members;

c) 5-6 membered heteroaryl ring containing one, two or three nitrogen members, optionally containing one oxygen member, substituted or unsubstituted with halo or -C_{1-4}alkyl; and

d) phenyl substituted or unsubstituted with halo, -CH_3, or -CF_3;

B) pyridine substituted or unsubstituted with one or two R^c members and substituted with R^d, wherein R^d is positioned adjacent to the point of attachment by R^1;

R^c is C_{1-4}alkyl;

R^d is a member selected from the group consisting of:

a) 5-6 membered heteroaryl ring selected from the group consisting of: 1H-1,2,3-triazol-1-yl, 2H-1,2,3-triazol-2-yl, 1H-pyrazol-5-yl, 3-methyl-1,2,4-oxadiazol-5-yl, pyridinyl, 3-methyl-

pyridin-2-yl; 1-(tetrahydro-2H-pyran-2-yl)-1H-pyrazol-5-yl), phenyl, and pyrimidin-2-yl; and

b) $-CF_3$, -Br, and $-C_{1-4}$alkoxy;

C) 5-membered heteroaryl ring selected from the group consisting of: 2-methyl-1,3-thiazol-yl, 1H-pyrazol-5-yl, oxazole, isoxazolyl, thiophen-2-yl, and furan-2-yl, each substituted with phenyl substituted or unsubstituted with -F; and

D) 5-13 membered aryl or heteroaryl ring selected from the group consisting of: 3-methylfuran-2-yl, 9H-fluorene, quinoline, cinnoline; 3-(1H-pyrrol-1-yl)thiophen-2-yl, 8-[1,2,3]-triazol-2-yl-naphthalen-1-yl, 2,3-dihydro-1,4-benzodioxin-5-yl, 1H-indol-7-yl, 4-fluoronaphthalen-1-yl, and naphthalen-1-yl;

R^2 is a member selected from the group consisting of:

A) 6-membered heteroaryl ring containing two nitrogen members substituted with one or more members independently selected from the group consisting of: halo, $-C_{1-4}$alkyl, $-CD_3$, -D, $-C_{1-4}$alkoxy, cyclopropyl, morpholin-2-yl, $-CO_2C_{1-4}$alkyl, $-CO_2H$, $-CH_2OH$, $-C(O)N(C_{1-4}alkyl)_2$, $-CF_3$, -CN, -OH, $-NO_2$, $-N(C_{1-4}alkyl)_2$, phenyl, furan-2-yl, thiophen-2-yl, 1H-pyrazol-4-yl, and pyrrolidin-1-yl;

B) pyridine substituted with one or two members independently selected from the group consisting of: halo, $-C_{1-4}$alkyl, $-C_{1-4}$alkoxy, and $-CF_3$;

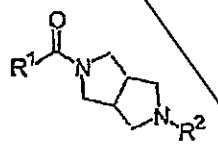
C) 9-membered heteroaryl ring selected from the group consisting of: benzooxazol-2-yl, 2-methylpyrimidin-4(3H)-one, 6-fluoro-1,3-benzothiazole, 1,3-benzothiazole, 6-methoxy-1,3-benzothiazole, 6-methyl-1,3-benzothiazole, 6-chloro-benzothiazol-2-yl, and 4-methyl-6,7-dihydro-5H-cyclopenta[d]pyrimidine;

D) 10-membered heteroaryl ring selected from the group consisting of: quinoxalin-2-yl, 3-methylquinoxalin-2-yl, 6,7-difluoroquinoxalin-2-yl, 3-(trifluoromethyl)quinoxaline, quinoline, 4-methylquinoline, and 6-fluoroquinazolin-2-yl; and

E) 4-methyl-1,3,5-triazin-2-yl;

and pharmaceutically acceptable salts of compounds of Formula (I), and at least one pharmaceutically acceptable excipient for use in the treatment of a disease, disorder, or medical condition wherein the disease, disorder, or medical condition is selected from the group consisting of: disorders of the sleep-wake cycle, insomnia, restless legs syndrome, jet-lag, disturbed sleep, sleep disorders secondary to neurological disorders, manias, depressions, manic depression, schizophrenia, pain syndromes, fibromyalgia, neuropathic pain , catatonia, Parkinson's disease, Tourette's syndrome, anxiety, delirium, dementias, overweight or obesity and conditions related to overweight or obesity, insulin resistance, type II diabetes, hyperlipidemia, gallstones, angina, hypertension, breathlessness, tachycardia, infertility, sleep apnea, back and joint pain, varicose veins, osteoarthritis, hypertension, tachycardia, arrhythmias, angina pectoris, acute heart failure, ulcers, irritable bowel syndrome, diarrhea and gastroesophageal reflux.

34. At least one chemical entity selected from compounds of Formula(I) :



Formula (I)

wherein:

R^1 is a member selected from the group consisting of:

A) phenyl substituted or unsubstituted with one or two R^a members and substituted in the *ortho* position with R^b;

R^a is independently selected from the group consisting of: -H, halo, -C_{1-4}alkyl, -C_{1-4}alkoxy, and -NO_2, wherein two adjacent R^a members may come together to form a six membered aromatic ring;

R^b is a member selected from the group consisting of:

a) halo, -C_{1-4}alkoxy, -C_{1-4}alkyl,-CF_3, -OCF_3, or -CN;

b) 5-membered heteroaryl ring containing one oxygen or one sulfur members;

c) 5-6 membered heteroaryl ring containing one, two or three nitrogen members, optionally containing one oxygen member, substituted or unsubstituted with halo or -C_{1-4}alkyl; and

d) phenyl substituted or unsubstituted with halo, -CH_3, or -CF_3;

B) pyridine substituted or unsubstituted with one or two R^c members and substituted with R^d, wherein R^d is positioned adjacent to the point of attachment by R^1;

R^c is C_{1-4}alkyl;

R^d is a member selected from the group consisting of:

a) 5-6 membered heteroaryl ring selected from the group consisting of: 1H-1,2,3-triazol-1-yl, 2H-1,2,3-triazol-2-yl, 1H-pyrazol-5-yl, 3-methyl-1,2,4-oxadiazol-5-yl, pyridinyl, 3-methyl-pyridin-2-yl; 1-(tetrahydro-2H-pyran-2-yl)-1H-pyrazol-5-yl), phenyl, and pyrimidin-2-yl; and

b) -CF_3, -Br, and -C_{1-4}alkoxy;

C) 5-membered heteroaryl ring selected from the group consisting of: 2-methyl-1,3-thiazol-yl, 1H-pyrazol-5-yl, oxazole, isoxazolyl, thiophen-2-yl, and furan-2-yl, each substituted with phenyl substituted or unsubstituted with -F; and

D) 5-13 membered aryl or heteroaryl ring selected from the group consisting of: 3-methylfuran-2-yl, 9H-fluorene, quinoline, cinnoline; 3-(1H-pyrrol-1-yl)thiophen-2-yl, 8-[1,2,3]-triazol-2-yl-naphthalen-1-yl, 2,3-dihydro-1,4-benzodioxin-5-yl, 1H-indol-7-yl, 4-fluoronaphthalen-1-yl, and naphthalen-1-yl;

R^2 is a member selected from the group consisting of:

A) 6-membered heteroaryl ring containing two nitrogen members substituted with one or more members independently selected from the group consisting of: halo, -C_{1-4}alkyl, -CD_3, -D, -C_{1-4}alkoxy, cyclopropyl, morpholin-2-yl, -CO_2C_{1-4}alkyl, -CO_2H, -CH_2OH, -$C(O)N(C_{1-4}alkyl)_2$, -CF_3, -CN, -OH, -NO_2, -$N(C_{1-4}alkyl)_2$, phenyl, furan-2-yl, thiophen-2-yl, 1H-pyrazol-4-yl, and pyrrolidin-1-yl;

B) pyridine substituted with one or two members independently selected from the group consisting of: halo, -C_{1-4}alkyl, -C_{1-4}alkoxy, and -CF_3;

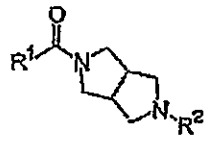
C) 9-membered heteroaryl ring selected from the group consisting of: benzooxazol-2-yl, 2-methylpyrimidin-4(3H)-one, 6-fluoro-1,3-benzothiazole, 1,3-benzothiazole, 6-methoxy-1,3-benzothiazole, 6-methyl-1,3-benzothiazole, 6-chloro-benzothiazol-2-yl, and 4-methyl-6,7-dihydro-5H-cyclopenta[d]pyrimidine;

D) 10-membered heteroaryl ring selected from the group consisting of: quinoxalin-2-yl, 3-methylquinoxalin-2-yl, 6,7-difluoroquinoxalin-2-yl, 3-(trifluoromethyl)quinoxaline, quinoline, 4-methylquinoline, and 6-fluoroquinazolin-2-yl; and

E) 4-methyl-1,3,5-triazin-2-yl;

and pharmaceutically acceptable salts of compounds of Formula (I), and at least one pharmaceutically acceptable excipient for use in the treatment of a disease, disorder, or medical condition wherein the disease, disorder, or medical condition is insomnia.

35. At least one chemical entity selected from compounds of Formula(I) :



Formula (I)

wherein:

R^1 is a member selected from the group consisting of:

A) phenyl substituted or unsubstituted with one or two R^a members and substituted in the *ortho* position with R^b;

R^a is independently selected from the group consisting of: -H, halo, -C_{1-4}alkyl, -C_{1-4}alkoxy, and -NO_2, wherein two adjacent R^a members may come together to form a six membered aromatic ring;

R^b is a member selected from the group consisting of:

a) halo, -C_{1-4}alkoxy, -C_{1-4}alkyl,-CF_3, -OCF_3, or -CN;

b) 5-membered heteroaryl ring containing one oxygen or one sulfur members;

c) 5-6 membered heteroaryl ring containing one, two or three nitrogen members, optionally containing one oxygen member, substituted or unsubstituted with halo or -C_{1-4}alkyl; and

d) phenyl substituted or unsubstituted with halo, -CH_3, or -CF_3;

B) pyridine substituted or unsubstituted with one or two R^c members and substituted with R^d, wherein R^d is positioned adjacent to the point of attachment by R^1;

R^c is C_{1-4}alkyl;

R^d is a member selected from the group consisting of:

a) 5-6 membered heteroaryl ring selected from the group consisting of: 1H-1,2,3-triazol-1-yl, 2H-1,2,3-triazol-2-yl, 1H-pyrazol-5-yl, 3-methyl-1,2,4-oxadiazol-5-yl, pyridinyl, 3-methyl-

pyridin-2-yl; 1-(tetrahydro-2H-pyran-2-yl)-1H-pyrazol-5-yl), phenyl, and pyrimidin-2-yl; and

b) $-CF_3$, -Br, and $-C_{1-4}$alkoxy;

C) 5-membered heteroaryl ring selected from the group consisting of: 2-methyl-1,3-thiazol-yl, 1H-pyrazol-5-yl, oxazole, isoxazolyl, thiophen-2-yl, and furan-2-yl, each substituted with phenyl substituted or unsubstituted with -F; and

D) 5-13 membered aryl or heteroaryl ring selected from the group consisting of: 3-methylfuran-2-yl, 9H-fluorene, quinoline, cinnoline; 3-(1H-pyrrol-1-yl)thiophen-2-yl, 8-[1,2,3]-triazol-2-yl-naphthalen-1-yl, 2,3-dihydro-1,4-benzodioxin-5-yl, 1H-indol-7-yl, 4-fluoronaphthalen-1-yl, and naphthalen-1-yl;

R^2 is a member selected from the group consisting of:

A) 6-membered heteroaryl ring containing two nitrogen members substituted with one or more members independently selected from the group consisting of: halo, $-C_{1-4}$alkyl, $-CD_3$, -D, $-C_{1-4}$alkoxy, cyclopropyl, morpholin-2-yl, $-CO_2C_{1-4}$alkyl, $-CO_2H$, $-CH_2OH$, $-C(O)N(C_{1-4}alkyl)_2$, $-CF_3$, -CN, -OH, $-NO_2$, $-N(C_{1-4}alkyl)_2$, phenyl, furan-2-yl, thiophen-2-yl, 1H-pyrazol-4-yl, and pyrrolidin-1-yl;

B) pyridine substituted with one or two members independently selected from the group consisting of: halo, $-C_{1-4}$alkyl, $-C_{1-4}$alkoxy, and $-CF_3$;

C) 9-membered heteroaryl ring selected from the group consisting of: benzooxazol-2-yl, 2-methylpyrimidin-4(3H)-one, 6-fluoro-1,3-benzothiazole, 1,3-benzothiazole, 6-methoxy-1,3-benzothiazole, 6-methyl-1,3-benzothiazole, 6-chloro-benzothiazol-2-yl, and 4-methyl-6,7-dihydro-5H-cyclopenta[d]pyrimidine;

D) 10-membered heteroaryl ring selected from the group consisting of: quinoxalin-2-yl, 3-methylquinoxalin-2-yl, 6,7-difluoroquinoxalin-2-yl, 3-(trifluoromethyl)quinoxaline, quinoline, 4-methylquinoline, and 6-fluoroquinazolin-2-yl; and

E) 4-methyl-1,3,5-triazin-2-yl;

and pharmaceutically acceptable salts of compounds of Formula (I), and at least one pharmaceutically acceptable excipient in the manufacture of a medicament for the treatment of a disease, disorder, or medical condition mediated by orexin receptor activity.

36. Use according to Claim 35, wherein the disease, disorder, or medical condition is selected from the group consisting of: disorders of the sleep-wake cycle, insomnia, restless legs syndrome, jet-lag, disturbed sleep, sleep disorders secondary to neurological disorders, manias, depressions, manic depression, schizophrenia, pain syndromes, fibromyalgia, neuropathic pain , catatonia, Parkinson's disease, Tourette's syndrome, anxiety, delirium, dementias, overweight or obesity and conditions related to overweight or obesity, insulin resistance, type II diabetes, hyperlipidemia, gallstones, angina, hypertension, breathlessness, tachycardia, infertility, sleep apnea, back and joint pain, varicose veins, osteoarthritis, hypertension, tachycardia, arrhythmias, angina pectoris, acute heart failure, ulcers, irritable bowel syndrome, diarrhea and gastroesophageal reflux.

37. Use according to Claim 35, wherein the disease, disorder, or medical condition is insomnia.

Body weight may also be affected by orexin-mediated regulation of appetite and metabolism (T. Sakurai *et al.*, *Cell*, 1998, 92(4), 573-585; T. Sakurai, *Reg. Pept*, 1999, 85(1), 25-30). Some effects of orexin on metabolism and appetite may be mediated in the gut, where, as mentioned, orexins alter gastric motility and gastric acid secretion.

Orexin receptor antagonists therefore are likely to be useful in treatment of overweight or obesity and conditions related to overweight or obesity, such as insulin resistance, type II diabetes, hyperlipidemia, gallstones, angina, hypertension, breathlessness, tachycardia, infertility, sleep apnea, back and joint pain, varicose veins and osteoarthritis.

Conversely, orexin receptor agonists are likely to be useful in treatment of underweight and related conditions such as hypotension, bradycardia, ammenorrhea and related infertility, and eating disorders such as anorexia and bulimia.

Intracerebroventricularly administered orexins have been shown to increase mean arterial pressure and heart rate in freely moving (awake) animals (Samson *et al.*, Brain Res. 1999, 831, 248-253; Shirasaka *et al.*, *Am. J. Physiol.* 1999, 277, R1780-R1785) and in urethane-anesthetized animals (Chen *et al.*, *Am. J. Physiol.* 2000, 278, R692-R697), with similar results.

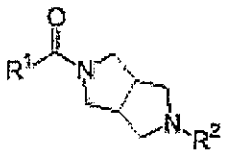
Orexin receptor agonists may therefore be candidates for treatment of hypotension, bradycardia and heart failure related thereto, while orexin receptor antagonists may be useful for treatment of hypertension, tachycardia and other arrhythmias, angina pectoris and acute heart failure.

From the foregoing discussion, it can be seen that the identification of orexin receptor modulators, in one embodiment modulators of the orexin-2 receptor, will be of great advantage in the development of therapeutic agents for the treatment of a wide variety of disorders that are mediated through these receptor systems.

Citation of a reference herein shall not be construed as an admission that such reference is prior art to the present invention.

Various small-molecule orexin receptor modulators have been reported e.g., N-aroyl cyclic amine derivatives (International Publication No. WO2003002561, January 9, 3003), ethylene diamine derivatives (International

independent and dependent claims appended hereto. In one general aspect, the invention is directed to a chemical entity of Formula (I):



Formula (I)

wherein:

R^1 is a member selected from the group consisting of:

A) phenyl substituted or unsubstituted with one or two R^a members, and substituted in the *ortho* position with R^b;

R^a is independently selected from the group consisting of: -H, halo, - C_{1-4}alkyl, -C_{1-4}alkoxy, and -NO_2, wherein two adjacent R^a members may come together to form a six membered aromatic ring; R^b is a member selected from the group consisting of:

a) halo, -C_{1-4}alkoxy, -C_{1-4}alkyl,-CF_3, -OCF_3, or -CN;

b) 5-membered heteroaryl ring containing one oxygen or one sulfur members;

c) 5-6 membered heteroaryl ring containing one, two or three nitrogen members, optionally containing one oxygen member, substituted or unsubstituted with halo or -C_{1-4}alkyl; and

d) phenyl substituted or unsubstituted with halo, -CH_3, or -CF_3;

B) pyridine substituted or unsubstituted with one or two R^c members and substituted with R^d, wherein R^d is positioned adjacent to the point of attachment by R^1 ;

R^c is C_{1-4}alkyl;

R^d is a member selected from the group consisting of:

a) 5-6 membered heteroaryl ring selected from the group consisting of: 1 H-1,2,3-triazol-1-yl, 2H-1,2,3-triazol-2-yl, 1H- pyrazol-5-yl, 3-methyl-1,2,4-oxadiazol-5-yl, pyridinyl, 3-methyl- pyridin-2-yl; 1-(tetrahydro-2H-pyran-2-yl)-1H-pyrazol-5-yl), phenyl, and pyrimidin-2-yl; and

Formula (II), and pharmaceutically active metabolites of compounds of Formula (I) or Formula (II).

In another aspect, the invention is directed to a method of treating a subject suffering from or diagnosed with a disease, disorder, or medical condition mediated by orexin receptor activity, comprising administering to the subject in need of such treatment an effective amount of at least one chemical entity selected from compounds of Formula (I) or Formula (II), pharmaceutically acceptable salts of compounds of Formula (I) or Formula (II), pharmaceutically acceptable prodrugs of compounds of Formula (I) or Formula (II), and pharmaceutically active metabolites of compounds of Formula (I) or Formula (II).

Additional embodiments of methods of treatment are set forth in the detailed description.

In another aspect, method of studying isotopically labeled compounds in metabolic studies (preferably with ^{14}C), reaction kinetic studies (with, for example ^{2}H or ^{3}H), detection or imaging techniques [such as positron emission tomography (PET) or single-photon emission computed tomography (SPECT)] including drug or substrate tissue distribution assays, or in radioactive treatment of patients. For example, an ^{18}F or ^{11}C labeled compound may be particularly preferred for PET or an I^{123} for SPECT studies.

An object of the present invention is to overcome or ameliorate at least one of the disadvantages of the conventional methodologies and/or prior art, or to provide a useful alternative thereto. Additional embodiments, features, and advantages of the invention will be apparent from the following detailed description and through practice of the invention.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 is a Powder X-Ray Diffraction of an exemplied compound X

DETAILED DESCRIPTION

The invention may be more fully appreciated by reference to the following description, including the following glossary of terms and the concluding examples.

As used herein, the terms "including", "containing" and "comprising" are used herein in their open, non-limiting sense.

The term "alkyl" refers to a straight- or branched-chain alkyl group having from 1 to 12 carbon atoms in the chain.

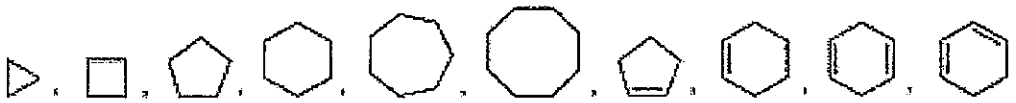
Examples of alkyl groups include methyl (Me, which also may be structurally depicted by the symbol, "/"), ethyl (Et), n-propyl, isopropyl, butyl, isobutyl, sec-butyl, *tert*-butyl (tBu), pentyl, isopentyl, *tert*-pentyl, hexyl, isohexyl, and groups that in light of the ordinary skill in the art and the teachings provided herein would be considered equivalent to any one of the foregoing examples.

The term "alkoxy" includes a straight chain or branched alkyl group with a terminal oxygen linking the alkyl group to the rest of the molecule. Alkoxy includes methoxy, ethoxy, propoxy, isopropoxy, butoxy, t-butoxy, pentoxy and so on. "Aminoalkyl", "thioalkyl", and "sulfonylalkyl" are analogous to alkoxy, replacing the terminal oxygen atom of alkoxy with, respectively, NH (or NR), S, and SO_2.

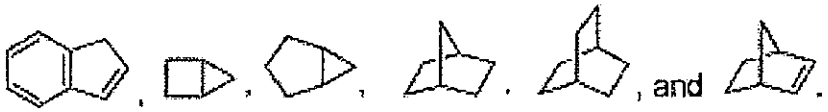
The term "cyano" refers to the group -CN.

The term "cycloalkyl" refers to a saturated or partially saturated, monocyclic, fused polycyclic, or spiro polycyclic carbocycle having from 3 to 12 ring atoms per carbocycle.

Illustrative examples of cycloalkyl groups include the foll wing entities, in the form of properly bonded moieties:



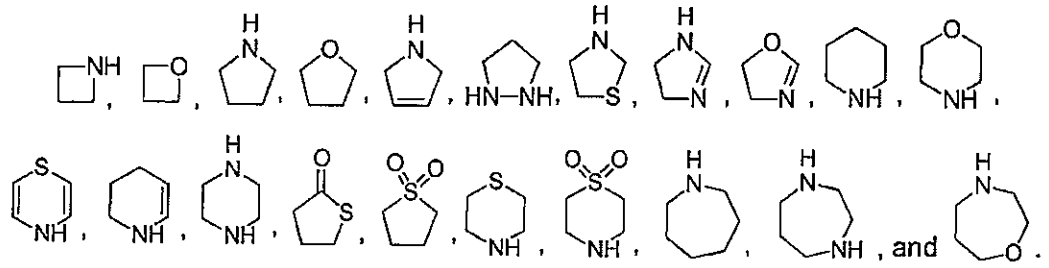




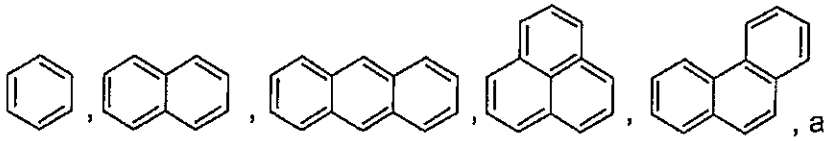
A "heterocycloalkyl" refers to a monocyclic ring structure that is saturated or partially saturated and has from 4 to 7 ring atoms per ring structure selected from carbon atoms and up to two heteroatoms selected from nitrogen, oxygen, and sulfur.

The ring structure may optionally contain up to two oxo

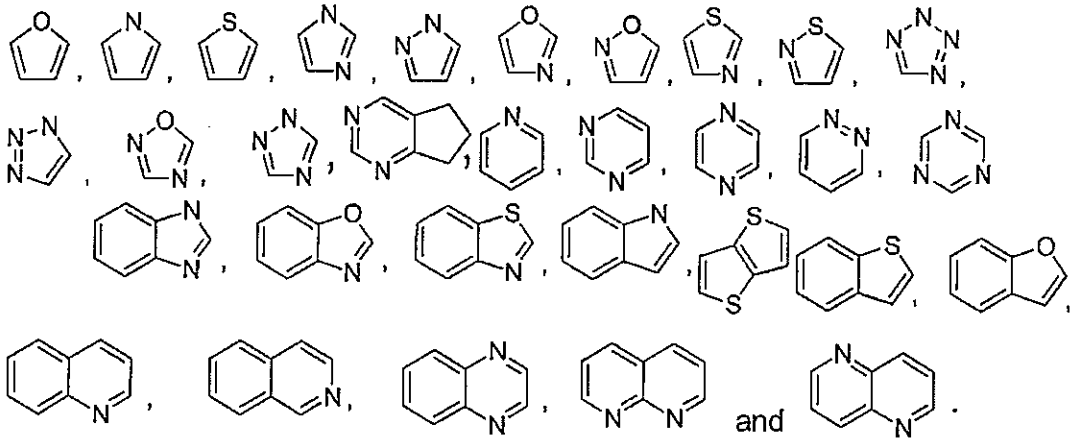
groups on sulfur ring members. Illustrative entities, in the form of properly bonded moieties, include:



The term "aryl" refers to a monocyclic, or fused or spiro polycyclic, aromatic carbocycle (ring structure having ring atoms that are all carbon) having from 3 to 12 ring atoms per ring. (Carbon atoms in aryl groups are sp^2 hybridized.) Illustrative examples of aryl groups include the following moieties:



The term "heteroaryl" refers to a monocyclic, fused bicyclic, or fused polycyclic aromatic heterocycle (ring structure having ring atoms selected from carbon atoms and up to four heteroatoms selected from nitrogen, oxygen, and sulfur) having from 3 to 12 ring atoms per heterocycle. Illustrative examples of heteroaryl groups include the following entities, in the form of properly bonded moieties:



Those skilled in the art will recognize that the species of heteroaryl,

group, or both types of functional groups, and accordingly react with a number of inorganic or organic bases, and inorganic and organic acids, to form a pharmaceutically acceptable salt, bases, and inorganic and organic acids, to form a pharmaceutically acceptable salt.

Examples of pharmaceutically acceptable salts include sulfates, pyrosulfates, bisulfates, sulfites, bisulfites, phosphates, monohydrogen-phosphates, dihydrogen-phosphates, metaphosphates, pyrophosphates, chlorides, bromides, iodides, acetates, propionates, decanoates, caprylates, acrylates, formates, isobutyrates, caproates, heptan-oates, propiolates, oxalates, malonates, succinates, suberates, sebacates, fumarates, maleates, butyne-1,4-dioates, hexyne-1,6-dioates, benzoates, chlorobenzoates, methyl-benzoates, dinitrobenzoates, hydroxybenzoates, methoxy-benzoates, phthalates, sulfon-ates, xylenesulfonates, phenylacetates, phenyl-propionates, phenylbutyrates, citrates, lactates, γ-hydroxybutyrates, glycolates, tartrates, methane-sulfonates, propanesulfonates, naphthalene-1-sulfonates, naphthalene-2-sulfonates, and mandelates.

When the compound of Formula (I) or Formula (II) contains a basic nitrogen, the desired pharmaceutically acceptable salt may be prepared by any suitable method available in the art, for example, treatment of the free base with an inorganic acid, such as hydrochloric acid, hydrobromic acid, sulfuric acid, sulfamic acid, nitric acid, boric acid, and phosphoric acid, or with an organic acid, such as acetic acid, phenylacetic acid, propionic acid, stearic acid, lactic acid, ascorbic acid, maleic acid, hydroxymaleic acid, isethionic acid, succinic acid, valeric acid, fumaric acid, malonic acid, pyruvic acid, oxalic acid, glycolic acid, salicylic acid, oleic acid, palmitic acid, lauric acid, a pyrano-sidyl acid, such as glucuronic acid or galacturonic acid, an alpha-hydroxy acid, such as mandelic acid, citric acid, or tartaric acid, an amino acid, such as aspartic acid, glutaric acid or glutamic acid, an aromatic acid, such as benzoic acid, 2-acetoxybenzoic acid, naphthoic acid, or cinnamic acid, a sulfonic acid, such as laurylsulfonic acid, p-toluene-sulfonic acid, methanesulfonic acid, ethanesulfonic acid, any compatible mixture of acids such as those given as examples herein, and any other acid and mixture thereof that are regarded as equivalents or acceptable substitutes in light of the ordinary level of skill in this technology.

Delivery forms of the pharmaceutical compositions containing one or more dosage units of the active agents may be prepared using suitable pharmaceutical excipients and compounding techniques known or that become available to those skilled in the art.

The compositions may be administered in the inventive methods by a suitable route of delivery, e.g., oral, parenteral, rectal, topical, or ocular routes, or by inhalation. The preparation may be in the form of tablets, capsules, sachets, dragees, powders, granules, lozenges, powders for reconstitution, liquid preparations, or suppositories. Preferably, the compositions are formulated for intravenous infusion, topical administration, or oral administration.

For oral administration, the compounds of the invention can be provided in the form of tablets or capsules, or as a solution, emulsion, or suspension. To prepare the oral compositions, the compounds may be formulated to yield a dosage of, e.g., from about 0.05 to about 100 mg/kg daily, or from about 0.05 to about 35 mg/kg daily, or from about 0.1 to about 10 mg/kg daily. For example, a total daily dosage of about 5 mg to 5 g daily may be accomplished by dosing once, twice, three, or four times per day.

Oral tablets may include a compound according to the invention mixed with pharmaceutically acceptable excipients such as inert diluents, disintegrating agents, binding agents, lubricating agents, sweetening agents, flavoring agents, coloring agents and preservative agents. Suitable inert fillers include sodium and calcium carbonate, sodium and calcium phosphate, lactose, starch, sugar, glucose, methyl cellulose, magnesium stearate, mannitol, and sorbitol. Exemplary liquid oral excipients include ethanol, glycerol, and water. Starch, polyvinyl-pyrrolidone (PVP), sodium starch glycolate, microcrystalline cellulose, and alginic acid are suitable disintegrating agents. Binding agents may include starch and gelatin. The lubricating agent, if present, may be magnesium stearate, stearic acid or talc. If desired, the tablets may be coated with a material such as glyceryl monostearate or glyceryl distearate to delay absorption in the gastrointestinal tract, or may be coated with an enteric coating.

Capsules for oral administration include hard and soft gelatin capsules. To prepare hard gelatin capsules, compounds of the invention may be mixed with a

solid, semi-solid, or liquid diluent. Soft gelatin capsules may be prepared by mixing the compound of the invention with water, an oil such as peanut oil or olive oil, liquid paraffin, a mixture of mono and di-glycerides of short chain fatty acids, polyethylene glycol 400, or propylene glycol.

Liquids for oral administration may be in the form of suspensions, solutions, emulsions or syrups or may be lyophilized or presented as a dry product for reconstitution with water or other suitable vehicle before use. Such liquid compositions may optionally contain: pharmaceutically-acceptable excipients such as suspending agents (for example, sorbitol, methyl cellulose, sodium alginate, gelatin, hydroxyl-ethylcellulose, carboxy-methylcellulose, and aluminum stearate gel); non-aqueous vehicles, e.g., oil (for example, almond oil or fractionated coconut oil), propylene glycol, ethyl alcohol, or water; preservatives (for example, methyl or propyl p-hydroxybenzoate or sorbic acid); wetting agents such as lecithin; and, if desired, flavoring or coloring agents.

The active agents of this invention may also be administered by non-oral routes. For example, the compositions may be formulated for rectal administration as a suppository.

For parenteral use, including intravenous, intramuscular, intra-peritoneal, or subcutaneous routes, the compounds of the invention may be provided in sterile aqueous solutions or suspensions, buffered to an appropriate pH and isotonicity or in parenterally acceptable oil. Suitable aqueous vehicles include Ringer's solution and isotonic sodium chloride.

Such forms will be presented in unit-dose form such as ampules or disposable injection devices, in multi-dose forms such as vials from which the appropriate dose may be withdrawn, or in a solid form or pre-concentrate that can be used to prepare an inject-able formulation. Illustrative infusion doses may range from about 1 to 1000 g/kg/minute of compound, admixed with a pharmaceutical carrier over a period ranging from several minutes to several days.

For topical administration, the compounds may be mixed with a pharmaceutical carrier at a concentration of about 0.1 % to about 10% of drug to vehicle. Another mode of administering the compounds of the invention may utilize a patch formulation to affect transdermal delivery.

that only one X member can be N), with commercially available HET compounds of formula (V), where HET is a 5-6 membered heteroaryl ring containing one to three nitrogen members, in the presence of copper(I)iodide, CS_2CO_3 and N,N'-dimethyl-cyclo-hexane-1,2-diamine; in a solvent such as DMF or dioxane, at temperatures ranging from 60 °C to 100 °C (using conventional or microwave heating).

One skilled in the art will recognize that 1,2,3-triazole can exist in two tautomeric forms defined as 2H-[1,2,3]-triazole and 1H-[1,2,3]triazole thus accounting for the formation of two regioisomers.

Alternatively, compounds of formula (VIb) are prepared by the reaction of halobenzonitrile compounds of formula (VII) with HET, where HET is a 5-membered heteroaryl ring selected from the group consisting of triazole or pyrazole, in a solvent such as DMF, in the presence of an inorganic base such as K_2CO_3, at temperatures ranging from 100 °C to 130 °C.

Subsequent hydrolysis of the nitrile using a base such as aqueous NaOH, in a solvent such as methanol provides compounds of formula (VIb).

Compounds of formula (VIb) are also prepared by the reaction of halobenzonitrile compounds of formula (VII) with HET-Sn(alkyl)$_3$, where HET-Sn(alkyl)$_3$ is a commercially available or synthetically accessible trialkyltinheteroaryl compound, in a solvent such as DME, in the presence of a palladium catalyst such as $Pd(PPh_3)_4$, in the presence or absence of a catalytic amount of copper iodide, at temperatures ranging from 100 °C to 160 °C, using conventional or microwave heating.

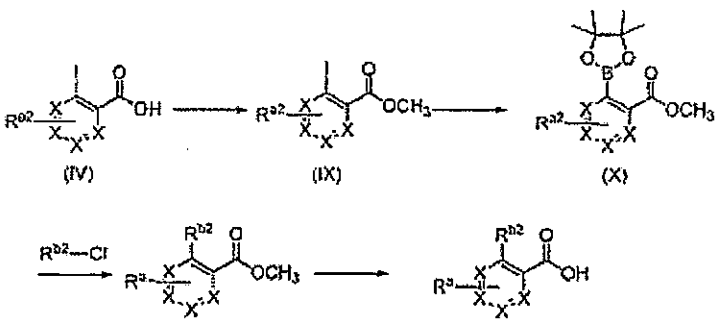
Subsequent hydrolysis of the nitrile using a base such as aqueous NaOH and the like, in a solvent such as methanol provides compounds of formula (VIb).

Compounds of formula (VIb) are also prepared by the reaction of halobenzonitrile compounds of formula (VII) with HET-boronic acid, where HET-boronic acid is a commercially available or synthetically accessible heteroarylboronic acid, in a solvent such as DME, in the presence of a base such as $NaHCO_3$, a palladium catalyst such as $Pd(PPh_3)_4$, at temperatures ranging from 80 °C to the reflux temperature of the solvent.

Subsequent hydrolysis using a base such as aqueous NaOH, in a solvent such as methanol provides compounds of formula (VIb).

Compounds of formula (I), where R^{b2} is -I, are further elaborated to compounds of formula (I), where R^{b2} is HET, where HET is a 5-6 membered hetero-aryl ring containg one to three nitrogen atoms optionally containing one oxygen member. Reaction of compounds of formula (I), where R^{b2} is -I, with HET-Sn(alkyl)$_3$, where HET-Sn(alkyl)$_3$ is a commercially available or synthetically accessible trialkyltinheteroaryl compound, in a solvent such as DME, in the presence of a palladium catalyst such as Pd(PPh$_3$) , in the presence or absence of a catalytic amount of copper iodide, at temperatures ranging from 100 °C to 160 °C, using conventional or microwave heating, provides compounds of formula (I).

SCHEME B



According to Scheme B, compounds of formula (VIc) are obtained from compounds of formula (IV), by first converting a commercially available or synthetically accessible compound of formula (IV), where R^{a2} is -H, halo, -C$_{1-4}$ alkyl, -C$_{1-4}$ alkoxy, -CF$_3$, or -NO$_2$, and where X is C or N (with the proviso that only one X may be N) to one of formula (IX) under esterification conditions, for example by treating an alcohol solution of a compound of formula (IV) with an acid. In a preferred method the compound of formula (IV) is dissolved in a solvent such as MeOH and treated with H_2SO_4 to afford a compound of formula (IX).

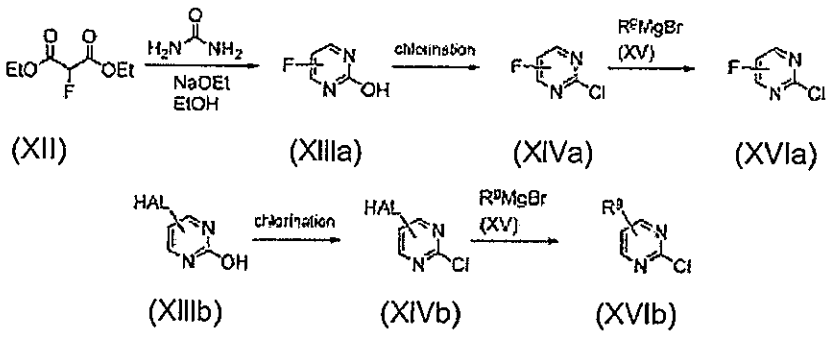
A compound of formula (X) is obtained by reacting a suitable compound of formula (IX) with pinacol borane in the presence of a phosphine and a palladium catalyst, in the presence of an amine base, in a solvent such as THF, at temperatures ranging from room temperature to 70 °C. In a preferred

method the phosphine is tri(o-tolyl)phosphine, the palladium catalyst is $Pd(OAc)_2$ and the amine base is triethylamine.

A compound of formula (Vic) is obtained by reacting a compound of formula (X) with a compound R^{b2}-Cl, where R^{b2}-Cl is a suitable commercially available or synthetic-ally accessible 6-membered chloro-substituted heteroaryl compound, in the presence of a palladium catalyst, a base such as Na_2CO3, in a solvent such as 2-methyl-tetrahydrofuran (2-methyl-THF), at temperatures ranging from room temperature to 80 °C.

In a preferred method the palladium catalyst is $PdCl_2$(dppf)-dcm adduct , the base is Na_2CO_3 and the solvent is 2-methyl-THF. A compound of formula (Vic) is obtained from a compound of formula (XI) via ester hydrolysis. In a preferred method of hydrolysis, a compound of formula (XI) in methyl-THF is treated with aqueous NaOH to afford a compound of formula (Vic).

SCHEME C



(XII) (XIIIa) (XIVa) (XVIa)

(XIIIb) (XIVb) (XVIb)

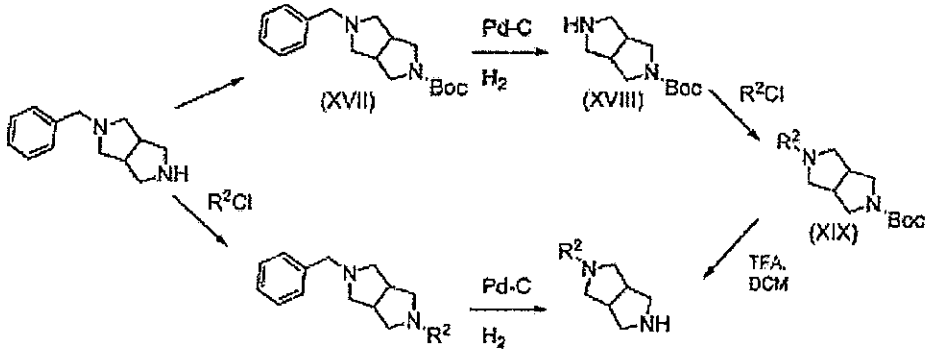
According to SCHEME C, substituted heteroaryl compounds R^2Cl of formula (XIVa) and (XVIb) are prepared from commercially available or synthetically accessible compounds of formula (XIIIa) or (XIIIb). Pyrimidols of formula (XIIIa) or formula (XIIIb) are commercially available or are prepared by reacting substituted alkyl malonates of formula (XII), where R^e is halo, with urea in the presence of a base such as sodium ethoxide; in a suitable solvent such as ethanol, at temperatures between room temperature and the reflux temperature of the solvent.

Chlorination of commercially available pyrimidinols of formula (XIIIb) or synthetically accessible compounds of formula (XIIIa) using a chlorinating agent such as oxalyl chloride; in a solvent such as CH_2Cl_2, in the presence of a base such as N,N-dimethylaniline

at temperatures ranging between room temperature and the reflux temperature of the solvent provides chloropyrimidines of formula (XIVa) or (XIVb).

Additionally, chloropyrimidines of formula (XIVa) or (XIVb) are further elaborated.

Chloropyrimidines of formula (XIVa) or (XIVb) are reacted with Grignard reagents (R^9MgBr) of formula (XV); in the presence of a catalytic amount of $Fe(acac)_3$, in a solvent such as Et_2O at 0 °C, provides alkyl chloropyrimidines of formula (XVIa) or (XVIb).



According to Scheme D, compounds of formula (XX) are obtained from synthetically accessible or commercially available 2-benzyl-octahydro-pyrrolo[3,4-c]-pyrrole by first protecting the secondary nitrogen of 2-benzyl-octahydro-pyrrolo[3,4-c]pyrrole as a carbamate. In a preferred embodiment the carbamate is the *tert*-butyl-carbamate (boc) which is introduced by treating 2-benzyl-octahydro-pyrrolo[3,4-c]-pyrrole with di-*tert*-butyl-dicarbonate, in a solvent such as DCM, affording compound (XVII).

Compound (XVIII) is obtained from treating compound (XVII) with hydrogen gas, in the presence of a catalyst. In a particularly preferred embodiment the catalyst is Pd on carbon, in a solvent such as MeOH in the presence of AcOH.

A compound of formula (XIX) is obtained by treating compound (XVIII) with a compound of formula R^2Cl, where R^2 is as defined in formula (I). Commercially available or synthetically accessible appropriately heteroaryl compounds of formula R^2Cl are reacted with compound (XVIII) in the presence of a suitably selected tertiary organic or inorganic base such as CS_2CO_3, Na_2CO_3, and TEA;

in a solvent such as DMF, dichloromethane, THF, and n-butanol; at a temperature between room temperature and the reflux temperature of the solvent, using conventional or microwave heating, to afford compounds of formula (XIX).

In a preferred embodiment the base is CS_2CO_3 and the solvent is DMF.

Removal of the *tert*-butyl-carbamate (boc) in compounds of formula (XIX) is accomplished by using methods known to one skilled in the art, such as, HCl, TFA, or p-toluenesulfonic acid, in a solvent such as CH_3OH, dioxane, or CH_2Cl_2.

In a preferred embodiment, a compound of formula (XIX) is treated with TFA in DCM or HCl to afford a compound of formula (XX).

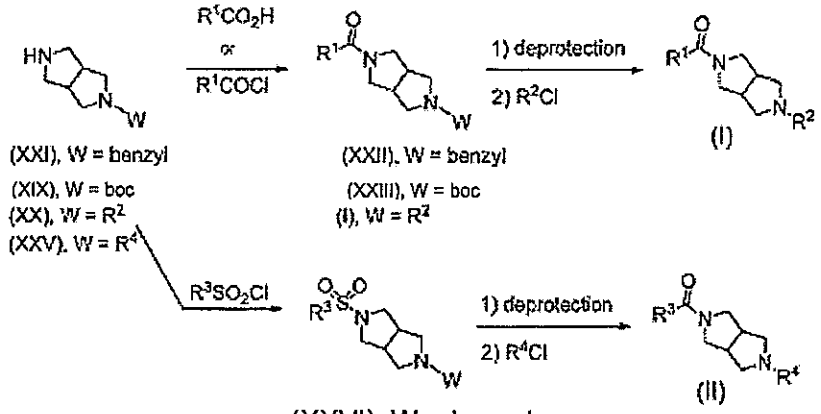
Compounds of formula (XX) are also obtained from 2-benzyl-octahydro-pyrrolo-[3,4-c]pyrrole. Referring to Scheme D, 2-benzyl-octahydro-pyrrolo[3,4-c]-pyrrole is treated with R^2Cl, where R^2 is as defined in a compound of formula (I).

Commercially available or synthetically accessible suitably substituted heteroaryl compounds of formula R^2Cl are reacted with compound 2-benzyl-octahydro-pyrrolo- [3,4-c]pyrrole in the presence of a tertiary organic or inorganic base such as CS_2CO_3, Na_2CO_3, and TEA; in a solvent such as DMF, dichloro-methane, and THF; at a temperature between room temperature and the reflux temperature of the solvent to afford a compound of formula (XXI).

In a preferred embodiment the base is CS_2CO_3 and the solvent is DMF. A compound of formula (XX) is obtained by treating a compound of formula (XXI) with hydrogen gas, in the presence of a catalyst, in a solvent such as AcOH.

In a preferred embodiment the catalyst is Pd on carbon.

SCHEME E



(XXVI), W = benzyl
(XXVII), W = boc
(XXVIII), W = R^4

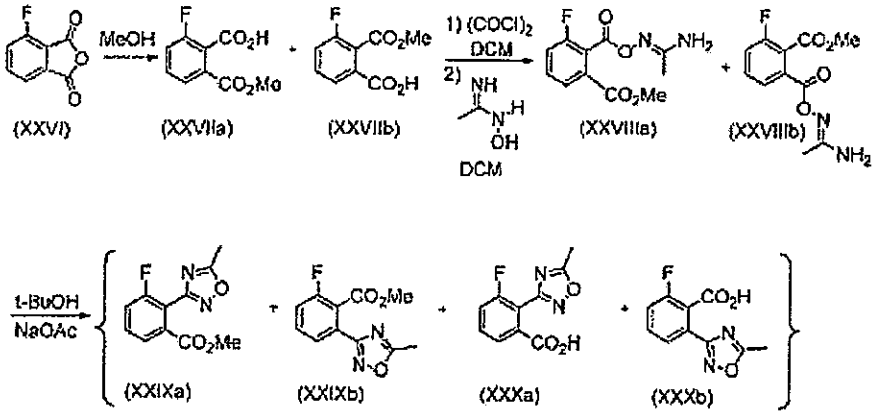
Referring to Scheme E, a compound of formula (I) is obtained from a compound of formula (XIX), (XX), or (XXI) by reacting a compound of formula (XIX), (XX), or (XXI) with a compound of formula R^1CO_2H under amide formation conditions. Compounds of formula R^1CO_2H, where R^1 is as defined in formula (I), are commercially available, as described, or synthetically accessible appropriately substituted aryl or heteroaryl carboxylic acids. In a preferred embodiment a compound of formula (XIX), (XX), or (XXI), either as a free base or as an acid salt, is reacted with a compound of formula R^1CO_2H, in the presence of a dehydrating agent such as HOBt/EDAC, CDI, HATU, HOAT; a suitably selected base such as DIPEA, and TEA; in an organic solvent or mixture thereof, such as toluene, acetonitrile, ethyl acetate, DMF, THF, and meth-ylene chloride; to afford a compound of formula (XXII), (XXIII) or (I). In a particularly preferred embodiment the dehydrating agent is HATU, and the base is DIPEA. In an alternative embodiment, a compound of formula R^1CO_2H (as described above) may be first converted to a compound of formula R^1COCl, or compound of formula R^1COCl is a commercially available substituted aryl sulfonyl chloride. In a preferred embodiment, a compound of formula R^1CO_2H is treated with thionyl chloride in a solvent such as toluene to afford a compound of formula R^1COCl.

A compound of formula (I) is obtained by treating a compound of formula R^1COCl with a compound of formula (XIX), (XX) , or (XXI), a suitably selected tertiary organic base such as TEA, in a solvent such as dichloromethane, and

THF, at a temperature between room temperature and the reflux temperature of the solvent. A compound of formula (II) is obtained by treating a compound of formula R^1SO_2Cl with a compound of formula (XIX), (XXI), or (XXV), where R^4 is (5-trifluoromethyl)-pyridin-2-yl, (5-tri-fluoro-methyl)-pyrimidin-2-yl, 4,6-dimethylpyrimidin-2-yl, or quinoxalin-2-yl; a suitably selected tertiary organic base such as TEA, in a solvent such as dichloromethane, and THF, at a temperature between room temperature and the reflux temperature of the solvent.

Referring to Scheme E, one skilled in the art will recognize that the sequence of transformations shown in Schemes D and E may be reordered such that amide bond formation may be the initial reaction to give compounds of formulae (XXII) and (XXIII). Removal of the N-benzyl group from a compound of formulae (XXII) or removal of the carbamate from a compound of formula (XXIII) followed by the reaction with a compound R^2Cl, where R^2Cl is as described above gives a compound of formula (I).

SCHEME F



3-Fluoro-2-(3-methyl-1,2,4-oxadiazol-5-yl)benzoic acid and 2-fluoro-6-(3-methyl -1,2,4-oxadiazol-5-yl)benzoic acid are prepared according to SCHEME H. 3-fluoro-phthalic anhydride was dissolved in a solvent such as MeOH, at temperatures ranging from room temperature to the reflux temperature of the solvent, to provide acid-esters (XXVIIa) and (XXIIb).

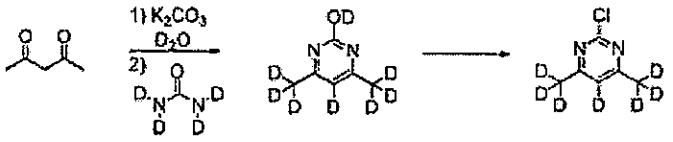
Conversion of the acid to the acid chloride is accomplished under standard chlorination conditions. In a preferred method the acid is heated with oxalyl chloride

in a solvent such as DCM. Subsequent reaction of the acid chloride with N-hydroxyacetamide in a solvent such as CH_2Cl_2 provides a mixture of esters (XXVIIIa) and (XXVIIIb). Finally, esters (XXVIIIa) and (XXVIIIb) are converted to a mixtue of esters (XXIXa) and (XXIXb) and acids (XXXa) and (XXXb) by treatment with a base, preferably sodium acetate, in the presence of a solvent, preferably t-BuOH.

Alternately, acid (XXXa) is prepared by first converting 2-fluoro-6-iodobenzoic acid to the acid chloride by reaction with a chlorinating agent such as oxalyl chloride, in a solvent such as DCM, with a catalytic amount of DMF, at a temperature of 0 °C.

Subsequent reaction of the acid chloride with N-hydroxyacetamide in a solvent such as CH_2Cl_2 provides (Z)-N'-((2-fluoro-6-iodobenzoyl)oxy)acetimidamide. 5-(2-fluoro-6-iodophenyl)-3-methyl-1,2,4-oxadiazole is prepared by reacting (Z)-N'-((2-fluoro -6-iodobenzoyl)oxy)acetimidamide with sodium acetate, in a solvent such as *tert*-butanol, at temperatures ranging from 100 °C to 1 10 °C. 3-fluoro-2-(3-methyl -1,2,4-oxadiazol-5-yl)benzoic acid (XXXa) is prepared by reacting 5-(2-fluoro-6-iodo-phenyl)-3-methyl-1,2, 4-oxadiazole with a grignard reagent such as i-PrMgCl, in a suitable solvent such as THF, at a temperature of -78 °C. Subsequent addition of CO_2 gas, at a temperature of -78 °C provides 3-fluoro-2-(3-methyl-1,2,4-oxadiazol-5-yl)benzoic acid (XXXa).

SCHEME H



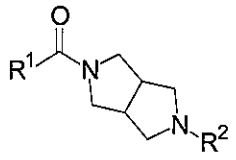
EtOD (XXXI) (XXXII)

Deuterated pyrimidine compounds of formula (XXXII) are prepared according to Scheme H.

Acetylacetone is reacted with an inorganic base such as K_2CO_3 in deuterated water, at temperatures ranging from 100 °C to 120 °C to provide 1,1,1,-3,3,3,5,5-octa-deuteriopentane-2,4-dione. 1,1,1,3,3,3,5,5-octadeuteriopentane-2,4-dione is subsequently reacted with deuterated urea, in a solvent such as deuterated ethanol, 35% wt. DCl in D_2O, at temperatures ranging from 90 °C to 100 °C to provide deuterated pyrimidinols of formula

CLAIMS

1. A chemical entity that is a compound of Formula (I):



Formula (I)

wherein:

R^1 is a member selected from the group consisting of:

A) phenyl substituted or unsubstituted with one or two R^a members and substituted in the *ortho* position with R^b;

R^a is independently selected from the group consisting of: -H, halo, -C_{1-4}alkyl, -C_{1-4}alkoxy, and -NO_2, wherein two adjacent R^a members may come together to form a six membered aromatic ring;

R^b is a member selected from the group consisting of:

a) halo, -C_{1-4}alkoxy, -C_{1-4}alkyl,-CF_3, -OCF_3, or -CN;

b) 5-membered heteroaryl ring containing one oxygen or one sulfur members;

c) 5-6 membered heteroaryl ring containing one, two or three nitrogen members, optionally containing one oxygen member, substituted or unsubstituted with halo or -C_{1-4}alkyl; and

d) phenyl substituted or unsubstituted with halo, -CH_3, or -CF_3;

B) pyridine substituted or unsubstituted with one or two R^c members and substituted with R^d, wherein R^d is positioned adjacent to the point of attachment by R^1;

R^c is C_{1-4}alkyl;

R^d is a member selected from the group consisting of:

a) 5-6 membered heteroaryl ring selected from the group consisting of: 1H-1,2,3-triazol-1-yl, 2H-1,2,3-triazol-2-yl, 1H-pyrazol-5-yl, 3-methyl-1,2,4-oxadiazol-5-yl, pyridinyl, 3-methyl-pyridin-2-yl; 1-(tetrahydro-2H-pyran-2-yl)-1H-pyrazol-5-yl), phenyl, and pyrimidin-2-yl; and

b) -CF_3, -Br, and -C_{1-4}alkoxy;

C) 5-membered heteroaryl ring selected from the group consisting of: 2-methyl-1,3-thiazol-yl, 1H-pyrazol-5-yl, oxazole, isoxazolyl, thiophen-2-yl, and furan-2-yl, each substituted with phenyl substituted or unsubstituted with -F; and

D) 5-13 membered aryl or heteroaryl ring selected from the group consisting of: 3-methylfuran-2-yl, 9H-fluorene, quinoline, cinnoline; 3-(1H-pyrrol-1-yl)thiophen-2-yl, 8-[1,2,3]-triazol-2-yl-naphthalen-1-yl, 2,3-dihydro-1,4-benzodioxin-5-yl, 1H-indol-7-yl, 4-fluoronaphthalen-1-yl, and naphthalen-1-yl;

R^2 is a member selected from the group consisting of:

A) 6-membered heteroaryl ring containing two nitrogen members substituted with one or more members independently selected from the group consisting of: halo, -C_{1-4}alkyl, -CD_3, -D, -C_{1-4}alkoxy, cyclopropyl, morpholin-2-yl, -CO_2C_{1-4}alkyl, -CO_2H, -CH_2OH, -$C(O)N(C_{1-4}alkyl)_2$, -CF_3, -CN, -OH, -NO_2, -$N(C_{1-4}alkyl)_2$, phenyl, furan-2-yl, thiophen-2-yl, 1H-pyrazol-4-yl, and pyrrolidin-1-yl;

B) pyridine substituted with one or two members independently selected from the group consisting of: halo, -C_{1-4}alkyl, -C_{1-4}alkoxy, and -CF_3;

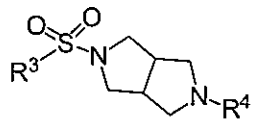
C) 9-membered heteroaryl ring selected from the group consisting of benzooxazol-2-yl, 6-fluoro-1,3-benzothiazole, 1,3-benzothiazole, 6-methoxy-1,3-benzothiazole, 6-methyl-1,3-benzothiazole, 6-chloro-benzothiazol-2-yl, and 4-methyl-6,7-dihydro-5H-cyclopenta[d]pyrimidine;

D) 10-membered heteroaryl ring selected from the group consisting of quinoxalin-2-yl, 3-methylquinoxalin-2-yl, 6,7-difluoroquinoxalin-2-yl, 3-(trifluoromethyl)quinoxaline, quinoline, 4-methylquinoline, and 6-fluoro-quinazolin-2-yl; and

E) 4-methyl-1,3,5-triazin-2-yl or 2-methylpyrimidin-4(3H)-one;

and pharmaceutically acceptable salts of compounds of Formula (I).

2. A chemical entity selected from compounds of Formula (II):



(II)

wherein

R^3 is phenyl substituted or unsubstituted with a member independently selected from the group consisting of: -C_{1-4}alkoxy, and phenyl; and

R^4 is a member selected from the group consisting of (5-trifluoromethyl)-pyridin-2-yl, (5-trifluoromethyl)-pyrimidin-2-yl, 4,6-dimethylpyrimidin-2-yl, and quinoxalin-2-yl;

and pharmaceutically acceptable salts of compounds of Formula (II).

3. A chemical entity defined in claim 1, wherein R^1 is phenyl, where R^a is a member independently selected from the group consisting of -F, -I, -Cl, -OCH_3, -OCH_2CH_3, -CH_3, -$CH(CH_3)_2$, -$C(CH_3)_3$ and -NO_2.

4. A chemical entity defined in claim 1, wherein R^1 is phenyl wherein R^b is a member selected from the group consisting of -Br, -F, -I, -C_{1-4}alkyl, -OCH_3, -OCH_2CH_3, -CN, -CF_3, and -OCF_3.

5. A chemical entity defined in claim 1, wherein R^1 is phenyl, where R^a is selected from the group consisting of -H, -F, -Cl, -CH_3, -$C(CH_3)_3$, -OCH_3, and -OCH_2CH_3, and R^b is selected from the group consisting of -Br, -F, -I, -C_{1-4}alkyl, -OCH_3, -OCH_2CH_3, -CN, -CF_3, and -OCF_3.

6. A chemical entity defined in claim 1, wherein R^1 is phenyl, where R^b is 2-thiophen-2-yl or 2-furan-2-yl.

7. A chemical entity defined in claim 1, wherein R^1 is phenyl, whereR^b is selected from the group consisting of phenyl, 3-chlorophenyl, 4-fluorophenyl, 3-fluorophenyl, 4-methylphenyl, and 4-trifluoromethylphenyl.

8. A chemical entity defined in claim 1, wherein R^1 is phenyl, where

R^b is a member selected from the group consisting of 1H-pyrrol-1-yl, 1H-pyrazol-1-yl, 1H-pyrazol-5-yl, 1H-imidazol-2-yl, 1-methyl-1H-imidazol-2-yl, 1H-1,2,3-triazol-1-yl, 2H-1,2,3-triazol-2-yl, 2H-1,2,3-triazol-1-yl, 1H-1,2,4-triazol-5-yl, 2H-1,2,4-triazol-1-yl, 2H-1,2,4-triazol-3-yl, 4H-1,2,4-triazol-3-yl, 4H-1,2,4-triazol-4-yl, 1-methyl-1H-1,2,4-triazol-3-yl, 1-methyl-1H-1,2,4-triazol-5-yl and 1-(tetrahydro-2H-pyran-2-yl)-1H-pyrazol-5-yl.

9. A chemical entity defined in claim 1, wherein R^1 is phenyl, where R^b is a member selected from the group consisting of pyridin-2-yl, 3-chloro-pyridin-2-yl, 3-fluoropyridin-2-yl, 3-methylpyridin-2-yl, 4-methylpyridin-2-yl, 5-methylpyridin-2-yl, 6-methylpyridin-2-yl, 2-pyridin-3-yl, and 2-pyrimidin-2-yl.

10. A chemical entity defined in claim 1, wherein R^1 is phenyl, whereR^b is a member selected from the group consisting of 3-methyl-1,2,4-oxadiazol-5-yl and oxazol-2-yl.

11. A chemical entity defined in claim 1, wherein R^1 is phenyl, whereR^a is halo, -C_{1-4}alkyl, or -C_{1-4}alkoxy, and R^b is triazole or pyrimidine substituted or unsubstituted with halo or -C_{1-4}alkyl.

12. A chemical entity defined in claim 1, wherein R^1 is (1-methylethyl)-2-(2H-1,2,3-triazol-2-yl)phenyl, 2-(1H-1,2,3-triazol-1-yl)phenyl, 2-(2H-1,2,3-triazol-2-yl)phenyl, 2-fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl, 2-methyl-6-(2H-1,2,3-triazol-2-yl)phenyl, 3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl, 3-fluoro-2-(1H-1,2,3-triazol-1-yl)phenyl, 3-methoxy-2-(1H-1,2,3-triazol-1-yl)phenyl, 3-methoxy-2-(2H-1,2,3-triazol-2-yl)phenyl, 3-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl, 3-methyl-2-(1H-1,2,3-triazol-1-yl)phenyl, 4-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl, 4-methoxy-2-(2H-1,2,3-triazol-2-yl)phenyl, 4-methoxy-2-(1H-1,2,3-triazol-2-yl)phenyl, 4,5-dimethoxy-2-[1,2,3]triazol-1-yl-phenyl, 4,5-dimethoxy-2-[1,2,3]triazol-2-yl-phenyl, 5-[1,2,3]triazol-2-yl-benzo[1,3]dioxol-4-yl, 5-chloro-2-(2H-1,2,3-triazol-2-yl)phenyl, 5-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl, 5-iodo-2-(2H-1,2,3-triazol-2-yl)phenyl, 5-methoxy-2-(2H-1,2,3-triazol-2-yl)phenyl, 5-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl, 1-[1,2,3]triazol-2-yl-naphthalen-2-yl, 2-(1H-1,2,4-triazol-1-yl)-

phenyl, 2-(1H-1,2,4-triazol-5-yl)phenyl, 2-(1-methyl-1H-1,2,4-triazol-5-yl)phenyl, 2-(1-methyl-1H-1,2,4-triazol-3-yl)phenyl, 2-(4H-1,2,4-triazol-3-yl)phenyl, 2-(4H-1,2,4-triazol-4-yl)phenyl, 2-(3-methyl-1,2,4-oxadiazol-5-yl)phenyl, 3-fluoro-2-(3-methyl-1,2,4-oxadiazol-5-yl)phenyl, 2-fluoro-6-(3-methyl-1,2,4-oxadiazol-5-yl)-phenyl, 4,5-difluoro-2-(4H-1,2,4-triazol-4-yl)phenyl), 2-fluoro-6-pyrimidin-2-yl-phenyl, 2-(pyrimidin-2-yl)pyridin-3-yl, 3-fluoro-2-pyrimidin-2-ylphenyl, 4-fluoro-2-(pyrimidin-2-yl)phenyl, 4-methoxy-2-(pyrimidin-2-yl)phenyl, 5-fluoro-2-pyrimidin-2-ylphenyl, and 5-methyl-2-pyrimidin-2-ylphenyl.

13. A chemical entity defined in claim 1, wherein R^1 is pyridine, whereR^d is a member selected from the group consisting of $-CF_3$, -Br, and $-OCH_2CH_2CH_3$.

14. A chemical entity defined in claim 1, wherein R^1 is pyridine, whereR^d is a member selected from the group consisting of 1H-pyrazol-5-yl, 2H-1,2,3-triazol-1-yl, 2H-1,2,3-triazol-2-yl, 4H-1,2,3-triazol-1-yl, 1-(tetrahydro-2H-pyran-2-yl)-1H-pyrazol-5-yl, 3-methylpyridin-2-yl, and 3-methyl-1,2,4-oxadiazol-5-yl.

15. A chemical entity defined in claim 1, wherein R^1 is pyridine, whereR^d is a member selected from the group consisting of 1H-pyrazol-5-yl, 2H-1,2,3-triazol-1-yl, and 2H-1,2,3-triazol-2-yl.

16. A chemical entity defined in claim 1, wherein R^1 is 1-phenyl-1H-pyrazol-5-yl, 3-phenylthiophen-2-yl, 3-phenylfuran-2-yl, 5-phenyl-1,3-oxazol-4-yl, 5-phenyl-isoxazol-4-yl, 5-(2-fluorophenyl)-2-methyl-1,3-thiazol-4-yl, 2-methyl-5-phenyl-thiazol-4-yl, or 5-(4-fluorophenyl)-2-methyl-1,3-thiazol-4-yl.

17. A chemical entity defined in claim 1, wherein R^1 is selected from the group consisting of 3-methylfuran-2-yl, 9H-fluorene, quinoline, cinnoline; 3-(1H-pyrrol-1-yl)thiophen-2-yl, 8-[1,2,3]-triazol-2-yl-naphthalen-1-yl, 2,3-dihydro-1,4-benzo-dioxin-5-yl, 1H-indol-7-yl, 4-fluoronaphthalen-1-yl, and naphthalen-1-yl and R^2 is selected from the group consisting of 4,6-dimethylpyrimidin-2-yl, 4-phenyl-pyrimidin-2-yl, quinoxaline, and 4-methoxypyrimidin-2-yl.

18. A chemical entity defined in claim 1, wherein R^2 is pyrimidine substituted with one or more members independently selected from the group consisting of -F, -Cl, -D, $-CD_3$, $-CH_3$, ethyl, isopropyl, propyl, tert-butyl, $-CF_3$, $-OCH_3$, $-N(CH_3)_2$, -CN, -OH, $-CH_2OH$, $-NO_2$, $-CO_2CH_3$, $-CO_2H$, $-C(O)N(CH_3)_2$, phenyl, furan-2-yl, thiophen-2-yl, 1H-pyrazol-4-yl, cyclopropyl, pyrrolidin-1-yl, and morpholin-4-yl.

19. A chemical entity defined in claim 1, wherein R^2 is 4,6-dimethylpyrimidin-2-yl, 4,5-dimethylpyrimidin-2-yl,4,6-dimethoxypyrimidin-2-yl,4-phenyl-pyrimidin-2-yl, 4-furan-2-ylpyrimidin-2-yl, 4-methylpyrimidin-2-yl, 4-methoxypyrimidin-2-yl, 4-thiophen-2-ylpyrimidin-2-yl, N,N,6-trimethyl-pyrimidin-4-amine, 4-(trifluoromethyl)pyrimidin-2-yl, 4,5,6-trimethylpyrimidin-2-yl, 4-(trifluoromethyl)-pyrimidine-5-carboxylate, 4-(trifluoromethyl)pyrimidine-5-carboxylic acid, 5-nitropyrimidin-2-yl, 6-methylpyrimidine-4-carboxylic acid, N,N-dimethyl-4-(triflouoromethyl)pyrimidine-5-carboxamide, N,N,6-trimethylpyrimidine-carbox-amide, 6-methylpyrimidine-4-carbonitrile, 4,6-bis(trifluoromethyl)-pyrimidin-2-yl, 6-methyl-pyrimidin-4-ol, 4-(furan-2-yl)-6-methylpyrimidin-2-yl, 5-fluoro-4-methylpyrimidin-2-yl, 5-fluoropyrimidin-2-yl, 4-methoxy-6-methyl-pyrimidin-2-yl, 4-ethyl-6-methylpyrimidin-2-yl, 4-isopropyl-6-methylpyrimidin-2-yl, 4-tertbutyl-6-methylpyrimidin-2-yl, 4-cyclopropyl-6-methylpyrimidin-2-yl, 4-methyl-6-morpholin-4-ylpyrimidin-2-yl, 5-chloro-4-methylpyrimidin-2-yl, 5-chloro-4,6-dimethylpyrimidin-2-yl, 5-fluoro-4,6-dimethylpyrimidin-2-yl, 5-trifluoromethylpyrimidin-2-yl, 4,6-bis[(^{2}H3)methyl]-(^{2}H)pyrimidin-2-yl, and 5-ethyl-4,6-dimethylpyrimidin-2-yl.

20. A chemical entity defined in claim 1, wherein R^2 is pyrimidine substituted with one or more members independently selected from the group consisting of -Cl, -F, $-CH_3$, $-CF_3$, $-N(CH_3)_2$, -D, and $-CD_3$.

21. A chemical entity defined in claim 1, wherein R^2 is 4,6-dimethylpyrimidin-2-yl, 4,5-dimethylpyrimidin-2-yl,4,6-dimethoxypyrimidin-2-yl, 4-methylpyrimidin-2-yl, 4-methoxypyrimidin-2-yl, N,N,6-trimethyl-pyrimidin-4-amine, 4-(trifluoromethyl)-pyrimidin-2-yl, 4,5,6-trimethylpyrimidin-2-yl, 4,6-bis(trifluoromethyl)-

pyrimidin-2-yl, 6-methyl-pyrimidin-4-ol, 5-fluoro-4-methylpyrimidin-2-yl, 5-fluoropyrimidin-2-yl, 4-methoxy-6-methylpyrimidin-2-yl, 5-chloro-4-methyl-pyrimidin-2-yl, 5-chloro-4,6-dimethylpyrimidin-2-yl, 5-fluoro-4,6-dimethyl-pyrimidin-2-yl, 5-trifluoromethylpyrimidin-2-yl, and 4,6-bis[(^{2}H3)-methyl]-(^{2}H)-pyrimidin-2-yl.

22. A chemical entity defined in claim 1, wherein R^2 is pyrazine or triazine substituted with one or more -CH_3.

23. A chemical entity defined in claim 1, wherein R^2 is pyridine substituted with one or more members independently selected from the group consisting of -F, -OCH_3, -OCH_2CH_3, -CH_3, and -CF_3.

24. A chemical entity defined in claim 1, wherein R^2 is a member selected from the group consisting of benzooxazol-2-yl, 2-methylpyrimidin-4(3H)-one and 4-methyl-6,7-dihydro-5H-cyclopenta[d]pyrimidine and R^1 is phenyl, substituted in the *ortho* position with R^b, where R^b is 2H-1,2,3-triazol-2-yl, 2H-1,2,3-triazol-1-yl, 3-methyl-1,2,4-oxadiazol-5-yl or 2-pyrimidin-2-yl.

25. A chemical entity defined in claim 1, wherein R^2 is a member selected from the group consisting of quinoxalin-2-yl, 3-methylquinoxalin-2-yl, 6,7-difluoro-quinoxalin-2-yl, 3-(trifluoromethyl)quinoxaline, 4-methylquinoline, and 6-fluoro-quinazolin-2-yl and R^1 is phenyl substituted in the *ortho* position with R^b, where R^b is 2H-1,2,3-triazol-2-yl, 2H-1,2,3-triazol-1-yl, 3-methyl-1,2,4-xadiazol-5-yl or 2-pyrimidin-2-yl.

26. A chemical entity defined in claim 2, wherein R^3 is biphenyl or 2-methoxy-phenyl and R^4 is (5-trifluoromethyl)-pyridin-2-yl, (5-trifluoromethyl)-pyrimidin-2-yl, 4,6-dimethylpyrimidin-2-yl, or quinoxalin-2-yl.

27. A chemical entity defined in claim 1, wherein R^1 is a member selected from the group consisting of 2-(1H-1,2,3-triazol-1-yl)phenyl, 2-(2H-1,2,3-triazol-2-yl)phenyl, 2-fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl, 2-methyl-6-(2H-1,2,3-triazol-

2-yl)phenyl, 3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl, 3-fluoro-2-(1H-1,2,3-triazol-1-yl)phenyl, 3-methoxy-2-(1H-1,2,3-triazol-1-yl)phenyl, 3-methoxy-2-(2H-1,2,3-triazol-2-yl)phenyl, 3-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl, 3-methyl-2-(1H-1,2,3-triazol-1-yl)phenyl, 4-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl, 4-methoxy-2-(2H-1,2,3-triazol-2-yl)phenyl, 4-methoxy-2-(1H-1,2,3-triazol-2-yl)phenyl, 4,5-dimethoxy-2-[1,2,3]triazol-1-yl-phenyl, 4,5-dimethoxy-2-[1,2,3]triazol-2-yl-phenyl, 5-chloro-2-(2H-1,2,3-triazol-2-yl)phenyl, 5-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl, 5-methoxy-2-(2H-1,2,3-triazol-2-yl)phenyl, 5-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl, 2-(1H-1,2,4-triazol-1-yl)phenyl, 2-(1H-1,2,4-triazol-5-yl)phenyl, 2-(1-methyl-1H-1,2,4-triazol-5-yl)phenyl, 2-(1-methyl-1H-1,2,4-triazol-3-yl)phenyl, 2-(4H-1,2,4-triazol-3-yl)phenyl, 2-(4H-1,2,4-triazol-4-yl)phenyl, 2-(3-methyl-1,2,4-oxadiazol-5-yl)phenyl, 3-fluoro-2-(3-methyl-1,2,4-oxadiazol-5-yl)phenyl, 2-fluoro-6-(3-methyl-1,2,4-oxadiazol-5-yl)phenyl, 4,5-difluoro-2-(4H-1,2,4-triazol-4-yl)phenyl), 2-fluoro-6-pyrimidin-2-ylphenyl, 2-(pyrimidin-2-yl)pyridin-3-yl, 3-fluoro-2-pyrimidin-2-ylphenyl, 4-fluoro-2-(pyrimidin-2-yl)phenyl, 4-methoxy-2-(pyrimidin-2-yl)phenyl, 5-fluoro-2-pyrimidin-2-ylphenyl, and 5-methyl-2-pyrimidin-2-ylphenyl and R^2 is a member selected from the group consisting of 4,6-dimethylpyrimidin-2-yl, 4,5-dimethylpyrimidin-2-yl,4,6-dimethoxypyrimidin-2-yl, 4-methylpyrimidin-2-yl, 4-methoxypyrimidin-2-yl, N,N,6-trimethyl-pyrimidin-4-amine, 4-(trifluoromethyl)pyrimidin-2-yl, 4,5,6-trimethylpyrimidin-2-yl, 4,6-bis(trifluoromethyl)pyrimidin-2-yl, 6-methyl-pyrimidin-4-ol, 5-fluoro-4-methylpyrimi-din-2-yl, 5-fluoropyrimidin-2-yl, 4-methoxy-6-methylpyrimidin-2-yl, 5-chloro-4-methylpyrimidin-2-yl, 5-chloro-4,6-dimethylpyrimidin-2-yl, 5-fluoro-4,6-dimethyl-pyrimidin-2-yl, 5-trifluoromethylpyrimidin-2-yl, and 4,6-bis[(^{2}H3)methyl]-(^{2}H)-pyrimidin-2-yl.

28. A chemical entity defined in claim 1, wherein R^1 is a member selected from the group consisting of 3-fluoro-2-(3-methyl-1,2,4-oxadiazol-5-yl)phenyl, 6-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl, 4-methoxy-2-(2H-1,2,3-triazol-2-yl)phenyl, and 3-[1,2,3]triazol-2-yl-pyridin-2-yl and R^2 is a member selected from the group consisting of 4,6-dimethylpyrimidin-2-yl, 5-fluoro-4,6-imethylpyrimidin-2-yl, and 5-fluoro-4-methylpyrimidin-2-yl.

29. A chemical entity as claimed in claim 1,selected from the group consisting of:

4-[5-{[2-Fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-6-methoxy-N,N-dimethylpyrimidin-2-amine;

N,N-Dimethyl-6-[5-{[2-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}hexahydro-pyrrolo[3,4-c]pyrrol-2(1H)-yl]-2-(trifluoromethyl)-pyrimidin-4-amine;

6-[5-{[2-Fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-N,N-dimethyl-2-(trifluoromethyl)pyrimidin-4-amine;

4-[5-{[5-Fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-6-methoxy-N,N-dimethylpyrimidin-2-amine;

4-Methoxy-N,N-dimethyl-6-[5-{[2-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}hexa-hydropyrrolo-[3,4-c]pyrrol-2(1H)-yl]pyrimidin-2-amine;

6-[5-{[4-Fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-N,N-dimethyl-2-(trifluoromethyl)pyrimidin-4-amine;

4-[5-{[4-Fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-6-methoxy-N,N-dimethylpyrimidin-2-amine;

2-(4,6-Dimethylpyrimidin-2-yl)-5-{[3-(1H-pyrrol-1-yl)thiophen-2-yl]carbonyl}octa-hydro-pyrrolo[3,4-c]pyrrole;

6-[5-{[5-Fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-N,N-dimethyl-2-(trifluoromethyl)pyrimidin-4-amine;

2-(4,6-Dimethylpyrimidin-2-yl)-5-[(1-phenyl-1H-pyrazol-5-yl)carbonyl]octa-hydropyrrolo[3,4-c]pyrrole;

8-{[5-(4,6-Dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-carbonyl}-quinoline;

2-(4,6-Dimethylpyrimidin-2-yl)-5-[(3-phenylthiophen-2-yl)carbonyl]octahydro-pyrrolo[3,4-c]pyrrole;

2-(4,6-Dimethylpyrimidin-2-yl)-5-[(3-phenylfuran-2-yl)carbonyl]octahydro-pyrrolo[3,4-c]pyrrole;

2-(4,6-Dimethylpyrimidin-2-yl)-5-{[2-(1H-1,2,4-triazol-5-yl)phenyl]carbonyl} octa-hydro-pyrrolo[3,4-c]pyrrole;

2-(4,6-Dimethylpyrimidin-2-yl)-5-{[3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl]-carbonyl} octahydropyrrolo[3,4-c]pyrrole;

2-{5-[(2,4-Dimethoxyphenyl)carbonyl]hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl}-6-fluoro-1,3-benzothiazole;

2-{5-[(2,4-Dimethoxyphenyl)carbonyl]hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl}-1,3-benzothiazole;

2-[5-{[2-(1H-Pyrazol-1-yl)phenyl]carbonyl}hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]quinoxaline;

2-{5-[(2-Thiophen-2-ylphenyl)carbonyl]hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl}-quinoxaline;

2-{5-[(2-Methylnaphthalen-1-yl)carbonyl]hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl}quinoxaline;

2-(2,3-Dihydro-1,4-benzodioxin-5-ylcarbonyl)-5-(4-phenylpyrimidin-2-yl)octahydropyrrolo[3,4-c]pyrrole;

2-(4-Phenylpyrimidin-2-yl)-5-[(2-thiophen-2-ylphenyl)carbonyl]octahydropyrrolo[3,4-c]pyrrole;

2-(4-Phenylpyrimidin-2-yl)-5-{[2-(1H-pyrazol-1-yl)phenyl]carbonyl}octahydropyrrolo[3,4-c]pyrrole;

2-(4-Phenylpyrimidin-2-yl)-5-{[2-(1H-pyrrol-1-yl)phenyl]carbonyl}octahydropyrrolo[3,4-c]pyrrole;

2-[(2-Methylnaphthalen-1-yl)carbonyl]-5-(4-phenylpyrimidin-2-yl)octahydropyrrolo[3,4-c]pyrrole;

2-(5-Quinoxalin-2-yl-hexahydro-pyrrolo[3,4-c]pyrrole;-2-carbonyl)-benzonitrile;

2-[5-{[2-(1H-Pyrrol-1-yl)phenyl]carbonyl}hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]quinoxaline;

2-{5-[(4'-Fluorobiphenyl-2-yl)carbonyl]hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl}-quinoxaline;

2-{5-[(3'-Fluorobiphenyl-2-yl)carbonyl]hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl}-quinoxaline;

2-{5-[(2-Methylphenyl)carbonyl]hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl}quinoxaline;

2-(Biphenyl-2-ylcarbonyl)-5-(4-furan-2-ylpyrimidin-2-yl)octahydropyrrolo[3,4-c]-pyrrole;

2-(4-Methylpyrimidin-2-yl)-5-[(2-thiophen-2-ylphenyl)carbonyl]octahydropyrrolo[3,4-c]pyrrole;

2-{5-[(2-Thiophen-2-ylphenyl)carbonyl]hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl}-quinoline;

2-(4-Furan-2-ylpyrimidin-2-yl)-5-[(2-thiophen-2-ylphenyl)carbonyl]octahydro-pyrrolo[3,4-c]pyrrole;

2-{5-[(2-Ethylphenyl)carbonyl]hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl}quin-oxaline;

2-[5-(1H-Indol-7-ylcarbonyl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]quinoxaline;

2-[(2-Thiophen-2-ylphenyl)carbonyl]-5-(4-thiophen-2-ylpyrimidin-2-yl)octahydro-pyrrolo[3,4-c]pyrrole;

2-(Biphenyl-2-ylcarbonyl)-5-(4-thiophen-2-ylpyrimidin-2-yl)octahydropyrrolo[3,4-c]pyrrole;

[5-(4,6-Dimethyl-pyrimidin-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-[2-(1-methyl-1H-imidazol-2-yl)-phenyl]-methanone;

2-[(2-Bromophenyl)carbonyl]-5-(4-phenylpyrimidin-2-yl)octahydropyrrolo[3,4-c]-pyrrole;

2-{5-[(3'-Chlorobiphenyl-2-yl)carbonyl]hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl}-quinoxaline;

2-{5-[(2-Bromophenyl)carbonyl]hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl}quin-oxaline;

2-(4,6-Dimethylpyrimidin-2-yl)-5-[(2-thiophen-2-ylphenyl)carbonyl]octahydro-pyrrolo[3,4-c]pyrrole;

2-(Biphenyl-2-ylcarbonyl)-5-(4,6-dimethylpyrimidin-2-yl)octahydropyrrolo[3,4-c]-pyrrole;

2-(4-Methoxypyrimidin-2-yl)-5-[(2-thiophen-2-ylphenyl)carbonyl]octahydro-pyrrolo[3,4-c]pyrrole;

6-Fluoro-2-{5-[(2-thiophen-2-ylphenyl)carbonyl]hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl}-1,3-benzothiazole

2-(4,6-Dimethylpyrimidin-2-yl)-5-[(2-methylnaphthalen-1-yl)carbonyl]octahydro-pyrrolo[3,4-c]pyrrole;

2-[(3'-Fluorobiphenyl-2-yl)carbonyl]-5-(4-methylpyrimidin-2-yl)octahydro-pyrrolo[3,4-c]pyrrole;

2-(4-Methoxypyrimidin-2-yl)-5-[(2-methylnaphthalen-1-yl)carbonyl]octahydro-pyrrolo[3,4-c]pyrrole;

2-[(2-Methylnaphthalen-1-yl)carbonyl]-5-(4-methylpyrimidin-2-yl)octahydropyrrolo[3,4-c]pyrrole;
2-[(3'-Fluorobiphenyl-2-yl)carbonyl]-5-(4-methoxypyrimidin-2-yl)octahydropyrrolo[3,4-c]pyrrole;
2-(4,6-Dimethylpyrimidin-2-yl)-5-[(3'-fluorobiphenyl-2-yl)carbonyl]octahydropyrrolo[3,4-c]pyrrole;
[5-(4,6-Dimethyl-pyrimidin-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-(2-fluorophenyl)-methanone;
2-(4-Methoxypyrimidin-2-yl)-5-[(4'-methylbiphenyl-2-yl)carbonyl]octahydropyrrolo[3,4-c]pyrrole;
2-[(3'-Chlorobiphenyl-2-yl)carbonyl]-5-(4-methoxypyrimidin-2-yl)octahydropyrrolo[3,4-c]pyrrole;
2-[(2-Ethoxynaphthalen-1-yl)carbonyl]-5-(4-methoxypyrimidin-2-yl)octahydropyrrolo[3,4-c]pyrrole;
2-[(4-Fluoronaphthalen-1-yl)carbonyl]-5-(4-methoxypyrimidin-2-yl)octahydropyrrolo[3,4-c]pyrrole;
2-(4-Methoxypyrimidin-2-yl)-5-(naphthalen-1-ylcarbonyl)octahydropyrrolo[3,4-c]pyrrole;
2-[(2-Ethoxyphenyl)carbonyl]-5-(4-methoxypyrimidin-2-yl)octahydropyrrolo[3,4-c]pyrrole;
2-[(2-Methoxynaphthalen-1-yl)carbonyl]-5-(4-methoxypyrimidin-2-yl)octahydropyrrolo[3,4-c]pyrrole;
2-(Biphenyl-2-ylcarbonyl)-5-[4-(1H-pyrazol-4-yl)pyrimidin-2-yl]octahydropyrrolo[3,4-c]pyrrole;
2-[4-(1H-Pyrazol-4-yl)pyrimidin-2-yl]-5-[(2-thiophen-2-ylphenyl)carbonyl]octahydro-pyrrolo[3,4-c]pyrrole;
2-(3,6-Dimethylpyrazin-2-yl)-5-[(2-thiophen-2-ylphenyl)carbonyl]octahydropyrrolo[3,4-c]pyrrole;
2-(Biphenyl-2-ylcarbonyl)-5-(3,5-dimethylpyrazin-2-yl)octahydropyrrolo[3,4-c]-pyrrole;
2-Methyl-3-{5-[(2-thiophen-2-ylphenyl)carbonyl]hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl}quinoxaline;

2-[5-(Biphenyl-2-ylcarbonyl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-3-methyl-quinoxaline;

2-(4,6-Dimethylpyrimidin-2-yl)-5-{[2-(1H-pyrazol-1-yl)phenyl]carbonyl}octa-hydro-pyrrolo[3,4-c]pyrrole;

2-(4,6-Dimethoxypyrimidin-2-yl)-5-[(2-fluoro-6-pyrimidin-2-ylphenyl)carbonyl] octahydropyrrolo[3,4-c]pyrrole;

2-(4,6-Dimethylpyrimidin-2-yl)-5-[(2-pyridin-2-ylphenyl)carbonyl]octahydro-pyrrolo[3,4-c]pyrrole;

2-(4,6-Dimethoxypyrimidin-2-yl)-5-[(2-pyridin-2-ylphenyl)carbonyl]octahydro-pyrrolo[3,4-c]pyrrole;

2-(4,6-Dimethoxypyrimidin-2-yl)-5-[(5-fluoro-2-pyrimidin-2-ylphenyl)carbonyl] octahydropyrrolo[3,4-c]pyrrole;

2-(4,6-Dimethoxypyrimidin-2-yl)-5-{[5-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl]-carbonyl}octahydropyrrolo[3,4-c]pyrrole;

2-(4,6-Dimethylpyrimidin-2-yl)-5-[(2-fluoro-6-pyrimidin-2-ylphenyl)carbonyl]octa-hydropyrrolo[3,4-c]pyrrole;

2-(4,6-Dimethylpyrimidin-2-yl)-5-[(5-fluoro-2-pyrimidin-2-ylphenyl)carbonyl]octa-hydropyrrolo[3,4-c]pyrrole;

2-(4,6-Dimethylpyrimidin-2-yl)-5-{[5-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl]-carbonyl}octahydropyrrolo[3,4-c]pyrrole;

2-(4,6-Dimethylpyrimidin-2-yl)-5-[(2-ethylphenyl)carbonyl]octahydropyrrolo[3,4-c]pyrrole;

2-(4,6-Dimethylpyrimidin-2-yl)-5-[(2-ethoxynaphthalen-1-yl)carbonyl]octahydro-pyrrolo[3,4-c]pyrrole;

2-(4,6-Dimethoxypyrimidin-2-yl)-5-{[2-(1H-pyrazol-1-yl)phenyl]carbonyl}octa-hydro-pyrrolo[3,4-c]pyrrole;

2-(4,6-Dimethylpyrimidin-2-yl)-5-[(5-phenyl-1,3-oxazol-4-yl)carbonyl]octahydro-pyrrolo[3,4-c]pyrrole;

2-(4,6-Dimethylpyrimidin-2-yl)-5-[(5-phenylisoxazol-4-yl)carbonyl]octahydro-pyrrolo[3,4-c]pyrrole;

[5-(2-Isopropyl-6-methyl-pyrimidin-4-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone;

2-[(2-Bromophenyl)carbonyl]-5-(4,6-dimethylpyrimidin-2-yl)octahydropyrrolo-[3,4-c]pyrrole;

2-(4,6-Dimethylpyrimidin-2-yl)-5-{[2-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl} octahydropyrrolo[3,4-c]pyrrole;

2-(4,6-Dimethoxypyrimidin-2-yl)-5-{[2-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl} octahydropyrrolo[3,4-c]pyrrole;

2-[5-{[2-(4H-1,2,4-Triazol-3-yl)phenyl]carbonyl}hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]quinoxaline;

2-[5-{[2-(4H-1,2,4-Triazol-3-yl)phenyl]carbonyl}hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-1,3-benzoxazole;

2-(4-Methylpyrimidin-2-yl)-5-{[2-(4H-1,2,4-triazol-3-yl)phenyl]carbonyl}octahydropyrrolo[3,4-c]pyrrole;

2-(4,6-Dimethylpyrimidin-2-yl)-5-[(2-ethoxyphenyl)carbonyl]octahydropyrrolo-[3,4-c]pyrrole;

2-(4,6-Dimethylpyrimidin-2-yl)-5-{[4-fluoro-2-(trifluoromethyl)phenyl]carbonyl} octahydropyrrolo[3,4-c]pyrrole;

2-(4,6-Dimethylpyrimidin-2-yl)-5-[(4-fluoronaphthalen-1-yl)carbonyl]octahydropyrrolo[3,4-c]pyrrole;

2-(4,6-Dimethylpyrimidin-2-yl)-5-{[2-(1-methylethyl)phenyl]carbonyl}octahydropyrrolo[3,4-c]pyrrole;

2-(4,6-Dimethylpyrimidin-2-yl)-5-[(3-methoxy-2-methylphenyl)carbonyl]octahydro-pyrrolo[3,4-c]pyrrole;

2-(4,6-Dimethylpyrimidin-2-yl)-5-(naphthalen-1-ylcarbonyl)octahydropyrrolo[3,4-c]pyrrole;

2-[5-{[2-(4H-1,2,4-Triazol-3-yl)phenyl]carbonyl}hexahydropyrrolo[3,4-c]pyrrol-2-(1H)-yl]-3-(trifluoromethyl)quinoxaline;

2-Methyl-3-[5-{[2-(4H-1,2,4-triazol-3-yl)phenyl]carbonyl}hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]quinoxaline;

2-[6-Methyl-2-(trifluoromethyl)pyrimidin-4-yl]-5-{[2-(4H-1,2,4-triazol-3-yl)phenyl]-carbonyl}octahydropyrrolo[3,4-c]pyrrole;

2-[6-Methyl-2-(trifluoromethyl)pyrimidin-4-yl]-5-{[2-(2H-1,2,3-triazol-2-yl)phenyl]-carbonyl}octahydropyrrolo[3,4-c]pyrrole;

2-{[2-Fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}-5-[6-methyl-2-(trifluoromethyl)pyrimidin-4-yl]octahydropyrrolo[3,4-c]pyrrole;

2-{[4-Fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}-5-[6-methyl-2-(trifluoromethyl)pyrimidin-4-yl]octahydropyrrolo[3,4-c]pyrrole;

2-(6-Methylpyrazin-2-yl)-5-{[5-methyl-2-(2H-1,2,3-triazol-2 yl)phenyl]carbonyl} octahydropyrrolo[3,4-c]pyrrole;

2-(3,6-Dimethylpyrazin-2-yl)-5-{[2-fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl]-carbonyl}octahydropyrrolo[3,4-c]pyrrole;

2-(4,6-Dimethylpyrimidin-2-yl)-5-[(5-methyl-2-pyrimidin-2-ylphenyl)carbonyl] octahydropyrrolo[3,4-c]pyrrole;

2-(3,6-Dimethylpyrazin-2-yl)-5-[(5-methyl-2-pyrimidin-2-ylphenyl)carbonyl] octahydropyrrolo[3,4-c]pyrrole;

2-(3,6-Dimethylpyrazin-2-yl)-5-{[4-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl]-carbonyl}octahydropyrrolo[3,4-c]pyrrole;

2-(4,6-Dimethylpyrimidin-2-yl)-5-{[5-iodo-2-(2H-1,2,3-triazol-2-yl)phenyl] carbonyl}octahydropyrrolo[3,4-c]pyrrole;

4-[5-{[2-Fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-N,N-dimethyl-6-(trifluoromethyl)pyrimidin-2-amine;

2-(4,6-Dimethylpyrimidin-2-yl)-5-{[2-fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl] carbonyl}octahydropyrrolo[3,4-c]pyrrole;

N,N-Dimethyl-4-{5-[(5-methyl-2-pyrimidin-2-ylphenyl)carbonyl]hexahydropyrrolo [3,4-c]pyrrol-2(1H)-yl}-6-(trifluoromethyl)pyrimidin-2-amine;

4-{5-[(5-Fluoro-2-pyrimidin-2-ylphenyl)carbonyl]hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl}-N,N-dimethyl-6-(trifluoromethyl)pyrimidin-2-amine;

4-[5-{[5-Fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-N,N-dimethyl-6-(trifluoromethyl)pyrimidin-2-amine;

4-[5-{[4-Fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-N,N-dimethyl-6-(trifluoromethyl)pyrimidin-2-amine;

2-[(5-Methyl-2-pyrimidin-2-ylphenyl)carbonyl]-5-[6-methyl-2-(trifluoromethyl) pyrimidin-4-yl]octahydropyrrolo[3,4-c]pyrrole;

2-[(5-Fluoro-2-pyrimidin-2-ylphenyl)carbonyl]-5-(4-phenylpyrimidin-2-yl)octahydropyrrolo[3,4-c]pyrrole;

2-{[5-Fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}-5-[6-methyl-2-(trifluoro-

methyl)pyrimidin-4-yl]octahydropyrrolo[3,4-c]pyrrole;

[5-(2,6-Dimethyl-pyrimidin-4-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-(5-fluoro-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

4-{5-[(2-Fluoro-6-pyrimidin-2-ylphenyl)carbonyl]hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl}-N,N-dimethyl-6-(trifluoromethyl)pyrimidin-2-amine

2-[(2-Fluoro-6-pyrimidin-2-ylphenyl)carbonyl]-5-[6-methyl-2-(trifluoromethyl) pyrimidin-4-yl]octahydropyrrolo[3,4-c]pyrrole;

2-(4,6-Dimethylpyrimidin-2-yl)-5-{[4-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl] carbonyl}octahydropyrrolo[3,4-c]pyrrole;

N,N,6-Trimethyl-2-[5-{[2-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}hexahydro pyrrolo[3,4-c]pyrrol-2(1H)-yl]pyrimidin-4-amine;

N,N,4-Trimethyl-6-[5-{[2-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}hexahydro pyrrolo[3,4-c]pyrrol-2(1H)-yl]pyrimidin-2-amine;

N,N-Dimethyl-4-[5-{[2-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}hexahydropyrrolo [3,4-c]pyrrol-2(1H)-yl]-6-(trifluoromethyl)pyrimidin-2-amine;

2-(2,6-Dimethylpyrimidin-4-yl)-5-{[2-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl} octahydropyrrolo[3,4-c]pyrrole;

[5-(3,6-Dimethyl-pyrazin-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-(5-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

2-[5-{[5-Fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-N,N,6-trimethylpyrimidin-4-amine;

2-(5-Methoxypyridin-2-yl)-5-[(2-thiophen-2-ylphenyl)carbonyl]octahydropyrrolo [3,4-c]pyrrole;

2-[(2-Ethoxynaphthalen-1-yl)carbonyl]-5-(4-phenylpyrimidin-2-yl)octahydro pyrrolo[3,4-c]pyrrole;

2-{[5-Methyl-2-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}-5-(4-phenylpyrimidin-2-yl)octahydropyrrolo[3,4-c]pyrrole;

(4-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[5-(4,6-dimethyl-pyrimidin-2-yl)-hexahydropyrrolo[3,4-c]pyrrol-2-yl]-methanone;

2-(4,6-Dimethoxypyrimidin-2-yl)-5-{[5-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl] carbonyl}octahydropyrrolo[3,4-c]pyrrole;

2-(4,6-Dimethylpyrimidin-2-yl)-5-{[5-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl] carbonyl}octahydropyrrolo[3,4-c]pyrrole;

2-(4-Phenylpyrimidin-2-yl)-5-{[2-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}octahydro pyrrolo[3,4-c]pyrrole;

2-(4,6-Dimethylpyrimidin-2-yl)-5-{[5-(2-fluorophenyl)-2-methyl-1,3-thiazol-4-yl]carbonyl}octahydropyrrolo[3,4-c]pyrrole;

2-[(2-Thiophen-2-ylphenyl)carbonyl]-5-[6-(trifluoromethyl)pyridin-2-yl]octahydro pyrrolo[3,4-c]pyrrole;

2-(6-Methylpyridin-2-yl)-5-[(2-thiophen-2-ylphenyl)carbonyl]octahydropyrrolo-[3,4-c]pyrrole;

2-(4-Methylpyrimidin-2-yl)-5-{[2-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}octahydropyrrolo[3,4-c]pyrrole;

2-(4-Methylpyridin-2-yl)-5-[(2-thiophen-2-ylphenyl)carbonyl]octahydropyrrolo-[3,4-c]pyrrole;

2-(6-Methoxypyridin-2-yl)-5-[(2-thiophen-2-ylphenyl)carbonyl]octahydropyrrolo-[3,4-c]pyrrole;

2-(4,6-Dimethoxypyrimidin-2-yl)-5-[(2-thiophen-2-ylphenyl)carbonyl]octahydro pyrrolo[3,4-c]pyrrole;

2-{5-[(2-Thiophen-2-ylphenyl)carbonyl]hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl}-1,3-benzoxazole;

2-[(2-Thiophen-2-ylphenyl)carbonyl]-5-[3-(trifluoromethyl)pyridin-2-yl]octahydro pyrrolo[3,4-c]pyrrole;

[5-(4-Phenyl-pyrimidin-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-[2-(4H-[1,2,4]-triazol-3-yl)-phenyl]-methanone;

2-(4,6-Dimethoxypyrimidin-2-yl)-5-{[5-(2-fluorophenyl)-2-methyl-1,3-thiazol-4-yl]carbonyl}octahydropyrrolo[3,4-c]pyrrole;

2-(4-Thiophen-2-ylpyrimidin-2-yl)-5-{[2-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl} octahydropyrrolo[3,4-c]pyrrole;

2-[5-{[2-(2H-1,2,3-Triazol-2-yl)phenyl]carbonyl}hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-1,3-benzoxazole;

2-{5-[(2-Ethoxynaphthalen-1-yl)carbonyl]hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl}quinoxaline;

2-{5-[(5-Fluoro-2-pyrimidin-2-ylphenyl)carbonyl]hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl}quinoxaline;

2-(6-Ethoxypyridin-2-yl)-5-{[2-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}octahydro

pyrrolo[3,4-c]pyrrole;
2-[(5-Fluoro-2-pyrimidin-2-ylphenyl)carbonyl]-5-[4-(trifluoromethyl)pyrimidin-2-yl]octahydropyrrolo[3,4-c]pyrrole;
2-[5-{[2-(2H-1,2,3-Triazol-2-yl)phenyl]carbonyl}hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]quinoxaline
2-[(5-Fluoro-2-pyrimidin-2-ylphenyl)carbonyl]-5-(4-methoxypyrimidin-2-yl)octahydropyrrolo[3,4-c]pyrrole;
2-(4-Furan-2-ylpyrimidin-2-yl)-5-{[2-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}octahydropyrrolo[3,4-c]pyrrole;
2-(5-Fluoropyridin-2-yl)-5-{[2-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}octahydro pyrrolo[3,4-c]pyrrole;
2-{[2-(2H-1,2,3-Triazol-2-yl)phenyl]carbonyl}-5-[4-(trifluoromethyl)pyrimidin-2-yl]octahydropyrrolo[3,4-c]pyrrole;
2-(4-Methoxypyrimidin-2-yl)-5-{[2-(1H-1,2,4-triazol-5-yl)phenyl]carbonyl} octahydropyrrolo[3,4-c]pyrrole;
2-(3,6-Dimethylpyrazin-2-yl)-5-{[2-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}octa hydropyrrolo[3,4-c]pyrrole;
2-(4-Methoxypyrimidin-2-yl)-5-{[2-(2H-1, 2,3-triazol-2-yl)phenyl]carbonyl}octahydropyrrolo[3,4-c]pyrrole;
2-{[5-Chloro-2-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}-5-(4,6-dimethylpyrimidin-2-yl)octahydropyrrolo[3,4-c]pyrrole;
2-{[4-Fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}-5-(6-methylpyrazin-2-yl)-octahydropyrrolo[3,4-c]pyrrole;
2-{[4-Fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}-5-(4-methoxypyrimidin-2-yl)octahydropyrrolo[3,4-c]pyrrole;
2-(4,6-Dimethoxypyrimidin-2-yl)-5-{[4-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl] carbonyl}octahydropyrrolo[3,4-c]pyrrole;
[5-(4,6-Dimethyl-pyrimidin-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-(5-methoxy-2-[1,2,3]triazol-2-yl-phenyl)-methanone;
(2-Fluoro-6-[1,2,3]triazol-2-yl-phenyl)-[5-(4-methoxy-pyrimidin-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-methanone;
6-Chloro-2-{5-[(2,4-dimethoxyphenyl)carbonyl]hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl}-1,3-benzothiazole;

2-(Biphenyl-2-ylcarbonyl)-5-(4-phenylpyrimidin-2-yl)octahydropyrrolo[3,4-c]-pyrrole;

2-{5-[(2,6-Dimethoxyphenyl)carbonyl]hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl}quinoxaline;

2-[(2,6-Dimethoxyphenyl)carbonyl]-5-(4-phenylpyrimidin-2-yl)octahydropyrrolo[3,4-c]pyrrole;

2-[(2,4-Dimethoxyphenyl)carbonyl]-5-(4-phenylpyrimidin-2-yl)octahydropyrrolo[3,4-c]pyrrole;

2-[5-(Biphenyl-2-ylcarbonyl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]quinoxaline;

2-[5-(Biphenyl-2-ylcarbonyl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-1,3-benzothiazole;

2-{5-[(2,4-Dimethoxyphenyl)carbonyl]hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl}-4-methylquinoline;

2-{5-[(2,4-Dimethoxyphenyl)carbonyl]hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl}-6-methoxy-1,3-benzothiazole;

2-{5-[(2,4-Dimethoxyphenyl)carbonyl]hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl}-6-methyl-1,3-benzothiazole;

2-(Biphenyl-2-ylcarbonyl)-5-(6-methylpyridin-2-yl)octahydropyrrolo[3,4-c]-pyrrole;

2-(Biphenyl-2-ylcarbonyl)-5-(4-methylpyrimidin-2-yl)octahydropyrrolo[3,4-c]-pyrrole;

2-[5-(Biphenyl-2-ylcarbonyl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]quinoline;

2-[5-(Biphenyl-2-ylcarbonyl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-6-fluoro-1,3-benzothiazole;

2-(Biphenyl-2-ylcarbonyl)-5-(4-methoxypyrimidin-2-yl)octahydropyrrolo[3,4-c]-pyrrole;

2-[5-(Biphenyl-2-ylcarbonyl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-4-methyl-quinoline;

(2,4-Dimethoxy-phenyl)-[5-(4-methoxy-pyrimidin-2-yl)-hexahydro-pyrrolo[3,4-c]-pyrrol-2-yl]-methanone;

(5-Benzooxazol-2-yl-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl)-(2-methoxy-phenyl)-methanone;

(2-Pyridin-3-yl-phenyl)-(5-quinoxalin-2-yl-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl)-

methanone;
[5-(4,6-Dimethyl-pyrimidin-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-[2-(1H-imidazol-2-yl)-phenyl]-methanone;
(5-Benzooxazol-2-yl-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl)-(2,4-dimethoxy-phenyl)-methanone;
(5-Benzooxazol-2-yl-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl)-biphenyl-2-yl-methanone;
(2,4-Dimethoxy-phenyl)-[5-(6-methyl-pyridin-2-yl)-hexahydro-pyrrolo[3,4-c]-pyrrol-2-yl]-methanone;
(2,4-Dimethoxy-phenyl)-[5-(4-methyl-pyrimidin-2-yl)-hexahydro-pyrrolo[3,4-c]-pyrrol-2-yl]-methanone;
Biphenyl-2-yl-[5-(6-methoxy-benzothiazol-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-methanone;
Biphenyl-2-yl-[5-(6-methyl-benzothiazol-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-methanone;
[5-(6-Chloro-benzothiazol-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-(2,6-dimethoxy-phenyl)-methanone;
Biphenyl-2-yl-[5-(6-chloro-benzothiazol-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-methanone;
(2,4-Dimethoxy-phenyl)-(5-quinoxalin-2-yl-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl)-methanone;
(5-Benzooxazol-2-yl-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl)-(2,6-dimethoxy-phenyl)-methanone;
(4'-Methyl-biphenyl-2-yl)-(5-quinoxalin-2-yl-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl)-methanone;
(5-Quinoxalin-2-yl-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl)-(4'-trifluoromethyl-biphenyl-2-yl)-methanone;
(4'-Methyl-biphenyl-2-yl)-[5-(4-phenyl-pyrimidin-2-yl)-hexahydro-pyrrolo[3,4-c]-pyrrol-2-yl]-methanone;
[5-(4-Phenyl-pyrimidin-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-(4'-trifluoro-methyl-biphenyl-2-yl)-methanone;
(4-Methoxy-2-methyl-phenyl)-(5-quinoxalin-2-yl-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl)-methanone;

(3'-Chloro-biphenyl-2-yl)-[5-(4-phenyl-pyrimidin-2-yl)-hexahydro-pyrrolo[3,4-c]-pyrrol-2-yl]-methanone;
(2-Methoxy-phenyl)-[5-(4-methoxy-pyrimidin-2-yl)-hexahydro-pyrrolo[3,4-c]-pyrrol-2-yl]-methanone;
(2-Methoxy-phenyl)-[5-(4-methyl-pyrimidin-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-methanone;
[5-(4,6-Dimethyl-pyrimidin-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-(2-methoxy-phenyl)-methanone;
2-[5-(4,6-Dimethyl-pyrimidin-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrole;-2-carbonyl]-benzonitrile;
Cinnolin-4-yl-[5-(4,6-dimethyl-pyrimidin-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-methanone;
(5-Fluoro-2-pyrimidin-2-yl-phenyl)-[5-(6-methyl-2-trifluoromethyl-pyrimidin-4-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-methanone;
[5-(4,6-Dimethyl-pyrimidin-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-(2-[1,2,3]-triazol-1-yl-phenyl)-methanone;
[5-(4,6-Dimethyl-pyrimidin-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-(2-[1,2,4]-triazol-1-yl-phenyl)-methanone;
[5-(4,6-Dimethoxy-pyrimidin-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-(3-phenyl-pyridin-2-yl)-methanone;
[5-(4,6-Dimethyl-pyrimidin-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-(3-phenyl-pyridin-2-yl)-methanone;
[5-(6-Methyl-2-propyl-pyrimidin-4-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone;
[5-(2-Methyl-pyrimidin-4-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone;
[5-(6-Methyl-pyrazin-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone;
[5-(3,6-Dimethyl-pyrazin-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-(5-fluoro-2-pyrimidin-2-yl-phenyl)-methanone;
[5-(3,6-Dimethyl-pyrazin-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-[2-(2H-[1,2,4]triazol-3-yl)-phenyl]-methanone;
[5-(2-Pyrrolidin-1-yl-6-trifluoromethyl-pyrimidin-4-yl)-hexahydro-pyrrolo[3,4-c]-

pyrrol-2-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone;
2-(2,6-Dimethylpyrimidin-4-yl)-5-{[5-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl]-carbonyl}octahydropyrrolo[3,4-c]pyrrole;
[5-(4,6-Dimethyl-pyrimidin-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-(2-nitro-6-[1,2,3]triazol-2-yl-phenyl)-methanone;
[5-(4,6-Dimethyl-pyrimidin-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-(2-furan-2-yl-phenyl)-methanone;
[5-(4,6-Dimethyl-pyrimidin-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-(2-methyl-5-phenyl-thiazol-4-yl)-methanone;
2-[(2,3-Dimethylphenyl)carbonyl]-5-(4,6-dimethylpyrimidin-2-yl)octahydro-pyrrolo[3,4-c]pyrrole;
2-(4,6-Dimethylpyrimidin-2-yl)-5-[(3-fluoro-2-methylphenyl)carbonyl]octahydro-pyrrolo[3,4-c]pyrrole;
2-(4,6-Dimethylpyrimidin-2-yl)-5-{[5-fluoro-2-(trifluoromethyl)phenyl]carbonyl}-octahydropyrrolo[3,4-c]pyrrole;
2-[(4-Chloro-2-methoxyphenyl)carbonyl]-5-(4,6-dimethylpyrimidin-2-yl)octa-hydropyrrolo[3,4-c]pyrrole;
2-[(5-Chloro-2-methylphenyl)carbonyl]-5-(4,6-dimethylpyrimidin-2-yl)octahydro-pyrrolo[3,4-c]pyrrole;
2-[(2,5-Dimethylphenyl)carbonyl]-5-(4,6-dimethylpyrimidin-2-yl)octahydro-pyrrolo[3,4-c]pyrrole;
2-[(2,6-Dimethylphenyl)carbonyl]-5-(4,6-dimethylpyrimidin-2-yl)octahydro-pyrrolo[3,4-c]pyrrole;
2-(4,6-Dimethylpyrimidin-2-yl)-5-[(5-fluoro-2-methylphenyl)carbonyl]octahydro-pyrrolo[3,4-c]pyrrole;
2-[(2,4-Dimethylphenyl)carbonyl]-5-(4,6-dimethylpyrimidin-2-yl)octahydro-pyrrolo[3,4-c]pyrrole;
2-[(2,5-Diethoxyphenyl)carbonyl]-5-(4,6-dimethylpyrimidin-2-yl)octahydro-pyrrolo[3,4-c]pyrrole;
2-[(2,6-Diethoxyphenyl)carbonyl]-5-(4,6-dimethylpyrimidin-2-yl)octahydro-pyrrolo-[3,4-c]pyrrole;
2-[(2-Chloro-6-methylphenyl)carbonyl]-5-(4,6-dimethylpyrimidin-2-yl)octahydro-pyrrolo[3,4-c]pyrrole;

(5-(4,6-Dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(4-fluoro-2-(pyrimidin-2-yl)phenyl)methanone;

(5-(4,6-dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(3-fluoro-2-iodophenyl)methanone;

2-(4,6-Dimethylpyrimidin-2-yl)-5-{[2-(trifluoromethyl)pyridin-3-yl]carbonyl}octahydropyrrolo[3,4-c]pyrrole;

2-Bromopyridin-3-yl)(5-(4,6-dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]-pyrrol-2(1H)-yl)methanone;

(5-(4,6-Dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(2-(pyrimidin-2-yl)pyridin-3-yl)methanone;

(5-(4,6-Dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(2-(1-(tetrahydro-2H-pyran-2-yl)-1H-pyrazol-5-yl)pyridin-3-yl)methanone;

(2-(1H-Pyrazol-5-yl)pyridin-3-yl)(5-(4,6-dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)methanone;

(2-(2H-1,2,3-Triazol-2-yl)pyridin-3-yl)(5-(4,6-dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)methanone;

(3-Fluoro-2-(pyrimidin-2-yl)phenyl)(5-(4,5,6-trimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)methanone;

(3-Fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)(5-(4,5,6-trimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)methanone;

(5-Methoxy-2-(2H-1,2,3-triazol-2-yl)phenyl)(5-(4,5,6-trimethylpyrimidin-2-yl)-hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)methanone;

(3-Fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)(5-(6-fluoroquinazolin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)methanone;

(3-Fluoro-2-(pyrimidin-2-yl)phenyl)(5-(6-fluoroquinazolin-2-yl)hexahydropyrrolo-[3,4-c]pyrrol-2(1H)-yl)methanone;

(5-(6,7-Difluoroquinoxalin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(3-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone;

(5-(6,7-Difluoroquinoxalin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(5-methoxy-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone;

(5-(6,7-Difluoroquinoxalin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(2-fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl)methanone;

(2-Bromo-3-fluorophenyl)(5-(6-fluoroquinazolin-2-yl)hexahydropyrrolo[3,4-c]-

pyrrol-2(1H)-yl)methanone;
(5-(4,6-dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(4-fluoro-2-(5-methylpyridin-2-yl)phenyl)methanone;
(2-Bromopyridin-3-yl)(5-(4,5,6-trimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]-pyrrol-2(1H)-yl)methanone;
(2-(1-(Tetrahydro-2H-pyran-2-yl)-1H-pyrazol-5-yl)pyridin-3-yl)(5-(4,5,6-trimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)methanone;
(2-(1H-Pyrazol-5-yl)pyridin-3-yl)(5-(4,5,6-trimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)methanone;
6-[5-{[2-Fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-2-methylpyrimidin-4(3H)-one;
2-(2,6-Dimethylpyrimidin-4-yl)-5-{[5-(4-fluorophenyl)-2-methyl-1,3-thiazol-4-yl]-carbonyl}octahydropyrrolo[3,4-c]pyrrole;
2-(4,6-Dimethylpyrimidin-2-yl)-5-{[5-(4-fluorophenyl)-2-methyl-1,3-thiazol-4-yl]-carbonyl}octahydropyrrolo[3,4-c]pyrrole;
6-[5-{[5-(4-Fluorophenyl)-2-methyl-1,3-thiazol-4-yl]carbonyl}hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-2-methylpyrimidin-4(3H)-one;
6-{5-[(5-Fluoro-2-pyrimidin-2-ylphenyl)carbonyl]hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl}-2-methylpyrimidin-4(3H)-one;
(5-(4,6-Dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(4-fluoro-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone;
(5-(4,6-Dimethoxypyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(2-fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl)methanone;
(5-(4,6-Dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(2-methyl-6-(2H-1,2,3-triazol-2-yl)phenyl)methanone;
(5-(4,6-Dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(3-methyl-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone;
(2-Fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl)(5-(5-nitropyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)methanone;
Methyl 2-(5-(2-fluoro-6-(2H-1,2,3-triazol-2-yl)benzoyl)hexahydropyrrolo[3,4-c]-pyrrol-2(1H)-yl)-4-(trifluoromethyl)pyrimidine-5-carboxylate;
2-(5-(2-Fluoro-6-(2H-1,2,3-triazol-2-yl)benzoyl)hexahydropyrrolo[3,4-c]pyrrol-

2(1H)-yl)-4-(trifluoromethyl)pyrimidine-5-carboxylic acid;
(2-(4H-1,2,4-Triazol-4-yl)phenyl)(5-(4,6-dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)methanone;
2-(5-(2-Fluoro-6-(2H-1,2,3-triazol-2-yl)benzoyl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)-6-methylpyrimidine-4-carboxylic acid;
(4,5-Difluoro-2-(4H-1,2,4-triazol-4-yl)phenyl)(5-(4,6-dimethylpyrimidin-2-yl)-hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)methanone;
(5-(4,6-Dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(3-methyl-2-(1H-1,2,3-triazol-1-yl)phenyl)methanone;
2-(5-(2-Fluoro-6-(2H-1,2,3-triazol-2-yl)benzoyl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)-N,N,6-trimethylpyrimidine-4-carboxamide;
2-(5-(2-Fluoro-6-(2H-1,2,3-triazol-2-yl)benzoyl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)-N,N-dimethyl-4-(trifluoromethyl)pyrimidine-5-carboxamide;
(5-(4,6-Dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(mesityl)-methanone;
(2,3-Difluorophenyl)(5-(4,6-dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]-pyrrol-2(1H)-yl)methanone;
(5-(4,6-Dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(4-methoxy-2-(pyrimidin-2-yl)phenyl)methanone;
(2,3-Dimethoxyphenyl)(5-(4,6-dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]-pyrrol-2(1H)-yl)methanone;
(5-(4,6-Dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(2-(trifluoromethoxy)phenyl)methanone;
[5-(4,6-Dimethyl-pyrimidin-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-(6-methyl-2-[1,2,3]triazol-2-yl-pyridin-3-yl)-methanone;
(5-(4,6-Dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(2-methoxy-4-methylphenyl)methanone;
(5-(4,6-Dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(4-methoxy-2-methylphenyl)methanone;
(2,6-Difluorophenyl)(5-(4,6-dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]-pyrrol-2(1H)-yl)methanone;
2-[5-{[2-Fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-6-methylpyrimidine-4-carbonitrile;

2-[4,6-Bis(trifluoromethyl)pyrimidin-2-yl]-5-{[2-fluoro-6-(2H-1,2,3-triazol-2-yl)-phenyl]carbonyl}octahydropyrrolo[3,4-c]pyrrole;

2-[5-{[2-Fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-6-methylpyrimidin-4-ol;

(2-Fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl)(5-(4-(furan-2-yl)-6-methylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)methanone;

2-(4,6-Dimethylpyrimidin-2-yl)-5-[(3-fluoro-2-pyrimidin-2-ylphenyl)carbonyl]-octahydropyrrolo[3,4-c]pyrrole;

2-(4,6-Dimethylpyrimidin-2-yl)-5-{[3-fluoro-2-(1H-pyrazol-5-yl)phenyl]carbonyl}-octahydropyrrolo[3,4-c]pyrrole;

2-(4,6-Dimethylpyrimidin-2-yl)-5-{[3-methoxy-2-(2H-1,2,3-triazol-2-yl)phenyl]-carbonyl}octahydropyrrolo[3,4-c]pyrrole;

2-(4,6-Dimethylpyrimidin-2-yl)-5-{[3-methoxy-2-(1H-1,2,3-triazol-1-yl)phenyl]-carbonyl}octahydropyrrolo[3,4-c]pyrrole;

2-(4,6-Dimethylpyrimidin-2-yl)-5-{[3-fluoro-2-(1H-1,2,3-triazol-1-yl)phenyl]-carbonyl}octahydropyrrolo[3,4-c]pyrrole;

2-(4,6-Dimethylpyrimidin-2-yl)-5-{[4-methoxy-2-(2H-1,2,3-triazol-2-yl)phenyl]-carbonyl}octahydropyrrolo[3,4-c]pyrrole;

2-(4,6-Dimethylpyrimidin-2-yl)-5-{[4-methoxy-2-(1H-1,2,3-triazol-2-yl)phenyl]-carbonyl}octahydropyrrolo[3,4-c]pyrrole;

2-(5-Fluoro-4-methylpyrimidin-2-yl)-5-{[2-(2H-1,2,3-triazol-2-yl)phenyl]-carbonyl}octahydropyrrolo[3,4-c]pyrrole;

2-(2-Chloro-5-fluoropyrimidin-4-yl)-5-{[2-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}-octahydropyrrolo[3,4-c]pyrrole;

2-(5-Fluoropyrimidin-2-yl)-5-{[2-fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}-octahydropyrrolo[3,4-c]pyrrole;

2-(5-Fluoro-4-methylpyrimidin-2-yl)-5-{[2-fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl]-carbonyl}octahydropyrrolo[3,4-c]pyrrole;

2-{[2-Fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}-5-(4,5,6-trimethyl-pyrimidin-2-yl)octahydropyrrolo[3,4-c]pyrrole;

2-(4,5-Dimethylpyrimidin-2-yl)-5-{[2-fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl]-carbonyl}octahydropyrrolo[3,4-c]pyrrole;

2-{[2-Fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}-5-(4-methoxy-6-methyl-

pyrimidin-2-yl)octahydropyrrolo[3,4-c]pyrrole;
2-(4-Ethyl-6-methylpyrimidin-2-yl)-5-{[2-fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl]-carbonyl}octahydropyrrolo[3,4-c]pyrrole;
2-{[2-Fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}-5-[4-methyl-6-(1-methyl-ethyl)pyrimidin-2-yl]octahydropyrrolo[3,4-c]pyrrole;
2-[4-Methyl-6-(1-methylethyl)pyrimidin-2-yl]-5-{[2-(2H-1,2,3-triazol-2-yl)phenyl]-carbonyl}octahydropyrrolo[3,4-c]pyrrole;
2-{[5-(1-Methylethyl)-2-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}-5-[4-methyl-6-(1-methylethyl)pyrimidin-2-yl]octahydropyrrolo[3,4-c]pyrrole;
2-(4-tert-Butyl-6-methylpyrimidin-2-yl)-5-{[2-fluoro-6-(2H-1,2,3-triazol-2-yl)-phenyl]carbonyl}octahydropyrrolo[3,4-c]pyrrole;
2-(4-Cyclopropyl-6-methylpyrimidin-2-yl)-5-{[2-fluoro-6-(2H-1,2,3-triazol-2-yl)-[phenyl]carbonyl}octahydropyrrolo[3,4-c]pyrrole;
2-{[2-Fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}-5-(4-methyl-1,3,5-triazin-2-yl)octahydropyrrolo[3,4-c]pyrrole;
2-{[2-Fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}-5-(4-methyl-6-morpholin-4-ylpyrimidin-2-yl)octahydropyrrolo[3,4-c]pyrrole;
2-{[2-(4H-1,2,4-Triazol-3-yl)phenyl]carbonyl}-5-(4,5,6-trimethylpyrimidin-2-yl)-octahydropyrrolo[3,4-c]pyrrole;
2-(4,6-Dimethylpyrimidin-2-yl)-5-{[2-(3-methyl-1,2,4-oxadiazol-5-yl)phenyl]-carbonyl}octahydropyrrolo[3,4-c]pyrrole;
2-(4,6-Dimethylpyrimidin-2-yl)-5-{[2-(1-methyl-1H-1,2,4-triazol-5-yl)phenyl]-carbonyl}octahydropyrrolo[3,4-c]pyrrole;
2-(4,6-Dimethylpyrimidin-2-yl)-5-{[2-(1-methyl-1H-1,2,4-triazol-3-yl)phenyl]-carbonyl}octahydropyrrolo[3,4-c]pyrrole;
2-{[2-(3-Methyl-1,2,4-oxadiazol-5-yl)phenyl]carbonyl}-5-(4,5,6-trimethyl-pyrimidin-2-yl)octahydropyrrolo[3,4-c]pyrrole;
2-(5-Fluoro-4-methylpyrimidin-2-yl)-5-{[2-(3-methyl-1,2,4-oxadiazol-5-yl)-phenyl]carbonyl}octahydropyrrolo[3,4-c]pyrrole;
2-{[2-(1-Methyl-1H-1,2,4-triazol-3-yl)phenyl]carbonyl}-5-(4,5,6-trimethyl-pyrimidin-2-yl)octahydropyrrolo[3,4-c]pyrrole;
2-(5-Fluoro-4-methylpyrimidin-2-yl)-5-{[2-(1-methyl-1H-1,2,4-triazol-3-yl)-phenyl]carbonyl}octahydropyrrolo[3,4-c]pyrrole;

2-[5-{[2-Fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}hexahydropyrrolo[3,4c]-pyrrol-2(1H)-yl]-4-methyl-6,7-dihydro-5H-cyclopenta[d]pyrimidine;

2-(4,6-Dimethylpyrimidin-2-yl)-5-{[3-fluoro-2-(3-methyl-1,2,4-oxadiazol-5-yl)-phenyl]carbonyl}octahydropyrrolo[3,4-c]pyrrole;

2-(4,6-Dimethylpyrimidin-2-yl)-5-{[2-fluoro-6-(3-methyl-1,2,4-oxadiazol-5-yl)-phenyl]carbonyl}octahydropyrrolo[3,4-c]pyrrole;

2-(5-Chloro-4-methylpyrimidin-2-yl)-5-{[2-fluoro-6-(2H-1,2,3-triazol-2-yl)-phenyl]carbonyl}octahydropyrrolo[3,4-c]pyrrole;

2-(5-Chloro-4,6-dimethylpyrimidin-2-yl)-5-{[2-fluoro-6-(2H-1,2,3-triazol-2-yl)-phenyl]carbonyl}octahydropyrrolo[3,4-c]pyrrole;

2-(5-Chloro-4,6-dimethylpyrimidin-2-yl)-5-{[2-(3-methyl-1,2,4-oxadiazol-5-yl)-phenyl]carbonyl}octahydropyrrolo[3,4-c]pyrrole;

4-Methyl-2-[5-{[2-(3-methyl-1,2,4-oxadiazol-5-yl)phenyl]carbonyl}hexahydro-pyrrolo[3,4-c]pyrrol-2(1H)-yl]-6,7-dihydro-5H-cyclopenta[d]pyrimidine;

2-(5-Chloro-4,6-dimethylpyrimidin-2-yl)-5-{[2-(1-methyl-1H-1,2,4-triazol-3-yl)-phenyl]carbonyl}octahydropyrrolo[3,4-c]pyrrole;

2-(5-Chloro-4-methylpyrimidin-2-yl)-5-{[2-(1-methyl-1H-1,2,4-triazol-3-yl)-phenyl]carbonyl}octahydropyrrolo[3,4-c]pyrrole;

2-(5-Ethyl-4,6-dimethylpyrimidin-2-yl)-5-{[2-(1-methyl-1H-1,2,4-triazol-3-yl)-phenyl]carbonyl}octahydropyrrolo[3,4-c]pyrrole;

2-{[3-(2H-1,2,3-Triazol-2-yl)pyridin-2-yl]carbonyl}-5-(4,5,6-trimethylpyrimidin-2-yl)octahydropyrrolo[3,4-c]pyrrole;

2-(5-Chloro-4,6-dimethylpyrimidin-2-yl)-5-{[3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl]-carbonyl}octahydropyrrolo[3,4-c]pyrrole;

2-(5-Fluoro-4,6-dimethylpyrimidin-2-yl)-5-{[3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl]-carbonyl}octahydropyrrolo[3,4-c]pyrrole;

2-(4,6-Dimethylpyrimidin-2-yl)-5-(9H-fluoren-4-ylcarbonyl)octahydropyrrolo[3,4-c]pyrrole;

[5-(4,6-Dimethyl-pyrimidin-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-(5-[1,2,3]-triazol-2-yl-benzo[1,3]dioxol-4-yl)-methanone;

[5-(4,6-Dimethyl-pyrimidin-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-(8-[1,2,3]-triazol-2-yl-naphthalen-1-yl)-methanone;

[5-(4,6-Dimethyl-pyrimidin-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-(4-[1,2,3]-

triazol-1-yl-pyridin-3-yl)-methanone;
(5-tert-Butyl-2-methoxy-phenyl)-[5-(4,6-dimethyl-pyrimidin-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-methanone;
[5-(4,6-Dimethyl-pyrimidin-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-(1-[1,2,3]-triazol-2-yl-naphthalen-2-yl)-methanone;
[5-(4,6-Dimethyl-pyrimidin-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-(3-[1,2,3]-triazol-2-yl-pyridin-2-yl)-methanone;
(2-Bromo-4,5-dimethoxy-phenyl)-[5-(4,6-dimethyl-pyrimidin-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-methanone;
(3,4-Dihydro-2H-benzo[b][1,4]dioxepin-6-yl)-[5-(4,6-dimethyl-pyrimidin-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-methanone;
(5-(4,6-Dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(4-fluoro-2-(6-methylpyridin-2-yl)phenyl)methanone;
[5-(4,6-Dimethyl-pyrimidin-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-(6-methyl-2-[1,2,3]triazol-1-yl-pyridin-3-yl)-methanone;
(1-Bromo-naphthalen-2-yl)-[5-(4,6-dimethyl-pyrimidin-2-yl)-hexahydro-pyrrolo-[3,4-c]pyrrol-2-yl]-methanone;
[5-(4,6-Dimethyl-pyrimidin-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-(3-methoxy-naphthalen-2-yl)-methanone;
[5-(4,6-Dimethyl-pyrimidin-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-(8-[1,2,3]-triazol-2-yl-naphthalen-1-yl)-methanone;
[5-(4,6-Dimethyl-pyrimidin-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-(1-methoxy-naphthalen-2-yl)-methanone;
(4,5-Dimethoxy-2-[1,2,3]triazol-1-yl-phenyl)-[5-(4,6-dimethyl-pyrimidin-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-methanone;
(4,5-Dimethoxy-2-[1,2,3]triazol-2-yl-phenyl)-[5-(4,6-dimethyl-pyrimidin-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-methanone;
(5-(4,6-Dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(4-fluoro-2-(4-methylpyridin-2-yl)phenyl)methanone;
(5-(4,6-Dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(3-propoxypyridin-2-yl)methanone;
(3-Propoxypyridin-2-yl)(5-(5-(trifluoromethyl)pyrimidin-2-yl)hexahydropyrrolo-[3,4-c]pyrrol-2(1H)-yl)methanone;

(5-(4,6-Dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(4-fluoro-2-(3-fluoropyridin-2-yl)phenyl)methanone;

(3-Propoxypyridin-2-yl)(5-(quinoxalin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)methanone;

2-[(2,6-Dimethoxyphenyl)carbonyl]-5-[5-(trifluoromethyl)pyridin-2-yl]octahydropyrrolo[3,4-c]pyrrole;

(2,6-Dimethoxyphenyl)(5-(5-(trifluoromethyl)pyrimidin-2-yl)hexahydropyrrolo-[3,4-c]pyrrol-2(1H)-yl)methanone;

(2,6-Dimethoxyphenyl)(5-(4,6-dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4c]-pyrrol-2(1H)-yl)methanone;

(5-(4,6-Dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(3-methylfuran-2-yl)methanone;

2-[(3-Methylfuran-2-yl)carbonyl]-5-[5-(trifluoromethyl)pyridin-2-yl]octahydropyrrolo[3,4-c]pyrrole;

(3-Methylfuran-2-yl)(5-(5-(trifluoromethyl)pyrimidin-2-yl)hexahydropyrrolo[3,4c]-pyrrol-2(1H)-yl)methanone;

(3-Methylfuran-2-yl)(5-(quinoxalin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)methanone;

(3,6'-Dimethyl-[2,3'-bipyridin]-2'-yl)(5-(quinoxalin-2-yl)hexahydropyrrolo[3,4-c]-pyrrol-2(1H)-yl)methanone;

(3,6'-Dimethyl-[2,3'-bipyridin]-2'-yl)(5-(5-(trifluoromethyl)pyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)methanone;

(3,6'-Dimethyl-[2,3'-bipyridin]-2'-yl)(5-(5-(trifluoromethyl)pyridin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)methanone;

(5-(4,6-Dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(4-fluoro-2-(pyridin-2-yl)phenyl)methanone;

(5-(4,6-Dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(3-fluoro-2-(pyridin-2-yl)phenyl)methanone;

[2,3'-Bipyridin]-2'-yl(5-(4,6-dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)methanone;

(5-(4,6-Dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(4-fluoro-2-(oxazol-2-yl)phenyl)methanone;

(5-(4,6-Dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(3-fluoro-

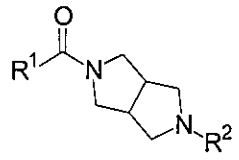
2-(6-methylpyridin-2-yl)phenyl)methanone;
(5-(4,6-Dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(3-fluoro-2-(3-methylpyridin-2-yl)phenyl)methanone;
(2-(3-Chloropyridin-2-yl)-3-fluorophenyl)(5-(4,6-dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)methanone;
(5-(4,6-Dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(3-fluoro-2-(4-methylpyridin-2-yl)phenyl)methanone;
(5-(4,6-Dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(3-fluoro-2-(5-methylpyridin-2-yl)phenyl)methanone;
(5-(4,6-Dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(3-fluoro-2-(3-fluoropyridin-2-yl)phenyl)methanone;
(5-(4,6-Dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(3-fluoro-2-(oxazol-2-yl)phenyl)methanone;
2-(5-Fluoro-4-methylpyrimidin-2-yl)-5-{[4-methoxy-2-(2H-1,2,3-triazol-2-yl)-phenyl]carbonyl}octahydropyrrolo[3,4-c]pyrrole;
2-(5-Chloro-4-methylpyrimidin-2-yl)-5-{[4-methoxy-2-(2H-1,2,3-triazol-2-yl)-phenyl]carbonyl}octahydropyrrolo[3,4-c]pyrrole;
2-(5-Fluoro-4,6-dimethylpyrimidin-2-yl)-5-{[4-methoxy-2-(2H-1,2,3-triazol-2-yl)-phenyl]carbonyl}octahydropyrrolo[3,4-c]pyrrole;
2-(4,5-Dimethylpyrimidin-2-yl)-5-{[4-methoxy-2-(2H-1,2,3-triazol-2-yl)phenyl]-carbonyl}octahydropyrrolo[3,4-c]pyrrole;
2-[(3-Propoxypyridin-2-yl)carbonyl]-5-[5-(trifluoromethyl)pyridin-2-yl]octahydro-pyrrolo[3,4-c]pyrrole;
2-{4,6-Bis[(2H3)methyl](2H)pyrimidin-2-yl}-5-{[2-fluoro-6-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}octahydropyrrolo[3,4-c]pyrrole;
2-{4,6-Bis[(2H3)methyl](2H)pyrimidin-2-yl}-5-{[3-fluoro-2-(3-methyl-1,2,4-oxadiazol-5-yl)phenyl]carbonyl}octahydropyrrolo[3,4-c]pyrrole;
2-{4,6-Bis[(2H3)methyl](2H)pyrimidin-2-yl}-5-{[4-methoxy-2-(2H-1,2,3-triazol-2-yl)phenyl]carbonyl}octahydropyrrolo[3,4-c]pyrrole;
2-(5-Ethyl-4,6-dimethylpyrimidin-2-yl)-5-{[3-(2H-1,2,3-triazol-2-yl)pyridin-2-yl]-carbonyl}octahydropyrrolo[3,4-c]pyrrole;
2-(4,6-Dimethylpyrimidin-2-yl)-5-{[3-(3-methyl-1,2,4-oxadiazol-5-yl)pyridin-2-yl]-carbonyl}octahydropyrrolo[3,4-c]pyrrole;

(5-(6,7-Difluoroquinoxalin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(3-fluoro-2-(pyrimidin-2-yl)phenyl)methanone;
(5-(6,7-Difluoroquinoxalin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(3-fluoro-2-(pyrimidin-2-yl)phenyl)methanone;
(5-(6,7-Difluoroquinoxalin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(4-methoxy-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone;
(5-(6-(Dimethylamino)pyrimidin-4-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(4-methoxy-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone;
(5-(6-(Dimethylamino)-2-methylpyrimidin-4-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(4-methoxy-2-(2H-1,2,3-triazol-2-yl)phenyl)methanone;
(5-(6-(Dimethylamino)-2-methylpyrimidin-4-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(3-fluoro-2-(pyrimidin-2-yl)phenyl)methanone;
(5-(6-(Dimethylamino)pyrimidin-4-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(3-fluoro-2-(pyrimidin-2-yl)phenyl)methanone;
(3-Fluoro-2-(pyrimidin-2-yl)phenyl)(5-(5-fluoro-4,6-dimethylpyrimidin-2-yl)-hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)methanone;
(5-(5-Chloro-4,6-dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(3-fluoro-2-(pyrimidin-2-yl)phenyl)methanone;
(5-(5-Chloro-4-methylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(3-fluoro-2-(pyrimidin-2-yl)phenyl)methanone;
(3-Fluoro-2-(pyrimidin-2-yl)phenyl)(5-(5-fluoro-4-methylpyrimidin-2-yl)hexa-hydropyrrolo[3,4-c]pyrrol-2(1H)-yl)methanone;
(5-(4,5-Dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(3-fluoro-2-(pyrimidin-2-yl)phenyl)methanone;
(5-(4,6-Dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(5-fluoro-2-(6-methylpyridin-2-yl)phenyl)methanone;
(5-(4,6-Dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(5-fluoro-2-(4-methylpyridin-2-yl)phenyl)methanone;
(5-(4,6-Dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(5-fluoro-2-(5-methylpyridin-2-yl)phenyl)methanone;
(5-(4,6-Dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(5-fluoro-2-(3-fluoropyridin-2-yl)phenyl)methanone;
(5-(4,6-Dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(5-fluoro-

2-(pyridin-2-yl)phenyl)methanone;
(5-(4,6-Dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(4-fluoro-2-(oxazol-2-yl)phenyl)methanone;
(5-(4,6-Dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(6-fluoro-2-(6-methylpyridin-2-yl)phenyl)methanone;
(5-(4,6-Dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(6-fluoro-2-(4-methylpyridin-2-yl)phenyl)methanone;
(5-(4,6-Dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(6-fluoro-2-(5-methylpyridin-2-yl)phenyl)methanone;
(5-(4,6-Dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(6-fluoro-2-(3-fluoropyridin-2-yl)phenyl)methanone;
(5-(4,6-Dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(6-fluoro-2-(pyridin-2-yl)phenyl)methanone;
(5-(4,6-Dimethylpyrimidin-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)(6-fluoro-2-(oxazol-2-yl)phenyl)methanone;
(3,6'-Dimethyl-[2,3'-bipyridin]-2'-yl)(5-(quinoxalin-2-yl)hexahydropyrrolo[3,4-c]-pyrrol-2(1H)-yl)methanone; and
[5-(4,6-Dimethyl-pyrimidin-2-yl)-hexahydro-pyrrolo[3,4-c]pyrrol-2-yl]-(2-fluoro-6-[1,2,3]triazol-2-yl-phenyl)-methanone•HCl•1.65H2O.

30. A pharmaceutical composition for treating a disease, disorder or medical condition mediated by orexin activity comprising:

(a) an effective amount of at least one chemical entity selected from compounds of Formula (I):



Formula (I)

wherein:

R^1 is a member selected from the group consisting of:

A) phenyl substituted or unsubstituted with one or two R^a members and substituted in the *ortho* position with R^b;

R^a is independently selected from the group consisting of: -H, halo, -C_{1-4}alkyl, -C_{1-4}alkoxy, and -NO_2, wherein two adjacent R^a members may come together to form a six membered aromatic ring;

R^b is a member selected from the group consisting of:

a) halo, -C_{1-4}alkoxy, -C_{1-4}alkyl,-CF_3, -OCF_3, or -CN;

b) 5-membered heteroaryl ring containing one oxygen or one sulfur members;

c) 5-6 membered heteroaryl ring containing one, two or three nitrogen members, optionally containing one oxygen member, substituted or unsubstituted with halo or -C_{1-4}alkyl; and

d) phenyl substituted or unsubstituted with halo, -CH_3, or -CF_3;

B) pyridine substituted or unsubstituted with one or two R^c members and substituted with R^d, wherein R^d is positioned adjacent to the point of attachment by R^1;

R^c is C_{1-4}alkyl;

R^d is a member selected from the group consisting of:

a) 5-6 membered heteroaryl ring selected from the group

b) consisting of: 1H-1,2,3-triazol-1-yl, 2H-1,2,3-triazol-2-yl, 1H-

c) pyrazol-5-yl, 3-methyl-1,2,4-oxadiazol-5-yl, pyridinyl, 3-methyl-pyridin-2-yl; 1-(tetrahydro-2H-pyran-2-yl)-1H-pyrazol-5-yl), phenyl, and pyrimidin-2-yl; and

d) -CF_3, -Br, and -C_{1-4}alkoxy;

C) 5-membered heteroaryl ring selected from the group consisting of: 2-methyl-1,3-thiazol-yl, 1H-pyrazol-5-yl, oxazole, isoxazolyl, thiophen-2-yl, and furan-2-yl, each substituted with phenyl substituted or unsubstituted with -F; and

D) 5-13 membered aryl or heteroaryl ring selected from the group consisting of: 3-methylfuran-2-yl, 9H-fluorene, quinoline, cinnoline; 3-(1H-pyrrol-1-yl)thiophen-2-yl, 8-[1,2,3]-triazol-2-yl-naphthalen-1-yl, 2,3-dihydro-1,4-benzodioxin-5-yl, 1H-indol-7-yl, 4-fluoronaphthalen-1-yl, and naphthalen-1-yl;

R^2 is a member selected from the group consisting of:

A) 6-membered heteroaryl ring containing two nitrogen members

substituted with one or more members independently selected from the group consisting of: halo, -C_{1-4}alkyl, -CD_3, -D, -C_{1-4}alkoxy, cyclopropyl, morpholin-2-yl, -CO_2C_{1-4}alkyl, -CO_2H, -CH_2OH, -$C(O)N(C_{1-4}alkyl)_2$, -CF_3, -CN, -OH, -NO_2, -$N(C_{1-4}alkyl)_2$, phenyl, furan-2-yl, thiophen-2-yl, 1H-pyrazol-4-yl, and pyrrolidin-1-yl;

B) pyridine substituted with one or two members independently selected from the group consisting of halo, -C_{1-4}alkyl, -C_{1-4}alkoxy, and -CF_3;

C) 9-membered heteroaryl ring selected from the group consisting of: benzooxazol-2-yl, 2-methylpyrimidin-4(3H)-one, 6-fluoro-1,3-benzothiazole, 1,3-benzothiazole, 6-methoxy-1,3-benzothiazole, 6-methyl-1,3-benzothiazole, 6-chloro-benzothiazol-2-yl, and 4-methyl-6,7-dihydro-5H-cyclopenta[d]pyrimidine;

D) 10-membered heteroaryl ring selected from the group consisting of: quinoxalin-2-yl, 3-methylquinoxalin-2-yl, 6,7-difluoroquinoxalin-2-yl, 3-(trifluoromethyl)quinoxaline, quinoline, 4-methylquinoline, and 6-fluoroquinazolin-2-yl; and

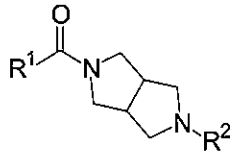
E) 4-methyl-1,3,5-triazin-2-yl;

and pharmaceutically acceptable salts of compounds of Formula (I); and

(b) at least one pharmaceutically acceptable excipient.

31. A pharmaceutical composition comprising and effective amount of at least one chemical entity of claim 29, and at least one pharmaceutically acceptable excipient.

32. At least one chemical entity selected from compounds of Formula(1) :



Formula (I)

wherein:

R^1 is a member selected from the group consisting of:

A) phenyl substituted or unsubstituted with one or two R^amembers and substituted in the *ortho*position with R^b;

$R^a$is independently selected from the group consisting of: -H. halo, -C_{1-4}alkyl, -C_{1-4}alkoxy, and –NO_2, wherein two adjacent R^a members may come together to form a six membered aromatic ring;

R^b is a member selected from the group consisting of:

a) halo, -C_{1-4}alkoxy, -C_{1-4}alkyl,-CF_3, -OCF_3 or -CN;

b) 5-membered heteroaryl ring containing one oxygen or one sulfur members;

c) 5-6 membered heteroaryl ring containing one, two or three nitrogen members, optionally containing one oxygen member, substituted or unsubstituted with halo or -C_{1-4}alkyl; and

d) phenyl substituted or unsubstituted with halo, -CH_3, or -CF_3;

B) pyridine substituted or unsubstituted with one or two R^cmembers and substituted with R^d wherein R^d is positioned adjacent to the point of attachment byR^1;

$R^c$is C-C_{1-4}alkyl;

R^d is a member selected from the group consisting of:

a) 5-6 membered heleroaryl ring selected from the group consisting of: 1H-1,2,3-triazol-1-yl, 2H-1,2,3-triazol-2-yl, 1H-pyrazol-5-yl,3-methyl-1,2,4-oxadiazol-5-yl. pyridinyl, 3-methylpyridin-2-yl; 1-(tetrahydro-2H-pyran-2-yl)-1H-pyrazol-5-yl), phenyl, and pyrimidin-2-yl; and

b) -CF_3, -Br, and -C_{1-4}alkoxy;

C) 5-membered heteroaryl ring selected from the group consisting of: 2-methyl-1,3-thiazol-yl, 1 H-pyrazol-5-yl, oxazole, isoxazolyl, thiophen-2-yl, and furan-2-yl, each substituted with phenyl substituted or unsubstituted with -F; and

D) 5-13 membered aryl or heteroaryl ring selected from the group consisting of: 3-methylfuran-2-yl, 9H-fluorene, quinoline, cinnoline; 3-(1H-pyrrol-1-yl)thiophen-2-yl, 8-[1,2,3]-triazol-2-ylnaphthalen-1-yl, 2,3-dihydro-1,4-benzodioxin-5-yl, 1H-indol-7-yl, 4-fluoronaphthalen-1-yl, and naphthalen-1-yl;

R^2 is a member selected from the group consisting of:

A) 6-membered heteroaryl ring containing two nitrogen members substituted with one or more members independently selected from the group consisting of: halo, -C_{1-4}alkyl, -CD_3, -D,-C_{1-4}alkoxy, cyclopropyl, morpholin-2-yl, -$C0_2$-C_{1-4}alkyl, -CO_2H, -CH_2OH, C(O)N(C_{1-4}Halkyl)$_2$,-CF_3, -CN, -OH, -NO_2, -N(C_{1-4}alkyl)$_2$, phenyl, furan-2-yl, thiophen-2-yl, 1 H-pyrazol-4-yl, and pyrrolidin-1-yl;

B) pyridine substituted with one or two members independently selected from

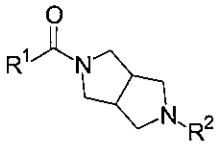
the group consisting of: halo, -C_{1-4}alkyl, -C_{1-4}alkoxy, and –CF_3;

C) 9-membered heteroaryl ring selected from the group consisting of: benzooxazol-2-yl, 2-methylpyrimidin-4(3H)-one, 6-fluoro-1,3benzothiazole, 1,3-benzothiazole, 6-methoxy-1,3-benzothiazole, 6-methyl-1,3-benzothiazole, 6-chloro-benzothiazol-2-yl, and 4-methyl-6,7-dihydro-5H-cyclopenta[d]pyrimidine;

D) 10-membered heteroaryl ring selected from the group consisting of: quinoxalin-2-yl, 3-methylquinoxalin-2-yl, 6,7-difluoroquinoxalin-2-yl, 3-(trifluoromethyl)quinoxaline, quinoline, 4-methylquinoline, and 6-fluoroquinazolin-2-yl; and

E) 4-methyl-1,3,5-triazin-2-yl; and pharmaceutically acceptable salts of compounds of Formula (I), and at least one pharmaceutically acceptable excipient for Use in the treatment of a disease, disorder, or medical condition mediated by orexin receptor activity.

33. At least one chemical entity selected from compounds of Formula(I) :



Formula (I)

wherein:

R^1 is a member selected from the group consisting of:

A) phenyl substituted or unsubstituted with one or two R^amembers and substituted in the *ortho*position with R^b;

$R^a$is independently selected from the group consisting of: -H. halo, -C_{1-4}alkyl, -C_{1-4}alkoxy, and –NO_2, wherein two adjacent R^a members may come together to form a six membered aromatic ring;

R^b is a member selected from the group consisting of:

a) halo, -C_{1-4}alkoxy, -C_{1-4}alkyl,-CF_3, -OCF_3 or -CN;

b) 5-membered heteroaryl ring containing one oxygen or one sulfur members;

c) 5-6 membered heteroaryl ring containing one, two or three nitrogen members, optionally containing one oxygen member, substituted or unsubstituted with halo or -C_{1-4}alkyl; and

d) phenyl substituted or unsubstituted with halo, -CH_3, or -CF_3;

B) pyridine substituted or unsubstituted with one or two R^cmembers and substituted with R^d. wherein R^d is positioned adjacent to the point of attachment by R^1;

$R^c$is C-C_{1-4}alkyl;

R^d is a member selected from the group consisting of:

a) 5-6 membered heteroaryl ring selected from the group consisting of: 1H-1,2,3-triazol-1-yl, 2H-1,2,3-triazol-2-yl, 1H-pyrazol-5-yl,3-methyl-1,2,4-oxadiazol-5-yl,pyridinyl, 3-methylpyridin-2-yl; 1-(tetrahydro-2H-pyran-2-yl)-1H-pyrazol-5-yl), phenyl, and pyrimidin-2-yl; and

b) -CF_3, -Br, and -C_{1-4}alkoxy;

C) 5-membered heteroaryl ring selected from the group consisting of: 2-methyl-1,3-thiazol-yl, 1 H-pyrazol-5-yl, oxazole, isoxazolyl, thiophen-2-yl, and furan-2-yl, each substituted with phenyl substituted or unsubstituted with -F; and

D) 5-13 membered aryl or heteroaryl ring selected from the group consisting of: 3-methylfuran-2-yl, 9H-fluorene, quinoline, cinnoline; 3-(1H-pyrrol-1-yl)thiophen-2-yl, 8-[1,2,3]-triazol-2-ylnaphthalen-1-yl, 2,3-dihydro-1,4-benzodioxin-5-yl, 1H-indol-7-yl, 4-fluoronaphthalen-1-yl, and naphthalen-1-yl;

R^2 is a member selected from the group consisting of:

A) 6-membered heteroaryl ring containing two nitrogen members substituted with one or more members independently selected from the group consisting of: halo, -C_{1-4}alkyl, -CD_3, -D, -C_{1-4}alkoxy, cyclopropyl, morpholin-2-yl, -$C0_2$-C_{1-4}alkyl, -CO_2H, -CH_2OH, C(O)N(C_{1-4}Halkyl)$_2$, -CF_3, -CN, -OH, -NO_2, -N(C_{1-4}alkyl)$_2$, phenyl, furan-2-yl, thiophen-2-yl, 1 H-pyrazol-4-yl, and pyrrolidin-1-yl;

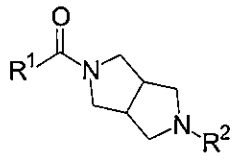
B) pyridine substituted with one or two members independently selected from the group consisting of: halo, -C_{1-4}alkyl, -C_{1-4}alkoxy, and –CF_3;

C) 9-membered heteroaryl ring selected from the group consisting of: benzooxazol-2-yl, 2-methylpyrimidin-4(3H)-one, 6-fluoro-1,3benzothiazole, 1,3-benzothiazole, 6-methoxy-1,3-benzothiazole, 6-methyl-1,3-benzothiazole, 6-chloro-benzothiazol-2-yl, and 4-methyl-6,7-dihydro-5H-cyclopenta[d]pyrimidine;

D) 10-membered heteroaryl ring selected from the group consisting of: quinoxalin-2-yl, 3-methylquinoxalin-2-yl, 6,7-difluoroquinoxalin-2-yl, 3-(trifluoromethyl)quinoxaline, quinoline, 4-methylquinoline, and 6-fluoroquinazolin-2-yl; and

E) 4-methyl-1,3,5-triazin-2-yl; and pharmaceutically acceptable salts of compounds of Formula (I), and at least one pharmaceutically acceptable excipient for use In the treatment of a disease. disorder, or medical condition wherein the disease, disorderor medical condition is selected from the group consisting of: disorders of the sleep-wake cycle, insomnia, restless legs syndrome, jet-lag, disturbed sleep, sleep disorders secondary to neurological disorders, manias, depressions, manic depression, schizophrenia, pain syndromes, fibromyalgia, neuropathic pain, catatonia, Parkinson's disease, Tourette's syndrome. anxiety, dellrium, dementias, overweight or obesity and conditions related to overweight or obesity, insulin resistance, type /I diabetes, hyperlipidemia, gallstones, angina, hypertension, breathlessness, tachycardia, infertility, sleep apnea, back and joint pain, varicose veins, osteoarthritis, hypertension, tachycardia, arrhythmias, angina pectoris, acute heart failure, ulcers, irritable bowel syndrome. diarrhea and gastroesophageal reflux.

34. At least one chemical entity selected from compounds of Formula(I):



Formula (I)

wherein:

R^1 is a member selected from the group consisting of:

A) phenyl substituted or unsubstituted with one or two R^amembers and substituted in the *ortho*position with R^b;

$R^a$is independently selected from the group consisting of: -H. halo, -C_{1-4}alkyl, -C_{1-4}alkoxy, and –NO_2, wherein two adjacent R^a members may come together to form a six membered aromatic ring;

R^b is a member selected from the group consisting of:

a) halo, -C_{1-4}alkoxy, -C_{1-4}alkyl,-CF_3, -OCF_3 or -CN;

b) 5-membered heteroaryl ring containing one oxygen or one sulfur members;

c) 5-6 membered heteroaryl ring containing one, two or three nitrogen members, optionally containing one oxygen member, substituted or unsubstituted with halo or -C_{1-4}alkyl; and

d) phenyl substituted or unsubstituted with halo, $-CH_3$, or $-CF_3$;

B) pyridine substituted or unsubstituted with one or two R^cmembers and substituted with R^d. wherein R^d is positioned adjacent to the point of attachment by R^1;

$R^c$is C-C_{1-4}alkyl;

R^d is a member selected from the group consisting of:

a) 5-6 membered heteroaryl ring selected from the group consisting of: 1H-1,2,3-triazol-1-yl, 2H-1,2,3-triazol-2-yl, 1H-pyrazol-5-yl,3-methyl-1,2,4-oxadiazol-5-yl. pyridinyl, 3-methylpyridin-2-yl; 1-(tetrahydro-2H-pyran-2-yl)-1H-pyrazol-5-yl), phenyl, and pyrimidin-2-yl; and

b) $-CF_3$, -Br, and -C_{1-4}alkoxy;

C) 5-membered heteroaryl ring selected from the group consisting of: 2-methyl-1,3-thiazol-yl, 1 H-pyrazol-5-yl, oxazole, isoxazolyl, thiophen-2-yl, and furan-2-yl, each substituted with phenyl substituted or unsubstituted with -F; and

D) 5-13 membered aryl or heteroaryl ring selected from the group consisting of: 3-methylfuran-2-yl, 9H-fluorene, quinoline, cinnoline; 3-(1H-pyrrol-1-yl)thiophen-2-yl, 8-[1,2,3]-triazol-2-ylnaphthalen-1-yl, 2,3-dihydro-1,4-benzodioxin-5-yl, 1H-indol-7-yl, 4-fluoronaphthalen-1-yl, and naphthalen-1-yl;

R^2 is a member selected from the group consisting of:

A) 6-membered heteroaryl ring containing two nitrogen members substituted with one or more members independently selected from the group consisting of: halo, -C_{1-4}alkyl, $-CD_3$, -D,-C_{1-4}alkoxy, cyclopropyl, morpholin-2-yl, -$C0_2$-C_{1-4}alkyl, $-CO_2H$, $-CH_2OH$, C(O)N(C_{1-4}Halkyl)$_2$,$-CF_3$, -CN, -OH, $-NO_2$, -N(C_{1-4}alkyl)$_2$, phenyl, furan-2-yl, thiophen-2-yl, 1 H-pyrazol-4-yl, and pyrrolidin-1-yl;

B) pyridine substituted with one or two members independently selected from the group consisting of: halo, -C_{1-4}alkyl, -C_{1-4}alkoxy, and $-CF_3$;

C) 9-membered heteroaryl ring selected from the group consisting of: benzooxazol-2-yl, 2-methylpyrimidin-4(3H)-one, 6-fluoro-1,3-benzothiazole, 1,3-benzothiazole, 6-methoxy-1,3-benzothiazole, 6-methyl-1,3-benzothiazole, 6-chloro-benzothiazol-2-yl, and 4-methyl-6,7-dihydro-5H-cyclopenta[d]pyrimidine;

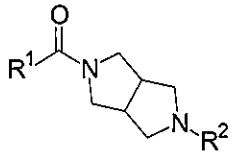
D) 10-membered heteroaryl ring selected from the group consisting of: quinoxalin-2-yl, 3-methylquinoxalin-2-yl, 6,7-difluoroquinoxalin-2-yl, 3-(trifluoro-

methyl)quinoxaline, quinoline, 4-methylquinoline, and 6-fluoroquinazolin-2-yl; and

E) 4-methyl-1,3,5-triazin-2-yl;

and pharmaceutically acceptable salts of compounds of Formula (I), and at least one pharmaceutically acceptable excipient for use in tile treatment of a disease, disorder, or medical condition wherein the disease, disorder, or medical condition is insomnia.

35. At least one chemical entity selected from compounds of Formula(1) :



Formula (I)

wherein

R^1 is a member selected from the group consisting of:

A) phenyl substituted or unsubstituted with one or two R^amembers and substituted in the *ortho*position with R^b;

$R^a$is independently selected from the group consisting of: -H. halo, -C_{1-4}alkyl, -C_{1-4}alkoxy, and –NO_2, wherein two adjacent R^a members may come together to form a six membered aromatic ring;

R^b is a member selected from the group consisting of:

a) halo, -C_{1-4}alkoxy, -C_{1-4}alkyl,-CF_3, -OCF_3 or -CN;

b) 5-membered heteroaryl ring containing one oxygen or one sulfur members;

c) 5-6 membered heteroaryl ring containing one, two or three nitrogen members, optionally containing one oxygen member, substituted or unsubstituted with halo or -C_{1-4}alkyl; and

d) phenyl substituted or unsubstituted with halo, -CH_3, or -CF_3;

B) pyridine substituted or unsubstituted with one or two R^cmembers and substituted with R^d. wherein R^d is positioned adjacent to the point of attachment by R^1;

$R^c$is C-C_{1-4}alkyl;

R^d is a member selected from the group consisting of:

a) 5-6 membered he!eroaryl ring selected from the group consisting of: 1H-

1,2,3-triazol-1-yl, 2H-1,2,3-triazol-2-yl, 1H-pyrazol-5-yl,3-methyl-1,2,4-oxadiazol-5-yl. pyridinyl, 3-methylpyridin-2-yl; 1-(tetrahydro-2H-pyran-2-yl)-1H-pyrazol-5-yl), phenyl, and pyrimidin-2-yl; and

b) $-CF_3$, -Br, and $-C_{1-4}$alkoxy;

C) 5-membered heteroaryl ring selected from the group consisting of: 2-methyl-1,3-thiazol-yl, 1 H-pyrazol-5-yl, oxazole, isoxazolyl, thiophen-2-yl, and furan-2-yl, each substituted with phenyl substituted or unsubstituted with -F; and

D) 5-13 membered aryl or heteroaryl ring selected from the group consisting of: 3-methylfuran-2-yl, 9H-fluorene, quinoline, cinnoline; 3-(1H-pyrrol-1-yl)thiophen-2-yl, 8-[1,2,3]-triazol-2-ylnaphthalen-1-yl, 2,3-dihydro-1,4-benzodioxin-5-yl, 1H-indol-7-yl, 4-fluoronaphthalen-1-yl, and naphthalen-1-yl;

R^2 is a member selected from the group consisting of:

A) 6-membered heteroaryl ring containing two nitrogen members substituted with one or more members independently selected from the group consisting of: halo, $-C_{1-4}$alkyl, $-CD_3$, -D,$-C_{1-4}$alkoxy, cyclopropyl, morpholin-2-yl, $-CO_2-C_{1-4}$alkyl, $-CO_2H$, $-CH_2OH$, $C(O)N(C_{1-4}Halkyl)_2$,$-CF_3$, -CN, -OH, $-NO_2$, $-N(C_{1-4}alkyl)_2$, phenyl, furan-2-yl, thiophen-2-yl, 1 H-pyrazol-4-yl, and pyrrolidin-1-yl;

B) pyridine substituted with one or two members independently selected from the group consisting of: halo, $-C_{1-4}$alkyl, $-C_{1-4}$alkoxy, and $-CF_3$;

C) 9-membered heteroaryl ring selected from the group consisting of: benzooxazol-2-yl, 2-methylpyrimidin-4(3H)-one, 6-fluoro-1,3benzothiazole, 1,3-benzothiazole, 6-methoxy-1,3-benzothiazole, 6-methyl-1,3-benzothiazole, 6-chloro-benzothiazol-2-yl, and 4-methyl-6,7-dihydro-5H-cyclopenta[d]pyrimidine;

D) 10-membered heteroaryl ring selected from the group consisting of: quinoxalin-2-yl, 3-methylquinoxalin-2-yl, 6,7-difluoroquinoxalin-2-yl, 3-(trifluoro-methyl)quinoxaline, quinoline, 4-methylquinoline, and 6-fluoroquinazolin-2-yl; and

E) 4-methyl-1,3,5-triazin-2-yl;

and pharmaceutically acceptable salts of compounds of Formula (I), and at least one pharmaceutically acceptable excipient inthe manufacture of a medicament for the treatment of a disease, disorder, or medical condition mediated by orexin receptor activity.

36. Use of the medicament according to Claim 35, wherein the disease, disorder, or medical con-dition is selected from the group consisting of: disorders of the sleep-wake cycle, insomnia, restless legs syndrome, jet-lag, disturbed sleep, sleep dis-orders secondary to neurological disorders, manias, depressions, manic depression, schizophrenia, pain syndromes, fibromyalgia, neuropathic pain, catatonia, Parkinson's disease, Tourette's syndrome, anxiety, delirium, dementias, overweight or obesity and conditions related to overweight or obesity, insulin resistance, type II diabetes, hyperlipidemia, gallstones, angina,hypertension, breathlessness, tachycardia, infertility, sleep apnea, back and joint pain, varicose veins, osteoarthritis, hypertension, tachycardia, arrhythmias, angina pectoris, acute heart failure, ulcers, irritable bowel syndrome, diarrhea and gastroesophageal reflux.

37. Use of the medicament according to Claim 35, wherein the disease, disorder, or medical condition is insomnia.

38. A chemical entity defined in claim 1, wherein R^3 is a member selected from the group consisting of:
2-([1,1'-Biphenyl]-2-ylsulfonyl)-5-(5-(trifluoromethyl) pyridin-2-yl)octahydropyrrolo[3,4-c]pyrrole;
2-([1,1'-Biphenyl]-2-ylsulfonyl)-5-(5-(trifluoromethyl)pyrimidin-2-yl)octahydropyrrolo[3,4-c]pyrrole;
2-([1,1'-Biphenyl]-2-ylsulfonyl)-5-(4,6-dimethylpyrimidin-2-yl)octahydropyrrolo-[3,4-c]pyrrole;
2-(4,6-Dimethylpyrimidin-2-yl)-5-((2-methoxyphenyl)sulfonyl)octahydropyrrolo[3,4-c]pyrrole;
2-((2-Methoxyphenyl)sulfonyl)-5-(5-(trifluoromethyl)pyrimidin-2-yl)octahydropyrrolo[3,4-c]pyrrole;
2-((2-Methoxyphenyl)sulfonyl)-5-(5-(trifluoromethyl)pyridin-2-yl)octahydropyrrolo[3,4-c]pyrrole;
2-(5-((2-Methoxyphenyl)sulfonyl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)-quinoxaline; and
2-(5-([1,1'-Biphenyl]-2-ylsulfonyl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)quin-

oxaline.