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(54) **Új NK-3 receptor szelektív antagonista vegyületek, gyógyászati készítmény és eljárások az NK-3 receptorok által közvetített rendellenességek során történő alkalmazásra**

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(54) **NOVEL NK-3 RECEPTOR SELECTIVE ANTAGONIST COMPOUNDS, PHARMACEUTICAL COMPOSITION AND METHODS FOR USE IN NK-3 RECEPTORS MEDIATED DISORDERS**

NEUE SELEKTIVEN NK-3-REZEPTOR ANTAGONISTEN VERBINDUNGEN, PHARMAZEUTISCHE ZUSAMMENSETZUNG UND VERFAHREN ZUR VERWENDUNG IN NK-3- REZEPTOREN VERMITTELTE STÖRUNGEN

NOUVEAUX COMPOSÉS ANTAGONISTES SÉLECTIFS DU RÉCEPTEUR NK-3, COMPOSITION PHARMACEUTIQUE ET PROCÉDÉ POUR UNE UTILISATION DANS DES TROUBLES MÉDIÉS PAR LES RÉCEPTEURS NK-3

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Description

[0001] The present invention relates to novel compounds including their pharmaceutically acceptable salts and solvates, which are selective antagonists of neurokinin 3 receptor (NK-3) and are useful as therapeutic compounds, particularly in the treatment and/or prevention of a broad array of CNS and peripheral diseases or disorders.

[BACKGROUND OF THE INVENTION]

[0002] Tachykinin receptors are the targets of a family of structurally related peptides which include substance P (SP), neurokinin A (NKA) and neurokinin B (NKB), named collectively "tachykinins". Tachykinins are synthesized in the central nervous system (CNS) and peripheral tissues, where they exert a variety of biological activities. Three tachykinin receptors are known which are named neurokinin-1 (NK-1), neurokinin-2 (NK-2) and neurokinin-3 (NK-3) receptors. Tachykinin receptors belong to the rhodopsin-like seven membrane G-protein coupled receptors. SP has the highest affinity and is believed to be the endogenous ligand of NK-1, NKA for NK-2 receptor and NKB for NK-3 receptor, although some crossreactivity probably exists. The NK-1, NK-2 and NK-3 receptors have been identified in different species. NK-1 and NK-2 receptors are expressed in a wide variety of peripheral tissues and NK-1 receptors are also expressed in the CNS; whereas NK-3 receptors are primarily expressed in the CNS.

[0003] The neurokinin receptors mediate a variety of tachykinin-stimulated biological effects that include transmission of excitatory neuronal signals in the CNS and periphery (e.g. pain), modulation of smooth muscle contractile activity, modulation of immune and inflammatory responses, induction of hypotensive effects via dilatation of the peripheral vasculature and stimulation of endocrine and exocrine gland secretions.

[0004] In the CNS, the NK-3 receptor is expressed in regions including the medial prefrontal cortex, the hippocampus, the thalamus and the amygdala. Moreover, NK-3 receptors are expressed on dopaminergic neurons. Activation of NK-3 receptors has been shown to modulate dopamine, acetylcholine and serotonin release suggesting a therapeutic utility for NK-3 receptor modulators for the treatment of a variety of disorders including psychotic disorders, anxiety, depression, schizophrenia as well as obesity, pain or inflammation (Exp. Opinion Ther. Patents (2000), 10(6); 939-960 Current Opinion in Investigational Drugs, 2001, 2(7), 950-956 and Current Pharmaceutical Design, 2010, 16, 344-357).

[0005] Schizophrenia is classified into subgroups. The paranoid type is characterized by delusions and hallucinations and absence of thought disorder, disorganized behavior, and affective flattening. In the disorganized type, which is also named 'hebephrenic schizophrenia' in the International Classification of Diseases (ICD), thought disorder and flat affect are present together. In the catatonic type, prominent psychomotor disturbances are evident, and symptoms may include catatonic stupor and waxy flexibility. In the undifferentiated type, psychotic symptoms are present but the criteria for paranoid, disorganized, or catatonic types have not been met. The symptoms of schizophrenia normally manifest themselves in three broad categories, i.e. positive, negative and cognitive symptoms. Positive symptoms are those, which represent an "excess" of normal experiences, such as hallucinations and delusions. Negative symptoms are those where the patient suffers from a lack of normal experiences, such as anhedonia and lack of social interaction. The cognitive symptoms relate to cognitive impairment in schizophrenics, such as a lack of sustained attention and deficits in decision making. The current antipsychotic drugs (APDs) are fairly successful in treating the positive symptoms but fare less well for the negative and cognitive symptoms. Contrary to that, NK3 antagonists have been shown clinically to improve on both positive and negative symptoms in schizophrenics (Meltzer et al, Am. J. Psychiatry, 161, 975-984, 2004) and ameliorate cognitive behavior of schizophrenics (Curr. Opion. Invest. Drug, 6, 717-721, 2005).

[0006] In rat, morphological studies provide evidence for putative interactions between NKB neurons and the hypothalamic reproductive axis (Krajewski et al, J. Comp. Neurol., 489(3), 372-386, 2005). In arcuate nucleus neurons, NKB expression co-localizes with estrogen receptor α and dynorphin, implicated in progesterone feedback to Gonadotropin Releasing Hormone (GnRH) secretion (Burke et al., J. Comp. Neurol., 498(5), 712-726, 2006; Goodman et al., Endocrinology, 145, 2959-2967, 2004). Moreover, NK-3 receptor is highly expressed in the hypothalamic arcuate nucleus in neurons which are involved in the regulation of GnRH release.

[0007] WO 00/43008 discloses a method of suppressing gonadotropin and/or androgen production with specific NK-3 receptor antagonists. More particularly, the WO 00/43008 application relates to lowering luteinizing hormone (LH) blood level by administering an NK-3 receptor antagonist. Concurently or alternatively with gonadotropin suppression, WO 00/43008 also relates to suppression of androgen production with NK-3 receptor antagonists. Recently it has been postulated that NKB acts autosynaptically on kisspeptin neurons in the arcuate nucleus to synchronize and shape the pulsatile secretion of kisspeptin and drive the release of GnRH from fibers in the median eminence (Navarro et al., J. of Neuroscience, 23, 2009 - pp11859-11866). All these observations suggest a therapeutic utility for NK-3 receptor modulators for sex hormone-dependent diseases.

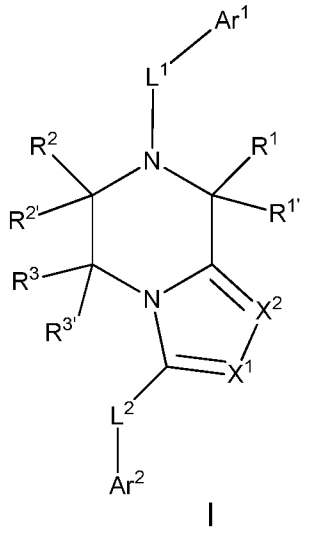
[0008] Non-peptide ligands have been developed for each of the tachykinin receptors. Some of them have been described as dual modulators able to modulate both NK-2 and NK-3 receptors (WO 06/120478). However known non-peptide NK-3 receptor antagonists suffer from a number of limitations such as poor drug bioavailability, poor CNS

penetration and weak potency particularly at mouse/rat ortholog receptors, all aspects which limit the potential to evaluate these compounds in preclinical models and/or clinical development. On this basis, new potent and selective antagonists of NK-3 receptor may be of therapeutic value for the preparation of drugs useful in the treatment and/or prevention of CNS and peripheral diseases or disorders in which NKB and the NK-3 receptors are involved.

[SUMMARY OF THE INVENTION]

[0009] The invention encompasses compounds of general Formula I, their pharmaceutically acceptable salts and solvates as well as methods of use of such compounds or compositions comprising such compounds as antagonists of NK-3 receptor activity.

[0010] In a general aspect, the invention provides compounds of general formula I:



I

and pharmaceutically acceptable salts and solvates thereof, wherein

Ar^1 is a 5- to 6-membered aryl or heteroaryl group, 3- to 6-membered cycloalkyl group a 3- to 6-membered heterocyclyl group or a C3-C6 alkyl group, each of the aryl, heteroaryl, cycloalkyl or heterocyclyl groups being optionally substituted by one or more group(s) selected from halo, cyano, alkyl, haloalkyl, cycloalkyl, heteroalkyl, heterocyclyl, aryl, aralkyl, heteroaryl, hydroxyl, alkoxy, haloalkoxy, alkoxyalkoxy, alkylamino, carboxy, alkoxycarbonyl, alkylcarbonyloxy, alkylcarbonylamino, haloalkylcarbonylamino, carbamoyl, alkylcarbamoyl, carbamoylamino, alkylcarbamoylamino, alkylsulfonyl, haloalkylsulfonyl, sulfamoyl, alkylsulfamoyl, alkylsulfonylamino, haloalkylsulfonylamino, or two substituents form an alkylenedioxy group or a haloalkylenedioxy group, or two substituents form a cycloalkyl or heterocycloalkyl moiety together with the cycloalkyl or heterocycloalkyl group they are attached to, or fused to the aryl, heteroaryl, cycloalkyl or heterocycloalkyl group may be one or more aryl moiety, each of said substituents being optionally substituted by one or more further substituent(s) selected from halo, cyano, alkyl, haloalkyl, cyclopropyl, alkoxy, haloalkoxy, heterocyclyl, aryl, heteroaryl, aryloxy or heteroaryloxy;

L^1 is carbonyl;

R^1 is H, a C_1-C_4 alkyl, aryl or aralkyl group, each of said alkyl, aryl or aralkyl groups being optionally substituted by one or more group(s) selected from halo or hydroxyl;

R$^{1'}$ is H or a C_1-C_4 alkyl group;

R^2 is H or a C_1-C_4 alkyl group;

R$^{2'}$ is H or a C_1-C_4 alkyl group;

R^3 is H or a C_1-C_4 alkyl group optionally substituted by one hydroxy;

R$^{3'}$ is H or a C_1-C_4 alkyl group;

X^1 and X^2 are N;

L^2 is a single bond or carbonyl;

Ar^2 is a 5- to 6-membered aryl or heteroaryl group, each of the aryl, or heteroaryl groups being optionally substituted by one or more group(s) selected from halo, cyano, alkyl, hydroxyalkyl, haloalkyl, cycloalkyl, heteroalkyl, heterocyclyl, aryl, heteroaryl, aralkyl, heteroarylalkyl, hydroxyl, alkoxy, haloalkoxy, alkylamino, carboxy, alkoxycarbonyl, alkylcarbonyloxy, alkylcarbonylamino, haloalkylcarbonylamino, acylamino, carbamoyl, alkylcarbamoyl, carbamoylalkyl, carbamoylamino, alkylcarbamoylamino, alkylsulfonyl, haloalkylsulfonyl, arylsulfonylalkyl, sulfamoyl, alkylsulfamoyl, alkylsulfonylamino, haloalkylsulfonylamino, or two substituents form an alkylenedioxy group or a haloalkylenedioxy group, or fused to the aryl or heteroaryl group may be one or more cycloalkyl, aryl, heterocyclyl or heteroaryl moiety, each of said substituents being optionally substituted by one or more further substituent(s) selected from halo, cyano, alkyl, haloalkyl, alkoxy, haloalkoxy, cycloalkyl, heterocyclyl optionally substituted by alkyl, aryl, heteroaryl, hydroxyl, alkoxyalkyl, hydroxyalkoxy, alkylamino, alkylsulfonylamino, alkoxycarbonylamino, aminoalkoxy, or alkoxycarbonylaminoalkoxy;
and wherein, when:

R^1, $R^{1'}$, R^2, $R^{2'}$, R^3, $R^{3'}$ are H, and

L^2 is single bond, and

Ar^1 is a 6-membered aryl optionally substituted by one or more group(s) selected from halo, cyano, C1-C3 alkyl, C1 haloalkyl, and

Ar^2 is a 5- to 6-membered aryl or heteroaryl group optionally substituted by one or more group(s) selected from halo, C1-C3 alkyl, hydroxyl, methoxy, or fused to an aryl or heteroaryl group optionally substituted by one or more further halo, C1-C3 alkyl, hydroxyl, methoxy,
then,

Ar^1 is phenyl, 3-halophenyl, 4-halophenyl, 2,3-dichlorophenyl, 2,4-difluorophenyl, 2,5-dihalophenyl, 2,6-difluorophenyl, 2,6-dichlorophenyl, 3,4-dihalophenyl, 3,5-dihalophenyl, 3,4,5-trihalophenyl, 2-cyanophenyl, 3-cyanophenyl, 4-cyanophenyl, 2,3-dicyanophenyl, 2,4-dicyanophenyl, 3,5-dicyanophenyl, 3-cyano-4-halophenyl, 4-(C1-C3 alkyl)phenyl, 3,4-di(C1-C3 alkyl)phenyl, 3,5-di(C1-C3 alkyl)phenyl, 4-(C1 haloalkyl)phenyl, and

Ar^2 is 2-(C1-C3 alkyl)thiazol-4-yl, 5-(C1-C3 alkyl)thiazol-4-yl, pyridin-2-yl, 4-halopyridin-2-yl, 4-(C1-C3 alkyl)pyridin-2-yl, 5-(C1-C3 alkyl)pyridin-2-yl, 6-(C1-C3 alkyl)pyridin-2-yl, quinolin-2-yl, isoquinolin-3-yl, 8-haloquinolin-2-yl, benzothiazol-2-yl, 4,5,6,7-tetrahydro-1,3-benzothiazol-2-yl;

with the following provisos:

- Ar^1 is neither a substituted or unsubstituted pyrazolo[1,5-a]pyridin-2yl nor a substituted or unsubstituted pyrazolo[1,5-a]pyrimidin-2yl moiety; and
  the compound of formula I is none of :

  (2,4-difluorophenyl)(3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
  (3-chlorophenyl)(3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
  2-(3-(pyridin-2-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazine-7-carbonyl)benzonitrile;
  (2,6-dichlorophenyl)(3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone,
  (2,3-dichlorophenyl)(3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone,
  (2,3-dichlorophenyl)(3-(5-methylpyridin-2-yl)-5,6-dihydro-[1,2,4] triazolo[4,3-a]pyrazin-7(8H)-yl)methanone,
  (2,3-dichlorophenyl)(3-(6-methylpyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone.

[0011] In another aspect, the present invention provides a pharmaceutical composition comprising at least one compound according to the invention or a pharmaceutically acceptable salt or solvate thereof.

[0012] The invention also relates to the use of the above compounds or their pharmaceutically acceptable salts and solvates as modulators of NK-3 receptors, preferably as antagonists of NK-3 receptors.

[0013] The invention further provides a compound of formula (I) or a pharmaceutically acceptable salt or solvate thereof for use in methods of treatment and/or prevention of depression, anxiety, pyschosis, schizophrenia, psychotic disorders, bipolar disorders, cognitive disorders, Parkinson's disease, Alzheimer's disease, attention deficit hyperactivity disorder (ADHD), pain, convulsion, obesity, inflammatory diseases including irritable bowel syndrome and inflammatory bowel disorders, emesis, pre-eclampsia, airway related diseases including chronic obstructive pulmonary disease, asthma, airway hyperresponsiveness, bronchoconstriction and cough, reproduction disorders and sex hormone-dependent diseases including but not limited to benign prostatic hyperplasia (BPH), metastatic prostatic carninoma, testicular cancer, breast cancer, androgen dependent acne, male pattern baldness, endometriosis, abnormal puberty, uterine fibrosis, hormone-dependent cancers, hyperandrogenism, hirsutism, virilization, polycystic ovary syndrome (PCOS), HAIR-AN syndrome (hyperandrogenism, insulin resistance and acanthosis nigricans), ovarian hyperthecosis (HAIR-AN with hyperplasia of luteinized theca cells in ovarian stroma), other manifestations of high intraovarian androgen concentrations (e.g. follicular maturation arrest, atresia, anovulation, dysmenorrhea, dysfunctional uterine bleeding, infertility) and androgen-producing tumor (virilizing ovarian or adrenal tumor) comprising the administration of a therapeutically effective amount of said compound to a patient in need thereof. Preferably the patient is a warm-blooded animal, more preferably a human.

[0014] The invention further provides a compound of formula (I) or a pharmaceutically acceptable salt or solvate thereof for use in methods of treatment for gynecological disorders and infertility. In particular, the invention provides a compound of formula (I) or a pharmaceutically acceptable salt or solvate thereof for use in methods to suppress the LH-surge in assisted conception comprising the administration of said compound to a patient in need thereof. Preferably the patient is a warm-blooded animal, more preferably a woman.

[0015] The invention further provides a compound of formula (I) or a pharmaceutically acceptable salt or solvate thereof for use in methods to affect androgen production to cause male castration and to inhibit the sex drive in male sexual offenders comprising the administration of a therapeutically effective amount of said compound to a patient in need thereof. Preferably the patient is a warm-blooded animal, more preferably a man.

[0016] The invention also provides the use of a compound of formula (I) or a pharmaceutically acceptable salt or solvate thereof as a medicament. Preferably, the medicament is used for the treatment and/or prevention of depression, anxiety, pyschosis, schizophrenia, psychotic disorders, bipolar disorders, cognitive disorders, Parkinson's disease, Alzheimer's disease, attention deficit hyperactivity disorder (ADHD), pain, convulsion, obesity, inflammatory diseases including irritable bowel syndrome and inflammatory bowel disorders, emesis, pre-eclampsia, airway related diseases including chronic obstructive pulmonary disease, asthma, airway hyperresponsiveness, bronchoconstriction and cough, reproduction disorders and sex hormone-dependent diseases including but not limited to benign prostatic hyperplasia (BPH), metastatic prostatic carninoma, testicular cancer, breast cancer, androgen dependent acne, male pattern baldness, endometriosis, abnormal puberty, uterine fibrosis, hormone-dependent cancers, hyperandrogenism, hirsutism, virilization, polycystic ovary syndrome (PCOS), HAIR-AN syndrome (hyperandrogenism, insulin resistance and acanthosis nigricans), ovarian hyperthecosis (HAIR-AN with hyperplasia of luteinized theca cells in ovarian stroma), other manifestations of high intraovarian androgen concentrations (e.g. follicular maturation arrest, atresia, anovulation, dysmenorrhea, dysfunctional uterine bleeding, infertility) and androgen-producing tumor (virilizing ovarian or adrenal tumor). The medicament may also be used for the treatment of gynecologic disorder, infertility and to affect androgen production to cause male castration.

[DETAILED DESCRIPTION OF THE INVENTION]

[0017] As noted above, the invention relates to compounds of formula I, as well as their pharmaceutically acceptable salts and solvates.

[0018] Preferred compounds of formula I and pharmaceutically acceptable salts and solvates thereof are those wherein **Ar^1** is a 5- to 6-membered aryl or heteroaryl group, 5- to 6-membered cycloalkyl group, C3-C6 alkyl group, each of the aryl or heteroaryl groups being optionally substituted by one or more group(s) selected from halo, cyano, alkyl, haloalkyl, C3-C6 cycloalkyl, heteroalkyl, heterocyclyl, aryl, heteroaryl, hydroxyl, alkoxy, haloalkoxy, alkylamino, carboxy, alkoxycarbonyl, alkylcarbonyloxy, alkylcarbonylamino, haloalkylcarbonylamino, carbamoyl, alkylcarbamoyl, carbamoylamino, alkylcarbamoylamino, alkylsulfonyl, haloalkylsulfonyl, sulfamoyl, alkylsulfamoyl, alkylsulfonylamino, haloalkylsulfonylamino, or two substituents form an alkylenedioxy group or a haloalkylenedioxy group, or fused to the aryl, heteroaryl, cycloalkyl or heterocycloalkyl group may be one aryl moiety, each of said substituents being optionally substituted by one or more further substituent(s) selected from halo, cyano, alkyl, haloalkyl, cyclopropyl, alkoxy, haloalkoxy, heterocyclyl, aryl, heteroaryl, aryloxy or heteroaryloxy, preferably **Ar^1** is a 5- to 6-membered aryl, preferably phenyl, heteroaryl group preferably pyridinyl, isopropyl, isobutyl, each of the aryl or heteroaryl groups being optionally substituted by one or more group(s) selected from halo, cyano, alkyl, haloalkyl, C3-C6 cycloalkyl, aryl, heteroaryl, or fused to the aryl or heteroaryl group may be one aryl, preferably phenyl, moiety, each of said substituents being optionally substituted by one or more further substituent(s) selected from halo, alkyl, haloalkyl, cyclopropyl, haloalkoxy, or aryloxy, more preferably **Ar^1** is a

phenyl, a biaryl, preferably 4-biphenyl, heterobiaryl preferably 4-(thiophen-2-yl)phenyl, 3-phenyl-1H-pyrazol-5-yl, 5-phenylpyridin-2-yl, 2-phenylpyridin-5-yl, more preferably 4-(thiophen-2-yl)phenyl, each of said biaryl or heterobiaryl being optionally substituted by one or more further substituent(s) selected from halo, alkyl, cyclopropyl, haloalkyl, haloalkoxy or aryloxy; and/or

L^1 is carbonyl; and/or

R^1 is H, a C_1-C_4 alkyl, aryl or aralkyl group, each of said alkyl, aryl or aralkyl groups being optionally substituted by one or more group(s) selected from halo or hydroxyl, preferably **R^1** is H, a C_1-C_3 alkyl, preferably methyl or isopropyl, hydroxyethyl, phenyl or benzyl group, each of said phenyl or benzyl groups being optionally substituted by one or more group(s) selected from halo, preferably fluoro or chloro, more preferably **R^1** is H, methyl or 2-hydroxyethyl; and/or

$R^{1'}$ is H or methyl preferably **$R^{1'}$** is H; and/or

R^2, **$R^{2'}$**, **R^3** and **$R^{3'}$** are H; and/or

X^1 and **X^2** are both N; and/or

L^2 is a single bond; and/or

Ar^2 is a 5- to 6-membered heteroaryl group optionally substituted by one or more group(s) selected from halo, cyano, alkyl, haloalkyl, C3-C6 cycloalkyl heterocyclyl, aryl, heteroaryl, aralkyl, heteroarylalkyl, arylsulfonylalkyl, alkoxy, or fused to the heteroaryl group may be one cycloalkyl, aryl, heterocyclyl or heteroaryl moiety, each of said substituents being optionally substituted by one or more further substituent(s) selected from halo, cyano, alkyl, haloalkyl, cyclopropyl, alkoxy, heterocyclyl optionally substituted by alkyl aryl, hydroxyl, alkoxyalkyl, hydroxyalkoxy, alkylamino, alkylsulfonylamino, alkoxycarbonylamino, aminoalkoxy, or alkoxycarbonylaminoalkoxy preferably **Ar^2** is a fused heteroaryl, preferably quinolin-2-yl, benzo[d]thiazol-2-yl, 4,5,6,7-tetrahydrobenzo[d]thiazol-2-yl, heterocyclylheteroaryl, preferably 2-(pyrrolidin-1-yl)thiazol-4-yl, 2-(piperidin-1-yl)thiazol-4-yl, 2-(morpholin-4-yl)thiazol-4-yl, 2-(piperazin-1-yl)thiazol-4-yl, heterobiaryl preferably 2-phenylthiazol-4-yl, 2-phenyloxazol-4-yl, 2-phenylthiazol-5-yl, 2-phenyloxazol-5-yl, 2-phenylimidazol-4-yl, 3-phenylpyrazol-5-yl, 5-phenylpyrazol-3-yl, 3-phenyl-1,2,4-oxadiazol-5-yl, 3-phenyl-1,2,4-thiadiazol-5-yl, 5-phenyl-1,2,4-oxadiazol-3-yl, 5-phenyl-1,2,4-triazol-3-yl, 2-(thiophen-2-yl)thiazol-4-yl, 2-(pyridin-2-yl)thiazol-4-yl, 2-(pyridin-4-yl)thiazol-4-yl, 2-(quinolin-2-yl)thiazol-4-yl, 2-(pyrazin-2-yl)thiazol-4-yl, each of said fused heteroaryl, heterocyclylheteroaryl and heterobiaryl being optionally substituted by one or more further substituent(s) selected from halo, cyano, alkyl, haloalkyl, cyclopropyl, alkoxy, heterocyclyl optionally substituted by alkyl, aryl, hydroxyl, alkoxyalkyl, hydroxyalkoxy, alkylamino, alkylsulfonylamino, aminoalkoxy, or alkoxycarbonylaminoalkoxy; and/or

wherein, when:

R^1, **$R^{1'}$**, **R^2**, **$R^{2'}$**, **R^3**, **$R^{3'}$** are H, and

L^2 is single bond, and

Ar^1 is a 6-membered aryl optionally substituted by one or more group(s) selected from halo, cyano, C1-C3 alkyl, C1 haloalkyl, and

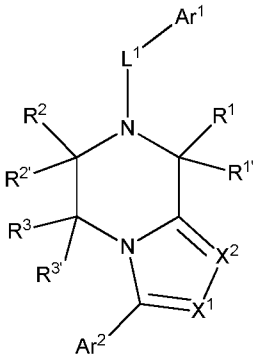
Ar^2 is a 5- to 6-membered aryl or heteroaryl group optionally substituted by one or more group(s) selected from halo, C1-C3 alkyl, hydroxyl, methoxy, or fused to an aryl or heteroaryl group optionally substituted by one or more further halo, C1-C3 alkyl, hydroxyl, methoxy,

then,

Ar^1 is phenyl, 3-halophenyl, 4-halophenyl, 2,3-dichlorophenyl 3,4-dihalophenyl, 3,4,5-trihalophenyl, 4-cyanophenyl, 4-(C1-C3 alkyl)phenyl, 4-(C1 haloalkyl)phenyl, preferably **Ar^1** is phenyl, 3-fluorophenyl, 3-chlorophenyl, 4-fluorophenyl, 4-chlorophenyl, 3,4-difluorophenyl, 3,4-dichlorophenyl, 4-chloro-3-fluorophenyl, 3-chloro-4-fluorophenyl, 3,4,5-trifluorophenyl, 4-cyanophenyl, 4-tolyl, 4-trifluoromethylphenyl, and

Ar^2 is 2-(C1-C3 alkyl)thiazol-4-yl, 5-(C1-C3 alkyl)thiazol-4-yl, pyridin-2-yl, 4-halopyridin-2-yl, 4-(C1-C3 alkyl)pyridin-2-yl, 5-(C1-C3 alkyl)pyridin-2-yl, 6-(C1-C3 alkyl)pyridin-2-yl, quinolin-2-yl, isoquinolin-3-yl, 8-haloquinolin-2-yl, benzothiazol-2-yl, 4,5,6,7-tetrahydro-1,3-benzothiazol-2-yl, preferably, **Ar^2** is 2-isopropylthiazol-4-yl, 5-methylthiazol-4-yl, pyridin-2-yl, 4-chloropyridin-2-yl, 4-methylpyridin-2-yl, 5-methylpyridin-2-yl, 6-methylpyridin-2-yl, quinolin-2-yl, isoquinolin-3-yl, 8-fluoroquinolin-2-yl, 8-chloroquinolin-2-yl, benzothiazol-2-yl, 4,5,6,7-tetrahydro-1,3-benzothiazol-2-yl.

[0019] In one embodiment, preferred compounds of Formula I are those of formula Ia:

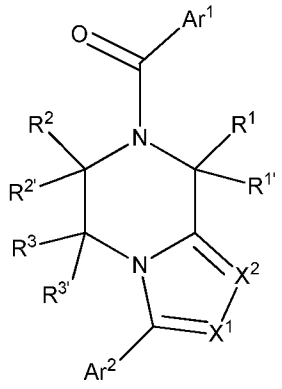


Ia

and pharmaceutically acceptable salts and solvates thereof, wherein

Ar^1, **Ar^2**, **L^1**, **R^1**, **R$^{1'}$**, **R^2**, **R$^{2'}$**, **R^3**, **R$^{3'}$**, **X^1** and **X^2** are as defined above in respect to formula I.

[0020] Preferred compounds of formula Ia are those of formula Ib:



Ib

and pharmaceutically acceptable salts and solvates thereof, wherein

Ar^1 is as defined above in respect to formula I, preferably **Ar^1** is a 5- to 6-membered aryl or heteroaryl group, 5- to 6-membered cycloalkyl group, or a C3-C6 alkyl group each of the aryl, heteroaryl or cycloalkyl groups being optionally substituted by one or more group(s) selected from halo, cyano, alkyl, haloalkyl, 3- to 6-membered cycloalkyl, heteroalkyl, heterocyclyl, aryl, heteroaryl, alkoxy, haloalkoxy, alkylamino, carboxy, alkoxycarbonyl, alkylcarbonyloxy, alkylcarbonylamino, carbamoyl, alkylcarbamoyl, alkylsulfonyl, sulfamoyl, alkylsulfamoyl, alkylsulfonylamino, or two substituents form an alkylenedioxy group, or fused to the aryl or heteroaryl group may be one or more aryl moiety, each of said substituents being optionally substituted by one or more further substituent(s) selected from halo, cyano, alkyl, haloalkyl, cyclopropyl, alkoxy, haloalkoxy, heterocyclyl, aryloxy or heteroaryloxy, more preferably **Ar^1** is a 5- to 6-membered aryl group preferably phenyl, or 5- to 6-membered heteroaryl group preferably pyrazolyl, pyridinyl, more preferably pyrazolyl, C3-C6 alkyl group, each of the aryl or heteroaryl group being optionally substituted by one or more group(s) selected from halo, cyano, alkyl, haloalkyl, C3-C6 cycloalkyl, heteroalkyl, heterocyclyl, aryl, heteroaryl, alkoxy, haloalkoxy, alkylamino, carboxy, alkoxycarbonyl, alkylcarbonyloxy, alkylcarbonylamino, carbamoyl, alkylcarbamoyl, alkylsulfonyl, sulfamoyl, alkylsulfamoyl, alkylsulfonylamino, or two substituents form an alkylenedioxy group, or fused to the aryl or heteroarylgroup may be one aryl moiety, each of said substituents being optionally substituted by one or more further substituent(s) selected from halo, cyano, alkyl, haloalkyl, cyclopropyl, alkoxy, haloalkoxy, heterocyclyl, aryloxy, or heteroaryloxy, even more preferably **Ar^1** is a 5-to 6-membered aryl

preferably phenyl, or heteroaryl preferably pyrrolyl, oxazolyl, thiazolyl, pyrazolyl, triazolyl, oxadiazolyl, thiadiazolyl, pyridinyl, pyrimidinyl, pyrazinyl, pyridazinyl, more preferably pyrazolyl group, isobutyl, each of the aryl or heteroaryl groups being optionally substituted by one or more group(s) selected from halo preferably chloro or fluoro, cyano, alkyl preferably methyl, haloalkyl preferably -CF_3 or -CHF_2, cycloalkyl preferably cyclopropyl, cyclohexyl, aryl preferably phenyl, heteroaryl preferably furanyl, thiophenyl, thiazolyl, isothiazolyl, more preferably thiophen-2-yl, thiophen-3-yl, thiazol-2-yl, thiazol-5-yl, isothiazol-5-yl, even more preferably thiophen-2-yl, thiophen-2-yl, furan-2-yl, or fused to the aryl or heteroaryl group may be one phenyl moiety, each of said substituents being optionally substituted by one or more further substituent(s) selected from halo preferably chloro or fluoro, alkyl preferably methyl, haloalkyl preferably -CF_3 or -CHF_2, cyclopropyl, haloalkoxy preferably -OCF_3 or -$OCHF_2$, or aryloxy preferably phenoxy; and

R^1 is as defined above in respect to formula I, preferably **R^1** is H, C_1-C_4 alkyl preferably isopropyl, methyl, aryl preferably phenyl, or aralkyl preferably benzyl, each of which being optionally substituted by one or more group(s) selected from halo, preferably chloro, fluoro, or hydroxyl, more preferably **R^1** is H, methyl, isopropyl, 2-hydroxyethyl, 4-fluorophenyl or benzyl, still more preferably **R^1** is H, methyl or 2-hydroxyethyl, even more preferably **R^1** is methyl; and

$R^{1'}$ is as defined above in respect to formula I, preferably **$R^{1'}$** is H or methyl, more preferably **$R^{1'}$** is H;

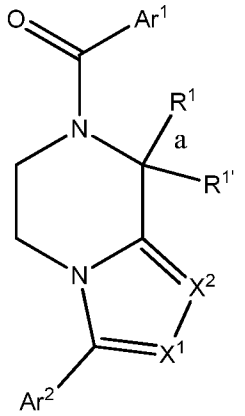
R^2, **$R^{2'}$**, **R^3** and **$R^{3'}$** are as defined above in respect to formula I, preferably **R^2**, **$R^{2'}$**, **R^3** and **$R^{3'}$** are H; and

X^1 and **X^2** are N; and

Ar^2 is as defined above in respect to formula I, preferably , **Ar^2** is a 5- to 6-membered heteroaryl group optionally substituted by one or more group(s) selected from halo, cyano, alkyl, hydroxyalkyl, haloalkyl, C3-C6 cycloalkyl, heteroalkyl, heterocyclyl, aryl, aralkyl, heteroaryl, heteroarylalkyl, hydroxyl, alkoxy, alkylamino, carboxy, alkoxycarbonyl, alkylcarbonyloxy, alkylcarbonylamino, acylamino, carbamoyl, alkylcarbamoyl, alkylsulfonyl, arylsulfonylalkyl, sulfamoyl, alkylsulfamoyl, alkylsulfonylamino, or two substituents form an alkylenedioxy group, or fused to the heteroaryl group may be one or more cycloalkyl, aryl, heterocyclyl or heteroaryl moiety, each of said substituents being optionally substituted by one or more further substituent(s) selected from halo, cyano, alkyl, haloalkyl, cyclopropyl, alkoxy, haloalkoxy, alkoxyalkyl, cycloalkyl, aryl, heterocyclyl optionally substituted by alkyl, heteroaryl, hydroxyl, alkoxy, alkoxyalkyl, hydroxyalkoxy, alkylamino, alkylsulfonylamino, alkoxycarbonylamino, aminoalkoxy or alkoxycarbonylaminoalkoxy,more preferably **Ar^2** is a 5- to 6-membered heteroaryl preferably imidazolyl, pyrazolyl, oxazolyl, thiazolyl, oxadiazolyl, triazolyl, thiadiazolyl or pyridyl group, each of the heteroaryl groups being optionally substituted by one or more group(s) selected from halo preferably chloro or fluoro, cyano, alkyl preferably methyl, isopropyl, isobutyl, haloalkyl preferably -CF_3 or -CHF_2, C3-C6 cycloalkyl preferably cyclopropyl, heterocyclyl preferably pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl, aryl preferably phenyl, aralkyl preferably benzyl, heteroarylalkyl preferably (imidazol-3-yl)methyl, arylsulfonylalkyl preferably phenylsulfonylmethyl, heteroaryl preferably thiophen-2-yl, pyridin-2-yl, pyridin-4-yl, pyrimidin-2-yl, pyrazin-2-yl, quinolin-2-yl, alkoxy preferably methoxy, or fused to the heteroaryl group may be one or more cycloalkyl, aryl, heterocyclyl or heteroaryl moiety, each of said substituents being optionally substituted by one or more further substituent(s) selected from halo preferably bromo, chloro or fluoro, cyano, alkyl preferably methyl, haloalkyl preferably -CF_3 or -CHF_2, cyclopropyl, alkoxy preferably methoxy heterocyclyl optionally substituted by alkyl, preferably pyrrolidin-1yl, piperidin-1-yl, morpholin-4-yl, 4-methylpiperazin-1-yl, aryl preferably phenyl, hydroxyl, alkoxy preferably methoxy, alkoxyalkyl preferably methoxymethyl, methoxyethyl, hydroxyalkoxy preferably hydroxyethoxy, alkylamino preferably dimethylamino, alkylsulfonylamino preferably methylsulfonylamino, alkoxycarbonylamino preferably *tert*-butoxycarbonylamino, aminoalkoxy preferably aminoethyloxy, or alkoxycarbonylaminoalkoxy preferably *tert*-butoxycarbonylaminoethoxy, more preferably **Ar^2** is a pyrazolyl, oxazolyl, thiazolyl, oxadiazolyl triazolyl, thiadiazolyl or pyridyl group, each of which being optionally substituted by one or more groups selected chloro, fluoro, cyano, methyl, isobutyl, C3-C6 cycloalkyl preferably cyclopropyl, heterocyclyl preferably pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl, aryl preferably phenyl, heteroaryl preferably thiophen-2-yl, pyridin-2-yl, pyridin-4-yl, or fused to the oxazolyl, thiazolyl or pyridyl group may be one cyclohexyl or phenyl moiety, each of said substituents being optionally substituted by one or more further substituent(s) selected from bromo, chloro, fluoro, cyano, haloalkyl preferably -CF_3, methoxy, cyclopropyl, heterocyclyl optionally substituted by methyl, preferably pyrrolidin-1yl, piperidin-1-yl, morpholin-4-yl, 4-methylpiperazin-1-yl, phenyl, hydroxyl, alkoxy preferably methoxy, alkoxyalkyl preferably methoxyethyl, hydroxyalkoxy preferably hydroxyethoxy, alkylamino preferably dimethylamino, alkylsulfonylamino preferably methylsulfonylamino, aminoalkoxy preferably aminoethyloxy, even more preferably **Ar^2** is a pyrazolyl, oxazolyl, thiazolyl, oxadiazolyl, thiadiazolyl or pyridyl group, each of which being optionally substituted by one or more groups selected chloro, fluoro, cyano, methyl, isobutyl, heterocyclyl

preferably pyrrolidin-1-yl, piperidin-1-yl, morpholin-4-yl, 4-phenylpiperazin-1-yl, aryl preferably phenyl, heteroaryl preferably thiophen-2-yl, pyridin-2-yl, or fused to the oxazolyl, thiazolyl or pyridyl group may be one cyclohexyl or phenyl moiety, each of said substituents being optionally substituted by one or more further substituent(s) selected from chloro, fluoro, cyano, methyl, cyclopropyl, phenyl, hydroxyl, alkoxy preferably methoxy, or methoxyethyl.

[0021] Preferred compounds of formula Ib are those of formula Ic:



Ic

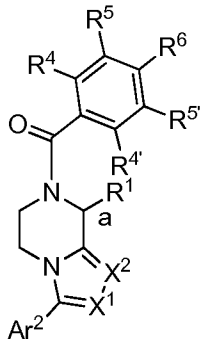
and pharmaceutically acceptable salts and solvates thereof, wherein a depicts the bond linking **R1** to the piperazine moiety, and **Ar1**, **Ar2**, **R1**, **R1'**, **X1**, and **X2** are as defined above in respect to formula Ib.

[0022] In one embodiment, compounds of formula Ic are those wherein **R1'** is H.

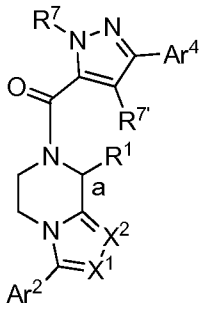
[0023] In another embodiment, compounds of formula Ic are those wherein bond **a** is drawn as a dotted wedge, **R1** is selected from the group consisting of C_1-C_4 alkyl, aryl or aralkyl group, each of said alkyl, aryl or aralkyl groups being optionally substituted by one or more group(s) selected from halo or hydroxyl, and/or **R1'** is H.

[0024] In yet another embodiment, compounds of formula Ic are those wherein bond **a** is drawn as a solid wedge, **R1** is selected from the group consisting of C_1-C_4 alkyl, aryl or aralkyl group, each of said alkyl, aryl or aralkyl groups being optionally substituted by one or more group(s) selected from halo or hydroxyl, and/or **R1'** is H.

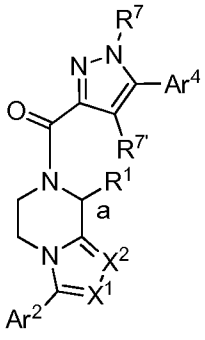
[0025] Preferred compounds of formula Ic are those of formulae Id-1, Id-2, Id-3 and Id-4:



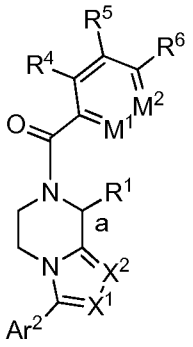
Id-1



Id-2



Id-3



Id-4

and pharmaceutically acceptable salts and solvates thereof, wherein

a depicts the bond linking **R1** to the piperazine moiety; and

Ar2, **R1**, **X1** and **X2** are as defined above in respect to formula Ib; and

R4, **R4'**, **R5**, **R5'** and **R6** are independently selected from H, halo, cyano, alkyl, haloalkyl, C3-C6 cycloalkyl, heteroalkyl, heterocyclyl, aryl, heteroaryl, hydroxyl, alkoxy, haloalkoxy, alkoxyalkoxy, alkylamino, carboxy, alkoxycarbonyl, alkyl-

carbonyloxy, alkylcarbonylamino, haloalkylcarbonylamino, carbamoyl, alkylcarbamoyl, carbamoylamino, alkylcarbamoylamino, alkylsulfonyl, haloalkylsulfonyl, sulfamoyl, alkylsulfamoyl, alkylsulfonylamino, haloalkylsulfonylamino, or R^5 together with R^4 or R^6, or $R^{5'}$ together with $R^{4'}$ or R^6 forms an alkylenedioxy group or a haloalkylenedioxy group, or R^5 together with R^4 or R^6, or $R^{5'}$ together with $R^{4'}$ or R^6 forms an aryl moiety fused to the phenyl group to which they are attached, each of said substituents being optionally substituted by one or more further substituent(s) selected from halo, cyano, alkyl, haloalkyl, cyclopropyl, preferably R^4 and $R^{4'}$ are H and at least one of R^5, $R^{5'}$, R^6 is independently selected from halo preferably chloro or fluoro, cyano, alkyl preferably methyl, haloalkyl preferably $-CF_3$ or $-CHF_2$, more preferably $-CF_3$, cyclopropyl, aryl preferably phenyl, heteroaryl preferably thiophen-2-yl, thiophen-3-yl, or furan-2-yl, the others, if applicable, being H, each of said aryl and heteroaryl group being optionally substituted by one or more further substituent(s) selected from halo preferably chloro or fluoro, alkyl preferably methyl, cyclopropyl, or R^5 together with R^4 or R^6, or $R^{5'}$ together with $R^{4'}$ or R^6 forms a phenyl moiety fused to the phenyl group to which they are attached, more preferably R^4, $R^{4'}$, R^5, and $R^{5'}$ are H and R^6 is selected from cyano, phenyl, thiophen-2-yl, thiophen-3-yl, or furan-2-yl, each of said group being optionally substituted by one or more further substituent(s) selected from chloro, fluoro or methyl, or R^4, $R^{4'}$, R^5 are H and $R^{5'}$, R^6 are independently selected from fluoro or chloro, or R^4 and $R^{4'}$ are H and R^5, $R^{5'}$, R^6 are fluoro; and

R^7 is H or methyl, preferably R^7 is H; and

$R^{7'}$ is H or methyl, preferably $R^{7'}$ is H; and

Ar^4 is a cycloalkyl preferably cyclohexyl or an aryl preferably phenyl group, each of said cycloalkyl or aryl groups being optionally substituted by one or more group(s) selected from halo preferably chloro or fluoro, alkyl preferably methyl, haloalkyl preferably $-CF_3$ or $-CHF_2$, more preferably $-CF_3$, cyclopropyl, haloalkoxy preferably $-OCF_3$ or $-OCHF_2$, more preferably $-OCF_3$, aryloxy preferably phenoxy; and

M^1 is N or C-$R^{4''}$ wherein $R^{4''}$ is selected from H, halo, cyano, alkyl, haloalkyl, C3-C6 cycloalkyl, heteroalkyl, heterocyclyl, aryl, heteroaryl, hydroxyl, alkoxy, haloalkoxy, alkoxyalkoxy, alkylamino, carboxy, alkoxycarbonyl, alkylcarbonyloxy, alkylcarbonylamino, haloalkylcarbonylamino, carbamoyl, alkylcarbamoyl, carbamoylamino, alkylcarbamoylamino, alkylsulfonyl, haloalkylsulfonyl, sulfamoyl, alkylsulfamoyl, alkylsulfonylamino, haloalkylsulfonylamino, each of said substituents being optionally substituted by one or more further substituent(s) selected from halo, cyano, alkyl, haloalkyl, cyclopropyl, preferably $R^{4''}$ is H; and

M^2 is N or M^2 is C-$R^{5''}$ under the condition that M^1 is N, wherein $R^{5''}$ is selected from H, halo, cyano, alkyl, haloalkyl, C3-C6 cycloalkyl, heteroalkyl, heterocyclyl, aryl, heteroaryl, hydroxyl, alkoxy, haloalkoxy, alkoxyalkoxy, alkylamino, carboxy, alkoxycarbonyl, alkylcarbonyloxy, alkylcarbonylamino, haloalkylcarbonylamino, carbamoyl, alkylcarbamoyl, carbamoylamino, alkylcarbamoylamino, alkylsulfonyl, haloalkylsulfonyl, sulfamoyl, alkylsulfamoyl, alkylsulfonylamino, haloalkylsulfonylamino, or $R^{5''}$ together with R^6 forms an alkylenedioxy group or a haloalkylenedioxy group, or an aryl moiety fused to the pyridinyl group to which they are attached, each of said substituents being optionally substituted by one or more further substituent(s) selected from halo, cyano, alkyl, haloalkyl, cyclopropyl, preferably $R^{5''}$ is selected from H, halo preferably chloro or fluoro, alkyl preferably methyl, haloalkyl preferably $-CF_3$ or $-CHF_2$, more preferably $-CF_3$, more preferably $R^{5''}$ is H; and

wherein, in formula Id-1 when:

R^1 is H, and

R^4, $R^{4'}$, R^5, $R^{5'}$ and R^6 are independently selected from H, halo, cyano, C1-C3 alkyl, C1 haloalkyl, and

Ar^2 is a 5- to 6-membered aryl or heteroaryl group optionally substituted by one or more group(s) selected from halo, C1-C3 alkyl, hydroxyl, alkoxy, or fused to an aryl group optionally substituted by one or more further halo, C1-C3 alkyl, hydroxyl, methoxy,
then,

R^4, $R^{4'}$, R^5, $R^{5'}$ and R^6 are H, or R^4, $R^{4'}$, $R^{5'}$, R^6 are H and R^5 is halo, or R^4, $R^{4'}$, R^5, $R^{5'}$ are H and R^6 is halo, cyano, C1-C3 alkyl, C1 haloalkyl, or $R^{4'}$, $R^{5'}$, R^6 are H and R^4, R^5 are halo, or R^4, $R^{4'}$, $R^{5'}$ are H and R^5, R^6 are independently halo, or R^4, $R^{4'}$ are H and R^5, $R^{5'}$, R^6 are halo, preferably, R^4, $R^{4'}$, R^5, $R^{5'}$ and R^6 are H, or R^4, $R^{4'}$, $R^{5'}$, R^6 are H and R^5 is fluoro, chloro, or R^4, $R^{4'}$, R^5, $R^{5'}$ are H and R^6 is fluoro, chloro, cyano, methyl, trifluoromethyl, or R^4, $R^{4'}$, $R^{5'}$ are H and R^5, R^6 are independently fluoro, chloro, or R^4, $R^{4'}$ are H and R^5, $R^{5'}$,

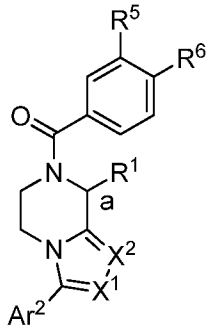
R^6 are fluoro, and

Ar^2 is 2-(C1-C3 alkyl)thiazol-4-yl, 5-(C1-C3 alkyl)thiazol-4-yl, pyridin-2-yl, 4-halopyridin-2-yl, 4-(C1-C3 alkyl)pyridin-2-yl, 5-(C1-C3 alkyl)pyridin-2-yl, 6-(C1-C3 alkyl)pyridin-2-yl, quinolin-2-yl, isoquinolin-3-yl, 8-haloquinolin-2-yl, benzothiazol-2-yl, 4,5,6,7-tetrahydro-1,3-benzothiazol-2-yl, preferably Ar^2 is 2-isopropylthiazol-4-yl, 5-methylthiazol-4-yl pyridin-2-yl, 6-methylpyridin-2-yl, 5-methylpyridin-2-yl, 4-methylpyridin-2-yl, 4-chloropyridin-2-yl, quinolin-2-yl, isoquinolin-3-yl, 8-fluoroquinolin-2-yl, 8-chloroquinolin-2-yl, benzothiazol-2-yl, 4,5,6,7-tetrahydro-1,3-benzothiazol-2-yl.

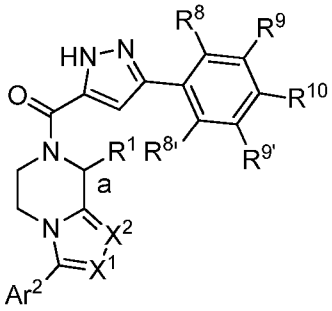
[0026] In another embodiment, compounds of formulae Id-1, Id-2, Id-3 and Id-4 are those wherein bond a is drawn as a dotted wedge, and/or R^1 is selected from the group consisting of C_1-C_4 alkyl, aryl or aralkyl group, each of said alkyl, aryl or aralkyl groups being optionally substituted by one or more group(s) selected from halo or hydroxyl.

[0027] In yet another embodiment, compounds of formulae Id-1, Id-2, Id-3 and Id-4 are those wherein bond a is drawn as a solid wedge, and/or R^1 is selected from the group consisting of C_1-C_4 alkyl, aryl or aralkyl group, each of said alkyl, aryl or aralkyl groups being optionally substituted by one or more group(s) selected from halo or hydroxyl.

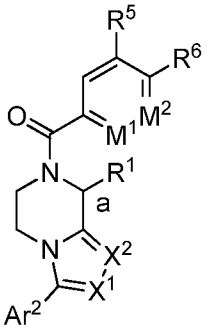
[0028] Preferred compounds of formulae Id-1, Id-2, Id-3 and Id-4 are those of formulae Ie-1, Ie-2 and Ie-3:



Ie-1



Ie-2



Ie-3

and pharmaceutically acceptable salts and solvates thereof, wherein

a depicts the bond linking R^1 to the piperazine moiety; and

Ar^2, R^1, X^1 and X^2 are as defined above in respect to formula Ib; and

R^5 and R^6 are independently selected from H, halo preferably chloro or fluoro, cyano, alkyl preferably methyl, cyclopropyl, aryl preferably phenyl, heteroaryl, preferably thiophen-2-yl, thiophen-2-yl, furan-2-yl, each of said aryl and heteroaryl groups being optionally substituted by one or more group(s) selected from halo, preferably chloro or fluoro, alkyl preferably methyl, cyclopropyl, or R^5 and R^6 together form a phenyl moiety fused to the phenyl ring they are attached to, preferably R^5 is H and R^6 is selected from H, chloro, fluoro, cyano, methyl, cyclopropyl, phenyl, 4-fluorophenyl, 4-chlorophenyl, 4-cyanophenyl, 4-tolyl, 3-tolyl, 2-tolyl, 2-fluorophenyl, 3,4-difluorophenyl, 3,4-dichlorophenyl, 3-fluoro-4-chlorophenyl, 3,5-difluorophenyl, thiophen-2-yl, 5-methylthiophen-2-yl, 2-methylthiophen-3-yl, furan-2-yl, or R^6 is H and R^5 is selected from chloro, fluoro, methyl, cyclopropyl or phenyl, or R^5 and R^6 are both chloro, more preferably R^5 is H and R^6 is selected from H, chloro, fluoro, phenyl, 4-fluorophenyl, 4-chlorophenyl, 4-cyanophenyl, 4-tolyl, 2-fluorophenyl, 3,4-difluorophenyl, thiophen-2-yl, 5-methylthiophen-2-yl, 2-methylthiophen-3-yl, or R^6 is H and R^5 is selected from chloro, fluoro, methyl or phenyl, or R^5 and R^6 are both chloro, even more preferably R^5 is H and R^6 is selected from phenyl, 4-fluorophenyl, thiophen-2-yl, 5-methylthiophen-2-yl, 2-methylthiophen-3-yl, or R^5 and R^6 are both chloro; and

R^8, $R^{8'}$, R^9, $R^{9'}$ and R^{10} are independently selected from H, halo preferably fluoro or chloro, haloalkyl preferably $-CF_3$ or $-CHF_2$, more preferably $-CF_3$, cyclopropyl or haloalkoxy preferably $-OCF_3$ or $-OCHF_2$ more preferably $-OCF_3$, or R^8, $R^{8'}$, R^9, $R^{9'}$ are H and R^{10} is phenoxy, preferably $R^{8'}$, R^9, $R^{9'}$, R^{10} are H and R^8 is $-CF_3$, or R^8, $R^{8'}$, $R^{9'}$, R^{10} are H and R^9 is selected from chloro or fluoro, or R^8, $R^{8'}$, R^9, $R^{9'}$ are H and R^{10} is selected from chloro, fluoro, $-CF_3$, $-OCF_3$ or $-OCHF_2$, phenoxy, or R^8, R^9, $R^{9'}$ are H, $R^{8'}$ is selected from chloro, fluoro $-CF_3$, and R^{10} is selected from fluoro or chloro, or R^8, $R^{8'}$, $R^{9'}$ are H and R^9, R^{10} are independently selected from fluoro or chloro, more preferably

R^8, $R^{8'}$, R^9, $R^{9'}$ are H and R^{10} is selected from chloro, fluoro or phenoxy, or R^8, R^9, $R^{9'}$ are H and $R^{8'}$, R^{10} are both chloro, or R^8 $R^{8'}$, $R^{9'}$ are H and R^9, R^{10} are both chloro; and

M^1 and M^2 are as defined above in respect to formula Id-4; and

wherein, in formula Ie-1 when:

R^1 is H, and

R^5 and R^6 are independently selected from H, halo, cyano, C1-C3 alkyl, and

Ar^2 is a 5- to 6-membered aryl or heteroaryl group optionally substituted by one or more group(s) selected from halo, C1-C3 alkyl, hydroxyl, alkoxy, or fused to an aryl group optionally substituted by one or more further halo, C1-C3 alkyl, hydroxyl, methoxy,
then,

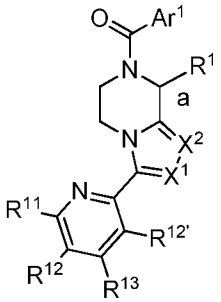
R^6 is H and R^5 is H, halo, or R^5 is H and R^6 is halo, cyano, C1-C3 alkyl, C1 haloalkyl, or R^5 and R^6 are independently halo, preferably R^6 is H and R^5 is fluoro, chloro, or R^5 is H and R^6 is fluoro, chloro, cyano, methyl, trifluoromethyl or R^5 and R^6 are independently fluoro, chloro, and

Ar^2 is 2-(C1-C3 alkyl)thiazol-4-yl, 5-(C1-C3 alkyl)thiazol-4-yl, pyridin-2-yl, 4-halopyridin-2-yl, 4-(C1-C3 alkyl)pyridin-2-yl, 5-(C1-C3 alkyl)pyridin-2-yl, 6-(C1-C3 alkyl)pyridin-2-yl, quinolin-2-yl, isoquinolin-3-yl, 8-haloquinolin-2-yl, benzothiazol-2-yl, 4,5,6,7-tetrahydro-1,3-benzothiazol-2-yl, preferably Ar^2 is 2-isopropylthiazol-4-yl, 5-methylthiazol-4-yl, pyridin-2-yl, 6-methylpyridin-2-yl, 5-methylpyridin-2-yl, 4-methylpyridin-2-yl, 4-chloropyridin-2-yl, quinolin-2-yl, isoquinolin-3-yl, 8-fluoroquinolin-2-yl, 8-chloroquinolin-2-yl, benzothiazol-2-yl, 4,5,6,7-tetrahydro-1,3-benzothiazol-2-yl.

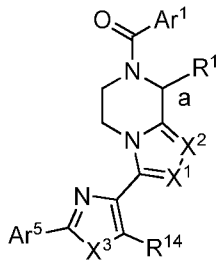
[0029] In another embodiment, compounds of formulae Ie-1, Ie-2 and Ie-3 are those wherein bond **a** is drawn as a dotted wedge, and/or R^1 is selected from the group consisting of C_1-C_4 alkyl, aryl or aralkyl group, each of said alkyl, aryl or aralkyl groups being optionally substituted by one or more group(s) selected from halo or hydroxyl.

[0030] In yet another embodiment, compounds of formulae Ie-1, Ie-2 and Ie-3 are those wherein bond a is drawn as a solid wedge, and/or R^1 is selected from the group consisting of C_1-C_4 alkyl, aryl or aralkyl group, each of said alkyl, aryl or aralkyl groups being optionally substituted by one or more group(s) selected from halo or hydroxyl.

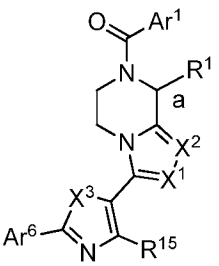
[0031] Other preferred compounds of formula Ic are those of formulae If-1, If-2, If-3, If-4, If-5, If-6, If-7 and If-8:



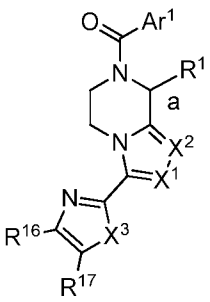
If-1



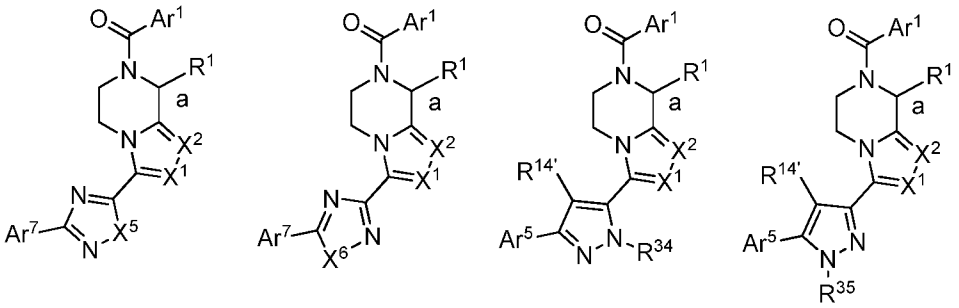
If-2



If-3



If-4



If-5 If-6 If-7 If-8

and pharmaceutically acceptable salts and solvates thereof, wherein

a designates the bond linking **R^1** to the piperazine moiety; and

Ar^1 **R^1**, **X^1** and **X^2** are as defined above in respect to formula Ib; and

R^{11}, **R^{12}**, **$R^{12'}$** and **R^{13}** are independently selected from H, halo, cyano, alkyl, hydroxyalkyl, haloalkyl, C3-C6 cycloalkyl, heteroalkyl, heterocyclyl, aryl, heteroaryl, hydroxyl, alkoxy, haloalkoxy, alkylamino, carboxy, alkoxycarbonyl, alkylcarbonyloxy, alkylcarbonylamino, haloalkylcarbonylamino, acylamino, carbamoyl, alkylcarbamoyl, carbamoylalkyl, carbamoylamino, alkylcarbamoylamino, alkylsulfonyl, haloalkylsulfonyl, sulfamoyl, alkylsulfamoyl, alkylsulfonylamino, haloalkylsulfonylamino, or **R^{12}** together with **R^{11}** or **R^{13}**, or **R^{13}** together with **$R^{12'}$** forms an alkylenedioxy group or a haloalkylenedioxy group, or **R^{12}** together with **R^{11}** or **R^{13}** forms a cycloalkyl, aryl, heterocyclyl or heteroaryl moiety fused to the pyridyl group to which they are attached, each of said groups being optionally substituted by one or more group(s) selected from halo, cyano, alkyl, haloalkyl, cyclopropyl, alkoxy, haloalkoxy or hydroxyl, preferably **R^{11}**, **R^{12}**, **$R^{12'}$** and **R^{13}** are independently selected from H, halo preferably chloro or fluoro, alkyl preferably methyl, haloalkyl preferably $-CF_3$ or $-CHF_2$, more preferably $-CF_3$, C3-C6 cycloalkyl, preferably cyclopropyl, heterocyclyl preferably pyrrolidin-1-yl, morpholin-4-yl, aryl preferably phenyl, or **R^{12}** together with **R^{11}** or **R^{13}** forms an aryl preferably phenyl moiety fused to the pyridyl group to which they are attached, each of said groups being optionally substituted by one or more group(s) selected from halo, cyano, alkyl, haloalkyl, alkoxy or haloalkoxy more preferably **R^{12}**, **$R^{12'}$** and **R^{13}** are H and **R^{11}** is selected from methyl, $-CF_3$, cyclopropyl, pyrrolidin-1-yl, morpholin-4-yl or phenyl, or **R^{11}**, **$R^{12'}$**, **R^{13}** are H and **R^{12}** is methyl, cyclopropyl, or **R^{11}**, **R^{12}**, **$R^{12'}$** are H and **R^{13}** is selected from chloro or methyl, cyclopropyl, or **R^{12}** together with **R^{11}** or **R^{13}** forms an aryl preferably phenyl moiety fused to the pyridyl group to which they are attached, thus forming a fused ring system, each of said phenyl and fused ring system being optionally substituted by one or more halo preferably chloro or fluoro, still more preferably **R^{12}**, **$R^{12'}$** and **R^{13}** are H and **R^{11}** is selected from methyl, pyrrolidin-1-yl or morpholin-4-yl, or **R^{12}** together with **R^{11}** forms a phenyl moiety fused to the pyridyl group to which they are attached, thus forming a quinoline moiety, each of said phenyl and quinoline groups being optionally substituted by one or more group(s) selected from halo preferably chloro or fluoro, even more preferably **R^{12}**, **$R^{12'}$** and **R^{13}** are H and **R^{11}** is methyl, or **R^{12}** together with **R^{11}** forms a phenyl moiety fused to the pyridyl group to which they are attached, thus forming a quinoline moiety; and

Ar^5 is a heterocyclyl, aryl, heteroaryl, aralkyl, heteroarylalkyl, or arylsulfonylalkyl group, each of which being optionally substituted by one or more group(s) selected from halo, cyano, alkyl, haloalkyl, cyclopropyl, alkoxy, haloalkoxy, heterocyclyl optionally substituted by alkyl, aryl, hydroxyl, alkoxy, alkoxyalkyl, hydroxyalkoxy, alkylamino, alkylsulfonylamino, aminoalkoxy, or alkoxycarbonylaminoalkoxy preferably *tert*-butyloxycarbonylaminoethoxy, preferably **Ar^5** is pyrrolidin-1-yl, morpholin-4-yl, piperidin-1-yl, 4-methylpiperazin-1-yl, each of which being optionally substituted by one or more halo preferably fluoro, alkyl preferably methyl, alkoxyalkyl preferably methoxymethyl, methoxyethyl, or **Ar^5** is 4-phenyl-piperazin-1-yl or a phenyl group optionally substituted by one or more group(s) selected from halo preferably bromo, chloro or fluoro, cyano, haloalkyl preferably $-CF_3$ or $-CHF_2$, more preferably $-CF_3$, cyclopropyl, hydroxyl, alkoxy preferably methoxy, heterocyclyl optionally substituted by alkyl, preferably pyrrolidin-1-yl, piperidin-1-yl, morpholin-4-yl, 4-methylpiperazin-1-yl, hydroxyalkoxy preferably hydroxyethoxy, alkylamino preferably dimethylamino, alkylsulfonylamino preferably methylsulfonylamino, aminoalkoxy preferably aminoethoxy, or **Ar^5** is thiophen-2-yl, pyridin-2-yl, pyridin-4-yl, pyrimidin-2-yl, pyrazin-2-yl, quinolin-2-yl, 4-chlorobenzyl, 4,5-dichloro(imidazol-3-yl)methyl, 4-chlorophenylsulfonylmethyl more preferably **Ar^5** is a phenyl optionally substituted by one or more group(s) selected from chloro or fluoro, cyano, $-CF_3$, hydroxyl, methoxy, 4-methylpiperazin-1-yl hydroxyethoxy or

Ar^5 is thiophen-2-yl, pyridin-2-yl even more preferably **Ar^5** is phenyl, 2-fluorophenyl, 4-fluorophenyl, 4-chlorophenyl, 3-fluorophenyl, 3-chlorophenyl, 2-chlorophenyl, 2,4-difluorophenyl or 2,4-dichlorophenyl, 4-cyanophenyl; and **X^3** is O or S, preferably **X^3** is S; and

R^{14} is H or methyl, preferably **R^{14}** is H; and

Ar^6 is a heterocyclyl, aryl or heteroaryl group, each of which being optionally substituted by one or more group(s) selected from halo, cyano, alkyl, haloalkyl, cyclopropyl, alkoxy, haloalkoxy, aryl or hydroxyl, preferably **Ar^6** is a phenyl group optionally substituted by one or more group(s) selected from halo preferably chloro or fluoro, haloalkyl preferably -CF_3 or -CHF_2, cyclopropyl, more preferably -CF_3, or alkoxy preferably methoxy, more preferably **Ar^6** is phenyl, 4-fluorophenyl, 2,4-difluorophenyl; and

R^{15} is H or methyl, preferably **R^{15}** is methyl; and

R^{16} is a heterocyclyl, aryl or heteroaryl group, each of said groups being optionally substituted by one or more group(s) selected from halo, cyano, alkyl, haloalkyl, cyclopropyl, alkoxy, haloalkoxy or hydroxyl, preferably **R^{16}** is a phenyl group optionally substituted by one or more group(s) selected from halo preferably chloro or fluoro, haloalkyl preferably-CF_3 or -CHF_2, more preferably -CF_3, alkoxy preferably methoxy, more preferably **R^{16}** is phenyl; and

R^{17} is H, methyl or **R^{17}** together with **R^{16}** forms a cycloalkyl or aryl moiety fused to the thiazolyl group to which they are attached, thus forming a fused ring system, said fused ring system being optionally substituted by one or more group(s) selected from halo, cyano, alkyl, haloalkyl, cyclopropyl, alkoxy, haloalkoxy or hydroxyl, preferably **R^{17}** is H or **R^{17}** together with **R^{16}** forms a cyclohexyl or phenyl moiety fused to the thiazolyl group to which they are attached, more preferably **R^{17}** together with **R^{16}** forms a cyclohexyl or phenyl moiety fused to the thiazolyl group to which they are attached; and

X^5 is O or S, or N-**R^{36}** wherein **R^{36}** is H or C1-C3 alkyl, preferably **X^5** is O or S, more preferably **X^5** is O; and

Ar^7 is a heterocyclyl, aryl or heteroaryl group, each of which being optionally substituted by one or more group(s) selected from halo, cyano, alkyl, haloalkyl, cyclopropyl, alkoxy, haloalkoxy, aryl or hydroxyl, preferably **Ar^7** is a phenyl group optionally substituted by one or more group(s) selected from halo preferably chloro or fluoro, haloalkyl preferably -CF_3 or -CHF_2, more preferably -CF_3, or alkoxy preferably methoxy, more preferably **Ar^7** is phenyl, 4-fluorophenyl, 2,4-difluorophenyl; and

X^6 is O, S or N-**$R^{36'}$** wherein **$R^{36'}$** is H or C1-C3 alkyl, preferably **X^6** is O or NH, more preferably **X^6** is O; and

$R^{14'}$ is H or methyl, preferably **$R^{14'}$** is H; and

R^{34} is H, alkyl, alkoxyalkyl, hydroxyalkyl, alkoxycarbonylaminoalkyl, preferably **R^{34}** is H, methyl, ethyl, hydroxyethyl, methoxyethyl, *tert*-butoxycarbonylaminoethyl, more preferably **R^{34}** is H, methyl, hydroxyethyl, methoxyethyl; and

R^{35} is H, alkyl, alkoxyalkyl, hydroxyalkyl, alkoxycarbonylaminoalkyl, preferably **R^{35}** is H, methyl, ethyl, hydroxyethyl, methoxyethyl, *tert*-butoxycarbonylaminoethyl, more preferably **R^{35}** is H, methyl, hydroxyethyl; and

wherein,

- in formula If-1 when:

  R^1 is H, and

  Ar^1 is a 6-membered aryl optionally substituted by one or more group(s) selected from halo, cyano, C1-C3 alkyl, C1-haloalkyl, and

  R^{11}, **R^{12}**, **$R^{12'}$** and **R^{13}** are independently selected from H, halo, C1-C3 alkyl, hydroxyl, methoxy, or **R^{12}** together with **R^{11}** or **R^{13}** forms an aryl or heterocyclyl or heteroaryl moiety fused to the pyridyl group to which they are attached and being optionally substituted by one or more group(s) selected from halo, C1-C3 alkyl, methoxy or hydroxyl,
  then,

Ar^1 is phenyl, 3-halophenyl, 4-halophenyl, 2,3-dichlorophenyl, 3,4-dihalophenyl, 3,4,5-trihalophenyl, 4-cyanophenyl, 4-(C1-C3 alkyl)phenyl, 4-(C1 haloalkyl)phenyl, preferably **Ar^1** is phenyl, 4-fluorophenyl, 4-chlorophenyl, 3-chlorophenyl, 3-fluorophenyl, 3,4-dichlorophenyl, 3,4-difluorophenyl, 3,4,5-trifluorophenyl, 4-chloro-3-fluorophenyl, 3-chloro-4-fluorophenyl, 4-cyanophenyl, 4-tolyl, 4-trifluoromethylphenyl, and

R^{11}, R^{12}, R$^{12'}$ and **R^{13}** are H, or **R^{11}**, **R^{12}**, **R$^{12'}$** are H and **R^{13}** is halo, C1-C3 alkyl, or **R^{11}**, **R$^{12'}$**, **R^{13}** are H and **R^{12}** is C1-C3 alkyl, or **R^{12}**, **R$^{12'}$**, **R^{13}** are H and **R^{11}** is C1-C3 alkyl, or **R^{11}**, **R^{12}**, **R$^{12'}$** and **R^{13}** together with the pyridyl group they are attached form a quinolin-2-yl, isoquinolin-3-yl or 8-haloquinolin-2-yl moiety, preferably **R^{11}**, **R^{12}**, **R$^{12'}$** and **R^{13}** are H, or **R^{11}**, **R^{12}**, **R$^{12'}$** are H and **R^{13}** is chloro, methyl, or **R^{11}**, **R$^{12'}$**, **R^{13}** are H and **R^{12}** is methyl, or **R^{12}**, **R$^{12'}$**, **R^{13}** are H and **R^{11}** is methyl, or **R^{11}**, **R^{12}**, **R$^{12'}$** and **R^{13}** together with the pyridyl group they are attached form a quinolin-2-yl, isoquinolin-3-yl, 8-fluoroquinolin-2-yl or 8-chloroquinolin-2-yl moiety; and

- in formula If-4 when:

R^1 is H, and

Ar^1 is a 6-membered aryl optionally substituted by one or more group(s) selected from halo, cyano, C1-C3 alkyl, C1-haloalkyl, and

R^{17} together with **R^{16}** forms a cycloalkyl or aryl moiety fused to the thiazolyl group to which they are attached, thus forming a fused ring system, said fused ring system being optionally substituted by one or more group(s) selected from halo, C1-3 alkyl, methoxy or hydroxyl,
then

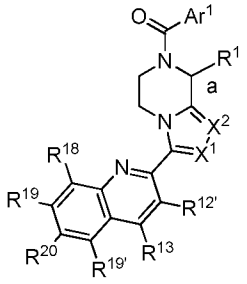
Ar^1 is phenyl, 3-halophenyl, 4-halophenyl, 2,3-dichlorophenyl, 3,4-dihalophenyl, 3,4,5-trihalophenyl, 4-cyanophenyl, 4-(C1-C3 alkyl)phenyl, 4-(C1 haloalkyl)phenyl, preferably **Ar^1** is phenyl, 4-fluorophenyl, 4-chlorophenyl, 3-chlorophenyl, 3-fluorophenyl, 3,4-dichlorophenyl, 3,4-difluorophenyl, 3,4,5-trifluorophenyl, 4-chloro-3-fluorophenyl, 3-chloro-4-fluorophenyl, 4-cyanophenyl, 4-tolyl, 4-trifluoromethylphenyl, and

R^{17} and **R^{16}** form together with the thiazolyl group to which they are attached a benzothiazol-2-yl or 4,5,6,7-tetrahydro-1,3-benzothiazol-2-yl moiety.

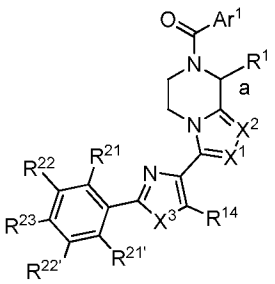
[0032] In another embodiment, compounds of formulae If-1, If-2, If-3, If-4, If-5, If-6, If-7 and If-8 are those wherein bond a is drawn as a dotted wedge, and/or **R^1** is selected from the group consisting of C_1-C_4 alkyl, aryl or aralkyl group, each of said alkyl, aryl or aralkyl groups being optionally substituted by one or more group(s) selected from halo or hydroxyl.

[0033] In yet another embodiment, compounds of formulae If-1, If-2, If-3, If-4, If-5, If-6, If-7 and If-8 are those wherein bond a is drawn as a solid wedge, and/or **R^1** is selected from the group consisting of C_1-C_4 alkyl, aryl or aralkyl group, each of said alkyl, aryl or aralkyl groups being optionally substituted by one or more group(s) selected from halo or hydroxyl.

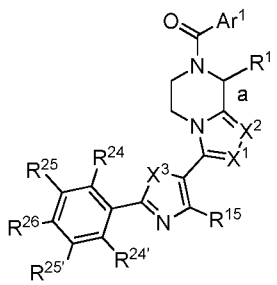
[0034] Preferred compounds of formulae If-1, If-2, If-3, If-4, If-5, If-6, If-7 and If-8 are those of formulae Ig-1, Ig-2, Ig-3, Ig-4, Ig-5, Ig-6, Ig-7 and Ig-8 respectively:



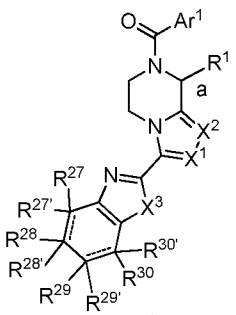
Ig-1



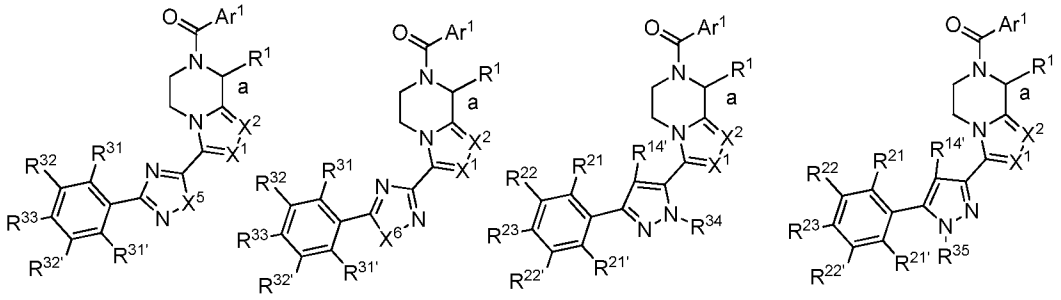
Ig-2



Ig-3



Ig-4



Ig-5 Ig-6 Ig-7 Ig-8

and pharmaceutically acceptable salts, and solvates thereof, wherein

a depicts the bond linking R^1 to the piperazine moiety; and

Ar^1, R^1, X^1 and X^2 are as defined above in respect to formula Ib; and

$R^{12'}$ and R^{13} are independently selected from H, halo, cyano, alkyl, hydroxyalkyl, haloalkyl, cycloalkyl, heteroalkyl, hydroxyl, alkoxy, haloalkoxy, carboxy, alkoxycarbonyl, alkylcarbonyloxy, alkylcarbonylamino, haloalkylcarbonylamino, acylamino, carbamoyl, alkylcarbamoyl, carbamoylalkyl, carbamoylamino, alkylcarbamoylamino, alkylsulfonyl, haloalkylsulfonyl, sulfamoyl, alkylsulfamoyl, alkylsulfonylamino, haloalkylsulfonylamino, or R^{13} together with $R^{12'}$ forms an alkylenedioxy group or a haloalkylenedioxy group, each of said groups being optionally substituted by one or more group(s) selected from halo, cyano, alkyl, haloalkyl, alkoxy, haloalkoxy, hydroxyl or oxo, preferably, $R^{12'}$ and R^{13} are independently selected from H, halo preferably chloro or fluoro, alkyl preferably methyl, haloalkyl preferably $-CF_3$ or $-CHF_2$, more preferably $-CF_3$, more preferably $R^{12'}$ and R^{13} are H; and

X^3 is as defined above in respect to formula If-2, preferably X^3 is S; and

R^{18}, R^{19}, $R^{19'}$ and R^{20} are independently selected from H, halo, cyano, alkyl, haloalkyl, cyclopropyl, alkoxy, haloalkoxy, preferably R^{19}, $R^{19'}$ and R^{20} are H and R^{18} is selected from H, fluoro or chloro, more preferably R^{18}, R^{19}, $R^{19'}$ and R^{20} are H; and

R^{14} is as defined above in respect to formula If-2; and

R^{21}, $R^{21'}$, R^{22}, $R^{22'}$ and R^{23} are independently selected from H, halo preferably bromo, chloro or fluoro, cyano, alkyl, haloalkyl preferably $-CF_3$ or $-CHF_2$, more preferably $-CF_3$, cyclopropyl, heterocyclyl optionally substituted by alkyl, preferably pyrrolidin-1-yl, piperidin-1-yl, morpholin-4-yl, 4-methylpiperazin-1-yl, hydroxyl, alkoxy preferably methoxy, haloalkoxy, hydroxyalkoxy preferably hydroxyethoxy, alkylamino preferably dimethylamino, alkylsulfonylamino preferably methylsulfonylamino, aminoalkoxy preferably aminoethoxy, alkoxycarbonylaminoalkoxy preferably *tert*-butyloxycarbonylaminoethoxy, preferably R^{21}, $R^{21'}$, R^{22} and $R^{22'}$ are H and R^{23} is selected from bromo, fluoro, chloro, cyano, methyl $-CF_3$, pyrrolidin-1-yl, piperidin-1-yl, morpholin-4-yl, 4-methylpiperazin-1-yl methoxy, dimethylamino or methylsulfonylamino, or R^{21}, $R^{21'}$, $R^{22'}$ and R^{23} are H and R^{22} is selected from fluoro, chloro, bromo, cyano, $-CF_3$, dimethylamino or methylsulfonylamino or $R^{21'}$, R^{22}, $R^{22'}$ and R^{23} are H and R^{21} is fluoro, chloro, bromo, cyano, hydroxyl, methoxy, hydroxyethoxy, dimethylamino, methylsulfonylamino, aminoethoxy or *tert*-butoxycarbonylaminoethoxy or $R^{21'}$, R^{22}, $R^{22'}$ are H and R^{21} and R^{23} are independently selected from H, chloro or fluoro, or $R^{21'}$, $R^{22'}$, and R^{23} are H and R^{21} and R^{22} are chloro, or R^{21}, $R^{21'}$ and R^{23} are H and R^{22} and $R^{22'}$ are chloro, more preferably R^{21}, $R^{21'}$, R^{22} and $R^{22'}$ are H and R^{23} is selected from fluoro or chloro, cyano, or R^{21}, $R^{21'}$, $R^{22'}$ and R^{23} are H and R^{22} is chloro, or $R^{21'}$, R^{22}, $R^{22'}$ and R^{23} are H and R^{21} is chloro, or $R^{21'}$, R^{22}, $R^{22'}$ are H and R^{21} and R^{23} are independently selected from H, chloro or fluoro, even more preferably R^{21}, $R^{21'}$, R^{22} and $R^{22'}$ are H and R^{23} is selected from H, fluoro, chloro, cyano, or $R^{21'}$, R^{22}, $R^{22'}$ are H and R^{21} and R^{23} are independently selected from H, chloro or fluoro; and

R^{15} is as defined above in respect to formula If-3, preferably R^{15} is methyl; and

R^{2a}, $R^{2a'}$, R^{25}, $R^{25'}$ and R^{26} are independently selected from H, halo preferably chloro or fluoro, haloalkyl preferably $-CF_3$ or $-CHF_2$, more preferably $-CF_3$, cyclopropyl, preferably R^{24}, $R^{24'}$, R^{25}, $R^{25'}$ are H and R^{26} is selected from H,

chloro or fluoro, more preferably R^{24}, $R^{2a'}$, R^{25}, $R^{25'}$ and R^{26} are H; and

R^{27}, R^{28}, R^{29} and R^{30} are independently selected from H, halo, cyano, alkyl, haloalkyl, cyclopropyl, alkoxy, haloalkoxy, preferably R^{28}, R^{29} and R^{30} are H and R^{27} is selected from H, fluoro or chloro, more preferably R^{27}, R^{28}, R^{29} and R^{30} are H; and

$R^{27'}$, $R^{28'}$, $R^{29'}$ and $R^{30'}$ are absent, or $R^{27'}$, $R^{28'}$, $R^{29'}$ and $R^{30'}$ are H under the condition that R^{28}, R^{29} and R^{30} are H and that R^{27} is selected from H, chloro or fluoro preferably $R^{27'}$, $R^{28'}$, $R^{29'}$ and $R^{30'}$ are absent or H under the condition that R^{27}, R^{28}, R^{29} and R^{30} are H; and

the two bonds represented by the dotted lines in formula Ig-4 are both absent, or both present under the condition that $R^{27'}$, $R^{28'}$, $R^{29'}$ and $R^{30'}$ are absent; and

X^5 is as defined above in respect to formula If-5, preferably X^5 is O; and

R^{31}, $R^{31'}$, R^{32}, $R^{32'}$ and R^{33} are independently selected from H, halo preferably chloro or fluoro, cyano, alkyl, haloalkyl preferably $-CF_3$ or $-CHF_2$, more preferably $-CF_3$, cyclopropyl, alkoxy preferably methoxy, haloalkoxy, preferably R^{31}, $R^{31'}$, R^{32} and $R^{32'}$ are H and R^{33} is selected from fluoro, chloro, cyano, $-CF_3$ or methoxy, or R^{31}, $R^{31'}$, $R^{32'}$ and R^{33} are H and R^{32} is selected from chloro or $-CF_3$, or $R^{31'}$, R^{32}, $R^{32'}$ and R^{33} are H and R^{31} is chloro, or $R^{31'}$, R^{32}, $R^{32'}$ are H and R^{31} and R^{33} are independently selected from H, chloro or fluoro, or $R^{31'}$, $R^{32'}$, and R^{33} are H and R^{31} and R^{32} are chloro, or R^{31}, $R^{31'}$ and R^{33} are H and R^{32} and $R^{32'}$ are chloro, more preferably R^{31}, $R^{31'}$, R^{32} and $R^{32'}$ are H and R^{33} is selected from fluoro, chloro or cyano or R^{31}, $R^{31'}$, $R^{32'}$ and R^{33} are H and R^{32} is chloro, or $R^{31'}$, R^{32}, $R^{32'}$ and R^{33} are H and R^{31} is chloro, or $R^{31'}$, R^{32}, $R^{32'}$ are H and R^{31} and R^{33} are independently selected from H, chloro or fluoro, even more preferably R^{31}, $R^{31'}$, R^{32} and $R^{32'}$ are H and R^{33} is selected from H, fluoro or chloro, or $R^{31'}$, R^{32}, $R^{32'}$ are H and R^{31} and R^{33} are fluoro; and

X^6 is as defined above in respect to formula If-6; and

$R^{14'}$ is as defined above in respect to formulae If-7 and If-8, preferably $R^{14'}$ is H; and

R^{34} and R^{35} are as defined above in respect to formula If-7; and

wherein,

- in formula Ig-1 when:

  R^1 is H, and

  Ar^1 is a 6-membered aryl optionally substituted by one or more group(s) selected from halo, cyano, C1-C3 alkyl, C1-haloalkyl, and

  $R^{12'}$, R^{13}, R^{18}, R^{19}, $R^{19'}$ and R^{20} are independently selected from H, halo, C1-3 alkyl, hydroxyl, methoxy, then,

  Ar^1 is phenyl, 3-halophenyl, 4-halophenyl, 2,3-dichlorophenyl, 3,4-dihalophenyl, 3,4,5-trihalophenyl, 4-cyanophenyl, 4-(C1-C3 alkyl)phenyl, 4-(C1 haloalkyl)phenyl, preferably Ar^1 is phenyl, 4-fluorophenyl, 4-chlorophenyl, 4-trifluoromethylphenyl, 3-chlorophenyl, 3-fluorophenyl, 3,4-dichlorophenyl, 3,4-difluorophenyl, 3,4,5-trifluorophenyl, 4-chloro-3-fluorophenyl, 3-chloro-4-fluorophenyl, 4-cyanophenyl, 4-tolyl, 4-trifluoromethylphenyl, and

  $R^{12'}$, R^{13}, R^{18}, R^{19}, $R^{19'}$ and R^{20} are H, or $R^{12'}$, R^{13}, R^{19}, $R^{19'}$, R^{20} are H and R^{18} is fluoro, chloro, and

- in formula Ig-4 when

  R^1 is H, and

  Ar^1 is a 6-membered aryl optionally substituted by one or more group(s) selected from halo, cyano, C1-C3 alkyl, C1-haloalkyl, and

R^{27}, R^{28}, R^{29} and R^{30} are independently selected from H, halo, C1-3 alkyl, methoxy, and

$R^{27'}$, $R^{28'}$, $R^{29'}$ and $R^{30'}$ are absent or H under the condition that R^{28}, R^{29} and R^{30} are H and R^{27} is selected from H, chloro or fluoro,
then

Ar^1 is phenyl, 3-halophenyl, 4-halophenyl, 2,3-dichlorophenyl, 3,4-dihalophenyl, 3,4,5-trihalophenyl, 4-cyanophenyl, 4-(C1-C3 alkyl)phenyl, 4-(C1 haloalkyl)phenyl, preferably Ar^1 is phenyl, 4-fluorophenyl, 4-chlorophenyl, 3-chlorophenyl, 3-fluorophenyl, 3,4-dichlorophenyl, 3,4-difluorophenyl, 3,4,5-trifluorophenyl, 4-chloro-3-fluorophenyl, 3-chloro-4-fluorophenyl, 4-cyanophenyl, 4-tolyl, 4-trifluoromethylphenyl, and

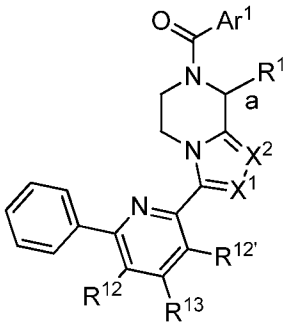
R^{27}, R^{28}, R^{29} and R^{30} are H, and

$R^{27'}$, $R^{28'}$, $R^{29'}$ and $R^{30'}$ are absent or H under the condition that R^{27}, R^{28}, R^{29} and R^{30} are H.

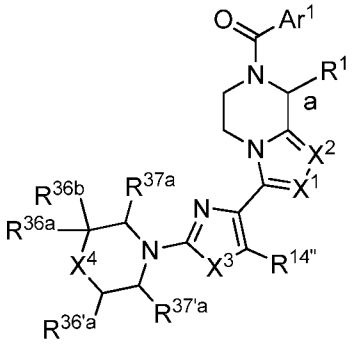
[0035] In another embodiment, compounds of formulae Ig-1, Ig-2, Ig-3, Ig-4, Ig-5, Ig-6, Ig-7 and Ig-8 are those wherein bond **a** is drawn as a dotted wedge, and/or R^1 is selected from the group consisting of C_1-C_4 alkyl, aryl or aralkyl group, each of said alkyl, aryl or aralkyl groups being optionally substituted by one or more group(s) selected from halo or hydroxyl.

[0036] In yet another embodiment, compounds of formulae Ig-1, Ig-2, Ig-3, Ig-4, Ig-5, Ig-6, Ig-7 and Ig-8 are those wherein bond **a** is drawn as a solid wedge, and/or R^1 is selected from the group consisting of C_1-C_4 alkyl, aryl or aralkyl group, each of said alkyl, aryl or aralkyl groups being optionally substituted by one or more group(s) selected from halo or hydroxyl.

[0037] Other preferred compounds of formulae If-1 and If-2, are those of formulae Ih-1 and Ih-2 respectively:



Ih-1



Ih-2

and pharmaceutically acceptable salts and solvates thereof, wherein

a designates the bond linking R^1 to the piperazine moiety; and

Ar^1, R^1, X^1 and X^2 are as defined above in respect to formula Ib; and

R^{12}, $R^{12'}$ and R^{13} are as defined above in respect to formula If-1, preferably R^{12}, $R^{12'}$ and R^{13} are H; and

$R^{14''}$ is H or methyl; and

X^3 is as defined above in respect to formula If-2, preferably X^3 is S; and

X^4 is O, CH_2, CF_2, $C(CH_3)_2$, N-(C1-C3 alkyl) N-phenyl, preferably X^4 is O, CH_2, CF_2, N-methyl or N-phenyl; and

R^{36a}, R^{36b}, $R^{36'a}$, R^{37a} and $R^{37'a}$ are independently selected from H, C1-C3 alkyl, alkoxyC1-C3 alkyl, preferably R^{36a}, R^{36b}, R^{37a} and $R^{37'a}$ are H and $R^{36'a}$ is H, methyl, methoxyethyl, or R^{36a}, R^{36b}, $R^{37'a}$ are H and R^{37a} and $R^{36'a}$ are methyl, or R^{36b}, R^{37a}, $R^{37'a}$ are H and R^{36a} and $R^{36'a}$ are methyl, or $R^{36'a}$, R^{37a}, $R^{37'a}$ are H and R^{36a} and R^{36b} are methyl, or R^{36a}, R^{36b}, $R^{36'a}$, R^{37a} are H and and $R^{37'a}$ is methoxymethyl.

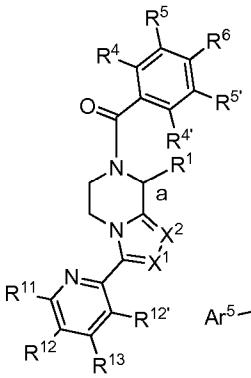
[0038] In another embodiment, compounds of formula Ih-1 are those wherein bond **a** is drawn as a dotted wedge.

[0039] In another embodiment, compounds of formula Ih-1 are those wherein bond **a** is drawn as a solid wedge.

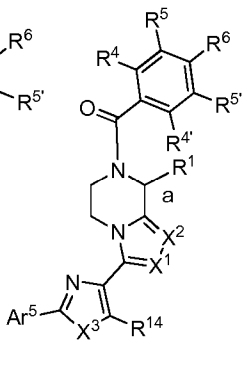
[0040] In another embodiment, compounds of formula Ih-2 are those wherein bond **a** is drawn as a dotted wedge. In one variant of this embodiment, compounds of formula Ih-2 are those wherein bond **a** is drawn as a dotted wedgeand $\mathbf{R^{36a}}$, $\mathbf{R^{36b}}$, $\mathbf{R^{36'a}}$, $\mathbf{R^{37a}}$ and $\mathbf{R^{37'a}}$ are H.

[0041] In yet another embodiment, compounds of formula Ih-2 are those wherein bond a is drawn as a solid wedge. In one variant of this embodiment, compounds of formula Ih-2 are those wherein bond **a** is drawn as a solid wedgeand $\mathbf{R^{36a}}$, $\mathbf{R^{36b}}$, $\mathbf{R^{36'a}}$, $\mathbf{R^{37a}}$ and $\mathbf{R^{37'a}}$ are H.

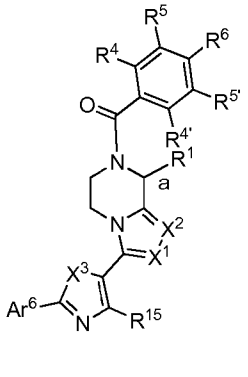
[0042] Other preferred compounds of formula Ic are those of formulae Ii-1, Ii-2, Ii-3, Ii-4, Ii-5, Ii-6, Ii-7, Ii-8, Ij-1, Ij-2, Ij-3, Ij-4, Ij-5, Ij-6, Ij-7, Ij-8, Ik-1, Ik-2, Ik-3, Ik-4 Ik-5, Ik-6, Ik-7, Ik-8, Ii'-1, Ii'-2, Ii'-3, Ii'-4, Ii'-5, Ii'-6, Ii'-7 and Ii'-8,



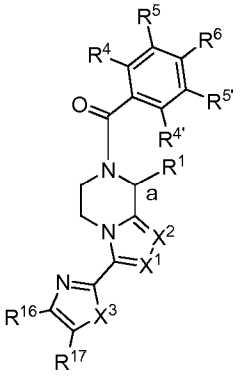
Ii-1



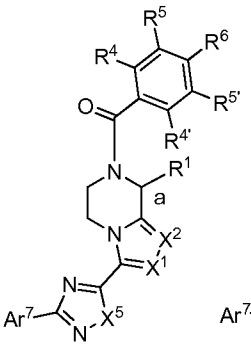
Ii-2



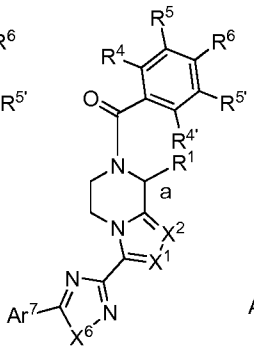
Ii-3



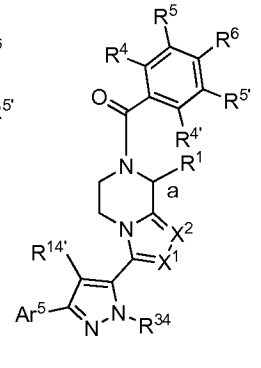
Ii-4



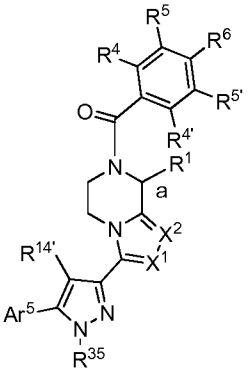
Ii-5



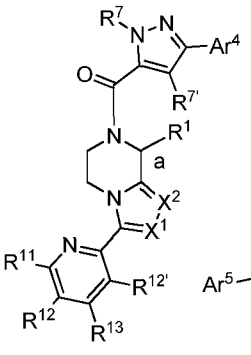
Ii-6



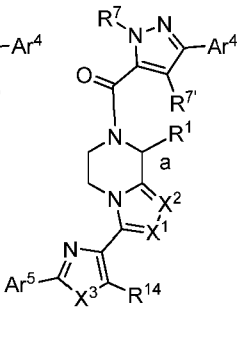
Ii-7



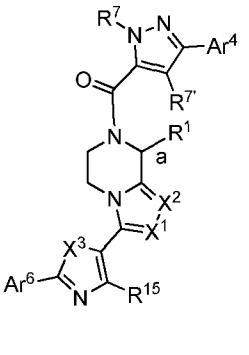
Ii-8



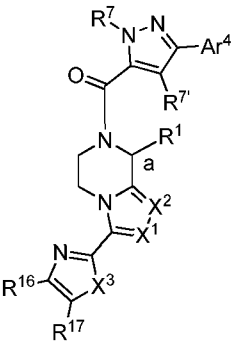
Ij-1



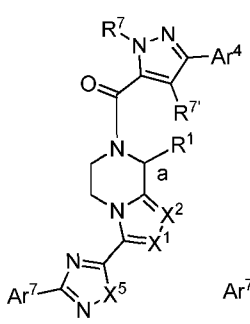
Ij-2



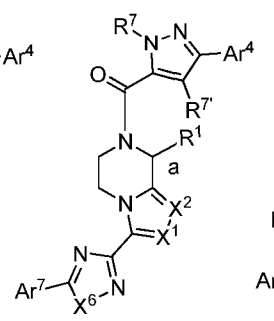
Ij-3



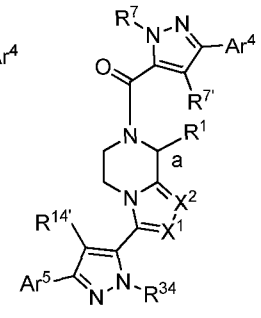
Ij-4



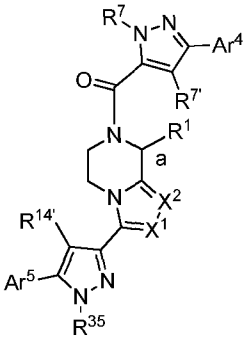
Ij-5



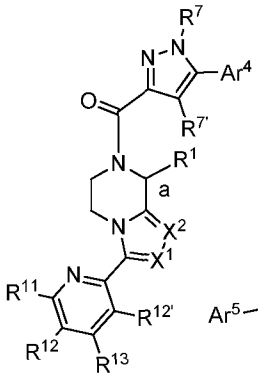
Ij-6



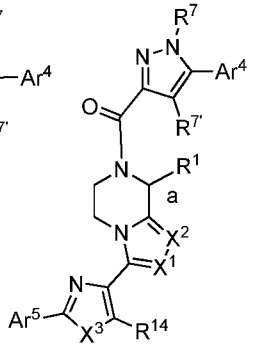
Ij-7



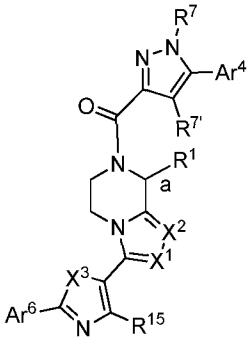
Ij-8



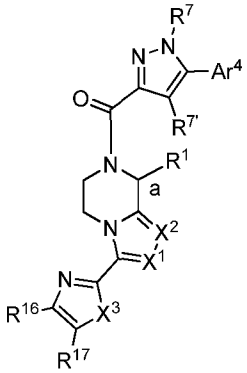
Ik-1



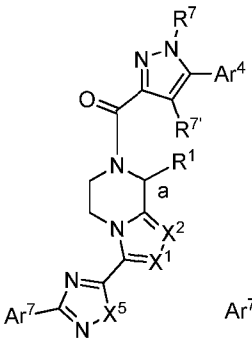
Ik-2



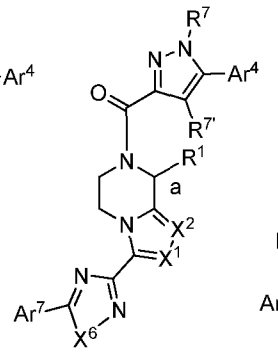
Ik-3



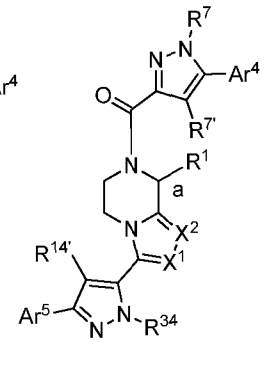
Ik-4



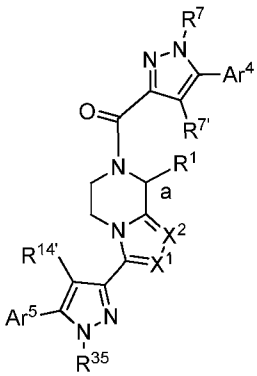
Ik-5



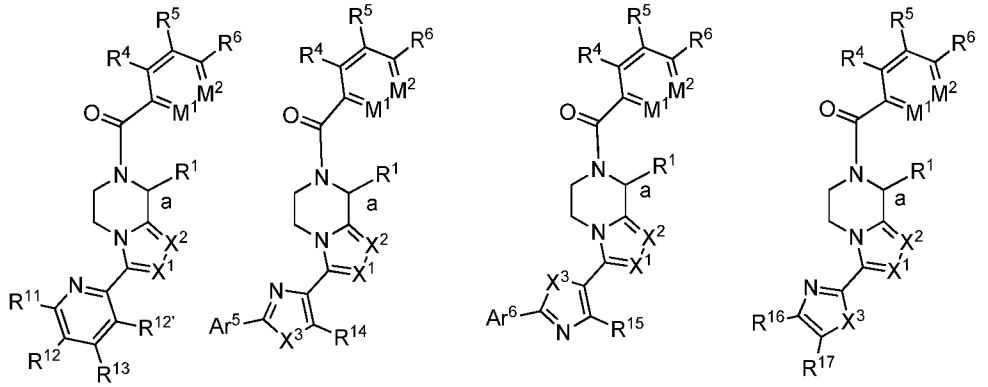
Ik-6



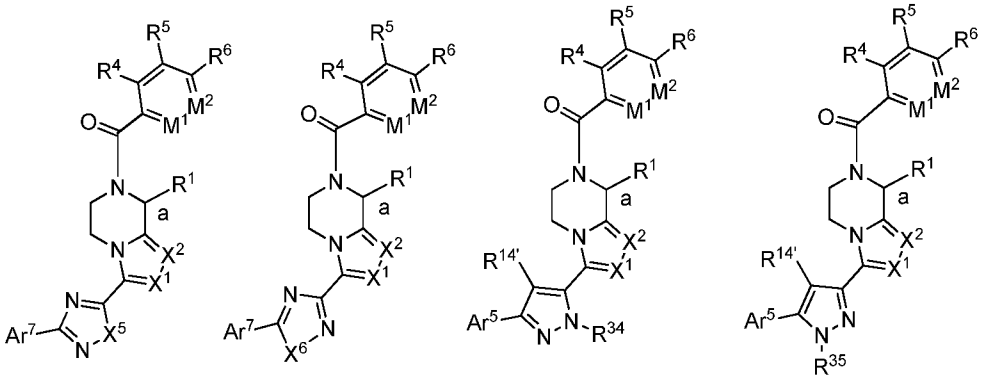
Ik-7



Ik-8



Ii'-1 Ii'-2 Ii'-3 Ii'-4



Ii'-5 Ii'-6 Ii'-7 Ii'-8

and pharmaceutically acceptable salts and solvates thereof, wherein

a depicts the bond linking $\mathbf{R^1}$ to the piperazine moiety; and
$\mathbf{R^1}$, $\mathbf{X^1}$ and $\mathbf{X^2}$ are as defined above in respect to formula Ib; and
$\mathbf{R^4}$, $\mathbf{R^{4'}}$, $\mathbf{R^5}$, $\mathbf{R^{5'}}$ and $\mathbf{R^6}$ are as defined above in respect to formula Id-1; and
$\mathbf{Ar^4}$, $\mathbf{R^7}$ and $\mathbf{R^{7'}}$ are as defined above in respect to formulae Id-2 and Id-3; and
$\mathbf{M^1}$ and $\mathbf{M^2}$ are as defined above in respect to formula Id-4; and
$\mathbf{R^{11}}$, $\mathbf{R^{12}}$, $\mathbf{R^{12'}}$ and $\mathbf{R^{13}}$ are as defined above in respect to formula If-1; and
$\mathbf{Ar^5}$, $\mathbf{R^{14}}$ and $\mathbf{X^3}$ are as defined above in respect to formula If-2; and
$\mathbf{Ar^6}$ and $\mathbf{R^{15}}$ are as defined above in respect to formula If-3; and
$\mathbf{R^{16}}$ and $\mathbf{R^{17}}$ are as defined above in respect to formula If-4: and
$\mathbf{Ar^7}$ and $\mathbf{X^5}$ are are as defined above in respect to formula If-5; and
$\mathbf{X^6}$ is as defined above in respect to formula If-6; and
$\mathbf{R^{14'}}$, $\mathbf{R^{34}}$ and $\mathbf{R^{35}}$ are as defined above in respect to formulae If-7 and If-8.

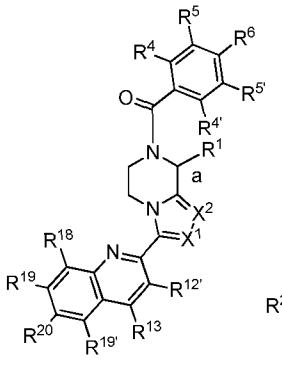
[0043] Among the compounds of formulae Ii-1, Ii-2, Ii-3, Ii-4, Ii-5, Ii-6, Ii-7, Ii-8, Ij-1, Ij-2, Ij-3, Ij-4, Ij-5, Ij-6, Ij-7, Ij-8, Ik-1, Ik-2, Ik-3, Ik-4 Ik-5, Ik-6, Ik-7, Ik-8, Ii'-1, Ii'-2, Ii'-3, Ii'-4, Ii'-5, Ii-6, Ii'-7 and Ii'-8, compounds of formulae Ii-1, Ii-2, Ii-3, Ii-4, Ii-5, Ii-6, Ii-7, Ii-8, Ii'-1, Ii'-2, Ii'-3, Ii'-4, Ii'-5, Ii-6, Ii'-7 and Ii'-8 are preferred.

[0044] In another embodiment, compounds of formulae Ii-1, Ii-2, Ii-3, Ii-4, Ii-5, Ii-6, Ii-7, Ii-8, Ij-1, Ij-2, Ij-3, Ij-4, Ij-5, Ij-6, Ij-7, Ij-8, Ik-1, Ik-2, Ik-3, Ik-4 Ik-5, Ik-6, Ik-7, Ik-8, Ii'-1, Ii'-2, Ii'-3, Ii'-4, Ii'-5, Ii-6, Ii-7 and Ii-8 are those wherein bond **a** is drawn as a dotted wedge, and/or $\mathbf{R^1}$ is selected from the group consisting of C_1-C_4 alkyl, aryl or aralkyl group, each of said alkyl, aryl or aralkyl groups being optionally substituted by one or more group(s) selected from halo or hydroxyl.

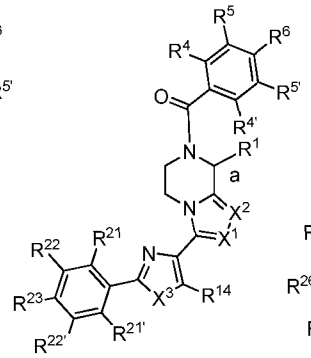
[0045] In yet another embodiment, compounds of formulae Ii-1, Ii-2, Ii-3, Ii-4, Ii-5, Ii-6, Ii-7, Ii-8, Ij-1, Ij-2, Ij-3, Ij-4, Ij-5, Ij-6, Ij-7, Ij-8, Ik-1, Ik-2, Ik-3, Ik-4 Ik-5, Ik-6, Ik-7, Ik-8, Ii'-1, Ii'-2, Ii'-3, Ii'-4, Ii'-5, Ii-6, Ii-7 and Ii-8 are those wherein bond **a** is drawn as a solid wedge, and/or $\mathbf{R^1}$ is selected from the group consisting of C_1-C_4 alkyl, aryl or aralkyl group, each of said alkyl, aryl or aralkyl groups being optionally substituted by one or more group(s) selected from halo or hydroxyl.

[0046] Preferred compounds of formulae Ii-1, Ii-2, Ii-3, Ii-4, Ii-5, Ii-6, Ii-7, Ii-8, Ii'-1, Ii'-2, Ii'-3, Ii'-4, Ii'-5, Ii'-6, Ii'-7 and Ii'-

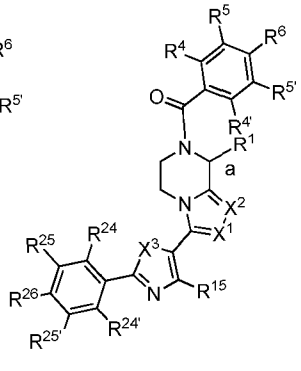
8 are those of formulae II-1, II-2, II-3, II-4, II-5, II-6, II-7, II-8, II'-1, II'-2, II'-3, II'-4, II'-5, II'-6, II'-7 and II'-8 respectively:



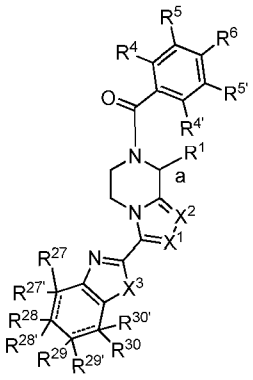
II-1



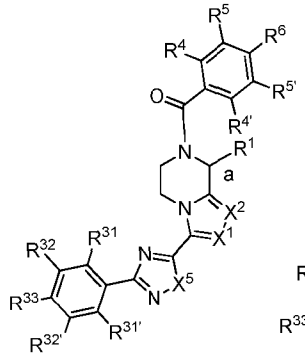
II-2



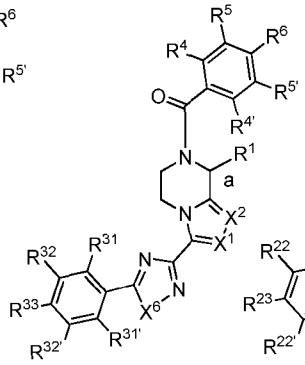
II-3



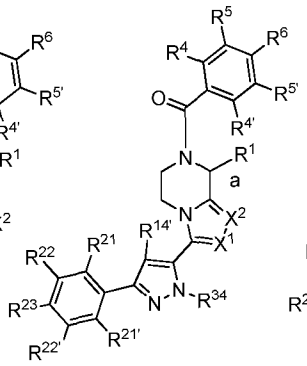
II-4



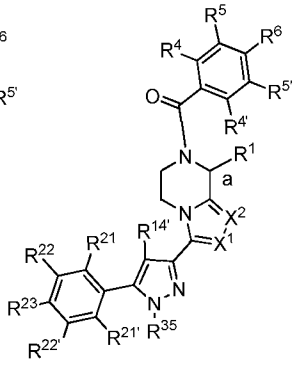
II-5



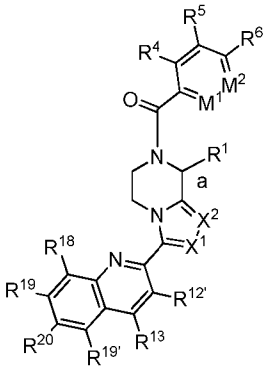
II-6



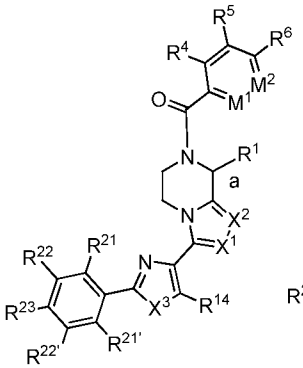
II-7



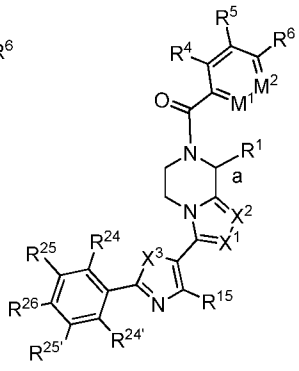
II-8



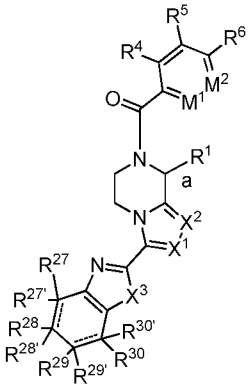
II'-1



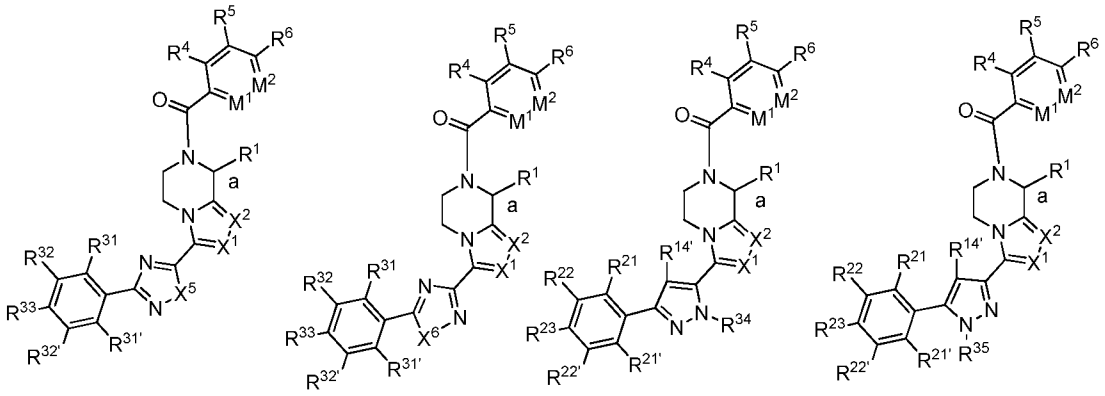
II'-2



II'-3



II'-4



II'-5 II'-6 II'-7 II'-8

and pharmaceutically acceptable salts and solvates thereof, wherein:

a depicts the bond linking **R^1** to the piperazine moiety; and

R^1, **X^1** and **X^2** are as defined above in respect to formula Ib; and

R^4, **$R^{4'}$**, **R^5**, **$R^{5'}$** and **R^6** are as defined above in respect to formula Id-1; and

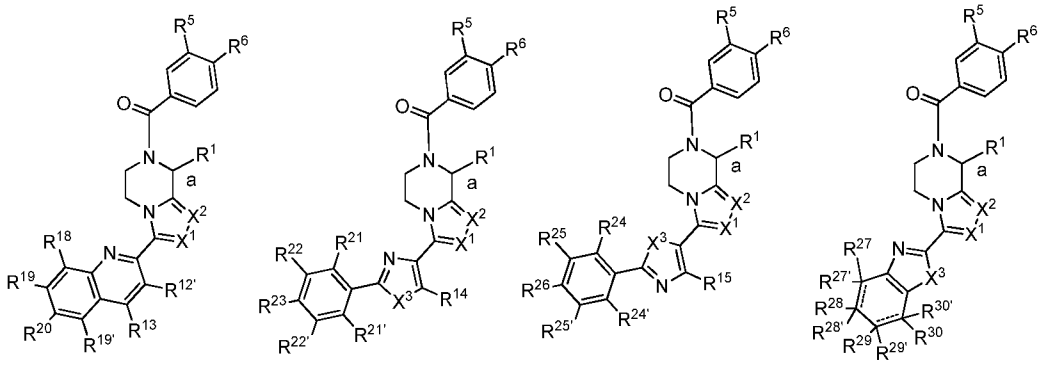
M^1 and **M^2** are as defined above in respect to formula Id-4; and

$R^{12'}$, **R^{13}**, **R^{14}**, **$R^{14'}$**, **R^{15}**, **R^{18}**, **R^{19}**, **$R^{19'}$**, **R^{20}**, **R^{21}**, **$R^{21'}$**, **R^{22}**, **$R^{22'}$**, **R^{23}**, **R^{24}**, **$R^{24'}$**, **R^{25}**, **$R^{25'}$**, **R^{26}**, **R^{27}**, **$R^{27'}$**, **R^{28}**, **$R^{28'}$**, **R^{29}**, **$R^{29'}$**, **R^{30}**, **$R^{30'}$**, **R^{31}**, **$R^{31'}$**, **R^{32}**, **$R^{32'}$**, **R^{33}**, **R^{34}**, **R^{35}**, **X^3**, **X^5**; **X^6**; and the two bonds represented by the dotted lines are as defined above in respect of formulae Ig-1, Ig-2, Ig-3, Ig-4, Ig-5, Ig-6, Ig-7 and Ig-8.

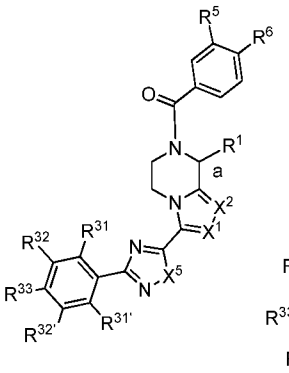
[0047] In another embodiment, compounds of formulae II-1, II-2, II-3, II-4, II-5, II-6, II-7, II-8, II'-1, II'-2, II'-3, II'-4, II'-5, II'-6, II'-7 and II'-8 are those wherein bond **a** is drawn as a dotted wedge, and/or **R^1** is selected from the group consisting of C_1-C_4 alkyl, aryl or aralkyl group, each of said alkyl, aryl or aralkyl groups being optionally substituted by one or more group(s) selected from halo or hydroxyl.

[0048] In yet another embodiment, compounds of formulae II-1, II-2, II-3, II-4, II-5, II-6, II-7, II-8, II'-1, II'-2, II'-3, II'-4, II'-5, II'-6, II'-7 and II'-8 are those wherein bond **a** is drawn as a solid wedge, and/or **R^1** is selected from the group consisting of C_1-C_4 alkyl, aryl or aralkyl group, each of said alkyl, aryl or aralkyl groups being optionally substituted by one or more group(s) selected from halo or hydroxyl.

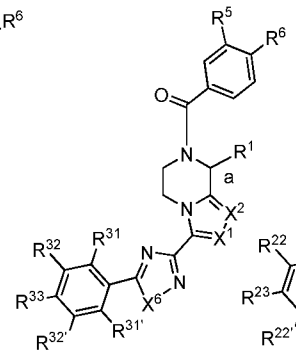
[0049] Preferred compounds of formulae II-1, II-2, II-3, II-4, II-5, II-6, II-7, II-8, II'-1, II'-2, II'-3, II'-4, II'-5, II'-6, II'-7 and II'-8 are those of formulae Im-1, Im-2, Im-3, Im-4, Im-5, Im-6, Im-7, Im-8, Im'-1, Im'-2, Im'-3, Im'-4, Im'-5, Im'-6, Im'-7 and Im'-8 respectively:



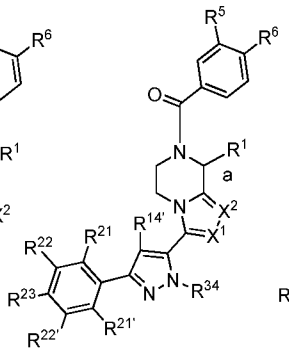
Im-1 Im-2 Im-3 Im-4



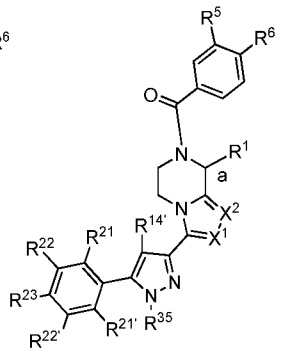
Im-5



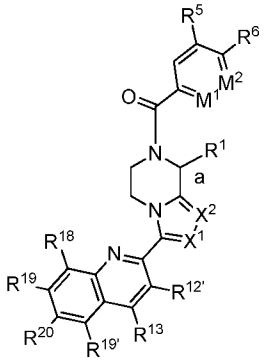
Im-6



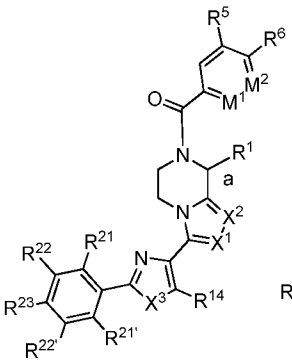
Im-7



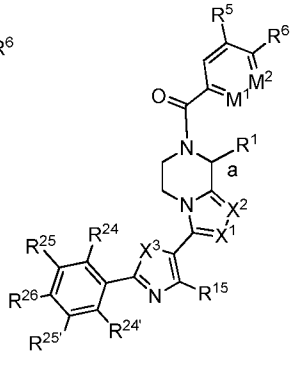
Im-8



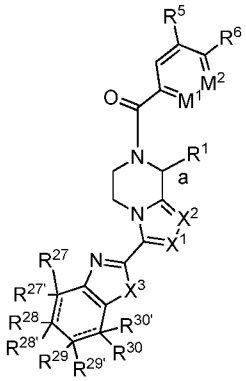
Im'-1



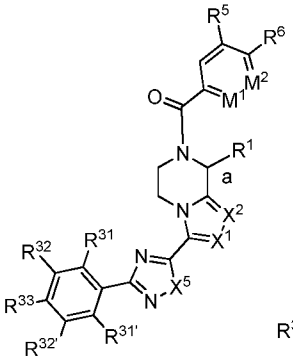
Im'-2



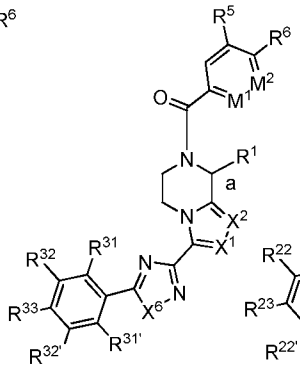
Im'-3



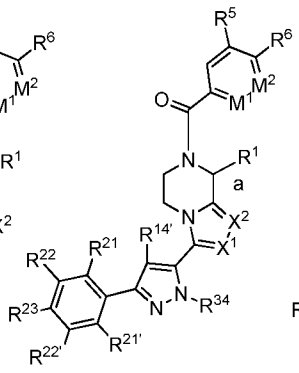
Im'-4



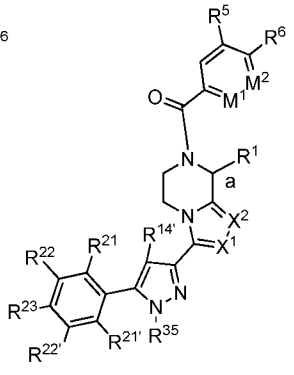
Im'-5



Im'-6



Im'-7



Im'-8

and pharmaceutically acceptable salts and solvates thereof, wherein:

a designates the bond linking **R^1** to the piperazine moiety; and

R^1, **X^1** and **X^2** are as defined above in respect to formula Ib; and

R^5 and **R^6** are as defined above in respect to formula Ie-1; and

M^1 and **M^2** are as defined above in respect to formula Ie-3; and

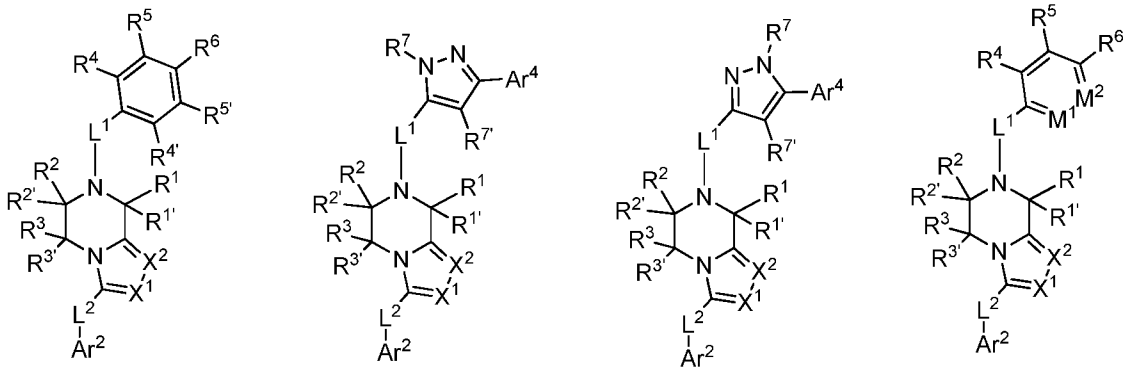
$R^{12'}$, R^{13}, R^{14}, $R^{14'}$, R^{15}, R^{18}, R^{19}, $R^{19'}$, R^{20}, R^{21}, $R^{21'}$, R^{22}, $R^{22'}$, R^{23}, R^{24}, $R^{24'}$, R^{25}, $R^{25'}$, R^{26}, R^{27}, $R^{27'}$, R^{28}, $R^{28'}$,

R^{29}, $R^{29'}$, R^{30}, $R^{30'}$, R^{31}, $R^{31'}$, R^{32}, $R^{32'}$, R^{33}, R^{34}, R^{35}, X^3, X^5, X^6; and the two bonds represented by the dotted lines are as defined above in respect to formulae Ig-1, Ig-2, Ig-3, Ig-4, Ig-5, Ig-6, Ig-7 and Ig-8.

[0050] In another embodiment, compounds of formulae Im-1, Im-2, Im-3, Im-4, Im-5, Im-6, Im-7, Im-8, Im'-1, Im'-2, Im'-3, Im'-4, Im'-5, Im'-6, Im'-7 and Im'-8 are those wherein bond **a** is drawn as a dotted wedge, and/or R^1 is selected from the group consisting of C_1-C_4 alkyl, aryl or aralkyl group, each of said alkyl, aryl or aralkyl groups being optionally substituted by one or more group(s) selected from halo or hydroxyl.

[0051] In yet another embodiment, compounds of Im-1, Im-2, Im-3, Im-4, Im-5, Im-6, Im-7, Im-8, Im'-1, Im'-2, Im'-3, Im'-4, Im'-5, Im'-6, Im'-7 and Im'-8 are those wherein bond **a** is drawn as a solid wedge, and/or R^1 is selected from the group consisting of C_1-C_4 alkyl, aryl or aralkyl group, each of said alkyl, aryl or aralkyl groups being optionally substituted by one or more group(s) selected from halo or hydroxyl.

[0052] Other preferred compounds of formula I are those of formulae In, Io, Ip and In'



In Io Ip In'

and pharmaceutically acceptable salts and solvates thereof, wherein:

Ar^2, L^1, L^2, R^1, $R^{1'}$, R^2, $R^{2'}$, R^3, $R^{3'}$, X^1 and X^2, are as defined above in respect to formula I.

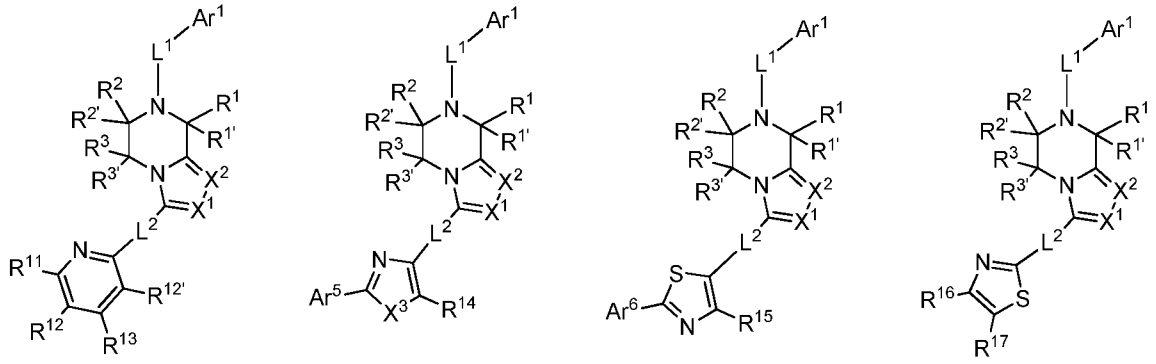
R^4, $R^{4'}$, R^5, $R^{5'}$ and R^6 are as defined above in respect to formula Id-1;

Ar^4, R^7 and $R^{7'}$ are as defined above in respect to formulae Id-2 and Id-3;

M^1 and M^2 are as defined above in respect to formula Id-4;

[0053] Preferred compounds of formulae In, Io and Ip are those wherein R^2, $R^{2'}$, R^3 and $R^{3'}$ are H.

[0054] Still other preferred compounds of formula I are those of formulae Iq, Ir, Is and It



Iq Ir Is It

and pharmaceutically acceptable salts and solvates thereof, wherein:

Ar^1, L^1, L^2, R^1, $R^{1'}$, R^2, $R^{2'}$, R^3, $R^{3'}$, X^1 and X^2, are as defined above in respect to formula I;

R^{11}, R^{12}, $R^{12'}$ and R^{13} are as defined above in respect to formula If-1;

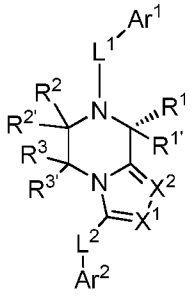
Ar^5, R^{14} and X^3 are as defined above in respect to formula If-2;

Ar^6 and R^{15} are as defined above in respect to formula If-3;

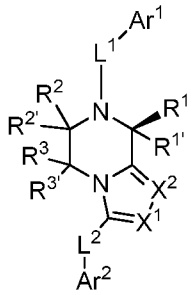
R^{16} and R^{17} are as defined above in respect to formula If-4.

[0055] Preferred compounds of formulae Iq, Ir, Is and It are those wherein R^2, $R^{2'}$, R^3 and $R^{3'}$ are H.

[0056] Other preferred compounds of formula I are those of formulae Iu and Iv



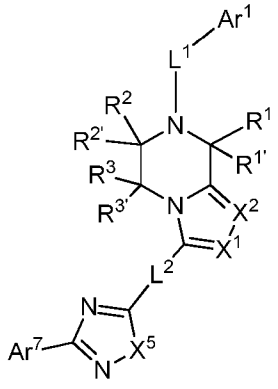
Iu



Iv

and pharmaceutically acceptable salts and solvates thereof, wherein Ar^1, Ar^2, L^1, L^2, R^1, $R^{1'}$, R^2, $R^{2'}$, R^3, $R^{3'}$, X^1 and X^2, are as defined above in respect to formula I, and R^1 and $R^{1'}$ are different.

[0057] Still other preferred compounds of formula I are those of formula Iw:



Iw

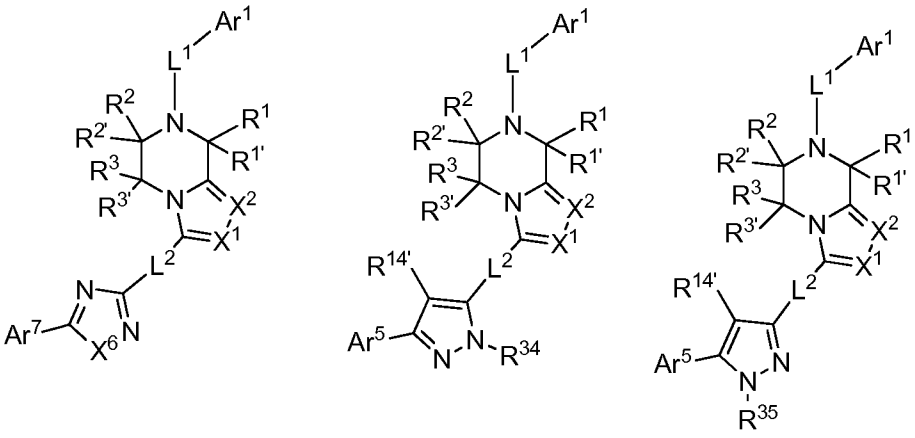
and pharmaceutically acceptable salts and solvates thereof, wherein

Ar^1, L^1, L^2, R^1, $R^{1'}$, R^2, $R^{2'}$, R^3, $R^{3'}$, X^1 and X^2, are as defined above in respect to formula I;

Ar^7 and X^5 are as defined above in respect to formula If-5;

[0058] Preferred compounds of formula Iw are those wherein R^2, $R^{2'}$, R^3 and $R^{3'}$ are H.

[0059] Still other preferred compounds of formula I are those of formulae Ix, Iy and Iz:



Ix Iy Iz

and pharmaceutically acceptable salts and solvates thereof, wherein

Ar^1, **L^1**, **L^2**, **R^1**, **$R^{1'}$**, **R^2**, **$R^{2'}$**, **R^3**, **$R^{3'}$**, **X^1** and **X^2**, are as defined above in respect to formula I;

Ar^5, **Ar^7**, **$R^{14'}$**, **R^{34}**, **R^{35}**, and **X^6** are as defined above in respect to formulae If-6, If-7 and If-8.

[0060] Preferred compounds of formula Ix, Iy and Iz are those wherein **R^2**, **$R^{2'}$**, **R^3** and **$R^{3'}$** are H and/or **$R^{14'}$** is H.

[0061] Particularly preferred compounds of the invention are those listed in Table 1 hereafter:

TABLE 1:

Compound n°	Name	$(M+H)^+$
1	(4-fluorophenyl)(3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	324.3
2	(4-chlorophenyl)(3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	340.8
3	(3-(4-chlorophenyl)-1H-pyrazol-5-yl)(3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	406.8
4	(3-(3,4-dichlorophenyl)-1H-pyrazol-5-yl)(3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	441.3
5	(3,4-dichlorophenyl)(3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	375.2
6	[1,1'-biphenyl]-4-yl(3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	382.4
7	(4-fluorophenyl)(3-(quinolin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	374.4
8	(4-fluorophenyl)(3-(2-phenylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	406.4
9	(4-fluorophenyl)(3-(2-morpholinothiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	415.5
10	(3-(5-chloropyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-fluorophenyl)methanone	358.8
11	(4-fluorophenyl)(3-(6-methylpyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	338.4
12	(4-fluorophenyl)(8-methyl-3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	338.4

(continued)

Compound n°	Name	$(M+H)^+$
13	(3-(2,4-dichlorophenyl)-1H-pyrazol-5-yl)(3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	441.3
14	(3-(3,4-dichlorophenyl)-1-methyl-1H-pyrazol-5-yl)(3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	455.3
15	(4-fluorophenyl)(3-(isoquinolin-3-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	374.4
16	(4'-fluoro-[1,1'-biphenyl]-4-yl)(3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	400.4
17	(3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(3-(4-(trifluoromethyl)phenyl)-1H-pyrazol-5-yl)methanone	440.4
18	(3-(4-phenoxyphenyl)-1H-pyrazol-5-yl)(3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	464.5
19	[1,1'-biphenyl]-4-yl(3-(quinolin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	432.5
20	[1,1'-biphenyl]-4-yl(3-(2-morpholinothiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	473.6
21	(3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone	388.5
22	(4-fluorophenyl)(3-(8-fluoroquinolin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	392.4
23	(3-(8-chloroquinolin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-fluorophenyl)methanone	408.8
24	(4-fluorophenyl)(3-(2-(4-(trifluoromethyl)phenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	474.4
25	(4-fluorophenyl)(3-(6-phenylpyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	400.4
26	[1,1'-biphenyl]-4-yl(3-(2-phenylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	464.6
27	(4-fluorophenyl)(3-(4,5,6,7-tetrahydrobenzo[d]thiazol-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	384.4
28	(4-fluorophenyl)(3-(2-(3-(trifluoromethyl)phenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	474.4
29	(3-(2-(2,4-difluorophenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-fluorophenyl)methanone	442.4
30	(3-(2-(2,3-dichlorophenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-fluorophenyl)methanone	475.3
31	(3-(2-(4-chlorophenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-fluorophenyl)methanone	440.9
32	(4-fluorophenyl)(3-(2-(4-fluorophenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	424.4
33	(4-fluorophenyl)(3-(2-(piperidin-1-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	413.5
34	(4-fluorophenyl)(3-(2-(4-phenylpiperazin-1-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	490.6

(continued)

Compound n°	Name	$(M+H)^+$
35	(3-(2-(2,4-dichlorophenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-fluorophenyl)methanone	475.3
36	(3-(2-(3,5-dichlorophenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-fluorophenyl)methanone	475.3
37	(4-fluorophenyl)(3-(6-(pyrrolidin-1-yl)pyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	393.4
38	(4-fluorophenyl)(3-(6-morpholinopyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	409.4
39	(4-fluorophenyl)(3-(6-(trifluoromethyl)pyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	392.3
40	(3-(2-(3,4-dimethoxyphenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-fluorophenyl)methanone	466.5
41	(4-fluorophenyl)(8-(4-fluorophenyl)-3-(2-phenylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	500.5
42	(3-(2-(3-chlorophenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-fluorophenyl)methanone	440.9
43	(4-fluorophenyl)(8-isopropyl-3-(2-phenylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	448.5
44	(R)-(4-fluorophenyl)(8-methyl-3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	338.4
45	(R)-(4-fluorophenyl)(8-methyl-3-(2-phenylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	420.5
46	[1,1'-biphenyl]-4-yl(8-methyl-3-(2-morpholinothiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	487.6
47	(4-fluorophenyl)(3-(2-phenyloxazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	390.4
48	(4-fluorophenyl)(8-methyl-3-(2-phenyloxazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	404.4
49	[1,1'-biphenyl]-4-yl(8-methyl-3-(2-phenyloxazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	462.5
50	[1,1'-biphenyl]-4-yl(3-(2-phenyloxazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	448.5
51	(4-fluorophenyl)(8-(2-hydroxyethyl)-3-(2-phenylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	450.5
52	(4-fluorophenyl)(8-methyl-3-(2-morpholinothiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	429.5
53	(4'-fluoro-[1,1'-biphenyl]-4-yl)(8-methyl-3-(2-morpholinothiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	505.6
54	(3-(2-phenylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone	470.6
55	(3-(2-morpholinothiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone	479.6
56	(8-methyl-3-(2-morpholinothiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone	493.6

(continued)

Compound n°	Name	$(M+H)^+$
57	(4-fluorophenyl)(3-(4-phenylthiazol-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	406.4
58	(3-(2-(2-chlorophenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-fluorophenyl)methanone	440.9
59	(3-(benzo[d]thiazol-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-fluorophenyl)methanone	380.4
60	(8,8-dimethyl-3-(2-phenylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-fluorophenyl)methanone	434.5
61	(4-fluorophenyl)(8-methyl-3-(quinolin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	388.4
62	(8-methyl-3-(2-phenylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone	484.6
63	(3-(2-phenylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-3-yl)phenyl)methanone	470.6
64	(8-methyl-3-(2-phenylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-3-yl)phenyl)methanone	484.6
65	(8-methyl-3-(quinolin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone	452.5
66	(3-(2-(2-chlorophenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone	505.0
67	[1,1'-biphenyl]-4-yl(3-(2-(2-chlorophenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	499.0
68	(R)-(3-(2-(4-chlorophenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-fluorophenyl)methanone	454.9
69	(3-(quinolin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone	438.5
70	(4-fluorophenyl)(3-(2-(4-fluorophenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	438.5
71	(R)-(4-fluorophenyl)(3-(2-(4-fluorophenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	438.5
72	[1,1'-biphenyl]-4-yl(8-methyl-3-(4-methyl-2-phenylthiazol-5-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	492.6
73	(3-(2-(4-fluorophenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone	488.6
74	(3-(2-(2-chlorophenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-fluorophenyl)methanone	454.9
75	(4-fluorophenyl)(8-methyl-3-(4-methyl-2-phenylthiazol-5-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	434.5
76	[1,1'-biphenyl]-4-yl(3-(2-(4-fluorophenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	496.6
77	(3-(2-(2,4-difluorophenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-fluorophenyl)methanone	456.5
78	(3-(2-(4-fluorophenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone	502.6

(continued)

Compound n°	Name	$(M+H)^+$
79	[1,1'-biphenyl]-4-yl(3-(2-(2,4-difluorophenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	514.6
80	(3-(2-(2,4-difluorophenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone	520.6
81	naphthalen-1-yl(3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	356.4
82	(3-(4-chlorophenyl)-1-methyl-1H-pyrazol-5-yl)(3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	420.9
83	(5-(4-chlorophenyl)-1-methyl-1H-pyrazol-3-yl)(3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	420.9
84	(8-methyl-3-(5-phenyl-1,2,4-oxadiazol-3-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone	469.5
85	(8-methyl-3-(3-phenyl-1,2,4-oxadiazol-5-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone	469.5
86	(R)-(3-(2-(4-fluorophenyl)oxazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone	486.5
90	(5-phenylpyridin-2-yl)(3-(quinolin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	433.5
91	(6-phenylpyridin-3-yl)(3-(quinolin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	433.5
92	(2-phenylpyrimidin-5-yl)(3-(quinolin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	434.5
93	(4-phenylcyclohexyl)(3-(quinolin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	438.5
94	cyclohexyl(3-(quinolin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	362.4
95	3-methyl-1-(3-(quinolin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)butan-1-one	336.4
96	[1,1'-biphenyl]-2-yl(3-(quinolin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	432.5
97	(4-(furan-3-yl)phenyl)(3-(quinolin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	422.5
98	(4-(pyrimidin-5-yl)phenyl)(3-(quinolin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	434.5
99	(9-methyl-9H-carbazol-2-yl)(3-(quinolin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	459.5
100	(4-(pyrimidin-2-yl)phenyl)(3-(quinolin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	434.5
101	(4-(pyrazin-2-yl)phenyl)(3-(quinolin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	434.5
102	(4-(pyridazin-3-yl)phenyl)(3-(quinolin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	434.5
103	4'-(3-(quinolin-2-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazine-7-carbonyl)-[1,1'-biphenyl]-4-carbonitrile	457.5

(continued)

Compound n°	Name	$(M+H)^+$
104	1-(4-(3-(quinolin-2-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazine-7-carbonyl)phenyl)piperidin-2-one	453.5
105	(4-morpholinophenyl)(3-(quinolin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	441.5
106	(4-(3,5-dimethyl-1H-pyrazol-1-yl)phenyl)(3-(quinolin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	450.5
107	(3-(2-(4-fluorophenyl)thiazol-4-yl)-6-methyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone	502.6
108	(3-(2-(4-fluorophenyl)thiazol-4-yl)-5-methyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone	502.6
109	(3,4-dichlorophenyl)(3-(2-(4-fluorophenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	489.4
110	(3,4-difluorophenyl)(3-(2-(4-fluorophenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	456.5
111	(3-chloro-4-fluorophenyl)(3-(2-(4-fluorophenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	472.9
112	(4-chloro-3-fluorophenyl)(3-(2-(4-fluorophenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	472.9
113	(3-(2-(4-fluorophenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(3,4,5-trifluorophenyl)methanone	474.4
114	(8-methyl-3-(2-phenyloxazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone	468.5
115	(R)-(4-fluorophenyl)(8-methyl-3-(quinolin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	388.4
117	(R)-[1,1'-biphenyl]-4-yl(8-methyl-3-(quinolin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	446.5
118	(R)-[1,1'-biphenyl]-4-yl(8-methyl-3-(2-morpholinothiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	487.6
119	(R)-(4-fluorophenyl)(8-methyl-3-(6-phenylpyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	414.4
120	(R)-[1,1'-biphenyl]-4-yl(8-methyl-3-(2-phenylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	478.6
121	(R)-(4-fluorophenyl)(8-methyl-3-(4,5,6,7-tetrahydrobenzo[d]thiazol-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	398.5
122	(R)-(3-(2-(2,4-difluorophenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-fluorophenyl)methanone	456.5
123	(R)-(3-(2-(2,3-dichlorophenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-fluorophenyl)methanone	489.4
126	(R)-(4-fluorophenyl)(8-methyl-3-(2-(4-phenylpiperazin-1-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	504.6
127	(R)-(3-(2-(2,4-dichlorophenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-fluorophenyl)methanone	489.4
128	(R)-(3-(2-(3-chlorophenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-fluorophenyl)methanone	454.9

(continued)

Compound n°	Name	$(M+H)^+$
130	(R)-(4-fluorophenyl)(8-methyl-3-(2-phenyloxazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	404.4
131	(R)-[1,1'-biphenyl]-4-yl(8-methyl-3-(2-phenyloxazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	462.5
133	(R)-(4-fluorophenyl)(8-(2-hydroxyethyl)-3-(2-phenylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	450.5
134	(R)-(4'-fluoro-[1,1'-biphenyl]-4-yl)(8-methyl-3-(2-morpholinothiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	505.6
135	(R)-(8-methyl-3-(2-phenylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone	484.6
136	(R)-(8-methyl-3-(2-morpholinothiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone	493.6
138	(R)-(4-fluorophenyl)(8-methyl-3-(4-phenylthiazol-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	420.5
139	(R)-(3-(2-(2-chlorophenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-fluorophenyl)methanone	454.9
142	(R)-(8-methyl-3-(2-phenylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-3-yl)phenyl)methanone	484.6
144	(R)-(8-methyl-3-(quinolin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone	452.5
145	(R)-(3-(2-(2-chlorophenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone	519.1
146	(R)- [1,1'-biphenyl]-4-yl(3-(2-(2-chlorophenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	513.0
149	(R)-[1,1'-biphenyl]-4-yl(8-methyl-3-(4-methyl-2-phenylthiazol-5-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	492.6
150	(R)-(3-(2-(4-fluorophenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone	502.6
152	(R)- [1,1'-biphenyl]-4-yl(3-(2-(4-fluorophenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	496.6
155	(R)-[1,1'-biphenyl]-4-yl(3-(2-(2,4-difluorophenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	514.6
156	(R)-(3-(2-(2,4-difluorophenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone	520.6
159	(S)-(4-fluorophenyl)(8-methyl-3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	338.4
160	(S)-(4-fluorophenyl)(3-(2-(4-fluorophenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	438.5
161	(S)-(4'-fluoro-[1,1'-biphenyl]-4-yl)(8-methyl-3-(2-morpholinothiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	505.6
162	(S)-(4-fluorophenyl)(8-methyl-3-(quinolin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	388.4
163	(S)-(8-methyl-3-(quinolin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone	452.5

(continued)

Compound n°	Name	$(M+H)^+$
164	(S)-(4-fluorophenyl)(3-(2-(4-fluorophenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	438.5
165	(S)-(3-(2-(2,4-difluorophenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone	520.6
166	(4-fluorophenyl)(8-methyl-3-(2-phenylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	420.5
167	(S)-(4-fluorophenyl)(8-methyl-3-(2-phenylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	420.5
168	(S)-(3-(3-(4-fluorophenyl)-1,2,4-oxadiazol-5-yl)-8-methyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone	487.5
169	(R)-(3-(3-(4-fluorophenyl)-1,2,4-oxadiazol-5-yl)-8-methyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone	487.5
170	(3-(2-(2,4-difluorophenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone	506.6
171	(3-(5-phenyl-1,2,4-oxadiazol-3-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone	455.5
172	(4-fluorophenyl)(3-(3-phenyl-1,2,4-oxadiazol-5-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	391.4
173	(4-fluorophenyl)(3-(5-phenyl-1,2,4-oxadiazol-3-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	391.4
174	(3-(3-phenyl-1,2,4-oxadiazol-5-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone	455.5
175	(4-fluorophenyl)(3-(3-(4-fluorophenyl)-1,2,4-oxadiazol-5-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	409.4
176	(3-(3-(4-fluorophenyl)-1,2,4-oxadiazol-5-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone	473.5
177	(3-(3-(2,4-difluorophenyl)-1,2,4-oxadiazol-5-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone	491.5
178	(4- fluorophenyl)(3-(5-phenyl-1H-1,2,4-triazol-3-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	390.4
179	(3-(5-phenyl-1H-1,2,4-triazol-3-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone	454.5
180	(4-fluorophenyl)(3-(2-(2-fluorophenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	424.4
181	(3-(2-(2-fluorophenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone	488.6
182	[1,1'-biphenyl]-4-yl(3-(2-(2-fluorophenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	482.5
183	(4'-fluoro-[1,1'-biphenyl]-4-yl)(3-(2-(2-fluorophenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	500.5
185	(3-(3-(2,4-difluorophenyl)-1,2,4-oxadiazol-5-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone	491.5
186	[1,1'-biphenyl]-4-yl(3-(2-((4,5-dichloro-1H-imidazol-1-yl)methyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	537.4

(continued)

Compound n°	Name	$(M+H)^+$
187	(3-(2-((4,5-dichloro-1H-imidazol-1-yl)methyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4'-fluoro-[1,1'-biphenyl]-4-yl)methanone	555.4
188	(3-(2-(4-chlorobenzyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-fluorophenyl)methanone	454.9
189	(3-(2-(4-chlorobenzyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone	519.1
190	(4-fluorophenyl)(3-(2-(p-tolyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	420.5
191	(4-(thiophen-2-yl)phenyl)(3-(2-(p-tolyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	484.6
192	[1,1'-biphenyl]-4-yl(3-(2-(p-tolyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	478.6
193	(4-fluorophenyl)(3-(2-(thiophen-2-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	412.5
194	(4-(thiophen-2-yl)phenyl)(3-(2-(thiophen-2-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	476.6
195	[1,1'-biphenyl]-4-yl(3-(2-(thiophen-2-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	470.6
196	(4'-fluoro-[1,1'-biphenyl]-4-yl)(3-(2-(thiophen-2-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	488.6
198	(3-(2-(((4-chlorophenyl)sulfonyl)methyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone	583.1
199	[1,1'-biphenyl]-4-yl(3-(2-(((4-chlorophenyl)sulfonyl)methyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	577.1
200	(3-(2-(((4-chlorophenyl)sulfonyl)methyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4'-fluoro-[1,1'-biphenyl]-4-yl)methanone	595.1
201	(4-fluorophenyl)(3-(2-(2-methoxyphenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	436.5
202	(3-(2-(2-methoxyphenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone	500.6
203	[1,1'-biphenyl]-4-yl(3-(2-(2-methoxyphenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	494.6
204	[1,1'-biphenyl]-4-yl(3-(3-(4-fluorophenyl)-1,2,4-oxadiazol-5-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	467.5
205	(4'-fluoro-[1,1'-biphenyl]-4-yl)(3-(3-(4-fluorophenyl)-1,2,4-oxadiazol-5-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	485.5
206	(4-fluorophenyl)(3-(2-(3-fluorophenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	424.4
207	(3-(2-(3-fluorophenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone	488.6
208	(4-fluorophenyl)(3-(2-isopropylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	372.4
209	(3-(3-(4-fluorophenyl)-1,2,4-oxadiazol-5-yl)-8-methyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone	487.5

(continued)

Compound n°	Name	$(M+H)^+$
211	(3-(3-phenyl-1,2,4-thiadiazol-5-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone	471.6
212	(4-fluorophenyl)(3-(3-phenyl-1,2,4-thiadiazol-5-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	407.4
213	(3-(2-(4-bromophenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone	549.5
214	(3-(2-(4-bromophenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-fluorophenyl)methanone	485.3
215	(3-(2-(4-fluorophenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(5-methylthiophen-2-yl)phenyl)methanone	516.6
216	4-(3-(2-(4-fluorophenyl)thiazol-4-yl)-8-methyl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazine-7-carbonyl)benzonitrile	445.5
217	[1,1'-biphenyl]-4-yl(3-(3-phenyl-1,2,4-oxadiazol-5-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	449.5
218	(4-fluorophenyl)(3-(2-(pyridin-4-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	407.4
219	(3-(2-(quinolin-2-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone	521.6
220	(3-(1-methyl-3-phenyl-1H-pyrazol-5-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone	467.6
221	(3-(2-(4-(dimethylamino)phenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-fluorophenyl)methanone	449.5
222	(3-(1-methyl-5-phenyl-1H-pyrazol-3-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone	467.6
223	(4'-fluoro-[1,1'-biphenyl]-4-yl)(3-(3-phenyl-1,2,4-oxadiazol-5-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	467.5
224	(3-(2-(pyridin-2-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone	471.6
225	(4-fluorophenyl)(3-(1-methyl-3-phenyl-1H-pyrazol-5-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	403.4
226	(3-(2-(pyrimidin-2-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone	472.6
227	(S)-(8-methyl-3-(2-morpholinothiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone	493.6
228	(3-(2-(pyridin-4-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone	471.6
229	(3-(2-(4-(dimethylamino)phenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone	513.6
230	(4-fluorophenyl)(3-(2-(pyridin-2-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	407.4
231	phenyl(3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	306.3
232	(3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(p-tolyl)methanone	320.4

(continued)

Compound n°	Name	$(M+H)^+$
233	(S)-(3-(2-(4-fluorophenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(2-methylthiophen-3-yl)phenyl)methanone	516.6
234	(R)-(3-(2-(4-fluorophenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(2-methylthiophen-3-yl)phenyl)methanone	516.6
235	(3-(2-(pyrazin-2-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone	472.6
236	4-(4-(7-(4-(thiophen-2-yl)benzoyl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)thiazol-2-yl)benzonitrile	495.6
237	(4-fluorophenyl)(3-(2-(pyrazin-2-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	408.4
238	(4-fluorophenyl)(3-(1-methyl-5-phenyl-1H-pyrazol-3-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	403.4
239	(3-(2-(4-morpholinophenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone	555.7
240	(4-fluorophenyl)(3-(2-(4-morpholinophenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	491.6
241	(3-(2-(4-(4-methylpiperazin-1-yl)phenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone	568.7
242	(4-fluorophenyl)(3-(2-(4-(4-methylpiperazin-1-yl)phenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	504.6
243	(3-(2-(4-(piperidin-1-yl)phenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone	553.7
244	(4-fluorophenyl)(3-(2-(4-(piperidin-1-yl)phenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	489.6
245	(3-(2-(4-(pyrrolidin-1-yl)phenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone	539.7
246	(4-fluorophenyl)(3-(2-(4-(pyrrolidin-1-yl)phenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	475.6
247	(3-(2-(piperidin-1-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone	477.6
248	(3-(2-(pyrrolidin-1-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone	463.6
249	(4-fluorophenyl)(3-(2-(pyrrolidin-1-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	399.5
250	(3-(2-(4-methylpiperazin-1-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone	492.6
251	(4-fluorophenyl)(3-(2-(4-methylpiperazin-1-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	428.5
252	(3-(1-methyl-2-phenyl-1H-imidazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone	467.6
253	(4-(dimethylamino)phenyl)(3-(2-(4-fluorophenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	449.5
254	(3-(1-(2-methoxyethyl)-3-phenyl-1H-pyrazol-5-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone	511.6

(continued)

Compound n°	Name	$(M+H)^+$
255	(4-fluorophenyl)(3-(1-(2-methoxyethyl)-3-phenyl-1H-pyrazol-5-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	447.5
256	(3-(2-isobutylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone	450.6
257	(3-(2-(2-(2-methoxyethyl)morpholino)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone	537.7
258	(3-(2-(4,4-difluoropiperidin-1-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-fluorophenyl)methanone	449.5
259	(4-fluorophenyl)(3-(2-isobutylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	386.5
261	(3-(2-(2,5-dimethylmorpholino)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone	507.6
262	(3-(2-(2-hydroxyphenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone	486.6
263	(3-(2-(4,4-difluoropiperidin-1-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone	513.6
265	(3-(2-(2,6-dimethylmorpholino)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone	507.6
266	(3-(2-(2,2-dimethylmorpholino)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone	507.6
267	(3-(3-phenyl-1H-pyrazol-5-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone	453.5
268	(3-(2-(4-fluorophenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(3-methylthiophen-2-yl)phenyl)methanone	516.6
269	(4- fluorophenyl)(3-(3- phenyl-1H-pyrazol-5-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	389.4
270	(R)-(3-(2-(4-fluorophenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(3-methylthiophen-2-yl)phenyl)methanone	516.6
271	(4-fluorophenyl)(3-(2-(2-hydroxyphenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	422.4
272	(S)-(3-(2-(4-fluorophenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(3-methylthiophen-2-yl)phenyl)methanone	516.6
273	(3-(2-(2-methylmorpholino)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone	493.6
274	(3-(2-(4,4-dimethylpiperidin-1-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone	505.7
275	(3-(5-methylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone	408.5
276	(3-(2-(4,4-dimethylpiperidin-1-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-fluorophenyl)methanone	441.5
277	(4-fluorophenyl)(3-(2-(2-(methoxymethyl)pipendin-1-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	457.5
278	(4-fluorophenyl)(8-methyl-3-(6-methylpyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	352.4

(continued)

Compound n°	Name	$(M+H)^+$
279	(3-(2-(2-(methoxymethyl)piperidin-1-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone	521.7
280	tert-butyl (2-(2-(4-(7-(4-(thiophen-2-yl)benzoyl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)thiazol-2-yl)phenoxy)ethyl)carbamate	629.8
281	(3-(2-(2-(2-hydroxyethoxy)phenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone	530.6
282	(3-(2-(2-(2-aminoethoxy)phenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone	529.6
283	N-(4-(4-(7-(4-(thiophen-2-yl)benzoyl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)thiazol-2-yl)phenyl)methanesulfonamide	563.7
284	(3-(1-(2-hydroxyethyl)-3-phenyl-1H-pyrazol-5-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone	497.6
285	(3-(1-(2-hydroxyethyl)-5-phenyl-1H-pyrazol-3-yl)-5,6-dihydro-[1,2,4] triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone	497.6
286	[1,1'-biphenyl]-4-yl(8-methyl-3-(6-methylpyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	410.5
287	(8-methyl-3-(6-methylpyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone	416.5
288	(3-(2-(2,4-difluorophenyl)-5-methylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone	520.6
289	(3-(2-(3-(dimethylamino)phenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone	513.6
290	(3-(2-(3-(dimethylamino)phenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-fluorophenyl)methanone	449.5
291	N-(3-(4-(7-(4-(thiophen-2-yl)benzoyl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)thiazol-2-yl)phenyl)methanesulfonamide	563.7
292	N-(2-(4-(7-(4-(thiophen-2-yl)benzoyl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)thiazol-2-yl)phenyl)methanesulfonamide	563.7
294	(3-(4-chlorophenyl)-1H-pyrazol-5-yl)(3-(2-(4-fluorophenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	507.0
295	(3-(4-chlorophenyl)-1-methyl-1H-pyrazol-5-yl)(3-(2-(4-fluorophenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	521.0
296	(3-(3,4-dichlorophenyl)-1-methyl-1H-pyrazol-5-yl)(3-(2-(4-fluorophenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	555.4
297	(5-(4-chlorophenyl)-1-methyl-1H-pyrazol-3-yl)(3-(2-(4-fluorophenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone	521.0
298	tert-butyl (2-(3-phenyl-5-(7-(4-(thiophen-2-yl)benzoyl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)-1H-pyrazol-1-yl)ethyl)carbamate	596.7
299	tert-butyl (2-(5-phenyl-3-(7-(4-(thiophen-2-yl)benzoyl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)-1H-pyrazol-1-yl)ethyl)carbamate	596.7
300	(3-(2-(2-bromophenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone	549.5
301	(3-(2-(3-bromophenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone	549.5

(continued)

Compound n°	Name	$(M+H)^+$
302	2-(4-(7-(4-(thiophen-2-yl)benzoyl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)thiazol-2-yl)benzonitrile	495.6
303	3-(4-(7-(4-(thiophen-2-yl)benzoyl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)thiazol-2-yl)benzonitrile	495.6
304	(3-(2-(4-fluorophenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(2-methylthiophen-3-yl)phenyl)methanone	516.6

[0062] The compounds of table 1 were named using ChemDraw Ultra 12 purchased from CambridgeSoft (Cambridge, MA, USA).

[0063] The compounds of formula I can be prepared by different ways with reactions known by the person skilled in the art. Reaction schemes as described in the example section illustrate by way of example different possible approaches.

[0064] The invention further provides the use of the compounds of the invention or pharmaceutically acceptable salts, or solvates thereof as antagonists of NK-3 receptor.

[0065] Accordingly, in a particularly preferred embodiment, the invention relates to the use of compounds of formula I and subformulae in particular those of table 1 above, or pharmaceutically acceptable salts and solvates thereof, as NK-3 receptor antagonists.

[APPLICATIONS]

[0066] The compounds of the invention are therefore useful as medicaments, in particular in the prevention and/or treatment of depression, anxiety, pyschosis, schizophrenia, psychotic disorders, bipolar disorders, cognitive disorders, Parkinson's disease, Alzheimer's disease, attention deficit hyperactivity disorder (ADHD), pain, convulsion, obesity, inflammatory diseases including irritable bowel syndrome and inflammatory bowel disorders, emesis, pre-eclampsia, airway related diseases including chronic obstructive pulmonary disease, asthma, airway hyperresponsiveness, bronchoconstriction and cough, reproduction disorders and sex hormone-dependent diseases including but not limited to benign prostatic hyperplasia (BPH), metastatic prostatic carninoma, testicular cancer, breast cancer, androgen dependent acne, male pattern baldness, endometriosis, abnormal puberty, uterine fibrosis, hormone-dependent cancers, hyperandrogenism, hirsutism, virilization, polycystic ovary syndrome (PCOS), HAIR-AN syndrome (hyperandrogenism, insulin resistance and acanthosis nigricans), ovarian hyperthecosis (HAIR-AN with hyperplasia of luteinized theca cells in ovarian stroma), other manifestations of high intraovarian androgen concentrations (e.g. follicular maturation arrest, atresia, anovulation, dysmenorrhea, dysfunctional uterine bleeding, infertility) and androgen-producing tumor (virilizing ovarian or adrenal tumor).

[0067] The invention also provides for the use of a compound of formula (I) or pharmaceutically salt thereof in a method for delaying in patient the onset of depression, anxiety, pyschosis, schizophrenia, psychotic disorders, bipolar disorders, cognitive disorders, Parkinson's disease, Alzheimer's disease, attention deficit hyperactivity disorder (ADHD), pain, convulsion, obesity, inflammatory diseases including irritable bowel syndrome and inflammatory bowel disorders, emesis, pre-eclampsia, airway related diseases including chronic obstructive pulmonary disease, asthma, airway hyperresponsiveness, bronchoconstriction and cough, reproduction disorders and sex hormone-dependent diseases including but not limited to benign prostatic hyperplasia (BPH), metastatic prostatic carninoma, testicular cancer, breast cancer, androgen dependent acne, male pattern baldness, endometriosis, abnormal puberty, uterine fibrosis, hormone-dependent cancers, hyperandrogenism, hirsutism, virilization, polycystic ovary syndrome (PCOS), HAIR-AN syndrome (hyperandrogenism, insulin resistance and acanthosis nigricans), ovarian hyperthecosis (HAIR-AN with hyperplasia of luteinized theca cells in ovarian stroma), other manifestations of high intraovarian androgen concentrations (e.g. follicular maturation arrest, atresia, anovulation, dysmenorrhea, dysfunctional uterine bleeding, infertility) and androgen-producing tumor (virilizing ovarian or adrenal tumor) comprising the administration of a pharmaceutically effective amount of said compound to a patient in need thereof.

[0068] Preferably, the patient is a warm-blooded animal, more preferably a human.

[0069] The compounds of the invention are also useful in the treatment of gynecological disorders and infertility. In particular, the invention provides methods to suppress the LH-surge in assisted conception.

[0070] The compounds of the invention are also useful to cause male castration and to inhibit the sex drive in men. This of particular interest in the treatment of male sexual offenders.

[0071] The invention further provides the use of a compound of formula (I) or a pharmaceutically acceptable salt or solvate thereof for the manufacture of a medicament for treating and/or preventing depression, anxiety, pyschosis,

schizophrenia, psychotic disorders, bipolar disorders, cognitive disorders, Parkinson's disease, Alzheimer's disease, attention deficit hyperactivity disorder (ADHD), pain, convulsion, obesity, inflammatory diseases including irritable bowel syndrome and inflammatory bowel disorders, emesis, pre-eclampsia, airway related diseases including chronic obstructive pulmonary disease, asthma, airway hyperresponsiveness, bronchoconstriction and cough, reproduction disorders and sex hormone-dependent diseases including but not limited to benign prostatic hyperplasia (BPH), metastatic prostatic carninoma, testicular cancer, breast cancer, androgen dependent acne, male pattern baldness, endometriosis, abnormal puberty, uterine fibrosis, hormone-dependent cancers, hyperandrogenism, hirsutism, virilization, polycystic ovary syndrome (PCOS), HAIR-AN syndrome (hyperandrogenism, insulin resistance and acanthosis nigricans), ovarian hyperthecosis (HAIR-AN with hyperplasia of luteinized theca cells in ovarian stroma), other manifestations of high intraovarian androgen concentrations (e.g. follicular maturation arrest, atresia, anovulation, dysmenorrhea, dysfunctional uterine bleeding, infertility) and androgen-producing tumor (virilizing ovarian or adrenal tumor) in a patient.

[0072] Preferably, the patient is a warm-blooded animal, more preferably a human.

[0073] The invention further provides the use of a compound of formula (I) or a pharmaceutically acceptable salt or solvate thereof for the manufacture of a medicament to suppress the LH-surge in assisted conception in a patient. Preferably the patient is a warm-blooded animal, more preferably a woman.

[0074] The invention further provides the use of a compound of formula (I) or a pharmaceutically acceptable salt or solvate thereof for the manufacture of a medicament to cause male castration and to inhibit the sex drive in men. This is of particular interest in the treatment of male sexual offenders.

[0075] According to a further feature of the present invention there is provided the use of a compound of the present invention, or a pharmaceutically acceptable salt or solvate thereof in a
method for modulating NK-3 receptor activity, in a patient, preferably a warm blooded animal, and even more preferably a human, in need of such treatment, which comprises administering to said patient an effective amount of said compound.

[0076] According to one embodiment, the compounds of the invention, their pharmaceutical acceptable salts or solvates may be administered as part of a combination therapy. Thus, are included within the scope of the present invention embodiments comprising coadministration of, and compositions and medicaments which contain, in addition to a compound of the present invention, a pharmaceutically acceptable salt or solvate thereof as active ingredient, additional therapeutic agents and/or active ingredients. Such multiple drug regimens, often referred to as combination therapy, may be used in the treatment and/or prevention of any of the diseases or conditions mediated by or associated with NK-3 receptor modulation. The use of such combinations of therapeutic agents is especially pertinent with respect to the treatment of the above-mentioned disorders within a patient in need of treatment or one at risk of becoming such a patient.

[0077] In addition to the requirement of therapeutic efficacy, which may necessitate the use of active agents in addition to the NK-3 receptor modulator compounds of Formula I or pharmaceutical acceptable salts or solvates thereof, there may be additional rationales which compel or highly recommend the use of combinations of drugs involving active ingredients which represent adjunct therapy, i.e., which complement and supplement the function performed by the NK-3 receptor modulator compounds of the present invention. Suitable supplementary therapeutic agents used for the purpose of auxiliary treatment include drugs which, instead of directly treating or preventing a disease or condition mediated by or associated with NK-3 receptor modulation, treat diseases or conditions which directly result from or indirectly accompany the basic or underlying NK-3 receptor modulated disease or condition.

[0078] According to a further feature of the present invention the compound of Formula I, a pharmaceutically acceptable salt or solvate thereof may be used in combination therapy with antipsychotic drugs (APD), to improve the efficacy and to minimize secondary effects associated to APD including but not limited to Dopamine 2/3 and 5-HT2 receptors antagonists. More particular the compound of Formula I, a pharmaceutically acceptable salt or solvate thereof may be used as an adjunct therapy in combination with an atypical antipsychotic drug, including but not limited to risperidone, clozapine, olanzapine, where the NK-3 receptor modulator may serve a role as dose-limiting for the atypical antipsychotic and therefore spare the patient from some of the side effect of those atypical antipsychotic drugs.

[0079] Thus, the methods of treatment and pharmaceutical compositions of the present invention may employ the compounds of Formula I or pharmaceutical acceptable salts or solvates thereof in the form of monotherapy, but said methods and compositions may also be used in the form of multiple therapy in which one or more compounds of Formula I or their pharmaceutically acceptable salts or solvates are coadministered in combination with one or more other therapeutic agents.

[0080] In the above-described embodiment combinations of the present invention, the compound of Formula I, a pharmaceutically acceptable salt or solvate thereof and other therapeutic active agents may be administered in terms of dosage forms either separately or in conjunction with each other, and in terms of their time of administration, either serially or simultaneously. Thus, the administration of one component agent may be prior to, concurrent with, or subsequent to the administration of the other component agent(s).

[0081] The invention also provides pharmaceutical compositions comprising a compound of formula I or a pharmaceutically acceptable salt or solvate thereof and at least one pharmaceutically acceptable carrier, diluent, excipient and/or adjuvant. As indicated above, the invention also covers pharmaceutical compositions which contain, in addition to a

compound of the present invention, a pharmaceutically acceptable salt or solvate thereof as active ingredient, additional therapeutic agents and/or active ingredients.

[0082] Another object of this invention is a medicament comprising at least one compound of the invention, or a pharmaceutically acceptable salt or solvate thereof, as active ingredient.

[0083] According to a further feature of the present invention there is provided the use of a compound of formula I or a pharmaceutically acceptable salt or solvate thereof for the manufacture of a medicament for modulating NK-3 receptor activity in a patient, in need of such treatment, which comprises administering to said patient an effective amount of compound of the present invention, or a pharmaceutically acceptable salt or solvate thereof.

[0084] Preferably, the patient is a warm-blooded animal, more preferably a human.

[0085] As set forth above, the compounds of the invention, their pharmaceutically acceptable salts or solvates may be used in monotherapy or in combination therapy. Thus, according to one embodiment, the invention provides the use of a compound of the invention for the manufacture of a medicament for at least one of the purposes described above, wherein said medicament is administered to a patient in need thereof, preferably a warm-blooded animal, and even more preferably a human, in combination with at least one additional therapeutic agent and/or active ingredient. The benefits and advantages of such a multiple drug regimen, possible administration regimens as well as suitable additional therapeutic agents and/or active ingredients are those described above.

[0086] Generally, for pharmaceutical use, the compounds of the inventions may be formulated as a pharmaceutical preparation comprising at least one compound of the invention and at least one pharmaceutically acceptable carrier, diluent, excipient and/or adjuvant, and optionally one or more further pharmaceutically active compounds.

[0087] By means of non-limiting examples, such a formulation may be in a form suitable for oral administration, for parenteral administration (such as by intravenous, intramuscular or subcutaneous injection or intravenous infusion), for topical administration (including ocular), for administration by inhalation, by a skin patch, by an implant, by a suppository, etc. Such suitable administration forms - which may be solid, semi-solid or liquid, depending on the manner of administration - as well as methods and carriers, diluents and excipients for use in the preparation thereof, will be clear to the skilled person; reference is made to the latest edition of Remington's Pharmaceutical Sciences.

[0088] Some preferred, but non-limiting examples of such preparations include tablets, pills, powders, lozenges, sachets, cachets, elixirs, suspensions, emulsions, solutions, syrups, aerosols, ointments, cremes, lotions, soft and hard gelatin capsules, suppositories, drops, sterile injectable solutions and sterile packaged powders (which are usually reconstituted prior to use) for administration as a bolus and/or for continuous administration, which may be formulated with carriers, excipients, and diluents that are suitable per se for such formulations, such as lactose, dextrose, sucrose, sorbitol, mannitol, starches, gum acacia, calcium phosphate, alginates, tragacanth, gelatin, calcium silicate, microcrystalline cellulose, polyvinylpyrrolidone, polyethylene glycol, cellulose, (sterile) water, methylcellulose, methyl- and propylhydroxybenzoates, talc, magnesium stearate, edible oils, vegetable oils and mineral oils or suitable mixtures thereof. The formulations can optionally contain other substances that are commonly used in pharmaceutical formulations, such as lubricating agents, wetting agents, emulsifying and suspending agents, dispersing agents, desintegrants, bulking agents, fillers, preserving agents, sweetening agents, flavoring agents, flow regulators, release agents, etc.. The compositions may also be formulated so as to provide rapid, sustained or delayed release of the active compound(s) contained therein.

[0089] The pharmaceutical preparations of the invention are preferably in a unit dosage form, and may be suitably packaged, for example in a box, blister, vial, bottle, sachet, ampoule or in any other suitable single-dose or multi-dose holder or container (which may be properly labeled); optionally with one or more leaflets containing product information and/or instructions for use. Generally, such unit dosages will contain between 0,05 and 1000 mg, and usually between 1 and 500 mg, of the at least one compound of the invention, e.g. about 10, 25, 50, 100, 200, 300 or 400 mg per unit dosage.

[0090] Usually, depending on the condition to be prevented or treated and the route of administration, the active compound of the invention will usually be administered between 0.01 to 100 mg per kilogram, more often betwen 0.1 and 50 mg, such as between 1 and 25 mg, for example about 0.5, 1, 5, 10, 15, 20 or 25 mg, per kilogram body weight of the patient per day, which may be administered as a single daily dose, divided over one or more daily doses, or essentially continuously, e.g. using a drip infusion.

[DEFINITIONS]

[0091] The definitions and explanations below are for the terms as used throughout the entire application, including both the specification and the claims.

[0092] When describing the compounds of the invention, the terms used are to be construed in accordance with the following definitions, unless indicated otherwise.

[0093] Where groups may be substituted, such groups may be substituted with one or more substituents, and preferably with one, two or three substituents. Substituents may be selected from but not limited to, for example, the group comprising halogen, hydroxyl, oxo, nitro, amido, carboxy, amino, cyano haloalkoxy, and haloalkyl.

[0094] As used herein the terms such as "alkyl, aryl, or cycloalkyl, each being optionally substituted with..." or "alkyl, aryl, or cycloalkyl, optionally substituted with..." encompasses "alkyl optionally substituted with...", "aryl optionally substituted with..." and "cycloalkyl optionally substituted with...".

[0095] The term "halo" or "halogen" means fluoro, chloro, bromo, or iodo. Preferred halo groups are fluoro and chloro.

[0096] The term "alkyl" by itself or as part of another substituent refers to a hydrocarbyl radical of Formula C_nH_{2n+1} wherein n is a number greater than or equal to 1. Generally, alkyl groups of this invention comprise from 1 to 6 carbon atoms, preferably from 1 to 4 carbon atoms, more preferably from 1 to 3 carbon atoms, still more preferably 1 to 2 carbon atoms. Alkyl groups may be linear or branched and may be substituted as indicated herein.

[0097] Suitable alkyl groups include methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl and t-butyl, pentyl and its isomers (e.g. n-pentyl, iso-pentyl), and hexyl and its isomers (e.g. n-hexyl, iso-hexyl). Preferred alkyl groups include methyl, ethyl, *n*-propyl, *i*-propyl, *n*-butyl, *i*-butyl, *s*-butyl and *t*-butyl. C_{x-y} -alkyl and Cx-Cy-alkyl refer to alkyl groups which comprise from x to y carbon atoms.

[0098] When the suffix "ene" ("alkylene") is used in conjunction with an alkyl group, this is intended to mean the alkyl group as defined herein having two single bonds as points of attachment to other groups. The term "alkylene" includes methylene, ethylene, methylmethylene, propylene, ethylethylene, and 1,2-dimethylethylene.

[0099] The term "haloalkyl" alone or in combination, refers to an alkyl radical having the meaning as defined above wherein one or more hydrogens are replaced with a halogen as defined above. Non-limiting examples of such haloalkyl radicals include chloromethyl, 1-bromoethyl, fluoromethyl, difluoromethyl, trifluoromethyl, 1,1,1-trifluoroethyl and the like. C_{x-y} -haloalkyl and Cx-Cy-alkyl refer to alkyl groups which comprise from x to y carbon atoms. Preferred haloalkyl groups are difluoromethyl, trifluoromethyl.

[0100] The term "cycloalkyl" as used herein is a cyclic alkyl group, that is to say, a monovalent, saturated, or unsaturated hydrocarbyl group having 1 or 2 cyclic structures. Cycloalkyl includes monocyclic or bicyclic hydrocarbyl groups. Cycloalkyl groups may comprise 3 or more carbon atoms in the ring and generally, according to this invention comprise from 3 to 10, more preferably from 3 to 8 carbon atoms still more preferably from 3 to 6 carbon atoms. Examples of cycloalkyl groups include but are not limited to cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, with cyclopropyl being particularly preferred.

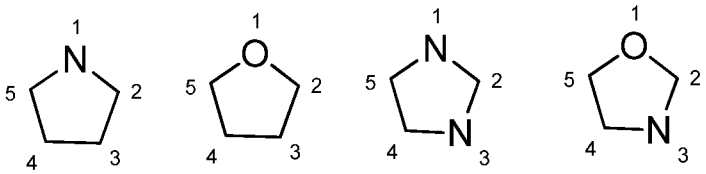
[0101] When the suffix "ene" is used in conjunction with a cyclic group, this is intended to mean the cyclic group as defined herein having two single bonds as points of attachment to other groups.

[0102] Therefore, "cycloalkylene" herein refers to a saturated homocyclic hydrocarbyl biradical of Formula C_nH_{2n-2}. Suitable cycloalkylene groups are C_{3-6} cycloalkylene group, preferably a C_{3-5} cycloalkylene (i.e. 1,2-cyclopropylene, 1,1-cyclopropylene, 1,1-cyclobutylene, 1,2-cyclobutylene, 1,3-cyclobutylene, 1,3-cyclopentylene, or 1,1-cyclopentylene), more preferably a C_{3-4} cycloalkylene (i.e. 1,2-cyclopropylene, 1,1-cyclopropylene, 1,1-cyclobutylene, 1,2-cyclobutylene).

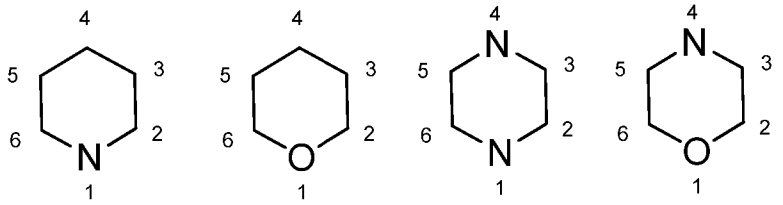
[0103] Where at least one carbon atom in a cycloalkyl group is replaced with a heteroatom, the resultant ring is referred to herein as "heterocycloalkyl" or "heterocyclyl".

[0104] The terms "heterocyclyl", "heterocycloalkyl" or "heterocyclo" as used herein by itself or as part of another group refer to non-aromatic, fully saturated or partially unsaturated cyclic groups (for example, 3 to 7 member monocyclic, 7 to 11 member bicyclic, or containing a total of 3 to 10 ring atoms) which have at least one heteroatom in at least one carbon atom-containing ring. Each ring of the heterocyclic group containing a heteroatom may have 1, 2, 3 or 4 heteroatoms selected from nitrogen, oxygen and/or sulfur atoms, where the nitrogen and sulfur heteroatoms may optionally be oxidized and the nitrogen heteroatoms may optionally be quaternized. Any of the carbon atoms of the heterocyclic group may be substituted by oxo (for example piperidone, pyrrolidinone).The heterocyclic group may be attached at any heteroatom or carbon atom of the ring or ring system, where valence allows. The rings of multi-ring heterocycles may be fused, bridged and/or joined through one or more spiro atoms. Non limiting exemplary heterocyclic groups include oxetanyl, piperidinyl, azetidinyl, 2-imidazolinyl, pyrazolidinyl imidazolidinyl, isoxazolinyl, oxazolidinyl, isoxazolidinyl, thiazolidinyl, isothiazolidinyl, piperidinyl, 3H-indolyl, indolinyl, isoindolinyl, 2-oxopiperazinyl, piperazinyl, homopiperazinyl, 2-pyrazolinyl, 3-pyrazolinyl, tetrahydro-2H-pyranyl, 2H-pyranyl, 4H-pyranyl, 3,4-dihydro-2H-pyranyl, 3-dioxolanyl, 1,4-dioxanyl, 2,5-dioximidazolidinyl, 2-oxopiperidinyl, 2-oxopyrrolodinyl, indolinyl, tetrahydropyranyl, tetrahydrofuranyl, tetrahydroquinolinyl, tetrahydroisoquinolin-1-yl, tetrahydroisoquinolin-2-yl, tetrahydroisoquinolin-3-yl, tetrahydroisoquinolin-4-yl, thiomorpholin-4-yl, thiomorpholin-4-ylsulfoxide, thiomorpholin-4-ylsulfone, 1,3-dioxolanyl, 1,4-oxathianyl, 1H-pyrrolizinyl, tetrahydro-1,1-dioxothiophenyl, N- formylpiperazinyl, and morpholin-4-yl.

[0105] The ring atoms of selected heterocyclyl and heterocyclylene moieties are numbered based on scheme below

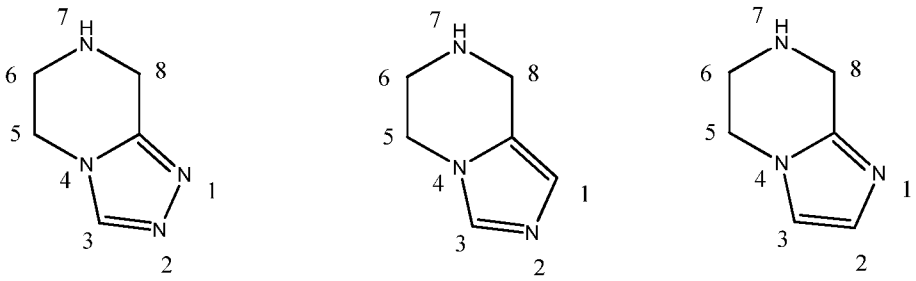


pyrrolidinyl tetrahydrofuranyl imidazolinyl oxazolidinyl



piperidinyl tetrahydropyranyl piperazinyl morpholinyl

[0106] The ring atoms of fused piperazine of the invention are numbered based on scheme below



5,6,7,8-tetrahydro-[1,2,4]triazolo [4,3-a]pyrazine

5,6,7,8-tetrahydroimidazo [1,5-a]pyrazine

5,6,7,8-tetrahydroimidazo [1,2-a]pyrazine

[0107] The term "aryl" as used herein refers to a polyunsaturated, aromatic hydrocarbyl group having a single ring (i.e. phenyl) or multiple aromatic rings fused together (e.g. naphtyl) or linked covalently, typically containing 5 to 12 atoms; preferably 6 to 10, wherein at least one ring is aromatic. The aromatic ring may optionally include one to two additional rings (either cycloalkyl, heterocyclyl or heteroaryl) fused thereto. Aryl is also intended to include the partially hydrogenated derivatives of the carbocyclic systems enumerated herein. Non-limiting examples of aryl comprise phenyl, biphenylyl, biphenylenyl, 5- or 6-tetralinyl, naphthalen-1- or -2-yl, 4-, 5-, 6 or 7-indenyl, 1- 2-, 3-, 4- or 5-acenaphtylenyl, 3-, 4- or 5-acenaphtenyl, 1- or 2-pentalenyl, 4- or 5-indanyl, 5-, 6-, 7- or 8-tetrahydronaphthyl, 1,2,3,4-tetrahydronaphthyl, 1,4-dihydronaphthyl, 1-, 2-, 3-, 4- or 5-pyrenyl.

[0108] The term "arylene" as used herein is intended to include divalent carbocyclic aromatic ring systems such as phenylene, biphenylylene, naphthylene, indenylene, pentalenylene, azulenylene and the like. Arylene is also intended to include the partially hydrogenated derivatives of the carbocyclic systems enumerated above. Non-limiting examples of such partially hydrogenated derivatives are 1,2,3,4-tetrahydronaphthylene, 1,4-dihydronaphthylene and the like.

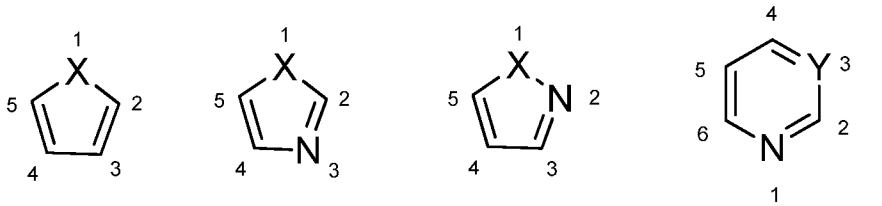
[0109] Where at least one carbon atom in an aryl group is replaced with a heteroatom, the resultant ring is referred to herein as a heteroaryl ring.

[0110] The term "heteroaryl" as used herein by itself or as part of another group refers but is not limited to 5 to 12 carbon-atom aromatic rings or ring systems containing 1 to 2 rings which are fused together or linked covalently, typically containing 5 to 6 atoms; at least one of which is aromatic, in which one or more carbon atoms in one or more of these rings is replaced by oxygen, nitrogen and/or sulfur atoms where the nitrogen and sulfur heteroatoms may optionally be oxidized and the nitrogen heteroatoms may optionally be quaternized. Such rings may be fused to an aryl, cycloalkyl, heteroaryl or heterocyclyl ring. Non-limiting examples of such heteroaryl, include: furanyl, thiophenyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, triazolyl, oxadiazolyl, thiadiazolyl, tetrazolyl, oxatriazolyl, thiatriazolyl, pyridinyl, pyrimidyl, pyrazinyl, pyridazinyl, oxazinyl, dioxinyl, thiazinyl, triazinyl, imidazo[2,1-b][1,3]thiazolyl, thieno[3,2-b]furanyl, thieno[3,2-b]thiophenyl, thieno[2,3-d][1,3]thiazolyl, thieno[2,3-d]imidazolyl, tetrazolo[1,5-a]pyridinyl, indolyl, indolizinyl, isoindolyl, benzofuranyl, isobenzofuranyl, benzothiophenyl, isobenzothiophenyl, indazolyl, benzimidazolyl, 1,3-

benzoxazolyl, 1,2-benzisoxazolyl, 2,1-benzisoxazolyl, 1,3-benzothiazolyl, 1,2-benzoisothiazolyl, 2,1-benzoisothiazolyl, benzotriazolyl, 1,2,3-benzoxadiazolyl, 2,1,3-benzoxadiazolyl, 1,2,3-benzothiadiazolyl, 2,1,3-benzothiadiazolyl, thienopyridinyl, purinyl, imidazo[1,2-a]pyridinyl, 6-oxo-pyridazin-1(6H)-yl, 2-oxopyridin-1(2H)-yl, 6-oxo-pyridazin-1(6H)-yl, 2-oxopyridin-1(2H)-yl, 1,3-benzodioxolyl, quinolinyl, isoquinolinyl, cinnolinyl, quinazolinyl, quinoxalinyl.

[0111] The term "heteroarylene" as used herein means divalent carbocyclic aromatic ring systems including pyridinylene and the like.

[0112] The ring atoms of selected heteroaryl or heteroarylene moieties are numbered on scheme below:



X is selected from: N, O or S

Examples:

pyrrolyl
furanyl
thiophenyl

X is selected from: N, O or S

Examples:

imidazolyl
oxazolyl
thiazolyl

X is selected from: N, O or S

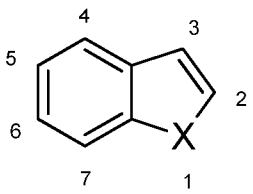
Examples:

pyrazolyl
isooxazolyl
isothiazolyl

Y is selected from: C, N

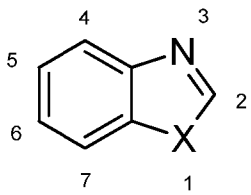
Examples:

pyridyl
pyrimidinyl



X is selected from: N, O or S

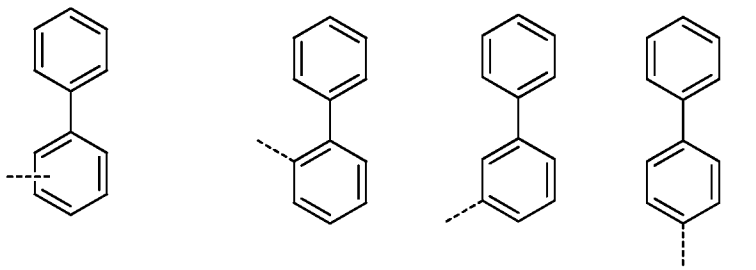
Examples:
indolyl
benzofuranyl
benzothiophenyl



X is selected from: N, O or S

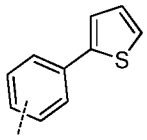
Examples:
benzimidazolyl
benzoxazolyl
benzothiazolyl

[0113] The term "biaryl" as used herein designates two aryl moieties as defined herein linked via a single bond. Non-limiting examples of such biaryl moieties include all biphenyl regioisomers 2-biphenyl, 3-biphenyl and 4-biphenyl.

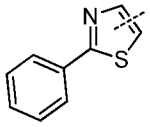


biphenyl 2-biphenyl 3-biphenyl 4-biphenyl

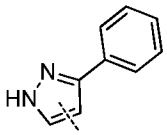
[0114] The term "heterobiaryl" as used herein designates two heteroaryl moieties as defined herein or a heteroaryl moiety and an aryl moity as defined herein linked via a single bond. Non-limiting examples of such heterobiaryl moieties are given hereunder.



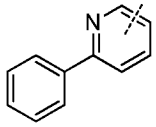
(thiophen-2-yl)phenyl



(2-phenyl)thiazolyl

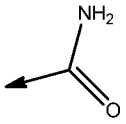


(3-phenyl)pyrazolyl



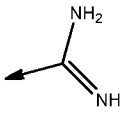
(2-phenyl)pyridyl or
(2-phenyl)pyridinyl

[0115] The term "carbamoyl" as used herein means a group of formula



wherein the arrow defines the attachment point.

[0116] The term "carbamimidoyl" as used herein means a group of formula

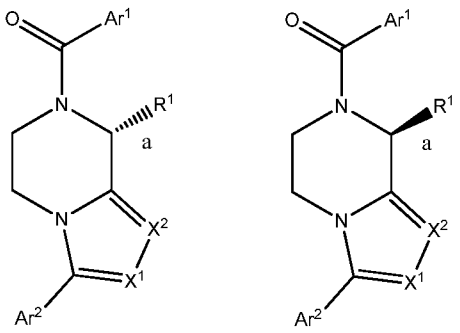


wherein the arrow defines the attachment point.

[0117] The compounds of Formula I and subformulae thereof contain at least one asymmetric center and thus may exist as different stereoisomeric forms. Accordingly, the present invention includes all possible stereoisomers and includes not only racemic compounds but the individual enantiomers and their non racemic mixtures as well. When a compound is desired as a single enantiomer, such may be obtained by stereospecific synthesis, by resolution of the final product or any convenient intermediate, or by chiral chromatographic methods as each are known in the art. Resolution of the final product, an intermediate, or a starting material may be effected by any suitable method known in the art. See, for example, Stereochemistry of Organic Compounds by E. L. Eliel, S. H. Wilen, and L. N. Mander (Wiley-Interscience, 1994), incorporated by reference with regard to stereochemistry.

[0118] The bonds from an asymmetric carbon in compounds of the present invention may be depicted herein using a solid line (-), a zigzag line (), a solid wedge (), or a dotted wedge (). The use of a solid line to depict bonds from an asymmetric carbon atom is meant to indicate that all possible stereoisomers in any relative ratio are meant to be included, unless it is clear from the context that a specific stereoisomer is intended. As a non limiting example, a solid line depicting bonds from an asymmetric carbon atom in a compound containing one asymmetric carbon encompasses a racemic mixture of both enantiomers. The term racemic used herein indicated a 1/1 ratio between the two enantiomers. The use of either a solid or dotted wedge to depict bonds from an asymmetric carbon atom is meant to indicate that only the stereoisomer shown is meant to be included.

[0119] As a non limiting example, compounds of formula Ic wherein **$R^{1'}$** is H, **R^1** is not H and bond **a,** which designates the bond linking **R^1** to the piperazine moiety, is drawn as a dotted wedge are stereoisomers of formula A. Compounds of formula Ic wherein **$R^{1'}$** is H, **R^1** is not H and bond a is drawn as a solid wedge are stereoisomers of formula B.



A

B

[0120] The compounds of the invention may also contain more than one asymmetric carbon atom. In those compounds, the use of a solid line to depict bonds from asymmetric carbon atoms is meant to indicate that all possible stereoisomers in any relative ratio are meant to be included, unless it is clear from the context that a specific stereoisomer is intended.

[0121] The compounds of the invention may be in the form of pharmaceutically acceptable salts. Pharmaceutically acceptable salts of the compounds of formula I include the acid addition and base salts thereof. Suitable acid addition salts are formed from acids which form non-toxic salts. Examples include the acetate, adipate, aspartate, benzoate, besylate, bicarbonate/carbonate, bisulphate/sulphate, borate, camsylate, citrate, cyclamate, edisylate, esylate, formate, fumarate, gluceptate, gluconate, glucuronate, hexafluorophosphate, hibenzate, hydrochloride/chloride, hydrobromide/bromide, hydroiodide/iodide, isethionate, lactate, malate, maleate, malonate, mesylate, methylsulphate, naphthylate, 2-napsylate, nicotinate, nitrate, orotate, oxalate, palmitate, pamoate, phosphate/hydrogen phosphate/dihydrogen phosphate, pyroglutamate, saccharate, stearate, succinate, tannate, tartrate, tosylate, trifluoroacetate and xinofoate salts. Suitable base salts are formed from bases which form non-toxic salts. Examples include the aluminium, arginine, benzathine, calcium, choline, diethylamine, diolamine, glycine, lysine, magnesium, meglumine, olamine, potassium, sodium, tromethamine, 2-(diethylamino)ethanol, ethanolamine, morpholine, 4-(2-hydroxyethyl)morpholine and zinc salts. Hemisalts of acids and bases may also be formed, for example, hemisulphate and hemicalcium salts. Preferred, pharmaceutically acceptable salts include hydrochloride/chloride, hydrobromide/bromide, bisulphate/sulphate, nitrate, citrate, and acetate.

[0122] When the compounds of the invention contain an acidic group as well as a basic group the compounds of the invention may also form internal salts, and such compounds are within the scope of the invention. When the compounds of the invention contain a hydrogen-donating heteroatom (e.g. NH), the invention also covers salts and/or isomers formed by transfer of said hydrogen atom to a basic group or atom within the molecule.

[0123] Pharmaceutically acceptable salts of compounds of Formula I may be prepared by one or more of these methods:

(i) by reacting the compound of Formula I with the desired acid;

(ii) by reacting the compound of Formula I with the desired base;

(iii) by removing an acid- or base-labile protecting group from a suitable precursor of the compound of Formula I or by ring-opening a suitable cyclic precursor, for example, a lactone or lactam, using the desired acid; or

(iv) by converting one salt of the compound of Formula I to another by reaction with an appropriate acid or by means of a suitable ion exchange column.

[0124] All these reactions are typically carried out in solution. The salt, may precipitate from solution and be collected by filtration or may be recovered by evaporation of the solvent. The degree of ionization in the salt may vary from completely ionized to almost non-ionized.

[0125] The term "solvate" is used herein to describe a molecular complex comprising the compound of the invention and one or more pharmaceutically acceptable solvent molecules, for example, ethanol. The term 'hydrate' is employed when said solvent is water.

[0126] All references to compounds of formula I include references to salts, solvates, multi- component complexes and liquid crystals thereof.

[0127] The compounds of the invention include compounds of formula I as hereinbefore defined, including all polymorphs and crystal habits thereof, prodrugs and isomers thereof (including optical, geometric and tautomeric isomers) and isotopically-labeled compounds of formula I.

[0128] In addition, although generally, with respect to the salts of the compounds of the invention, pharmaceutically acceptable salts are preferred, it should be noted that the invention in its broadest sense also included non-pharmaceutically acceptable salts, which may for example be used in the isolation and/or purification of the compounds of the invention. For example, salts formed with optically active acids or bases may be used to form diastereoisomeric salts that can facilitate the separation of optically active isomers of the compounds of Formula I above.

[0129] The invention also generally covers all pharmaceutically acceptable predrugs and prodrugs of the compounds of Formula I.

[0130] The term "prodrug" as used herein means the pharmacologically acceptable derivatives of compounds of formula I such as esters whose in vivo biotransformation product is the active drug. Prodrugs are characterized by increased bio-availability and are reaily metabolized into the active compounds in vivo.

[0131] The term "predrug", as used herein, means any compound that will be modified to form a drug species, wherein the modification may take place either inside or outside of the body, and either before or after the predrug reaches the area of the body where administration of the drug is indicated.

[0132] The term "patient" refers to a warm-blooded animal, more preferably a human, who/which is awaiting or receiving

medical care or is or will be the object of a medical procedure.

[0133] The term "human" refers to suject of both genders and at any stage of development (i.e. neonate, infant, juvenile, adolescent, adult).

[0134] The terms "treat", "treating" and "treatment, as used herein, are meant to include alleviating or abrogating a condition or disease and/or its attendant symptoms.

[0135] The terms "prevent", "preventing" and "prevention", as used herein, refer to a method of delaying or precluding the onset of a condition or disease and/or its attendant symptoms, barring a patient from acquiring a condition or disease, or reducing a patient's risk of acquiring a condition or disease.

[0136] The term "therapeutically effective amount" (or more simply an "effective amount") as used herein means the amount of active agent or active ingredient (e. g. NK-3 antagonist) which is sufficient to achieve the desired therapeutic or prophylactic effect in the individual to which it is administered.

[0137] The term "administration", or a variant thereof (e.g., "administering"), means providing the active agent or active ingredient (e. g. a NK-3 antagonist), alone or as part of a pharmaceutically acceptable composition, to the patient in whom/which the condition, symptom, or disease is to be treated or prevented.

[0138] By "pharmaceutically acceptable" is meant that the ingredients of a pharmaceutical composition are compatible with each other and not deleterious to the patient thereof.

[0139] The term "antagonist" as used herein means a compound which competitively or non-competitively binds to a receptor at the same site as an agonist (for example, the endogenous ligand), but does not activate an intracellular response initiated by an active form of the receptor. An antagonist thereby inhibits the intracellular response induced by an agonist.

[0140] The term "sex hormone-dependent disease" as used herein means a disease which is exacerbated by, or caused by, excessive, inappropriate or unregulated sex hormone production. Exemple of such diseases in men include but not limited to benign prostatic hyperplasia (BPH), metastatic prostatic carninoma, testicular cancer, breast cancer, androgen dependent acne, male pattern baldness. Exemple of such diseases in women include but not limited to endometriosis, abnormal puberty, uterine fibrosis, hormone-dependent cancers (ovarian cancer, breast cancer), hyperandrogenism, hirsutism, virilization, polycystic ovary syndrome (PCOS), HAIR-AN syndrome (hyperandrogenism, insulin resistance and acanthosis nigricans), ovarian hyperthecosis (HAIR-AN with hyperplasia of luteinized theca cells in ovarian stroma), other manifestations of high intraovarian androgen concentrations (e.g. follicular maturation arrest, atresia, anovulation, dysmenorrhea, dysfunctional uterine bleeding, infertility) and androgen-producing tumor (virilizing ovarian or adrenal tumor).

[0141] The term "Psychotic disorders" as used herein means a group of illnesses that affect the mind. These illnesses alter a patient's ability to think clearly, make good judgments, respond emotionally, communicate effectively, understand reality, and behave appropriately. When symptoms are severe, patient with psychotic disorders have difficulty staying in touch with reality and often are unable to meet the ordinary demands of daily life. Psychotic disorders include, and are not limited to, schizophrenia, schizophreniform disorder, schizoaffective disorder, delusional disorder, brief psychotic disorder, shared psychotic disorder, psychotic disorder due to a general medical condition, substance-induced psychotic disorder or psychotic disorder not otherwise specified (Diagnostic and Statistical Manual of Mental Disorders, Ed. 4th, American Psychiatric Association, Washington, D.C. 1994).

[0142] The term "pharmaceutical vehicle" as used herein means a carrier or inert medium used as solvent or diluent in which the pharmaceutically active agent is formulated and/or administered. Non-limiting examples of pharmaceutical vehicles include creams, gels, lotions, solutions, and liposomes.

[0143] The present invention will be better understood with reference to the following examples. These examples are intended to representative of specific embodiments of the invention, and are not intended as limiting the scope of the invention.

CHEMISTRY EXAMPLES

[0144] All temperatures are expressed in °C and all reactions were carried out at room temperature (RT) unless otherwise stated.

[0145] Analytical thin layer chromatography (TLC) was used to monitor reactions, establish flash chromatography conditions and verify purity of intermediates or final products. TLC plates used were Merck TLC aluminium sheet silica gel 60 F_{254}. TLC plates were revealed using ultraviolet irradiation (wavelength=254nm) at room temperature or bromocresol green spray reagent at 0.1% in propan-2-ol purchased from VWR International upon heating at 160°C or $KMnO_4$ revelator upon heating at 160°C. The $KMnO_4$ TLC revealing agent was prepared by dissolving 3g of potassium permanganate, 20g of sodium carbonate, 0.5g of sodium hydroxide in 100mL of distilled water.

[0146] HPLC-MS spectra were obtained on Agilent LCMS using Electropsray ionization (ESI). The Agilent instrument includes an Autosampler 1200, a binary pump 1100, a 5 wave length detector 1100 and a 6100 Single Quad. The column used was an XBridge C18, 4.6 x 50 mm, 3.5 μm.

Eluent was a mixture of solution A (0.1% TFA in H_2O) and solution B (0.1% TFA in ACN). Gradient was applied at a flow rate of 2 mL min^{-1} as follows: gradient A: held the initial conditions of 5% solution B for 1 min, increased linearly to 95% solution B in 4 min, held at 95% during 1 min, returned to initial conditions in 0.5 min and maintained for 1 min; gradient B: held the initial conditions of 5% solution B for 1 min, increased linearly to 60% in 10 min, increased linearly to 95% in 0.5 min, held at 95% during 3 min, returned to initial conditions in 0.5 min and maintained for 1 min.

[0147] Determination of ee was performed on an Agilent 1100 (binary pump and 5 wavelengths detector) with manual or automatic (Autosampler 1100) injection. Columns used were CHIRALPAK IA CHIRALPAK IB or CHIRALPAK IC in isocratic mode. Mixtures of eluents were selected depending on the separation obtained of enantiomers or diastereosiomers. Usual mixtures were:

- hexane and ethanol (0.1% DEA)
- hexane and isoropanol (0.1% DEA)
- hexane and ethyl acetate (0.1% DEA)
- hexane and dichloromethane (0.1% DEA)
- heptane and THF (0.1% DEA)

[0148] Preparative HPLC purifications were carried out on Fractionlynx instrument, from Waters. This instrument consists of a Fraction Collector, a 2767 Sample Manager, a pump control a module II, a 515 HPLC Pump, a 2525 Binary Gradient Module, a Switching Valve, a 2996 Photodiode Array Detector and a Micromass ZQ. The column used was a Waters Sunfire C18 Eluent was a mixture of solution A (0.1% TFA in H_2O) and solution B (0.1% TFA in ACN). The gradient was adapted depending on impurities present in samples, to allow sufficient separation between impurities and target compound.

[0149] Chiral preparative HPLC purification were performed on an Agilent 1100 instrument (binary pump and 5 wavelengths detector) with manual injection using a CHIRALPAK IA or a CHIRALPAK IB column in isocratic mode.Mixtures of eluents were selected depending on the separation of enantiomers or diastereosiomers obtained with the analytical method. Usual mixtures were the same as those used for the determination of ee.

[0150] ^1H and ^{13}C NMR spectra were recorded on a Bruker Avance DRX 300MHz. Chemical shifts are expressed in parts per million, (ppm, δ units). Coupling constants are expressed in Hertz units (Hz). Splitting patterns describe apparent multiplicities and are described as s (singlet), d (doublet), t (triplet), q (quadruplet), m (multiplet), or br (broad).

[0151] Solvents, reagents and starting materials were purchased from well known chemical suppliers such as for example Sigma Aldrich, Acros Organics, Fluorochem, Eurisotop, VWR International, Sopachem and Polymer labs and the following abbreviations are used:

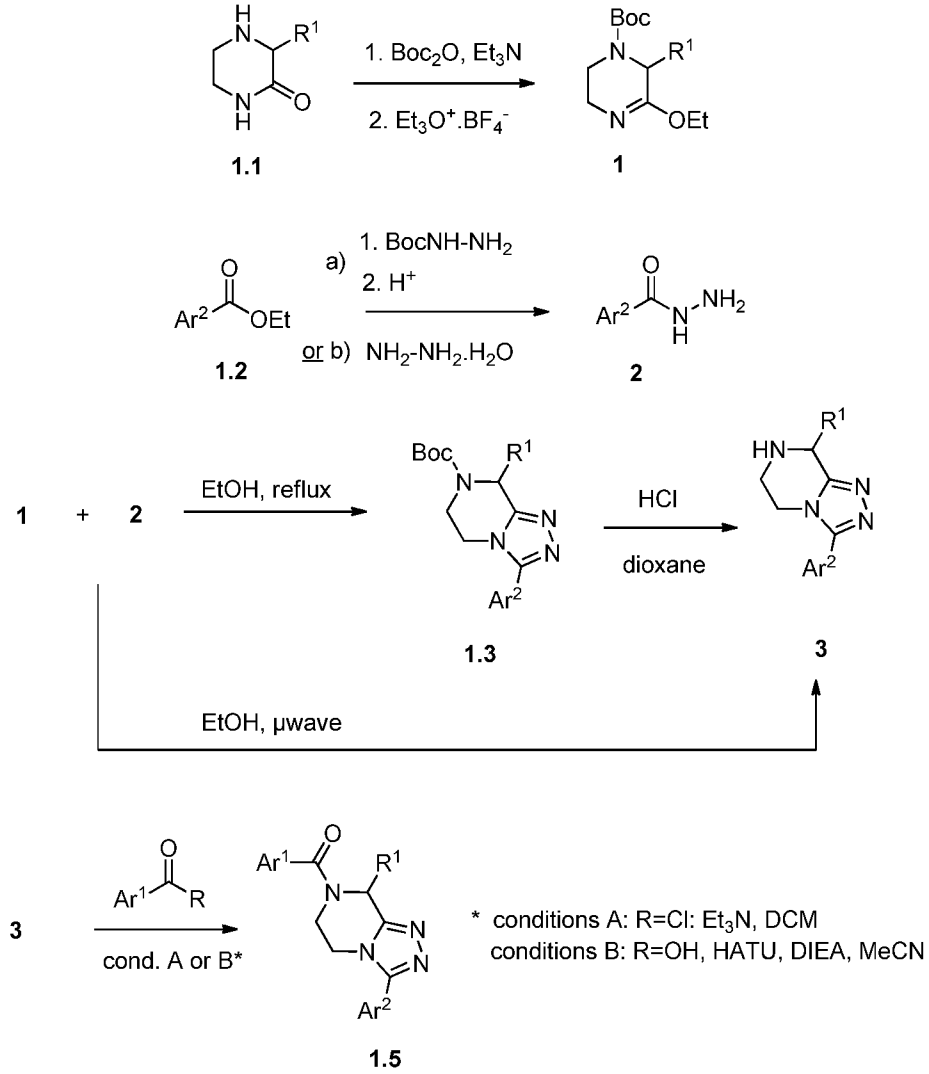
ACN: Acetonitrile,
DCM: Dichloromethane,
DMF: N,N-dimethylformamide,
EtOAc: Ethyl acetate,
EtOH: Ethanol,
MeOH: Methanol,
IPA: isopropanol,
RT: Room temperature,
Y: Yield,
g: Gram(s),
mg: Milligram(s),
L: Liter(s),
mL: Milliliter(s),
μL: Microliter(s),
mol: Mole(s),
mmol: Millimole(s),
h: Hour(s),
mn or min: Minute(s),
TLC: Thin layer chromatography,
MW: Molecular weight,
eq: Equivalent,
μW or μwave: Microwave,
THF: Tetrahydrofuran,
Ac: Acetyl,
ee: Enantiomeric excess,

tBu: tert-Butyl
P: UV purity at 254nm or 215nm determined by HPLC-MS,
SPE: Solid phase extraction,
rt: Retention time.
DEA: diethylamine,
HATU: O-(7-azabenzotriazol-1-yl)-N,N,N',N'-tretramethyluronium hexafluorophosphate,
TFA: trifluoroacetic acid,
DBU: 1,8-Diazabicyclo[5.4.0]undec-7-ene
TMS: trimethylsilyl,
CDI: carbonyldiimidazole,
rm or RM: reaction mixture,
dba: dibenzylideneacetone,
X-Phos: 2-Dicyclohexylphosphino-2',4',6'-triisopropylbiphenyl,
THP: tetrahydropyran,
Boc: *tert*-butoxycarbonyl,
DPPF: Diphenylphosphinoferrocene.

[0152] The intermediates and compounds disclosed hereunder were named using ChemDraw Ultra 12 purchased from CambridgeSoft (Cambridge, MA, USA).

General synthetic scheme

[0153] Most compounds of the invention were synthesized using the methodology described in *scheme 1.* The chiral compounds were obtained either by purification using chiral HPLC, or by employing the appropriate chiral ketopiperazine building block.

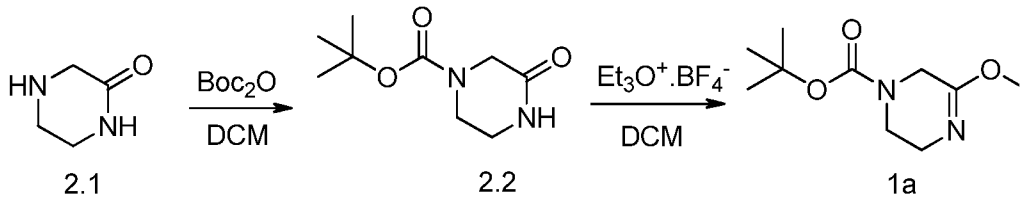


Scheme 1: General synthetic scheme for the preparation of the majority of compounds in the present invention

[0154] Ketopiperazine **1.1** was protected with a Boc group and converted to iminoether **1** by using Meerwein reagent (i.e., Et_3OBF_4). Ester **1.2** was subsequently converted to acyl hydrazide **2** through its reaction with hydrazine, either in N-Boc-protected form (i.e. **1.2** → **2**, condition a), or without protection (i.e. **1.2** → **2**, condition b). Condensation reaction between the acyl hydrazide thus generated and the iminoether aforementioned was conducted either under thermal reflux conditions, or by applying microwave irradiation. In case of reactions conducted using microwave irradiation, the N-Boc deprotection occurred during the condensation reaction, thus a deprotection step was not necessary to carry out (i.e. **1 + 2** → **3** in Scheme 1). However, when condensation reaction was carried out under thermal conditions, it was necessary to introduce a deprotection step (i.e. **1 + 2** → **1.3** → **3**). Acylation of the amine in the triazolopiperazine intermediate **1.5,** either through reaction with the appropriate acid chloride or through reaction with the appropriate activated ester, i.e. conditions A and B respectively, afforded the final target structure. This synthetic approach was used for the majority of the compounds described in the present invention.

General Method A:

[0155] General Method A is the general procedure used for the synthesis of the iminoether intermediates **1** (cf. Scheme 1) and is detailed below using the example of *tert*-butyl 3-ethoxy-5,6-dihydropyrazine-1(2H)-carboxylate **1a.**



2.1 2.2 1a

Scheme 2: Synthesis of *tert*-butyl 3-ethoxy-5,6-dihydropyrazine-1(2H)-carboxylate

Step 1: Synthesis of *tert*-butyl 3-oxopiperazine-1-carboxylate **2.2**

[0156] Boc_2O (10.9 g, 0.05 mol) was added in portions under stirring and cooling on an ice bath to a suspension of piperazin-2-one **2.1** (5 g, 0.05 mol) in anhydrous dichloromethane (100 mL). The reaction mixture was stirred at 20 °C overnight (evolution of gas was observed at the beginning of the reaction), during which time a homogeneous solution formed. The solvent was evaporated, and the solid residue was vacuum-dried (10 - 15 mm Hg) at 40 -50°C to constant weight to give **2.2.** Yield: 100 g (100%).

Step 2: Synthesis of *tert*-butyl 5-ethoxy-3,6-dihydropyrazine-1(2*H*)-carboxylate **1a**

[0157] Solid triethyloxonium tetrafluoroborate (2.3 g, 0.012 mol) was added in portions under stirring and cooling on an ice bath to a solution of **2.2** (2 g, 0.01 mol) in anhydrous dichloromethane (20 mL). After the addition was completed, the cooling was removed, and the reaction mixture was stirred at room temperature overnight. Then a 20% K_2CO_3 aqueous solution was added in portions under cooling on an ice bath to the obtained slightly muddy solution to obtain pH 8-9. The formed precipitate of potassium tetrafluoroborate was removed by filtration and washed on filter with dichloromethane. The filtrate was placed into a separatory funnel, and the organic layer was separated. The aqueous layer was extracted with dichloromethane (3 x 10 mL), and the combined organic extracts were washed with water (20 mL), dried over Na_2SO_4 and concentrated on a rotary evaporator. Hexane was added to the residue, and the obtained mixture was left to stand in a refrigerator for ~4 h. The formed precipitate was removed by filtration using a thin pad of Celite, and the filtrate was evaporated. The obtained viscous yellowish oil was vacuum-dried (10-15 mm Hg) at 40-50 °C for ~6 h to give title intermediate **1a.** Yield: 2.03g (88 %). ^{1}HNMR ($CDCl_3$): δ: 4.1ppm (q, 2H), 3.85 (s, 2H), 3.5ppm (m, 1H), 3.35ppm (t, 2H), 1.45ppm (s, 9H), 1.3ppm (t, 3H).

[0158] Alternatively, general method A was carried out as follows:

Step 1: Synthesis of *tert*-butyl 3-oxopiperazine-1-carboxylate **2.2**

[0159] To a solution of piperazin-2-one **2.1** (5.0 g, 33.2 mmol) in commercial anhydrous CH_2Cl_2 (100 mL) under N_2 at RT was added NEt_3 (5.1 mL, 35.5 mmol). After 10 min stirring, the RM. was cooled down to 0°C with an ice bath and Boc_2O (8.33 g, 38.2 mmol) was added in one portion. TheRM. was then stirred at RT for 1h. The mixture was diluted with 50 mL of CH_2Cl_2 and washed with HCl 0.5M (30 mL), brine (30 mL), dried over magnesium sulfate, filtered and concentrated to constant weight furnishing **2.2** as a yellow oil. Yield: 7.1g (100%). LCMS and ^{1}HNMR data are consistent with those described above.

Step 2: Synthesis of *tert*-butyl 5-ethoxy-3,6-dihydropyrazine-1(2*H*)-carboxylate **1a**

[0160] To a pre-made solution of triethyloxonium tetrafluoroborate (2.3 g, 0.012 mol) in anhydrous dichloromethane (20 mL) was added **2.2** (2 g, 0.01 mol) at 0 °C. After the addition was completed, the ice-bath was removed, and the reaction mixture was allowed to warm to room temperature and stirred for an additional hour (reaction progress monitored by LC-MS). Upon completion of the reaction, a saturated solution of $NaHCO_3$ (500 mL) was slowly added to the reaction mixture and it was stirred for 5 min. The organic layer was separated and the aqueous layer was further extracted with dichloromethane. The combined organic layers were subsequently washed with brine, dried over $MgSO_4$, filtered and further dried *in vacuo* to obtain the title intermediate **1a** as a viscous yellow oil. Yield: 2.03 g (88%). ^{1}HNMR ($CDCl_3$): δ: 4.1ppm (q, 2H), 3.85 (s, 2H), 3.5ppm (m, 1H), 3.35ppm (t, 2H), 1.45ppm (s, 9H), 1.3ppm (t, 3H).

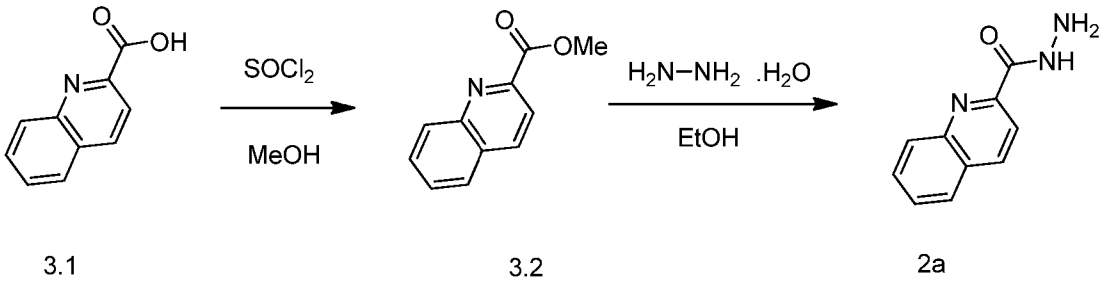
[0161] The following intermediates were also prepared from the *ad hoc* reagents using General Method A:

intermediate **1b:** (R)-*tert*-butyl 3-ethoxy-2-methyl-5,6-dihydropyrazine-1(2H)-carboxylate,
intermediate **1c:** (S)-*tert*-butyl 3-ethoxy-2-methyl-5,6-dihydropyrazine-1(2H)-carboxylate,
intermediate **1d:** *tert*-butyl 3-ethoxy-2-methyl-5,6-dihydropyrazine-1(2H)-carboxylate,

intermediate **1e:** *tert*-butyl 3-ethoxy-2-(4-fluorophenyl)-5,6-dihydropyrazine-1(2H)-carboxylate,
intermediate **1f**: *tert*-butyl 3-ethoxy-2-isopropyl-5,6-dihydropyrazine-1(2H)-carboxylate,
intermediate **1g:** *tert*-butyl 3-ethoxy-2-(2-hydroxyethyl)-5,6-dihydropyrazine-1(2H)-carboxylate,
intermediate **1h:** *tert*-butyl 3-ethoxy-2,2-dimethyl-5,6-dihydropyrazine-1(2H)-carboxylate,
intermediate **1i:** *tert*-butyl 3-ethoxy-6-methyl-5,6-dihydropyrazine-1(2H)-carboxylate,
intermediate **1j:** *tert*-butyl 3-ethoxy-5-methyl-5,6-dihydropyrazine-l(2H)-carboxylate.

General Method B:

[0162] General Method B is the general procedure used for the synthesis of hydrazide intermediates **2** and is detailed below using the example of quinoline-2-carbohydrazide **2a.**



3.1 3.2 2a

Scheme 3: Synthesis of quinoline-2-carbohydrazide **2a**

Step 1: Synthesis of methyl quinoline-2-carboxylate **3.2**

[0163] To an ice-cooled solution of quinoline-2-carboxylic acid **3.1** (10g, 0.0578 mol) in 100 mL of absolute methanol was added dropwise thionyl chloride (20 g, 0.173 mol). After the addition was completed, the mixture was heated to reflux for 2 h. The solvent was then evaporated to dryness under reduced pressure and treated with 100 mL of 10% aqueous solution of K_2CO_3. The mixture was extracted with ethyl acetate; combined organic extracts were dried over sodium sulfate and evaporated to dryness to afford of methyl quinoline-2-carboxylate. Yield: 10.1g (93%).

Step 2: Synthesis of quinoline-2-carbohydrazide **2a**

[0164] Methyl quinoline-2-carboxylate **3.2** (10.1 g, 0.054 mol) was dissolved in 50 mL of ethanol and hydrazine hydrate (8.1 g, 0.16 mol) was added. The mixture was heated to reflux for 1 h and cooled down to RT at which point a precipitate formed. The mixture was concentrated to approximately 1/3 of the volume and the precipitate was filtered off, washed with small volumes of ethanol to afford intermediate **2a** solvated by ½ equivalent of ethanol.. Yield 10 g (99%). ^{1}HNMR (DMSO-d^6): δ: 9.95ppm (s, 1H), 8.55 (d, 1H), 8.1ppm (d, 2H), 8.05ppm (d, 1H), 8.85ppm (t, 1H), 7.65ppm (t, 1H), 4.6ppm (s, 2H), 4.3ppm (t, 0.5H), 4.4ppm (q, 1H), 1.05ppm (q, 1.5H).

[0165] In one embodiment 5 to 20 equivalents of hydrazine hydrate was used to carry out this reaction.

[0166] The following intermediates were also prepared from the *ad hoc* reagents using General Method B:

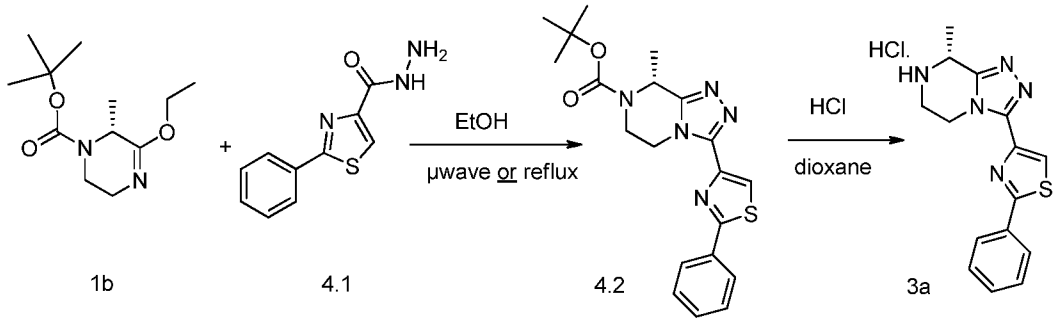
intermediate **2b:** 6-chloropicolinylhydrazide,
intermediate **2c:** 6-methylpicolinylhydrazide,
intermediate **2d:** isoquinoline-3-carbohydrazide,
intermediate **2e:** 8-fluoroquinoline-2-carbohydrazide,
intermediate **2f:** 8-chloroquinoline-2-carbohydrazide,
intermediate **2g:** 2-(4-(trifluoromethyl)phenyl)thiazole-4-carbohydrazide,
intermediate **2h:** 6-phenylpicolinohydrazide,
intermediate **2i:** 4,5,6,7-tetrahydrobenzo[d]thiazole-2-carbohydrazide,
intermediate **2j:** benzo[d]thiazole-2-carbohydrazide,
intermediate **2k:** 2-(2,4-difluorophenyl)thiazole-4-carbohydrazide,
intermediate **2l:** 2-(4-chlorophenyl)thiazole-4-carbohydrazide,
intermediate **2m:** 2-(4-fluorophenyl)thiazole-4-carbohydrazide,
intermediate **2n:** 2-(piperidin-1yl)thiazole-4-carbohydrazide,
intermediate **2o:** 2-(4-phenylpiperazin-1-yl)thiazole-4-carbohydrazide,

intermediate **2p:** 2-(2,4-dichlorophenyl)thiazole-4-carbohydrazide,
intermediate **2q:** 2-(3,5-dichlorophenyl)thiazole-4-carbohydrazide,
intermediate **2r:** 6-(pyrrolidin-1yl)picolinohydrazide,
intermediate **2s:** 6-morpholinopicolinohydrazide,
intermediate **2t:** 6-(trifluoromethyl)picolinohydrazide,
intermediate **2u:** 2-(3,4-dimethoxyphenyl)thiazole-4-carbohydrazide,
intermediate **2v:** 2-(3-chlorophenyl)thiazole-4-carbohydrazide,
intermediate **2w:** 2-phenyloxazole-4-carbohydrazide,
intermediate **2x:** 2-(2-chlorophenyl)thiazole-4-carbohydrazide,
intermediate **2y:** 5-methyl-2-phenylthiazole-4-carbohydrazide,
intermediate **2z:** 3-phenyl-1,2,4-oxadiazole-5-carbohydrazide,
intermediate **2a1:** 5-phenyl-1,2,4-oxadiazole-3-carbohydrazide,
intermediate **2b1:** 3-(4-fluorophenyl)-1,2,4-oxadiazole-5-carbohydrazide,
intermediate **2c1** 3-(2,4-difluorophenyl)-1,2,4-oxadiazole-5-carbohydrazide, was synthesized from intermediate **5a** obtained using General Method E,
intermediate **2d1:** 5-phenyl-1H-1,2,4-triazole-3-carbohydrazide, was synthesized from methyl 5-phenyl-1H-1,2,4-triazole-3-carboxylate whose preparation is disclosed in J. Med. Chem. 1995, 38, 2196,
intermediate **2e1:** 2-((4,5-dichloro-1H-imidazol-1-yl)methyl)thiazole-4-carbohydrazide,
intermediate **2f1:** 2-(4-chlorobenzyl)thiazole-4-carbohydrazide
intermediate **2g1:** 2-(p-tolyl)thiazole-4-carbohydrazide,
intermediate **2h1:** 2-(2-methoxyphenyl)thiazole-4-carbohydrazide,
intermediate **2i1:** 2-(3-fluorophenyl)thiazole-4-carbohydrazide,
intermediate **2j1:** 3-(4-fluorophenyl)-1,2,4-oxadiazole-5-carbohydrazide,
intermediate **2k1:** 3-phenyl-1,2,4-thiadiazole-5-carbohydrazide,
intermediate **2l1:** 2-(4-bromophenyl)thiazole-4-carbohydrazide,
intermediate **2m1:** 2-(pyridin-4-yl)thiazole-4-carbohydrazide, was synthesized from intermediate **6b** obtained using the General Method F,
intermediate **2n1:** 2-(quinolin-2-yl)thiazole-4-carbohydrazide,
intermediate **2o1:** 1-methyl-3-phenyl-1H-pyrazole-5-carbohydrazide,
intermediate **2p1:** 2-(4-(dimethylamino)phenyl)thiazole-4-carbohydrazide,
intermediate **2q1:** 1-methyl-5-phenyl-1H-pyrazole-3-carbohydrazide,
intermediate **2r1:** 2-(pyridin-2-yl)thiazole-4-carbohydrazide,
intermediate **2s1:** 2-(pyrimidin-2-yl)thiazole-4-carbohydrazide, was synthesized from intermediate **6d** obtained using General Method F
intermediate **2t1:** 2-(pyrazin-2-yl)thiazole-4-carbohydrazide, was synthesized from intermediate **6e** obtained using General Method F,
intermediate **2u1:** 2-(4-morpholinophenyl)thiazole-4-carbohydrazide, was synthesized from intermediate **7b** obtained using General Method G,
intermediate **2v1:** 2-(4-(4-methylpiperazin-1-yl)phenyl)thiazole-4-carbohydrazide,
intermediate **2w1:** 2-(4-(piperidin-1-yl)phenyl)thiazole-4-carbohydrazide, was synthesized from intermediate **7c** obtained using General Method G,
intermediate **2x1:** 2-(4-(pyrrolidin-1-yl)phenyl)thiazole-4-carbohydrazide, was synthesized from intermediate **7d** obtained using General Method G,
intermediate **2y1:** 2-(piperidin-1-yl)thiazole-4-carbohydrazide, was synthesized from intermediate **7e** obtained using General Method G,
intermediate **2z1:** 2-(pyrrolidin-1-yl)thiazole-4-carbohydrazide, was synthesized from intermediate **7f** obtained using General Method G,
intermediate **2a2:** 2-(4-methylpiperazin-1-yl)thiazole-4-carbohydrazide, was synthesized from intermediate **7g** obtained using General Method G,
intermediate **2b2:** 1-methyl-2-phenyl-1H-imidazole-4-carbohydrazide,
intermediate **2c2:** 1-(2-methoxyethyl)-3-phenyl-1H-pyrazole-5-carbohydrazide, was synthesized from intermediate **8a** obtained using General Method H,
intermediate **2d2:** 2-isobutylthiazole-4-carbohydrazide, was synthesized from ethyl 2-isobutylthiazole-4-carboxylate, which was obtained from 3-methylbutanethioamide using the methodology reported by Ciufolini, et al. in Journal of Organic Chemistry, 1997 , vol. 62, issue 12, p. 3804 - 3805,
intermediate **2e2:** 2-(2-(2-methoxyethyl)morpholino)thiazole-4-carbohydrazide, was synthesized from intermediate **7h** obtained using General Method G,
intermediate **2f2:** 2-(4,4-difluoropiperidin-1-yl)thiazole-4-carbohydrazide, was synthesized from intermediate **7i** ob-

tained using General Method G,
intermediate **2g2:** 2-(2,5-dimethylmorpholino)thiazole-4-carbohydrazide, was synthesized from intermediate **7i** obtained using General Method G,
intermediate **2h2:** 2-(2-hydroxyphenyl)thiazole-4-carbohydrazide, was synthesized from ethyl 2-(2-hydroxyphenyl)thiazole-4-carboxylate, which was obtained from 2-hydroxybenzothioamide using the methodology reported by Ciufolini, et al. in Journal of Organic Chemistry, 1997, vol. 62, issue 12, p. 3804 - 3805,
intermediate **2i2:** 2-(2,6-dimethylmorpholino)thiazole-4-carbohydrazide, was synthesized from intermediate **7k** obtained using General Method G,
intermediate **2j2:** 2-(2,2-dimethylmorpholino)thiazole-4-carbohydrazide, was synthesized from intermediate **7l** obtained using General Method G,
intermediate **2k2:** 3-phenyl-1H-pyrazole-5-carbohydrazide,
intermediate **212:** 2-(2-methylmorpholino)thiazole-4-carbohydrazide, was synthesized from intermediate **7m** obtained using General Method G,
intermediate **2m2:** 2-(4,4-dimethylpiperidin-1-yl)thiazole-4-carbohydrazide, was synthesized from intermediate **7n** obtained using General Method G,
intermediate **2n2:** 5-methylthiazole-4-carbohydrazide,
intermediate **2o2:** 2-(2-(methoxymethyl)piperidin-1-yl)thiazole-4-carbohydrazide, was synthesized from intermediate **7o** obtained using General Method G,
intermediate **2p2:** 2-(2-bromophenyl)thiazole-4-carbohydrazide, was synthesized from ethyl 2-(2-bromophenyl)thiazole-4-carboxylate, which was obtained from 2-bromobenzothioamide using the methodology reported by Ciufolini, et al. in Journal of Organic Chemistry, 1997 , vol. 62, issue 12, p. 3804 - 3805,
intermediate **2q2:** 2-(3-bromophenyl)thiazole-4-carbohydrazide, was synthesized from ethyl 2-(3-bromophenyl)thiazole-4-carboxylate, which was obtained from 3-bromobenzothioamide using the methodology reported by Ciufolini, et al. in Journal of Organic Chemistry, 1997 , vol. 62, issue 12, p. 3804 - 3805,

General Method C:

[0167] General Method C is the general procedure used for the synthesis of triazolopiperazine intermediates **3** and is detailed below with the synthesis of (R)-4-(8-methyl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)-2-phenylthiazole hydrochloride **3a.**



1b 4.1 4.2 3a

Scheme 4: Synthesis of (R)-4-(8-methyl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)-2-phenylthiazole hydrochloride salt

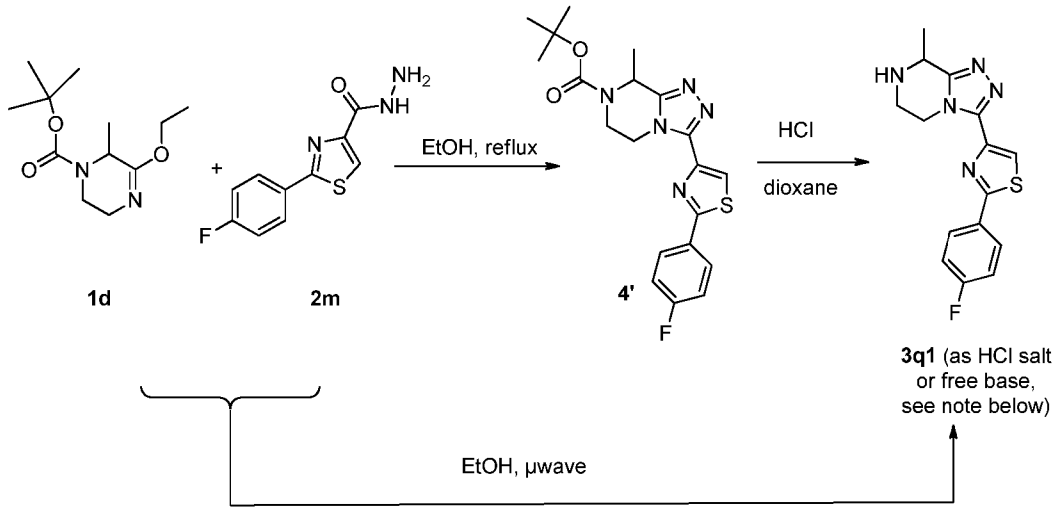
Step 1: Synthesis of (R)-*tert*-butyl 8-methyl-3-(2-phenylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazine-7(8H)-carboxylate **4.2**

[0168] To a solution of hydrazide 2-phenylthiazole-4-carbohydrazide **4.1** (100 mg, 0.4 mmol) in ethanol (7 mL) was added (2R)-*tert*-butyl 3-ethoxy-2-methyl-5,6-dihydropyrazine-1(2H)-carboxylate **1b** (75 mg, 0.34 mmol). To this reaction mixture was applied microwave radiation (110 °C, 220 psi) for 25 h. The solvent was then evaporated to dryness and the residue was purified on silica gel using CH_2Cl_2-Ethyl acetate (5:1→5:2 + MeOH from 1% to 5%). Yield: 50 mg of **4.2** + 40 mg of de-Boc product **3a.** Combined yield: 76%. %. LCMS: P=96%, rt =1.86mn, m/z=398, 298.

Step 2: Synthesis of (R)-4-(8-methyl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)-2-phenylthiazole hydrochloride **3a**

[0169] Compound **4.2** (50 mg, 0.125 mmol) obtained in the previous step was dissolved in isopropyl alcohol (10 mL) to which was added 0.3 mL of HCl 4M in dioxane. The mixture was stirred at 50 °C overnight. After cooling down to RT, 10 mL of diethyl ether was added. The precipitate was filtered to afford title intermediate. Yield: 42mg, 99%. LCMS: P=100%, rt=1.08mn, m/z=298. ^{1}H NMR (DMSO-d^6): δ: 8.3 ppm (s, 1H), 8.05 ppm (m, 2H), 7.55 ppm (m, 3H), 4.5 ppm (m, 1H), 4.25-4.05 ppm (m, 2H), 3.3ppm (m, 1H), 2.95-3.1 ppm (m, 1H), 2.8 ppm (br s, 1H), 1.95ppm (d, 3H).

[0170] Variant of General Method C is detailed below using the example of 2-(4-fluorophenyl)-4-(8-methyl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)thiazole **3q1.**



NB: When HCl/dioxane deprotection was applied, **3q1** was obtained as HCl salt. When μwave conditions were used, the Boc deprotection occurred during the cyclization, and no HCl deprotection step was required; thus, **3q1** was obtained in free-base form under the latter condition.

Scheme 4': Synthesis of 2-(4-fluorophenyl)-4-(8-methyl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)thiazole

Step 1: Synthesis of *tert*-butyl 3-(2-(4-fluorophenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazine-7(8H)-carboxylate **4**

[0171] To a solution of hydrazide **2m** (1.65 g, 6.95 mmol) in anhydrous ethanol (15 mL, ~ 0.5M) was added iminoether **1d** (1.69 g, 6.95 mmol) in one portion. The reaction mixture was then stirred under reflux. After 45h (nearly complete conversion by LC-MS), the solvent was evaporated to dryness and the residue was purified on silica gel using a CH_2Cl_2/MeOH mixture (0% to 4% MeOH) as eluent, furnishing **4'** as a yellow solid. Yield: 2.1g (73%). LCMS: P= 92%, rt=4.4 mn, m/z=416. ^{1}HNMR ($CDCl_3$): δ: 8.11 ppm (s, 1H), 7.97 ppm (t, 2H), 7.20 ppm (t, 2H), 4.75 (m, 1H), 4.52 (m, 1H), 4.23 (dt, 1H), 4.17 (m, 1H), 3.48 (dt, 1H), 1.64 ppm (d, 3H), 1.51 ppm (s, 9H).

Step *2* Synthesis of 2-(4-fluorophenyl)-4-(8-methyl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)thiazole **3q1**

[0172] To a solution of Boc-triazolo-piperazine **4'** (2.17 g, 5.22 mmol) in *iso*-propanol (150 mL) was added HCl 4M solution in 1,4-dioxane (26.1 mL, 104 mmol) in one portion. The reaction mixture was stirred at 60°C and the reaction progress was monitored by LC-MS. After 1h (complete conversion by LC-MS), the reaction mixture was allowed to cool to room temperature and then further cooled to 0°C with an ice bath. Thereupon, 150 mL of Et_2O was added. After 15 min stirring, the precipitate was filtered off and dried *in vacuo* to afford **3q1** as an off-white solid. Yield: 1.313g (72%). LCMS: P= 98%, rt=3.3 mn, m/z=316. ^{1}HNMR (CD_3OD): δ: 8.57 ppm (s, 1H), 8.15 ppm (t, 2H), 7.30 ppm (t, 2H), 5.22 (m, 1H), 5.08 (q, 1H), 4.13 (m, 1H), 3.77 (m, 1H), 3.12 (m, 1H), 1.94 ppm (d, 3H).

[0173] As noted in Scheme 4' above, an alternative procedure to thermal reflux to effect the condensation step to form the triazolopiperazine intermediate entailed use of microwave irradiation. Such reactions were run in anhydrous ethanol and the following conditions were typically applied (CEM Discover): 300 W μwave (143 °C) with air-cooling.

[0174] The following intermediates were also prepared from the *ad hoc* reagents and intermediates using General Method C:

intermediate **3b:** 3-(pyridin-2-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazine dihydrochloride salt,
intermediate **3c:** 4-(4-(5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)thiazol-2-yl)morpholine dihydrochloride salt,
intermediate **3d:** 3-(5-chloropyridin-2-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazine dihydrochloride salt,
intermediate **3e:** 3-(6-methylpyridin-2-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazine dihydrochloride salt,
intermediate **3f:** 8-methyl-3-(pyridin-2-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazine dihydrochloride salt,
intermediate **3g:** 3-(5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)isoquinoline hydrochloride salt,
intermediate **3h:** 2-(5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)quinoline hydrochloride salt,
intermediate **3i:** 8-fluoro-2-(5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)quinoline hydrochloride salt,
intermediate **3j:** 8-chloro-2-(5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)quinoline hydrochloride salt,
intermediate **3k:** 4-(5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)-2-(4-(trifluoromethyl)phenyl)thiazole hydrochloride salt,
intermediate **3l:** 3-(6-phenylpyridin-2-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazine dihydrochloride salt,
intermediate **3m:** 2-(5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)-4,5,6,7-tetrahydrobenzo[d]thiazole hydrochloride salt,
intermediate **3n:** 2-(5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)benzo[d]thiazole hydrochloride salt,
intermediate **3o:** 2-phenyl-4-(5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)thiazole hydrochloride salt,
intermediate **3p:** 4-(5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)-2-(3-(trifluoromethyl)phenyl)thiazole hydrochloride salt,
intermediate **3q:** 2-(2,4-difluorophenyl)-4-(5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)thiazole hydrochloride salt,
intermediate **3r:** 2-(2,3-dichlorophenyl)-4-(5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)thiazole hydrochloride salt,
intermediate **3s:** 2-(4-chlorophenyl)-4-(5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)thiazole hydrochloride salt,
intermediate **3t:** 2-(4-fluorophenyl)-4-(5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)thiazole hydrochloride salt,
intermediate **3u:** 2-(piperidin-1-yl)-4-(5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)thiazole dihydrochloride salt,
intermediate **3v:** 2-(4-phenylpiperazin-1-yl)-4-(5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)thiazole dihydrochloride salt,
intermediate **3w:** 2-(2,4-dichlorophenyl)-4-(5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)thiazole hydrochloride salt,
intermediate **3x:** 2-(3,5-dichlorophenyl)-4-(5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)thiazole hydrochloride salt,
intermediate **3y:** 3-(6-(pyrrolidin-1-yl)pyridin-2-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazine dihydrochloride salt,
intermediate **3z:** 4-(6-(5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)pyridin-2-yl)morpholine dihydrochloride salt,
intermediate **3a1:** 3-(6-(trifluoromethyl)pyridin-2-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazine dihydrochloride salt,
intermediate **3b1:** 2-(3,4-dimethoxyphenyl)-4-(5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)thiazole hydrochloride salt,
intermediate **3c1:** 4-(8-(4-fluorophenyl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)-2-phenylthiazole hydrochloride salt,
intermediate **3d1:** 2-(3-chlorophenyl)-4-(5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)thiazole hydrochloride salt,
intermediate **3e1:** 4-(8-isopropyl-5,6,7,8-te trahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)-2-phenylthiazole hydrochloride salt,
intermediate **3f1:** (R)-8-methyl-3-(pyridin-2-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazine dihydrochloride salt,
intermediate **3g1:** 4-(4-(8-methyl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)thiazol-2-yl)morpholine dihydrochloride salt,
intermediate **3h1:** 2-phenyl-4-(5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)oxazole hydrochloride salt,
intermediate **3i1:** 4-(8-methyl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)-2-phenyloxazole,
intermediate **3j1:** 2-(3-(2-phenylthiazol-4-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-8-yl)ethanol hydrochlo-

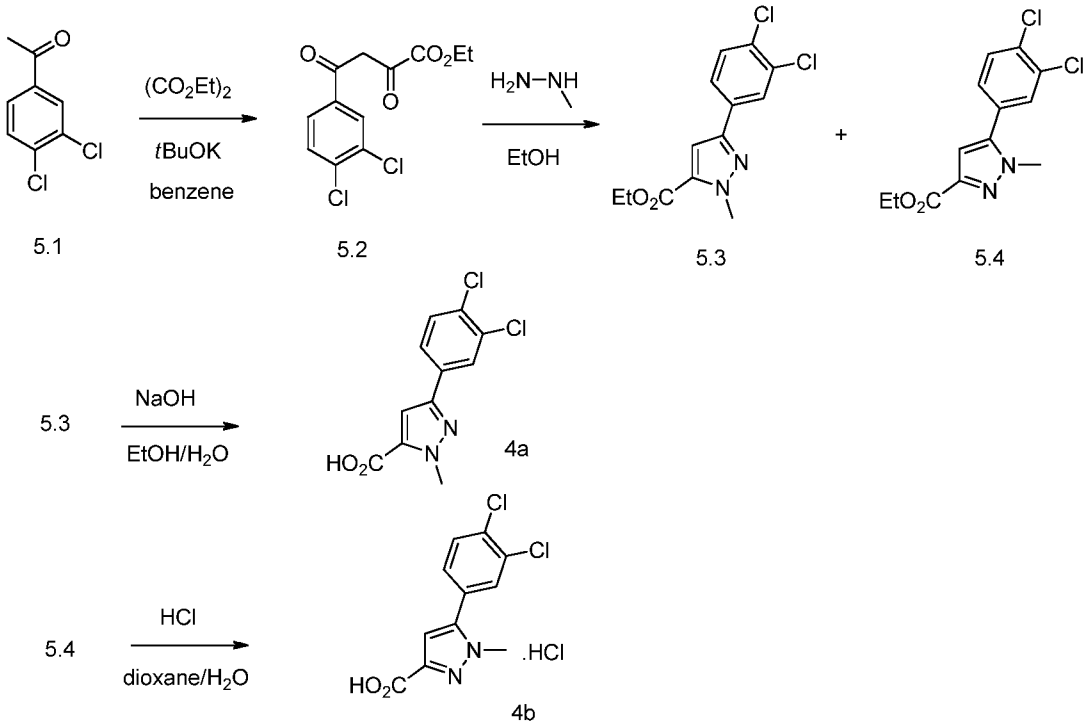
ride salt,
intermediate **3k1:** 4-phenyl-2-(5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)thiazole hydrochloride salt,
intermediate **3l1:** 2-(2-chlorophenyl)-4-(5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)thiazole hydrochloride salt,
intermediate **3m1:** 4-(8,8-dimethyl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)-2-phenylthiazole hydrochloride salt,
intermediate **3n1:** 2-(8-methyl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)quinoline hydrochloride salt,
intermediate **3o1:** 4-(8-methyl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)-2-phenylthiazole hydrochloride salt,
intermediate **3p1:** (R)-2-(4-chlorophenyl)-4-(8-methyl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)thiazole hydrochloride salt,
intermediate **3q1:** 2-(4-fluorophenyl)-4-(8-methyl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)thiazole hydrochloride salt,
intermediate **3r1:** (R)-2-(4-fluorophenyl)-4-(8-methyl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)thiazole hydrochloride salt,
intermediate **3s1:** 5-methyl-4-(8-methyl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)-2-phenylthiazole hydrochloride salt,
intermediate **3t1:** 2-(2-chlorophenyl)-4-(8-methyl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)thiazole hydrochloride salt,
intermediate **3u1:** 2-(2,4-difluorophenyl)-4-(8-methyl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)thiazole hydrochloride salt,
intermediate **3v1:** 5-(8-methyl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)-3-phenyl-1,2,4-oxadiazole hydrochloride salt,
intermediate **3w1:** 2-(4-fluorophenyl)-4-(6-methyl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)thiazole hydrochloride salt,
intermediate **3x1:** 2-(4-fluorophenyl)-4-(5-methyl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)thiazole hydrochloride salt,
intermediate **3y1:** (S)-8-methyl-3-(pyridin-2-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazine,
intermediate **3z1:** (S)-2-(4-fluorophenyl)-4-(8-methyl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)thiazole,
intermediate **3a2:** (S)-4-(4-(8-methyl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)thiazol-2-yl)morpholine,
intermediate **3b2:** 5-phenyl-3-(5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)-1,2,4-oxadiazole hydrochloride salt,
intermediate **3c2:** 3-phenyl-5-(5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)-1,2,4-oxadiazole hydrochloride salt,
intermediate **3d2** 3-(4-fluorophenyl)-5-(5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)-1,2,4-oxadiazole hydrochloride salt,
intermediate **3e2:** 3-(2,4-difluorophenyl)-5-(5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)-1,2,4-oxadiazole hydrochloride salt,
intermediate **3f2:** 3-(5-phenyl-1H-1,2,4-triazol-3-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazine hydrochloride salt,
intermediate **3g2:** 2-(2-fluorophenyl)-4-(5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)thiazole hydrochloride salt,
intermediate **3h2:** 2-((4,5-dichloro-1H-imidazol-1-yl)methyl)-4-(5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)thiazole dihydrochloride salt,
intermediate **3i2:** 2-(4-chlorobenzyl)-4-(5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)thiazole hydrochloride salt,
intermediate **3j2:** 4-(5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)-2-(p-tolyl)thiazole hydrochloride salt,
intermediate **3k2:** 4-(5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)-2-(thiophen-2-yl)thiazole hydrochloride salt,
intermediate **3l2:** 2-(((4-chlorophenyl)sulfonyl)methyl)-4-(5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)thiazole hydrochloride salt,
intermediate 3m2: 2-(2-methoxyphenyl)-4-(5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)thiazole hydrochloride salt,
intermediate 3n2: 2-(3-fluorophenyl)-4-(5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)thiazole hydrochloride salt,
intermediate **3o2:** 2-isopropyl-4-(5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)thiazole hydrochloride salt,
intermediate **3p2:** 3-(4-fluorophenyl)-5-(8-methyl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)-1,2,4-oxadiazole hydrochloride salt,

intermediate **3q2:** 3-phenyl-5-(5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)-1,2,4-thiadiazole hydrochloride salt,
intermediate **3r2:** 2-(4-bromophenyl)-4-(5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)thiazole hydrochloride salt,
intermediate **3s2:** 2-(pyridin-4-yl)-4-(5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)thiazole dihydrochloride salt,
intermediate **3t2:** 2-(quinolin-2-yl)-4-(5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)thiazole dihydrochloride salt,
intermediate **3u2:** 3-(1-methyl-3-phenyl-1H-pyrazol-5-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazine hydrochloride salt,
intermediate **3v2:** N,N-dimethyl-4-(4-(5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)thiazol-2-yl)aniline dihydrochloride salt,
intermediate **3w2:** 3-(1-methyl-5-phenyl-1H-pyrazol-3-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazine hydrochloride salt,
intermediate **3y2:** 2-(pyridin-2-yl)-4-(5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)thiazole dihydrochloride salt,
intermediate **3z2:** 2-(pyrimidin-2-yl)-4-(5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)thiazole dihydrochloride salt,
intermediate **3a3:** 2-(pyrazin-2-yl)-4-(5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)thiazole dihydrochloride salt,
intermediate **3b3:** 4-(4-(4-(5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)thiazol-2-yl)phenyl)morpholine hydrochloride salt,
intermediate **3c3:** 2-(4-(4-methylpiperazin-1-yl)phenyl)-4-(5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)thiazole dihydrochloride salt,
intermediate **3d3:** 2-(4-(piperidin-1-yl)phenyl)-4-(5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)thiazole hydrochloride salt,
intermediate **3e3:** 2-(4-(pyrrolidin-1-yl)phenyl)-4-(5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)thiazole hydrochloride salt,
intermediate **3f3:** 2-(piperidin-1-yl)-4-(5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)thiazole hydrochloride salt,
intermediate **3g3:** 2-(pyrrolidin-1-yl)-4-(5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)thiazole hydrochloride salt,
intermediate **3h3:** 2-(4-methylpiperazin-1-yl)-4-(5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)thiazole dihydrochloride salt,
intermediate **3i3:** 3-(1-methyl-2-phenyl-1H-imidazol-4-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazine dihydrochloride salt,
intermediate **3j3:** 3-(1-(2-methoxyethyl)-3-phenyl-1H-pyrazol-5-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazine hydrochloride salt,
intermediate **3k3:** 2-isobutyl-4-(5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)thiazole hydrochloride salt,
intermediate **3l3:** 2-(2-methoxyethyl)-4-(4-(5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)thiazol-2-yl)morpholine hydrochloride salt,
intermediate **3m3:** 2-(4,4-difluoropiperidin-1-yl)-4-(5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)thiazole hydrochloride salt,
intermediate **3n3:** 2,5-dimethyl-4-(4-(5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)thiazol-2-yl)morpholine hydrochloride salt,
intermediate **3o3:** 2-(4-(5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)thiazol-2-yl)phenol hydrochloride salt,
intermediate **3p3:** 2,6-dimethyl-4-(4-(5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)thiazol-2-yl)morpholine hydrochloride salt,
intermediate **3q3:** 2,2-dimethyl-4-(4-(5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)thiazol-2-yl)morpholine hydrochloride salt,
intermediate **3r3:** 3-(3-phenyl-1H-pyrazol-5-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazine dihydrochloride salt,
intermediate **3s3:** 2-methyl-4-(4-(5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)thiazol-2-yl)morpholine hydrochloride salt,
intermediate **3t3:** 2-(4,4-dimethylpiperidin-1-yl)-4-(5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)thiazole hydrochloride salt,
intermediate **3u3** 5-methyl-4-(5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)thiazole hydrochloride salt,
intermediate **3v3** 2-(2-(methoxymethyl)piperidin-1-yl)-4-(5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)thia-

zole hydrochloride salt,
intermediate **3w3:** 8-methyl-3-(6-methylpyridin-2-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazine dihydrochloride salt,
intermediate **3x3:** 2-(2-bromophenyl)-4-(5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)thiazole,
intermediate **3y3:** 2-(3-bromophenyl)-4-(5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)thiazole,

General Method D:

[0175] General Method D is the general procedure used for the synthesis of 3-phenylpyrazole-5-carboxylic acid intermediates **4** and is exemplified below using the synthesis of 3-(3,4-dichlorophenyl)-1-methyl-1H-pyrazole-5-carboxylic acid **4a** and 5-(3,4-dichlorophenyl)-1-methyl-1H-pyrazole-3-carboxylic acid **4b.**



Scheme 5: Synthesis of intermediates **4a** and **4b**

Step 1: Synthesis of ethyl 4-(3,4-dichlorophenyl)-2,4-dioxobutanoate **5.2**

[0176] To a solution of *t*-BuOK (0.05 mol, 5.6 g) in benzene (200 mL) was added dropwise a benzene (50 mL) solution of 3,4-dichloroacetophenone **5.1** (0.05 mol, 9.45 g) and diethyloxalate (0.055 mol, 8.1 g). The resultant mixture was stirred for 8 h at room temperature, then 10% aqueous HCl solution (100 mL) was added to the mixture. The organic layer was separated and washed with brine, dried over sodium sulfate and concentrated *in vacuo.* The crude product was purified by column chromatography using dichloromethane as eluent to yield the title compound. Yield: 7.5 g (52%).

Step 2: synthesis of ethyl 3-(3,4-dichlorophenyl)-1-methyl-1H-pyrazole-5-carboxylate **5.3** and ethyl 5-(3,4-dichlorophenyl)-1-methyl-1H-pyrazole-3-carboxylate **5.4**

[0177] To a solution of compound **5.2** (0.035 mol, 10.2 g) in ethanol (100 mL) was added monomethyl hydrazine (0.0353 mol, 1.63 g) and the resultant mixture was refluxed for 2 h, and subsequently stirred overnight at RT. The mixture was then evaporated to dryness and the thus obtained crude product was subjected to column chromatography (eluent: ethyl acetate/hexane 2:3). This afforded 3.68 g of compound **5.3** (R_f=0.8) and 3.28 g of compound **5.4** (R_f=0.6). The structure assignment of the thus obtained regioisomers was accomplished on the basis of NOE in 2D-NOESY spectra and ^{1}H-^{13}C cross-coupling constants in 2D-^{1}H-^{13}C-HMBC spectra between N-methyl protons and quaternary carbons in the pyrazole rings.

Step 3: synthesis of 3-(3,4-dichlorophenyl)-1-methyl-1H-pyrazole-5-carboxylic acid **4a** and 5-(3,4-dichlorophenyl)-1-methyl-1H-pyrazole-3-carboxylic acid hydrochloride salt **4b**

Synthesis of 3-(3,4-dichlorophenyl)-1-methyl-1H-pyrazole-5-carboxylate **4a**

[0178] Compound **5.3** (0.0123 mol, 3.68 g) and sodium hydroxide (2 g) were dissolved in water-ethanol (1:1 v/v, 300 mL) solution. The mixture was refluxed for 3 h and then most of the ethanol was evaporated. The pH of the thus obtained mixture was adjusted to pH 3 by addition of 10% HCl whereupon a precipitate formed, which was filtered, washed with water and air dried to afford compound **5.5.** Yield: 3.05 g (91.6%). LCMS: P= 97.5%, rt=1.86 mn, m/z=271. ^{1}HNMR (DMSO-d^6): δ: 13.5 ppm (br s, 1H), 8.05 ppm (s, 1H), 7.8 ppm (d, 1H), 7.6 ppm (d, 1H), 7.4 ppm (s, 1H), 4.15 ppm (s, 3H).

Synthesis of 5-(3,4-dichlorophenyl)-1-methyl-1H-pyrazole-3-carboxylate **4b**

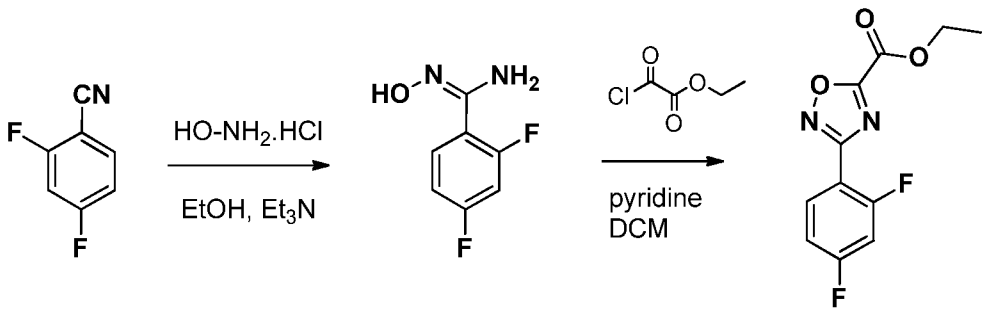
[0179] Compound **5.4** (10.08 mmol, 3.24 g) was refluxed in a mixture of conc. HCl 50mL/ water 75 mL/dioxane 125 mL for 3h. The volatiles were evaporated until the formation of a precipitate, which was filtered, washed with water and air dried to afford product **5.6** as HCl salt. Yield: 2.79 g (90%). LCMS: P=95%, rt=1.67mn, m/z=271. ^{1}H NMR (DMSO-d^6): δ: 7.9 ppm (s, 1H), 7.75 ppm (d, 1H), 7.6 ppm (d, 1H), 6.95ppm (s, 1H), 3.9 ppm (s, 3H).

[0180] The following intermediates were also prepared from the *ad hoc* reagents and intermediates using General Method D:

Intermediate **4c:** 3-(4-chlorophenyl)-1H-pyrazole-5-carboxylic acid,
Intermediate **4d:** 3-(3,4-dichlorophenyl)-1H-pyrazole-5-carboxylic acid,
Intermediate **4e:** 3-(2,4-dichlorophenyl)-1H-pyrazole-5-carboxylic acid,
Intermediate **4f:** 3-(4-trifluoromethylphenyl)-1H-pyrazole-5-carboxylic acid,
Intermediate **4g:** 3-(4-phenoxyphenyl)-1H-pyrazole-5-carboxylic acid,
Intermediate **4h:** 3-(4-chlorophenyl)-1-methyl-1H-pyrazole-5-carboxylic acid,
Intermediate **4i:** 5-(4-chlorophenyl)-1-methyl-1H-pyrazole-3-carboxylic acid.

General Method E:

[0181] General Method E is the general procedure used for the synthesis of ethyl 3-phenyl-1,2,4-oxadiazol-5-carboxylate intermediates **1.2** and is exemplified below with the synthesis of ethyl 3-(2,4-difluorophenyl)-1,2,4-oxadiazole-5-carboxylate **5a.**



5.1 **5 2** **5a**

Scheme 6: synthesis of intermediate **5a**

***Step 1*:** Synthesis of 2,4-difluoro-N'-hydroxybenzimidamide **5.2**

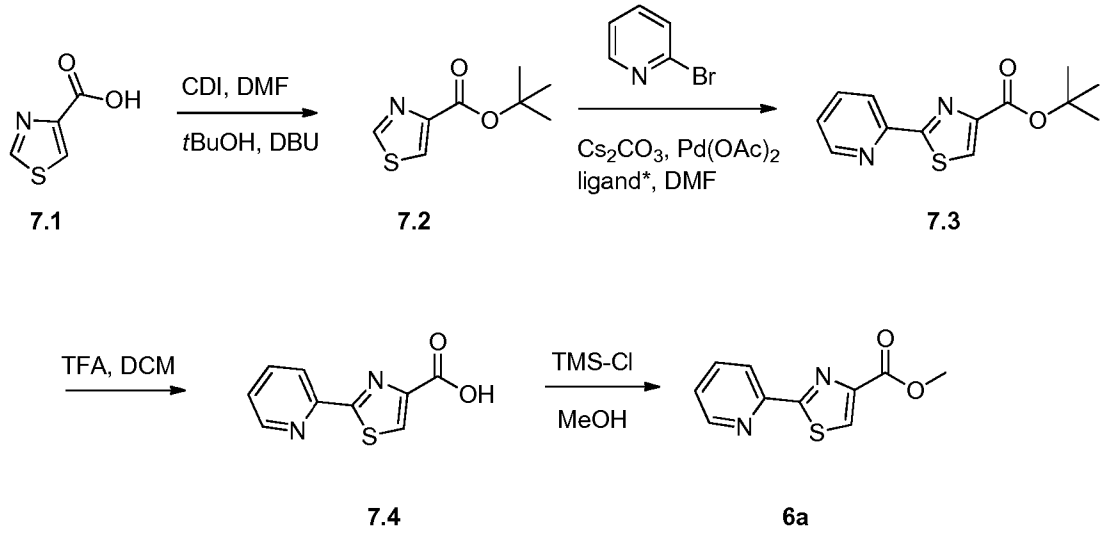
[0182] To a solution of 2,4-difluorobenzonitrile **5.1** (1 g, 7.2 mmol) and hydroxylamine hydrochloride (1 g, 14.4 mmol) in commercial dry EtOH (5 mL) under N_2 was added NEt_3 (2 mL, 14.4 mmol) dropwise over 2 min at RT. The mixture was stirred under reflux overnight. The mixture was then allowed to cool down to RT and concentrated. The white solid obtained was used crude in the next step. Yield: 3.52 g (quantitative).LCMS: P= 33 %, rt = 0.84mn, m/z = 173.

Step 2: Synthesis of ethyl 3-(2,4-difluorophenyl)-1,2,4-oxadiazole-5-carboxylate **5a**

[0183] To a solution of 2,4-difluoro-N'-hydroxybenzimidamide **5.2** (3.52 g, 33% purity, max. 7.2 mmol) and pyridine (2.32 mL, 28.7 mmol) in anhydrous CH_2Cl_2 under N_2 was added ethyl chlorooxoacetate (1.27 g, 9.32 mmol) dropwise over 5 min at RT. The mixture was stirred under reflux. After 1h30, the rxn mixt. was concentrated and purified on silica gel using CH_2Cl_2, furnishing 1.414 g of title product **5a** as colorless oil. Yield: 1.414 g (78 %). LCMS: P= 94 %, rt = 4.21mn, m/z = 255, 277 (M+Na).

General Method F:

[0184] General Method E is the general procedure used for the synthesis of methyl 2-pyridyl-thiazol-4-carboxylate intermediates **1.2** and is exemplified below with the synthesis of methyl 2-(pyridin-2-yl)thiazole-4-carboxylate **6a.**



7.1 **7.2** **7.3**

7.4 **6a**

*(2-biphenyl)dicyclohexyl phosphine

Scheme 7: Synthesis of intermediate **6a**

Step 1: Synthesis of *tert*-butyl thiazole-4-carboxylate **7.2**

[0185] To a solution of thiazole-4-carboxylic acid **7.1** (1 g, 7.2 mmol) and carbonyldiimidazole (6.3 g, 38.7 mmol) in commercial dry DMF (50 mL) under N_2 was stirred at 50 °C for 20 min. *Tert*-butanol (8.6 g, 116.0 mmol) and DBU (5.8 mL, 38.7 mmol) were then successively added at once and the reaction was warmed at 60 °C for 48h. The RM was then allowed to cool down to RT and the pH was adjusted to 4 with a solution of HCl (2M, ~ 80 mL). The mixture was diluted with water (250 mL) and extracted with Et_2O (3x 100 mL). The combined org. layers were washed with brine (250 mL), dried over $MgSO_4$, concentrated and purified on silica gel using DCM to afford title product as yellowish oil (47%). Yield: 3.37 g (47 %). LCMS: P= 98 %, rt = 3.65 mn, m/z = 186.

Step 2: Synthesis of *tert*-butyl 2-(pyridin-2-yl)thiazole-4-carboxylate **7.3**

[0186] To a solution of *tert*-butyl thiazole-4-carboxylate **7.2** (256 mg, 1.62 mmol), anhydrous cesium carbonate (1 g, 3.24 mmol) and 2-bromo-pyridine (300 mg, 1.62 mmol) sequentially added in commercial anhydrous DMF (6 mL) at RT under N_2 was added $Pd(OAc)_2$ (18 mg, 0.08 mmol) and (2-biphenyl)dicyclohexyl phosphine (57 mg, 0.16 mmol). The RM was heated at 110°C overnight. The RM was then allowed to cool down to RT, filtered on Celite pad and concentrated. The residue was purified on silica gel using cyclohexane/EtOAc (5% to 20% of EtOAc), furnishing 7.3 as yellow oil. Yield: 340 mg (80 %). LCMS: P= 96 %, rt = 4.28 mn, m/z = 263.

Step 3: Synthesis of 2-(pyridin-2-yl)thiazole-4-carboxylic acid **7.4**

[0187] To a solution of *tert*-butyl 2-(pyridin-2-yl)thiazole-4-carboxylate **7.3** (340 mg, 1.3 mmol) in commercial anhydrous CH_2Cl_2 (5 mL) at RT was added TFA (0.93 mL, 13 mmol) under N_2. The mixture was stirred at RT overnight. The mixture

was diluted with CH_2Cl_2 (25 mL), washed with an aqueous solution of $NaHSO_3$ 10% (5x 25 mL), brine (25 mL) and then water (25 mL). The organic layer was dried over $MgSO_4$ and evaporated to afford title product as a yellow oil. Yield: 250 mg (94 %). LCMS: P= 93 %, rt = 3.03 mn, m/z = 207.

***Step** 4:* Synthesis of methyl 2-(pyridin-2-yl)thiazole-4-carboxylate **6a**

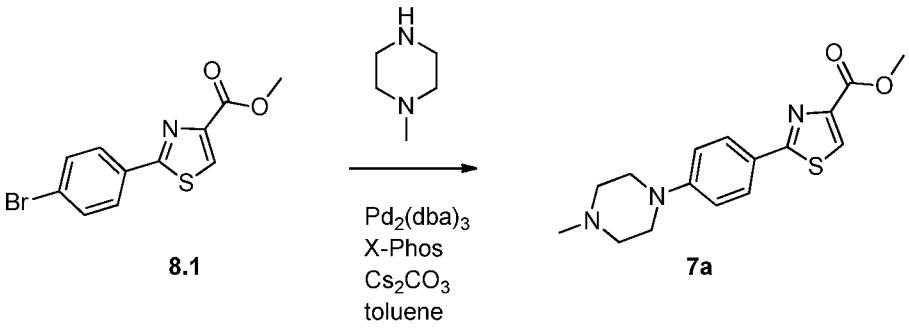
[0188] To a solution of 2-(pyridin-2-yl)thiazole-4-carboxylic acid **7.4** (500 mg, 2.425 mmol) in commercial anhydrous methanol (10 mL) was added TMS-Cl (0.77 mL, 6.06 mmol) at once. The RM was heated to 50°C overnight. The RM. was concentrated under reduced pressure and the residue was used crude in next step. Yield: 649 mg (quantitative). LCMS: P= 94 %, rt = 4.07 mn, m/z = 221.

[0189] The following intermediates were also prepared from the *ad hoc* reagents and intermediates using General Method F:

intermediate **6b:** methyl 2-(pyridin-4-yl)thiazole-4-carboxylate,
intermediate **6c:** methyl 2-(quinolin-2-yl)thiazole-4-carboxylate,
intermediate **6d:** methyl 2-(pyrimidin-2-yl)thiazole-4-carboxylate,
intermediate **6e:** methyl 2-(pyrazin-2-yl)thiazole-4-carboxylate.

General Method G:

[0190] General Method G is the general procedure used for the synthesis of methyl 2-(4-heterocyclylphenyl)thiazole-4-carboxylate intermediates **1.2** and is exemplified below with the synthesis of methyl 2-(4-(4-methylpiperazin-1-yl)phenyl)thiazole-4-carboxylate **7a.**



Scheme 8: Synthesis of intermediate **7a**

[0191] In a tube previously dried in a 113°C-heated oven overnight were introduced successively 2-(4-bromophenyl)thiazole-4-carboxylate **8.1** (500 mg, 1.6 mmol), 1-methylpiperazine (0.21 mL, 1.9 mmol) and anhydrous cesium carbonate (1.04 g, 3.0 mmol) under N_2. Commercial anhydrous toluene (10 mL) was then added and RM was degassed (argon bubbling for ~ 5 min).
$Pd_2(dba)_3$ (73 mg, 0.08 mmol) and X-Phos (76 mg, 0.16 mmol) were quickly added successively and the mixture was heated under reflux overnight. The reaction mixture was then allowed to cool down to RT and EtOAc (50 mL) was added. This mixture was washed with brine (30 mL) and the aqueous layer was further extracted twice with EtOAc (30 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified on silica gel using CH_2Cl_2/MeOH (2% of MeOH) to afford title product as a yellow solid. Yield: 374 mg (71 %). LCMS: P= 92 %, rt = 3.31 mn, m/z = 332.

[0192] This General Method was also applied to the synthesis of methyl 2-heterocyclylthiazole-4-carboxylate intermediates, starting from methyl 2-bromothiazole-4-carboxylate.

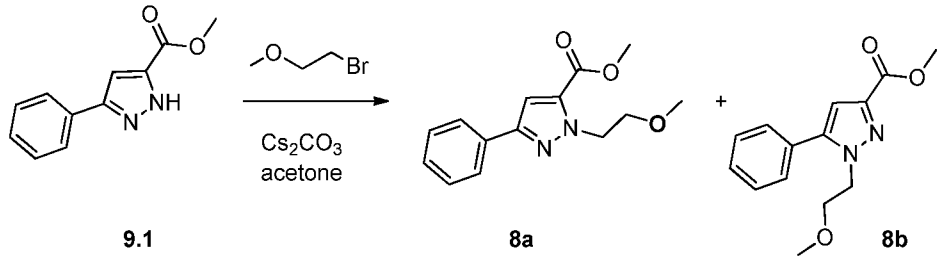
[0193] The following intermediates were also prepared from the *ad hoc* reagents and intermediates using General Method G

intermediate **7b:** methyl 2-(4-morpholinophenyl)thiazole-4-carboxylate,
intermediate **7c:** methyl 2-(4-(piperidin-1-yl)phenyl)thiazole-4-carboxylate,
intermediate **7d:** methyl 2-(4-(pyrrolidin-1-yl)phenyl)thiazole-4-carboxylate,
intermediate **7e:** methyl 2-(piperidin-1-yl)thiazole-4-carboxylate,
intermediate **7f:** methyl 2-(pyrrolidin-1-yl)thiazole-4-carboxylate,

intermediate **7g:** methyl 2-(4-methylpiperazin-1-yl)thiazole-4-carboxylate,
intermediate **7h:** methyl 2-(2-(2-methoxyethyl)morpholino)thiazole-4-carboxylate,
intermediate **7i:** methyl 2-(4,4-difluoropiperidin-1-yl)thiazole-4-carboxylate,
intermediate **7j:** methyl 2-(2,5-dimethylmorpholino)thiazole-4-carboxylate,
intermediate **7k:** methyl 2-(2,6-dimethylmorpholino)thiazole-4-carboxylate,
intermediate **7l:** methyl 2-(2,2-dimethylmorpholino)thiazole-4-carboxylate,
intermediate **7m:** methyl 2-(2-methylmorpholino)thiazole-4-carboxylate,
intermediate **7n:** methyl 2-(4,4-dimethylpiperidin-1-yl)thiazole-4-carboxylate,
intermediate **7o:** methyl 2-(2-(methoxymethyl)piperidin-1-yl)thiazole-4-carboxylate,

General Method H:

[0194] General Method H is the general procedure used for the synthesis of methyl 3-phenylpyrazole-5-carboxylate and methyl 5-phenylpyrazole-3-carboxylate intermediates **1.2** and is exemplified below with the synthesis of methyl 1-(2-methoxyethyl)-3-phenyl-1H-pyrazole-5-carboxylate **8a** and methyl 1-(2-methoxyethyl)-5-phenyl-1H-pyrazole-3-carboxylate **8b.**



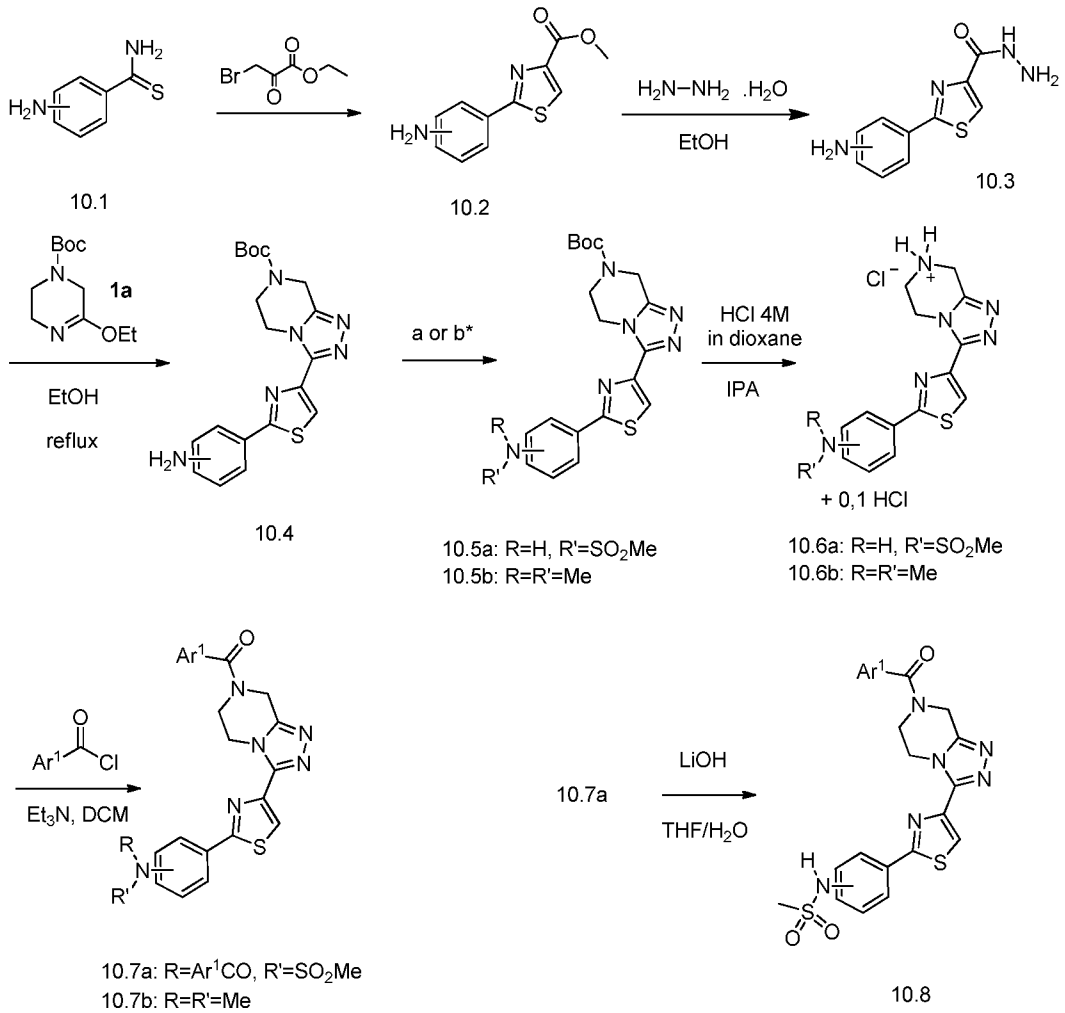
9.1 **8a** **8b**

Scheme 9: Synthesis of intermediates **8a** and **8b**

[0195] To a solution of methyl 3-phenyl-1H-pyrazole-5-carboxylate **9.1** (250 mg, 1.24 mmol) in commercial anhydrous acetone (30 mL) at RT under N_2 was added cesium carbonate at once (806 mg, 2.47 mmol). After 10 min stirring, 2-bromoethyl-methylether (258 mg, 1.85 mmol) was added at once. The reaction mixture was refluxed for 2h and then allowed to cool down and concentrated, diluted with CH_2Cl_2 (50 mL) and washed with water (50 mL). The organic layer was then dried over $MgSO_4$, filtered and evaporated to dryness. The residue was purified on silica gel using CH_2Cl_2/MeOH (1% of MeOH) to afford a mixture of **8a** alongside with **8b** (~ 10%) as a pale yellow oil. Yield: 359 mg (71 %). LCMS: P = 100 %, ratio 8a/8b = 9/1, **8a:** rt = 4.41 mn, m/z = 261; **8b** . rt = 3.95 mn, m/z = 261.

Additional synthetic schemes

[0196] The synthesis of compounds n° 283, 289, 290, 291, 292 was carried out according to scheme 10

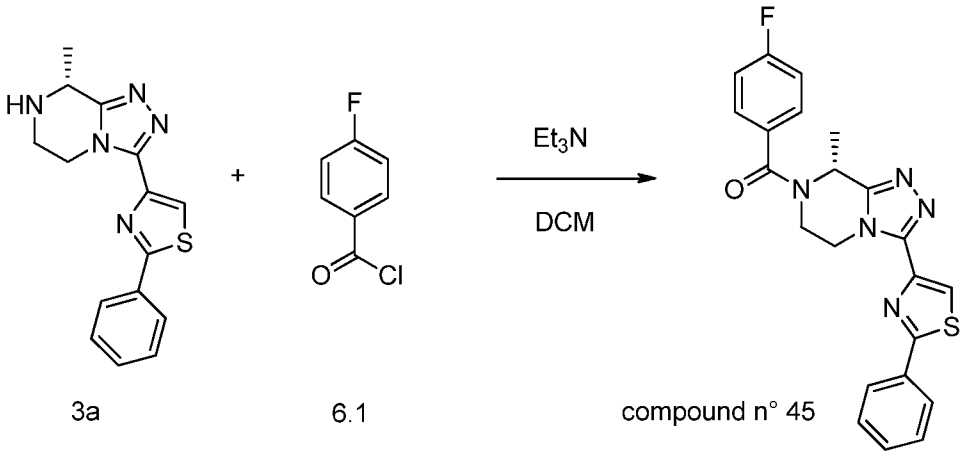


Scheme 10: Synthesis of compounds n° 283, 289, 290, 291, 292

[0197] Thioamide **10.1** is condensed with ethyl 3-bromo-2-oxopropanoate to yield thiazole ester intermediate **10.2** which was further converted to thiazolylhydrazide **10.3.** Condensation of **10.3** with iminoether 1 provided aniline **10.4** which could be further converted to N-methylsulfonylaniline **10.5a** or dimethylaniline **10.5b.** Boc deprotection followed acylation yielded compounds **10.7a** and **10.7b.** Di-acylated product **10.7a** could be deacylated on the aniline part to provided target compound **10.8.**

Example 1: synthesis of compound n°45

[0198] The general procedure used for the synthesis of triazolopiperazine compounds of the invention is detailed below using the synthesis of
compound n° 45: (R)-(4-fluorophenyl)(8-methyl-3-(2-phenylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone



3a 6.1 compound n° 45

Scheme 12: synthesis of (R)-(4-fluorophenyl)(8-methyl-3-(2-phenylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone (compound n°45).

[0199] To a solution of intermediate **3a** (80 mg, 0.27 mmol) in 7 mL of DCM there was added Et_3N (68 mg, 0.67 mmol) and then a solution of 4-fluorobenzoyl chloride **6.1** in DCM (43 mg, 0.27 mmol). The solution was left stirring at room temperature for 2 h. The reaction mixture was washed with water, brine, dried over sodium sulfate and approximately ¾ of the volatiles were evaporated. Diethyl ether was added and the precipitate was filtered and dried to yield the title compound. Yield: 68 mg, 60%. LCMS: P=100%, rt=1.96mn, $(M+H)^+$: 420.1; chiral: 7.22 mn, ee=91%. ^{1}HNMR (DMSO-d^6): δ: 8.4 ppm (s, 1H), 8.05 ppm (m, 2H), 7.6 ppm (m, 2H), 7.5 ppm (m, 3H), 7.35 ppm (t, 2H), 5.7 ppm (br m, 1H), 4.8 ppm (dd, 1H), 4.3 ppm (m, 1H), 4.1 ppm (br m, 1H), 3.7 ppm (m, 1H), 1.6 ppm (d, 3H).

Examples 2 to 84:

[0200] The general procedure detailed in example 1 was used for the preparation of compounds in examples 2 to 84 starting from the appropriate intermediates or commercially available reagents. Example n°, compound n°, compound names, triazolopiperazine intermediates 3 and acyl chloride intermediates **4** are listed in Table 2A below.

TABLE2A

Example_n°	Compound_n°	Triazolopiperazine intermediae 3	Acyl chloride intermediate 4
2	1	**3b**	4-fluorobenzoyl chloride
3	2	**3b**	4-chlorobenzoyl chloride
4	3	**3b**	**4c**
5	4	**3b**	**4d**
6	5	**3b**	3,4-dichlorobenzoyl chloride
7	6	**3b**	4-phenylbenzoyl chloride
8	7	**3h**	4-fluorobenzoyl chloride
9	8	**3o**	4-fluorobenzoyl chloride
10	9	**3c**	4-fluorobenzoyl chloride
11	10	**3d**	4-fluorobenzoyl chloride
12	11	**3e**	4-fluorobenzoyl chloride
13	12	**3f**	4-fluorobenzoyl chloride
14	13	**3b**	**4e**
15	14	**3b**	**4a**

(continued)

Example_n°	Compound_n°	Triazolopiperazine intermediae 3	Acyl chloride intermediate 4
16	15	**3g**	4-fluorobenzoic chloride
17	16	**3b**	4-(4-fluorophenyl)benzoyl chloride
18	17	**3b**	**4f**
19	18	**3b**	**4g**
20	19	**3h**	4-phenylbenzoyl chloride
21	20	**3c**	4-phenylbenzoyl chloride
22	21	**3b**	4-(thiophen-2-yl)benzoyl chloride
23	22	**3i**	4-fluorobenzoyl chloride
24	23	**3j**	4-fluorobenzoyl chloride
25	24	**3k**	4-fluorobenzoyl chloride
26	25	**3l**	4-fluorobenzoyl chloride
27	26	**3o**	4-phenylbenzoyl chloride
28	27	**3m**	4-fluorobenzoyl chloride
29	28	**3p**	4-fluorobenzoyl chloride
30	29	**3q**	4-fluorobenzoyl chloride
31	30	**3r**	4-fluorobenzoyl chloride
32	31	**3s**	4-fluorobenzoyl chloride
33	32	**3t**	4-fluorobenzoyl chloride
34	33	**3u**	4-fluorobenzoyl chloride
35	34	**3v**	4-fluorobenzoyl chloride
36	35	**3w**	4-fluorobenzoyl chloride
37	36	**3x**	4-fluorobenzoyl chloride
38	37	**3y**	4-fluorobenzoyl chloride
39	38	**3z**	4-fluorobenzoyl chloride
40	39	**3a1**	4-fluorobenzoyl chloride
41	40	**3b1**	4-fluorobenzoyl chloride
42	41	**3c1**	4-fluorobenzoyl chloride
43	42	**3d1**	4-fluorobenzoyl chloride
44	43	**3e1**	4-fluorobenzoyl chloride
45	44	**3f1**	4-fluorobenzoyl chloride
46	46	**3g1**	4-phenylbenzoyl chloride
47	47	**3h1**	4-phenylbenzoyl chloride
48	48	**3i1**	4-fluorobenzoyl chloride
49	49	**3i1**	4-fluorobenzoyl chloride
50	50	**3h1**	4-fluorobenzoyl chloride
51	51	**3j1**	4-fluorobenzoyl chloride
52	52	**3g1**	4-fluorobenzoyl chloride
53	53	**3g1**	4-(4-fluorophenyl)benzoyl chloride

(continued)

Example_n°	Compound_n°	Triazolopiperazine intermediae 3	Acyl chloride intermediate 4
54	54	**3o**	4-(thiophen-2-yl)benzoyl chloride
55	55	**3c**	4-(thiophen-2-yl)benzoyl chloride
56	56	**3g1**	4-(thiophen-2-yl)benzoyl chloride
57	57	**3k1**	4-fluorobenzoyl chloride
58	58	**3l1**	4-fluorobenzoyl chloride
59	59	**3n**	4-fluorobenzoyl chloride
60	60	**3m1**	4-fluorobenzoyl chloride
61	61	**3n1**	4-fluorobenzoyl chloride
62	62	**3o1**	4-(thiophen-2-yl)benzoyl chloride
63	63	**3o**	4-(thiophen-3-yl)benzoyl chloride
64	64	**3o1**	4-(thiophen-3-yl)benzoyl chloride
65	65	**3n1**	4-(thiophen-2-yl)benzoyl chloride
66	66	**3l1**	4-(thiophen-2-yl)benzoyl chloride
67	67	**3l1**	4-phenylbenzoyl chloride
68	68	**3p1**	4-fluorobenzoyl chloride
69	69	**3h**	4-(thiophen-2-yl)benzoyl chloride
70	70	**3q1**	4-fluorobenzoyl chloride
71	71	**3r1**	4-fluorobenzoyl chloride
72	72	**3s1**	4-phenylbenzoyl chloride
73	73	**3t**	4-(thiophen-2-yl)benzoyl chloride
74	74	**3t1**	4-fluorobenzoyl chloride
75	75	**3s1**	4-fluorobenzoyl chloride
76	76	**3q1**	4-phenylbenzoyl chloride
77	77	**3u1**	4-fluorobenzoyl chloride
78	78	**3q1**	4-(thiophen-2-yl)benzoyl chloride
79	79	**3u1**	4-phenylbenzoyl chloride
80	80	**3u1**	4-(thiophen-2-yl)benzoyl chloride
81	81	**3b**	1-naphthoyl chloride
82	82	**3b**	**4h** converted to acyl chloride
83	83	**3b**	**4i** converted to acyl chloride
84	85	**3v1**	4-(thiophen-2-yl)benzoyl chloride

Examples 87 to 111:

[0201] The general procedure detailed in example 1 was used for the preparation of compounds in examples 87 to 111 starting from the appropriate intermediates or commercially available reagents. Example n°, compound n°, compound names, triazolopiperazine intermediates **3** and carboxylic acidacyl chloride intermediates **4** are listed in table 2B hereunder.

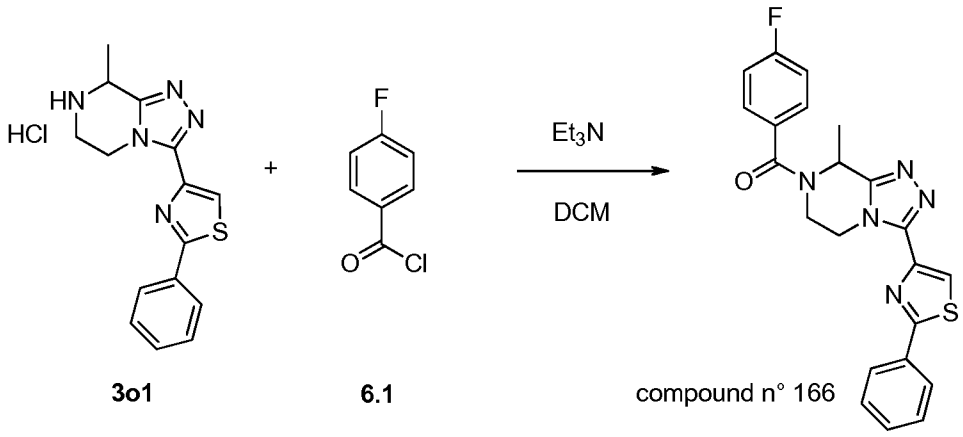
TABLE 2B

Example_n°	Compound_n°	Triazolopiperazine intermediate 3	Acyl chloride intermediate 4
88	90	**3h**	5-phenylpicolinyl chloride
89	91	**3h**	6-phenylnicotinyl chloride
90	92	**3h**	2-phenylpyrimidine-5-carbonyl chloride
91	93	**3h**	4-phenylcyclohexanecarbonyl chloride
92	95	**3h**	3-methylbutanoyl chloride
93	96	**3h**	2-phenylbenzoyl chloride
94	98	**3h**	4-(pyrimidin-5-yl)benzoyl chloride
95	100	**3h**	4-(pyrimidin-2-yl)benzoyl chloride
96	101	**3h**	4-(pyrazin-2-yl)benzoic chloride
97	102	**3h**	4-(pyridazin-3-yl)benzoyl chloride
98	103	**3h**	4'-cyano-[1,1'-biphenyl]-4-carbonyl chloride
99	104	**3h**	4-(2-oxopiperidin-1-yl)benzoyl chloride
100	105	**3h**	4-morpholinobenzoyl chloride
101	106	**3h**	4-(3,5-dimethyl-1H-pyrazol-1-yl)benzoyl chloride
102	107	**3w1**	4-(thiophen-2-yl)benzoyl chloride
103	108	**3x1**	4-(thiophen-2-yl)benzoyl chloride
104	109	**3q1**	3,4-dichlorobenzoyl chloride
105	110	**3q1**	3,4-difluorobenzoyl chloride
106	111	**3q1**	3-chloro-4-fluorobenzoyl chloride
107	112	**3q1**	3-fluoro-4-chlorobenzoyl chloride
108	113	**3q1**	3,4,5-trifluorobenzoyl chloride
109	114	**3i1**	4-(thiophen-2-yl)benzoyl chloride
110	135	**3a**	4-(thiophen-2-yl)benzoyl chloride
111	136	**3g1**	4-(thiophen-2-yl)benzoyl chloride

[0202] It was noted that synthesis from chiral intermediate **3** could lead to compounds with low enantiomeric excess. It could therefore be advantageous to make the synthesis of compounds of invention from racemic bulding block **3** and perform futher purification by chiral preparative HPLC.

Example 112: Synthesis of compound n° 166

[0203] A variant to the general procedure used for the synthesis of triazolopiperazine compounds of the invention is detailed below using the synthesis of compound n° 166: (4-fluorophenyl)(8-methyl-3-(2-phenylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone:



3o1 **6.1** compound n° 166

Scheme 13: synthesis of (4-fluorophenyl)(8-methyl-3-(2-phenylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone (compound n°166).

[0204] To a solution of intermediate **3o1** (500 mg, 1.50 mmol) in 20 mL of anhydrous DCM was added 4-fluorobenzoyl chloride **6.1** (261 mg, 1.65 mmol) and Et_3N (0.625 mL, 455 mg, 4.49 mmol). The reaction mixture was stirred for 2 h. Thereupon the reaction mixture was washed with water, and the extracted organic layer further washed with brine, dried over sodium sulfate. Thereafter the volatiles were concentrated and diethyl ether was added to precipitate the product. The filtered precipitate was then dried *in vacuo.* Yield: 630 mg, 100%. LCMS: P=100%, rt= 8.2 min, $(M+H)^+$: 420.1. ^{1}HNMR ($CDCl_3$): δ: 8.3 ppm (s, 1H), 8.0 ppm (m, 2H), 7.5 ppm (m, 5H), 7.2 ppm (t, 2H), 5.7 ppm (br m, 1H), 5.0 ppm (dd, 1H), 4.4 ppm (m, 1H), 3.5 ppm (m, 1H), 1.6 ppm (d, 3H).

[0205] The general procedure variant detailed in example 112 was used for the preparation of compounds in examples 113 to 257 starting from the appropriate intermediates or commercially available reagents.

[0206] Example n°, compound n°, compound names, triazolopiperazine intermediates 3 and acyl chloride intermediates **4** are listed in table 2C hereunder.

TABLE 2C

Example_n°	Compound_n°	Triazolopiperazine intermediate 3	Acyl chloride intermediate 4
113	115	chiral preparative HPLC of compound n°61	
114	118	chiral preparative HPLC of compound n°46	
115	131	chiral preparative HPLC of compound n°49	
116	134	chiral preparative HPLC of compound n°53	
117	144	chiral preparative HPLC of compound n°65	
118	156	chiral preparative HPLC of compound n°80	
119	159	**3y1**	4-fluorobenzoyl chloride
120	160	**3z1**	4-fluorobenzoyl chloride
121	161	**3a2**	4'-fluoro-[1,1'-biphenyl]-4-carbonyl chloride
122	162	chiral preparative HPLC of compound n°61	
123	163	chiral preparative HPLC of compound n°65	
124	164	chiral preparative HPLC of compound n°70	
125	165	chiral preparative HPLC of compound n°80	
126	167	chiral preparative HPLC of compound n°166	

(continued)

Example_n°	Compound_n°	Triazolopiperazine intermediate 3	Acyl chloride intermediate 4
127	168	chiral preparative HPLC of compound n°209	
128	169	chiral preparative HPLC of compound n°209	
129	170	**3q**	4-(thiophen-2-yl)benzoyl chloride
130	171	**3b2**	4-(thiophen-2-yl)benzoyl chloride
131	172	**3c2**	4-fluorobenzoyl chloride
132	173	**3b2**	4-fluorobenzoyl chloride
133	174	**3c2**	4-(thiophen-2-yl)benzoyl chloride
134	175	**3d2**	4-fluorobenzoyl chloride
135	176	**3d2**	4-(thiophen-2-yl)benzoyl chloride
136	177	**3e2**	4-(thiophen-2-yl)benzoyl chloride
137	178	**3f2**	4-fluorobenzoyl chloride
138	179	**3f2**	4-(thiophen-2-yl)benzoyl chloride
139	180	**3g2**	4-fluorobenzoyl chloride
140	181	**3g2**	4-(thiophen-2-yl)benzoyl chloride
141	182	**3g2**	4-phenylbenzoyl chloride
142	183	**3g2**	4'-fluoro-[1,1'-biphenyl]-4-carbonyl chloride
143	185	**3h2**	4-(thiophen-2-yl)benzoyl chloride
144	186	**3h2**	4-phenylbenzoyl chloride
145	187	**3h2**	4'-fluoro-[1,1'-biphenyl]-4-carbonyl chloride
146	188	**3i2**	4-fluorobenzoyl chloride
147	189	**3i2**	4-(thiophen-2-yl)benzoyl chloride
148	190	**3j2**	4-fluorobenzoyl chloride
149	191	**3j2**	4-(thiophen-2-yl)benzoyl chloride
150	192	**3j2**	4-phenylbenzoyl chloride
151	193	**3k2**	4-fluorobenzoyl chloride
152	194	**3k2**	4-(thiophen-2-yl)benzoyl chloride
153	195	**3k2**	4-phenylbenzoyl chloride
154	196	**3k2**	4'-fluoro-[1,1'-biphenyl]-4-carbonyl chloride
155	198	**312**	4-(thiophen-2-yl)benzoyl chloride
156	199	**312**	4-phenylbenzoyl chloride
157	200	**312**	4'-fluoro-[1,1'-biphenyl]-4-carbonyl chloride
158	201	**3m2**	4-fluorobenzoyl chloride
159	202	**3m2**	4-(thiophen-2-yl)benzoyl chloride
160	203	**3m2**	4-phenylbenzoyl chloride

(continued)

Example_n°	Compound_n°	Triazolopiperazine intermediate 3	Acyl chloride intermediate 4
161	204	**3d2**	4-phenylbenzoyl chloride
162	205	**3d2**	4'-fluoro-[1,1'-biphenyl]-4-carbonyl chloride
163	206	**3n2**	4-fluorobenzoyl chloride
164	207	**3n2**	4-(thiophen-2-yl)benzoyl chloride
165	208	**3o2**	4-fluorobenzoyl chloride
166	209	**3p2**	4-(thiophen-2-yl)benzoyl chloride
167	211	**3q2**	4-(thiophen-2-yl)benzoyl chloride
168	212	**3q2**	4-fluorobenzoyl chloride
169	213	**3r2**	4-(thiophen-2-yl)benzoyl chloride
170	214	**3r2**	4-fluorobenzoyl chloride
171	215	**3q1**	4-(5-methylthiophen-2-yl)benzoyl chloride
4-(5-methylthiophen-2-yl)benzoyl chloride was prepared from a classical Suzuki coupling between 2-bromo-5-methylthiophene and 4-methoxycarbonylphenylboronic acid followed by a saponification and acyl chloride formation			
172	216	**3q1**	4-cyanobenzoyl chloride
173	217	**3c2**	4-phenylbenzoyl chloride
174	218	**3s2**	4-fluorobenzoyl chloride
175	219	**3t2**	4-(thiophen-2-yl)benzoyl chloride
176	220	**3u2**	4-(thiophen-2-yl)benzoyl chloride
177	221	**3v2**	4-fluorobenzoyl chloride
178	222	**3w2**	4-(thiophen-2-yl)benzoyl chloride
179	223	**3x2**	4'-fluoro-[1,1'-biphenyl]-4-carbonyl chloride
180	224	**3y2**	4-(thiophen-2-yl)benzoyl chloride
181	225	**3u2**	4-fluorobenzoyl chloride
182	226	**3z2**	4-(thiophen-2-yl)benzoyl chloride
183	227	chiral preparative HPLC of compound n°56	
184	228	**3s2**	4-(thiophen-2-yl)benzoyl chloride
185	229	**3v2**	4-(thiophen-2-yl)benzoyl chloride
186	230	**3y2**	4-fluorobenzoyl chloride
187	231	**3b**	benzoyl chloride
188	232	**3b**	4-methylbenzoyl chloride
189	304	**3q1**	4-(2-methylthiophen-3-yl)benzoyl chloride
4-(2-methylthiophen-3-yl)benzoyl chloride was prepared from a classical Suzuki coupling between methyl 4-iodobenzoate & 4,4,5,5-tetramethyl-2-(2-methylthiophen-3-yl)-1,3,2-dioxaborolane followed by a saponification and acyl chloride formation			
190	233	chiral preparative HPLC of compound n°304	

(continued)

Example_n°	Compound_n°	Triazolopiperazine intermediate 3	Acyl chloride intermediate 4
191	234	chiral preparative HPLC of compound n°304	
192	235	**3a3**	4-(thiophen-2-yl)benzoyl chloride
193	236	Cyanation of compound n°213 using the procedure described in WO2008/103500 A1	
194	237	**3a3**	4-fluorobenzoyl chloride
195	238	**3w2**	4-fluorobenzoyl chloride
196	239	**3b3**	4-(thiophen-2-yl)benzoyl chloride
197	240	**3b3**	4-fluorobenzoyl chloride
198	241	**3c3**	4-(thiophen-2-yl)benzoyl chloride
199	242	**3c3**	4-fluorobenzoyl chloride
200	244	**3d3**	4-fluorobenzoyl chloride
201	245	**3e3**	4-(thiophen-2-yl)benzoyl chloride
202	246	**3e3**	4-fluorobenzoyl chloride
203	247	**3f3**	4-(thiophen-2-yl)benzoyl chloride
204	248	**3g3**	4-(thiophen-2-yl)benzoyl chloride
205	249	**3g3**	4-fluorobenzoyl chloride
206	250	**3h3**	4-(thiophen-2-yl)benzoyl chloride
207	251	**3h3**	4-fluorobenzoyl chloride
208	252	**3i3**	4-(thiophen-2-yl)benzoyl chloride
209	253	**3t**	4-(dimethylamino)benzoyl chloride
210	254	**3j3**	4-(thiophen-2-yl)benzoyl chloride
211	255	**3j3**	4-fluorobenzoyl chloride
212	256	**3k3**	4-(thiophen-2-yl)benzoyl chloride
213	257	**3l3**	4-(thiophen-2-yl)benzoyl chloride
214	258	**3m3**	4-fluorobenzoyl chloride
215	259	**3k3**	4-fluorobenzoyl chloride
217	261	**3n3**	4-(thiophen-2-yl)benzoyl chloride
218	262	**2o3**	4-(thiophen-2-yl)benzoyl chloride
219	263	**3l3**	4-(thiophen-2-yl)benzoyl chloride
220	265	**3p3**	4-(thiophen-2-yl)benzoyl chloride
221	266	**3q3**	4-(thiophen-2-yl)benzoyl chloride
222	267	**3r3**	4-(thiophen-2-yl)benzoyl
			chloride
223	268	**3q1**	4-(3-methylthiophen-2-yl)benzoyl chloride
4-(3-methylthiophen-2-yl)benzoyl chloride was prepared from a classical Suzuki coupling between methyl 4-iodobenzoate & 4,4,5,5-tetramethyl-2-(3-methylthiophen-2-yl)-1,3,2-dioxaborolane followed by a saponification and acyl chloride formation			

(continued)

Example_n°	Compound_n°	Triazolopiperazine intermediate 3	Acyl chloride intermediate 4
224	269	**3r3**	4-fluorobenzoyl chloride
225	270	chiral preparative HPLC of compound n°268	
226	271	**3o3**	4-fluorobenzoyl chloride
227	272	chiral preparative HPLC of compound n°268	
228	273	**3s3**	4-(thiophen-2-yl)benzoyl chloride
229	274	**3t3**	4-(thiophen-2-yl)benzoyl chloride
230	275	**3u3**	4-(thiophen-2-yl)benzoyl chloride
231	276	**3t3**	4-fluorobenzoyl chloride
232	277	**3v3**	4-fluorobenzoyl chloride
233	278	**3w3**	4-fluorobenzoyl chloride
234	279	**3v3**	4-(thiophen-2-yl)benzoyl chloride
235	280	Compound n°262 was alkylated with *tert*-butyl (2-bromoethyl)carbamate using the same alkylation procedure that is described in General Method H	
236	281	Compound n°262 was alkylated with 2-(2-bromoethoxy)tetrahydro-2H-pyran using the same alkylation procedure that is described in General	
		Method H, then the THP group was removed with HCl in dioxane	
237	282	Compound n°280 was treated with TFA in DCM (Boc deprotection)	
238	283	According to scheme 10	
239	284	Compound n°267 was alkylated with 2-(2-bromoethoxy)tetrahydro-2H-pyran using the same alkylation procedure that is described in General Method H, then the THP group was removed with HCl in dioxane. Chiral preparative HPLC yielded compounds n° 284 and 285	
	285		
240	286	**3w3**	4-phenylbenzoyl chloride
241	287	**3w3**	4-(thiophen-2-yl)benzoyl chloride
242	288	Compound n°275 was reacted with 2,4-difluoro-iodobenzene according to General Method F (C2-arylation described in Org. Lett. 2008, 10 (13), 2909)	
243	289	According to scheme 10	
244	290	According to scheme 10	
245	291	According to scheme 10	
246	292	According to scheme 10	
248	294	**3t**	**4c**
249	295	**3t**	**4h**
250	296	**3t**	**4a**
251	297	**3t**	**4i**
252	298	Compound n°267 was alkylated with *tert*-butyl (2-bromoethyl)carbamate using the same alkylation procedure that is described in General Method H, Chiral preparative HPLC yielded compounds n° 284 and 285	
	299		
253	300	**3x3**	4-(thiophen-2-yl)benzoyl chloride
254	301	**2y3**	4-(thiophen-2-yl)benzoyl chloride

(continued)

Example_n°	Compound_n°	Triazolopiperazine intermediate 3	Acyl chloride intermediate 4
255	302	Compound n° 300 was converted to compound n° 302 using the cyanation procedure described in WO2008/103500 A1	
256	303	Compound n° 301 was converted to compound n° 303 using the cyanation procedure described in WO2008/103500 A1	
257	243	**3d3**	4-(thiophen-2-yl)benzoyl chloride

BIOLOGY EXAMPLES

BRIEF DESCRIPTION OF THE DRAWINGS

[0207]

Figure 1 shows the effects of a single intravenous 10 mg/kg dose of compound n°156 on LH serum levels in castrated male rats, measured 60 min and 120 min following dosing. LH hormone levels are expressed as means ± S.E.M. (** $p < 0.001$ vs. baseline, determined by one-Way ANOVA and Dunnett's post hoc).

Figure 2 shows the effects of a single intravenous dose of compound n°144 (10 mg/kg), compound 71 (15 mg/kg) and compound 114 (20 mg/kg) on LH serum levels in castrated male rats, measured 60 min following dosing. LH hormone levels are expressed as means ± S.E.M. (** $p < 0.001$ vs. baseline, determined by one-Way ANOVA and Dunnett's post hoc).

Figure 3 shows the effect of a single intravenous 20 mg/kg dose of compound n° 156 on testosterone plasma levels in gonad-intact male rats (N=5 rats/group). Plasma testosterone levels are represented as an integrated testosterone response (AUC) over a 420 min period following dosing.

Competitive binding assays

[0208] The affinity of compounds of the invention for the tachykinin receptors was determined by measuring the ability of the compounds of the invention to displace a radiolabeled ligand from its specifics binding site.

^{3}H-SB222200 binding competition assay with human NK-3 receptor

[0209] The ability of the compounds of the invention to inhibit the binding of the NK-3 receptor selective antagonist SB222200 was assessed by an in vitro radioligand binding assay. Membranes were prepared from Chinese hamster ovary recombinant cells which express the human NK3 receptor. The membranes were incubated with 5nM ^{3}H-SB222200_(ARC) in a HEPES 25mM/ NaCl 0.1M/$CaCl_2$ 1mM/$MgCl_2$ 5Mm/ BSA 0.5%/ Saponin 10μg/ml buffer at pH 7.4 and various concentrations of the compounds of the invention. The amount of tritiated SB222200 bound to the receptor was determined after filtration by the quantification of membrane associated radioactivity using the TopCount-NXT reader (Packard). Competition curves were obtained for compounds of the invention and the concentrations of compounds which displaced 50% of bound radioligand (IC_{50}) were determined and then apparent inihibition constant Ki values were calculated by the following equation: $Ki = IC_{50}/(1+[L]/K_D)$ where [L] is the concentration of free radioligand and K_D is its dissociation constant at the receptor, derived from saturation binding experiments (Cheng and Prusoff, 1973) (see results in table 3 below).

[0210] In Table 3 biological results obtained using the ^{3}H-SB222200 binding competition assay with compounds of the invention are set out in tabulated form. In this table the calculated Ki is given. The Ki value obtained (in accordance with the protocol set forth above) is represented as follows: "+++" means Ki<500nM; "++" means 500nM < Ki ≤1μM; "+" means 1μM < Ki ≤5μM; "#" means Ki >5μM.

TABLE 3

Compound n°	Ki range
1	+

(continued)

Compound n°	Ki range
2	+
3	+
4	+
5	+
6	+
7	+++
8	+++
9	+++
10	+++
11	+++
13	+
14	+
15	+
16	+
17	+
18	+
19	+++
20	+++
21	+++
22	++
23	++
24	+++
25	+++
26	+++
27	+++
28	+++
29	+++
30	+++
31	+++
32	+++
33	+++
34	+++
35	+++
36	+++
37	+++
38	+++
39	++
40	+++

(continued)

Compound n°	Ki range
41	+++
42	+++
43	+
44	+
45	+++
46	+++
47	+++
48	+++
49	+++
50	+++
51	+++
52	+++
53	+++
54	+++
55	+++
56	+++
57	+++
58	+++
59	+++
60	+++
61	+++
62	+++
63	+++
64	+++
65	+++
66	+++
67	+++
68	+++
69	+++
70	+++
71	+++
72	+++
73	+++
74	+++
75	++
76	+++
77	+++
78	+++

(continued)

Compound n°	Ki range
79	+++
80	+++
83	#
85	+++
90	+++
91	+++
92	+
93	+
95	+
96	#
103	+
107	++
108	++
109	+++
110	+++
111	+++
112	+++
113	+++
114	+++
115	+++
118	+++
131	+++
134	+++
135	+++
136	+++
144	+++
156	+++
159	#
160	+
161	+
162	+++
163	++
164	+++
165	+++
166	+++
167	++
168	+++
169	+++

(continued)

Compound n°	Ki range
170	+++
171	+++
172	+++
173	+++
174	+++
175	+++
176	+++
177	+++
178	+
179	+++
180	+++
181	+++
182	+++
183	+++
185	#
186	+
187	+
188	++
189	+++
190	+++
191	#
193	+++
194	+++
195	+++
196	+++
198	+
199	+
200	++
201	+
202	+++
203	++
204	+++
205	++
206	+
207	+++
208	+
209	+++
211	+++

(continued)

Compound n°	Ki range
212	+++
213	+++
214	+++
215	+++
216	+++
217	+++
218	+
219	+++
220	+++
221	++
222	+++
223	+++
224	+++
225	+
226	#
227	++
228	+++
229	+++
230	+
231	+
232	+
233	+++
234	+++
235	+++
236	+++
238	+++
239	+
240	++
241	+++
242	++
244	++
245	+++
246	+++
247	+++
248	+++
249	+++
250	++
252	++

(continued)

Compound n°	Ki range
253	++
254	+++
255	++
256	+++
257	+++
258	+++
259	+
261	+++
262	+++
263	+++
265	+++
266	+++
267	+++
268	+++
269	++
271	+++
273	+++
274	++
275	#
276	#
277	#
278	+++
279	+++
280	+++
281	+++
282	++
283	++
284	+++
285	+++
286	+++
287	+++

[^{125}I]-His-MePhe7-Neurokinin B binding competition assay with rat NK-3 receptor

[0211] The affinity of compounds of the invention for the rat NK3 receptor was evaluated in CHO recombinant cells which express the rat NK3 receptor. Membrane suspensions were prepared from these cells. The following radioligand: [^{125}I]-His-MePhe7-Neurokinin B (PerkinElmer Cat#NEX285) was used in this assay. Binding assays were performed in a 25nM HEPES / 1mM $CaCl_2$ / 5mM $MgCl_2$ / 0.5% BSA / 10μg/ml Saponin, at pH 7.4. Binding assays consisted of 25 μl of membrane suspension (approximately 5 μg protein/well in a 96 well plate), 50 μl of compound or reference ligand (MePhe7-Neurokinin B) at increasing concentrations (diluted in assay buffer) and 0.09 nM [^{125}I]-His-MePhe7-Neurokinin B. The plate was incubated 60 min at 25°C in a water bath and then filtered over GF/C filters (Perkin Elmer, 6005174,

presoaked in assay buffer without saponine for 2h at room temperature) with a Filtration unit (Perkin Elmer). The radioactivity retained on the filters was measured by using the TopCount-NXT reader (Packard). Competition curves were obtained for compounds of the invention and the concentrations of compounds which displaced 50% of bound radioligand (IC_{50}) were determined and then apparent inhibition constant Ki values were calculated by the following equation: $Ki = IC_{50}/(1+[L]/K_D)$ where [L] is the concentration of free radioligand and K_D is its dissociation constant at the receptor, derived from saturation binding experiments (Cheng and Prusoff, 1973).

[0212] When tested in above described assay, preferred compounds of the invention showed an inhibition constant (Ki) for rat NK-3 receptor < 50 nM.

Selectivity assay

[0213] Selectivity of the compounds of the invention was determined over the other human NK receptors, namely NK-1 and NK2 receptors.

Human NK1

[0214] The affinity of compounds of the invention for the NK1 receptor was evaluated in CHO recombinant cells which express the human NK1 receptor. Membrane suspensions were prepared from these cells. The following radioligand: [^{3}H] substance P (PerkinElmer Cat#NET111520) was used in this assay. Binding assays were performed in a 50 mM Tris / 5 mM MnCl2 / 150 mM NaCl / 0.1% BSA at pH 7.4. Binding assays consisted of 25 µl of membrane suspension (approximately 5 µg of protein/well in a 96 well plate), 50 µl of compound or reference ligand (Substance P) at increasing concentrations (diluted in assay buffer) and 2nM [^{3}H] substance P. The plate was incubated 60 min at 25°C in a water bath and then filtered over GF/C filters (Perkin Elmer, 6005174, presoaked in 0.5% PEI for 2h at room temperature) with a Filtration unit (Perkin Elmer). The radioactivity retained on the filters was measured by using the TopCount-NXT reader (Packard). Competition curves were obtained for compounds of the invention and the concentrations of compounds which displaced 50% of bound radioligand (IC_{50}) were determined and then apparent inhibition constant Ki values were calculated by the following equation: $Ki = IC_{50}/(1+[L]/K_D)$ where [L] is the concentration of free radioligand and K_D is its dissociation constant at the receptor, derived from saturation binding experiments (Cheng and Prusoff, 1973).

Human NK2

[0215] The affinity of compounds of the invention for the NK2 receptor was evaluated in CHO recombinant cells which express the human NK2 receptor. Membrane suspensions were prepared from these cells. The following radioligand [^{125}I]-Neurokinin A (PerkinElmer Cat#NEX252) was used in this assay. Binding assays were performed in a 25 mM HEPES / 1 mM CaCl2 / 5 mM MgCl2/ 0.5% BSA / 10µg/ml saponin, at pH 7.4. Binding assays consisted of 25 µl of membrane suspension (approximately 3.75 µg of protein/well in a 96 well plate), 50 µl of compound or reference ligand (Neurokinin A) at increasing concentrations (diluted in assay buffer) and 0.1 nM [^{125}I]-Neurokinin A. The plate was incubated 60 min at 25°C in a water bath and then filtered over GF/C filters (Perkin Elmer, 6005174, presoaked in assay buffer without saponine for 2h at room temperature) with a Filtration unit (Perkin Elmer). The radioactivity retained on the filters was measured by using the TopCount-NXT reader (Packard). Competition curves were obtained for compounds of the invention and the concentrations of compounds which displaced 50% of bound radioligand (IC_{50}) were determined and then apparent inhibition constant Ki values were calculated by the following equation: $Ki = IC_{50}/(1+[L]/K_D)$ where [L] is the concentration of free radioligand and K_D is its dissociation constant at the receptor, derived from saturation binding experiments (Cheng and Prusoff, 1973).

[0216] The compounds of the invention, which were tested in the above NK-1 and NK-2 described assays, demonstrated a low affinity at the human NK-1 and human NK-2 receptors: 100-200 fold shift of the Ki compared to the human NK-3 receptor. Thus, compounds according to the invention have been shown to be selective over NK1 and NK2 receptors.

In vivo assay to assess compound activity in rat

[0217] The inhibitory effect of the compounds of the invention in luteinizing hormone (LH) secretion and on circulating steroid levels are determined by the following biological studies.

Castrated male rat model to assess the effect of compound of invention on circulating levels of luteinizing hormone (LH).

[0218] In humans and rodents, castration is well-precedented to permit heightened, persistent GnRH signaling and consequently elevation of circulating LH. Thus, in this animal model, LH is measured in castrated rats as a marker of test compound inhibition of the GnRH signaling pathway.

[0219] Castrated adult male Sprague-Dawley (SD) rats (150-175 g,) were purchased from Janvier (St Berthevin, France). All animals were housed 3 per cage in a temperature-controlled room (22 ± 2°C) and 50 ± 5% relative humidity with a 12 hour light/12 hour dark photoperiod (lights off at 6h00 pm). The animals were allowed 2 weeks of postoperative recovery prior to study. Animals were handled on a daily basis. Standard diet and tap water were provided *ad libitum.* Animal cage litters were changed once a week. On the study day, animals were acclimated to the procedure room for a period of one hour prior to the initiation of the experiment.

[0220] Compounds of the invention were formulated as 10%DMSO, 10% Cremophore EL, and 80% saline solutions.

[0221] After basal sampling (TO) a single dose of compounds of the invention or vehicule was administrated intravenously to rats. Blood was then collected at 60 min and 120 min post dosing. Blood samples were obtained via tail vein bleed, drawn into EDTA-containing tubes and centrifuged immediately. Plasma samples were collected and stored in a -80°C freezer until assayed. Serum LH levels were determined using radioimmunoassay kit from IDS (Liege, Belgium). Baseline was defined as the initial basal blood sample.

[0222] When tested in the castrated male rat model described above, the compounds n°144, 71, 156 and 114 significantly suppressed GnRH-mediated elevation of LH (Figures 1 and 2).

[0223] This result also shows that the compounds according to the invention pass through the blood-brain barrier and that they are capable of blocking the action of the NK-3 receptors in the CNS. The brain to plasma ratio values (B/P) obtained with the compounds according to the invention were generally greater than 0.1 indicating a significant brain penetration.

Gonad-intact adult male to assess the effect of compounds of the invention on circulating levels of testosterone.

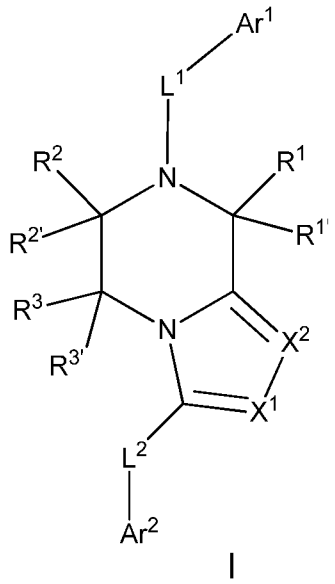
[0224] Gonad-intact adult male Sprague-Dawley (SD) rats (300-385 g N=5/group were single housed in a temperature-controlled room (22 ± 2°C) and 50 ± 5% relative humidity with a 12 hour light/12 hour dark photoperiod (lights off at 6h00 pm). Purina rat chow (Ralston Purina Co., St. Louis, MO) and tap water were made available to rats, *ad libitum.* Chronic intracardiac venous cannulae were implanted under sodium pentobarbital anaesthesia (50 mg/kg, i.p.). After surgery, rats were placed directly into isolation test chambers and provided with food and water *ad libitum* until body weight returned to preoperative levels (a period of at least five days). On the test day, food was removed 1.5 h before the start of sampling and was returned at the end of the experiment. After basal blood sampling, free-moving rats were intravenously injected at time = 0 min with either a single dose (20 mg/kg) of compound n°156 or vehicle. Blood was then collected through a heparinized line at regular intervals up to 420 min and centrifuged immediately. Plasma samples were collected and stored in a -80°C freezer until assayed. Plasma testosterone levels were determined using a radioimmunoassay kit (Immunotech).

[0225] Compound n°156 was formulated as 40%DMA, 50% PEG400, and 10% sterile water solution.

[0226] When tested in gonad-intact male rats, compound n°156 significantly suppressed plasma testosterone levels over the 420 minute test period (Figure 3).

Claims

1. A compound of formula I:



I

and pharmaceutically acceptable salts and solvates thereof, wherein

Ar^1 is a 5- to 6-membered aryl or heteroaryl group, 3- to 6-membered cycloalkyl group a 3- to 6-membered heterocyclyl group or a C3-C6 alkyl group, each of the aryl, heteroaryl, cycloalkyl or heterocyclyl groups being optionally substituted by one or more group(s) selected from halo, cyano, alkyl, haloalkyl, cycloalkyl, heteroalkyl, heterocyclyl, aryl, aralkyl, heteroaryl, hydroxyl, alkoxy, haloalkoxy, alkoxyalkoxy, alkylamino, carboxy, alkoxycarbonyl, alkylcarbonyloxy, alkylcarbonylamino, haloalkylcarbonylamino, carbamoyl, alkylcarbamoyl, carbamoylamino, alkylcarbamoylamino, alkylsulfonyl, haloalkylsulfonyl, sulfamoyl, alkylsulfamoyl, alkylsulfonylamino, haloalkylsulfonylamino, or two substituents form an alkylenedioxy group or a haloalkylenedioxy group, or two substituents form a cycloalkyl or heterocycloalkyl moiety together with the cycloalkyl or heterocycloalkyl group they are attached to, or fused to the aryl, heteroaryl, cycloalkyl or heterocycloalkyl group may be one or more aryl moiety, each of said substituents being optionally substituted by one or more further substituent(s) selected from halo, cyano, alkyl, haloalkyl, cyclopropyl, alkoxy, haloalkoxy, heterocyclyl, aryl, heteroaryl, aryloxy heteroaryloxy;

L^1 is carbonyl;

R^1 is H, a C_1-C_4 alkyl, aryl or aralkyl group, each of said alkyl, aryl or aralkyl groups being optionally substituted by one or more group(s) selected from halo or hydroxyl;

$R^{1'}$ is H or a C_1-C_4 alkyl group;

R^2 is H or a C_1-C_4 alkyl group;

$R^{2'}$ is H or a C_1-C_4 alkyl group;

R^3 is H or a C_1-C_4 alkyl group optionally substituted by one hydroxy;

$R^{3'}$ is H or a C_1-C_4 alkyl group;

X^1 and **X^2** are N;

L^2 is a single bond or carbonyl,

Ar^2 is a 5- to 6-membered aryl or heteroaryl group, each of the aryl, or heteroaryl groups being optionally substituted by one or more group(s) selected from halo, cyano, alkyl, hydroxyalkyl, haloalkyl, cycloalkyl, heteroalkyl, heterocyclyl, aryl, heteroaryl, aralkyl, heteroarylalkyl, hydroxyl, alkoxy, haloalkoxy, alkylamino, carboxy, alkoxycarbonyl, alkylcarbonyloxy, alkylcarbonylamino, haloalkylcarbonylamino, acylamino, carbamoyl, alkylcarbamoyl, carbamoylalkyl, carbamoylamino, alkylcarbamoylamino, alkylsulfonyl, haloalkylsulfonyl, arylsulfonylalkyl, sulfamoyl, alkylsulfamoyl, alkylsulfonylamino, haloalkylsulfonylamino, or two substituents form an alkylenedioxy group or a haloalkylenedioxy group, or fused to the aryl or heteroaryl group may be one or more cycloalkyl, aryl, heterocyclyl or heteroaryl moiety, each of said substituents being optionally substituted by one or more further substituent(s) selected from halo, cyano, alkyl, haloalkyl, alkoxy, haloalkoxy, cycloalkyl, heterocyclyl optionally substituted by alkyl, aryl, heteroaryl, hydroxyl, alkoxyalkyl, hydroxyalkoxy, alkylamino, alkylsulfonylamino, alkoxycarbonylamino, aminoalkoxy, or alkoxycarbonylaminoalkoxy;

and wherein, when:

R^1, $R^{1'}$, R^2, $R^{2'}$, R^3, $R^{3'}$ are H, and

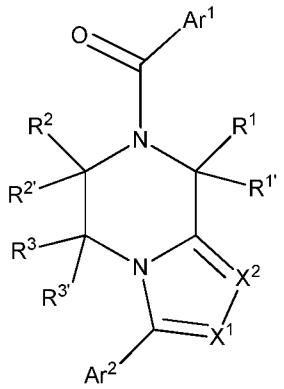
L^2 is single bond, and
Ar^1 is a 6-membered aryl optionally substituted by one or more group(s) selected from halo, cyano, C1-C3 alkyl, C1 haloalkyl, and
Ar^2 is a 5- to 6-membered aryl or heteroaryl group optionally substituted by one or more group(s) selected from halo, C1-C3 alkyl, hydroxyl, methoxy, or fused to an aryl or heteroaryl group optionally substituted by one or more further halo, C1-C3 alkyl, hydroxyl, methoxy,
then,
Ar^1 is phenyl, 3-halophenyl, 4-halophenyl, 2,3-dichlorophenyl, 2,4-difluorophenyl, 2,5-dihalophenyl, 2,6-difluorophenyl, 2,6-dichlorophenyl, 3,4-dihalophenyl, 3,5-dihalophenyl, 3,4,5-trihalophenyl, 2-cyanophenyl, 3-cyanophenyl, 4-cyanophenyl, 2,3-dicyanophenyl, 2,4-dicyanophenyl, 3,5-dicyanophenyl, 3-cyano-4-halophenyl, 4-(C1-C3 alkyl)phenyl, 3,4-di(C1-C3 alkyl)phenyl, 3,5-di(C1-C3 alkyl)phenyl, 4-(C1 haloalkyl)phenyl, and
Ar^2 is 2-(C1-C3 alkyl)thiazol-4-yl, 5-(C1-C3 alkyl)thiazol-4-yl, pyridin-2-yl, 4-halopyridin-2-yl, 4-(C1-C3 alkyl)pyridin-2-yl, 5-(C1-C3 alkyl)pyridin-2-yl, 6-(C1-C3 alkyl)pyridin-2-yl, quinolin-2-yl, isoquinolin-3-yl, 8-haloquinolin-2-yl, benzothiazol-2-yl, 4,5,6,7-tetrahydro-1,3-benzothiazol-2-yl;
with the following provisos:

- Ar^1 is neither a substituted or unsubstituted pyrazolo[1,5-a]pyridin-2yl nor a substituted or unsubstituted pyrazolo[1,5-a]pyrimidin-2yl moiety; and

the compound of formula I is none of :

(2,4-difluorophenyl)(3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(3-chlorophenyl)(3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
2-(3-(pyridin-2-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazine-7-carbonyl)benzonitrile;
(2,6-dichlorophenyl)(3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone,
(2,3-dichlorophenyl)(3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone,
(2,3-dichlorophenyl)(3-(5-methylpyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone,
(2,3-dichlorophenyl)(3-(6-methylpyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone.

2. The compound of claim **1** having formula Ib

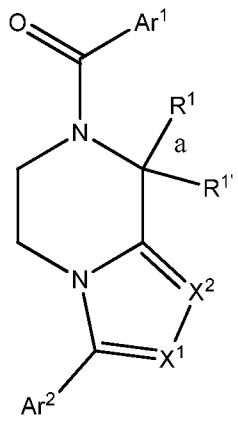


Ib

and pharmaceutically acceptable salts and solvates thereof, wherein

Ar^1, Ar^2, R^1, $R^{1'}$ R^2, $R^{2'}$, R^3, $R^{3'}$ X^1, X^2, are as defined in claim **1.**

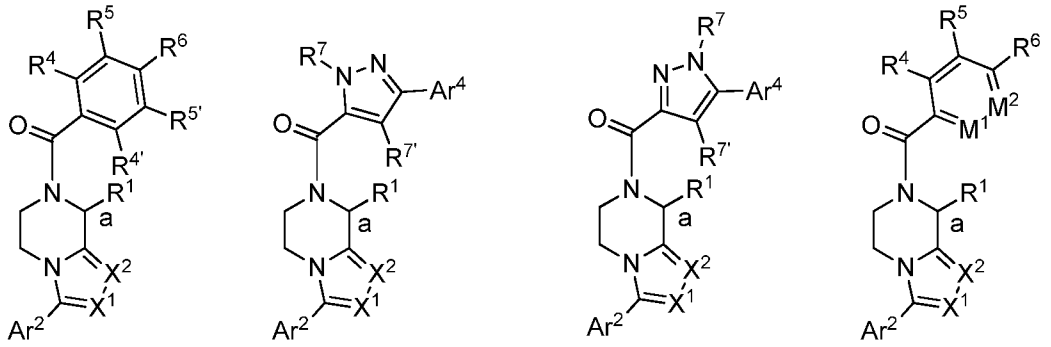
3. The compound of claim **2** having formula Ic



Ic

and pharmaceutically acceptable salts and solvates thereof, wherein a depicts the bond linking **R1** to the piperazine moiety, and **Ar1, Ar2, R1, R1', X1,** and **X2** are as defined in claim **2.**

4. The compound of claim **3** selected from formulae Id-1, Id-2, Id-3 and Id-4



Id-1 Id-2 Id-3 Id-4

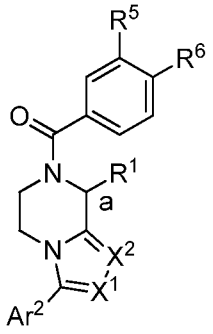
and pharmaceutically acceptable salts and solvates thereof, wherein

a depicts the bond linking **R1** to the piperazine moiety; and
Ar2, R1, X1 and **X2** are as defined in claim **2**; and
R4, R4', R5, R5' and **R6** are independently selected from H, halo, cyano, alkyl, haloalkyl, C3-C6 cycloalkyl, heteroalkyl, heterocyclyl, aryl, heteroaryl, hydroxyl, alkoxy, haloalkoxy, alkoxyalkoxy, alkylamino, carboxy, alkoxycarbonyl, alkylcarbonyloxy, alkylcarbonylamino, haloalkylcarbonylamino, carbamoyl, alkylcarbamoyl, carbamoylamino, alkylcarbamoylamino, alkylsulfonyl, haloalkylsulfonyl, sulfamoyl, alkylsulfamoyl, alkylsulfonylamino, haloalkylsulfonylamino, or **R5** together with **R4** or **R6,** or **R5'** together with **R4'** or **R6** forms an alkylenedioxy group or a haloalkylenedioxy group, or **R5** together with **R4** or **R6,** or **R5'** together with **R4'** or **R6** forms an aryl moiety fused to the phenyl group to which they are attached, each of said substituents being optionally substituted by one or more further substituent(s) selected from halo, cyano, alkyl, haloalkyl, cyclopropyl; and
R7 is H or methyl; and
R7' is H or methyl; and
Ar4 is a cycloalkyl or an aryl group, each of said cycloalkyl or aryl groups being optionally substituted by one or more group(s) selected from halo, alkyl, haloalkyl, cyclopropyl, haloalkoxy, aryloxy; and
M1 is N or C-**R4"** wherein **R4"** is selected from H, halo, cyano, alkyl, haloalkyl, C3-C6 cycloalkyl, heteroalkyl, heterocyclyl, aryl, heteroaryl, hydroxyl, alkoxy, haloalkoxy, alkoxyalkoxy, alkylamino, carboxy, alkoxycarbonyl, alkylcarbonyloxy, alkylcarbonylamino, haloalkylcarbonylamino, carbamoyl, alkylcarbamoyl, carbamoylamino, alkylcarbamoylamino, alkylsulfonyl, haloalkylsulfonyl, sulfamoyl, alkylsulfamoyl, alkylsulfonylamino, haloalkylsulfonylamino, each of said substituents being optionally substituted by one or more further substituent(s)

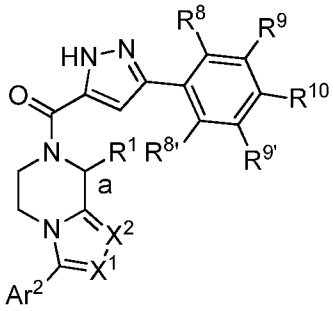
selected from halo, cyano, alkyl, haloalkyl, cyclopropyl; and
M² is N or **M²** is C-**R⁵"** under the condition that **M¹** is N, wherein **R⁵"** is selected from H, halo, cyano, alkyl, haloalkyl, C3-C6 cycloalkyl, heteroalkyl, heterocyclyl, aryl, heteroaryl, hydroxyl, alkoxy, haloalkoxy, alkoxy-alkoxy, alkylamino, carboxy, alkoxycarbonyl, alkylcarbonyloxy, alkylcarbonylamino, haloalkylcarbonylamino, carbamoyl, alkylcarbamoyl, carbamoylamino, alkylcarbamoylamino, alkylsulfonyl, haloalkylsulfonyl, sulfamoyl, alkylsulfamoyl, alkylsulfonylamino, haloalkylsulfonylamino, or **R⁵"** together with **R⁶** forms an alkylenedioxy group or a haloalkylenedioxy group, or an aryl moiety fused to the pyridinyl group to which they are attached, each of said substituents being optionally substituted by one or more further substituent(s) selected from halo, cyano, alkyl, haloalkyl, cyclopropyl; and
wherein, in formula Id-1 when:

R¹ is H, and
R⁴, R⁴', R⁵, R⁵' and **R⁶** are independently selected from H, halo, cyano, C1-C3 alkyl, C1 haloalkyl, and
Ar² is a 5- to 6-membered aryl or heteroaryl group optionally substituted by one or more group(s) selected from halo,C1-C3 alkyl, hydroxyl, alkoxy, or fused to an aryl group optionally substituted by one or more further halo, C1-C3 alkyl, hydroxyl, methoxy
then,
R⁴, R⁴', R⁵, R⁵' and **R⁶** are H, or **R⁴, R⁴', R⁵', R⁶** are H and **R⁵** is halo, or **R⁴, R⁴', R⁵, R⁵'** are H and **R⁶** is halo, cyano, C1-C3 alkyl, C1 haloalkyl, or **R⁴', R⁵', R⁶** are H and **R⁴, R⁵** are halo, or **R⁴, R⁴', R⁵'** are H and **R⁵, R⁶** are independently halo, or **R⁴, R⁴'** are H and **R⁵, R⁵', R⁶** are halo, and
Ar² is 2-(C1-C3 alkyl)thiazol-4-yl, 5-(C1-C3 alkyl)thiazol-4-yl, pyridin-2-yl, 4-halopyridin-2-yl, 4-(C1-C3 alkyl)pyridin-2-yl, 5-(C1-C3 alkyl)pyridin-2-yl, 6-(C1-C3 alkyl)pyridin-2-yl, quinolin-2-yl, isoquinolin-3-yl, 8-haloquinolin-2-yl, benzothiazol-2-yl, 4,5,6,7-tetrahydro-1,3-benzothiazol-2-yl.

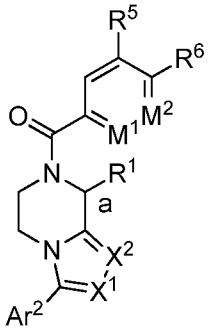
5. The compound of claim **4** selected from formulae formula Ie-1, Ie-2 and Ie-3



Ie-1



Ie-2



Ie-3

and pharmaceutically acceptable salts and solvates thereof, wherein

a depicts the bond linking **R¹** to the piperazine moiety; and
Ar², R¹, X¹ and **X²** are as defined in claim **2**; and
R⁵ and **R⁶** are independently selected from H, halo, cyano, alkyl, cyclopropyl, aryl, heteroaryl, each of said aryl and heteroaryl groups being optionally substituted by one or more group(s) selected from halo, alkyl, cyclopropyl, or **R⁵** and **R⁶** together form a phenyl moiety fused to the phenyl ring they are attached to; and
R⁸, R⁸', R⁹, R⁹' and **R¹⁰** are independently selected from H, halo, haloalkyl, cyclopropyl or haloalkoxy, or **R⁸, R⁸', R⁹, R⁹'** are H and **R¹⁰** is phenoxy;
M¹ and **M²** are as defined in claim **4**; and
wherein, in formula Ie-1 when:

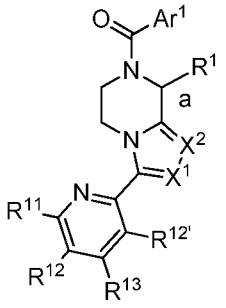
R¹ is H, and
R⁵ and **R⁶** are independently selected from H, halo, cyano, C1-C3 alkyl, and
Ar² is a 5- to 6-membered aryl or heteroaryl group optionally substituted by one or more group(s) selected from halo, C1-C3alkyl, hydroxyl, alkoxy, or fused to an aryl group optionally substituted by one or more further halo, C1-C3 alkyl, hydroxyl, methoxy

then,

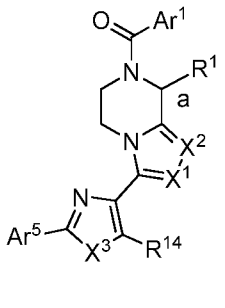
R^6 is H and R^5 is H, halo, or R^5 is H and R^6 is halo, cyano, C1-C3 alkyl, C1 haloalkyl, or R^5 and R^6 are independently halo, and

Ar^2 is 2-(C1-C3 alkyl)thiazol-4-yl, 5-(C1-C3 alkyl)thiazol-4-yl, pyridin-2-yl, 4-halopyridin-2-yl, 4-(C1-C3 alkyl)pyridin-2-yl, 5-(C1-C3 alkyl)pyridin-2-yl, 6-(C1-C3 alkyl)pyridin-2-yl, quinolin-2-yl, isoquinolin-3-yl, 8-haloquinolin-2-yl, benzothiazol-2-yl, 4,5,6,7-tetrahydro-1,3-benzothiazol-2-yl.

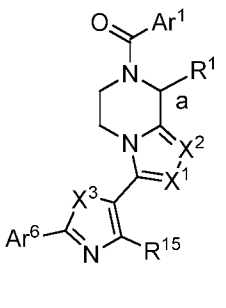
6. The compound of claim **3** selected from formulae If-1, If-2, If-3, If-4, If-5, If-6, If-7 and If-8



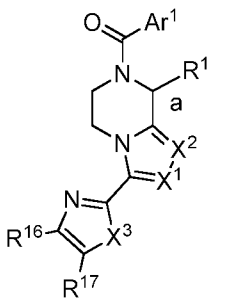
If-1



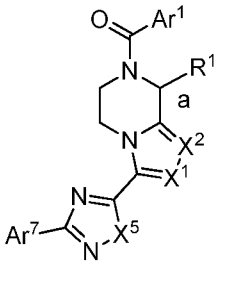
If-2



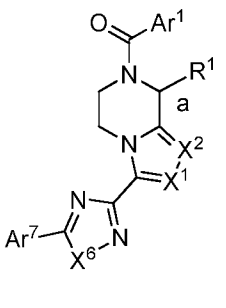
If-3



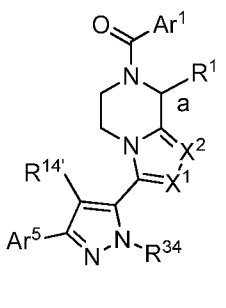
If-4



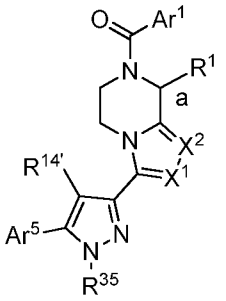
If-5



If-6



If-7



If-8

and pharmaceutically acceptable salts and solvates thereof, wherein

a designates the bond linking R^1 to the piperazine moiety; and

Ar^1, R^1, X^1 and X^2 are as defined in claim **2**; and

R^{11}, R^{12}, $R^{12'}$ and R^{13} are independently selected from H, halo, cyano, alkyl, hydroxyalkyl, haloalkyl, C3-C6 cycloalkyl, heteroalkyl, heterocyclyl, aryl, heteroaryl, - hydroxyl, alkoxy, haloalkoxy, alkylamino, carboxy, alkoxycarbonyl, alkylcarbonyloxy, alkylcarbonylamino, haloalkylcarbonylamino, acylamino, carbamoyl, alkylcarbamoyl, carbamoylalkyl, carbamoylamino, alkylcarbamoylamino, alkylsulfonyl, haloalkylsulfonyl, sulfamoyl, alkylsulfamoyl, alkylsulfonylamino, haloalkylsulfonylamino, or R^{12} together with R^{11} or R^{13}, or R^{13} together with $R^{12'}$ forms an alkylenedioxy group or a haloalkylenedioxy group, or R^{12} together with R^{11} or R^{13} forms a cycloalkyl, aryl, heterocyclyl or heteroaryl moiety fused to the pyridyl group to which they are attached, each of said groups being optionally substituted by one or more group(s) selected from halo, cyano, alkyl, haloalkyl, cyclopropyl, alkoxy, haloalkoxy or hydroxyl; and

Ar^5 is a heterocyclyl, aryl, heteroaryl, aralkyl, heteroarylalkyl, or arylsulfonylalkyl group, each of which being optionally substituted by one or more group(s) selected from halo, cyano, alkyl, haloalkyl, cyclopropyl, alkoxy, haloalkoxy, heterocyclyl optionally substituted by alkyl, aryl, hydroxyl, alkoxy, alkoxyalkyl, hydroxyalkoxy, alkylamino, alkylsulfonylamino, aminoalkoxy, or alkoxycarbonylaminoalkoxy; and

X^3 is O or S; and

R^{14} is H or methyl; and

Ar^6 is a heterocyclyl, aryl or heteroaryl group, each of which being optionally substituted by one or more group(s) selected from halo, cyano, alkyl, haloalkyl, cyclopropyl, alkoxy, haloalkoxy, aryl or hydroxyl; and

R^{15} is H or methyl; and
R^{16} is a heterocyclyl, aryl or heteroaryl group, each of said groups being optionally substituted by one or more group(s) selected from halo, cyano, alkyl, haloalkyl, cyclopropyl, alkoxy, haloalkoxy or hydroxyl;
R^{17} is H, methyl or R^{17} together with R^{16} forms a cycloalkyl or aryl moiety fused to the thiazolyl group to which they are attached, thus forming a fused ring system, said fused ring system being optionally substituted by one or more group(s) selected from halo, cyano, alkyl, haloalkyl, cyclopropyl, alkoxy, haloalkoxy or hydroxyl; and
X^5 is O or S, or N-R^{36} wherein R^{36} is H or C1-C3 alkyl; and
Ar^7 is a heterocyclyl, aryl or heteroaryl group, each of which being optionally substituted by one or more group(s) selected from halo, cyano, alkyl, haloalkyl, cyclopropyl, alkoxy, haloalkoxy, aryl or hydroxyl; and
X^6 is O, S or N-$R^{36'}$ wherein $R^{36'}$ is H or C1-C3 alkyl; and
$R^{14'}$ is H or methyl; and
R^{34} is H, alkyl, alkoxyalkyl, hydroxyalkyl, alkoxycarbonylaminoalkyl; and
R^{35} is H, alkyl, alkoxyalkyl, hydroxyalkyl, alkoxycarbonylaminoalkyl; and
wherein,

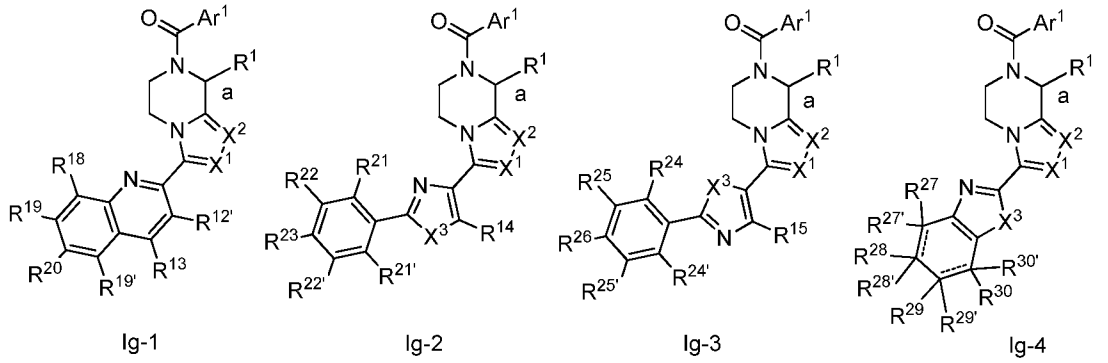
- in formula If-1 when:

  R^1 is H, and
  Ar^1 is a 6-membered aryl optionally substituted by one or more group(s) selected from halo, cyano, C1-C3 alkyl, C1-haloalkyl, and
  R^{11}, R^{12}, $R^{12'}$ and R^{13} are independently selected from H, halo, C1-C3 alkyl, hydroxyl, methoxy, or R^{12} together with R^{11} or R^{13} forms an aryl or heterocyclyl or heteroaryl moiety fused to the pyridyl group to which they are attached and being optionally substituted by one or more group(s) selected from halo, C1-C3 alkyl, methoxy or hydroxyl,
  then,
  Ar^1 is phenyl, 3-halophenyl, 4-halophenyl, 2,3-dichlorophenyl, 3,4-dihalophenyl, 3,4,5-trihalophenyl, 4-cyanophenyl, 4-(C1-C3 alkyl)phenyl, 4-(C1 haloalkyl)phenyl, and
  R^{11}, R^{12}, $R^{12'}$ and R^{13} are H, or R^{11}, R^{12}, $R^{12'}$ are H and R^{13} is halo, C1-C3 alkyl, or R^{11}, $R^{12'}$, R^{13} are H and R^{12} is C1-C3 alkyl, or R^{12}, $R^{12'}$, R^{13} are H and R^{11} is C1-C3 alkyl, or R^{11}, R^{12}, $R^{12'}$ and R^{13} together with the pyridyl group they are attached form a quinolin-2-yl, isoquinolin-3-yl or 8-haloquinolin-2-yl moiety; and

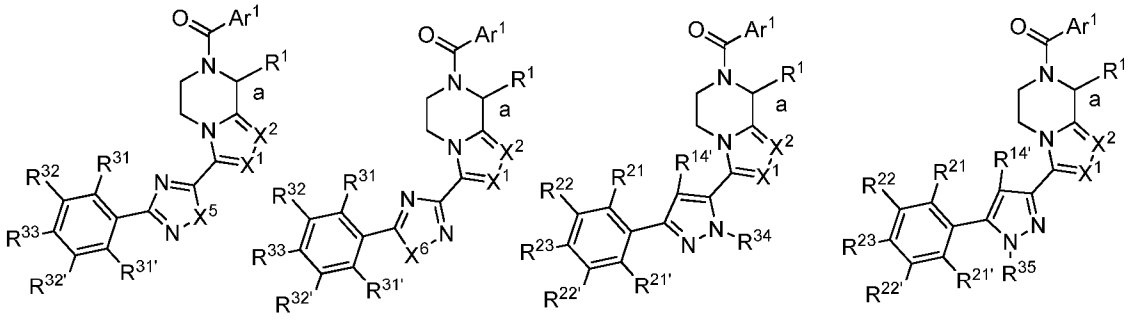
- in formula If-4 when:

  R^1 is H, and
  Ar^1 is a 6-membered aryl optionally substituted by one or more group(s) selected from halo, cyano, C1-C3 alkyl, C1-haloalkyl, and
  R^{17} together with R^{16} forms a cycloalkyl or aryl moiety fused to the thiazolyl group to which they are attached, thus forming a fused ring system, said fused ring system being optionally substituted by one or more group(s) selected from halo, C1-3 alkyl, methoxy or hydroxyl,
  then
  Ar^1 is phenyl, 3-halophenyl, 4-halophenyl, 2,3-dichlorophenyl, 3,4-dihalophenyl, 3,4,5-trihalophenyl, 4-cyanophenyl, 4-(C1-C3 alkyl)phenyl, 4-(C1 haloalkyl)phenyl, and
  R^{17} and R^{16} form together with the thiazolyl group to which they are attached a benzothiazol-2-yl or 4,5,6,7-tetrahydro-1,3-benzothiazol-2-yl moiety.

7. The compound of claim **6** selected from formulae Ig-1, Ig-2, Ig-3, Ig-4, Ig-5, Ig-6, Ig-7 and Ig-8



Ig-1 Ig-2 Ig-3 Ig-4



Ig-5 Ig-6 Ig-7 Ig-8

and pharmaceutically acceptable salts, and solvates thereof, wherein

a depicts the bond linking R^1 to the piperazine moiety; and
Ar^1, R^1, X^1 and **X^2** are as defined in claim **2**; and
R^{14}, $R^{14'}$, R^{15}, R^{34}, R^{35}, X^3 X^5 and **X^6** are as defined in claim **6**; and
$R^{12'}$ and **R^{13}** are independently selected from H, halo, cyano, alkyl, hydroxyalkyl, haloalkyl, cycloalkyl, heteroalkyl, hydroxyl, alkoxy, haloalkoxy, carboxy, alkoxycarbonyl, alkylcarbonyloxy, alkylcarbonylamino, haloalkylcarbonylamino, acylamino, carbamoyl, alkylcarbamoyl, carbamoylalkyl, carbamoylamino, alkylcarbamoylamino, alkylsulfonyl, haloalkylsulfonyl, sulfamoyl, alkylsulfamoyl, alkylsulfonylamino, haloalkylsulfonylamino, or **R^{13}** together with **$R^{12'}$** forms an alkylenedioxy group or a haloalkylenedioxy group, each of said groups being optionally substituted by one or more group(s) selected from halo, cyano, alkyl, haloalkyl, alkoxy, haloalkoxy, hydroxyl or oxo; and
R^{18}, R^{19}, $R^{19'}$ and **R^{20}** are independently selected from H, halo, cyano, alkyl, haloalkyl, cyclopropyl, alkoxy, haloalkoxy; and
R^{21}, $R^{21'}$, R^{22}, $R^{22'}$ and **R^{23}** are independently selected from H, halo, cyano, alkyl, haloalkyl, cyclopropyl, heterocyclyl optionally substituted by alkyl, hydroxyl, alkoxy, haloalkoxy, hydroxyalkoxy, alkylamino, alkylsulfonylamino, aminoalkoxy, alkoxycarbonylaminoalkoxy; and
R^{24}, $R^{24'}$, R^{25}, $R^{25'}$ and **R^{26}** are independently selected from H, halo haloalkyl, cyclopropyl; and
R^{27}, R^{28}, R^{29} and **R^{30}** are independently selected from H, halo, cyano, alkyl, haloalkyl, cyclopropyl, alkoxy, haloalkoxy; and
$R^{27'}$, $R^{28'}$, $R^{29'}$ and **$R^{30'}$** are absent, or **$R^{27'}$, $R^{28'}$, $R^{29'}$** and **$R^{30'}$** are H under the condition that **R^{28}, R^{29}** and **R^{30}** are H and that **R^{27}** is selected from H, chloro or fluoro; and
the two bonds represented by the dotted lines in formula Ig-4 are both absent, or both present under the condition that **$R^{27'}$, $R^{28'}$, $R^{29'}$** and **$R^{30'}$** are absent; and
R^{31}, $R^{31'}$, R^{32}, $R^{32'}$ and **R^{33}** are independently selected from H, halo, cyano, alkyl, haloalkyl, cyclopropyl, alkoxy, haloalkoxy; and
wherein,

- in formula Ig-1 when:

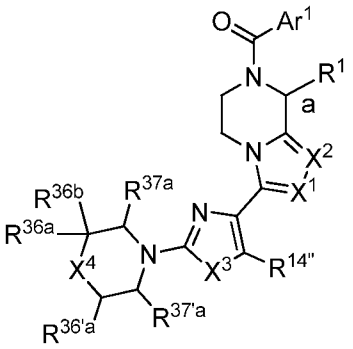
  R^1 is H, and

Ar^1 is a 6-membered aryl optionally substituted by one or more group(s) selected from halo, cyano, C1-C3 alkyl, C1-haloalkyl, and
$R^{12'}$, R^{13}, R^{18}, R^{19}, $R^{19'}$ and **R^{20}** are independently selected from H, halo, C1-3 alkyl, hydroxyl, methoxy, then,
Ar^1 is phenyl, 3-halophenyl, 4-halophenyl, 2,3-dichlorophenyl, 3,4-dihalophenyl, 3,4,5-trihalophenyl, 4-cyanophenyl, 4-(C1-C3 alkyl)phenyl, 4-(C1 haloalkyl)phenyl, and
$R^{12'}$, R^{13}, R^{18}, R^{19}, $R^{19'}$ and **R^{20}** are H, or **$R^{12'}$, R^{13}, R^{19}, $R^{19'}$, R^{20}** are H and **R^{18}** is fluoro, chloro, and

- in formula Ig-4 when

R^1 is H, and
Ar^1 is a 6-membered aryl optionally substituted by one or more group(s) selected from halo, cyano, C1-C3 alkyl, C1-haloalkyl, and
R^{27}, R^{28}, R^{29} and **R^{30}** are independently selected from H, halo, C1-3 alkyl, methoxy, and
$R^{27'}$, $R^{28'}$, $R^{29'}$ and **$R^{30'}$** are absent or H under the condition that **R^{28}, R^{29}** and **R^{30}** are H and **R^{27}** is selected from H, chloro or fluoro,
then
Ar^1 is phenyl, 3-halophenyl, 4-halophenyl, 2,3-dichlorophenyl, 3,4-dihalophenyl, 3,4,5-trihalophenyl, 4-cyanophenyl, 4-(C1-C3 alkyl)phenyl, 4-(C1 haloalkyl)phenyl, and
R^{27}, R^{28}, R^{29} and **R^{30}** are H, and
$R^{27'}$, $R^{28'}$, $R^{29'}$ and **$R^{30'}$** are absent or H under the condition that **R^{27}, R^{28}, R^{29}** and **R^{30}** are H.

8. The compound of formula If-2 of claim **6** having formula Ih-2

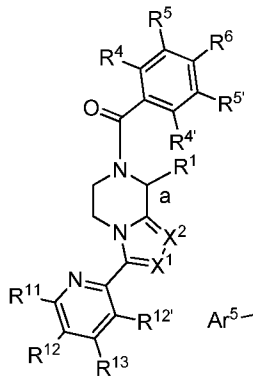


Ih-2

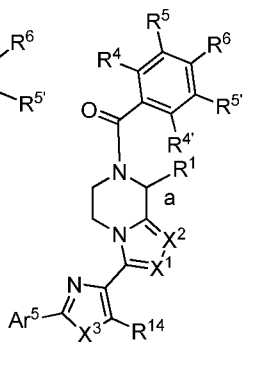
and pharmaceutically acceptable salts and solvates thereof, wherein

a designates the bond linking **R^1** to the piperazine moiety; and
Ar^1, R^1, X^1 and **X^2** are as defined in claim **2**; and
X^3 is as defined in claim **6**; and
$R^{14"}$ is H or methyl; and
X^4 is O, CH_2, CF_2, $C(CH_3)_2$, N-(C1-C3 alkyl) N-phenyl; and
R^{36a}, R^{36b}, $R^{36'a}$, R^{37a} and **$R^{37'a}$** are independently selected from H, C1-C3 alkyl, alkoxyC1-C3 alkyl.

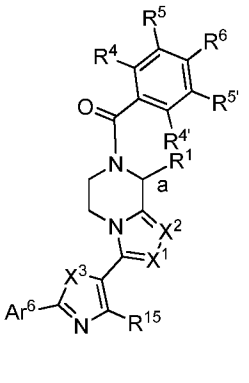
9. The compound of claim **3** selected from formulae Ii-1, Ii-2, Ii-3, Ii-4, Ii-5, Ii-6, Ii-7, Ii-8, Ij-1, Ij-2, Ij-3, Ij-4, Ij-5, Ij-6, Ij-7, Ij-8, Ik-1, Ik-2, Ik-3, Ik-4, Ik-5, Ik-6, Ik-7, Ik-8, Ii'-1, Ii'-2, Ii'-3, Ii'-4, Ii'-5, Ii'-6, Ii'-7 and Ii'-8



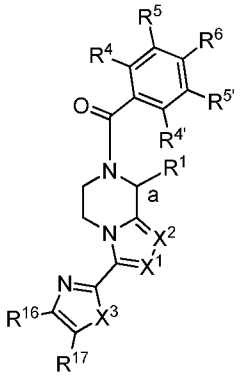
Ii-1



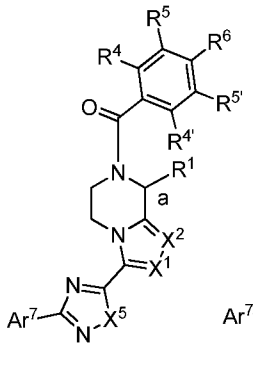
Ii-2



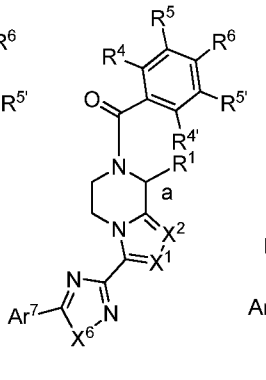
Ii-3



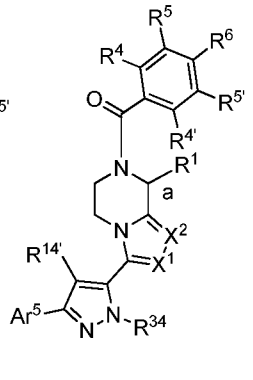
Ii-4



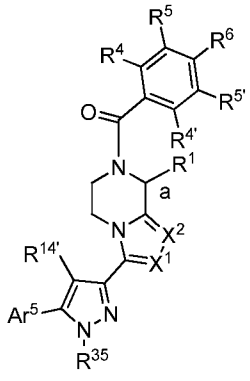
Ii-5



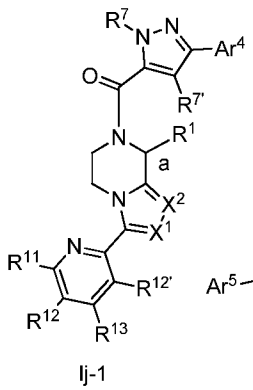
Ii-6



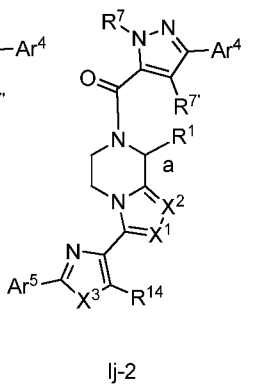
Ii-7



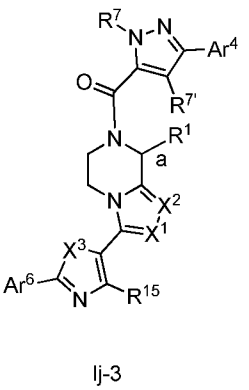
Ii-8



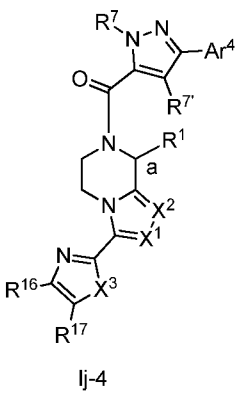
Ij-1



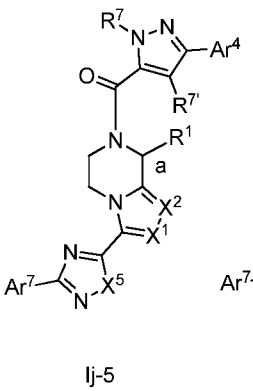
Ij-2



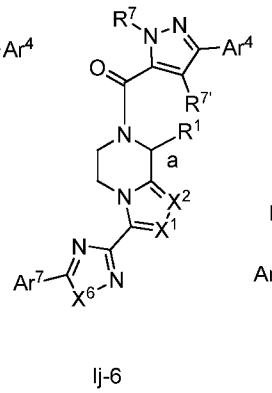
Ij-3



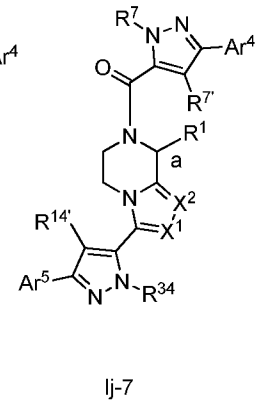
Ij-4



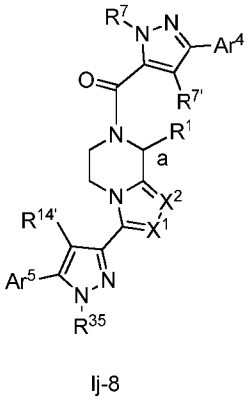
Ij-5



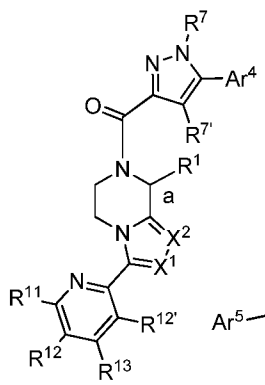
Ij-6



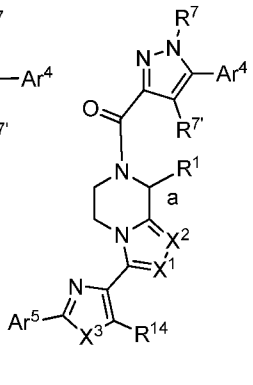
Ij-7



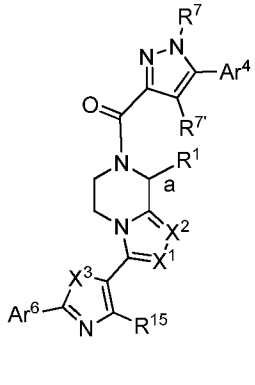
Ij-8



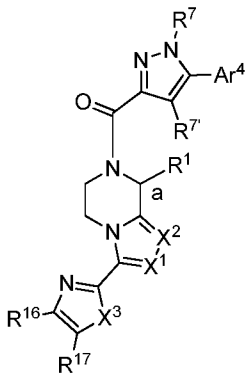
Ik-1



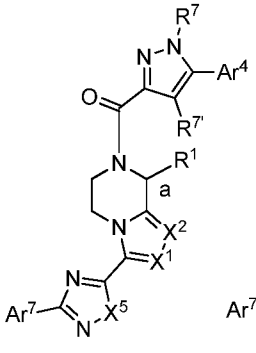
Ik-2



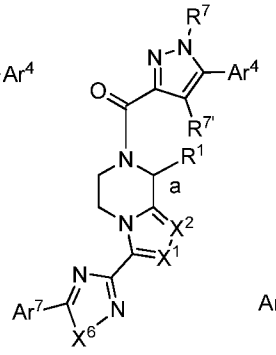
Ik-3



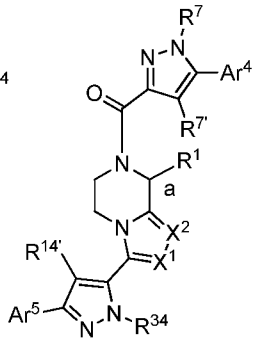
Ik-4



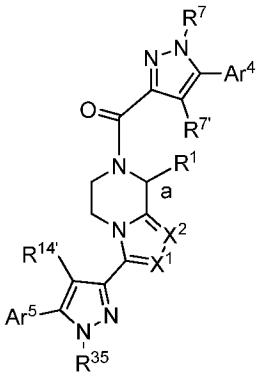
Ik-5



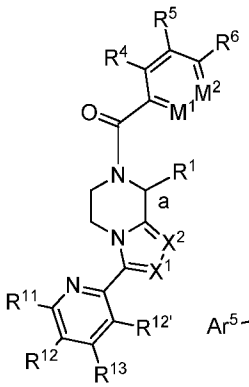
Ik-6



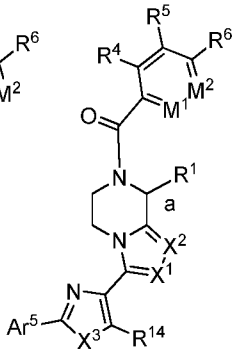
Ik-7



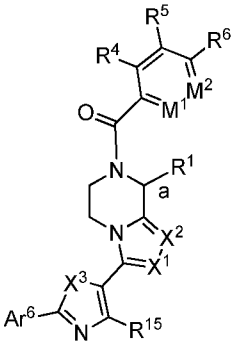
Ik-8



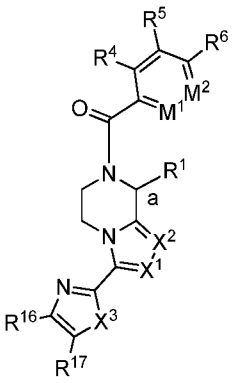
Ii'-1



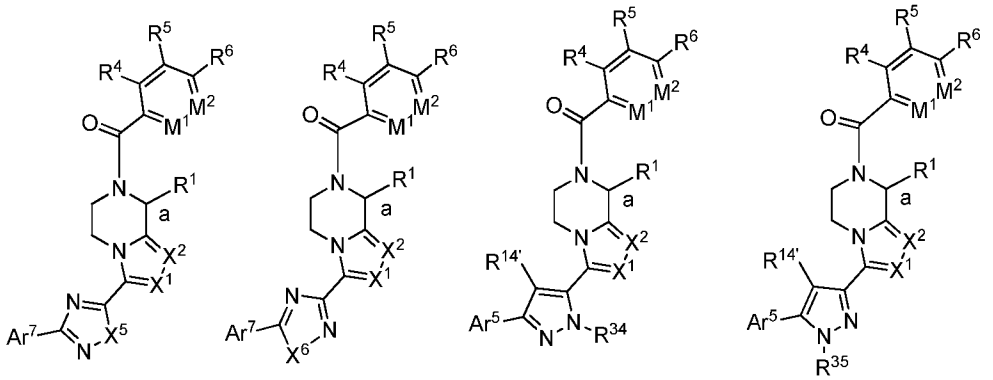
Ii'-2



Ii'-3



Ii'-4

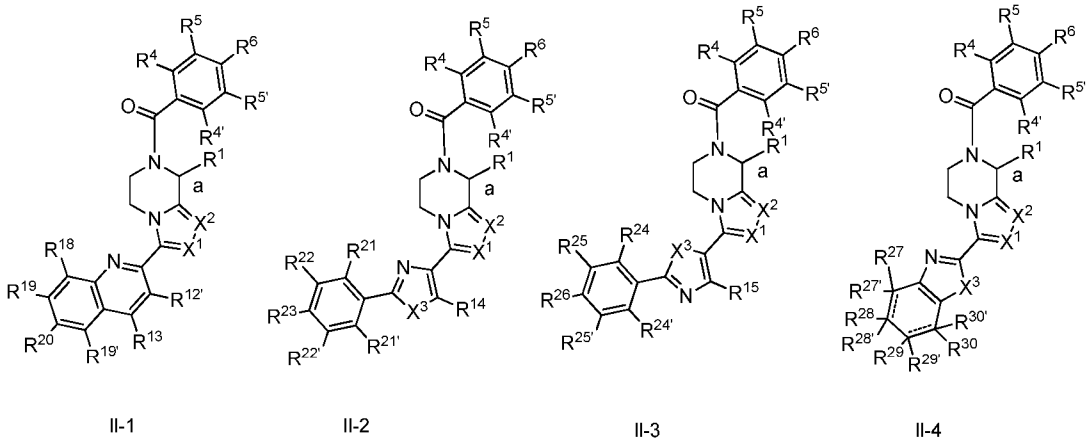


Ii'-5 Ii'-6 Ii'-7 Ii'-8

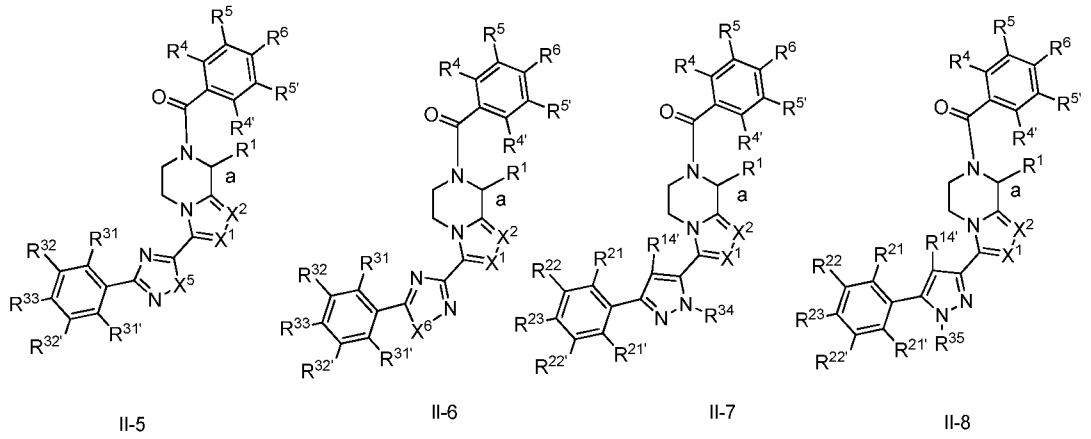
and pharmaceutically acceptable salts and solvates thereof, wherein

a depicts the bond linking R^1 to the piperazine moiety; and
R^1, X^1 and X^2 are as defined in claim **2**; and
Ar^4, R^4, $R^{4'}$, R^5, $R^{5'}$, R^6, R^7, $R^{7'}$, M^1, M^2 are as defined in claim 4; and
Ar^5, Ar^6, Ar^7, R^{11}, R^{12}, $R^{12'}$, R^{13}, R^{14}, $R^{14'}$, R^{15}, R^{16}, R^{17}, R^{34}, R^{35}, X^3, X^5, X^6, and are as defined in claim **6.**

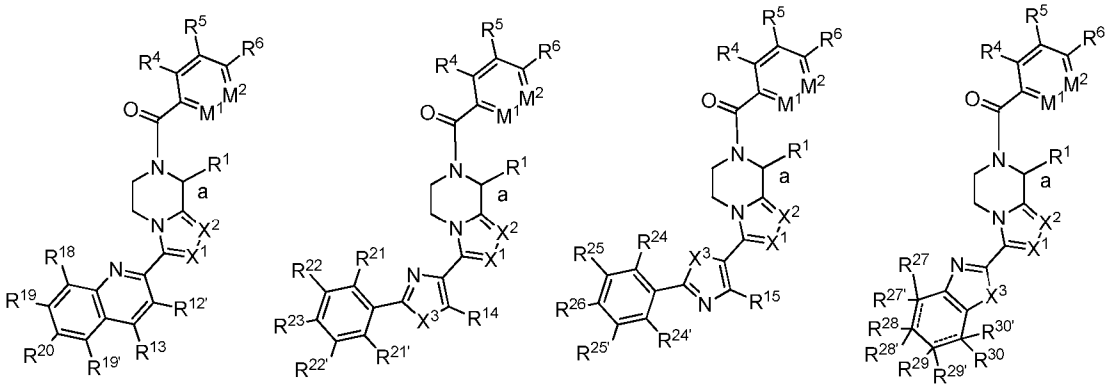
10. The compound of claim **9** selected from formulae II-1, II-2, II-3, II-4, II-5, II-6, II-7, II-8, II'-1, II'-2, II'-3, II'-4, II'-5, II'-6, II'-7, II'-8



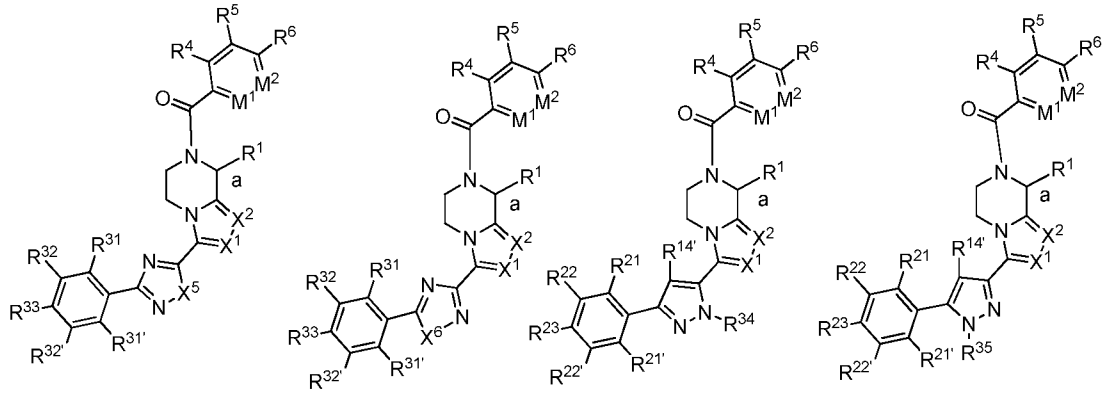
II-1 II-2 II-3 II-4



II-5 II-6 II-7 II-8



II'-1 II'-2 II'-3 II'-4

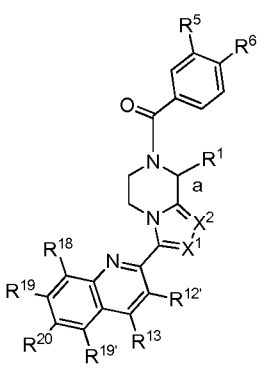


II'-5 II'-6 II'-7 II'-8

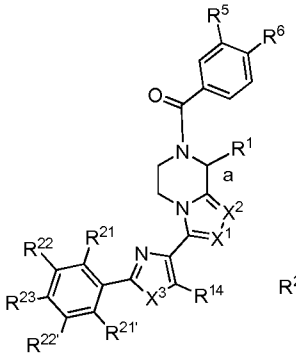
and pharmaceutically acceptable salts and solvates thereof, wherein:

a depicts the bond linking R^1 to the piperazine moiety; and
R^1, X^1 and X^2 are as defined in claim **2**; and
R^4, $R^{4'}$, R^5, $R^{5'}$, R^6, M^1 and M^2 are as defined in claim **4**; and
$R^{12'}$, R^{13}, R^{14}, $R^{14'}$, R^{15}, R^{18}, R^{19}, $R^{19'}$, R^{20}, R^{21}, $R^{21'}$, R^{22}, $R^{22'}$, R^{23}, R^{24}, $R^{24'}$, R^{25}, $R^{25'}$ R^{26}, R^{27}, $R^{27'}$, R^{28}, $R^{28'}$, R^{29}, $R^{29'}$, R^{30}, $R^{30'}$, R^{31}, $R^{31'}$, R^{32}, $R^{32'}$, R^{33}, R^{34}, R^{35}, X^3, X^5; X^6; and the two bonds represented by the dotted lines are as defined in claim 7.

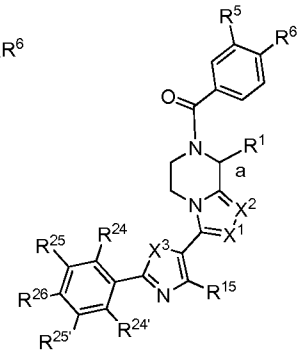
11. The compound of claim **10** selected from formulae Im-1, Im-2, Im-3, Im-4, Im-5, Im-6, Im-7, Im-8, Im'-1, Im'-2, Im'-3, Im'-4, Im'-5, Im'-6, Im'-7 and Im'-8



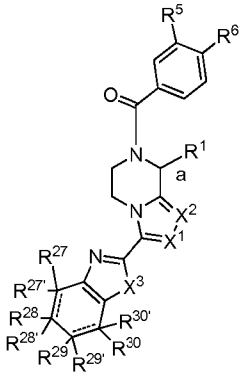
Im-1



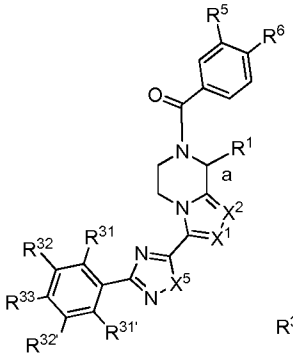
Im-2



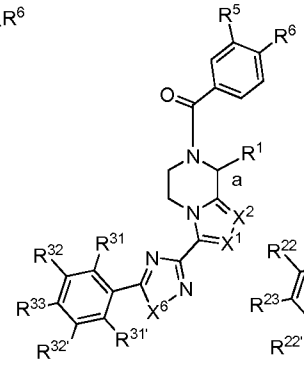
Im-3



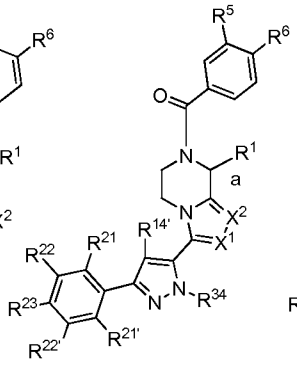
Im-4



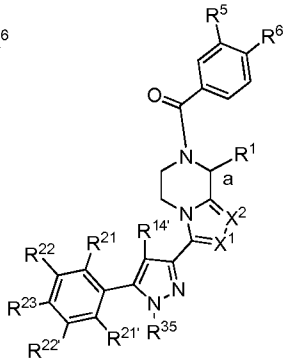
Im-5



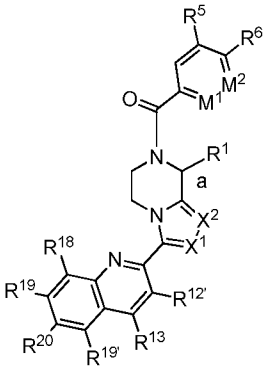
Im-6



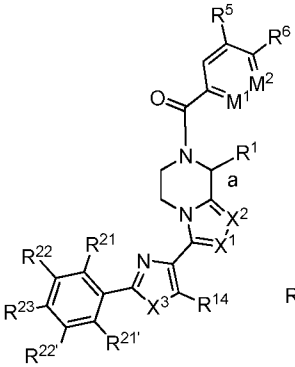
Im-7



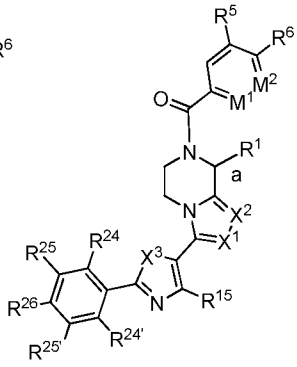
Im-8



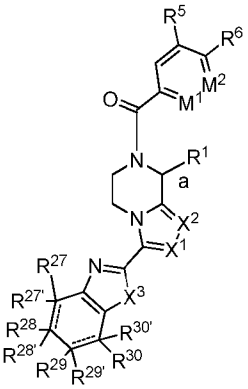
Im'-1



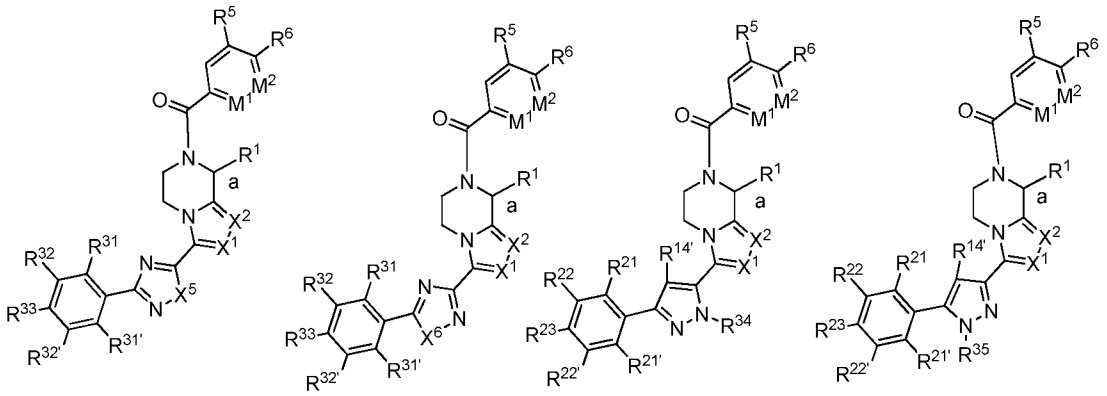
Im'-2



Im'-3



Im'-4



Im'-5 Im'-6 Im'-7 Im'-8

and pharmaceutically acceptable salts and solvates thereof, wherein:

a designates the bond linking R^1 to the piperazine moiety; and
R^1, X^1 and X^2 are as defined in claim **2**; and
R^5, R^6, M^1 and M^2 are as defined in claim **5**; and
$R^{12'}$, R^{13}, R^{14}, $R^{14'}$, R^{15}, R^{18}, R^{19}, $R^{19'}$, R^{20}, R^{21}, $R^{21'}$, R^{22}, $R^{22'}$, R^{23}, R^{24}, $R^{24'}$, R^{25}, $R^{25'}$, R^{26}, R^{27}, $R^{27'}$, R^{28}, $R^{28'}$, R^{29}, $R^{29'}$, R^{30}, $R^{30'}$, R^{31}, $R^{31'}$, R^{32}, $R^{32'}$, R^{33}, R^{34}, R^{35}, X^3, X^5 , X^6; and the two bonds represented by the dotted lines are as defined in claim **7.**

12. The compound of claim **1** selected from the group consisting of:

(4-fluorophenyl)(3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(4-chlorophenyl)(3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(3-(4-chlorophenyl)-1H-pyrazol-5-yl)(3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(3-(3,4-dichlorophenyl)-1H-pyrazol-5-yl)(3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(3,4-dichlorophenyl)(3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
[1,1'-biphenyl]-4-yl(3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(4-fluorophenyl)(3-(quinolin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(4-fluorophenyl)(3-(2-phenylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(4-fluorophenyl)(3-(2-morpholinothiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(3-(5-chloropyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-fluorophenyl)methanone;
(4-fluorophenyl)(3-(6-methylpyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(4-fluorophenyl)(8-methyl-3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(3-(2,4-dichlorophenyl)-1H-pyrazol-5-yl)(3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(3-(3,4-dichlorophenyl)-1-methyl-1H-pyrazol-5-yl)(3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(4-fluorophenyl)(3-(isoquinolin-3-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(4'-fluoro-[1,1'-biphenyl]-4-yl)(3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(3-(4-(trifluoromethyl)phenyl)-1H-pyrazol-5-yl)methanone;
(3-(4-phenoxyphenyl)-1H-pyrazol-5-yl)(3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
[1,1'-biphenyl]-4-yl(3-(quinolin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
[1,1'-biphenyl]-4-yl(3-(2-morpholinothiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone;
(4-fluorophenyl)(3-(8-fluoroquinolin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(3-(8-chloroquinolin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-fluorophenyl)methanone;
(4-fluorophenyl)(3-(2-(4-(trifluoromethyl)phenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;

(4-fluorophenyl)(3-(6-phenylpyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
[1,1'-biphenyl]-4-yl(3-(2-phenylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(4-fluorophenyl)(3-(4,5,6,7-tetrahydrobenzo[d]thiazol-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(4-fluorophenyl)(3-(2-(3-(trifluoromethyl)phenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(3-(2-(2,4-difluorophenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-fluorophenyl)methanone;
(3-(2-(2,3-dichlorophenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-fluorophenyl)methanone;
(3-(2-(4-chlorophenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-fluorophenyl)methanone;
(4-fluorophenyl)(3-(2-(4-fluorophenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(4-fluorophenyl)(3-(2-(piperidin-1-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(4-fluorophenyl)(3-(2-(4-phenylpiperazin-1-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(3-(2-(2,4-dichlorophenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-fluorophenyl)methanone;
(3-(2-(3,5-dichlorophenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-fluorophenyl)methanone;
(4-fluorophenyl)(3-(6-(pyrrolidin-1-yl)pyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(4-fluorophenyl)(3-(6-morpholinopyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(4-fluorophenyl)(3-(6-(trifluoromethyl)pyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(3-(2-(3,4-dimethoxyphenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-fluorophenyl)methanone;
(4-fluorophenyl)(8-(4-fluorophenyl)-3-(2-phenylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(3-(2-(3-chlorophenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-fluorophenyl)methanone;
(4-fluorophenyl)(8-isopropyl-3-(2-phenylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(R)-(4-fluorophenyl)(8-methyl-3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(R)-(4-fluorophenyl)(8-methyl-3-(2-phenylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
[1,1'-biphenyl]-4-yl(8-methyl-3-(2-morpholinothiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(4-fluorophenyl)(3-(2-phenyloxazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(4-fluorophenyl)(8-methyl-3-(2-phenyloxazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
[1,1'-biphenyl]-4-yl(8-methyl-3-(2-phenyloxazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
[1,1'-biphenyl]-4-yl(3-(2-phenyloxazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(4-fluorophenyl)(8-(2-hydroxyethyl)-3-(2-phenylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(4-fluorophenyl)(8-methyl-3-(2-morpholinothiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(4'-fluoro-[1,1'-biphenyl]-4-yl)(8-methyl-3-(2-morpholinothiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(3-(2-phenylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone;
(3-(2-morpholinothiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone;
(8-methyl-3-(2-morpholinothiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone;
(4-fluorophenyl)(3-(4-phenylthiazol-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;

(3-(2-(2-chlorophenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-fluorophenyl)methanone;
(3-(benzo[d]thiazol-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-fluorophenyl)methanone;
(8,8-dimethyl-3-(2-phenylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-fluorophenyl)methanone;
(4-fluorophenyl)(8-methyl-3-(quinolin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(8-methyl-3-(2-phenylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone;
(3-(2-phenylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-3-yl)phenyl)methanone;
(8-methyl-3-(2-phenylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-3-yl)phenyl)methanone;
(8-methyl-3-(quinolin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone;
(3-(2-(2-chlorophenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone;
[1,1'-biphenyl]-4-yl(3-(2-(2-chlorophenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(R)-(3-(2-(4-chlorophenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-fluorophenyl)methanone;
(3-(quinolin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone;
(4-fluorophenyl)(3-(2-(4-fluorophenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(R)-(4-fluorophenyl)(3-(2-(4-fluorophenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
[1,1'-biphenyl]-4-yl(8-methyl-3-(4-methyl-2-phenylthiazol-5-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(3-(2-(4-fluorophenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone;
(3-(2-(2-chlorophenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-fluorophenyl)methanone;
(4-fluorophenyl)(8-methyl-3-(4-methyl-2-phenylthiazol-5-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
[1,1'-biphenyl]-4-yl(3-(2-(4-fluorophenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(3-(2-(2,4-difluorophenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-fluorophenyl)methanone;
(3-(2-(4-fluorophenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone;
[1,1'-biphenyl]-4-yl(3-(2-(2,4-difluorophenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(3-(2-(2,4-difluorophenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone;
naphthalen-1-yl(3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(3-(4-chlorophenyl)-1-methyl-1H-pyrazol-5-yl)(3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(5-(4-chlorophenyl)-1-methyl-1H-pyrazol-3-yl)(3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(8-methyl-3-(5-phenyl-1,2,4-oxadiazol-3-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone;
(8-methyl-3-(3-phenyl-1,2,4-oxadiazol-5-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone;
(R)-(3-(2-(4-fluorophenyl)oxazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone;
(5-phenylpyridin-2-yl)(3-(quinolin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(6-phenylpyridin-3-yl)(3-(quinolin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(2-phenylpyrimidin-5-yl)(3-(quinolin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(4-phenylcyclohexyl)(3-(quinolin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;

cyclohexyl(3-(quinolin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
3-methyl-1-(3-(quinolin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)butan-1-one;
[1,1'-biphenyl]-2-yl(3-(quinolin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(4-(furan-3-yl)phenyl)(3-(quinolin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(4-(pyrimidin-5-yl)phenyl)(3-(quinolin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(9-methyl-9H-carbazol-2-yl)(3-(quinolin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(4-(pyrimidin-2-yl)phenyl)(3-(quinolin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(4-(pyrazin-2-yl)phenyl)(3-(quinolin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(4-(pyridazin-3-yl)phenyl)(3-(quinolin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
4'-(3-(quinolin-2-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazine-7-carbonyl)-[1,1'-biphenyl]-4-carbonitrile;
1-(4-(3-(quinolin-2-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazine-7-carbonyl)phenyl)piperidin-2-one;
(4-morpholinophenyl)(3-(quinolin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(4-(3,5-dimethyl-1H-pyrazol-1-yl)phenyl)(3-(quinolin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(3-(2-(4-fluorophenyl)thiazol-4-yl)-6-methyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone;
(3-(2-(4-fluorophenyl)thiazol-4-yl)-5-methyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone;
(3,4-dichlorophenyl)(3-(2-(4-fluorophenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(3,4-difluorophenyl)(3-(2-(4-fluorophenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(3-chloro-4-fluorophenyl)(3-(2-(4-fluorophenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(4-chloro-3-fluorophenyl)(3-(2-(4-fluorophenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(3-(2-(4-fluorophenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(3,4,5-trifluorophenyl)methanone;
(8-methyl-3-(2-phenyloxazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone;
(R)-(4-fluorophenyl)(8-methyl-3-(quinolin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(R)-[1,1'-biphenyl]-4-yl(8-methyl-3-(quinolin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(R)-[1,1'-biphenyl]-4-yl(8-methyl-3-(2-morpholinothiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(R)-(4-fluorophenyl)(8-methyl-3-(6-phenylpyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(R)-[1,1'-biphenyl]-4-yl(8-methyl-3-(2-phenylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(R)-(4-fluorophenyl)(8-methyl-3-(4,5,6,7-tetrahydrobenzo[d]thiazol-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(R)-(3-(2-(2,4-difluorophenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-fluorophenyl)methanone;
(R)-(3-(2-(2,3-dichlorophenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-fluorophenyl)methanone;
R)-(4-fluorophenyl)(8-methyl-3-(2-(4-phenylpiperazin-1-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(R)-(3-(2-(2,4-dichlorophenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-fluorophenyl)methanone;
(R)-(3-(2-(3-chlorophenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-fluorophenyl)methanone;
(R)-(4-fluorophenyl)(8-methyl-3-(2-phenyloxazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(R)-[1,1'-biphenyl]-4-yl(8-methyl-3-(2-phenyloxazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(R)-(4-fluorophenyl)(8-(2-hydroxyethyl)-3-(2-phenylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(R)-(4'-fluoro-[1,1-biphenyl]-4-yl)(8-methyl-3-(2-morpholinothiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-

a]pyrazin-7(8H)-yl)methanone;
(R)-(8-methyl-3-(2-phenylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone;
(R)-(8-methyl-3-(2-morpholinothiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone;
(R)-(4-fluorophenyl)(8-methyl-3-(4-phenylthiazol-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(R)-(3-(2-(2-chlorophenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-fluorophenyl)methanone;
(R)-(8-methyl-3-(2-phenylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-3-yl)phenyl)methanone;
(R)-(8-methyl-3-(quinolin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone;
(R)-(3-(2-(2-chlorophenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone;
(R)-[1,1'-biphenyl]-4-yl(3-(2-(2-chlorophenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(R)-[1,1'-biphenyl]-4-yl(8-methyl-3-(4-methyl-2-phenylthiazol-5-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(R)-(3-(2-(4-fluorophenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone;
(R)-[1,1'-biphenyl]-4-yl(3-(2-(4-fluorophenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(R)-[1,1'-biphenyl]-4-yl(3-(2-(2,4-difluorophenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(R)-(3-(2-(2,4-difluorophenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone;
(S)-(4-fluorophenyl)(8-methyl-3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(S)-(4-fluorophenyl)(3-(2-(4-fluorophenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(S)-(4'-fluoro-[1,1'-biphenyl]-4-yl)(8-methyl-3-(2-morpholinothiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(S)-(4-fluorophenyl)(8-methyl-3-(quinolin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(S)-(8-methyl-3-(quinolin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone;
(S)-(4-fluorophenyl)(3-(2-(4-fluorophenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(S)-(3-(2-(2,4-difluorophenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone;
(4-fluorophenyl)(8-methyl-3-(2-phenylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(S)-(4-fluorophenyl)(8-methyl-3-(2-phenylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(S)-(3-(3-(4-fluorophenyl)-1,2,4-oxadiazol-5-yl)-8-methyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone;
(R)-(3-(3-(4-fluorophenyl)-1,2,4-oxadiazol-5-yl)-8-methyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone;
(3-(2-(2,4-difluorophenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone;
(3-(5-phenyl-1,2,4-oxadiazol-3-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone;
(4-fluorophenyl)(3-(3-phenyl-1,2,4-oxadiazol-5-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(4-fluorophenyl)(3-(5-phenyl-1,2,4-oxadiazol-3-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(3-(3-phenyl-1,2,4-oxadiazol-5-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone;
(4-fluorophenyl)(3-(3-(4-fluorophenyl)-1,2,4-oxadiazol-5-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-

7(8H)-yl)methanone;
(3-(3-(4-fluorophenyl)-1,2,4-oxadiazol-5-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone;
(3-(3-(2,4-difluorophenyl)-1,2,4-oxadiazol-5-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone;
(4-fluorophenyl)(3-(5-phenyl-1H-1,2,4-triazol-3-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(3-(5-phenyl-1H-1,2,4-triazol-3-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone;
(4-fluorophenyl)(3-(2-(2-fluorophenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(3-(2-(2-fluorophenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone;
[1,1'-biphenyl]-4-yl(3-(2-(2-fluorophenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(4'-fluoro-[1,1'-biphenyl]-4-yl)(3-(2-(2-fluorophenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(3-(3-(2,4-difluorophenyl)-1,2,4-oxadiazol-5-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone;
[1,1'-biphenyl]-4-yl(3-(2-((4,5-dichloro-1H-imidazol-1-yl)methyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(3-(2-((4,5-dichloro-1H-imidazol-1-yl)methyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4'-fluoro-[1,1'-biphenyl]-4-yl)methanone;
(3-(2-(4-chlorobenzyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-fluorophenyl)methanone;
(3-(2-(4-chlorobenzyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone;
(4-fluorophenyl)(3-(2-(p-tolyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(4-(thiophen-2-yl)phenyl)(3-(2-(p-tolyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
[1,1'-biphenyl]-4-yl(3-(2-(p-tolyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(4-fluorophenyl)(3-(2-(thiophen-2-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(4-(thiophen-2-yl)phenyl)(3-(2-(thiophen-2-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
[1,1'-biphenyl]-4-yl(3-(2-(thiophen-2-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(4'-fluoro-[1,1'-biphenyl]-4-yl)(3-(2-(thiophen-2-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(3-(2-(((4-chlorophenyl)sulfonyl)methyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone;
[1,1'-biphenyl]-4-yl(3-(2-(((4-chlorophenyl)sulfonyl)methyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(3-(2-(((4-chlorophenyl)sulfonyl)methyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4'-fluoro-[1,1'-biphenyl]-4-yl)methanone;
(4-fluorophenyl)(3-(2-(2-methoxyphenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(3-(2-(2-methoxyphenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone;
[1,1'-biphenyl]-4-yl(3-(2-(2-methoxyphenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
[1,1'-biphenyl]-4-yl(3-(3-(4-fluorophenyl)-1,2,4-oxadiazol-5-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(4'-fluoro-[1,1'-biphenyl]-4-yl)(3-(3-(4-fluorophenyl)-1,2,4-oxadiazol-5-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(4-fluorophenyl)(3-(2-(3-fluorophenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(3-(2-(3-fluorophenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phe-

nyl)methanone;
(4-fluorophenyl)(3-(2-isopropylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(3-(3-(4-fluorophenyl)-1,2,4-oxadiazol-5-yl)-8-methyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone;
(3-(3-phenyl-1,2,4-thiadiazol-5-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone;
(4-fluorophenyl)(3-(3-phenyl-1,2,4-thiadiazol-5-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(3-(2-(4-bromophenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone;
(3-(2-(4-bromophenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-fluorophenyl)methanone;
(3-(2-(4-fluorophenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(5-methylthiophen-2-yl)phenyl)methanone;
4-(3-(2-(4-fluorophenyl)thiazol-4-yl)-8-methyl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazine-7-carbonyl)benzonitrile;
[1,1'-biphenyl]-4-yl(3-(3-phenyl-l,2,4-oxadiazol-5-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(4-fluorophenyl)(3-(2-(pyridin-4-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(3-(2-(quinolin-2-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone;
(3-(1-methyl-3-phenyl-1H-pyrazol-5-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone;
(3-(2-(4-(dimethylamino)phenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-fluorophenyl)methanone;
(3-(1-methyl-5-phenyl-1H-pyrazol-3-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone;
(4'-fluoro-[1,1'-biphenyl]-4-yl)(3-(3-phenyl-1,2,4-oxadiazol-5-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(3-(2-(pyridin-2-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone;
(4-fluorophenyl)(3-(1-methyl-3-phenyl-1H-pyrazol-5-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(3-(2-(pyrimidin-2-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone;
(S)-(8-methyl-3-(2-morpholinothiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone;
(3-(2-(pyridin-4-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone;
(3-(2-(4-(dimethylamino)phenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone;
(4-fluorophenyl)(3-(2-(pyridin-2-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
phenyl(3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(p-tolyl)methanone;
(S)-(3-(2-(4-fluorophenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(2-methylthiophen-3-yl)phenyl)methanone;
(R)-(3-(2-(4-fluorophenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(2-methylthiophen-3-yl)phenyl)methanone;
(3-(2-(pyrazin-2-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone;
4-(4-(7-(4-(thiophen-2-yl)benzoyl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)thiazol-2-yl)benzonitrile;
(4-fluorophenyl)(3-(2-(pyrazin-2-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(4-fluorophenyl)(3-(1-methyl-5-phenyl-1H-pyrazol-3-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(3-(2-(4-morpholinophenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone;
(4-fluorophenyl)(3-(2-(4-morpholinophenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;

(3-(2-(4-(4-methylpiperazin-1-yl)phenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone;
(4-fluorophenyl)(3-(2-(4-(4-methylpiperazin-1-yl)phenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(3-(2-(4-(piperidin-1-yl)phenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone;
(4-fluorophenyl)(3-(2-(4-(piperidin-1-yl)phenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(3-(2-(4-(pyrrolidin-1-yl)phenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone;
(4-fluorophenyl)(3-(2-(4-(pyrrolidin-1-yl)phenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(3-(2-(piperidin-1-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone;
(3-(2-(pyrrolidin-1-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone;
(4-fluorophenyl)(3-(2-(pyrrolidin-1-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(3-(2-(4-methylpiperazin-1-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone;
(4-fluorophenyl)(3-(2-(4-methylpiperazin-1-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(3-(1-methyl-2-phenyl-1H-imidazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone;
(4-(dimethylamino)phenyl)(3-(2-(4-fluorophenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(3-(1-(2-methoxyethyl)-3-phenyl-1H-pyrazol-5-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone;
(4-fluorophenyl)(3-(1-(2-methoxyethyl)-3-phenyl-1H-pyrazol-5-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(3-(2-isobutylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone;
(3-(2-(2-(2-methoxyethyl)morpholino)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone;
(3-(2-(4,4-difluoropiperidin-1-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-fluorophenyl)methanone;
(4-fluorophenyl)(3-(2-isobutylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(3-(2-(2,5-dimethylmorpholino)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone;
(3-(2-(2-hydroxyphenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone;
(3-(2-(4,4-difluoropiperidin-1-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone;
(3-(2-(2,6-dimethylmorpholino)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone;
(3-(2-(2,2-dimethylmorpholino)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone;
(3-(3-phenyl-1H-pyrazol-5-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone;
(3-(2-(4-fluorophenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(3-methylthiophen-2-yl)phenyl)methanone;
(4-fluorophenyl)(3-(3-phenyl-1H-pyrazol-5-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(R)-(3-(2-(4-fluorophenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(3-methylthiophen-2-yl)phenyl)methanone;
(4-fluorophenyl)(3-(2-(2-hydroxyphenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(S)-(3-(2-(4-fluorophenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(3-methylthiophen-2-yl)phenyl)methanone;

(3-(2-(2-methylmorpholino)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone;
(3-(2-(4,4-dimethylpiperidin-1-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone;
(3-(5-methylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone;
(3-(2-(4,4-dimethylpiperidin-1-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-fluorophenyl)methanone;
(4-fluorophenyl)(3-(2-(2-(methoxymethyl)piperidin-1-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(4-fluorophenyl)(8-methyl-3-(6-methylpyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(3-(2-(2-(methoxymethyl)piperidin-1-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone;
tert-butyl (2-(2-(4-(7-(4-(thiophen-2-yl)benzoyl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)thiazol-2-yl)phenoxy)ethyl)carbamate;
(3-(2-(2-(2-hydroxyethoxy)phenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone;
(3-(2-(2-(2-aminoethoxy)phenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone;
N-(4-(4-(7-(4-(thiophen-2-yl)benzoyl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)thiazol-2-yl)phenyl)methanesulfonamide;
(3-(1-(2-hydroxyethyl)-3-phenyl-1H-pyrazol-5-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone;
(3-(1-(2-hydroxyethyl)-5-phenyl-1H-pyrazol-3-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone;
[1,1'-biphenyl]-4-yl(8-methyl-3-(6-methylpyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(8-methyl-3-(6-methylpyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone;
(3-(2-(2,4-difluorophenyl)-5-methylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone;
(3-(2-(3-(dimethylamino)phenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone;
(3-(2-(3-(dimethylamino)phenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-fluorophenyl)methanone;
N-(3-(4-(7-(4-(thiophen-2-yl)benzoyl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)thiazol-2-yl)phenyl)methanesulfonamide;
N-(2-(4-(7-(4-(thiophen-2-yl)benzoyl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)thiazol-2-yl)phenyl)methanesulfonamide;
(3-(4-chlorophenyl)-1H-pyrazol-5-yl)(3-(2-(4-fluorophenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(3-(4-chlorophenyl)-1-methyl-1H-pyrazol-5-yl)(3-(2-(4-fluorophenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(3-(3,4-dichlorophenyl)-1-methyl-1H-pyrazol-5-yl)(3-(2-(4-fluorophenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
(5-(4-chlorophenyl)-1-methyl-1H-pyrazol-3-yl)(3-(2-(4-fluorophenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)methanone;
tert-butyl (2-(3-phenyl-5-(7-(4-(thiophen-2-yl)benzoyl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)-1H-pyrazol-1-yl)ethyl)carbamate;
tert-butyl (2-(5-phenyl-3-(7-(4-(thiophen-2-yl)benzoyl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)-1H-pyrazol-1-yl)ethyl)carbamate;
(3-(2-(2-bromophenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone;
(3-(2-(3-bromophenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanone;
2-(4-(7-(4-(thiophen-2-yl)benzoyl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)thiazol-2-yl)benzonitrile;
3-(4-(7-(4-(thiophen-2-yl)benzoyl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)thiazol-2-yl)benzonitrile;

(3-(2-(4-fluorophenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(2-methylthiophen-3-yl)phenyl)methanone;
and pharmaceutically acceptable salts and solvates thereof.

13. A pharmaceutical composition comprising a compound according to any of claims **1** to **12** or a pharmaceutically acceptable salt or solvate thereof and at least one pharmaceutically acceptable carrier, diluent, excipient and/or adjuvant.

14. Medicament comprising a compound according to any of claims **1** to **12** or a pharmaceutically acceptable salt or solvate thereof.

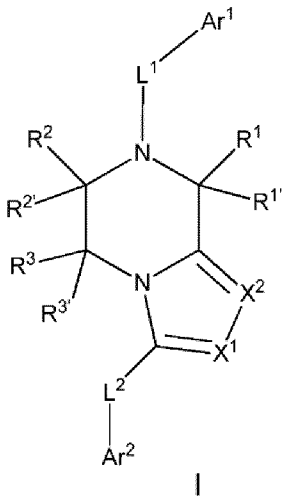
15. A compound according to any of claims **1** to **12** or a pharmaceutically acceptable salt or solvate thereof for use in treating and/or preventing depression, anxiety, pyschosis, schizophrenia, psychotic disorders, bipolar disorders, cognitive disorders, Parkinson's disease, Alzheimer's disease, attention deficit hyperactivity disorder (ADHD), pain, convulsion, obesity, inflammatory diseases including irritable bowel syndrome and inflammatory bowel disorders, emesis, pre-eclampsia, airway related diseases including chronic obstructive pulmonary disease, asthma, airway hyperresponsiveness, bronchoconstriction and cough, reproduction disorders and sex hormone-dependent diseases including but not limited to benign prostatic hyperplasia (BPH), metastatic prostatic carninoma, testicular cancer, breast cancer, androgen dependent acne, male pattern baldness, endometriosis, abnormal puberty, uterine fibrosis, hormone-dependent cancers, hyperandrogenism, hirsutism, virilization, polycystic ovary syndrome (PCOS), HAIR-AN syndrome (hyperandrogenism, insulin resistance and acanthosis nigricans), ovarian hyperthecosis (HAIR-AN with hyperplasia of luteinized theca cells in ovarian stroma), other manifestations of high intraovarian androgen concentrations (e.g. follicular maturation arrest, atresia, anovulation, dysmenorrhea, dysfunctional uterine bleeding, infertility), gynecological disorders, infertility and androgen-producing tumor (virilizing ovarian or adrenal tumor).

16. A compound according to any of claims **1** to **12** or a pharmaceutically acceptable salt or solvate thereof for use in suppressing the LH-surge in assisted conception in a patient.

17. A compound according to any of claims **1** to **12** or a pharmaceutically acceptable salt or solvate thereof for use in causing male castration and inhibiting the sex drive in men.

Patentansprüche

1. Verbindung der Formel I:



I

und pharmazeutisch verträgliche Salze und Solvate davon, wobei

Ar^1 eine 5- bis 6-gliedrige Aryl- oder Heteroarylgruppe, eine 3- bis 6-gliedrige Cycloalkylgruppe, eine 3- bis 6-gliedrige Heterocyclylgruppe oder eine C3-C6-Alkylgruppe ist, wobei jede der Aryl-, Heteroaryl-, Cycloalkyl- oder Heterocyclylgruppen gegebenenfalls mit einer oder mehreren Gruppe(n), ausgewählt aus Halogen, Cyano,

Alkyl, Halogenalkyl, Cycloalkyl, Heteroalkyl, Heterocyclyl, Aryl, Aralkyl, Heteroaryl, Hydroxyl, Alkoxy, Halogenalkoxy, Alkoxyalkoxy, Alkylamino, Carboxy, Alkoxycarbonyl, Alkylcarbonyloxy, Alkylcarbonylamino, Halogenalkylcarbonylamino, Carbamoyl, Alkylcarbamoyl, Carbamoylamino, Alkylcarbamoylamino, Alkylsulfonyl, Halogenalkylsulfonyl, Sulfamoyl, Alkylsulfamoyl, Alkylsulfonylamino, Halogenalkylsulfonylamino substituiert ist, oder zwei Substituenten eine Alkylendioxygruppe oder eine Halogenalkylendioxygruppe bilden, oder zwei Substituenten zusammen mit der Cycloalkyl- oder Heterocycloalkylgruppe, an die sie gebunden sind, einen Cycloalkyl- oder Heterocycloalkylrest bilden, oder ein oder mehrere Arylreste mit der Aryl-, Heteroaryl-, Cycloalkyl- oder Heterocycloalkylgruppe fusioniert sein können, wobei jeder der besagten Substituenten gegebenenfalls mit einem oder mehreren weiteren Substituenten, ausgewählt aus Halogen, Cyano, Alkyl, Halogenalkyl, Cyclopropyl, Alkoxy, Halogenalkoxy, Heterocyclyl, Aryl, Heteroaryl, Aryloxy, Heteroaryloxy, substituiert ist;
L^1 Carbonyl ist;
R^1 H, eine C_1-C_4-Alkyl-, Aryl- oder Aralkylgruppe ist, wobei jede der besagten Alkyl-, Aryl- oder Aralkylgruppen gegebenenfalls mit einer oder mehreren Gruppe(n), ausgewählt aus Halogen oder Hydroxyl, substituiert ist;
$R^{1'}$ H oder eine C_1-C_4-Alkylgruppe ist;
R^2 H oder eine C_1-C_4-Alkylgruppe ist;
$R^{2'}$ H oder eine C_1-C_4-Alkylgruppe ist;
R^3 H oder eine gegebenenfalls mit einem Hydroxy substituierte C_1-C_4-Alkylgruppe ist;
$R^{3'}$ H oder eine C_1-C_4-Alkylgruppe ist;
X^1 und **X^2** N sind;
L^2 eine Einfachbindung oder Carbonyl ist,
Ar^2 eine 5- bis 6-gliedrige Aryl- oder Heteroarylgruppe ist, wobei jede der Aryl- oder Heteroarylgruppen gegebenenfalls mit einer oder mehreren Gruppe(n), ausgewählt aus Halogen, Cyano, Alkyl, Hydroxyalkyl, Halogenalkyl, Cycloalkyl, Heteroalkyl, Heterocyclyl, Aryl, Heteroaryl, Aralkyl, Heteroarylalkyl, Hydroxyl, Alkoxy, Halogenalkoxy, Alkylamino, Carboxy, Alkoxycarbonyl, Alkylcarbonyloxy, Alkylcarbonylamino, Halogenalkylcarbonylamino, Acylamino, Carbamoyl, Alkylcarbamoyl, Carbamoylalkyl, Carbamoylamino, Alkylcarbamoylamino, Alkylsulfonyl, Halogenalkylsulfonyl, Arylsulfonylalkyl, Sulfamoyl, Alkylsulfamoyl, Alkylsulfonylamino, Halogenalkylsulfonylamino substituiert ist, oder zwei Substituenten eine Alkylendioxygruppe oder eine Halogenalkylendioxygruppe bilden, oder eine oder mehrere Cycloalkyl-, Aryl-, Heterocyclyl- oder Heteroarylreste mit der Aryl- oder Heteroarylgruppe fusioniert sein können, wobei jeder der besagten Substituenten gegebenenfalls mit einem oder mehreren weiteren Substituenten, ausgewählt aus Halogen, Cyano, Alkyl, Halogenalkyl, Alkoxy, Halogenalkoxy, Cycloalkyl, Heterocyclyl substituiert ist, welche gegebenenfalls mit Alkyl, Aryl, Heteroaryl, Hydroxyl, Alkoxyalkyl, Hydroxyalkoxy, Alkylamino, Alkylsulfonylamino, Alkoxycarbonylamino, Aminoalkoxy, oder Alkoxycarbonylaminoalkoxy substituiert sind;
und wobei, wenn:

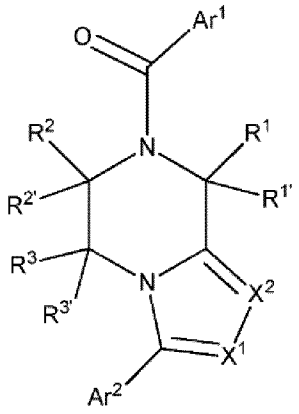
R^1, **$R^{1'}$**, **R^2**, **$R^{2'}$**, **R^3**, **$R^{3'}$** H sind, und
L^2 eine Einfachbindung ist, und
Ar^1 ein gegebenenfalls mit einer oder mehreren Gruppe(n), ausgewählt aus Halogen, Cyano, C1-C3-Alkyl, C1-Halogenalkyl substituiertes 6-gliedriges Aryl ist, und
Ar^2 eine 5- bis 6-gliedrige Aryl- oder Heteroarylgruppe ist, die gegebenenfalls mit einer oder mehreren Gruppe(n), ausgewählt aus Halogen, C1-C3-Alkyl, Hydroxyl, Methoxy substituiert, oder mit einer Aryl- oder Heteroarylgruppe fusioniert ist, welche gegebenenfalls mit einem oder mehreren weiteren Halogen, C1-C3-Alkyl, Hydroxyl, Methoxy substituiert ist,
dann
ist **Ar^1** Phenyl, 3-Halogenphenyl, 4-Halogenphenyl, 2,3-Dichlorphenyl, 2,4-Difluorphenyl, 2,5-Dihalogenphenyl, 2,6-Difluorphenyl, 2,6-Dichlorphenyl, 3,4-Dihalogenphenyl, 3,5-Dihalogenphenyl, 3,4,5-Trihalogenphenyl, 2-Cyanophenyl, 3-Cyanophenyl, 4-Cyanophenyl, 2,3-Dicyanophenyl, 2,4-Dicyanophenyl, 3,5-Dicyanophenyl, 3-Cyano-4-halogenphenyl, 4-(C1-C3-Alkyl)phenyl, 3,4-Di(C1-C3-alkyl)phenyl, 3,5-Di(C1-C3-alkyl)phenyl, 4-(C1-Halogengenalkyl)phenyl, und
ist **Ar^2** 2-(C1-C3-Alkyl)thiazol-4-yl, 5-(C1-C3-Alkyl)thiazol-4-yl, Pyridin-2-yl, 4-Halogenpyridin-2-yl, 4-(C1-C3-Alkyl)pyridin-2-yl, 5-(C1-C3-Alkyl)pyridin-2-yl, 6-(C1-C3-Alkyl)pyridin-2-yl, Chinolin-2-yl, Isochinolin-3-yl, 8-Halogenchinolin-2-yl, Benzothiazol-2-yl, 4,5,6,7-Tetrahydro-1,3-benzothiazol-2-yl;
mit den folgenden Bestimmungen:

- **Ar^1** ist weder ein substituiertes oder unsubstituiertes Pyrazol[1,5-a]pyridin-2-yl noch ein substituierter oder unsubstituierter Pyrazol[1,5-a]pyrimidin-2-yl-Rest; und die Verbindung nach Formel I keines von:

(2,4-Difluorphenyl)(3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;

(3-Chlorphenyl)(3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
2-(3-(Pyridin-2-yl)-5,6,7,8-tetrahydro-[1,2,4]triazol[4,3-a]pyrazin-7-carbonyl)benzonitril;
(2,6-Dichlorphenyl)(3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon,
(2,3-Dichlorphenyl)(3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon,
(2,3-Dichlorphenyl)(3-(5-methylpyridin-2-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon,
(2,3-Dichlorphenyl)(3-(6-methylpyridin-2-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon.

2. Verbindung nach Anspruch 1 mit der Formel Ib

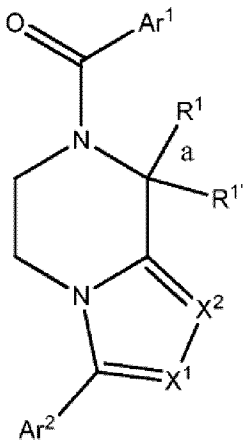


Ib

und pharmazeutisch verträgliche Salze und Solvate davon, wobei

Ar^1, **Ar^2**, **R^1**, **$R^{1'}$**, **R^2**, **$R^{2'}$**, **R^3**, **$R^{3'}$**, **X^1**, **X^2** wie in Anspruch 1 definiert sind.

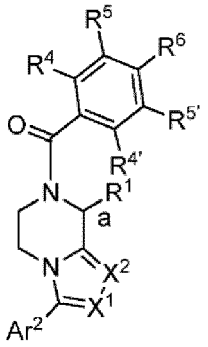
3. Verbindung nach Anspruch 2 mit der Formel Ic



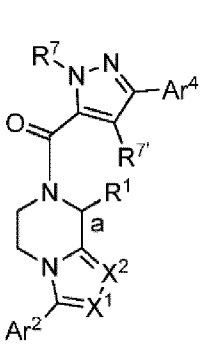
Ic

und pharmazeutisch verträgliche Salze und Solvate davon, wobei **a** die Bindung zeigt, die **R^1** mit dem Piperazinrest verbindet, und **Ar^1**, **Ar^2**, **R^1**, **$R^{1'}$**, **X^1** und **X^2** wie in Anspruch **2** definiert sind.

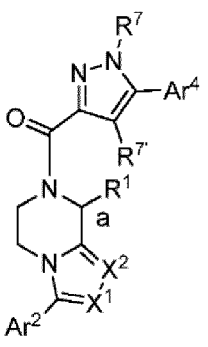
4. Verbindung nach Anspruch **3,** ausgewählt aus den Formeln Id-1, Id-2, Id-3 und Id-4,



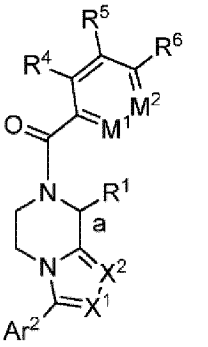
Id-1



Id-2



Id-3



Id-4

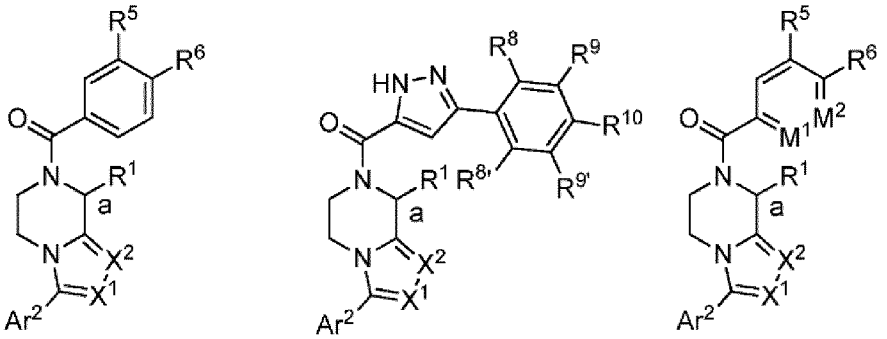
und pharmazeutisch verträgliche Salze und Solvate davon, wobei

a die Bindung zeigt, die **R1** mit dem Piperazinrest verbindet; und
Ar2, **R1**, **X1** und **X2** wie in Anspruch **2** definiert sind; und
R4, **R4'**, **R5**, **R5'** und **R6** unabhängig ausgewählt sind aus H, Halogen, Cyano, Alkyl, Halogenalkyl, C3-C6-Cycloalkyl, Heteroalkyl, Heterocyclyl, Aryl, Heteroaryl, Hydroxyl, Alkoxy, Halogenalkoxy, Alkoxyalkoxy, Alkylamino, Carboxy, Alkoxycarbonyl, Alkylcarbonyloxy, Alkylcarbonylamino, Halogenalkylcarbonylamino, Carbamoyl, Alkylcarbamoyl, Carbamoylamino, Alkylcarbamoylamino, Alkylsulfonyl, Halogenalkylsulfonyl, Sulfamoyl, Alkylsulfamoyl, Alkylsulfonylamino, Halogenalkylsulfonylamino, oder **R5** zusammen mit **R4** oder **R6**, oder **R5'** zusammen mit **R4'** oder **R6** eine Alkylendioxygruppe oder eine Halogenalkylendioxygruppe bildet, oder **R5** zusammen mit **R4** oder **R6**, oder **R5'** zusammen mit **R4'** oder **R6** einen Arylrest bildet, der mit der Phenylgruppe, an die sie gebunden sind, fusioniert ist, wobei jeder der besagten Substituenten gegebenenfalls mit einem oder mehreren weiteren Substituenten, ausgewählt aus Halogen, Cyano, Alkyl, Halogenalkyl, Cyclopropyl, substituiert ist; und
R7 H oder Methyl ist; und
R7' H oder Methyl ist; und
Ar4 eine Cycloalkyl- oder eine Arylgruppe ist, wobei jede der besagten Cycloalkyl- oder Arylgruppen gegebenenfalls mit einer oder mehreren Gruppe(n), ausgewählt aus Halogen, Alkyl, Halogenalkyl, Cyclopropyl, Halogenalkoxy, Aryloxy, substituiert ist; und
M1 N oder C-**R4"** ist, wobei **R4"** ausgewählt ist aus H, Halogen, Cyano, Alkyl, Halogenalkyl, C3-C6-Cycloalkyl, Heteroalkyl, Heterocyclyl, Aryl, Heteroaryl, Hydroxyl, Alkoxy, Halogenalkoxy, Alkoxyalkoxy, Alkylamino, Carboxy, Alkoxycarbonyl, Alkylcarbonyloxy, Alkylcarbonylamino, Halogenalkylcarbonylamino, Carbamoyl, Alkylcarbamoyl, Carbamoylamino, Alkylcarbamoylamino, Alkylsulfonyl, Halogenalkylsulfonyl, Sulfamoyl, Alkylsulfamoyl, Alkylsulfonylamino, Halogenalkylsulfonylamino, wobei jeder der besagten Substituenten gegebenenfalls mit einem oder mehreren weiteren Substituenten, ausgewählt aus Halogen, Cyano, Alkyl, Halogenalkyl, Cyclopropyl, substituiert ist; und
M2 N ist oder **M2** C-**R5"** ist unter der Bedingung, dass **M1** N ist, wobei **R5"** ausgewählt ist aus H, Halogen, Cyano, Alkyl, Halogenalkyl, C3-C6-Cycloalkyl, Heteroalkyl, Heterocyclyl, Aryl, Heteroaryl, Hydroxyl, Alkoxy, Halogenalkoxy, Alkoxyalkoxy, Alkylamino, Carboxy, Alkoxycarbonyl, Alkylcarbonyloxy, Alkylcarbonylamino, Halogenalkylcarbonylamino, Carbamoyl, Alkylcarbamoyl, Carbamoylamino, Alkylcarbamoylamino, Alkylsulfonyl, Halogenalkylsulfonyl, Sulfamoyl, Alkylsulfamoyl, Alkylsulfonylamino, Halogenalkylsulfonylamino, oder **R5"** zusammen mit **R6** eine Alkylendioxygruppe oder eine Halogenalkylendioxygruppe, oder einen Arylrest bildet, der mit der Pyridinylgruppe, an die sie gebunden sind, fusioniert ist, wobei jeder der besagten Substituenten gegebenenfalls mit einem oder mehreren weiteren Substituenten, ausgewählt aus Halogen, Cyano, Alkyl, Halogenalkyl, Cyclopropyl, substituiert ist; und
wobei, in Formel Id-1, wenn:

R1 H ist, und
R4, **R4'**, **R5**, **R5'** und **R6** unabhängig ausgewählt sind aus H, Halogen, Cyano, C1-C3-Alkyl, C1-Halogenalkyl, und
Ar2 eine 5- bis 6-gliedrige Aryl- oder Heteroarylgruppe ist, die gegebenenfalls mit einer oder mehreren Gruppe(n), ausgewählt aus Halogen, C1-C3-Alkyl, Hydroxyl, Alkoxy substituiert, oder mit einer Arylgruppe fusioniert ist, die gegebenenfalls mit einem oder mehreren weiteren Halogen, C1-C3-Alkyl, Hydroxyl, Me-

thoxy substituiert ist, dann,
sind **R4**, **R4'**, **R5**, **R5'** und **R6** H, oder sind **R4**, **R4'**, **R5'**, **R6** H und ist **R5** Halogen, oder sind **R4**, **R4'**, **R5**, **R5'** H und ist **R6** Halogen, Cyano, C1-C3-Alkyl, C1-Halogenalkyl, oder sind **R4'**, **R5'**, **R6** H und sind **R4**, **R5** Halogen, oder sind **R4**, **R4'**, **R5'** H und sind **R5**, **R6** unabhängig Halogen, oder sind **R4**, **R4'** H und sind **R5**, **R5'**, **R6** Halogen, und
ist **Ar2** 2-(C1-C3-Alkyl)thiazol-4-yl, 5-(C1-C3-Alkyl)thiazol-4-yl, Pyridin-2-yl, 4-Halogenpyridin-2-yl, 4-(C1-C3-Alkyl)pyridin-2-yl, 5-(C1-C3-Alkyl)pyridin-2-yl, 6-(C1-C3-Alkyl)pyridin-2-yl, Chinolin-2-yl, Isochinolin-3-yl, 8-Halogenchinolin-2-yl, Benzothiazol-2-yl, 4,5,6,7-Tetrahydro-1,3-benzothiazol-2-yl.

5. Verbindung nach Anspruch **4,** ausgewählt aus den Formeln Ie-1, Ie-2 und Ie-3,



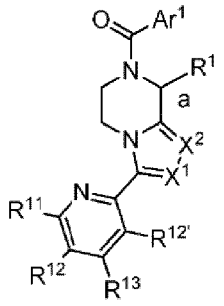
Ie-1 Ie-2 Ie-3

und pharmazeutisch verträgliche Salze und Solvate davon, wobei

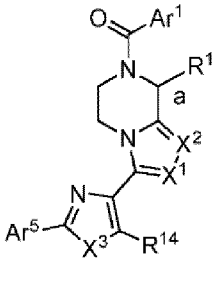
a die Bindung zeigt, die **R1** mit dem Piperazinrest verbindet; und
Ar2, **R1**, **X1** und **X2** wie in Anspruch **2** definiert sind; und
R5 und **R6** unabhängig ausgewählt sind aus H, Halogen, Cyano, Alkyl, Cyclopropyl, Aryl, Heteroaryl, wobei jede der besagten Aryl- und Heteroarylgruppen gegebenenfalls mit einer oder mehreren Gruppe(n), ausgewählt aus Halogen, Alkyl, Cyclopropyl substituiert ist, oder **R5** und **R6** zusammen einen Phenylrest bilden, der mit dem Phenylring, an den sie gebunden sind, fusioniert ist; und
R8, **R8'**, **R9**, **R9'** und **R10** unabhängig ausgewählt sind aus H, Halogen, Halogenalkyl, Cyclopropyl oder Halogenalkoxy, oder **R8**, **R8'**, **R9**, **R9'** H sind und **R10** Phenoxy ist; **M1** und **M2** wie in Anspruch **4** definiert sind; und wobei, in Formel Ie-1, wenn:

R1 H ist, und
R5 und **R6** unabhängig ausgewählt sind aus H, Halogen, Cyano, C1-C3-Alkyl, und
Ar2 eine 5- bis 6-gliedrige Aryl- oder Heteroarylgruppe ist, die gegebenenfalls mit einer oder mehreren Gruppe(n), ausgewählt aus Halogen, C1-C3-Alkyl, Hydroxyl, Alkoxy substituiert, oder mit einer Arylgruppe fusioniert ist, welche gegebenenfalls mit einem oder mehreren weiteren Halogen, C1-C3-Alkyl, Hydroxyl, Methoxy substituiert ist,
dann,
ist **R6** H und ist **R5** H, Halogen, oder ist **R5** H und ist **R6** Halogen, Cyano, C1-C3-Alkyl, C1-Halogenalkyl, oder sind **R5** und **R6** unabhängig Halogen, und
ist **Ar2** 2-(C1-C3-Alkyl)thiazol-4-yl, 5-(C1-C3-Alkyl)thiazol-4-yl, Pyridin-2-yl, 4-Halogenpyridin-2-yl, 4-(C1-C3-Alkyl)pyridin-2-yl, 5-(C1-C3-Alkyl)pyridin-2-yl, 6-(C1-C3-Alkyl)pyridin-2-yl, Chinolin-2-yl, Isochinolin-3-yl, 8-Halogenchinolin-2-yl, Benzothiazol-2-yl, 4,5,6,7-Tetrahydro-1,3-benzothiazol-2-yl.

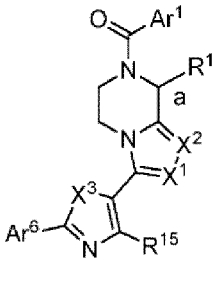
6. Verbindung nach Anspruch **3,** ausgewählt aus den Formeln If-1, If-2, If-3, If-4, If-5, If-6, If-7 und If-8,



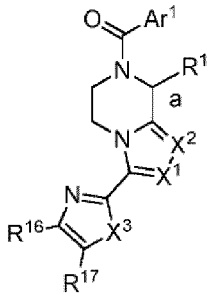
If-1



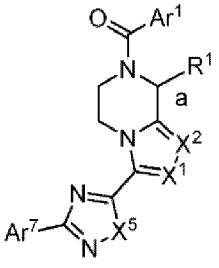
If-2



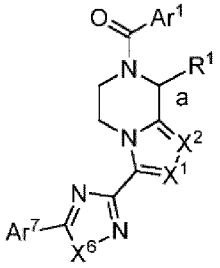
If-3



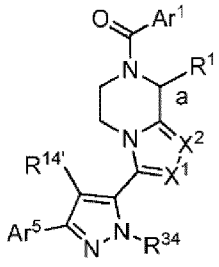
If-4



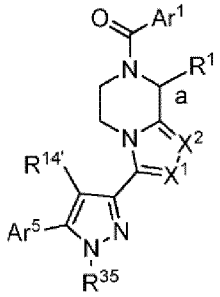
If-5



If-6



If-7



If-8

und pharmazeutisch verträgliche Salze und Solvate davon, wobei

a die Bindung bezeichnet, die **R^1** mit dem Piperazinrest verbindet; und
Ar^1, **R^1**, **X^1** und **X^2** wie in Anspruch **2** definiert sind; und
R^{11}, **R^{12}**, **R$^{12'}$** und **R^{13}** unabhängig ausgewählt sind aus H, Halogen, Cyano, Alkyl, Hydroxyalkyl, Halogenalkyl, C3-C6-Cycloalkyl, Heteroalkyl, Heterocyclyl, Aryl, Heteroaryl, Hydroxyl, Alkoxy, Halogenalkoxy, Alkylamino, Carboxy, Alkoxycarbonyl, Alkylcarbonyloxy, Alkylcarbonylamino, Halogenalkylcarbonylamino, Acylamino, Carbamoyl, Alkylcarbamoyl, Carbamoylalkyl, Carbamoylamino, Alkylcarbamoylamino, Alkylsulfonyl, Halogenalkylsulfonyl, Sulfamoyl, Alkylsulfamoyl, Alkylsulfonylamino, Halogenalkylsulfonylamino, oder **R^{12}** zusammen mit **R^{11}** oder **R^{13}**, oder **R^{13}** zusammen mit **R$^{12'}$** eine Alkylendioxygruppe oder eine Halogenalkylendioxygruppe bildet, oder **R^{12}** zusammen mit **R^{11}** oder **R^{13}** einen Cycloalkyl-, Aryl-, Heterocyclyl- oder Heteroarylrest bildet, der mit der Pyridylgruppe, an die sie gebunden sind, fusioniert ist, wobei jede der besagten Gruppen gegebenenfalls mit einer oder mehreren Gruppe(n), ausgewählt aus Halogen, Cyano, Alkyl, Halogenalkyl, Cyclopropyl, Alkoxy, Halogenalkoxy oder Hydroxyl substituiert ist; und
Ar^5 eine Heterocyclyl-, Aryl-, Heteroaryl-, Aralkyl-, Heteroarylalkyl- oder Arylsulfonylalkylgruppe ist, von denen jede gegebenenfalls mit einer oder mehreren Gruppe(n), ausgewählt aus Halogen, Cyano, Alkyl, Halogenalkyl, Cyclopropyl, Alkoxy, Halogenalkoxy, Heterocyclyl substituiert ist, welche gegebenenfalls mit Alkyl, Aryl, Hydroxyl, Alkoxy, Alkoxyalkyl, Hydroxyalkoxy, Alkylamino, Alkylsulfonylamino, Aminoalkoxy oder Alkoxycarbonylaminoalkoxy substituiert sind; und
X^3 O oder S ist; und
R^{14} H oder Methyl ist; und
Ar^6 eine Heterocyclyl-, Aryl- oder Heteroarylgruppe ist, von denen jede gegebenenfalls mit einer oder mehreren Gruppe(n), ausgewählt aus Halogen, Cyano, Alkyl, Halogenalkyl, Cyclopropyl, Alkoxy, Halogenalkoxy, Aryl oder Hydroxyl substituiert ist; und
R^{15} H oder Methyl ist; und
R^{16} eine Heterocyclyl-, Aryl- oder Heteroarylgruppe ist, wobei jede der besagten Gruppen gegebenenfalls mit einer oder mehreren Gruppe(n), ausgewählt aus Halogen, Cyano, Alkyl, Halogenalkyl, Cyclopropyl, Alkoxy, Halogenalkoxy oder Hydroxyl substituiert ist;
R^{17} H, Methyl ist, oder **R^{17}** zusammen mit **R^{16}** einen Cycloalkyl- oder Arylrest bildet, der mit der Thiazolylgruppe, an die sie gebunden sind, fusioniert ist und somit ein kondensiertes Ringsystem bildet, wobei das besagte

kondensierte Ringsystem gegebenenfalls mit einer oder mehreren Gruppe(n), ausgewählt aus Halogen, Cyano, Alkyl, Halogenalkyl, Cyclopropyl, Alkoxy, Halogenalkoxy oder Hydroxyl substituiert ist; und
X^5 O oder S, oder N-**R^{36}** ist, wobei **R^{36}** H oder C1-C3-Alkyl ist; und
Ar^7 eine Heterocyclyl-, Aryl- oder Heteroarylgruppe ist, von denen jede gegebenenfalls mit einer oder mehreren Gruppe(n), ausgewählt aus Halogen, Cyano, Alkyl, Halogenalkyl, Cyclopropyl, Alkoxy, Halogenalkoxy, Aryl oder Hydroxyl substituiert ist; und
X^6 0, S oder N-**R$^{36'}$** ist, wobei **R$^{36'}$** H oder C1-C3-Alkyl ist; und
R$^{14'}$ H oder Methyl ist; und
R^{34} H, Alkyl, Alkoxyalkyl, Hydroxyalkyl, Alkoxycarbonylaminoalkyl ist; und
R^{35} H, Alkyl, Alkoxyalkyl, Hydroxyalkyl, Alkoxycarbonylaminoalkyl ist; und
wobei,

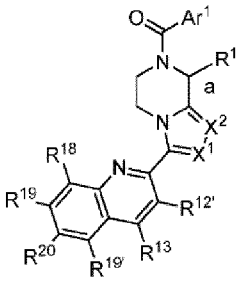
- in Formel If-1, wenn:

  R^1 H ist, und
  Ar^1 ein gegebenenfalls mit einer oder mehreren Gruppe(n), ausgewählt aus Halogen, Cyano, C1-C3-Alkyl, C1-Halogenalkyl substituiertes 6-gliedriges Aryl ist, und
  R^{11}, **R^{12}**, **R$^{12'}$** und **R^{13}** unabhängig ausgewählt sind aus H, Halogen, C1-C3-Alkyl, Hydroxyl, Methoxy, oder **R^{12}** zusammen mit **R^{11}** oder **R^{13}** einen Aryl- oder Heterocyclyl- oder Heteroarylrest bildet, der mit der Pyridylgruppe, an die sie gebunden sind, fusioniert ist und gegebenenfalls mit einer oder mehreren Gruppe(n), ausgewählt aus Halogen, C1-C3-Alkyl, Methoxy oder Hydroxyl substituiert ist, dann, ist **Ar^1** Phenyl, 3-Halogenphenyl, 4-Halogenphenyl, 2,3-Dichlorphenyl, 3,4-Dihalogenphenyl, 3,4,5-Trihalogenphenyl, 4-Cyanophenyl, 4-(C1-C3-Alkyl)phenyl, 4-(C1-Halogenalkyl)phenyl, und sind **R^{11}**, **R^{12}**, **R$^{12'}$** und **R^{13}** H, oder sind **R^{11}**, **R^{12}**, **R$^{12'}$** H und ist **R^{13}** Halogen, C1-C3-Alkyl, oder sind **R^{11}**, **R$^{12'}$**, **R^{13}** H und ist **R^{12}** C1-C3-Alkyl, oder sind **R^{12}**, **R$^{12'}$**, **R^{13}** H und ist **R^{11}** C1-C3-Alkyl, oder bilden **R^{11}**, **R^{12}**, **R$^{12'}$** und **R^{13}** zusammen mit der Pyridylgruppe, an die sie gebunden sind, einen Chinolin-2-yl-, Isochinolin-3-yl- oder 8-Halogenchinolin-2-yl-Rest; und

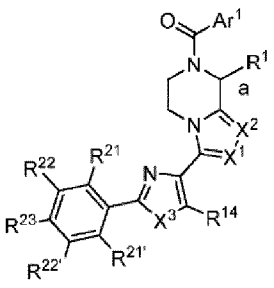
- in Formel If-4, wenn:

  R^1 H ist, und
  Ar^1 ein gegebenenfalls mit einer oder mehreren Gruppe(n), ausgewählt aus Halogen, Cyano, C1-C3-Alkyl, C1-Halogenalkyl substituiertes 6-gliedriges Aryl ist, und
  R^{17} zusammen mit **R^{16}** einen Cycloalkyl- oder Arylrest bildet, der mit der Thiazolylgruppe, an die sie gebunden sind, fusioniert ist und somit ein kondensiertes Ringsystem bildet, wobei das besagte kondensierte Ringsystem gegebenenfalls mit einer oder mehreren Gruppe(n), ausgewählt aus Halogen, C1-3-Alkyl, Methoxy oder Hydroxyl substituiert ist,
  dann
  ist **Ar^1** Phenyl, 3-Halogenphenyl, 4-Halogenphenyl, 2,3-Dichlorphenyl, 3,4-Dihalogenphenyl, 3,4,5-Trihalogenphenyl, 4-Cyanophenyl, 4-(C1-C3-Alkyl)phenyl, 4-(C1-Halogenalkyl)phenyl, und
  bilden **R^{17}** und **R^{16}** zusammen mit der Thiazolylgruppe, an die sie gebunden sind, einen Benzothiazol-2-yl- oder 4,5,6,7-Tetrahydro-1,3-benzothiazol-2-yl-Rest.

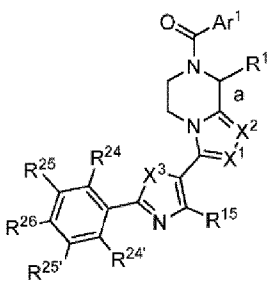
7. Verbindung nach Anspruch **6,** ausgewählt aus den Formeln Ig-1, Ig-2, Ig-3, Ig-4, Ig-5, Ig-6, Ig-7 und Ig-8,



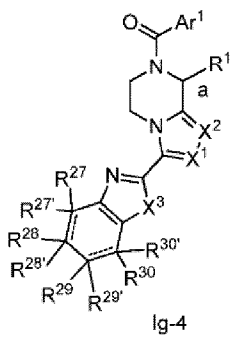
Ig-1



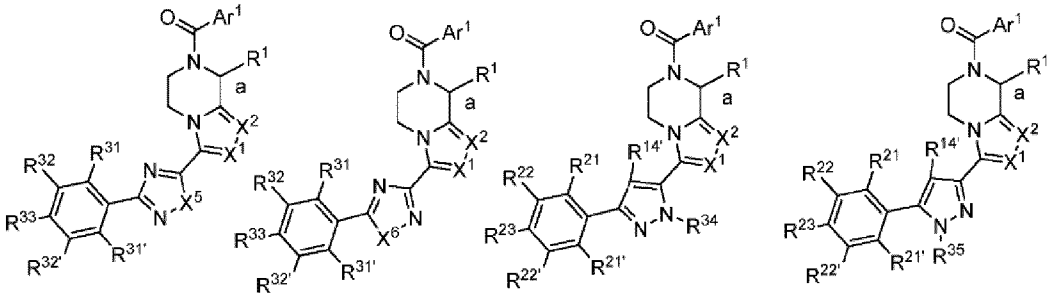
Ig-2



Ig-3



Ig-4



Ig-5 Ig-6 Ig-7 Ig-8

und pharmazeutisch verträgliche Salze und Solvate davon, wobei

a die Bindung zeigt, die **R^1** mit dem Piperazinrest verbindet; und
Ar^1, **R^1**, **X^1** und **X^2** wie in Anspruch **2** definiert sind; und
R^{14}, **R$^{14'}$**, **R^{15}**, **R^{34}**, **R^{35}**, **X^3**, **X^5** und **X^6** wie in Anspruch **6** definiert sind; und
R$^{12'}$ und **R^{13}** unabhängig ausgewählt sind aus H, Halogen, Cyano, Alkyl, Hydroxyalkyl, Halogenalkyl, Cycloalkyl, Heteroalkyl, Hydroxyl, Alkoxy, Halogenalkoxy, Carboxy, Alkoxycarbonyl, Alkylcarbonyloxy, Alkylcarbonylamino, Halogenalkylcarbonylamino, Acylamino, Carbamoyl, Alkylcarbamoyl, Carbamoylalkyl, Carbamoylamino, Alkylcarbamoylamino, Alkylsulfonyl, Halogenalkylsulfonyl, Sulfamoyl, Alkylsulfamoyl, Alkylsulfonylamino, Halogenalkylsulfonylamino, oder **R^{13}** zusammen mit **R$^{12'}$** eine Alkylendioxygruppe oder eine Halogenalkylendioxygruppe bildet, wobei jede der besagten Gruppen gegebenenfalls mit einer oder mehreren Gruppe(n), ausgewählt aus Halogen, Cyano, Alkyl, Halogenalkyl, Alkoxy, Halogenalkoxy, Hydroxyl oder Oxo substituiert ist; und
R^{18}, **R^{19}**, **R$^{19'}$** und **R^{20}** unabhängig ausgewählt sind aus H, Halogen, Cyano, Alkyl, Halogenalkyl, Cyclopropyl, Alkoxy, Halogenalkoxy; und
R^{21}, **R$^{21'}$**, **R^{22}**, **R$^{22'}$** und **R^{23}** unabhängig ausgewählt sind aus H, Halogen, Cyano, Alkyl, Halogenalkyl, Cyclopropyl, Heterocyclyl, die gegebenenfalls mit Alkyl, Hydroxyl, Alkoxy, Halogenalkoxy, Hydroxyalkoxy, Alkylamino, Alkylsulfonylamino, Aminoalkoxy, Alkoxycarbonylaminoalkoxy substituiert sind; und
R^{24}, **R$^{24'}$**, **R^{25}**, **R$^{25'}$** und **R^{26}** unabhängig ausgewählt sind aus H, Halogen Halogenalkyl, Cyclopropyl; und
R^{27}, **R^{28}**, **R^{29}** und **R^{30}** unabhängig ausgewählt sind aus H, Halogen, Cyano, Alkyl, Halogenalkyl, Cyclopropyl, Alkoxy, Halogenalkoxy; und
R$^{27'}$, **R$^{28'}$**, **R$^{29'}$** und **R$^{30'}$** fehlen, oder **R$^{27'}$**, **R^{28}**, **R$^{29'}$** und **R$^{30'}$** H sind unter der Bedingung, dass **R^{28}**, **R^{29}** und **R^{30}** H sind und dass **R^{27}** ausgewählt ist aus H, Chlor oder Fluor; und
die zwei in Formel Ig-4 von den gestrichelten Linien dargestellten Bindungen beide fehlen oder beide vorhanden sind unter der Bedingung, dass **R$^{27'}$**, **R$^{28'}$**, **R$^{29'}$** und **R$^{30'}$** fehlen; und
R^{31}, **R$^{31'}$**, **R^{32}**, **R$^{32'}$** und **R^{33}** unabhängig ausgewählt sind aus H, Halogen, Cyano, Alkyl, Halogenalkyl, Cyclopropyl, Alkoxy, Halogenalkoxy; und
wobei,

- in Formel Ig-1, wenn:

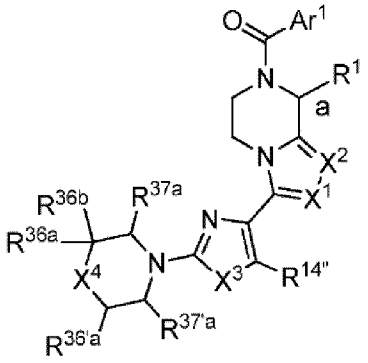
  R^1 H ist, und
  Ar^1 ein gegebenenfalls mit einer oder mehreren Gruppe(n), ausgewählt aus Halogen, Cyano, C1-C3-Alkyl, C1-Halogenalkyl substituiertes 6-gliedriges Aryl ist, und
  R$^{12'}$, **R^{13}**, **R^{18}**, **R^{19}**, **R$^{19'}$** und **R^{20}** unabhängig ausgewählt sind aus H, Halogen, C1-3-Alkyl, Hydroxyl, Methoxy,
  dann,
  ist **Ar^1** Phenyl, 3-Halogenphenyl, 4-Halogenphenyl, 2,3-Dichlorphenyl, 3,4-Dihalogenphenyl, 3,4,5-Trihalogenphenyl, 4-Cyanophenyl, 4-(C1-C3-Alkyl)phenyl, 4-(C1-Halogenalkyl)phenyl, und
  sind **R$^{12'}$**, **R^{13}**, **R^{18}**, **R^{19}**, **R$^{19'}$** und **R^{20}** H, oder sind **R$^{12'}$**, **R^{13}**, **R^{19}**, **R$^{19'}$**, **R^{20}** H und ist **R^{18}** Fluor, Chor, und

- in Formel Ig-4, wenn

  R^1 H ist, und
  Ar^1 ein gegebenenfalls mit einer oder mehreren Gruppe(n), ausgewählt aus Halogen, Cyano, C1-C3-Alkyl, C1-Halogenalkyl substituiertes 6-gliedriges Aryl ist, und

R^{27}, R^{28}, R^{29} und R^{30} unabhängig ausgewählt sind aus H, Halogen, C1-C3-Alkyl, Methoxy, und
$R^{27'}$, $R^{28'}$, $R^{29'}$ und $R^{30'}$ fehlen oder H sind unter der Bedingung, dass R^{28}, R^{29} und R^{30} H sind und
R^{27} ausgewählt ist aus H, Chlor oder Fluor,
dann
ist Ar^1 Phenyl, 3-Halogenphenyl, 4-Halogenphenyl, 2,3-Dichlorphenyl, 3,4-Dihalogenphenyl, 3,4,5-Trihalogenphenyl, 4-Cyanophenyl, 4-(C1-C3-Alkyl)phenyl, 4-(C1-Halogenalkyl)phenyl, und
sind R^{27}, R^{28}, R^{29} und R^{30} H, und
fehlen $R^{27'}$, $R^{28'}$, $R^{29'}$ und $R^{30'}$ oder sind H unter der Bedingung, dass R^{27}, R^{28}, R^{29} und R^{30} H sind.

8. Verbindung der Formel If-2 nach Anspruch **6,** mit der Formel Ih-2

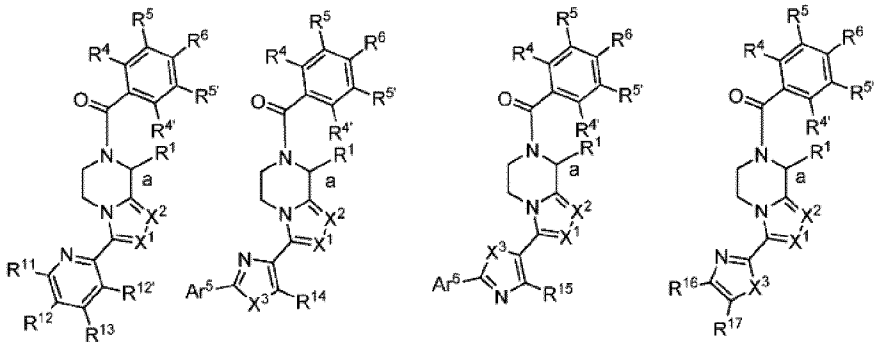


Ih-2

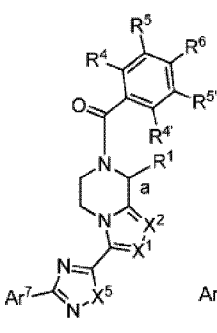
und pharmazeutisch verträgliche Salze und Solvate davon, wobei

a die Bindung bezeichnet, die R^1 mit dem Piperazinrest verbindet; und
Ar^1, R^1, X^1 und X^2 wie in Anspruch **2** definiert sind; und
X^3 wie in Anspruch **6** definiert ist; und
$R^{14"}$ H oder Methyl ist; und
X^4 O, CH_2, CF_2, $C(CH_3)_2$, N-(Cl-C3-Alkyl)-N-phenyl ist; und
R^{36a}, R^{36b}, $R^{36'a}$, R^{37a} und $R^{37'a}$ unabhängig ausgewählt sind aus H, C1-C3-Alkyl, Alkoxy-C1-C3-alkyl.

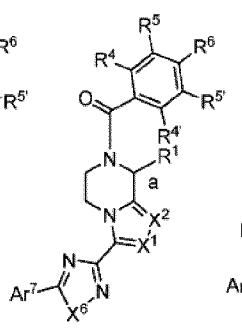
9. Verbindung nach Anspruch **3,** ausgewählt aus den Formeln Ii-1, Ii-2, Ii-3, Ii-4, Ii-5, Ii-6, Ii-7, Ii-8, Ij-1, Ij-2, Ij-3, Ij-4, Ij-5, Ij-6, Ij-7, Ij-8, Ik-1, Ik-2, Ik-3, Ik-4, Ik-5, Ik-6, Ik-7, Ik-8, Ii'-1, Ii'-2, Ii'-3, Ii'-4, Ii'-5, Ii'-6, Ii'-7 und Ii'-8,



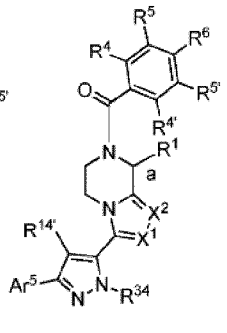
Ii-1 Ii-2 Ii-3 Ii-4



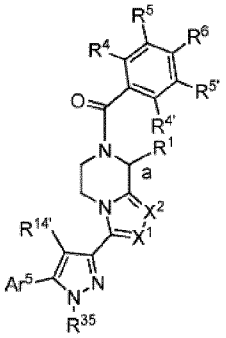
Ii-5



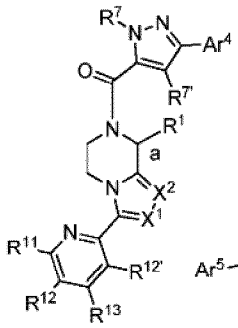
Ii-6



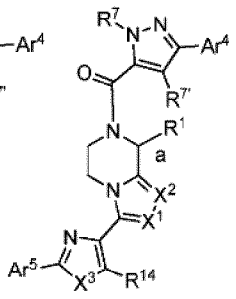
Ii-7



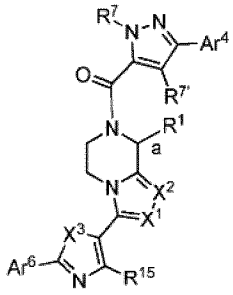
Ii-8



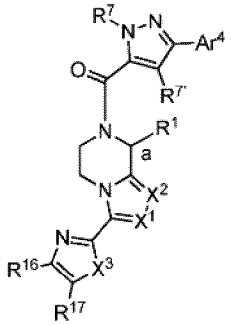
Ij-1



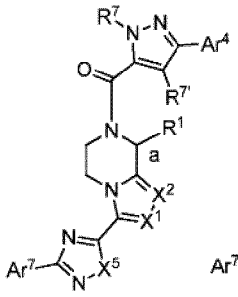
Ij-2



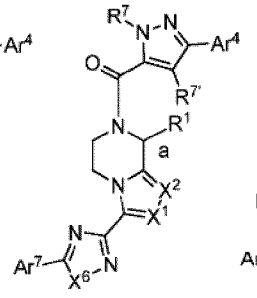
Ij-3



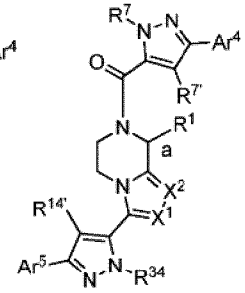
Ij-4



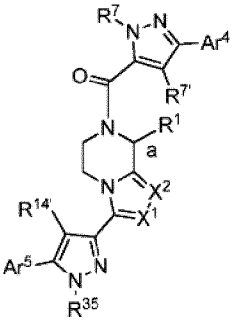
Ij-5



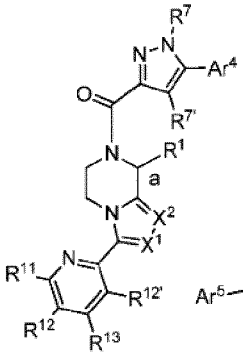
Ij-6



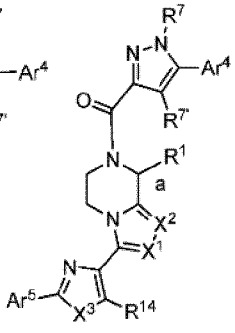
Ij-7



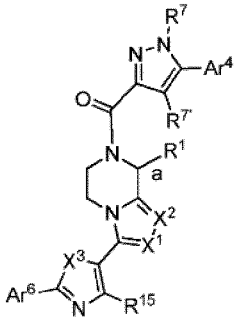
Ij-8



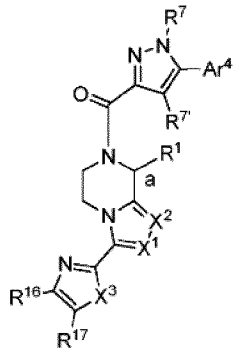
Ik-1



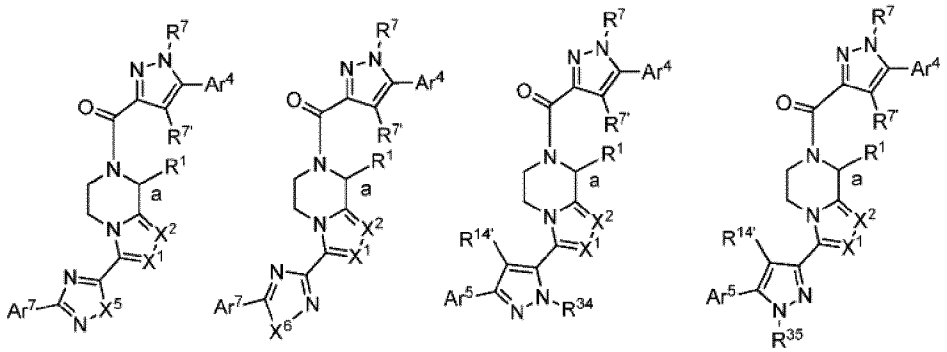
Ik-2



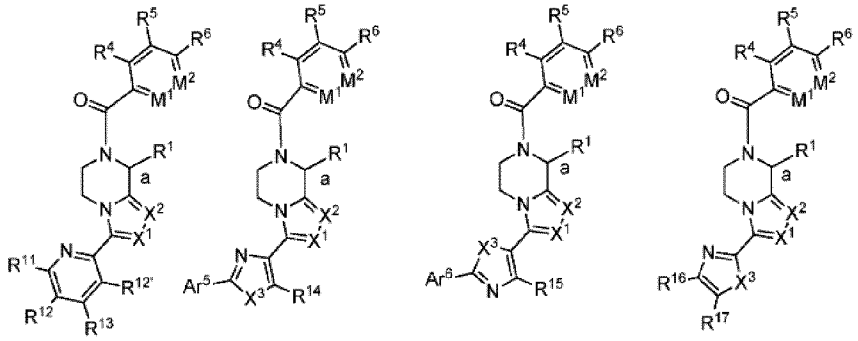
Ik-3



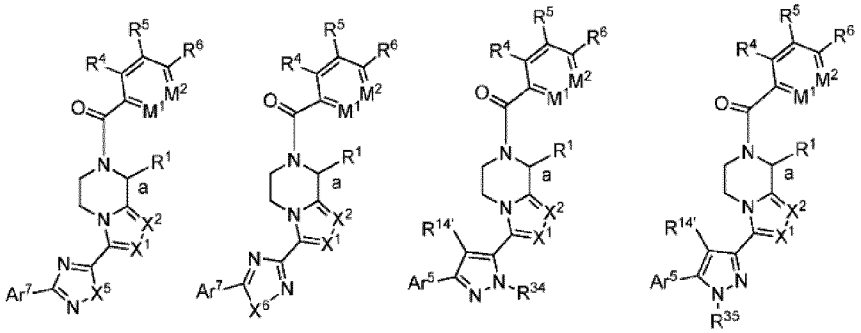
Ik-4



Ik-5 Ik-6 Ik-7 Ik-8



Ii'-1 Ii'-2 Ii'-3 Ii'-4

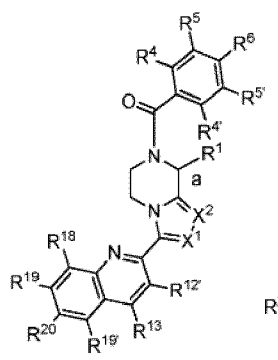


Ii'-5 Ii'-6 Ii'-7 Ii'-8

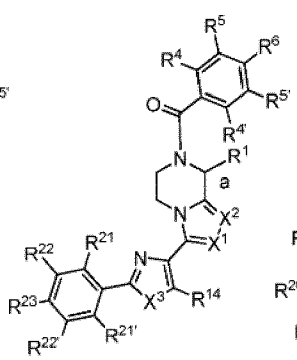
und pharmazeutisch verträgliche Salze und Solvate davon, wobei

a die Bindung zeigt, die **R^1** mit dem Piperazinrest verbindet; und
R^1, **X^1** und **X^2** wie in Anspruch **2** definiert sind; und
Ar^4, **R^4**, **$R^{4'}$**, **R^5**, **$R^{5'}$**, **R^6**, **R^7**, **$R^{7'}$**, **M^1**, **M^2** wie in Anspruch 4 definiert sind; und
Ar^5, **Ar^6**, **Ar^7**, **R^{11}**, **R^{12}**, **$R^{12'}$**, **R^{13}**, **R^{14}**, **$R^{14'}$**, **R^{15}**, **R^{16}**, **R^{17}**, **R^{34}**, **R^{35}**, **X^3**, **X^5** und **X^6** wie in Anspruch **6** definiert sind.

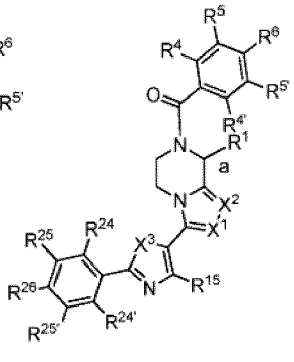
10. Verbindung nach Anspruch **9,** ausgewählt aus den Formeln II-1, II-2, II-3, II-4, II-5, II-6, II-7, II-8, II'-1, II'-2, II'-3, II'-4, II'-5, II'-6, II'-7, II'-8,



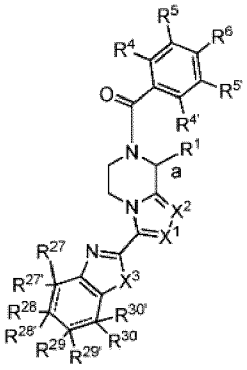
II-1



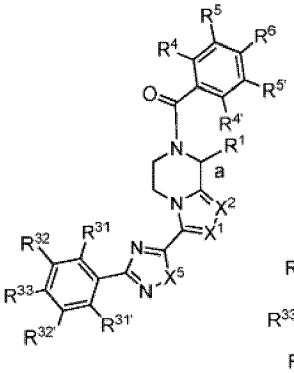
II-2



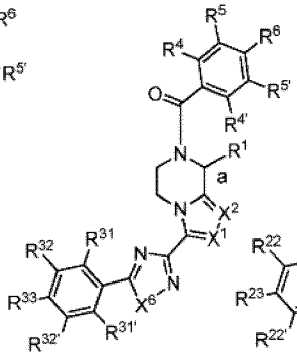
II-3



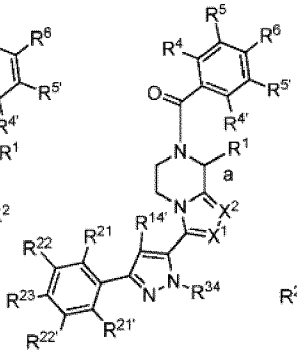
II-4



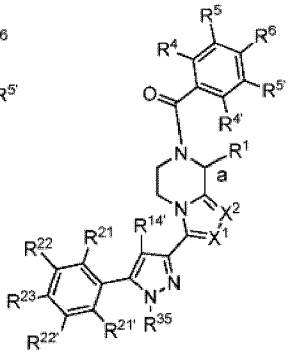
II-5



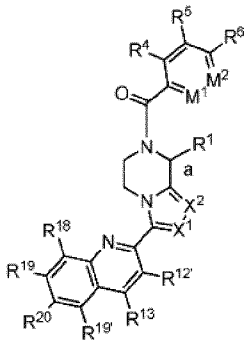
II-6



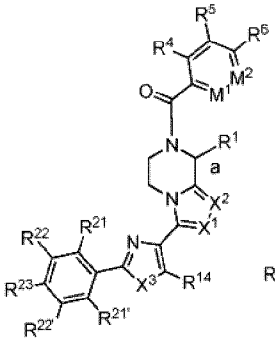
II-7



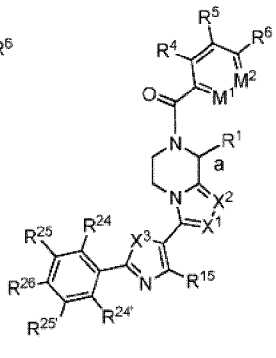
II-8



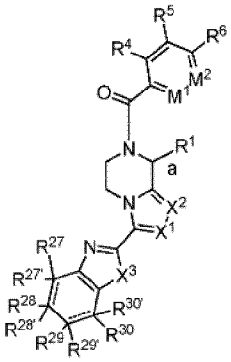
II'-1



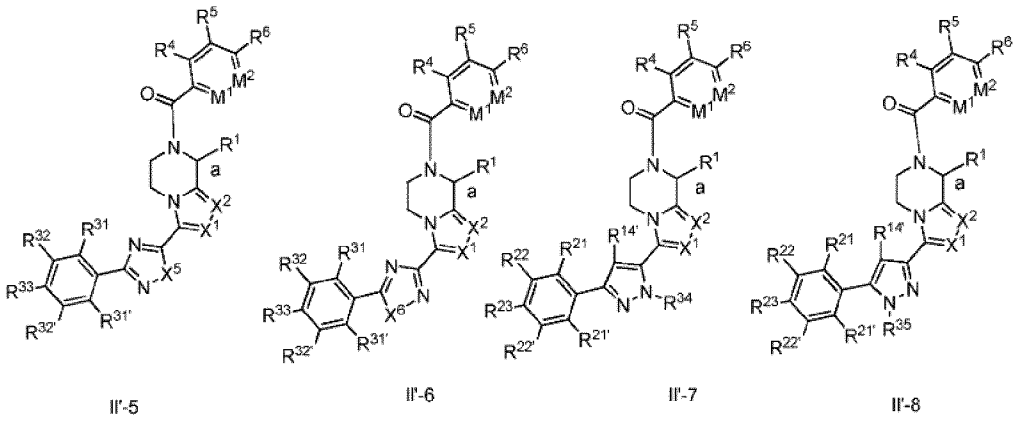
II'-2



II'-3



II'-4

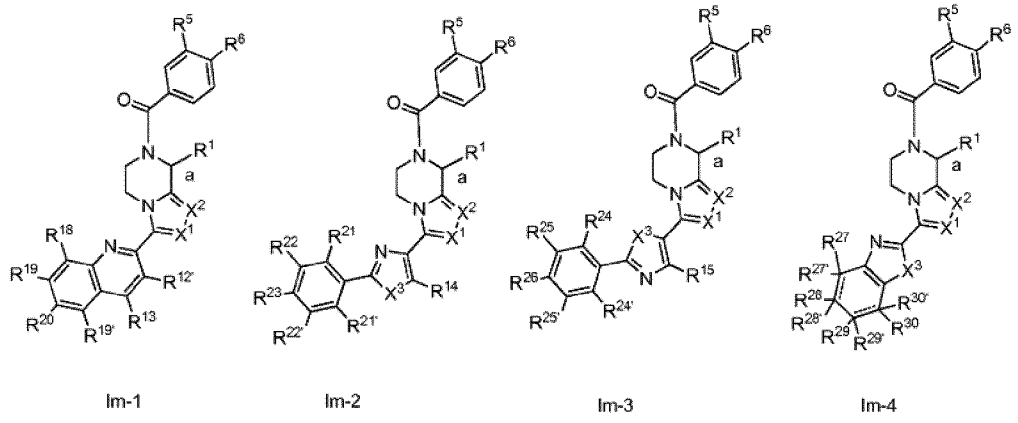


Il'-5 Il'-6 Il'-7 Il'-8

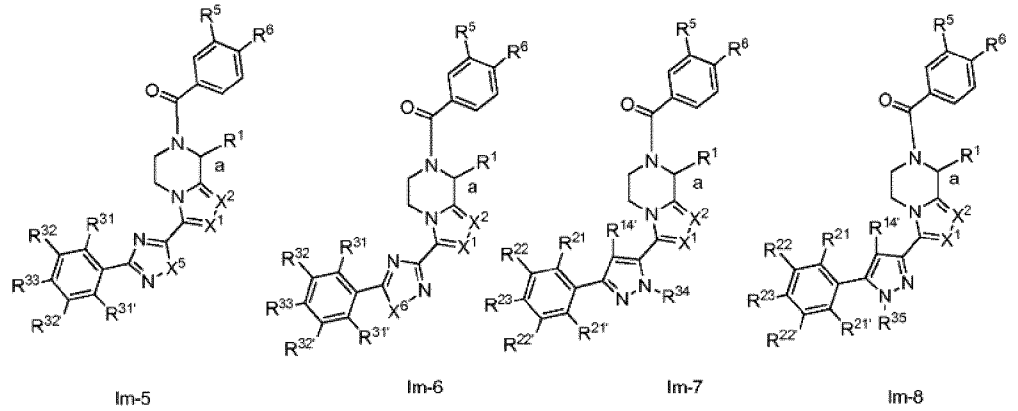
und pharmazeutisch verträgliche Salze und Solvate davon, wobei:

a die Bindung zeigt, die R^1 mit dem Piperazinrest verbindet; und
R^1, X^1 und X^2 wie in Anspruch **2** definiert sind; und
R^4, $R^{4'}$, R^5, $R^{5'}$, R^6, M^1 und M^2 wie in Anspruch **4** definiert sind; und
$R^{12'}$, R^{13}, R^{14}, $R^{14'}$, R^{15}, R^{18}, R^{19}, $R^{19'}$, R^{20}, R^{21}, $R^{21'}$, R^{22}, $R^{22'}$, R^{23}, R^{24}, $R^{24'}$, R^{25}, $R^{25'}$, R^{26}, R^{27}, $R^{27'}$, R^{28}, $R^{28'}$, R^{29}, $R^{29'}$, R^{30}, $R^{30'}$, R^{31}, $R^{31'}$, R^{32}, $R^{32'}$, R^{33}, R^{34}, R^{35}, X^3, X^5, X^6 und die zwei von den gestrichelten Linien dargestellten Bindungen wie in Anspruch **7** definiert sind.

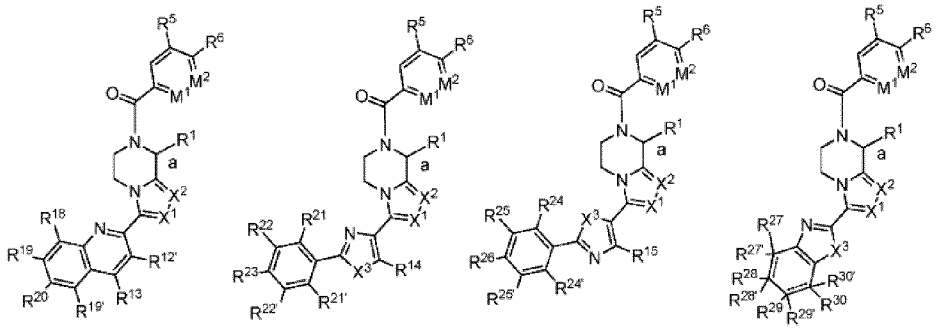
11. Verbindung nach Anspruch **10,** ausgewählt aus den Formeln Im-1, Im-2, Im-3, Im-4, Im-5, Im-6, Im-7, Im-8, Im'-1, Im'-2, Im'-3, Im'-4, Im'-5, Im'-6, Im'-7 und Im'-8,



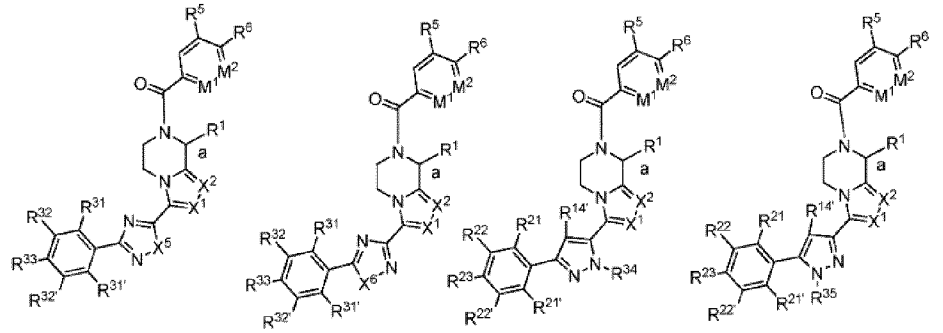
Im-1 Im-2 Im-3 Im-4



Im-5 Im-6 Im-7 Im-8



Im'-1 Im'-2 Im'-3 Im'-4



Im'-5 Im'-6 Im'-7 Im'-8

und pharmazeutisch verträgliche Salze und Solvate davon, wobei:

a die Bindung bezeichnet, die R^1 mit dem Piperazinrest verbindet; und
R^1, X^1 und X^2 wie in Anspruch **2** definiert sind; und
R^5, R^6, M^1 und M^2 wie in Anspruch **5** definiert sind; und
$R^{12'}$, R^{13}, R^{14}, $R^{14'}$, R^{15}, R^{18}, R^{19}, $R^{19'}$, R^{20}, R^{21}, $R^{21'}$, R^{22}, $R^{22'}$, R^{23}, R^{24}, $R^{24'}$, R^{25}, $R^{25'}$, R^{26}, R^{27}, $R^{27'}$, R^{28}, $R^{28'}$, R^{29}, $R^{29'}$, R^{30}, $R^{30'}$, R^{31}, $R^{31'}$, R^{32}, $R^{32'}$, R^{33}, R^{34}, R^{35}, X^3, X^5, X^6 und die zwei von den gestrichelten Linien dargestellten Bindungen wie in Anspruch **7** definiert sind.

12. Verbindung nach Anspruch **1,** ausgewählt aus der Gruppe bestehend aus:

(4-Fluorphenyl)(3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(4-Chlorphenyl)(3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(3-(4-Chlorphenyl)-1H-pyrazol-5-yl)(3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(3-(3,4-Dichlorphenyl)-1H-pyrazol-5-yl)(3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(3,4-Dichlorphenyl)(3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
[1,1'-Biphenyl]-4-yl(3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(4-Fluorphenyl)(3-(chinolin-2-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(4-Fluorphenyl)(3-(2-phenylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(4-Fluorphenyl)(3-(2-morpholinothiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(3-(5-Chlorpyridin-2-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-fluorphenyl)methanon;
(4-Fluorphenyl)(3-(6-methylpyridin-2-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(4-Fluorphenyl)(8-methyl-3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(3-(2,4-Dichlorphenyl)-1H-pyrazol-5-yl)(3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(3-(3,4-Dichlorphenyl)-1-methyl-1H-pyrazol-5-yl)(3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(4-Fluorphenyl)(3-(isochinolin-3-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;

(4'-Fluor-[1,1'-biphenyl]-4-yl)(3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(3-(Pyridin-2-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(3-(4-(trifluormethyl)phenyl)-1H-pyrazol-5-yl)methanon;
(3-(4-Phenoxyphenyl)-1H-pyrazol-5-yl)(3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
[1,1'-Biphenyl]-4-yl(3-(chinolin-2-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
[1,1'-Biphenyl]-4-yl(3-(2-morpholinothiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(3-(Pyridin-2-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanon;
(4-Fluorphenyl)(3-(8-fluorchinolin-2-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(3-(8-Chlorchinolin-2-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-fluorphenyl)methanon;
(4-Fluorphenyl)(3-(2-(4-(trifluormethyl)phenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(4-Fluorphenyl)(3-(6-phenylpyridin-2-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
[1,1'-Biphenyl]-4-yl(3-(2-phenylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(4-Fluorphenyl)(3-(4,5,6,7-tetrahydrobenzo[d]thiazol-2-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(4-Fluorphenyl)(3-(2-(3-(trifluormethyl)phenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(3-(2-(2,4-Difluorphenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-fluorphenyl)methanon;
(3-(2-(2,3-Dichlorphenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-fluorphenyl)methanon;
(3-(2-(4-Chlorphenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-fluorphenyl)methanon;
(4-Fluorphenyl)(3-(2-(4-fluorphenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(4-Fluorphenyl)(3-(2-(piperidin-1-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(4-Fluorphenyl)(3-(2-(4-phenylpiperazin-1-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(3-(2-(2,4-Dichlorphenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-fluorphenyl)methanon;
(3-(2-(3,5-Dichlorphenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-fluorphenyl)methanon;
(4-Fluorphenyl)(3-(6-(pyrrolidin-1-yl)pyridin-2-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(4-Fluorphenyl)(3-(6-morpholinopyridin-2-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(4-Fluorphenyl)(3-(6-(trifluormethyl)pyridin-2-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(3-(2-(3,4-Dimethoxyphenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-fluorphenyl)methanon;
(4-Fluorphenyl)(8-(4-fluorphenyl)-3-(2-phenylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(3-(2-(3-Chlorphenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-fluorphenyl)methanon;
(4-Fluorphenyl)(8-isopropyl-3-(2-phenylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(R)-(4-Fluorphenyl)(8-methyl-3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(R)-(4-Fluorphenyl)(8-methyl-3-(2-phenylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
[1,1'-Biphenyl]-4-yl(8-methyl-3-(2-morpholinothiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(4-Fluorphenyl)(3-(2-phenyloxazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(4-Fluorphenyl)(8-methyl-3-(2-phenyloxazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
[1,1'-Biphenyl]-4-yl(8-methyl-3-(2-phenyloxazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
[1,1'-Biphenyl]-4-yl(3-(2-phenyloxazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(4-Fluorphenyl)(8-(2-hydroxyethyl)-3-(2-phenylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(4-Fluorphenyl)(8-methyl-3-(2-morpholinothiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(4'-Fluor-[1,1'-biphenyl]-4-yl)(8-methyl-3-(2-morpholinothiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(3-(2-Phenylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanon;

(3-(2-Morpholinothiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4- (thiophen-2-yl)phenyl)methanon;
(8-Methyl-3-(2-morpholinothiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanon;
(4-Fluorphenyl)(3-(4-phenylthiazol-2-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(3-(2-(2-Chlorphenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-fluorphenyl)methanon;
(3-(Benzo[d]thiazol-2-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-fluorphenyl)methanon;
(8,8-Dimethyl-3-(2-phenylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-fluorphenyl)methanon;
(4-Fluorphenyl)(8-methyl-3-(chinolin-2-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(8-Methyl-3-(2-phenylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanon;
(3-(2-Phenylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-3-yl)phenyl)methanon;
(8-Methyl-3-(2-phenylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-3-yl)phenyl)methanon;
(8-Methyl-3-(chinolin-2-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanon;
(3-(2-(2-Chlorphenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanon;
[1,1'-Biphenyl]-4-yl(3-(2-(2-chlorphenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(R)-(3-(2-(4-Chlorphenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-fluorphenyl)methanon;
(3-(Chinolin-2-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanon;
(4-Fluorphenyl)(3-(2-(4-fluorphenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(R)-(4-Fluorphenyl)(3-(2-(4-fluorphenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
[1,1'-Biphenyl]-4-yl(8-methyl-3-(4-methyl-2-phenylthiazol-5-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(3-(2-(4-Fluorphenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanon;
(3-(2-(2-Chlorphenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-fluorphenyl)methanon;
(4-Fluorphenyl)(8-methyl-3-(4-methyl-2-phenylthiazol-5-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
[1,1'-Biphenyl]-4-yl(3-(2-(4-fluorphenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(3-(2-(2,4-Difluorphenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-fluorphenyl)methanon;
(3-(2-(4-Fluorphenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanon;
[1,1'-Biphenyl]-4-yl(3-(2-(2,4-difluorphenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(3-(2-(2,4-Difluorphenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanon;
Naphthalen-1-yl(3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(3-(4-Chlorphenyl)-1-methyl-1H-pyrazol-5-yl)(3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(5-(4-Chlorphenyl)-1-methyl-1H-pyrazol-3-yl)(3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(8-Methyl-3-(5-phenyl-1,2,4-oxadiazol-3-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanon;
(8-Methyl-3-(3-phenyl-1,2,4-oxadiazol-5-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanon;
(R)-(3-(2-(4-Fluorphenyl)oxazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanon;
(5-Phenylpyridin-2-yl)(3-(chinolin-2-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;

(6-Phenylpyridin-3-yl)(3-(chinolin-2-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(2-Phenylpyrimidin-5-yl) (3-(chinolin-2-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(4-Phenylcyclohexyl)(3-(chinolin-2-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
Cyclohexyl(3-(chinolin-2-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
3-Methyl-1-(3-(chinolin-2-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)butan-1-on;
[1,1'-Biphenyl]-2-yl(3-(chinolin-2-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(4-(Furan-3-yl)phenyl)(3-(chinolin-2-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(4-(Pyrimidin-5-yl)phenyl)(3-(chinolin-2-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(9-Methyl-9H-carbazol-2-yl)(3-(chinolin-2-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(4-(Pyrimidin-2-yl)phenyl)(3-(chinolin-2-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(4-(Pyrazin-2-yl)phenyl)(3-(chinolin-2-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(4-(Pyridazin-3-yl)phenyl)(3-(chinolin-2-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
4'-(3-(Chinolin-2-yl)-5,6,7,8-tetrahydro-[1,2,4]triazol[4,3-a]pyrazin-7-carbonyl)-[1,1'-biphenyl]-4-carbonitril;
1-(4-(3-(Chinolin-2-yl)-5,6,7,8-tetrahydro-[1,2,4]triazol[4,3-a]pyrazin-7-carbonyl)phenyl)piperidin-2-on;
(4-Morpholinophenyl)(3-(chinolin-2-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(4-(3,5-Dimethyl-1H-pyrazol-1-yl)phenyl)(3-(chinolin-2-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(3-(2-(4-Fluorphenyl)thiazol-4-yl)-6-methyl-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanon;
(3-(2-(4-Fluorphenyl)thiazol-4-yl)-5-methyl-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanon;
(3,4-Dichlorphenyl)(3-(2-(4-fluorphenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(3,4-Difluorphenyl)(3-(2-(4-fluorphenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(3-Chlor-4-fluorphenyl)(3-(2-(4-fluorphenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(4-Chlor-3-fluorphenyl)(3-(2-(4-fluorphenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(3-(2-(4-Fluorphenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(3,4,5-trifluorphenyl)methanon;
(8-Methyl-3-(2-phenyloxazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanon;
(R)-(4-Fluorphenyl)(8-methyl-3-(chinolin-2-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(R)-[1,1'-Biphenyl]-4-yl(8-methyl-3-(chinolin-2-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(R)-[1,1'-Biphenyl]-4-yl(8-methyl-3-(2-morpholinothiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(R)-(4-Fluorphenyl)(8-methyl-3-(6-phenylpyridin-2-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(R)-[1,1'-Biphenyl]-4-yl(8-methyl-3-(2-phenylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(R)-(4-Fluorphenyl)(8-methyl-3-(4,5,6,7-tetrahydrobenzo[d]thiazol-2-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(R)-(3-(2-(2,4-Difluorphenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-fluorphenyl)methanon;
(R)-(3-(2-(2,3-Dichlorphenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-fluorphenyl)methanon;
(R)-(4-Fluorphenyl)(8-methyl-3-(2-(4-phenylpiperazin-1-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(R)-(3-(2-(2,4-Dichlorphenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-fluorphenyl)methanon;
(R)-(3-(2-(3-Chlorphenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-fluorphenyl)methanon;
(R)-(4-Fluorphenyl)(8-methyl-3-(2-phenyloxazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(R)-[1,1'-Biphenyl]-4-yl(8-methyl-3-(2-phenyloxazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(R)-(4-Fluorphenyl)(8-(2-hydroxyethyl)-3-(2-phenylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-

7(8H)-yl)methanon;
(R)-(4'-Fluor-[1,1'-biphenyl]-4-yl)(8-methyl-3-(2-morpholinothiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(R)-(8-Methyl-3-(2-phenylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanon;
(R)-(8-Methyl-3-(2-morpholinothiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanon;
(R)-(4-Fluorphenyl)(8-methyl-3-(4-phenylthiazol-2-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(R)-(3-(2-(2-Chlorphenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-fluorphenyl)methanon;
(R)-(8-Methyl-3-(2-phenylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-3-yl)phenyl)methanon;
(R)-(8-Methyl-3-(chinolin-2-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanon;
(R)-(3-(2-(2-Chlorphenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanon;
(R)-[1,1'-Biphenyl]-4-yl(3-(2-(2-chlorphenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(R)-[1,1'-Biphenyl]-4-yl(8-methyl-3-(4-methyl-2-phenylthiazol-5-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(R)-(3-(2-(4-Fluorphenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanon;
(R)-[1,1'-Biphenyl]-4-yl(3-(2-(4-fluorphenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(R)-[1,1'-Biphenyl]-4-yl(3-(2-(2,4-difluorphenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(R)-(3-(2-(2,4-Difluorphenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanon;
(S)-(4-Fluorphenyl)(8-methyl-3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(S)-(4-Fluorphenyl)(3-(2-(4-fluorphenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(S)-(4'-Fluor-[1,1'-biphenyl]-4-yl)(8-methyl-3-(2-morpholinothiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(S)-(4-Fluorphenyl)(8-methyl-3-(chinolin-2-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(S)-(8-Methyl-3-(chinolin-2-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanon;
(S)-(4-Fluorphenyl)(3-(2-(4-fluorphenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(S)-(3-(2-(2,4-Difluorphenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanon;
(4-Fluorphenyl)(8-methyl-3-(2-phenylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(S)-(4-Fluorphenyl)(8-methyl-3-(2-phenylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(S)-(3-(3-(4-Fluorphenyl)-1,2,4-oxadiazol-5-yl)-8-methyl-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanon;
(R)-(3-(3-(4-Fluorphenyl)-1,2,4-oxadiazol-5-yl)-8-methyl-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanon;
(3-(2-(2,4-Difluorphenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanon;
(3-(5-Phenyl-1,2,4-oxadiazol-3-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanon;
(4-Fluorphenyl)(3-(3-phenyl-1,2,4-oxadiazol-5-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(4-Fluorphenyl)(3-(5-phenyl-1,2,4-oxadiazol-3-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(3-(3-Phenyl-1,2,4-oxadiazol-5-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanon;
(4-Fluorphenyl)(3-(3-(4-fluorphenyl)-1,2,4-oxadiazol-5-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;

(3-(3-(4-Fluorphenyl)-1,2,4-oxadiazol-5-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanon;
(3-(3-(2,4-Difluorphenyl)-1,2,4-oxadiazol-5-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanon;
(4-Fluorphenyl)(3-(5-phenyl-1H-1,2,4-triazol-3-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(3-(5-Phenyl-1H-1,2,4-triazol-3-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanon;
(4-Fluorphenyl)(3-(2-(2-fluorphenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(3-(2-(2-Fluorphenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanon;
[1,1'-Biphenyl]-4-yl(3-(2-(2-fluorphenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(4'-Fluor-[1,1'-biphenyl]-4-yl)(3-(2-(2-fluorphenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(3-(3-(2,4-Difluorphenyl)-1,2,4-oxadiazol-5-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanon;
[1,1'-Biphenyl]-4-yl(3-(2-((4,5-dichlor-1H-imidazol-1-yl)methyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(3-(2-((4,5-Dichlor-1H-imidazol-1-yl)methyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4'-fluor-[1,1'-biphenyl]-4-yl)methanon;
(3-(2-(4-Chlorbenzyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-fluorphenyl)methanon;
(3-(2-(4-Chlorbenzyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanon;
(4-Fluorphenyl)(3-(2-(p-tolyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(4-(Thiophen-2-yl)phenyl)(3-(2-(p-tolyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
[1,1'-Biphenyl]-4-yl(3-(2-(p-tolyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(4-Fluorphenyl)(3-(2-(thiophen-2-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(4-(Thiophen-2-yl)phenyl)(3-(2-(thiophen-2-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
[1,1'-Biphenyl]-4-yl(3-(2-(thiophen-2-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(4'-Fluor-[1,1'-biphenyl]-4-yl)(3-(2-(thiophen-2-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(3-(2-(((4-Chlorphenyl)sulfonyl)methyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanon;
[1,1'-Biphenyl]-4-yl(3-(2-(((4-chlorphenyl)sulfonyl)methyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(3-(2-(((4-Chlorphenyl)sulfonyl)methyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4'-fluor-[1,1'-biphenyl]-4-yl)methanon;
(4-Fluorphenyl)(3-(2-(2-methoxyphenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(3-(2-(2-Methoxyphenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanon;
[1,1'-Biphenyl]-4-yl(3-(2-(2-methoxyphenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
[1,1'-Biphenyl]-4-yl(3-(3-(4-fluorphenyl)-1,2,4-oxadiazol-5-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(4'-Fluor-[1,1'-biphenyl]-4-yl)(3-(3-(4-fluorphenyl)-1,2,4-oxadiazol-5-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(4-Fluorphenyl)(3-(2-(3-fluorphenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(3-(2-(3-Fluorphenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanon;
(4-Fluorphenyl)(3-(2-isopropylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(3-(3-(4-Fluorphenyl)-1,2,4-oxadiazol-5-yl)-8-methyl-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanon;
(3-(3-Phenyl-1,2,4-thiadiazol-5-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanon;

(4-Fluorphenyl)(3-(3-phenyl-1,2,4-thiadiazol-5-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(3-(2-(4-Bromphenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanon;
(3-(2-(4-Bromphenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-fluorphenyl)methanon;
(3-(2-(4-Fluorphenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(5-methylthiophen-2-yl)phenyl)methanon;
4-(3-(2-(4-Fluorphenyl)thiazol-4-yl)-8-methyl-5,6,7,8-tetrahydro-[1,2,4]triazol[4,3-a]pyrazin-7-carbonyl)benzonitril;
[1,1'-Biphenyl]-4-yl(3-(3-phenyl-1,2,4-oxadiazol-5-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(4-Fluorphenyl)(3-(2-(pyridin-4-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(3-(2-(Chinolin-2-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanon;
(3-(1-Methyl-3-phenyl-1H-pyrazol-5-yl)-5,6-dihydro-[1,2,4] triazol[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanon;
(3-(2-(4-(Dimethylamino)phenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-fluorphenyl)methanon;
(3-(1-Methyl-5-phenyl-1H-pyrazol-3-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanon;
(4'-Fluor-[1,1'-biphenyl]-4-yl)(3-(3-phenyl-1,2,4-oxadiazol-5-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(3-(2-(Pyridin-2-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanon;
(4-Fluorphenyl)(3-(1-methyl-3-phenyl-1H-pyrazol-5-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(3-(2-(Pyrimidin-2-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanon;
(S)-(8-Methyl-3-(2-morpholinothiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanon;
(3-(2-(Pyridin-4-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanon;
(3-(2-(4-(Dimethylamino)phenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanon;
(4-Fluorphenyl)(3-(2-(pyridin-2-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
Phenyl(3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(3-(Pyridin-2-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(p-tolyl)methanon;
(S)-(3-(2-(4-Fluorphenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(2-methylthiophen-3-yl)phenyl)methanon;
(R)-(3-(2-(4-Fluorphenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(2-methylthiophen-3-yl)phenyl)methanon;
(3-(2-(Pyrazin-2-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanon;
4-(4-(7-(4-(Thiophen-2-yl)benzoyl)-5,6,7,8-tetrahydro-[1,2,4]triazol[4,3-a]pyrazin-3-yl)thiazol-2-yl)benzonitril;
(4-Fluorphenyl)(3-(2-(pyrazin-2-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(4-Fluorphenyl)(3-(1-methyl-5-phenyl-1H-pyrazol-3-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(3-(2-(4-Morpholinophenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanon;
(4-Fluorphenyl)(3-(2-(4-morpholinophenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(3-(2-(4-(4-Methylpiperazin-1-yl)phenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanon;
(4-Fluorphenyl)(3-(2-(4-(4-methylpiperazin-1-yl)phenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(3-(2-(4-(Piperidin-1-yl)phenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanon;
(4-Fluorphenyl)(3-(2-(4-(piperidin-1-yl)phenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;

(3-(2-(4-(Pyrrolidin-1-yl)phenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanon;
(4-Fluorphenyl)(3-(2-(4-(pyrrolidin-1-yl)phenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(3-(2-(Piperidin-1-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanon;
(3-(2-(Pyrrolidin-1-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanon;
(4-Fluorphenyl)(3-(2-(pyrrolidin-1-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(3-(2-(4-Methylpiperazin-1-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanon;
(4-Fluorphenyl)(3-(2-(4-methylpiperazin-1-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(3-(1-Methyl-2-phenyl-1H-imidazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanon;
(4-(Dimethylamino)phenyl)(3-(2-(4-fluorphenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(3-(1-(2-Methoxyethyl)-3-phenyl-1H-pyrazol-5-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanon;
(4-Fluorphenyl)(3-(1-(2-methoxyethyl)-3-phenyl-1H-pyrazol-5-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(3-(2-Isobutylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanon;
(3-(2-(2-(2-Methoxyethyl)morpholino)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanon;
(3-(2-(4,4-Difluorpiperidin-1-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-fluorphenyl)methanon;
(4-Fluorphenyl)(3-(2-isobutylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(3-(2-(2,5-Dimethylmorpholino)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanon;
(3-(2-(2-Hydroxyphenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanon;
(3-(2-(4,4-Difluorpiperidin-1-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanon;
(3-(2-(2,6-Dimethylmorpholino)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanon;
(3-(2-(2,2-Dimethylmorpholino)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanon;
(3-(3-Phenyl-1H-pyrazol-5-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanon;
(3-(2-(4-Fluorphenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(3-methylthiophen-2-yl)phenyl)methanon;
(4-Fluorphenyl)(3-(3-phenyl-1H-pyrazol-5-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(R)-(3-(2-(4-Fluorphenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(3-methylthiophen-2-yl)phenyl)methanon;
(4-Fluorphenyl)(3-(2-(2-hydroxyphenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(S)-(3-(2-(4-Fluorphenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(3-methylthiophen-2-yl)phenyl)methanon;
(3-(2-(2-Methylmorpholino)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanon;
(3-(2-(4,4-Dimethylpiperidin-1-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanon;
(3-(5-Methylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanon;
(3-(2-(4,4-Dimethylpiperidin-1-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-fluorphenyl)methanon;
(4-Fluorphenyl)(3-(2-(2-(methoxymethyl)piperidin-1-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(4-Fluorphenyl)(8-methyl-3-(6-methylpyridin-2-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;

(3-(2-(2-(Methoxymethyl)piperidin-1-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanon;
Tert-butyl (2-(2-(4-(7-(4-(thiophen-2-yl)benzoyl)-5,6,7,8-tetrahydro-[1,2,4]triazol[4,3-a]pyrazin-3-yl)thiazol-2-yl)phenoxy)ethyl)carbamat;
(3-(2-(2-(2-Hydroxyethoxy)phenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanon;
(3-(2-(2-(2-Aminoethoxy)phenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanon;
N-(4-(4-(7-(4-(Thiophen-2-yl)benzoyl)-5,6,7,8-tetrahydro-[1,2,4]triazol[4,3-a]pyrazin-3-yl)thiazol-2-yl)phenyl)methansulfonamid;
(3-(1-(2-Hydroxyethyl)-3-phenyl-1H-pyrazol-5-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanon;
(3-(1-(2-Hydroxyethyl)-5-phenyl-1H-pyrazol-3-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanon;
[1,1'-Biphenyl]-4-yl(8-methyl-3-(6-methylpyridin-2-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(8-Methyl-3-(6-methylpyridin-2-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanon;
(3-(2-(2,4-Difluorphenyl)-5-methylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanon;
(3-(2-(3-(Dimethylamino)phenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanon;
(3-(2-(3-(Dimethylamino)phenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-fluorphenyl)methanon;
N-(3-(4-(7-(4-(Thiophen-2-yl)benzoyl)-5,6,7,8-tetrahydro-[1,2,4]triazol[4,3-a]pyrazin-3-yl)thiazol-2-yl)phenyl)methansulfonamid;
N-(2-(4-(7-(4-(Thiophen-2-yl)benzoyl)-5,6,7,8-tetrahydro-[1,2,4]triazol[4,3-a]pyrazin-3-yl)thiazol-2-yl)phenyl)methansulfonamid;
(3-(4-Chlorphenyl)-1H-pyrazol-5-yl)(3-(2-(4-fluorphenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(3-(4-Chlorphenyl)-1-methyl-1H-pyrazol-5-yl)(3-(2-(4-fluorphenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(3-(3,4-Dichlorphenyl)-1-methyl-1H-pyrazol-5-yl)(3-(2-(4-fluorphenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
(5-(4-Chlorphenyl)-1-methyl-1H-pyrazol-3-yl)(3-(2-(4-fluorphenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)methanon;
Tert-butyl(2-(3-phenyl-5-(7-(4-(thiophen-2-yl)benzoyl)-5,6,7,8-tetrahydro-[1,2,4]triazol[4,3-a]pyrazin-3-yl)-1H-pyrazol-1-yl)ethyl)carbamat;
Tert-butyl(2-(5-phenyl-3-(7-(4-(thiophen-2-yl)benzoyl)-5,6,7,8-tetrahydro-[1,2,4]triazol[4,3-a]pyrazin-3-yl)-1H-pyrazol-1-yl)ethyl)carbamat;
(3-(2-(2-Bromphenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanon;
(3-(2-(3-Bromphenyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(thiophen-2-yl)phenyl)methanon;
2-(4-(7-(4-(Thiophen-2-yl)benzoyl)-5,6,7,8-tetrahydro-[1,2,4]triazol[4,3-a]pyrazin-3-yl)thiazol-2-yl)benzonitril;
3-(4-(7-(4-(Thiophen-2-yl)benzoyl)-5,6,7,8-tetrahydro-[1,2,4]triazol[4,3-a]pyrazin-3-yl)thiazol-2-yl)benzonitril;
(3-(2-(4-Fluorphenyl)thiazol-4-yl)-8-methyl-5,6-dihydro-[1,2,4]triazol[4,3-a]pyrazin-7(8H)-yl)(4-(2-methylthiophen-3-yl)phenyl)methanon;
und pharmazeutisch verträgliche Salze und Solvate davon.

13. Pharmazeutische Zusammensetzung, welche eine Verbindung nach einem der Ansprüche **1** bis **12** oder ein pharmazeutisch verträgliches Salz oder Solvat davon und mindestens einen pharmazeutisch verträglichen Träger, Verdünner, Exzipienten und/oder Hilfsstoff umfasst.

14. Arzneimittel, welches eine Verbindung nach einem der Ansprüche **1** bis **12** oder ein pharmazeutisch verträgliches Salz oder Solvat davon umfasst.

15. Verbindung nach einem der Ansprüche **1** bis **12** oder ein pharmazeutisch verträgliches Salz oder Solvat davon zur

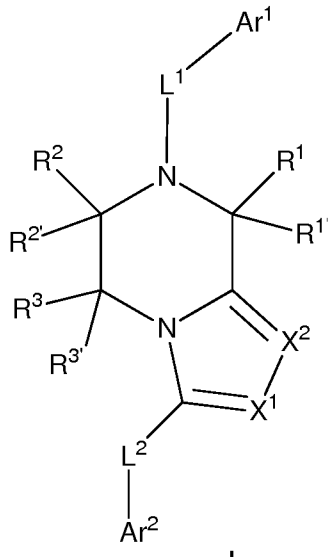
Verwendung in der Behandlung und/oder Vorbeugung von Depressionen, Angstzuständen, Psychosen, Schizophrenie, psychotischen Störungen, bipolaren Störungen, kognitiven Störungen, Parkinson-Krankheit, Alzheimer-Krankheit, Aufmerksamkeitsdefizit-/Hyperaktivitätsstörung (ADHS), Schmerzen, Krämpfen, Fettleibigkeit, entzündlichen Erkrankungen einschließlich Reizdarmsyndrom und entzündlichen Darmerkrankungen, Erbrechen, Präeklampsie, Erkrankungen der Luftwege einschließlich chronisch obstruktiver Lungenerkrankung, Asthma, Hyperreagibilität der Atemwege, Bronchokonstriktion und Husten, Fortpflanzungsstörungen und geschlechtshormonabhängigen Erkrankungen einschließlich, aber nicht beschränkt auf benigne Prostatahyperplasie (BPH), metastasierendes Prostatakarzinom, Hodenkrebs, Brustkrebs, androgenabhängige Akne, Alopezie des männlichen Typs, Endometriose, abnorme Pubertät, Uterusfibrose, hormonabhängige Krebserkrankungen, Hyperandrogenismus, Hirsutismus, Virilisierung, polyzystisches Ovarialsyndrom (PCOS), HAIR-AN-Syndrom (Hyperandrogenismus, Insulinresistenz und Acanthosis nigricans), ovarielle Hyperthekose (HAIR-AN mit Hyperplasie der luteinisierten Thekazellen im ovariellen Stroma), sonstigen Manifestationen hoher intraovarieller Androgenkonzentrationen (z. B. follikulärer Maturationsarrest, Atresie, Anovulation, Dysmenorrhoe, dysfunktionelle uterine Blutungen, Unfruchtbarkeit), gynäkologischen Erkrankungen, Unfruchtbarkeit und androgenproduzierenden Tumoren (virilisierender Ovarial- oder Nebennierenrindentumor).

16. Verbindung nach einem der Ansprüche **1** bis **12** oder ein pharmazeutisch verträgliches Salz oder Solvat davon zur Verwendung in der Unterdrückung des LH-Anstiegs bei der künstlichen Befruchtung einer Patientin.

17. Verbindung nach einem der Ansprüche **1** bis **12** oder ein pharmazeutisch verträgliches Salz oder Solvat davon zur Verwendung in der Herbeiführung der Kastration und Hemmung des Geschlechtstriebes beim Mann.

Revendications

1. Composé de formule I :



I

et sels et solvates pharmaceutiquement acceptables de celui-ci, dans lquelle

Ar^1 est un groupe aryle ou hétéroaryle à 5 ou 6 chaînons, un groupe cycloalkyle à 3 à 6 chaînons, un groupe hétérocyclyle à 3 à 6 chaînons ou un groupe alkyle en C_3-C_6, chacun des groupes aryle, hétéroaryle, cycloalkyle ou hétérocyclyle étant optionnellement substitué par un ou plusieurs groupe(s) choisi(s) parmi un halo, un cyano, un alkyle, un haloalkyle, un cycloalkyle, un hétéroalkyle, un hétérocyclyle, un aryle, un aralkyle, un hétéroaryle, un hydroxyle, un alkoxy, un haloalkoxy, un alkoxyalkoxy, un alkylamino, un carboxy, un alkoxycarbonyle, un alkylcarbonyloxy, un alkylcarbonylamino, un haloalkylcarbonylamino, un carbamoyle, un alkylcarbamoyle, un carbamoylamino, un alkylcarbamoylamino, un alkylsulfonyle, un haloalkylsulfonyle, un sulfamoyle, un alkylsulfamoyle, un alkylsulfonylamino, un haloalkylsulfonylamino, ou deux substituants forment un groupe alkylenedioxy ou un groupe haloalkylenedioxy, ou deux substituants forment un groupe cycloalkyle ou hétéro-

cycloalkyle avec le groupe cycloalkyle ou hétérocycloalkyle auquel ils sont attachés, ou un ou plusieurs groupes aryle peuvent être fusionnés au groupe aryle, hétéroaryle, cycloalkyle ou hétérocycloalkyle, chacun desdits substituants étant optionnellement substitué par un ou plusieurs autre(s) substituant(s) choisi(s) parmi un halo, un cyano, un alkyle, un haloalkyle, un cyclopropyle, un alkoxy, un haloalkoxy, un hétérocyclyle, un aryle, un hétéroaryle, un aryloxy, un hétéroaryloxy;

L^1 est un carbonyle ;

R^1 est H, un groupe alkyle en C_1-C_4, un aryle ou un aralkyle, chacun desdits groupes alkyle, aryle ou aralkyle étant optionnellement substitué par un ou plusieurs groupe(s) choisi(s) parmi un halo ou un hydroxyle ;

$R^{1'}$ est H ou un groupe alkyle en C_1-C_4 ;

R^2 est H ou un groupe alkyle en C_1-C_4 ;

$R^{2'}$ est H ou un groupe alkyle en C_1-C_4 ;

R^3 est H ou un groupe alkyle en C_1-C_4 optionnellement substitué par un hydroxyle ;

$R^{3'}$ est H ou un groupe alkyle en C_1-C_4 ;

X^1 et X^2 sont N ;

L^2 est une liaison simple ou un carbonyle,

Ar^2 est un groupe aryle ou hétéroaryle à 5 ou 6 chaînons, chacun des groupes aryle ou hétéroaryle étant optionnellement substitué par un ou plusieurs groupe(s) choisi(s) parmi un halo, un cyano, un alkyle, un hydroxyalkyle, un haloalkyle, un cycloalkyle, un hétéroalkyle, un hétérocyclyle, un aryle, un hétéroaryle, un aralkyle, un hétéroarylalkyle, un hydroxyle, un alkoxy, un haloalkoxy, un alkylamino, un carboxy, un alkoxycarbonyle, un alkylcarbonyloxy, un alkylcarbonylamino, un haloalkylcarbonylamino, un acylamino, un carbamoyle, un alkylcarbamoyle, un carbamoylalkyle, un carbamoylamino, un alkylcarbamoylamino, un alkylsulfonyle, un haloalkylsulfonyle, un arylsulfonylalkyle, un sulfamoyle, un alkylsulfamoyle, un alkylsulfonylamino, un haloalkylsulfonylamino, ou deux substituants forment un groupe alkylenedioxy ou un groupe haloalkylenedioxy,
ou un ou plusieurs groupes cycloalkyle, aryle, hétérocyclyle ou hétéroaryle peuvent être fusionnés au groupe aryle ou hétéroaryle, chacun desdits substituants étant optionnellement substitué par un ou plusieurs autres substituants(s) choisi(s) parmi un halo, un cyano, un alkyle, un haloalkyle, un alkoxy, un haloalkoxy, un cycloalkyle, un hétérocyclyle optionnellement substitué par un alkyle, un aryle, un hétéroaryle, un hydroxyle, un alkoxyalkyle, un hydroxyalkoxy, un alkylamino, un alkylsulfonylamino, un alkoxycarbonylamino, un aminoalkoxy, ou un alkoxycarbonylaminoalkoxy;

et dans laquelle, quand :

R^1, $R^{1'}$, R^2, $R^{2'}$, R^3, $R^{3'}$ sont H, et

L^2 est une liaison simple, et

Ar^1 est un aryle à 6 chaînons optionnellement substitué par un ou plusieurs groupe(s) choisi(s) parmi un halo, un cyano, un alkyle en C_1-C_3, haloalkyle en Ci, et

Ar^2 est un groupe aryle ou hétéroaryle à 5 ou 6 chaînons optionnellement substitué par un ou plusieurs groupe(s) choisi(s) parmi un halo, un alkyle en C_1-C_3, un hydroxyle, un méthoxy, ou fusionné à un groupe aryle ou hétéroaryle optionnellement substitué par un ou plusieurs autres halo, alkyle en C_1-C_3, hydroxyle, méthoxy,

alors,

Ar^1 est un phényle, 3-halophényle, 4-halophényle, 2,3-dichlorophényle, 2,4-difluorophényle, 2,5-dihalophényle, 2,6-difluorophényle, 2,6-dichlorophényle, 3,4-dihalophényle, 3,5-dihalophényle, 3,4,5-trihalophényle, 2-cyanophényle, 3-cyanophényle, 4-cyanophényle, 2,3-dicyanophényle, 2,4-dicyanophényle, 3,5-dicyanophényle, 3-cyano-4-halophényle, 4-(C1-C3 alkyl)phényle, 3,4-di(C1-C3 alkyl)phényle, 3,5-di(C1-C3 alkyl)phényle, 4-(C1 haloalkyl)phényle, et

Ar^2 est un 2-(C1-C3 alkyl)thiazol-4-yl, 5-(C1-C3 alkyle)thiazol-4-yl, pyridin-2-yl, 4-halopyridin-2-yl, 4-(C1-C3 alkyl)pyridin-2-yl, 5-(C1-C3 alkyl)pyridin-2-yl, 6-(C1-C3 alkyl)pyridin-2-yl, quinolin-2-yl, isoquinolin-3-yl, 8-haloquinolin-2-yl, benzothiazol-2-yl, 4,5,6,7-tétrahydro-1,3-benzothiazol-2-yl;

avec les exclusions suivantes :

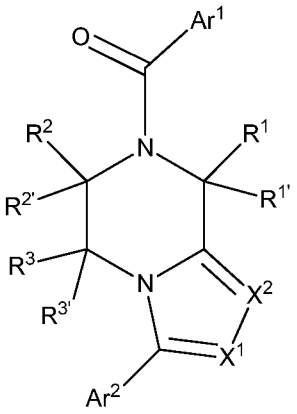
- Ar^1 n'est ni un pyrazolo[1,5-a]pyridin-2-yl substitué ou non-substitué, ni un groupe pyrazolo[1,5-a]pyrimidin-2yl substitué ou non-substitué; et

le compose de formule I n'est aucun de :

(2,4-difluorophényl)(3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(3-chlorophényl)(3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
2-(3-(pyridin-2-yl)-5,6,7,8-tétrahydro-[1,2,4]triazolo[4,3-a]pyrazine-7-carbonyl)benzonitrile;

(2,6-dichlorophényl)(3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone,
(2,3-dichlorophényl)(3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone,
(2,3-dichlorophényl)(3-(5-méthylpyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone,
(2,3-dichlorophényl)(3-(6-méthylpyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone.

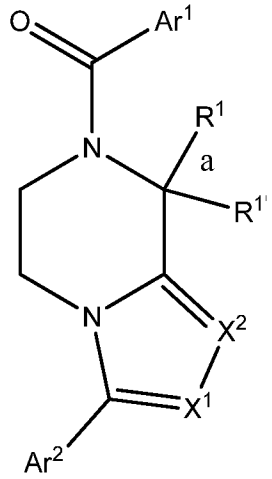
2. Le composé selon la revendication 1, ayant pour formule Ib



Ib

et sels et solvates pharmaceutiquement acceptables de celui-ci, dans laquelle **Ar^1, Ar^2, R^1, $R^{1'}$ R^2, $R^{2'}$, R^3, $R^{3'}$ X^1, X^2** sont tels que définis dans la revendication **1.**

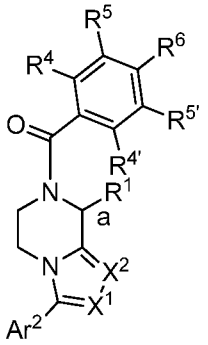
3. Le composé selon la revendication 2, ayant pour formule Ic



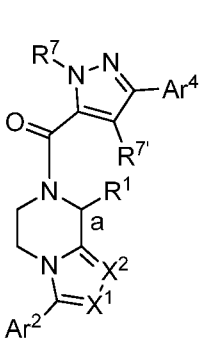
Ic

et sels et solvates pharmaceutiquement acceptables de celui-ci, dans laquelle a représente la liaison reliant **R^1** au groupe pipérazine, et **Ar^1**, **Ar^2**, **R^1**, **$R^{1'}$**, **X^1**, et **X^2** sont tels que définis dans la revendication **2.**

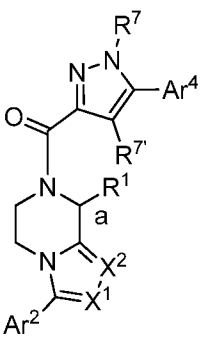
4. Le composé selon la revendication **3,** choisi parmi les formules Id-1, Id-2, Id-3 et Id-4



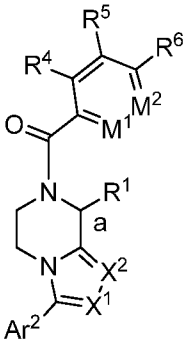
Id-1



Id-2



Id-3



Id-4

et sels et solvates pharmaceutiquement acceptables de ceux-ci, dans lesquelles-

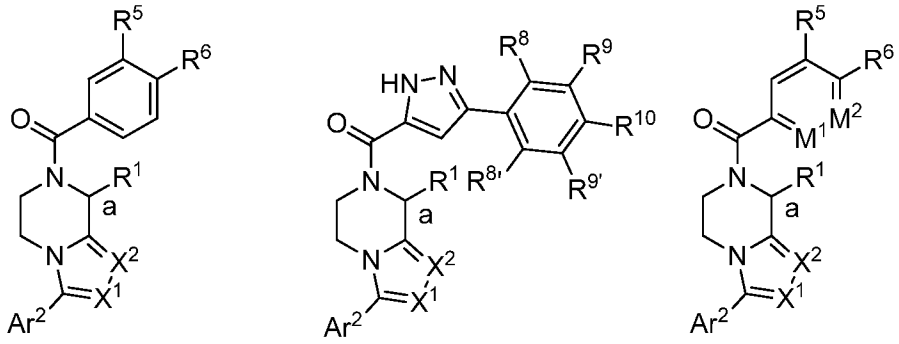
a représente la liaison reliant **R^1** au groupe pipérazine; et
Ar^2, **R^1**, **X^1** et **X^2** sont tels que définis dans la revendication **2 ;** et
R^4, **$R^{4'}$**, **R^5**, **$R^{5'}$** et **R^6** sont indépendamment choisis parmi H, un halo, un cyano, un alkyle, un haloalkyle, un cycloalkyle en C_3-C_6, un hétéroalkyle, un hétérocyclyle, un aryle, un hétéroaryle, un hydroxyle, un alkoxy, un haloalkoxy, un alkoxyalkoxy, un alkylamino, un carboxy, un alkoxycarbonyle, un alkylcarbonyloxy, un alkylcarbonylamino, un haloalkylcarbonylamino, un carbamoyle, un alkylcarbamoyle, un carbamoylamino, un alkylcarbamoylamino, un alkylsulfonyle, un haloalkylsulfonyle, un sulfamoyle, un alkylsulfamoyle, un alkylsulfonylamino, un haloalkylsulfonylamino, ou **R^5** avec **R^4** ou **R^6**, ou **$R^{5'}$** avec **$R^{4'}$** ou **R^6** forme un groupe alkylenedioxy ou un groupe haloalkylenedioxy, ou **R^5** avec **R^4** ou **R^6**, ou **$R^{5'}$** avec **$R^{4'}$** ou **R^6** forme un groupe aryle fusionné au groupe phényle auquel ils sont attachés, chacun desdits substituants étant optionnellement substitué par un ou plusieurs autres substituant(s) choisi(s) parmi un halo, un cyano, un alkyle, un haloalkyle, un cyclopropyle; et
R^7 est H ou méthyl ; et
$R^{7'}$ est H ou méthyl ; et
Ar^4 est un groupe cycloalkyle ou aryle, chacun desdits groupes cycloalkyle ou aryle étant optionnellement substitué avec un ou plusieurs groupe(s) choisi(s) parmi un halo, un alkyle, un haloalkyle, un cyclopropyle, un haloalkoxy, un aryloxy ; et
M^1 est N ou C-**$R^{4"}$** dans lequel **$R^{4"}$** est choisi parmi H, un halo, un cyano, un alkyle, un haloalkyle, un cycloalkyle en C_3-C_6, un hétéroalkyle, un hétérocyclyle, un aryle, un hétéroaryle, un hydroxyle, un alkoxy, un haloalkoxy, un alkoxyalkoxy, un alkylamino, un carboxy, un alkoxycarbonyle, un alkylcarbonyloxy, un alkylcarbonylamino, un haloalkylcarbonylamino, un carbamoyle, un alkylcarbamoyle, un carbamoylamino, un alkylcarbamoylamino, un alkylsulfonyle, un haloalkylsulfonyle, un sulfamoyle, un alkylsulfamoyle, un alkylsulfonylamino, un haloalkylsulfonylamino, chacun desdits substituants étant optionnellement substitué par un ou plusieurs autre(s) substituants(s) choisi(s) parmi un halo, un cyano, un alkyle, un haloalkyle, un cyclopropyle; et
M^2 est N ou **M^2** est C-**$R^{5"}$** à condition que **M^1** soit N, dans lequel **$R^{5"}$** est choisi parmi H, un halo, un cyano, un alkyle, un haloalkyle, un cycloalkyle en C_3-C_6, un hétéroalkyle, un hétérocyclyle, un aryle, un hétéroaryle, un hydroxyle, un alkoxy, un haloalkoxy, un alkoxyalkoxy, un alkylamino, un carboxy, un alkoxycarbonyle, un alkylcarbonyloxy, un alkylcarbonylamino, un haloalkylcarbonylamino, un carbamoyle, un alkylcarbamoyle, un carbamoylamino, un alkylcarbamoylamino, un alkylsulfonyle, un haloalkylsulfonyle, un sulfamoyle, un alkylsulfamoyle, un alkylsulfonylamino, un haloalkylsulfonylamino, ou **$R^{5"}$** avec **R^6** forme un groupe alkylenedioxy ou un groupe haloalkylenedioxy, ou un groupe aryle fusionné au groupe pyridinyl auquel ils sont attachés, chacun desdits substituants étant optionnellement substitué par un ou plusieurs autres substituant(s) choisi(s) parmi un halo, un cyano, un alkyle, un haloalkyle, un cyclopropyle; et
dans la formule Id-1, quand :

R^1 est H, et
R^4, **$R^{4'}$**, **R^5**, **$R^{5'}$** et **R^6** sont indépendamment choisis parmi H, un halo, un cyano, un alkyle en C_1-C_3, un haloalkyle en Ci, et
Ar^2 est un groupe aryle ou hétéroaryle à 5 ou 6 chaînons optionnellement substitué par un ou plusieurs groupe(s) choisi(s) parmi un halo, un alkyle en C_1-C_3, un hydroxyle, un alkoxy, ou fusionné au groupe aryle optionnellement substitué par un ou plusieurs autre(s) halo, alkyle en C_1-C_3, hydroxyle, méthoxy
alors,

R^4, $R^{4'}$, R^5, $R^{5'}$ et R^6 sont H, ou R^4, $R^{4'}$, $R^{5'}$, R^6 sont H et R^5 est un halo, ou R^4, $R^{4'}$, R^5, $R^{5'}$ sont H et R^6 est un halo, un cyano, un alkyle en C_1-C_3, un haloalkyle en Ci, ou $R^{4'}$, $R^{5'}$, R^6 sont H et R^4, R^5 sont un halo, ou R^4, $R^{4'}$, $R^{5'}$ sont H et R^5, R^6 sont indépendamment un halo, ou R^4, $R^{4'}$ sont H et R^5, $R^{5'}$, R^6 sont un halo, et

Ar^2 est 2-(C1-C3 alkyl)thiazol-4-yl, 5-(C1-C3 alkyl)thiazol-4-yl, pyridin-2-yl, 4-halopyridin-2-yl, 4-(C1-C3 alkyl)pyridin-2-yl, 5-(C1-C3 alkyl)pyridin-2-yl, 6-(C1-C3 alkyl)pyridin-2-yl, quinolin-2-yl, isoquinolin-3-yl, 8-haloquinolin-2-yl, benzothiazol-2-yl, 4,5,6,7-tétrahydro-1,3-benzothiazol-2-yl.

5. Le composé selon la revendication **4,** choisi parmi les formules Ie-1, Ie-2 et Ie-3



Ie-1 Ie-2 Ie-3

et sels et solvates pharmaceutiquement acceptables de ceux-ci, dans lesquelles

a représente la liaison reliant R^1 au groupe pipérazine; et

Ar^2, R^1, X^1 et X^2 sont tels que définis dans la revendication **2 ;** et

R^5 et R^6 sont indépendamment choisis parmi H, un halo, un cyano, un alkyle, un cyclopropyle, un aryle, un hétéroaryle, chacun desdits groupes aryle et hétéroaryle étant optionnellement substitué par un ou plusieurs groupe(s) choisi(s) parmi un halo, un alkyle, un cyclopropyle, ou R^5 et R^6 forment ensemble un groupe phényle fusionné au groupe phényle auquel ils sont attachés ; et

R^8, $R^{8'}$, R^9, $R^{9'}$ et R^{10} sont indépendamment choisis parmi H, un halo, un haloalkyle, un cyclopropyle ou un haloalkoxy, ou R^8, $R^{8'}$, R^9, $R^{9'}$ sont H et R^{10} est un phénoxy ; M^1 et M^2 sont tels que définis dans la revendication **4 ;** et

dans la formule Ie-1, quand :

R^1 est H, et

R^5 et R^6 sont indépendamment choisis parmi H, un halo, un cyano, un alkyle en C_1-C_3, et

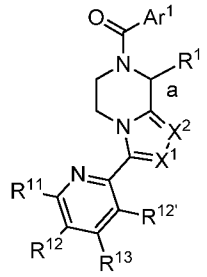
Ar^2 est un groupe aryle ou hétéroaryle à 5 ou 6 chaînons optionnellement substitué par un ou plusieurs groupe(s) choisi(s) parmi un halo, un alkyle en C_1-C_3, un hydroxyle, un alkoxy, ou fusionné au groupe aryle optionnellement substitué par un ou plusieurs autres halo, alkyle en C_1-C_3, hydroxyle, méthoxy ;

alors,

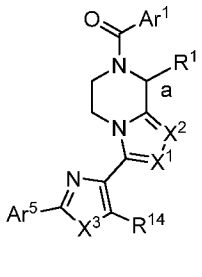
R^6 est H et R^5 est H, un halo, ou R^5 est H et R^6 est un halo, un cyano, un alkyle en C_1-C_3, un haloalkyle en Ci, ou R^5 et R^6 sont indépendamment halo, et

Ar^2 est 2-(C1-C3 alkyl)thiazol-4-yl, 5-(C1-C3 alkyl)thiazol-4-yl, pyridin-2-yl, 4-halopyridin-2-yl, 4-(C1-C3 alkyl)pyridin-2-yl, 5-(C1-C3 alkyl)pyridin-2-yl, 6-(C1-C3 alkyl)pyridin-2-yl, quinolin-2-yl, isoquinolin-3-yl, 8-haloquinolin-2-yl, benzothiazol-2-yl, 4,5,6,7-tétrahydro-1,3-benzothiazol-2-yl.

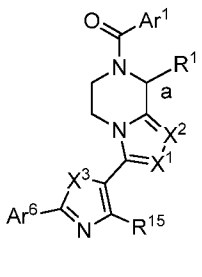
6. Le composé selon la revendication **3,** choisi parmi les formules If-1, If-2, If-3, If-4, If-5, If-6, If-7 et If-8



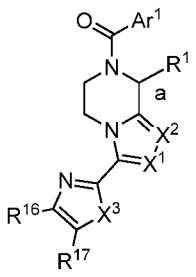
If-1



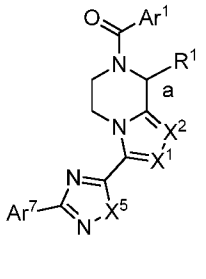
If-2



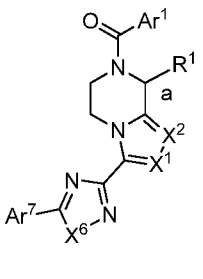
If-3



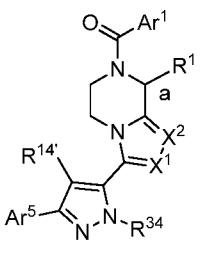
If-4



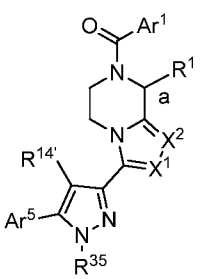
If-5



If-6



If-7



If-8

et sels et solvates pharmaceutiquement acceptables de ceux-ci, dans lesquelles

a représente la liaison entre **R^1** et le groupe pipérazine; et
Ar^1, **R^1**, **X^1** et **X^2** sont tels que définis dans la revendication **2 ;** et
R^{11}, **R^{12}**, **$R^{12'}$** et **R^{13}** sont indépendamment choisis parmi H, un halo, un cyano, un alkyle, un hydroxyalkyle, un haloalkyle, un cycloalkyle en C_3-C_6, un hétéroalkyle, un hétérocyclyle, un aryle, un hétéroaryle, un hydroxyle, un alkoxy, un haloalkoxy, un alkylamino, un carboxy, un alkoxycarbonyle, un alkylcarbonyloxy, un alkylcarbonylamino, un haloalkylcarbonylamino, un acylamino, un carbamoyle, un alkylcarbamoyle, un carbamoylalkyle, un carbamoylamino, un alkylcarbamoylamino, un alkylsulfonyle, un haloalkylsulfonyle, un sulfamoyle, un alkylsulfamoyle, un alkylsulfonylamino, un haloalkylsulfonylamino, ou **R^{12}** avec **R^{11}** ou **R^{13}**, ou **R^{13}** avec **$R^{12'}$** forme un groupe alkylenedioxy ou un groupe haloalkylenedioxy, ou **R^{12}** avec **R^{11}** ou **R^{13}** forme un groupe cycloalkyle, aryle, hétérocyclyle ou hétéroaryle fusionné au groupe pyridyl auquel ils sont attachés, chacun desdits groupes étant optionnellement substitué par un ou plusieurs groupe(s) choisi(s) parmi un halo, un cyano, un alkyle, un haloalkyle, un cyclopropyle, un alkoxy, un haloalkoxy ou un hydroxyle; et
Ar^5 est un groupe hétérocyclyle, aryle, hétéroaryle, aralkyle, hétéroarylalkyle, ou arylsulfonylalkyle, chacun étant optionnellement substitué par un ou plusieurs groupe(s) choisi(s) parmi un halo, un cyano, un alkyle, un haloalkyle, un cyclopropyle, un alkoxy, un haloalkoxy, un hétérocyclyle optionnellement substitué par un alkyle, un aryle, un hydroxyle, un alkoxy, un alkoxyalkyle, un hydroxyalkoxy, un alkylamino, un alkylsulfonylamino, un aminoalkoxy, ou un alkoxycarbonylaminoalkoxy; et
X^3 est O ou S ; et
R^{14} est H ou un méthyl ; et
Ar^6 est un groupe hétérocyclyle, aryle ou hétéroaryle, chacun étant optionnellement substitué par un ou plusieurs groupe(s) choisi(s) parmi un halo, un cyano, un alkyle, un haloalkyle, un cyclopropyle, un alkoxy, un haloalkoxy, un aryle ou un hydroxyle ; et
R^{15} est H ou un méthyl ; et
R^{16} est un groupe hétérocyclyle, aryle ou hétéroaryle, chacun desdits groupes étant optionnellement substitué par un ou plusieurs groupe(s) choisi(s) parmi un halo, un cyano, un alkyle, un haloalkyle, un cyclopropyle, un alkoxy, un haloalkoxy ou un hydroxyle ;
R^{17} est H, un méthyl ou **R^{17}** avec **R^{16}** forme un groupe cycloalkyle ou aryle fusionné au groupe thiazolyle auquel ils sont attachés, formant ainsi un système cyclique fusionné, ledit système cyclique fusionné étant optionnellement substitué par un ou plusieurs groupe(s) choisi(s) parmi un halo, un cyano, un alkyle, un haloalkyle, un cyclopropyle, un alkoxy, un haloalkoxy ou un hydroxyle ; et

X^5 est O ou S, ou N-R^{36} dans lequel R^{36} est H ou un alkyle en C_1-C_3 ; et
Ar^7 est un groupe hétérocyclyle, aryle ou hétéroaryle, chacun étant optionnellement substitué par un ou plusieurs groupe(s) choisi(s) parmi un halo, un cyano, un alkyle, un haloalkyle, un cyclopropyle, un alkoxy, un haloalkoxy, un aryle ou un hydroxyle ; et
X^6 est O, S ou N-$R^{36'}$ dans lequel $R^{36'}$ est H ou un alkyle en C_1-C_3 ; et
$R^{14'}$ est H ou un méthyl ; et
R^{34} est H, un alkyle, un alkoxyalkyle, un hydroxyalkyle, un alkoxycarbonylaminoalkyle ; et
R^{35} est H, un alkyle, un alkoxyalkyle, un hydroxyalkyle, un alkoxycarbonylaminoalkyle ; et
dans lesquelles,

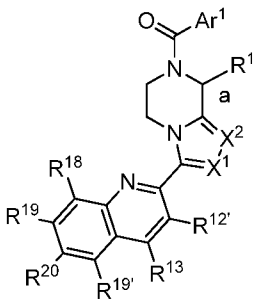
- dans la formule If-1 quand :

  R^1 est H, et
  Ar^1 est un groupe aryle à 6 chaînons optionnellement substitué par un ou plusieurs groupe(s) choisi(s) parmi un halo, un cyano, un alkyle en C_1-C_3, un haloalkyle en Ci, et
  R^{11}, R^{12}, $R^{12'}$ et R^{13} sont indépendamment choisis parmi H, un halo, un alkyle en C_1-C_3, un hydroxyle, un méthoxy, ou R^{12} avec R^{11} ou R^{13} forme un groupe aryle ou hétérocyclyle ou hétéroaryle fusionné au groupe pyridyle auquel ils sont attachés et étant optionnellement substitué par un ou plusieurs groupe(s) choisi(s) parmi un halo, un alkyle en C_1-C_3, un méthoxy ou un hydroxyle,
  alors,
  Ar^1 est un phényle, un 3-halophényle, un 4-halophényle, un 2,3-dichlorophényle, un 3,4-dihalophényle, un 3,4,5-trihalophényle, un 4-cyanophényle, un 4-(alkyle en C_1-C_3)phényle, un 4-(haloalkyle en C_1)phényle, et
  R^{11}, R^{12}, $R^{12'}$ et R^{13} sont H, ou R^{11}, R^{12}, $R^{12'}$ sont H et R^{13} est un halo, un alkyle en C_1-C_3, ou R^{11}, $R^{12'}$, R^{13} sont H et R^{12} est un alkyle en C_1-C_3, ou R^{12}, $R^{12'}$, R^{13} sont H et R^{11} est un alkyle en C_1-C_3, ou R^{11}, R^{12}, $R^{12'}$ et R^{13} avec le groupe pyridyle auquel ils sont attachés forment un groupe quinolin-2-yl, isoquinolin-3-yl ou 8-haloquinolin-2-yl ; et

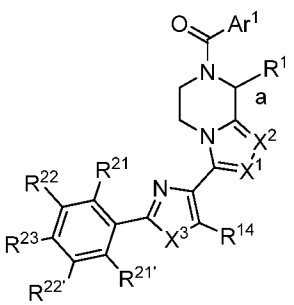
- dans la formule If-4, quand :

  R^1 est H, et
  Ar^1 est un aryle à 6 chainons optionnellement substitué par un ou plusieurs groupe(s) choisi(s) parmi un halo, un cyano, un alkyle en C_1-C_3, un haloalkyle en Ci, et
  R^{17} avec R^{16} forme un groupe cycloalkyle ou aryle fusionné au groupe thiazolyle auquel ils sont attachés, formant ainsi système cyclique fusionné, ledit système cyclique fusionné étant optionnellement substitué par un ou plusieurs groupe(s) choisi(s) parmi un halo, un alkyle en C_1-C_3, un méthoxy ou un hydroxyle,
  alors,
  Ar^1 est un phényle, un 3-halophényle, un 4-halophényle, un 2,3-dichlorophényle, un 3,4-dihalophényle, un 3,4,5-trihalophényle, un 4-cyanophényle, un 4-(alkyle en C_1-C_3)phényle, un 4-(C1 haloalkyle)phényle, et
  R^{17} et R^{16} forment avec le groupe thiazolyle auquel ils sont attachés un groupe benzothiazol-2-yl ou 4,5,6,7-tétrahydro-1,3-benzothiazol-2-yl.

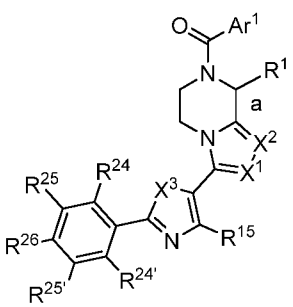
7. Le composé selon la revendication **6,** choisi parmi les formules Ig-1, Ig-2, Ig-3, Ig-4, Ig-5, Ig-6, Ig-7 et Ig-8



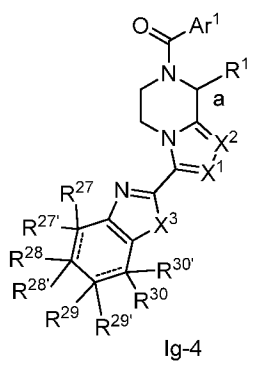
Ig-1



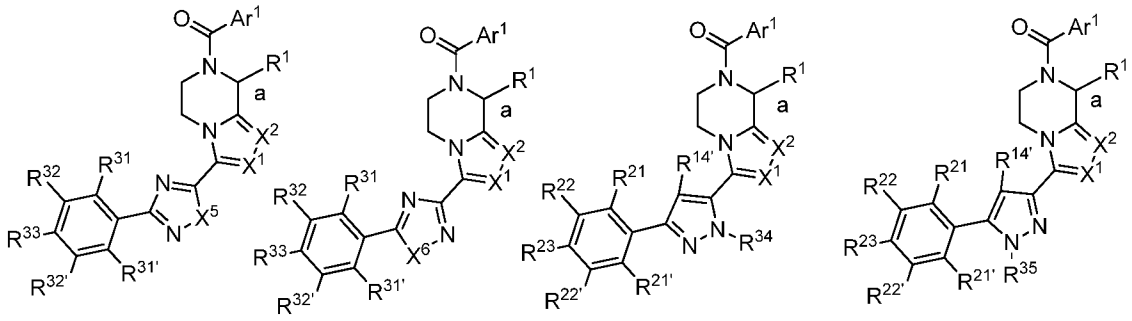
Ig-2



Ig-3



Ig-4



Ig-5 Ig-6 Ig-7 Ig-8

et sels et solvates pharmaceutiquement acceptables de ceux-ci, dans lesquelles

a représente la liaison entre R^1 et le groupe pipérazine; et
Ar^1, R^1, X^1 et X^2 sont tels que définis dans revendication **2** ; et
R^{14}, $R^{14'}$, R^{15}, R^{34}, R^{35}, X^3 X^5 et X^6 sont tels que définis dans revendication **6** ; et
$R^{12'}$ et R^{13} sont indépendamment choisis parmi un H, un halo, un cyano, un alkyle, un hydroxyalkyle, un haloalkyle, un cycloalkyle, un hétéroalkyle, un hydroxyle, un alkoxy, un haloalkoxy, un carboxy, un alkoxycarbonyle, un alkylcarbonyloxy, un alkylcarbonylamino, un haloalkylcarbonylamino, un acylamino, un carbamoyle, un alkylcarbamoyle, un carbamoylalkyle, un carbamoylamino, un alkylcarbamoylamino, un alkylsulfonyle, un haloalkylsulfonyle, un sulfamoyle, un alkylsulfamoyle, un alkylsulfonylamino, un haloalkylsulfonylamino, ou R^{13} avec $R^{12'}$ forme un groupe alkylenedioxy ou un groupe haloalkylenedioxy, chacun desdits groupes étant optionnellement substitué par un ou plusieurs groupe(s) choisi(s) parmi un halo, un cyano, un alkyle, un haloalkyle, un alkoxy, un haloalkoxy, un hydroxyle ou un oxo; et
R^{18}, R^{19}, $R^{19'}$ et R^{20} sont indépendamment choisis parmi H, un halo, un cyano, un alkyle, un haloalkyle, un cyclopropyle, un alkoxy, un haloalkoxy ; et
R^{21}, $R^{21'}$, R^{22}, $R^{22'}$et R^{23} sont indépendamment choisis parmi H, un halo, un cyano, un alkyle, un haloalkyle, un cyclopropyle, un hétérocyclyle optionnellement substitué par un alkyle, un hydroxyle, un alkoxy, un haloalkoxy, un hydroxyalkoxy, un alkylamino, un alkylsulfonylamino, un aminoalkoxy, un alkoxycarbonylaminoalkoxy ; et
R^{24}, $R^{24'}$, R^{25}, $R^{25'}$et R^{26} sont indépendamment choisis parmi H, un halo, un haloalkyle, un cyclopropyle ; et
R^{27}, R^{28}, R^{29} et R^{30} sont indépendamment choisis parmi H, un halo, un cyano, un alkyle, un haloalkyle, un cyclopropyle, un alkoxy, un haloalkoxy ; et
$R^{27'}$, $R^{28'}$, $R^{29'}$ et $R^{30'}$ sont absents, ou $R^{27'}$, $R^{28'}$, $R^{29'}$ et $R^{30'}$ sont H à condition que R^{28}, R^{29} et R^{30} soient H et que R^{27} est choisi parmi H, un chloro ou un fluoro ; et
les deux liaisons représentées par les lignes en pointillé dans la formule Ig-4 sont toutes les deux absentes, ou toutes les deux présentes à condition que $R^{27'}$, $R^{28'}$, $R^{29'}$ et $R^{30'}$ soient absents ; et
R^{31}, $R^{31'}$, R^{32}, $R^{32'}$et R^{33} sont indépendamment choisis parmi H, un halo, un cyano, un alkyle, un haloalkyle, un cyclopropyle, un alkoxy, un haloalkoxy ; et
dans lesquelles,

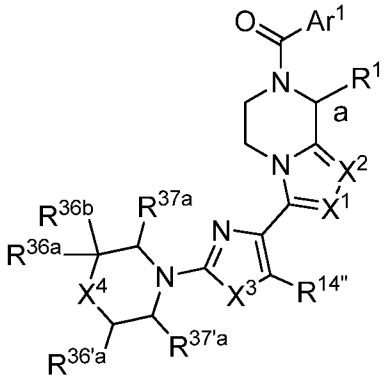
- dans la formule Ig-1, quand :

  R^1 est H, et
  Ar^1 est un aryle à 6 chainons optionnellement substitué par un ou plusieurs groupe(s) choisi(s) parmi un halo, un cyano, un alkyle en C_1-C_3, un haloalkyle en Ci, et
  $R^{12'}$, R^{13}, R^{18}, R^{19}, $R^{19'}$ et R^{20} sont indépendamment choisis parmi H, un halo, un alkyle en C_1-C_3, un hydroxyle, un méthoxy,
  alors,
  Ar^1 est un phényle, un 3-halophényle, un 4-halophényle, un 2,3-dichlorophényle, un 3,4-dihalophényle, un 3,4,5-trihalophényle, un 4-cyanophényle, un 4-(alkyle en C_1-C_3)phényle, un 4-(haloalkyle en C_1)phényle, et
  $R^{12'}$, R^{13}, R^{18}, R^{19}, $R^{19'}$ et R^{20} sont H, ou $R^{12'}$, R^{13}, R^{19}, $R^{19'}$, R^{20} sont H et R^{18} est un fluoro, un chloro, et

- dans la formule Ig-4, quand

R^1 est H, et
Ar^1 est un aryle à 6 chainons optionnellement substitué par un ou plusieurs groupe(s) choisi(s) parmi un halo, un cyano, un alkyle en C_1-C_3, un haloalkyle en Ci, et
R^{27}, **R^{28}**, **R^{29}** et **R^{30}** sont indépendamment choisis parmi H, un halo, un alkyle en C_1-C_3, un méthoxy, et
$R^{27'}$, **$R^{28'}$**, **$R^{29'}$** et **$R^{30'}$** sont absents ou H à condition que **R^{28}**, **R^{29}** et **R^{30}** soient H et **R^{27}** est choisi parmi H, un chloro ou un fluoro,
alors,
Ar^1 est un phényle, un 3-halophényle, un 4-halophényle, un 2,3-dichlorophényle,
un 3,4-dihalophényle, un 3,4,5-trihalophényle, un 4-cyanophényle, un 4-(alkyle en C_1-C_3)phényle, un 4-(haloalkyle en C_1)phényle, et
R^{27}, **R^{28}**, **R^{29}** et **R^{30}** sont H, et
$R^{27'}$, **$R^{28'}$**, **$R^{29'}$** et **$R^{30'}$** sont absents ou H à condition que **R^{27}**, **R^{28}**, **R^{29}** et **R^{30}** soient H.

8. Le composé de formule If-2 selon la revendication **6** ayant pour formule Ih-2 :

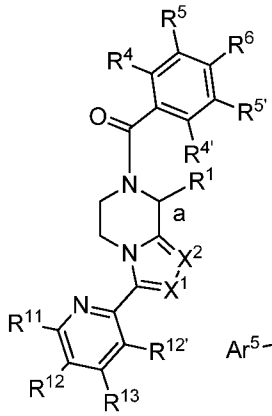


Ih-2

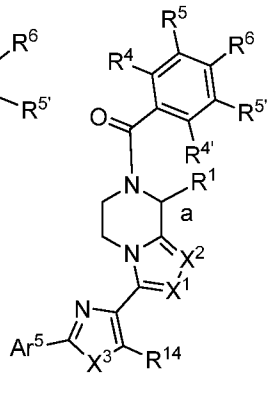
et sels et solvates pharmaceutiquement acceptables de celui-ci, dans laquelle

a représente la liaison entre **R^1** et le groupe pipérazine; et
Ar^1, **R^1**, **X^1** et **X^2** sont tels que définis dans revendication **2 ;** et
X^3 est tel que défini dans revendication **6 ;** et
$R^{14"}$ est H ou un méthyl ; et
X^4 est O, CH_2, CF_2, $C(CH_3)_2$, N-(alkyle en C_1-C_3) N-phényle ; et
R^{36a}, **R^{36b}**, **$R^{36'a}$**, **R^{37a}** et **$R^{37'a}$** sont indépendamment choisis parmi H, un alkyle en C_1-C_3, un alkoxyalkyle en C_1-C_3.

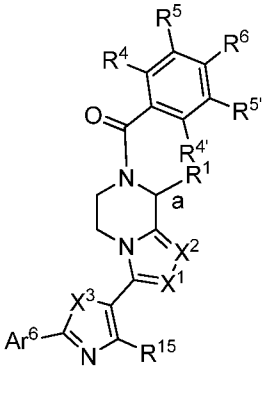
9. Le composé selon la revendication 3, choisi parmi les formules Ii-1, Ii-2, Ii-3, Ii-4, Ii-5, Ii-6, Ii-7, Ii-8, Ij-1, Ij-2, Ij-3, Ij-4, Ij-5, Ij-6, Ij-7, Ij-8, Ik-1, Ik-2, Ik-3, Ik-4, Ik-5, Ik-6, Ik-7, Ik-8, Ii'-1, Ii'-2, Ii'-3, Ii'-4, Ii'-5, Ii'-6, Ii'-7 et Ii'-8



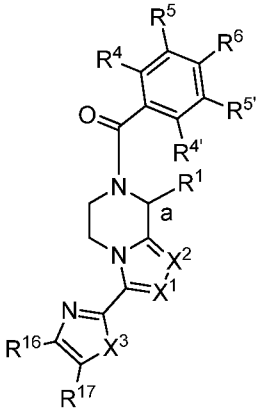
Ii-1



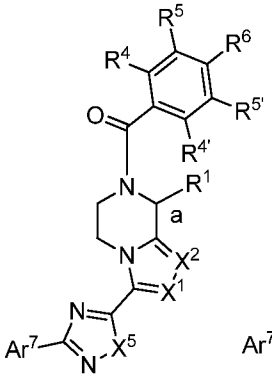
Ii-2



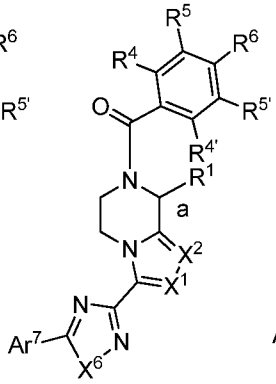
Ii-3



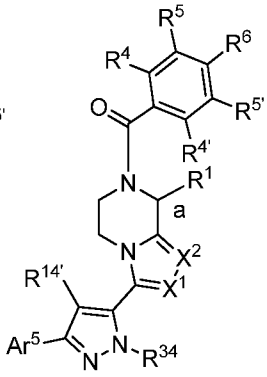
Ii-4



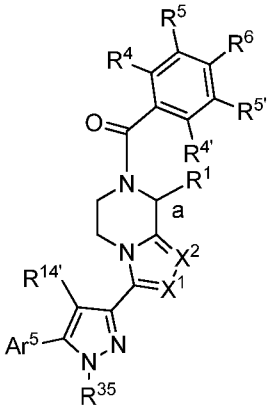
Ii-5



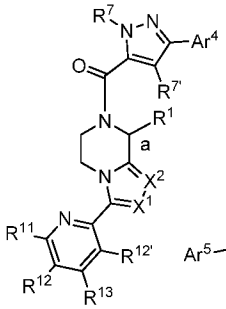
Ii-6



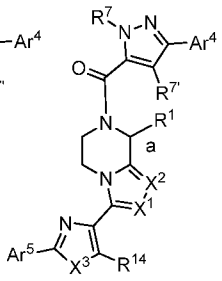
Ii-7



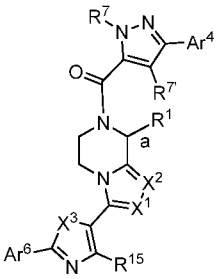
Ii-8



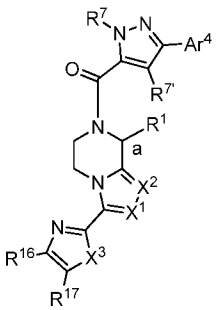
Ij-1



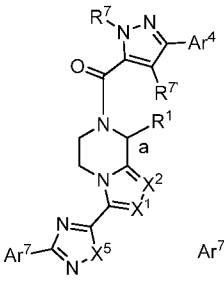
Ij-2



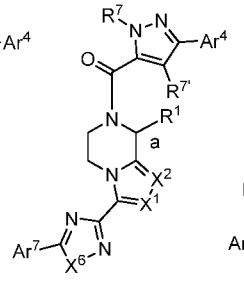
Ij-3



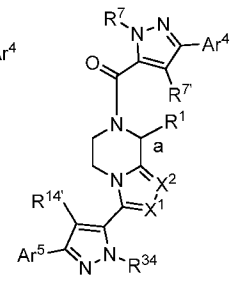
Ij-4



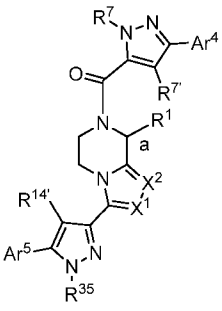
Ij-5



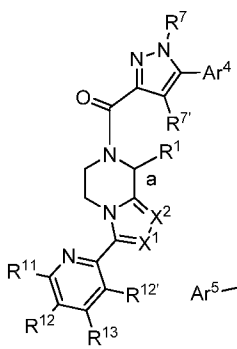
Ij-6



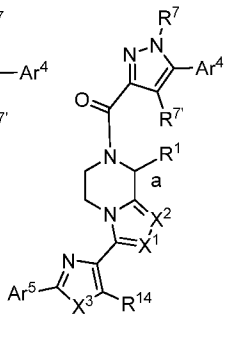
Ij-7



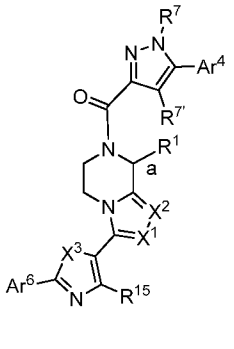
Ij-8



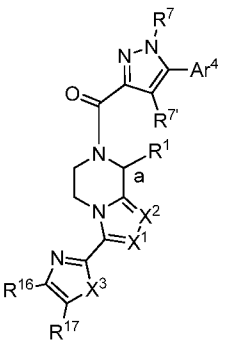
Ik-1



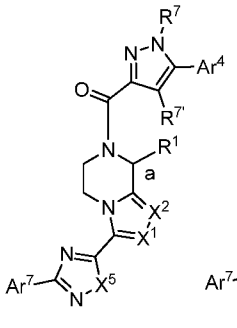
Ik-2



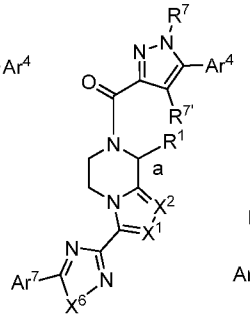
Ik-3



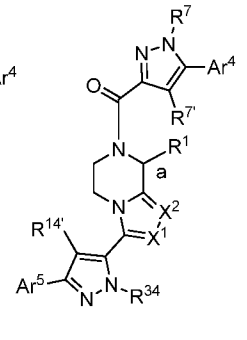
Ik-4



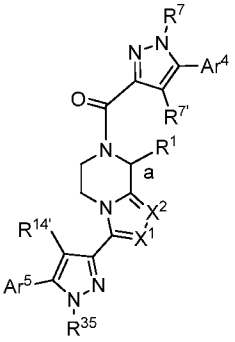
Ik-5



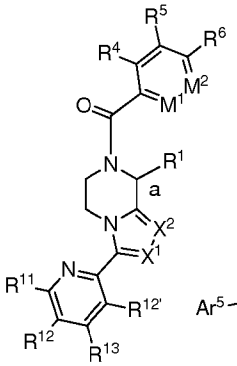
Ik-6



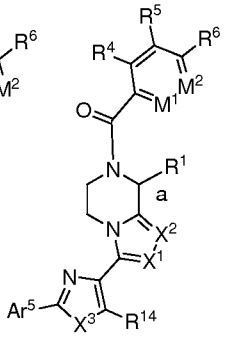
Ik-7



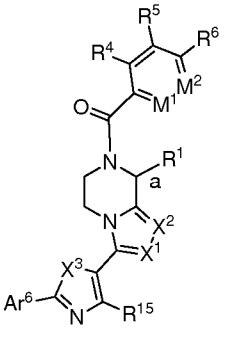
Ik-8



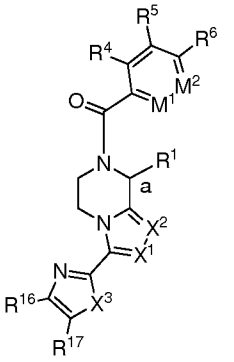
Ii'-1



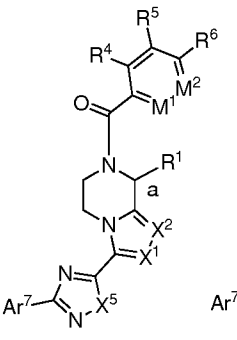
Ii'-2



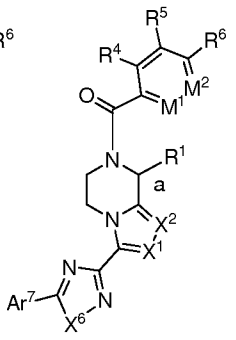
Ii'-3



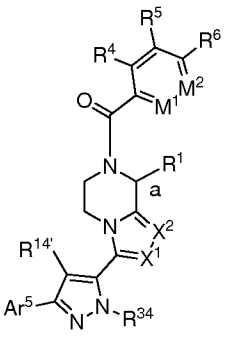
Ii'-4



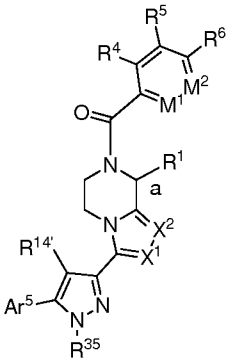
Ii'-5



Ii'-6



Ii'-7

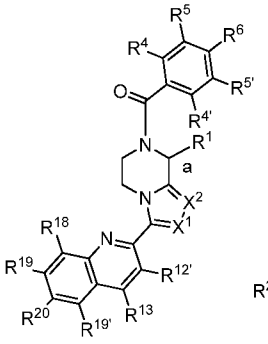


Ii'-8

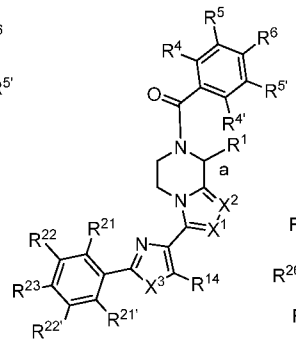
et sels et solvates pharmaceutiquement acceptables de ceux-ci, dans lesquelles

a représente la liaison entre **R^1** et le groupe pipérazine; et
Ar^1, **R^1**, **X^1** et **X^2** sont tels que définis dans revendication **2 ;** et
Ar^4, **R^4**, **$R^{4'}$**, **R^5**, **$R^{5'}$**, **R^6**, **R^7**, **$R^{7'}$**, **M^1**, **M^2** sont tels que définis dans la revendication 4 ; et
Ar^5, **Ar^6**, **Ar^7**, **R^{11}**, **R^{12}**, **$R^{12'}$**, **R^{13}, R^{14}, $R^{14'}$**, **R^{15}**, **R^{16}, R^{17}, R^{34},** R^{35}, **X^3**, **X^5, X^6** sont tels que définis dans la revendication **6.**

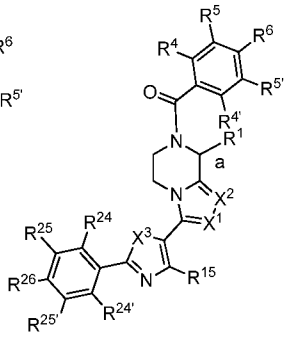
10. Le composé selon la revendication **9,** choisi parmi les formules II-1, II-2, II-3,II-4, II-5, II-6, II-7, II-8, II'-1, II'-2, II'-3, II'-4, II'-5, II'-6, II'-7, II'-8



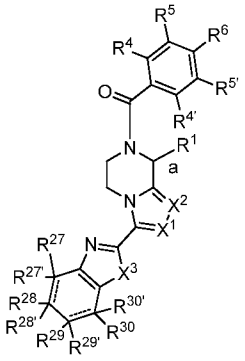
II-1



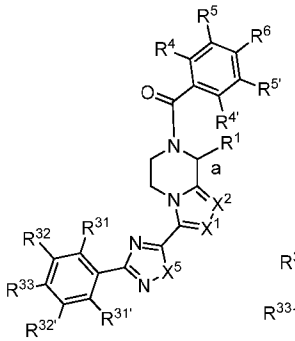
II-2



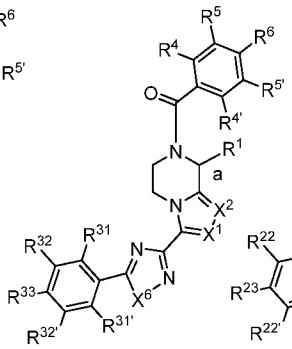
II-3



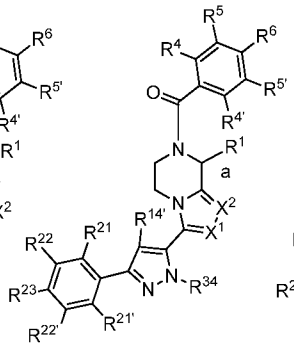
II-4



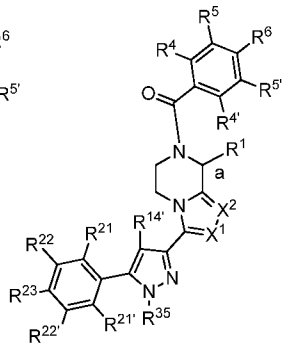
II-5



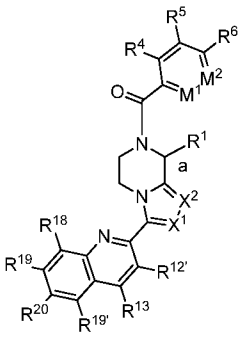
II-6



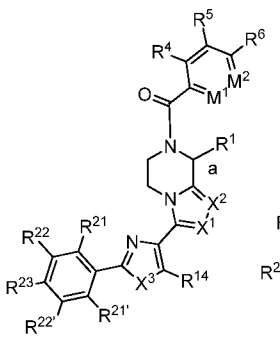
II-7



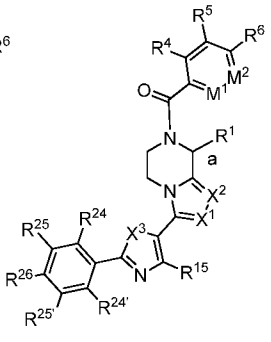
II-8



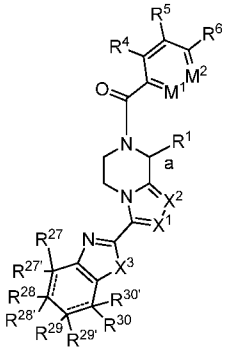
II'-1



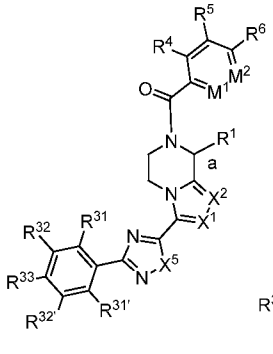
II'-2



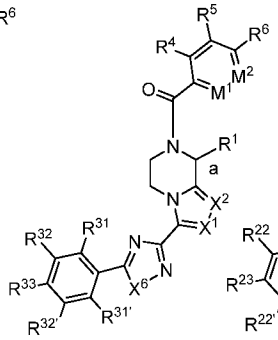
II'-3



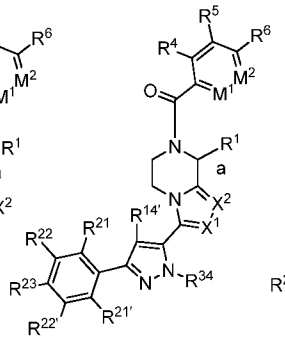
II'-4



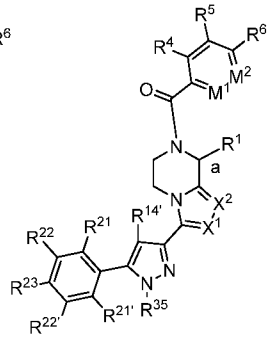
II'-5



II'-6



II'-7

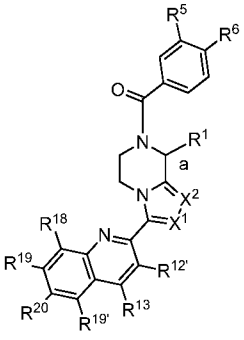


II'-8

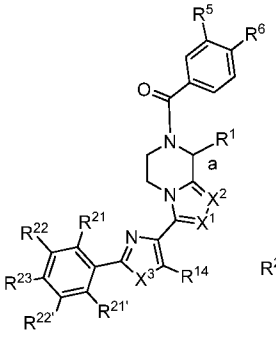
et sels et solvates pharmaceutiquement acceptables de ceux-ci, dans lesquelles :

a représente la liaison entre **R^1** et le groupe pipérazine ; et
R^1, X^1 et **X^2** sont tels que définis dans la revendication **2 ;** et
R^4, **$R^{4'}$**, **R^5**, **$R^{5'}$**, **R^6**, **M^1** et **M^2** sont tels que définis dans la revendication **4 ;** et
$R^{12'}$, **R^{13}**, **R^{14}**, **$R^{14'}$**, **R^{15}**, **R^{18}**, **R^{19}**, **$R^{19'}$**, **R^{20}**, **R^{21}**, **$R^{21'}$**, **R^{22}**, **$R^{22'}$**, **R^{23}**, **R^{24}**, **$R^{24'}$**, **R^{25}**, **$R^{25'}$**, **R^{26}**, **R^{27}**, **$R^{27'}$**, **R^{28}**, **$R^{28'}$**, **R^{29}**, **$R^{29'}$**, **R^{30}**, **$R^{30'}$**, **R^{31}**, **$R^{31'}$**, **$R^{32'}$**, **$R^{32'}$**, **R^{33}**, **R^{34}**, **R^{35}**, **X^3**, **X^5**; **X^6**; et les deux liaisons représentées par les lignes en pointillé sont tels que définis dans la revendication **7.**

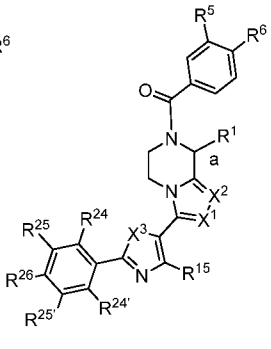
11. Le composé selon la revendication **10,** choisi parmi les formules Im-1, Im-2, Im-3, Im-4, Im-5, Im-6, Im-7, Im-8, Im'-1, Im'-2, Im'-3, Im'-4, Im'-5, Im'-6, Im'-7 et Im'-8



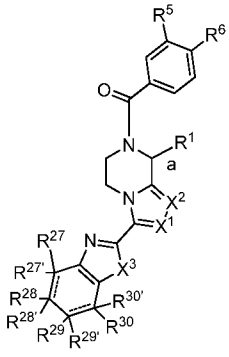
Im-1



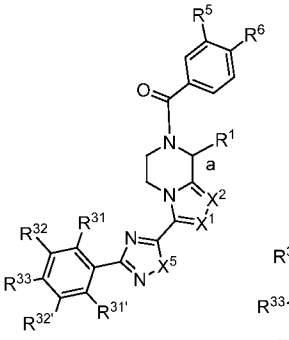
Im-2



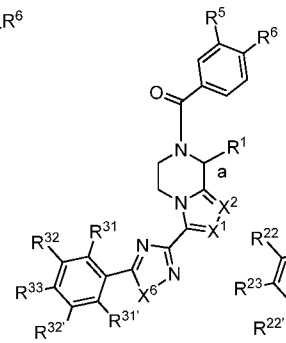
Im-3



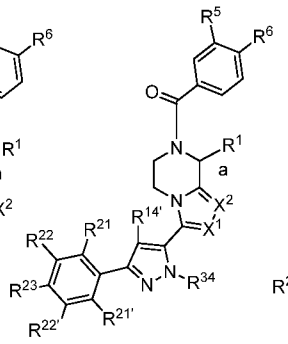
Im-4



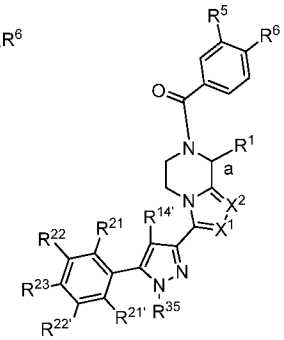
Im-5



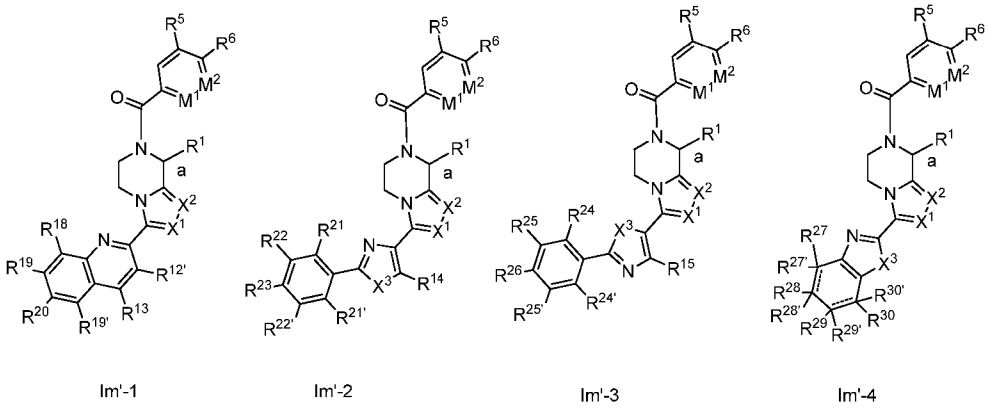
Im-6



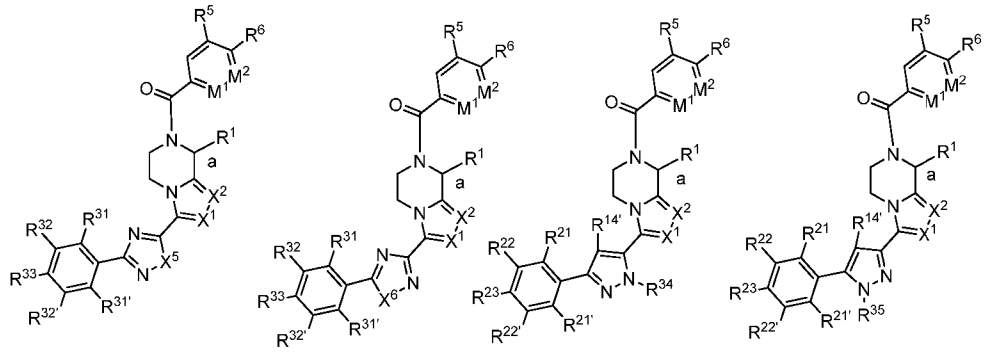
Im-7



Im-8



Im'-1 Im'-2 Im'-3 Im'-4



Im'-5 Im'-6 Im'-7 Im'-8

et sels et solvates pharmaceutiquement acceptables de ceux-ci, dans lesquelles :

a représente la liaison entre R^1 et le groupe pipérazine ; et
R^1, X^1 et X^2 sont tels que définis dans la revendication **2 ;** et
R^5, R^6, M^1 et M^2 sont tels que définis dans la revendication **5 ;** et
$R^{12'}$, R^{13}, R^{14}, $R^{14'}$, R^{15}, R^{18}, R^{19}, $R^{19'}$, R^{20}, R^{21}, $R^{21'}$, R^{22}, $R^{22'}$, R^{23}, R^{24}, $R^{24'}$, R^{25}, $R^{25'}$, R^{26}, R^{27}, $R^{27'}$, R^{28}, $R^{28'}$, R^{29}, $R^{29'}$, R^{30}, $R^{30'}$, R^{31}, $R^{31'}$, R^{32}, $R^{32'}$, R^{33}, R^{34}, R^{35}, X^3, X^5 X^6; et et les deux liaisons représentées par les lignes en pointillé sont tels que définis dans la revendication **7.**

12. Le composé selon la revendication **1,** choisi dans le groupe constitué par :

(4-fluorophényl)(3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(4-chlorophényl)(3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(3-(4-chlorophényle)-1H-pyrazol-5-yl)(3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(3-(3,4-dichlorophényl)-1H-pyrazol-5-yl)(3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(3,4-dichlorophényl)(3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
[1,1'-biphényl]-4-yl(3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(4-fluorophényl)(3-(quinolin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(4-fluorophényl)(3-(2-phénylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(4-fluorophényl)(3-(2-morpholinothiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(3-(5-chloropyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-fluorophényl)méthanone;
(4-fluorophényl)(3-(6-méthylpyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(4-fluorophényl)(8-méthyl-3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(3-(2,4-dichlorophényl)-1H-pyrazol-5-yl)(3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(3-(3,4-dichlorophényl)-1-méthyl-1H-pyrazol-5-yl)(3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;

(4-fluorophényl)(3-(isoquinolin-3-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(4'-fluoro-[1,1'-biphényle]-4-yl)(3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(3-(4-(trifluorométhyl)phényl)-1H-pyrazol-5-yl)méthanone;
(3-(4-phenoxyphényl)-1H-pyrazol-5-yl)(3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
[1,1'-biphényl]-4-yl(3-(quinolin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
[1,1'-biphényl]-4-yl(3-(2-morpholinothiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophén-2-yl)phényl)méthanone;
(4-fluorophényl)(3-(8-fluoroquinolin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(3-(8-chloroquinolin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-fluorophényl)méthanone;
(4-fluorophényl)(3-(2-(4-(trifluorométhyl)phényl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(4-fluorophényl)(3-(6-phénylpyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
[1,1'-biphényl]-4-yl(3-(2-phénylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(4-fluorophényl)(3-(4,5,6,7-tétrahydrobenzo[d]thiazol-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(4-fluorophényl)(3-(2-(3-(trifluorométhyl)phényl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(3-(2-(2,4-difluorophényl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-fluorophényl)méthanone;
(3-(2-(2,3-dichlorophényl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-fluorophényl)méthanone;
(3-(2-(4-chlorophényl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-fluorophényl)méthanone;
(4-fluorophényl)(3-(2-(4-fluorophényl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(4-fluorophényl)(3-(2-(pipéridin-1-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(4-fluorophényl)(3-(2-(4-phénylpipérazin-1-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(3-(2-(2,4-dichlorophényl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-fluorophényl)méthanone;
(3-(2-(3,5-dichlorophényl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-fluorophényl)méthanone;
(4-fluorophényl)(3-(6-(pyrrolidin-1-yl)pyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(4-fluorophényl)(3-(6-morpholinopyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(4-fluorophényl)(3-(6-(trifluorométhyl)pyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(3-(2-(3,4-diméthoxyphényl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-fluorophényl)méthanone;
(4-fluorophényl)(8-(4-fluorophényl)-3-(2-phénylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(3-(2-(3-chlorophényl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-fluorophényl)méthanone;
(4-fluorophényl)(8-isopropyl-3-(2-phénylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(R)-(4-fluorophényl)(8-méthyl-3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(R)-(4-fluorophényl)(8-méthyl-3-(2-phénylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
[1,1'-biphényl]-4-yl(8-méthyl-3-(2-morpholinothiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(4-fluorophényl)(3-(2-phényloxazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(4-fluorophényl)(8-méthyl-3-(2-phényloxazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
[1,1'-biphényl]-4-yl(8-méthyl-3-(2-phényloxazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
[1,1'-biphényl]-4-yl(3-(2-phényloxazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;

(4-fluorophényl)(8-(2-hydroxyéthyl)-3-(2-phénylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(4-fluorophényl)(8-méthyl-3-(2-morpholinothiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(4'-fluoro-[1,1'-biphényl]-4-yl)(8-méthyl-3-(2-morpholinothiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(3-(2-phénylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophén-2-yl)phényl)méthanone;
(3-(2-morpholinothiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophén-2-yl)phényl)méthanone;
(8-méthyl-3-(2-morpholinothiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophén-2-yl)phényl)méthanone;
(4-fluorophényl)(3-(4-phénylthiazol-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(3-(2-(2-chlorophényl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-fluorophényl)méthanone;
(3-(benzo[d]thiazol-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-fluorophényl)méthanone;
(8,8-diméthyl-3-(2-phénylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-fluorophényl)méthanone;
(4-fluorophényl)(8-méthyl-3-(quinolin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(8-méthyl-3-(2-phénylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophén-2-yl)phényl)méthanone;
(3-(2-phénylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophén-3-yl)phényl)méthanone;
(8-méthyl-3-(2-phénylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophén-3-yl)phényl)méthanone;
(8-méthyl-3-(quinolin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophén-2-yl)phényl)méthanone;
(3-(2-(2-chlorophényl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophén-2-yl)phényl)méthanone;
[1,1'-biphényl]-4-yl(3-(2-(2-chlorophényl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(R)-(3-(2-(4-chlorophényl)thiazol-4-yl)-8-méthyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-fluorophényl)méthanone;
(3-(quinolin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophén-2-yl)phényl)méthanone;
(4-fluorophényl)(3-(2-(4-fluorophényl)thiazol-4-yl)-8-méthyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(R)-(4-fluorophényl)(3-(2-(4-fluorophényl)thiazol-4-yl)-8-méthyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
[1,1'-biphényl]-4-yl(8-méthyl-3-(4-méthyl-2-phénylthiazol-5-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(3-(2-(4-fluorophényl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophén-2-yl)phényl)méthanone;
(3-(2-(2-chlorophényl)thiazol-4-yl)-8-méthyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-fluorophényl)méthanone;
(4-fluorophényl)(8-méthyl-3-(4-méthyl-2-phénylthiazol-5-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
[1,1'-biphényl]-4-yl(3-(2-(4-fluorophényl)thiazol-4-yl)-8-méthyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(3-(2-(2,4-difluorophényl)thiazol-4-yl)-8-méthyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-fluorophényl)méthanone;
(3-(2-(4-fluorophényl)thiazol-4-yl)-8-méthyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophén-2-yl)phényl)méthanone;
[1,1'-biphényl]-4-yl(3-(2-(2,4-difluorophényl)thiazol-4-yl)-8-méthyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(3-(2-(2,4-difluorophényl)thiazol-4-yl)-8-méthyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophén-2-yl)phényl)méthanone;
naphthalèn-1-yl(3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(3-(4-chlorophényl)-1-méthyl-1H-pyrazol-5-yl)(3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-

7(8H)-yl)méthanone;
(5-(4-chlorophényl)-1-méthyl-1H-pyrazol-3-yl)(3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(8-méthyl-3-(5-phényl-1,2,4-oxadiazol-3-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophén-2-yl)phényl)méthanone;
(8-méthyl-3-(3-phényl-1,2,4-oxadiazol-5-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophén-2-yl)phényl)méthanone;
(R)-(3-(2-(4-fluorophényl)oxazol-4-yl)-8-méthyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophén-2-yl)phényl)méthanone;
(5-phénylpyridin-2-yl)(3-(quinolin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(6-phénylpyridin-3-yl)(3-(quinolin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(2-phénylpyrimidin-5-yl)(3-(quinolin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(4-phénylcyclohexyl)(3-(quinolin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
cyclohexyl(3-(quinolin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
3-méthyl-1-(3-(quinolin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)butan-1-one;
[1,1'-biphényl]-2-yl(3-(quinolin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(4-(furan-3-yl)phényl)(3-(quinolin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(4-(pyrimidin-5-yl)phényl)(3-(quinolin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(9-méthyl-9H-carbazol-2-yl)(3-(quinolin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(4-(pyrimidin-2-yl)phényl)(3-(quinolin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(4-(pyrazin-2-yl)phényl)(3-(quinolin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(4-(pyridazin-3-yl)phényl)(3-(quinolin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
4'-(3-(quinolin-2-yl)-5,6,7,8-tétrahydro-[1,2,4]triazolo[4,3-a]pyrazine-7-carbonyle)-[1,1'-biphényl]-4-carbonitrile;
1-(4-(3-(quinolin-2-yl)-5,6,7,8-tétrahydro-[1,2,4]triazolo[4,3-a]pyrazine-7-carbonyle)phényle)pipéridin-2-one;
(4-morpholinophényl)(3-(quinolin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(4-(3,5-diméthyl-1H-pyrazol-1-yl)phényl)(3-(quinolin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(3-(2-(4-fluorophényl)thiazol-4-yl)-6-méthyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophén-2-yl)phényl)méthanone;
(3-(2-(4-fluorophényl)thiazol-4-yl)-5-méthyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophén-2-yl)phényl)méthanone;
(3,4-dichlorophényl)(3-(2-(4-fluorophényl)thiazol-4-yl)-8-méthyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(3,4-difluorophényl)(3-(2-(4-fluorophényl)thiazol-4-yl)-8-méthyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(3-chloro-4-fluorophényl)(3-(2-(4-fluorophényl)thiazol-4-yl)-8-méthyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(4-chloro-3-fluorophényl)(3-(2-(4-fluorophényl)thiazol-4-yl)-8-méthyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(3-(2-(4-fluorophényl)thiazol-4-yl)-8-méthyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(3,4,5-trifluorophényl)méthanone;
(8-méthyl-3-(2-phényloxazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophén-2-yl)phényl)méthanone;
(R)-(4-fluorophényl)(8-méthyl-3-(quinolin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(R)-[1,1'-biphényl]-4-yl(8-méthyl-3-(quinolin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(R)-[1,1'-biphényl]-4-yl(8-méthyl-3-(2-morpholinothiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(R)-(4-fluorophényl)(8-méthyl-3-(6-phénylpyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(R)-[1,1'-biphényl]-4-yl(8-méthyl-3-(2-phénylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(R)-(4-fluorophényl)(8-méthyl-3-(4,5,6,7-tétrahydrobenzo[d]thiazol-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(R)-(3-(2-(2,4-difluorophényl)thiazol-4-yl)-8-méthyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-fluorophényl)méthanone;
(R)-(3-(2-(2,3-dichlorophényl)thiazol-4-yl)-8-méthyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-fluo-

rophényl)méthanone;
(R)-(4-fluorophényl)(8-méthyl-3-(2-(4-phénylpipérazin-1-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(R)-(3-(2-(2,4-dichlorophényl)thiazol-4-yl)-8-méthyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-fluorophényl)méthanone;
(R)-(3-(2-(3-chlorophényl)thiazol-4-yl)-8-méthyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-fluorophényl)méthanone;
(R)-(4-fluorophényl)(8-méthyl-3-(2-phényloxazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(R)-[1,1'-biphényl]-4-yl(8-méthyl-3-(2-phényloxazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(R)-(4-fluorophényl)(8-(2-hydroxyéthyl)-3-(2-phénylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(R)-(4'-fluoro-[1,1'-biphényl]-4-yl)(8-méthyl-3-(2-morpholinothiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(R)-(8-méthyl-3-(2-phénylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophén-2-yl)phényl)méthanone;
(R)-(8-méthyl-3-(2-morpholinothiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophén-2-yl)phényl)méthanone;
(R)-(4-fluorophényl)(8-méthyl-3-(4-phénylthiazol-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(R)-(3-(2-(2-chlorophényl)thiazol-4-yl)-8-méthyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-fluorophényl)méthanone;
(R)-(8-méthyl-3-(2-phénylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophén-3-yl)phényl)méthanone;
(R)-(8-méthyl-3-(quinolin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophén-2-yl)phényl)méthanone;
(R)-(3-(2-(2-chlorophényl)thiazol-4-yl)-8-méthyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophén-2-yl)phényl)méthanone;
(R)-[1,1'-biphényl]-4-yl(3-(2-(2-chlorophényl)thiazol-4-yl)-8-méthyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(R)-[1,1'-biphényl]-4-yl(8-méthyl-3-(4-méthyl-2-phénylthiazol-5-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(R)-(3-(2-(4-fluorophényl)thiazol-4-yl)-8-méthyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophén-2-yl)phényl)méthanone;
(R)-[1,1'-biphényl]-4-yl(3-(2-(4-fluorophényl)thiazol-4-yl)-8-méthyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(R)-[1,1'-biphényl]-4-yl(3-(2-(2,4-difluorophényl)thiazol-4-yl)-8-méthyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(R)-(3-(2-(2,4-difluorophényl)thiazol-4-yl)-8-méthyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophén-2-yl)phényl)méthanone;
(S)-(4-fluorophényl)(8-méthyl-3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(S)-(4-fluorophényl)(3-(2-(4-fluorophényl)thiazol-4-yl)-8-méthyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(S)-(4'-fluoro-[1,1'-biphényl]-4-yl)(8-méthyl-3-(2-morpholinothiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(S)-(4-fluorophényl)(8-méthyl-3-(quinolin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(S)-(8-méthyl-3-(quinolin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophén-2-yl)phényl)méthanone;
(S)-(4-fluorophényl)(3-(2-(4-fluorophényl)thiazol-4-yl)-8-méthyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(S)-(3-(2-(2,4-difluorophényl)thiazol-4-yl)-8-méthyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophén-2-yl)phényl)méthanone;
(4-fluorophényl)(8-méthyl-3-(2-phénylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(S)-(4-fluorophényl)(8-méthyl-3-(2-phénylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(S)-(3-(3-(4-fluorophényl)-1,2,4-oxadiazol-5-yl)-8-méthyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-

7(8H)-yl)(4-(thiophén-2-yl)phényl)méthanone;
(R)-(3-(3-(4-fluorophényl)-1,2,4-oxadiazol-5-yl)-8-méthyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophén-2-yl)phényl)méthanone;
(3-(2-(2,4-difluorophényl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophén-2-yl)phényl)méthanone;
(3-(5-phényl-1,2,4-oxadiazol-3-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophén-2-yl)phényl)méthanone;
(4-fluorophényl)(3-(3-phényl-1,2,4-oxadiazol-5-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(4-fluorophényl)(3-(5-phényl-1,2,4-oxadiazol-3-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(3-(3-phényl-1,2,4-oxadiazol-5-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophén-2-yl)phényl)méthanone;
(4-fluorophényl)(3-(3-(4-fluorophényl)-1,2,4-oxadiazol-5-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(3-(3-(4-fluorophényl)-1,2,4-oxadiazol-5-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophén-2-yl)phényl)méthanone;
(3-(3-(2,4-difluorophényl)-1,2,4-oxadiazol-5-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophén-2-yl)phényl)méthanone;
(4-fluorophényl)(3-(5-phényl-1H-1,2,4-triazol-3-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(3-(5-phényl-1H-1,2,4-triazol-3-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophén-2-yl)phényl)méthanone;
(4-fluorophényl)(3-(2-(2-fluorophényl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(3-(2-(2-fluorophényl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophén-2-yl)phényl)méthanone;
[1,1'-biphényl]-4-yl(3-(2-(2-fluorophényl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(4'-fluoro-[1,1'-biphényl]-4-yl)(3-(2-(2-fluorophényl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(3-(3-(2,4-difluorophényl)-1,2,4-oxadiazol-5-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophén-2-yl)phényl)méthanone;
[1,1'-biphényl]-4-yl(3-(2-((4,5-dichloro-1H-imidazol-1-yl)méthyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(3-(2-((4,5-dichloro-1H-imidazol-1-yl)méthyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4'-fluoro-[1,1'-biphényl]-4-yl)méthanone;
(3-(2-(4-chlorobenzyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-fluorophényl)méthanone;
(3-(2-(4-chlorobenzyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophén-2-yl)phényl)méthanone;
(4-fluorophényl)(3-(2-(p-tolyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(4-(thiophén-2-yl)phényl)(3-(2-(p-tolyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
[1,1'-biphényl]-4-yl(3-(2-(p-tolyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(4-fluorophényl)(3-(2-(thiophén-2-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(4-(thiophén-2-yl)phényl)(3-(2-(thiophén-2-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
[1,1'-biphényl]-4-yl(3-(2-(thiophén-2-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(4'-fluoro-[1,1'-biphényl]-4-yl)(3-(2-(thiophén-2-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(3-(2-(((4-chlorophényl)sulfonyl)méthyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophén-2-yl)phényl)méthanone;
[1,1'-biphényl]-4-yl(3-(2-(((4-chlorophényl)sulfonyl)méthyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(3-(2-(((4-chlorophényl)sulfonyl)méthyl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4'-

fluoro-[1,1'-biphényl]-4-yl)méthanone;
(4-fluorophényl)(3-(2-(2-méthoxyphényl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(3-(2-(2-méthoxyphényl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophén-2-yl)phényl)méthanone;
[1,1'-biphényl]-4-yl(3-(2-(2-méthoxyphényl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
[1,1'-biphényl]-4-yl(3-(3-(4-fluorophényl)-1,2,4-oxadiazol-5-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(4'-fluoro-[1,1'-biphényl]-4-yl)(3-(3-(4-fluorophényl)-1,2,4-oxadiazol-5-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(4-fluorophényl)(3-(2-(3-fluorophényl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(3-(2-(3-fluorophényl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophén-2-yl)phényl)méthanone;
(4-fluorophényl)(3-(2-isopropylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(3-(3-(4-fluorophényl)-1,2,4-oxadiazol-5-yl)-8-méthyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophén-2-yl)phényl)méthanone;
(3-(3-phényl-1,2,4-thiadiazol-5-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophén-2-yl)phényl)méthanone;
(4-fluorophényl)(3-(3-phényl-1,2,4-thiadiazol-5-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(3-(2-(4-bromophényl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophén-2-yl)phényl)méthanone;
(3-(2-(4-bromophényl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-fluorophényl)méthanone;
(3-(2-(4-fluorophényl)thiazol-4-yl)-8-méthyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(5-méthylthiophén-2-yl)phényl)méthanone;
4-(3-(2-(4-fluorophényl)thiazol-4-yl)-8-méthyl-5,6,7,8-tétrahydro-[1,2,4]triazolo[4,3-a]pyrazine-7-carbonyl)benzonitrile;
[1,1'-biphényl]-4-yl(3-(3-phényl-1,2,4-oxadiazol-5-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(4-fluorophényl)(3-(2-(pyridin-4-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(3-(2-(quinolin-2-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophén-2-yl)phényl)méthanone;
(3-(1-méthyl-3-phényl-1H-pyrazol-5-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophén-2-yl)phényl)méthanone;
(3-(2-(4-(diméthylamino)phényl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-fluorophényl)méthanone;
(3-(1-méthyl-5-phényl-1H-pyrazol-3-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophén-2-yl)phényl)méthanone;
(4'-fluoro-[1,1'-biphényl]-4-yl)(3-(3-phényl-1,2,4-oxadiazol-5-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(3-(2-(pyridin-2-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophén-2-yl)phényl)méthanone;
(4-fluorophényl)(3-(1-méthyl-3-phényl-1H-pyrazol-5-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(3-(2-(pyrimidin-2-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophén-2-yl)phényl)méthanone;
(S)-(8-méthyl-3-(2-morpholinothiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophén-2-yl)phényl)méthanone;
(3-(2-(pyridin-4-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophén-2-yl)phényl)méthanone;
(3-(2-(4-(diméthylamino)phényl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophén-2-yl)phényl)méthanone;
(4-fluorophényl)(3-(2-(pyridin-2-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
phényl(3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(3-(pyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(p-tolyl)méthanone;

(S)-(3-(2-(4-fluorophényl)thiazol-4-yl)-8-méthyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(2-méthylthiophén-3-yl)phényl)méthanone;
(R)-(3-(2-(4-fluorophényl)thiazol-4-yl)-8-méthyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(2-méthylthiophén-3-yl)phényl)méthanone;
(3-(2-(pyrazin-2-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophén-2-yl)phényl)méthanone;
4-(4-(7-(4-(thiophén-2-yl)benzoyl)-5,6,7,8-tétrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)thiazol-2-yl)benzonitrile;
(4-fluorophényl)(3-(2-(pyrazin-2-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(4-fluorophényl)(3-(1-méthyl-5-phényl-1H-pyrazol-3-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(3-(2-(4-morpholinophényl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophén-2-yl)phényl)méthanone;
(4-fluorophényl)(3-(2-(4-morpholinophényl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(3-(2-(4-(4-méthylpipérazin-1-yl)phényl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophén-2-yl)phényl)méthanone;
(4-fluorophényl)(3-(2-(4-(4-méthylpipérazin-1-yl)phényl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(3-(2-(4-(pipéridin-1-yl)phényl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophén-2-yl)phényl)méthanone;
(4-fluorophényl)(3-(2-(4-(pipéridin-1-yl)phényl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(3-(2-(4-(pyrrolidin-1-yl)phényl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophén-2-yl)phényl)méthanone;
(4-fluorophényl)(3-(2-(4-(pyrrolidin-1-yl)phényl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(3-(2-(pipéridin-1-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophén-2-yl)phényl)méthanone;
(3-(2-(pyrrolidin-1-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophén-2-yl)phényl)méthanone;
(4-fluorophényl)(3-(2-(pyrrolidin-1-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(3-(2-(4-méthylpipérazin-1-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophén-2-yl)phényl)méthanone;
(4-fluorophényl)(3-(2-(4-méthylpipérazin-1-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(3-(1-méthyl-2-phényl-1H-imidazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophén-2-yl)phényl)méthanone;
(4-(diméthylamino)phényl)(3-(2-(4-fluorophényl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(3-(1-(2-méthoxyethyl)-3-phényl-1H-pyrazol-5-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophén-2-yl)phényl)méthanone;
(4-fluorophényl)(3-(1-(2-méthoxyethyl)-3-phényl-1H-pyrazol-5-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(3-(2-isobutylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophén-2-yl)phényl)méthanone;
(3-(2-(2-(2-méthoxyethyl)morpholino)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophén-2-yl)phényl)méthanone;
(3-(2-(4,4-difluoropipéridin-1-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-fluorophényl)méthanone;
(4-fluorophényl)(3-(2-isobutylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(3-(2-(2,5-diméthylmorpholino)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophén-2-yl)phényl)méthanone;
(3-(2-(2-hydroxyphényl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophén-2-yl)phényl)méthanone;
(3-(2-(4,4-difluoropipéridin-1-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophén-2-yl)phényl)méthanone;
(3-(2-(2,6-diméthylmorpholino)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophén-2-

yl)phényl)méthanone;
(3-(2-(2,2-diméthylmorpholino)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophén-2-yl)phényl)méthanone;
(3-(3-phényl-1H-pyrazol-5-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophén-2-yl)phényl)méthanone;
(3-(2-(4-fluorophényl)thiazol-4-yl)-8-méthyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(3-méthylthiophén-2-yl)phényl)méthanone;
(4-fluorophényl)(3-(3-phényl-1H-pyrazol-5-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(R)-(3-(2-(4-fluorophényl)thiazol-4-yl)-8-méthyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(3-méthylthiophén-2-yl)phényl)méthanone;
(4-fluorophényl)(3-(2-(2-hydroxyphényl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(S)-(3-(2-(4-fluorophényl)thiazol-4-yl)-8-méthyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(3-méthylthiophén-2-yl)phényl)méthanone;
(3-(2-(2-méthylmorpholino)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophén-2-yl)phényl)méthanone;
(3-(2-(4,4-diméthylpipéridin-1-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophén-2-yl)phényl)méthanone;
(3-(5-méthylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophén-2-yl)phényl)méthanone;
(3-(2-(4,4-diméthylpipéridin-1-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-fluorophényl)méthanone;
(4-fluorophényl)(3-(2-(2-(méthoxyméthyl)pipéridin-1-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(4-fluorophényl)(8-méthyl-3-(6-méthylpyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(3-(2-(2-(méthoxyméthyl)pipéridin-1-yl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophén-2-yl)phényl)méthanone;
tert-butyl (2-(2-(4-(7-(4-(thiophén-2-yl)benzoyl)-5,6,7,8-tétrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)thiazol-2-yl)phenoxy)éthyl)carbamate;
(3-(2-(2-(2-hydroxyéthoxy)phényl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophén-2-yl)phényl)méthanone;
(3-(2-(2-(2-aminoéthoxy)phényl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophén-2-yl)phényl)méthanone;
N-(4-(4-(7-(4-(thiophén-2-yl)benzoyl)-5,6,7,8-tétrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)thiazol-2-yl)phényl)méthanesulfonamide;
(3-(1-(2-hydroxyéthyl)-3-phényl-1H-pyrazol-5-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophén-2-yl)phényl)méthanone;
(3-(1-(2-hydroxyéthyl)-5-phényl-1H-pyrazol-3-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophén-2-yl)phényl)méthanone;
[1,1'-biphényl]-4-yl(8-méthyl-3-(6-méthylpyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(8-méthyl-3-(6-méthylpyridin-2-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophén-2-yl)phényl)méthanone;
(3-(2-(2,4-difluorophényl)-5-méthylthiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophén-2-yl)phényl)méthanone;
(3-(2-(3-(diméthylamino)phényl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophén-2-yl)phényl)méthanone;
(3-(2-(3-(diméthylamino)phényl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-fluorophényl)méthanone;
N-(3-(4-(7-(4-(thiophén-2-yl)benzoyl)-5,6,7,8-tétrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)thiazol-2-yl)phényl)méthanesulfonamide;
N-(2-(4-(7-(4-(thiophén-2-yl)benzoyl)-5,6,7,8-tétrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)thiazol-2-yl)phényl)méthanesulfonamide;
(3-(4-chlorophényl)-1H-pyrazol-5-yl)(3-(2-(4-fluorophényl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(3-(4-chlorophényl)-1-méthyl-1H-pyrazol-5-yl)(3-(2-(4-fluorophényl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;

(3-(3,4-dichlorophényl)-1-méthyl-1H-pyrazol-5-yl)(3-(2-(4-fluorophényl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
(5-(4-chlorophényl)-1-méthyl-1H-pyrazol-3-yl)(3-(2-(4-fluorophényl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)méthanone;
tert-butyl (2-(3-phényl-5-(7-(4-(thiophén-2-yl)benzoyl)-5,6,7,8-tétrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)-1H-pyrazol-1-yl)éthyl)carbamate;
tert-butyl (2-(5-phényl-3-(7-(4-(thiophén-2-yl)benzoyl)-5,6,7,8-tétrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)-1H-pyrazol-1-yl)éthyl)carbamate;
(3-(2-(2-bromophényl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophén-2-yl)phényl)méthanone;
(3-(2-(3-bromophényl)thiazol-4-yl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(thiophén-2-yl)phényl)méthanone;
2-(4-(7-(4-(thiophén-2-yl)benzoyl)-5,6,7,8-tétrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)thiazol-2-yl)benzonitrile;
3-(4-(7-(4-(thiophén-2-yl)benzoyl)-5,6,7,8-tétrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)thiazol-2-yl)benzonitrile;
(3-(2-(4-fluorophényl)thiazol-4-yl)-8-méthyl-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(4-(2-méthylthiophén-3-yl)phényl)méthanone;
et les sels et solvates pharmaceutiquement acceptables de ceux-ci.

13. Composition pharmaceutique comprenant un composé selon l'une quelconque des revendications **1** à **12** ou un sel ou solvate pharmaceutiquement acceptable de celui-ci et au moins un véhicule, diluant, excipient et/ou adjuvant pharmaceutiquement acceptable.

14. Médicament comprenant un composé selon l'une quelconque des revendications **1** à **12** ou un sel ou solvate pharmaceutiquement acceptable de celui-ci.

15. Composé selon l'une quelconque des revendications **1** à **12** ou un sel ou solvate pharmaceutiquement acceptable de celui-ci pour son utilisation dans le traitement et/ou la prévention de la dépression, de l'anxiété, de la psychose, de la schizophrénie, des troubles psychotiques, des troubles bipolaires, des troubles cognitifs, de la maladie de Parkinson, de la maladie d'Alzheimer, du trouble déficitaire de l'attention avec hyperactivité (TDAH), de la douleur, des convulsions, de l'obésité, des maladies inflammatoires telles que le syndrome du côlon irritable et les troubles intestinaux inflammatoires, des vomissements, de la pré-éclampsie, des maladies associées aux voies respiratoires telles que la bronchopneumopathie obstructive chronique, l'asthme, l'hypersensibilité des voies respiratoires, la broncoconstruction et la toux, les troubles de la reproduction et des maladies dépendantes des hormones sexuelles telles que, mais sans s'y limiter, l'hypertrophie bénigne de la prostate (HBP), le carcinome métastasique de la prostate, le cancer des testicules, le cancer du sein, l'acné dépendant des androgènes, la calvitie masculine, l'endométriose, une puberté anormale, la fibrose utérine, les cancers hormono-dépendants, l'hyperandrogénie, l'hirsutisme, le virilisme, le syndrome des ovaires polykystiques (SOPK), le syndrome HAIR-AN (hyperandrogénie, résistance insuline et acanthosis nigricans), l'hyperthécose ovarienne (HAIR-AN avec hyperplasie des cellules thécales lutéinisées du stoma ovarien), d'autres manifestations de concentrations intra-ovariennes élevées en androgènes (par exemple, l'arrêt de la maturation folliculaire, l'atrésie, l'anovulation, les dysménorrhées, des saignements utérins dysfonctionnels, la stérilité), les troubles gynécologiques, la stérilité et une tumeur produisant des androgènes (tumeur ovarienne virilisante ou tumeur surrénalienne).

16. Composé selon l'une quelconque des revendications **1** à **12** ou un sel ou solvate pharmaceutiquement acceptable de celui-ci pour son utilisation dans la suppression de l'augmentation soudaine de LH lors d'une procréation assistée chez une patiente.

17. Composé selon l'une quelconque des revendications **1** à **12** ou un sel ou solvate pharmaceutiquement acceptable de celui-ci, pour son utilisation à des fins de castration chez les hommes et pour inhiber les pulsions sexuelles chez les hommes.

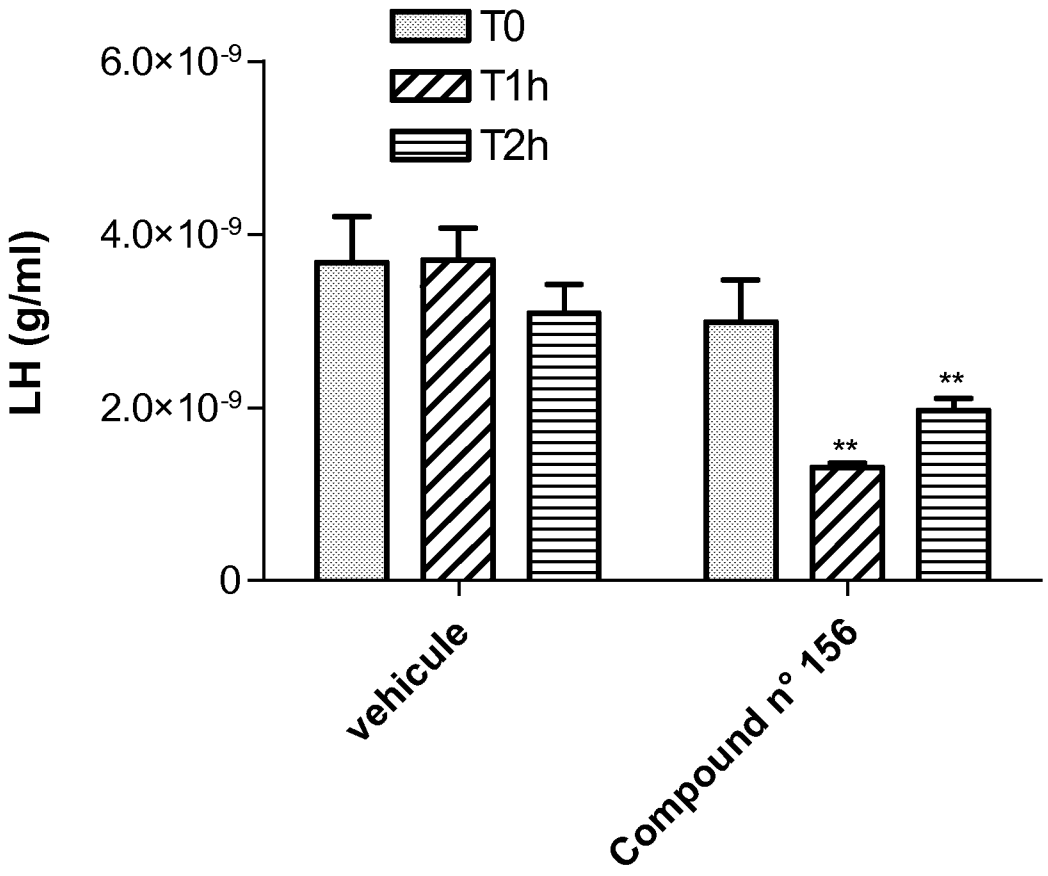
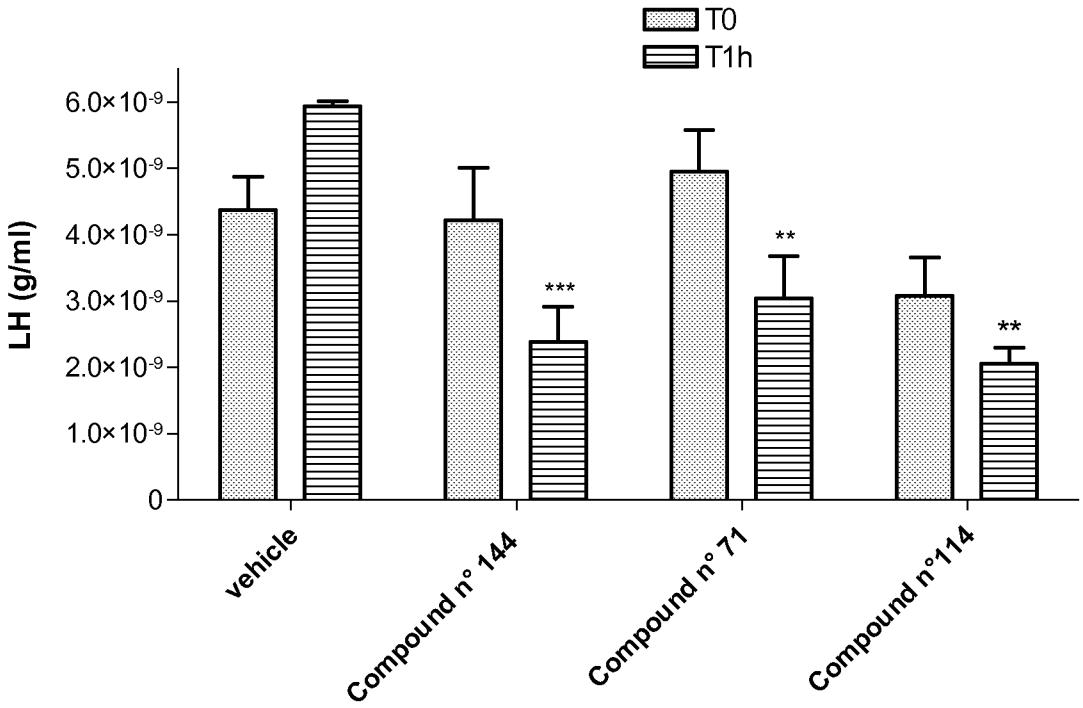
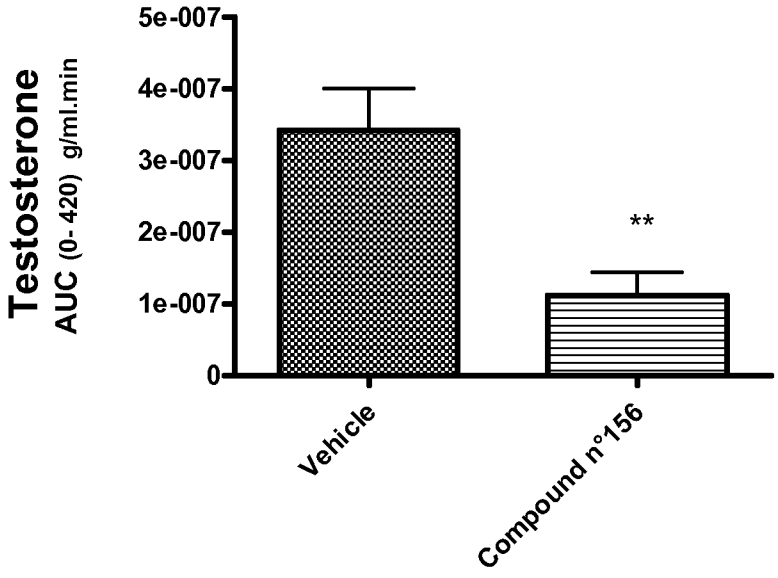


FIGURE 1



Statistics: One-Way ANOVA and Dunnett's post hoc
**** p<0.01 et ** p<0.05*

FIGURE 2



** p< 0.01 vs vehicle, determined by one-Way ANOVA and Dunnett's post hoc

FIGURE 3

REFERENCES CITED IN THE DESCRIPTION

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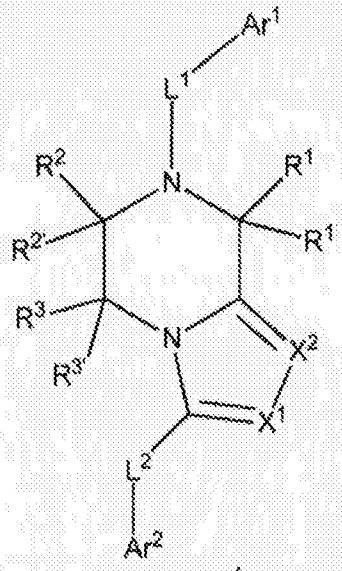
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ÚJ NK-3 RECEPTOR SZELEKTÍV ANTAGONISTA VEGYÜLETEK, GYÓGYÁSZATI KÉSZÍTMÉNY ÉS ELJÁRÁSOK AZ NK-3 RECEPTOROK ÁLTAL KÖZVETÍTETT RENDELLENESSÉGEK SORÁN TÖRTÉNŐ ALKALMAZÁSRA

Szabadalmi igénypontok

1. Vegyület, amely a következő I általános képletű:



I

SZTNH-100051921

és annak gyógyászatilag elfogadható sói és szolvátjai, ahol

Ar^1 jelentése egy 5-6-tagú aril vagy heteroaril csoport, egy 3-6-tagú cikloalkil csoport, egy 3-6-tagú heterociklil csoport vagy egy C3-C6-alkil csoport, ahol mindegyik az aril, heteroaril, cikloalkil vagy heterociklil csoportok közül opcionálisan szubsztituálva (helyettesítve) van egy vagy több csoporttal, amely a következők közül van választva: halogén, ciano, alkil, halogén-alkil, cikloalkil, heteroalkil, heterociklil, aril, aralkil, heteroaril, hidroxil, alkoxi, halogén-alkoxi, alkox-alkoxi, alkil-amino, karboxi, alkoxi-karbonil, alkil-karbonil-oxi, alkil-karbonil-amino, halogén-alkil-karbonil-amino, karbamoil, alkil-karbamoil, karbamoil-amino, alkil-karbamoil-amino, alkil-szulfonil, halogén-alkil-szulfonil, szulfamoil, alkil-szulfamoil, alkil-szulfonil-amino, halogén-alkil-szulfonil-amino, vagy két szubstituens egy alkilén-dioxi csoportot vagy egy halogén-alkilén-dioxi csoportot képez, vagy két szubstituens egy cikloalkil vagy heterocikloalkil molekularészt (csoportot) képez együtt a cikloalkil vagy heterocikloalkil csoporttal, amelyhez azok kapcsolódnak, vagy az aril, heteroaril, cikloalkil vgy heterocikloalkil csoporttal kondenzálva lehet egy vagy több aril molekularész (csoport), ahol a nevezett szubsztituensek közül mindegyik opcionálisan szubsztituálva (helyettesítve) van egy vagy több további szubsztituenssel, amely a következők közül van választva: halogén, ciano, alkil, halogén-alkil, ciklopropil, alkoxi, halogén-alkoxi, heterociklil, aril, heteroaril, aril-oxi, heteroaril-oxi;

L^1 jelentése karbonil;

R^1 jelentése H, egy C_1-C_4-alkil, aril vagy aralkil csoport, ahol a nevezett alkil, aril vagy aralkil csoportok opcionálisan szubsztituálva (helyettesítve) vannak egy vagy több csoporttal, amely a következők közül van választva: halogén vagy hidroxil;

$R^{1'}$ jelentése H vagy egy C_1-C_4-alkil csoport;

R^2 jelentése H vagy egy C_1-C_4-alkil csoport;

$R^{2'}$ jelentése H vagy egy C_1-C_4-alkil csoport;

R^3 jelentése H vagy egy C_1-C_4-alkil csoport, amely opcionálisan szubsztituálva (helyettesítve) van egy hidroxi csoporttal;

$R^{3'}$ jelentése H vagy egy C_1-C_4-alkil csoport;

X^1 és X^2 jelentése N;

L^2 jelentése egy egyes kötés vagy karbonil,

Ar^2 jelentése egy 5-6-tagú aril vagy heteroaril csoport, ahol mindegyik az aril vagy heteroaril csoportok közül opcionálisan szubsztituálva (helyettesítve) van egy vagy több csoporttal, amely a következők közül van választva: halogén, ciano, alkil, hidroxi-alkil, halogén-alkil, cikloalkil, heteroalkil, heterociklil, aril, heteroaril, aralkil, heteroaril-alkil, hidroxil, alkoxi, halogén-alkoxi, alkil-amino, karboxi, alkoxi-karbonil, alkil-karbonil-oxi, alkil-karbonil-amino, halogén-alkil-karbonil-amino, acil-amino, karbamoil, alkil-karbamoil, karbamoil-alkil, karbamoil-amino, alkil-karbamoil-amino, alkil-szulfonil, halogén-alkil-szulfonil, aril-szulfonil-alkil, szulfamoil, alkil-szulfamoil, alkil-szulfonil-amino, halogén-alkil-szulfonil-amino, vagy két szubstituens egy alkilén-dioxi csoportot vagy egy halogén-alkilén-dioxi csoportot képez, vagy az aril vagy heteroaril csoporttal kondenzálva lehet egy vagy több cikloalkil, aril, heterociklil vagy heteroaril molekularész (csoport), ahol a nevezett szubsztituensek közül mindegyik opcionálisan szubsztituálva (helyettesítve) van egy vagy több további szubsztituenssel, amely a következők közül van választva: halogén, ciano, alkil, halogén-alkil, alkoxi, halogén-alkoxi, cikloalkil, heterociklil, amelyek opcionálisan szubsztituálva (helyettesítve) vannak a következőkkel: alkil, aril, heteroaril, hidroxil, alkoxi-alkil, hidroxi-alkoxi, alkil-amino, alkil-szulfonil-amino, alkoxi-karbonil-amino, amino-alkoxi, vagy alkoxi-karbonil-amino-alkoxi;

és ahol, ha:

R^1, $R^{1'}$, R^2, $R^{2'}$, R^3, $R^{3'}$ jelentése H, és

L^2 jelentése egyes kötés, és

Ar^1 jelentése egy 6-tagú aril csoport, amely opcionálisan szubsztituálva (helyettesítve) van egy vagy több csoporttal, amely a következők közül van választva: halogén, ciano, C1-C3-alkil, C1-halogén-alkil, és

Ar^2 jelentése egy 5-6-tagú aril vagy heteroaril csoport, amely opcionálisan szubsztituálva (helyettesítve) van egy vagy több csoporttal, amely a következők közül van választva: halogén, C1-C3-alkil, hidroxil, metoxi, vagy kondenzálva van egy aril vagy heteroaril csoporttal, amely opcionálisan szubsztituálva (helyettesítve) van egy vagy több további halogén, C1-C3-alkil, hidroxil, metoxi csoporttal,

akkor

Ar^1 jelentése fenil, 3-halogén-fenil, 4-halogén-fenil, 2,3-diklór-fenil, 2,4-difluor-fenil, 2,5-dihalogén-fenil, 2,6-difluor-fenil, 2,6-diklór-fenil, 3,4-dihalogén-fenil, 3,5-dihalogén-fenil, 3,4,5-trihalogén-fenil, 2-ciano-fenil, 3-ciano-fenil, 4-ciano-fenil, 2,3-diciano-fenil, 2,4-diciano-fenil, 3,5-diciano-fenil, 3-ciano-4-halogén-fenil, 4-(C1-C3-alkil)fenil, 3,4-di(C1-C3-alkil)fenil, 3,5-di(C1-C3-alkil)fenil, 4-(C1-halogén-alkil)fenil, és

Ar² jelentése 2-(C1-C3-alkil)tiazol-4-il, 5-(C1-C3-alkil)tiazol-4-il, piridin-2-il, 4-halogén-piridin-2-il, 4-(C1-C3-alkil)piridin-2-il, 5-(C1-C3-alkil)piridin-2-il, 6-(C1-C3-alkil)pridin-2-il, kinolin-2-il, izokinolin-3-il, 8-halogén-kinolin-2-il, benzotiazol-2-il, 4,5,6,7-tetrahidro-1,3-benzotiazol-2-il;

a következő feltételekkel:

- **Ar¹** jelentése sem egy szubstituált vagy szubstituálatlan pirazolo[1,5-a]piridin-2il sem egy szubstituált vagy szubstituálatlan pirazolo[1,5-a]pirimidin-2-il molekularész (csoport); és

az I általános képletű vegyületet az egyik sem képezi a következők közül:

(2,4-difluor-fenil)(3-(piridin-2-il)-5,6-dihidro-[1,2,4]triazolo[4,3-a]pirazin-7(8H)-il)metanon;

(3-klór-fenil)(3-(piridin-2-il)-5,6-dihidro-[1,2,4]triazolo[4,3-a]pirazin-7(8H)-il)metanon;

2-(3-(piridin-2-il)-5,6,7,8-tetrahidro-[1,2,4]triazolo[4,3-a]pirazin-7-karbonil)benzonitril;

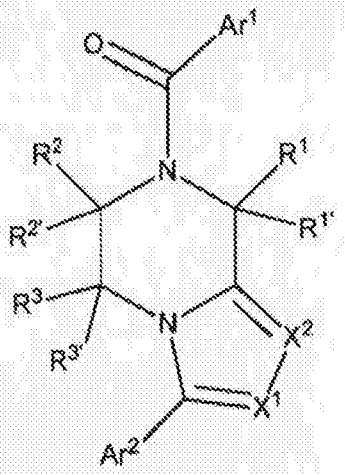
(2,6-diklór-fenil)(3-(piridin-2-il)-5,6-dihidro-[1,2,4]triazolo[4,3-a]pirazin-7(8H)-il)metanon,

(2,3-diklór-fenil)(3-(piridin-2-il)-5,6-dihidro-[1,2,4]triazolo[4,3-a]pirazin-7(8H)-il)metanon,

(2,3-diklór-fenil)(3-(5-metil-piridin-2-il)-5,6-dihidro-[1,2,4]triazolo[4,3-a]pirazin-7(8H)-il)metanon,

(2,3-diklór-fenil)(3-(6-metil-piridin-2-il)-5,6-dihidro-[1,2,4]triazolo[4,3-a]pirazin-7(8H)-il)metanon.

2. Vegyület az 1. igénypont szerint, amely a következő Ib általános képlettel rendelkezik:

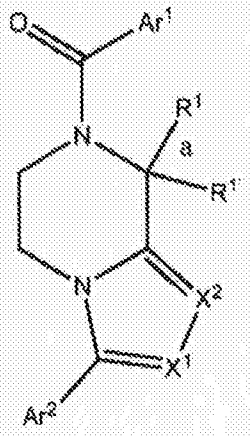


Ib

és annak gyógyászatilag elfogadható sói és szolvátjai, ahol

Ar¹, **Ar²**, **R¹**, **R¹'**, **R²**, **R²'**, **R³**, **R³'**, **X¹**, **X²** jelentése az 1. igénypontban meghatározottak szerinti.

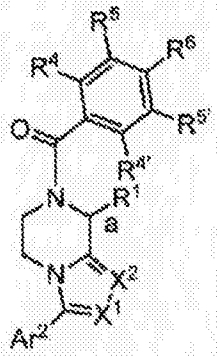
3. Vegyület a 2. igénypont szerint, amely a következő Ic általános képlettel rendelkezik:



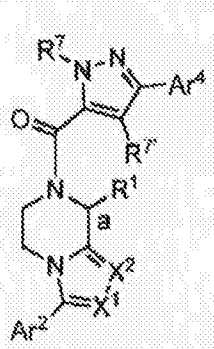
Ic

és annak gyógyászatilag elfogadható sói és szolvátjai, ahol **a** ábrázolja a kötést, amely által $\mathbf{R^1}$ kapcsolódik a piperazin molekularészhez (csoporthoz), és ahol $\mathbf{Ar^1}$, $\mathbf{Ar^2}$, $\mathbf{R^1}$, $\mathbf{R^{1'}}$, $\mathbf{X^1}$ és $\mathbf{X^2}$ jelentése a 2. igénypontban meghatározottak szerinti.

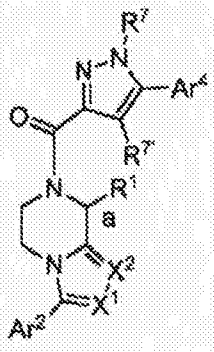
4. Vegyület a 3. igénypont szerint, amely a következő Id-1, Id-2, Id-3 és Id-4 általános képletek közül van választva:



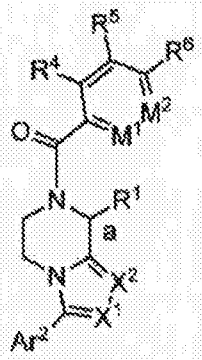
Id-1



Id-2



Id-3



Id-4

és azok gyógyászatilag elfogadható sói és szolvátjai, ahol

a ábrázolja a kötést, amely által $\mathbf{R^1}$ kapcsolódik a piperazin molekularészhez (csoporthoz); és

$\mathbf{Ar^2}$, $\mathbf{R^1}$, $\mathbf{X^1}$ és $\mathbf{X^2}$ jelentése a 2. igénypontban meghatározottak szerinti; és

$\mathbf{R^4}$, $\mathbf{R^{4'}}$, $\mathbf{R^5}$, $\mathbf{R^{5'}}$ és $\mathbf{R^6}$ jelentése egymástól függetlenül a következők közül van választva: H, halogén, ciano, alkil, halogén-alkil, C3-C6-cikloalkil, heteroalkil, heterociklil, aril, heteroaril, hidroxil, alkoxi, halogén-alkoxi, alkoxi-alkoxi, alkil-amino, karboxi, alkoxi-karbonil, alkil-karbonil-oxi, alkil-karbonil-amino, halogén-alkil-karbonil-amino, karbamoil, alkil-karbamoil, karbamoil-amino, alkil-karbamoil-amino, alkil-szulfonil, halogén-alkil-szulfonil, szulfamoil, alkil-szulfamoil, alkil-szulfonil-amino, halogén-alkil-szulfonil-amino, vagy $\mathbf{R^5}$ együtt $\mathbf{R^4}$-gyel vagy $\mathbf{R^6}$-tal, vagy $\mathbf{R^{5'}}$ együtt $\mathbf{R^{4'}}$-vel vagy $\mathbf{R^6}$-tal egy alkilén-dioxi csoportot vagy egy halogén-alkilén-dioxi csoportot képez, vagy $\mathbf{R^5}$ együtt $\mathbf{R^4}$-gyel vagy $\mathbf{R^6}$-tal, vagy $\mathbf{R^{5'}}$ együtt $\mathbf{R^{4'}}$-vel vagy $\mathbf{R^6}$-tal egy aril molekularészt (csoportot) képez, amely kondenzálva van a fenil csoporttal, amelyekhez azok kapcsolódnak, ahol mindegyik a nevezett szubsztituensek közül opcionálisan szubsztituálva (helyettesítve) van egy vagy több további szubsztituenssel, amely a következők közül van választva: halogén, ciano, alkil, halogén-alkil, ciklopropil; és

R^7 jelentése H vagy metil; és

$R^{7'}$ jelentése H vagy metil; és

Ar^4 jelentése egy cikloalkil vagy egy aril csoport, ahol mindegyik a nevezett cikloalkil vagy aril csoportok közül opcionálisan szubsztituálva (helyettesítve) van egy vagy több csoporttal, amely a következők közül van választva: halogén, alkil, halogén-alkil, ciklopropil, halogén-alkoxi, aril-oxi; és

M^1 jelentése N vagy C-$R^{4''}$, ahol $R^{4''}$ jelentése a következők közül van választva: H, halogén, ciano, alkil, halogén-alkil, C3-C6-cikloalkil, heteroalkil, heterociklil, aril, heteroaril, hidroxil, alkoxi, halogén-alkoxi, alkoxi-alkoxi, alkil-amino, karboxi, alkoxi-karbonil, alkil-karbonil-oxi, alkil-karbonil-amino, halogén-alkil-karbonil-amino, karbamoil, alkil-karbamoil, karbamoil-amino, alkil-karbamoil-amino, alkil-szulfonil, halogén-alkil-szulfonil, szulfamoil, alkil-szulfamoil, alkil-szulfonil-amino, halogén-alkil-szulfonil-amino, ahol mindegyik a nevezett szubsztituensek közül opcionálisan szubsztituálva (helyettesítve) van egy vagy több további szubsztituenssel, amely a következők közül van választva: halogén, ciano, alkil, halogén-alkil, ciklopropil; és

M^2 jelentése N vagy M^2 jelentése C-$R^{5''}$ azzal a feltétellel, hogy M^1 jelentése N, ahol $R^{5''}$ jelentése a következők közül van választva: H, halogén, ciano, alkil, halogén-alkil, C3-C6-cikloalkil, heteroalkil, heterociklil, aril, heteroaril, hidroxil, alkoxi, halogén-alkoxi, alkoxi-alkoxi, alkil-amino, karboxi, alkoxi-karbonil, alkil-karbonil-oxi, alkil-karbonil-amino, halogén-alkil-karbonil-amino, karbamoil, alkil-karbamoil, karbamoil-amino, alkil-karbamoil-amino, alkil-szulfonil, halogén-alkil-szulfonil, szulfamoil, alkil-szulfamoil, alkil-szulfonil-amino, halogén-alkil-szulfonil-amino, vagy $R^{5''}$ együtt R^6-tal egy alkilén-dioxi csoportot vagy egy halogén-alkilén-dioxi csoportot képez, vagy egy aril molekularészt (csoportot) képez, amely kondenzálva van a piridinil csoporttal, amelyekhez azok kapcsolódnak, ahol mindegyik a nevezett szubsztituensek közül opcionálisan szubsztituálva (helyettesítve) van egy vagy több további szubsztituenssel, amely a következők közül van választva: halogén, ciano, alkil, halogén-alkil, ciklopropil; és

ahol, az Id-1 általános képletben, ha:

R^1 jelentése H, és

R^4, $R^{4'}$, R^5, $R^{5'}$ és R^6 jelentése egymástól függetlenül a következők közül van választva: H, halogén, ciano, C1-C3-alkil, C1-halogén-alkil, és

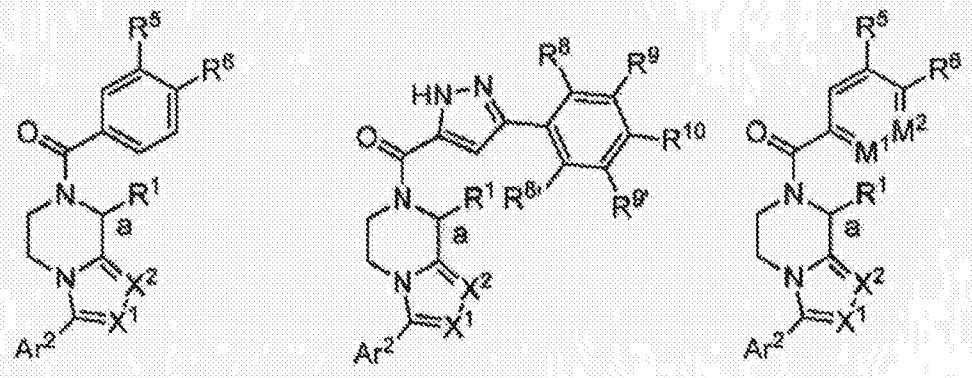
Ar^2 jelentése egy 5-6-tagú aril vagy heteroaril csoport, amely opcionálisan szubsztituálva (helyettesítve) van egy vagy több csoporttal, amely a következők közül van választva: halogén, C1-C3-alkil, hidroxil, alkoxi, vagy kondenzálva van egy aril csoporttal, amely opcionálisan szubsztituálva (helyettesítve) van egy vagy több további halogén, C1-C3-alkil, hidroxil, metoxi csoporttal,

akkor

R^4, $R^{4'}$, R^5, $R^{5'}$ és R^6 jelentése H, vagy R^4, $R^{4'}$, $R^{5'}$, R^6 jelentése H és R^5 jelentése halogén, vagy R^4, $R^{4'}$, R^5, $R^{5'}$ jelentése H és R^6 jelentése halogén, ciano, C1-C3-alkil, C1-halogén-alkil, vagy $R^{4'}$, $R^{5'}$, R^6 jelentése H és R^4, R^5 jelentése halogén, vagy R^4, $R^{4'}$, $R^{5'}$ jelentése H és R^5, R^6 jelentése egymástól függetlenül halogén, vagy R^4, $R^{4'}$ jelentése H és R^5, $R^{5'}$, R^6 jelentése halogén, és

Ar^2 jelentése 2-(C1-C3-alkil)tiazol-4-il, 5-(C1-C3-alkil)tiazol-4-il, piridin-2-il, 4-halogén-piridin-2-il, 4-(C1-C3-alkil)piridin-2-il, 5-(C1-C3-alkil)piridin-2-il, 6-(C1-C3-alkil)piridin-2-il, kinolin-2-il, izokinolin-3-il, 8-halogén-kinolin-2-il, benzotiazol-2-il, 4,5,6,7-tetrahidro-1,3-benzotiazol-2-il.

5. Vegyület a 4. igénypont szerint, amely a következő Ie-1, Ie-2 és Ie-3 általános képletek közül van választva:



Ie-1 Ie-2 Ie-3

és azok gyógyászatilag elfogadható sói és szolvátjai, ahol

a ábrázolja a kötést, amely által R^1 kapcsolódik a piperazin molekularészhez (csoporthoz); és

Ar^2, R^1, X^1 és X^2 jelentése a 2. igénypontban meghatározottak szerinti; és

R^5 és R^6 jelentése egymástól függetlenül a következők közül van választva: H, halogén, ciano, alkil, ciklopropil, aril, heteroaril, ahol mindegyik a nevezett aril és heteroaril csoportok közül opcionálisan szubsztituálva (helyettesítve) van egy vagy több csoporttal, amely a következők közül van választva: halogén, alkil, ciklopropil, vagy R^5 és R^6 együtt egy fenil molekularészt (csoportot) képeznek, amely kondenzálva van a fenil gyűrűhöz, amelyekhez azok kapcsolódnak; és

R^8, $R^{8'}$, R^9, $R^{9'}$ és R^{10} jelentése egymástól függetlenül a következők közül van választva: H, halogén, halogén-alkil, ciklopropil vagy halogén-alkoxi, vagy R^8, $R^{8'}$, R^9, $R^{9'}$ jelentése H és R^{10} jelentése fenoxi;

M^1 és M^2 jelentése a 4. igénypontban meghatározottak szerinti; és

ahol, az Ie-1 általános képletben, ha:

R^1 jelentése H, és

R^5 és R^6 jelentése egymástól függetlenül a következők közül van választva: H, halogén, ciano, C1-C3-alkil, és

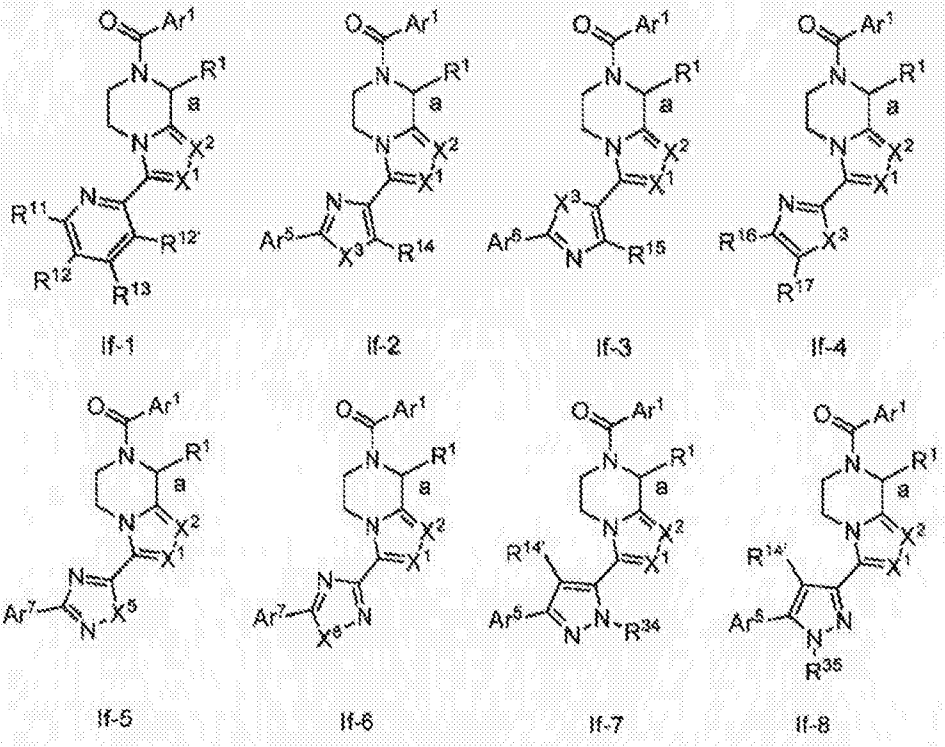
Ar^2 jelentése egy 5-6-tagú aril vagy heteroaril csoport, amely opcionálisan szubsztituálva (helyettesítve) van egy vagy több csoporttal, amely a következők közül van választva: halogén, C1-C3-alkil, hidroxil, alkoxi, vagy kondenzálva van egy aril csoporttal, amely opcionálisan szubsztituálva (helyettesítve) van egy vagy több további halogén, C1-C3-alkil, hidroxil, metoxi csoporttal,

akkor

R^6 jelentése H és R^5 jelentése H, halogén, vagy R^5 jelentése H és R^6 jelentése halogén, ciano, C1-C3-alkil, C1-halogén-alkil, vagy R^5 és R^6 jelentése egymástól függetlenül halogén, és

Ar^2 jelentése 2-(C1-C3-alkil)tiazol-4-il, 5-(C1-C3-alkil)tiazol-4-il, piridin-2-il, 4-halogén-piridin-2-il, 4-(C1-C3-alkil)piridin-2-il, 5-(C1-C3-alkil)piridin-2-il, 6-(C1-C3-alkil)piridin-2-il, kinolin-2-il, izokinolin-3-il, 8-halogén-kinolin-2-il, benzotiazol-2-il, 4,5,6,7-tetrahidro-1,3-benzotiazol-2-il.

6. Vegyület a 3. igénypont szerint, amely a következő If-1, If-2, If-3, If-4, If-5, If-6, If-7 és If-8 általános képletek közül van választva:



If-1 If-2 If-3 If-4

If-5 If-6 If-7 If-8

és azok gyógyászatilag elfogadható sói és szolvátjai, ahol

a ábrázolja a kötést, amely által $\mathbf{R^1}$ kapcsolódik a piperazin molekularészhez (csoporthoz); és

$\mathbf{Ar^1}$, $\mathbf{R^1}$, $\mathbf{X^1}$ és $\mathbf{X^2}$ jelentése a 2. igénypontban meghatározottak szerinti; és

$\mathbf{R^{11}}$, $\mathbf{R^{12}}$, $\mathbf{R^{12'}}$ és $\mathbf{R^{13}}$ jelentése egymástól függetlenül a következők közül van választva: H, halogén, ciano, alkil, hidroxi-alkil, halogén-alkil, C3-C6-cikloalkil, heteroalkil, heterociklil, aril, heteroaril, hidroxil, alkoxi, halogén-alkoxi, alkil-amino, karboxi, alkoxi-karbonil, alkil-karbonil-oxi, alkil-karbonil-amino, halogén-alkil-karbonil-amino, acil-amino, karbamoil, alkil-karbamoil, karbamoil-alkil, karbamoil-amino, alkil-karbamoil-amino, alkil-szulfonil, halogén-alkil-szulfonil, szulfamoil, alkil-szulfamoil, alkil-szulfonil-amino, halogén-alkil-szulfonil-amino, vagy $\mathbf{R^{12}}$ együtt $\mathbf{R^{11}}$-gyel vagy $\mathbf{R^{13}}$-mal, vagy $\mathbf{R^{13}}$ együtt $\mathbf{R^{12'}}$-vel egy alkilén-dioxi csoportot vagy egy halogén-alkilén-dioxi csoportot képez, vagy $\mathbf{R^{12}}$ együtt $\mathbf{R^{11}}$-gyel vagy $\mathbf{R^{13}}$-mal egy cikloalkil, aril, heterociklil vagy heteroaril molekularészt (csoportot) képez, amely kondenzálva van a piridil csoporttal, amelyekhez azok kapcsolódnak, ahol mindegyik a nevezett csoportok közül opcionálisan szubsztituálva (helyettesítve) van egy vagy több csoporttal, amely a következők közül van választva: halogén, ciano, alkil, halogén-alkil, ciklopropil, alkoxi, halogén-alkoxi vagy hidroxil; és

$\mathbf{Ar^5}$ jelentése egy heterociklil, aril, heteroaril, aralkil, heteroaril-alkil, vagy aril-szulfonil-alkil csoport, amelyek közül mindegyik opcionálisan szubsztituálva (helyettesítve) van egy vagy több csoporttal, amely a következők közül van választva: halogén, ciano, alkil, halogén-alkil, ciklopropil, alkoxi, halogén-alkoxi, heterociklil, amelyek opcionálisan szubsztituálva (helyettesítve) vannak a következőkkel: alkil, aril, hidroxil, alkoxi, alkoxi-alkil, hidroxi-alkoxi, alkil-amino, alkil-szulfonil-amino, amino-alkoxi, vagy alkoxi-karbonil-amino-alkoxi; és

$\mathbf{X^3}$ jelentése O vagy S; és

R^{14} jelentése H vagy metil; és

Ar^6 jelentése egy heterociklil, aril vagy heteroaril csoport, amelyek közül mindegyik opcionálisan szubsztituálva (helyettesítve) van egy vagy több csoporttal, amely a következők közül van választva: halogén, ciano, alkil, halogén-alkil, ciklopropil, alkoxi, halogén-alkoxi, aril vagy hidroxil; és

R^{15} jelentése H vagy metil; és

R^{16} jelentése egy heterociklil, aril vagy heteroaril csoport, ahol mindegyik a nevezett csoportok közül opcionálisan szubsztituálva (helyettesítve) van egy vagy több csoporttal, amely a következők közül van választva: halogén, ciano, alkil, halogén-alkil, ciklopropil, alkoxi, halogén-alkoxi vagy hidroxil;

R^{17} jelentése H, metil, vagy R^{17} együtt R^{16}-tal egy cikloalkil vagy aril molekularészt (csoportot) képez, amely kondenzálva van a tiazolil csoporttal, amelyhez azok kapcsolódnak, ily módon egy kondenzált gyűrűrendszer van képezve, ahol a nevezett kondenzált gyűrűrendszer opcionálisan szubsztituálva (helyettesítve) van egy vagy több csoporttal, amely a következők közül van választva: halogén, ciano, alkil, halogén-alkil, ciklopropil, alkoxi, halogén-alkoxi vagy hidroxil; és

X^5 jelentése O vagy S, vagy N-R^{36}, ahol R^{36} jelentése H vagy C1-C3-alkil; és

Ar^7 jelentése egy heterociklil, aril vagy heteroaril csoport, amelyek közül mindegyik opcionálisan szubsztituálva (helyettesítve) van egy vagy több csoporttal, amely a következők közül van választva: halogén, ciano, alkil, halogén-alkil, ciklopropil, alkoxi, halogén-alkoxi, aril vagy hidroxil; és

X^6 jelentése O, S vagy N-$R^{36'}$, ahol $R^{36'}$ jelentése H vagy C1-C3-alkil; és

$R^{14'}$ jelentése H vagy metil; és

R^{34} jelentése H, alkil, alkoxi-alkil, hidroxi-alkil, alkoxi-karbonil-amino-alkil; és

R^{35} jelentése H, alkil, alkoxi-alkil, hidroxi-alkil, alkoxi-karbonil-amino-alkil; és

ahol,

- az If-1 általános képletben, ha:

  R^1 jelentése H, és

  Ar^1 jelentése egy 6-tagú aril csoport, amely opcionálisan szubsztituálva (helyettesítve) van egy vagy több csoporttal, amely a következők közül van választva: halogén, ciano, C1-C3-alkil, C1-halogén-alkil, és

  R^{11}, R^{12}, $R^{12'}$ és R^{13} jelentése egymástól függetlenül a következők közül van választva: H, halogén, C1-C3-alkil, hidroxil, metoxi, vagy R^{12} együtt R^{11}-gyel vagy R^{13}-mal egy aril vagy heterociklil vagy heteroaril molekularészt (csoportot) képez, amely kondenzálva van a piridil csoporttal, amelyekhez azok kapcsolódnak, és opcionálisan szubsztituálva (helyettesítve) van egy vagy több csoporttal, amely a következők közül van választva: halogén, C1-C3-alkil, metoxi vagy hidroxil,

  akkor

  Ar^1 jelentése fenil, 3-halogén-fenil, 4-halogén-fenil, 2,3-diklór-fenil, 3,4-dihalogén-fenil, 3,4,5-trihalogén-fenil, 4-ciano-fenil, 4-(C1-C3-alkil)fenil, 4-(C1-halogén-alkil)fenil, és

  R^{11}, R^{12}, $R^{12'}$ és R^{13} jelentése H, vagy R^{11}, R^{12}, $R^{12'}$ jelentése H és R^{13} jelentése halogén, C1-C3-alkil, vagy R^{11}, $R^{12'}$, R^{13} jelentése H és R^{12} jelentése C1-C3-alkil,

vagy R^{12}, $R^{12'}$, R^{13} jelentése H és R^{11} jelentése C1-C3-alkil, vagyR^{11}, R^{12}, $R^{12'}$ és R^{13} együtt a piridil csoporttal, amelyhez azok kapcsolódnak egy kinolin-2-il, izokinolin-3-il vagy 8-halogén-kinolin-2-il molekularészt (csoportot) képeznek; és

- az If-4 általános képletben, ha:

  R^1 jelentése H, és

  Ar^1 jelentése egy 6-tagú aril csoport, amely opcionálisan szubsztituálva (helyettesítve) van egy vagy több csoporttal, amely a következők közül van választva: halogén, ciano, C1-C3-alkil, C1-halogén-alkil, és

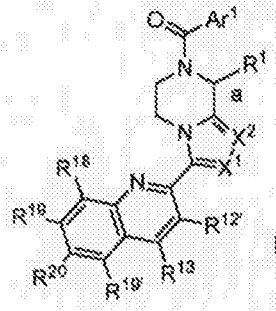
  R^{17} együtt R^{16}-tal egy cikloalkil vagy aril molekularészt (csoportot) képez, amely kondenzálva van a tiazolil csoporttal, amelyekhez azok kapcsolódnak, ily módon egy kondenzált gyűrűrendszer van képezve, ahol a nevezett kondenzált gyűrűrendszer opcionálisan szubsztituálva (helyettesítve) van egy vagy több csoporttal, amely a következők közül van választva: halogén, C1-3-alkil, metoxi vagy hidroxil,

  akkor

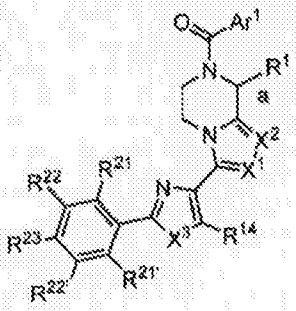
  Ar^1 jelentése fenil, 3-halogén-fenil, 4-halogén-fenil, 2,3-diklór-fenil, 3,4-dihalogén-fenil, 3,4,5-trihalogén-fenil, 4-ciano-fenil, 4-(C1-C3-alkil)fenil, 4-(C1-halogén-alkil)fenil, és

  R^{17} és R^{16} együtt a tiazolil csoporttal, amelyekhez azok kapcsolódnak, egy benzotiazol-2-il vagy 4,5,6,7-tetrahidro-1,3-benzotiazol-2-il molekularészt (csoportot) képeznek.

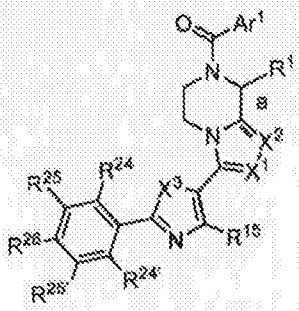
7. Vegyület a 6. igénypont szerint, amely a következő Ig-1, Ig-2, Ig-3, Ig-4, Ig-5, Ig-6, Ig-7 és Ig-8 általános képletek közül van választva:



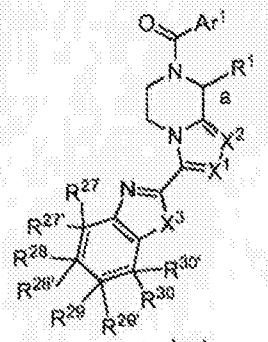
Ig-1



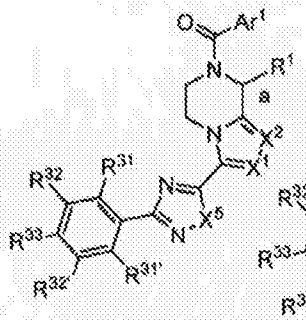
Ig-2



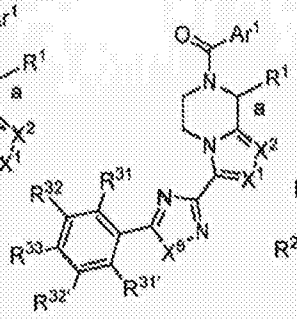
Ig-3



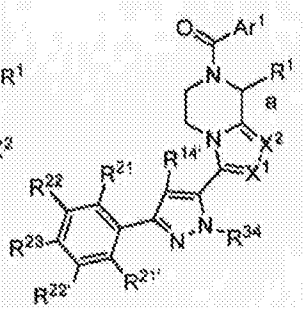
Ig-4



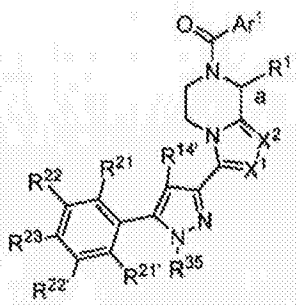
Ig-5



Ig-6



Ig-7



Ig-8

és azok gyógyászatilag elfogadható sói és szolvátjai, ahol

a ábrázolja a kötést, amely által R^1 kapcsolódik a piperazin molekularészhez (csoporthoz); és

Ar^1, R^1, X^1 és X^2 jelentése a 2. igénypontban meghatározottak szerinti; és

R^{14}, $R^{14'}$, R^{15}, R^{34}, R^{35}, X^3, X^5 és X^6 jelentése a 6. igénypontban meghatározottak szerinti; és

$R^{12'}$ és R^{13} jelentése egymástól függetlenül a következők közül van választva: H, halogén, ciano, alkil, hidroxi-alkil, halogén-alkil, cikloalkil, heteroalkil, hidroxil, alkoxi, halogén-alkoxi, karboxi, alkoxi-karbonil, alkil-karbonil-oxi, alkil-karbonil-amino, halogén-alkil-karbonil-amino, acil-amino, karbamoil, alkil-karbamoil, karbamoil-alkil, karbamoil-amino, alkil-karbamoil-amino, alkil-szulfonil, halogén-alkil-szulfonil, szulfamoil, alkil-szulfamoil, alkil-szulfonil-amino, halogén-alkil-szulfonil-amino, vagy R^{13} együtt $R^{12'}$-vel egy alkilén-dioxi csoportot vagy egy halogén-alkilén-dioxi csoportot képez, ahol mindegyik a nevezett csoportok közül opcionálisan szubsztituálva (helyettesítve) van egy vagy több csoporttal, amely a következők közül van választva: halogén, ciano, alkil, halogén-alkil, alkoxi, halogén-alkoxi, hidroxil vagy oxo; és

R^{18}, R^{19}, $R^{19'}$ és R^{20} jelentése egymástól függetlenül a következők közül van választva: H, halogén, ciano, alkil, halogén-alkil, ciklopropil, alkoxi, halogén-alkoxi; és

R^{21}, $R^{21'}$, R^{22}, $R^{22'}$ és R^{23} jelentése egymástól függetlenül a következők közül van választva: H, halogén, ciano, alkil, halogén-alkil, ciklopropil, heterociklil, amelyek opcionálisan szubsztituálva (helyettesítve) vannak a következőkkel: alkil, hidroxil, alkoxi, halogén-alkoxi, hidroxi-alkoxi, alkil-amino, alkl-szulfonil-amino, amino-alkoxi, alkoxi-karbonil-amino-alkoxi; és

R^{24}, $R^{24'}$, R^{25}, $R^{25'}$ és R^{26} jelentése egymástól függetlenül a következők közül van választva: H, halogén, halogén-alkil, ciklopropil; és

R^{27}, R^{28}, R^{29} és R^{30} jelentése egymástól függetlenül a következők közül van választva: H, halogén, ciano, alkil, halogén-alkil, ciklopropil, alkoxi, halogén-alkoxi; és

$R^{27'}$, $R^{28'}$, $R^{29'}$ és $R^{30'}$ hiányoznak, vagy $R^{27'}$, $R^{28'}$, $R^{29'}$ és $R^{30'}$ jelentése H, azzal a feltétellel, hogy R^{28}, R^{29} és R^{30} jelentése H és hogy R^{27} jelentése a következők közül van választva: H, klór vagy fluor; és

a két kötés esetében, amely a pontozott vonalakkal van ábrázolva az Ig-4 általános képletben, mindkettő hiányzik, vagy mindkettő jelen van, azzal a feltétellel, hogy $R^{27'}$, $R^{28'}$, $R^{29'}$ és $R^{30'}$ hiányoznak; és

R^{31}, $R^{31'}$, R^{32}, $R^{32'}$ és R^{33} jelentése egymástól függetlenül a következők közül van választva: H, halogén, ciano, alkil, halogén-alkil, ciklopropil, alkoxi, halogén-alkoxi; és

ahol,

- az Ig-1 általános képletben, ha:

  R^1 jelentése H, és

  Ar^1 jelentése egy 6-tagú aril csoport, amely opcionálisan szubsztituálva (helyettesítve) van egy vagy több csoporttal, amely a következők közül van választva: halogén, ciano, C1-C3-alkil, C1-halogén-alkil, és

  $R^{12'}$, R^{13}, R^{18}, R^{19}, $R^{19'}$ és R^{20} jelentése egymástól függetlenül a következők közül van választva: H, halogén, C1-3-alkil, hidroxil, metoxi,

  akkor

Ar^1 jelentése fenil, 3-halogén-fenil, 4-halogén-fenil, 2,3-diklór-fenil, 3,4-dihalogén-fenil, 3,4,5-trihalogén-fenil, 4-ciano-fenil, 4-(C1-C3-alkil)fenil, 4-(C1-halogén-alkil)fenil, és

$R^{12'}$, R^{13}, R^{18}, R^{19}, $R^{19'}$ és R^{20} jelentése H, vagy $R^{12'}$, R^{13}, R^{19}, $R^{19'}$, R^{20} jelentése H és R^{18} jelentése fluor, klór, és

- az Ig-4 általános képletben, ha

R^1 jelentése H, és

Ar^1 jelentése egy 6-tagú aril csoport, amely opcionálisan szubsztituálva (helyettesítve) van egy vagy több csoporttal, amely a következők közül van választva: halogén, ciano, C1-C3-alkil, C1-halogén-alkil, és

R^{27}, R^{28}, R^{29} és R^{30} jelentése egymástól függetlenül a következők közül van választva: H, halogén, C1-3-alkil, metoxi, és

$R^{27'}$, $R^{28'}$, $R^{29'}$ és $R^{30'}$ hiányoznak vagy jelentésük H, azzal a feltétellel, hogy R^{28}, R^{29} és R^{30} jelentése H és R^{27} jelentése a következők közül van választva: H, klór vagy fluor,

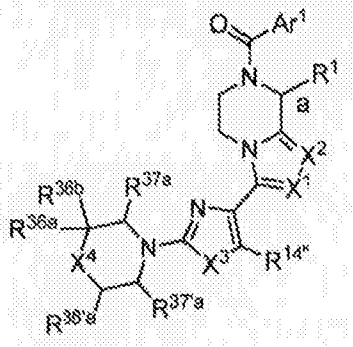
akkor

Ar^1 jelentése fenil, 3-halogén-fenil, 4-halogén-fenil, 2,3-diklór-fenil, 3,4-dihalogén-fenil, 3,4,5-trihalogén-fenil, 4-ciano-fenil, 4-(C1-C3-alkil)fenil, 4-(C1-halogén-alkil)fenil, és

R^{27}, R^{28}, R^{29} és R^{30} jelentése H, és

$R^{27'}$, $R^{28'}$, $R^{29'}$ és $R^{30'}$ hiányoznak vagy jelentésük H, azzal a feltétellel, hogy R^{27}, R^{28}, R^{29} és R^{30} jelentése H.

8. Az If-2 általános képletű vegyület a 6. igénypont szerint, amely a következő Ih-2 általános képlettel rendelkezik:



Ih-2

és annak gyógyászatilag elfogadható sói és szolvátjai, ahol

a ábrázolja a kötést, amely által R^1 kapcsolódik a piperazin molekularészhez (csoporthoz); és

Ar^1, R^1, X^1 és X^2 jelentése a 2. igénypontban meghatározottak szerinti; és

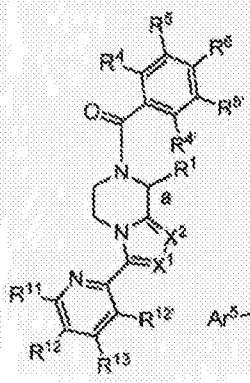
X^3 jelentése a 6. igénypontban meghatározottak szerinti; és

$R^{14''}$ jelentése H vagy metil; és

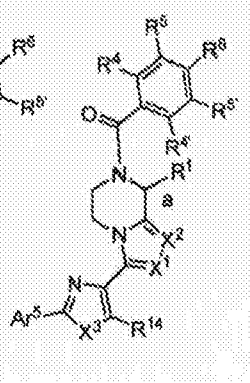
X^4 jelentése O, CH_2, CF_2, $C(CH_3)_2$, N-(C1-C3-alkil)-N-fenil; és

R^{36a}, R^{36b}, $R^{36'a}$, R^{37a} és $R^{37'a}$ jelentése egymástól függetlenül a következők közül van választva: H, C1-C3-alkil, alkoxi-C1-C3-alkil.

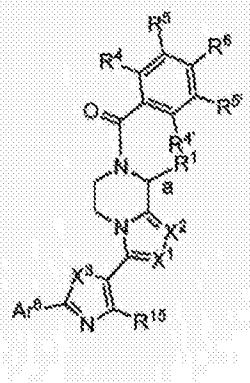
9. Vegyület a 3. igénypont szerint, amely a következő Ii-1, Ii-2, Ii-3, Ii-4, Ii-5, Ii-6, Ii-7, Ii-8, Ij-1, Ij-2, Ij-3, Ij-4, Ij-5, Ij-6, Ij-7, Ij-8, Ik-1, Ik-2, Ik-3, Ik-4, Ik-5, Ik-6, Ik-7, Ik-8, Ii'-1, Ii'-2, Ii'-3, Ii'-4, Ii'-5, Ii'-6, Ii'-7 és Ii'-8 általános képletek közül van választva:



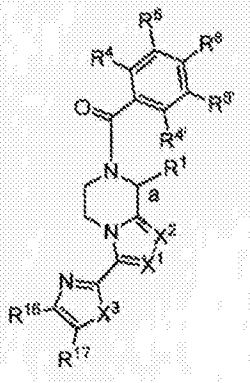
Ii-1



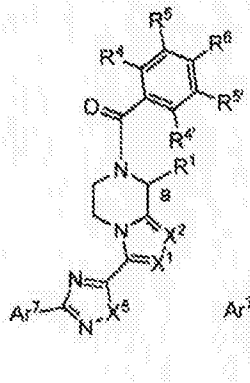
Ii-2



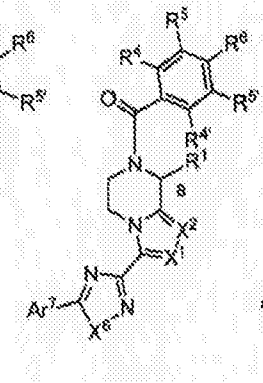
Ii-3



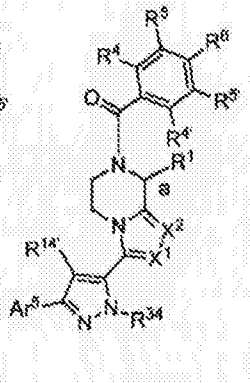
Ii-4



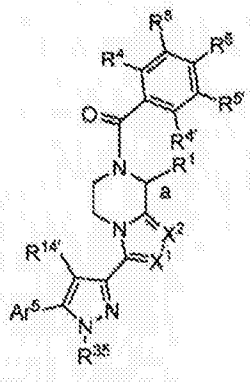
Ii-5



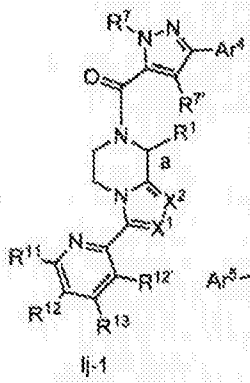
Ii-6



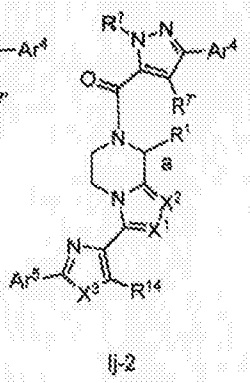
Ii-7



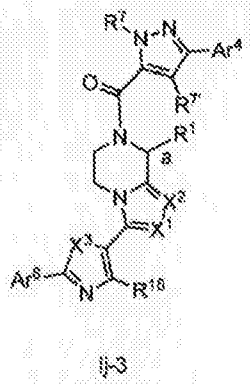
Ii-8



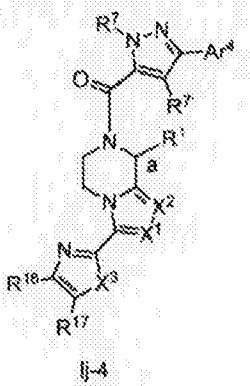
Ij-1



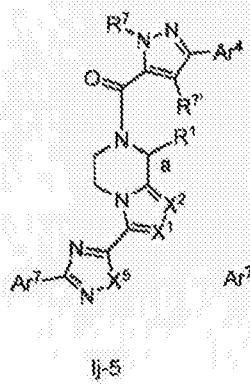
Ij-2



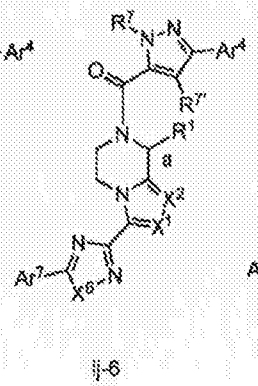
Ij-3



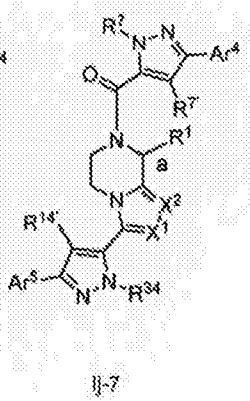
Ij-4



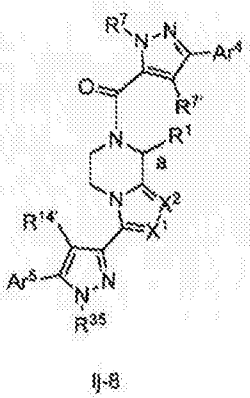
Ij-5



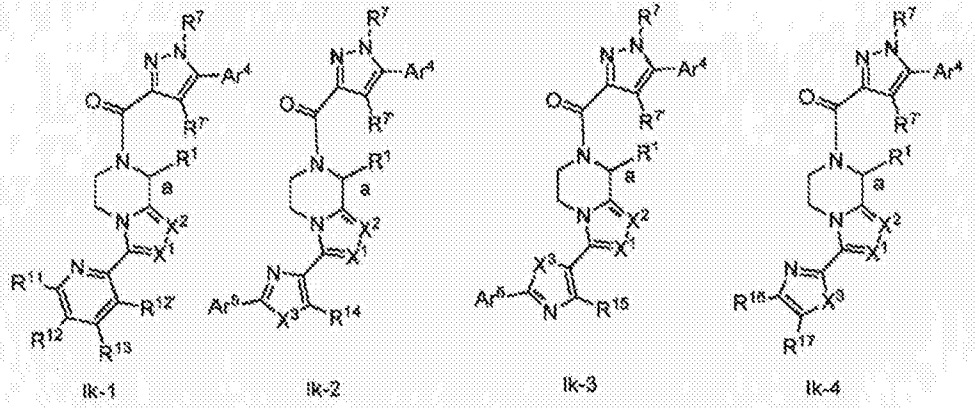
Ij-6



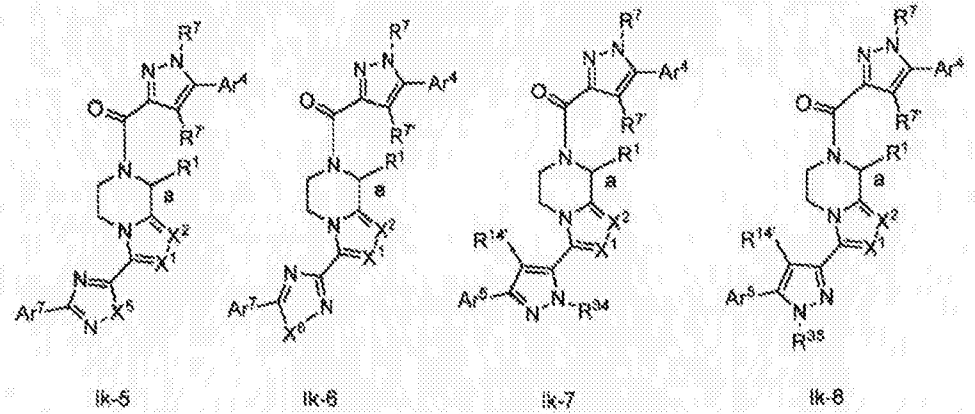
Ij-7



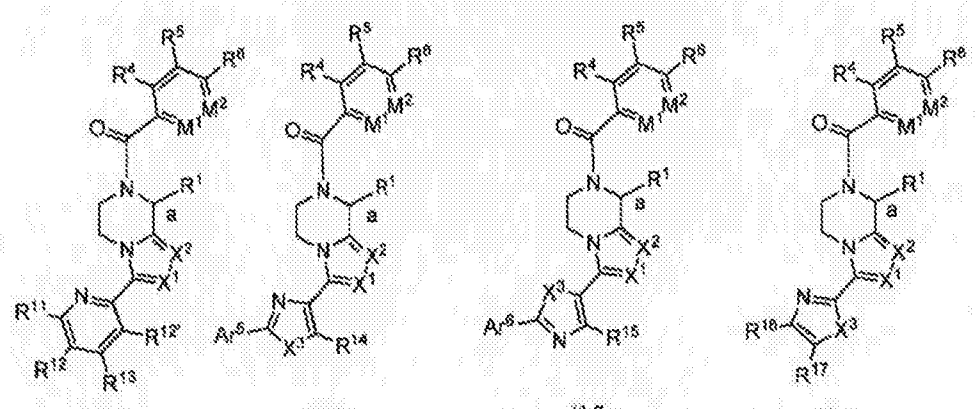
Ij-8



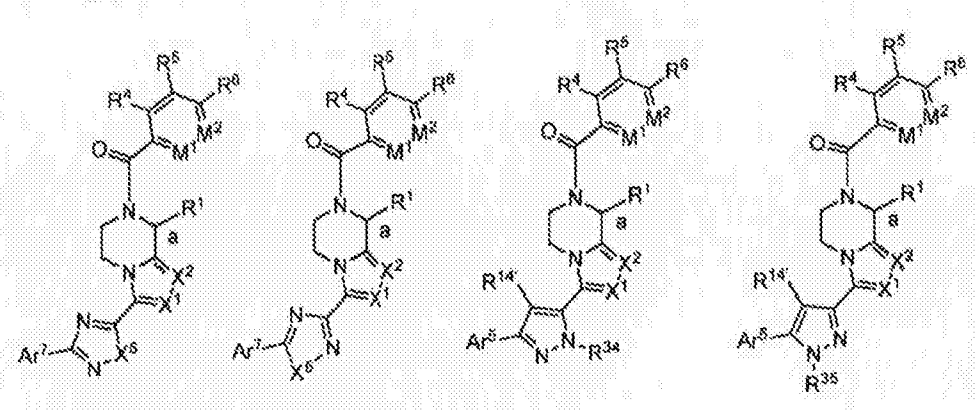
Ik-1 Ik-2 Ik-3 Ik-4



Ik-5 Ik-6 Ik-7 Ik-8



If-1 If-2 If-3 If-4



If-5 If-6 If-7 If-8

és azok gyógyászatilag elfogadható sói és szolvátjai, ahol

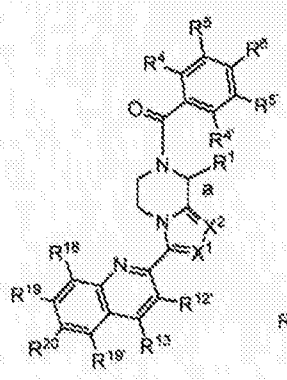
a ábrázolja a kötést, amely által $\mathbf{R^1}$ kapcsolódik a piperazin molekularészhez (csoporthoz); és

$\mathbf{R^1}$, $\mathbf{X^1}$ és $\mathbf{X^2}$ jelentése a 2. igénypontban meghatározottak szerinti; és

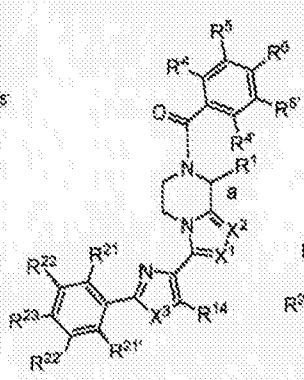
$\mathbf{Ar^3}$, $\mathbf{R^4}$, $\mathbf{R^{4'}}$, $\mathbf{R^5}$, $\mathbf{R^{5'}}$, $\mathbf{R^6}$, $\mathbf{R^7}$, $\mathbf{R^{7'}}$, $\mathbf{M^1}$, $\mathbf{M^2}$ jelentése a 4. igénypontban meghatározottak szerinti; és

$\mathbf{Ar^5}$, $\mathbf{Ar^6}$, $\mathbf{Ar^7}$, $\mathbf{R^{11}}$, $\mathbf{R^{12}}$, $\mathbf{R^{12'}}$, $\mathbf{R^{13}}$, $\mathbf{R^{14}}$, $\mathbf{R^{14'}}$, $\mathbf{R^{15}}$, $\mathbf{R^{16}}$, $\mathbf{R^{17}}$, $\mathbf{R^{34}}$, $\mathbf{R^{35}}$, $\mathbf{X^3}$, $\mathbf{X^5}$, $\mathbf{X^6}$ jelentése a 6. igénypontban meghatározottak szerinti.

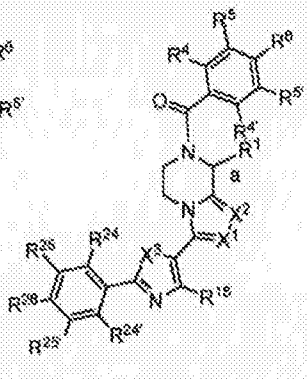
10. Vegyület a 9. igénypont szerint, amely a következő II-1, II-2, II-3, II-4, II-5, II-6, II-7, II-8, II'-1, II'-2, II'-3, II'-4, II'-5, II'-6, II'-7, II'-8 általános képletek közül van választva:



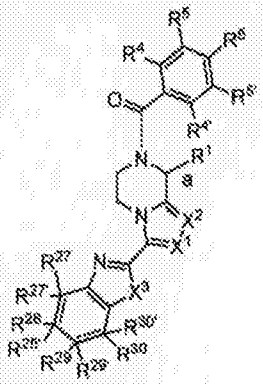
II-1



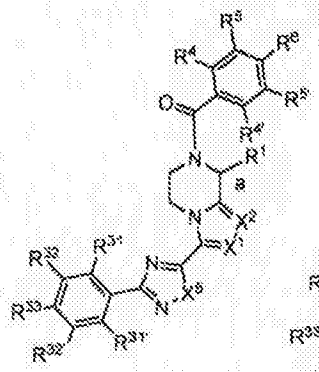
II-2



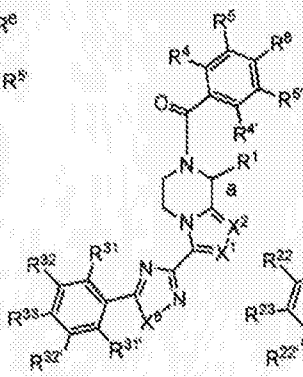
II-3



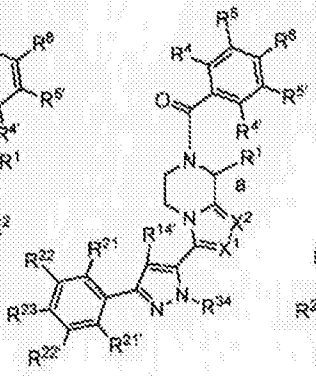
II-4



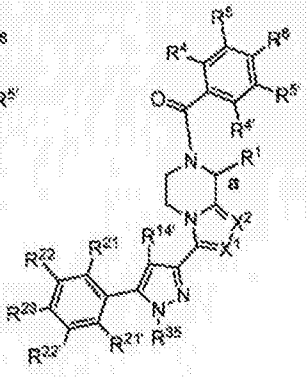
II-5



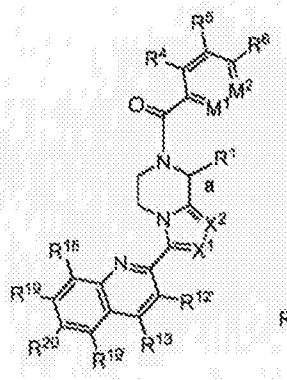
II-6



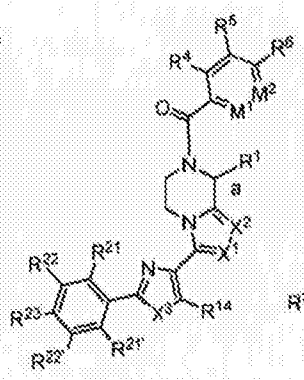
II-7



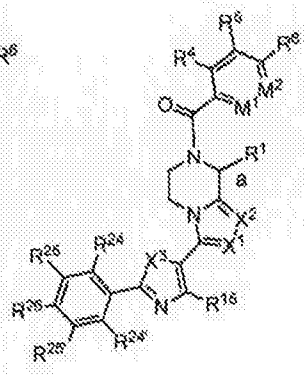
II-8



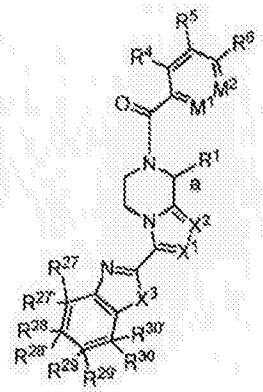
II'-1



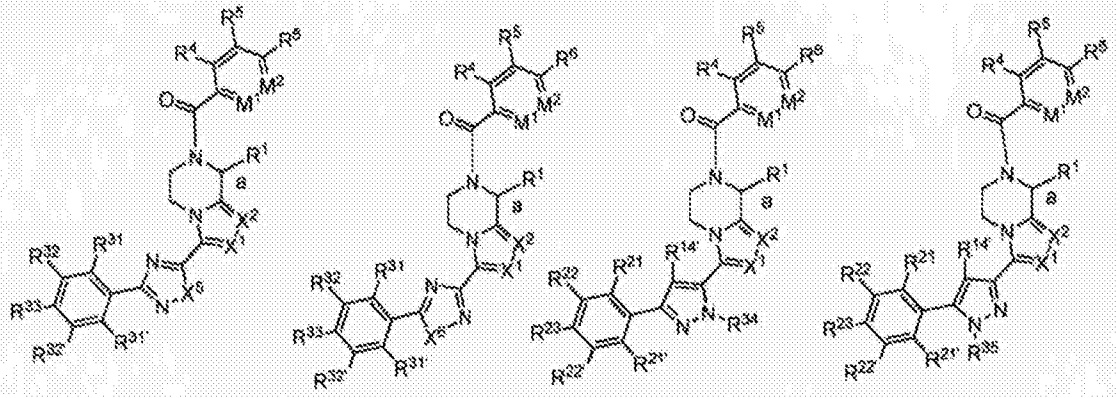
II'-2



II'-3



II'-4



Ir'-5 Ir-6 Ir-7 Ir-8

és azok gyógyászatilag elfogadható sói és szolvátjai, ahol

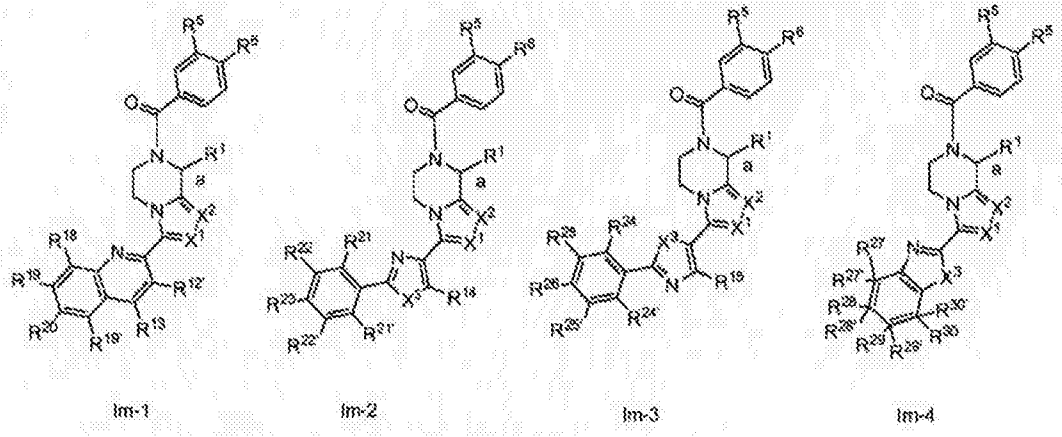
a ábrázolja a kötést, amely által $\mathbf{R^1}$ kapcsolódik a piperazin molekularészhez (csoporthoz); és

$\mathbf{R^1}$, $\mathbf{X^1}$ és $\mathbf{X^2}$ jelentése a 2. igénypontban meghatározottak szerinti; és

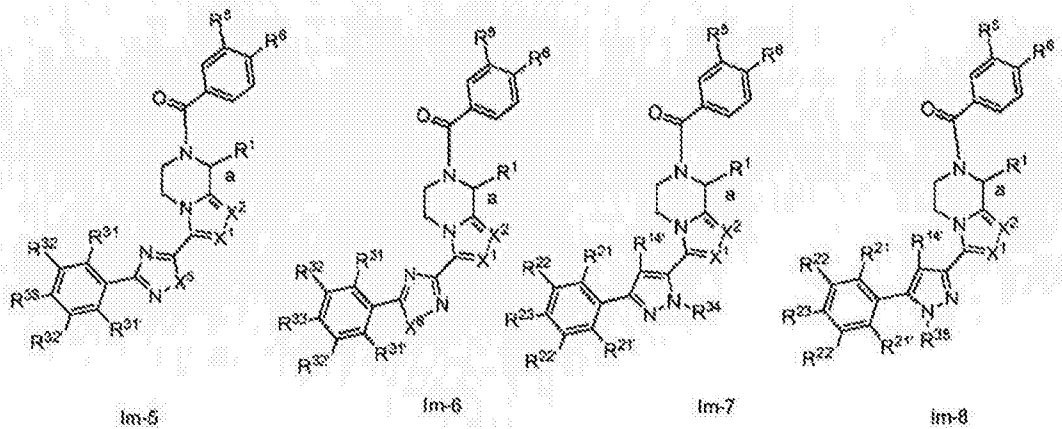
$\mathbf{R^4}$, $\mathbf{R^{4'}}$, $\mathbf{R^5}$, $\mathbf{R^{5'}}$, $\mathbf{R^6}$, $\mathbf{M^1}$ és $\mathbf{M^2}$ jelentése a 4. igénypontban meghatározottak szerinti; és

$\mathbf{R^{12'}}$, $\mathbf{R^{13}}$, $\mathbf{R^{14}}$, $\mathbf{R^{14'}}$, $\mathbf{R^{15}}$, $\mathbf{R^{18}}$, $\mathbf{R^{19}}$, $\mathbf{R^{19'}}$, $\mathbf{R^{20}}$, $\mathbf{R^{21}}$, $\mathbf{R^{21'}}$, $\mathbf{R^{22}}$, $\mathbf{R^{22'}}$, $\mathbf{R^{23}}$, $\mathbf{R^{24}}$, $\mathbf{R^{24'}}$, $\mathbf{R^{25}}$, $\mathbf{R^{25'}}$, $\mathbf{R^{26}}$, $\mathbf{R^{27}}$, $\mathbf{R^{27'}}$, $\mathbf{R^{28}}$, $\mathbf{R^{28'}}$, $\mathbf{R^{29}}$, $\mathbf{R^{29'}}$, $\mathbf{R^{30}}$, $\mathbf{R^{30'}}$, $\mathbf{R^{31}}$, $\mathbf{R^{31'}}$, $\mathbf{R^{32}}$, $\mathbf{R^{32'}}$, $\mathbf{R^{33}}$, $\mathbf{R^{34}}$, $\mathbf{R^{35}}$, $\mathbf{X^3}$, $\mathbf{X^5}$, $\mathbf{X^6}$ jelentése; és a két kötés, amely a pontozott vonalakkal van ábrázolva, a 7. igénypontban meghatározottak szerinti.

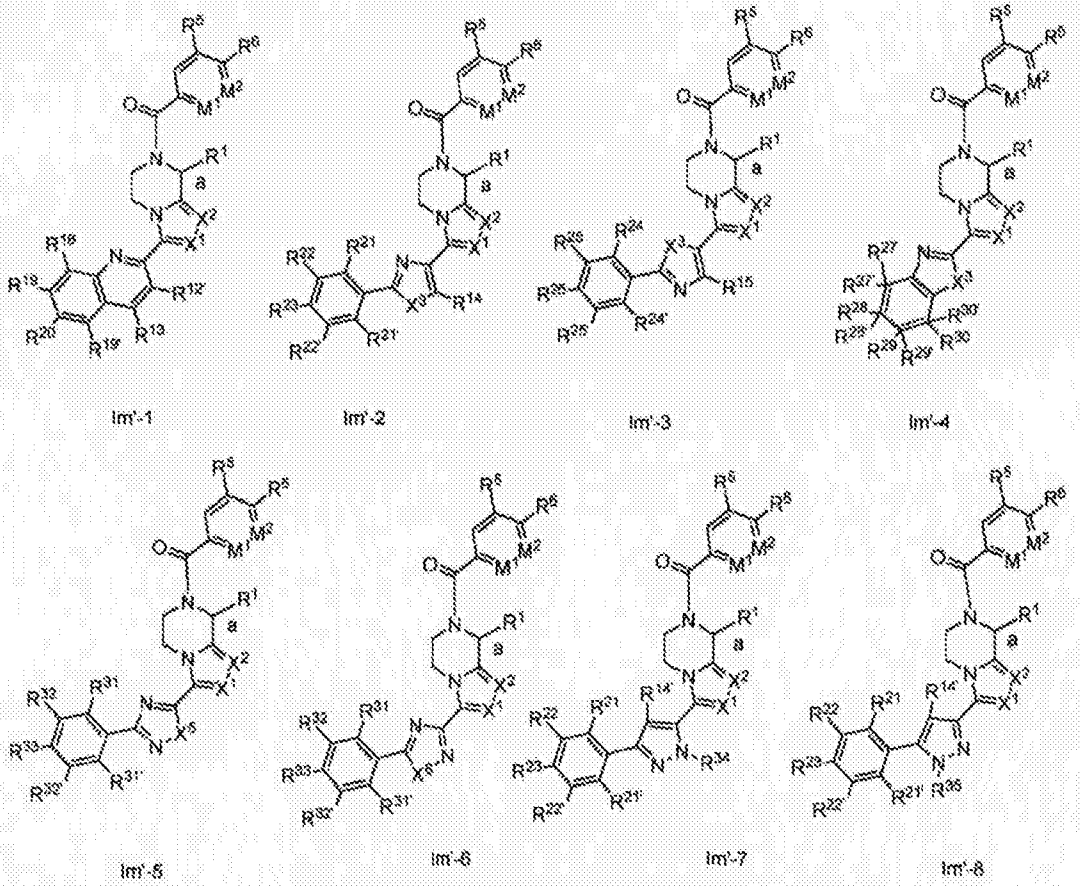
11. Vegyület a 10. igénypont szerint, amely a következő Im-1, Im-2, Im-3, Im-4, Im-5, Im-6, Im-7, Im-8, Im'-1, Im'-2, Im'-3, Im'-4, Im'-5, Im'-6, Im'-7 és Im'-8 általános képletek közül van választva:



Im-1 Im-2 Im-3 Im-4



Im-5 Im-6 Im-7 Im-8



és azok gyógyászatilag elfogadható sói és szolvátjai, ahol

a ábrázolja a kötést, amely által $\mathbf{R^1}$ kapcsolódik a piperazin molekularészhez (csoporthoz); és

$\mathbf{R^1}$, $\mathbf{X^1}$ és $\mathbf{X^2}$ jelentése a 2. igénypontban meghatározottak szerinti; és

$\mathbf{R^5}$, $\mathbf{R^6}$, $\mathbf{M^1}$ és $\mathbf{M^2}$ jelentése az 5. igénypontban meghatározottak szerinti; és

$\mathbf{R^{12'}}$, $\mathbf{R^{13}}$, $\mathbf{R^{14}}$, $\mathbf{R^{14'}}$, $\mathbf{R^{15}}$, $\mathbf{R^{18}}$, $\mathbf{R^{19}}$, $\mathbf{R^{19'}}$, $\mathbf{R^{20}}$, $\mathbf{R^{21}}$, $\mathbf{R^{21'}}$, $\mathbf{R^{22}}$, $\mathbf{R^{22'}}$, $\mathbf{R^{23}}$, $\mathbf{R^{24}}$, $\mathbf{R^{24'}}$, $\mathbf{R^{25}}$, $\mathbf{R^{25'}}$, $\mathbf{R^{26}}$, $\mathbf{R^{27}}$, $\mathbf{R^{27'}}$, $\mathbf{R^{28}}$, $\mathbf{R^{28'}}$, $\mathbf{R^{29}}$, $\mathbf{R^{29'}}$, $\mathbf{R^{30}}$, $\mathbf{R^{30'}}$, $\mathbf{R^{31}}$, $\mathbf{R^{31'}}$, $\mathbf{R^{32}}$, $\mathbf{R^{32'}}$, $\mathbf{R^{33}}$, $\mathbf{R^{34}}$, $\mathbf{R^{35}}$, $\mathbf{X^3}$, $\mathbf{X^5}$, $\mathbf{X^6}$ jelentése; és a két kötés, amely a pontozott vonalakkal van ábrázolva, a 7. igénypontban meghatározottak szerinti.

12. Vegyület az 1. igénypont szerint, amely a következőkből álló csoportból van választva:

(4-fluor-fenil)(3-(piridin-2-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(4-klór-fenil)(3-(piridin-2-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(3-(4-klór-fenil)-1H-pirazol-5-il)(3-(piridin-2-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(3-(3,4-diklór-fenil)-1H-pirazol-5-il)(3-(piridin-2-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(3,4-diklór-fenil)(3-(piridin-2-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

[1,1'-bifenil]-4-il(3-(piridin-2-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(4-fluor-fenil)(3-(kinolin-2-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(4-fluor-fenil)(3-(2-fenil-tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(4-fluor-fenil)(3-(2-morfolino-tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(3-(5-klór-piridin-2-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-fluor-fenil)metanon;

(4-fluor-fenil)(3-(6-metil-piridin-2-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(4-fluor-fenil)(8-metil-3-(piridin-2-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(3-(2,4-diklór-fenil)-1H-pirazol-5-il)(3-(piridin-2-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(3-(3,4-diklór-fenil)-1-metil-1H-pirazol-5-il)(3-(piridin-2-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(4-fluor-fenil)(3-(izokinolin-3-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(4'-fluor-[1,1'-bifenil]-4-il)(3-(piridin-2-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(3-(piridin-2-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(3-(4-(trifluor-metil)fenil)-1H-pirazol-5-il)metanon;

(3-(4-fenoxi-fenil)-1H-pirazol-5-il)(3-(piridin-2-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

[1,1'-bifenil]-4-il(3-(kinolin-2-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

[1,1'-bifenil]-4-il(3-(2-morfolino-tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(3-(piridin-2-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(tiofén-2-il)fenil)metanon;

(4-fluor-fenil)(3-(8-fluor-kinolin-2-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(3-(8-klór-kinolin-2-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-fluor-fenil)metanon;

(4-fluor-fenil)(3-(2-(4-(trifluor-metil)fenil)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(4-fluor-fenil)(3-(6-fenil-piridin-2-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

[1,1'-bifenil]-4-il(3-(2-fenil-tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(4-fluor-fenil)(3-(4,5,6,7-tetrahidrobenzo[d]tiazol-2-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(4-fluor-fenil)(3-(2-(3-(trifluor-metil)fenil)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(3-(2-(2,4-difluor-fenil)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-fluor-fenil)metanon;

(3-(2-(2,3-diklór-fenil)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-fluor-fenil)metanon;

(3-(2-(4-klór-fenil)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-fluor-fenil)metanon;

(4-fluor-fenil)(3-(2-(4-fluor-fenil)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(4-fluor-fenil)(3-(2-(piperidin-1-il)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(4-fluor-fenil)(3-(2-(4-fenilpiperazin-1-il)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(3-(2-(2,4-diklór-fenil)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-fluor-fenil)metanon;

(3-(2-(3,5-diklór-fenil)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-fluor-fenil)metanon;

(4-fluor-fenil)(3-(6-(pirrolidin-1-il)piridin-2-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(4-fluor-fenil)(3-(6-morfolino-piridin-2-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(4-fluor-fenil)(3-(6-(trifluor-metil)piridin-2-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(3-(2-(3,4-dimetoxi-fenil)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-fluor-fenil)metanon;

(4-fluor-fenil)(8-(4-fluor-fenil)-3-(2-fenil-tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(3-(2-(3-klór-fenil)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-fluor-fenil)metanon;

(4-fluor-fenil)(8-izopropil-3-(2-fenil-tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(R)-(4-fluor-fenil)(8-metil-3-(piridin-2-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(R)-(4-fluor-fenil)(8-metil-3-(2-fenil-tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

[1,1'-bifenil]-4-il(8-metil-3-(2-morfolino-tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(4-fluor-fenil)(3-(2-fenil-oxazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(4-fluor-fenil)(8-metil-3-(2-fenil-oxazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

[1,1'-bifenil]-4-il(8-metil-3-(2-fenil-oxazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

[1,1'-bifenil]-4-il(3-(2-fenil-oxazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(4-fluor-fenil)(8-(2-hidroxi-etil)-3-(2-fenil-tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(4-fluor-fenil)(8-metil-3-(2-morfolino-tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(4'-fluor-[1,1'-bifenil]-4-il)(8-metil-3-(2-morfolino-tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(3-(2-fenil-tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(tiofén-2-il)fenil)metanon;

(3-(2-morfolino-tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(tiofén-2-il)fenil)metanon;

(8-metil-3-(2-morfolino-tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(tiofén-2-il)fenil)metanon;

(4-fluor-fenil)(3-(4-fenil-tiazol-2-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(3-(2-(2-klór-fenil)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-fluor-fenil)metanon;

(3-(benzo[d]tiazol-2-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-fluor-fenil)metanon;

(8,8-dimetil-3-(2-fenil-tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-fluor-fenil)metanon;

(4-fluor-fenil)(8-metil-3-(kinolin-2-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(8-metil-3-(2-fenil-tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(tiofén-2-il)fenil)metanon;

(3-(2-fenil-tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(tiofén-3-il)fenil)metanon;

(8-metil-3-(2-fenil-tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(tiofén-3-il)fenil)metanon;

(8-metil-3-(kinolin-2-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(tiofén-2-il)fenil)metanon;

(3-(2-(2-klór-fenil)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(tiofén-2-il)fenil)metanon;

[1,1'-bifenil]-4-il(3-(2-(2-klór-fenil)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(R)-(3-(2-(4-klór-fenil)tiazol-4-il)-8-metil-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-fluor-fenil)metanon;

(3-(kinolin-2-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(tiofén-2-il)fenil)metanon;

(4-fluor-fenil)(3-(2-(4-fluor-fenil)tiazol-4-il)-8-metil-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(R)-(4-fluor-fenil)(3-(2-(4-fluor-fenil)tiazol-4-il)-8-metil-5,6-dihidro[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

[1,1'-bifenil]-4-il(8-metil-3-(4-metil-2-fenil-tiazol-5-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(3-(2-(4-fluor-fenil)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(tiofén-2-il)fenil)metanon;

(3-(2-(2-klór-fenil)tiazol-4-il)-8-metil-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-fluor-fenil)metanon;

(4-fluor-fenil)(8-metil-3-(4-metil-2-fenil-tiazol-5-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

[1,1`-bifenil]-4-il(3-(2-(4-fluor-fenil)tiazol-4-il)-8-metil-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(3-(2-(2,4-difluor-fenil)tiazol-4-il)-8-metil-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-fluor-fenil)metanon;

(3-(2-(4-fluor-fenil)tiazol-4-il)-8-metil-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(tiofén-2-il)fenil)metanon;

[1,1'-bifenil]-4-il(3-(2-(2,4-difluor-fenil)tiazol-4-il)-8-metil-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(3-(2-(2,4-difluor-fenil)tiazol-4-il)-8-metil-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(tiofén-2-il)fenil)metanon;

naftalin-1-il(3-(piridin-2-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(3-(4-klór-fenil)-1-metil-1H-pirazol-5-il)(3-(piridin-2-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(5-(4-klór-fenil)-1-metil-1H-pirazol-3-il)(3-(piridin-2-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(8-metil-3-(5-fenil-1,2,4-oxadiazol-3-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(tiofén-2-il)fenil)metanon;

(8-metil-3-(3-fenil-1,2,4-oxadiazol-5-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(tiofén-2-il)fenil)metanon;

(R)-(3-(2-(4-fluor-fenil)oxazol-4-il)-8-metil-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(tiofén-2-il)fenil)metanon;

(5-fenil-piridin-2-il)(3-(kinolin-2-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(6-fenil-piridin-3-il)(3-(kinolin-2-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(2-fenil-pirimidin-5-il)(3-(kinolin-2-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(4-fenil-ciklohexil)(3-(kinolin-2-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

ciklohexil(3-(kinolin-2-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

3-metil-1-(3-(kinolin-2-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)bután-1-on;

[1,1'-bifenil]-2-il(3-(kinolin-2-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(4-(furán-3-il)fenil)(3-(kinolin-2-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(4-(pirimidin-5-il)fenil)(3-(kinolin-2-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(9-metil-9H-karbazol-2-il)(3-(kinolin-2-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(4-(pirimidin-2-il)fenil)(3-(kinolin-2-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(4-(pirazin-2-il)fenil)(3-(kinolin-2-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(4-(piridazin-3-il)fenil)(3-(kinolin-2-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

4'-(3-(kinolin-2-il)-5,6,7,8-tetrahidro-[1,2,4]triazol[4,3-a]pirazine-7-karbonil)-[1,1'-bifenil]-4-karbonitril;

1-(4-(3-(kinolin-2-il)-5,6,7,8-tetrahidro-[1,2,4]triazol[4,3-a]pirazine-7-karbonil)fenil)piperidin-2-on;

(4-morfolino-fenil)(3-(kinolin-2-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(4-(3,5-dimetil-1H-pirazol-1-il)fenil)(3-(kinolin-2-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(3-(2-(4-fluor-fenil)tiazol-4-il)-6-metil-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(tiofén-2-il)fenil)metanon;

(3-(2-(4-fluor-fenil)tiazol-4-il)-5-metil-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(tiofén-2-il)fenil)metanon;

(3,4-diklór-fenil)(3-(2-(4-fluor-fenil)tiazol-4-il)-8-metil-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(3,4-difluor-fenil)(3-(2-(4-fluor-fenil)tiazol-4-il)-8-metil-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(3-klór-4-fluor-fenil)(3-(2-(4-fluor-fenil)tiazol-4-il)-8-metil-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(4-klór-3-fluor-fenil)(3-(2-(4-fluor-fenil)tiazol-4-il)-8-metil-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(3-(2-(4-fluor-fenil)tiazol-4-il)-8-metil-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(3,4,5-trifluor-fenil)metanon;

(8-metil-3-(2-fenil-oxazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(tiofén-2-il)fenil)metanon;

(R)-(4-fluor-fenil)(8-metil-3-(kinolin-2-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(R)-[1,1'-bifenil]-4-il(8-metil-3-(kinolin-2-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(R)-[1,1'-bifenil]-4-il(8-metil-3-(2-morfolino-tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(R)-(4-fluor-fenil)(8-metil-3-(6-fenil-piridin-2-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(R)-[1,1'-bifenil]-4-il(8-metil-3-(2-fenil-tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(R)-(4-fluor-fenil)(8-metil-3-(4,5,6,7-tetrahidrobenzo[d]tiazol-2-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(R)-(3-(2-(2,4-difluor-fenil)tiazol-4-il)-8-metil-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-fluor-fenil)metanon;

(R)-(3-(2-(2,3-diklór-fenil)tiazol-4-il)-8-metil-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-fluor-fenil)metanon;

R)-(4-fluor-fenil)(8-metil-3-(2-(4-fenil-piperazin-1-il)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(R)-(3-(2-(2,4-diklór-fenil)tiazol-4-il)-8-metil-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-fluor-fenil)metanon;

(R)-(3-(2-(3-klór-fenil)tiazol-4-il)-8-metil-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-fluor-fenil)metanon;

(R)-(4-fluor-fenil)(8-metil-3-(2-fenil-oxazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(R)-[1,1'-bifenil]-4-il(8-metil-3-(2-fenil-oxazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(R)-(4-fluor-fenil)(8-(2-hidroxi-etil)-3-(2-fenil-tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(R)-(4'-fluor-[1,1-bifenil]-4-il)(8-metil-3-(2-morfolino-tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(R)-(8-metil-3-(2-fenil-tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(tiofén-2-il)fenil)metanon;

(R)-(8-metil-3-(2-morfolino-tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(tiofén-2-il)fenil)metanon;

(R)-(4-fluor-fenil)(8-metil-3-(4-fenil-tiazol-2-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(R)-(3-(2-(2-klór-fenil)tiazol-4-il)-8-metil-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-fluor-fenil)metanon;

(R)-(8-metil-3-(2-fenil-tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(tiofén-3-il)fenil)metanon;

(R)-(8-metil-3-(kinolin-2-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(tiofén-2-il)fenil)metanon;

(R)-(3-(2-(2-klór-fenil)tiazol-4-il)-8-metil-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(tiofén-2-il)fenil)metanon;

(R)-[1,1'-bifenil]-4-il(3-(2-(2-klór-fenil)tiazol-4-il)-8-metil-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(R)-[1,1`-bifenil]-4-il(8-metil-3-(4-metil-2-fenil-tiazol-5-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(R)-(3-(2-(4-fluor-fenil)tiazol-4-il)-8-metil-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(tiofén-2-il)fenil)metanon;

(R)-[1,1'-bifenil]-4-il(3-(2-(4-fluor-fenil)tiazol-4-il)-8-metil-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(R)-[1,1'-bifenil]-4-il(3-(2-(2,4-difluor-fenil)tiazol-4-il)-8-metil-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(R)-(3-(2-(2,4-difluor-fenil)tiazol-4-il)-8-metil-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(tiofén-2-il)fenil)metanon;

(S)-(4-fluor-fenil)(8-metil-3-(piridin-2-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(S)-(4-fluor-fenil)(3-(2-(4-fluor-fenil)tiazol-4-il)-8-metil-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(S)-(4'-fluor-[1,1'-bifenil]-4-il)(8-metil-3-(2-morfolino-tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(S)-(4-fluor-fenil)(8-metil-3-(kinolin-2-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(S)-(8-metil-3-(kinolin-2-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(tiofén-2-il)fenil)metanon;

(S)-(4-fluor-fenil)(3-(2-(4-fluor-fenil)tiazol-4-il)-8-metil-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(S)-(3-(2-(2,4-difluor-fenil)tiazol-4-il)-8-metil-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(tiofén-2-il)fenil)metanon;

(4-fluor-fenil)(8-metil-3-(2-fenil-tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(S)-(4-fluor-fenil)(8-metil-3-(2-fenil-tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(S)-(3-(3-(4-fluor-fenil)-1,2,4-oxadiazol-5-il)-8-metil-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(tiofén-2-il)fenil)metanon;

(R)-(3-(3-(4-fluor-fenil)-1,2,4-oxadiazol-5-il)-8-metil-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(tiofén-2-il)fenil)metanon;

(3-(2-(2,4-difluor-fenil)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(tiofén-2-il)fenil)metanon;

(3-(5-fenil-1,2,4-oxadiazol-3-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(tiofén-2-il)fenil)metanon;

(4-fluor-fenil)(3-(3-fenil-1,2,4-oxadiazol-5-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(4-fluor-fenil)(3-(5-fenil-1,2,4-oxadiazol-3-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(3-(3-fenil-1,2,4-oxadiazol-5-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(tiofén-2-il)fenil)metanon;

(4-fluor-fenil)(3-(3-(4-fluor-fenil)-1,2,4-oxadiazol-5-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(3-(3-(4-fluor-fenil)-1,2,4-oxadiazol-5-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(tiofén-2-il)fenil)metanon;

(3-(3-(2,4-difluor-fenil)-1,2,4-oxadiazol-5-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(tiofén-2-il)fenil)metanon;

(4-fluor-fenil)(3-(5-fenil-1H-1,2,4-triazol-3-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(3-(5-fenil-1H-1,2,4-triazol-3-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(tiofén-2-il)fenil)metanon;

(4-fluor-fenil)(3-(2-(2-fluor-fenil)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(3-(2-(2-fluor-fenil)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(tiofén-2-il)fenil)metanon;

[1,1'-bifenil]-4-il(3-(2-(2-fluor-fenil)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(4'-fluor-[1,1'-bifenil]-4-il)(3-(2-(2-fluor-fenil)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(3-(3-(2,4-difluor-fenil)-1,2,4-oxadiazol-5-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(tiofén-2-il)fenil)metanon;

[1,1'-bifenil]-4-il(3-(2-((4,5-diklór-1H-imidazol-1-il)metil)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(3-(2-((4,5-diklór-1H-imidazol-1-il)metil)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4'-fluor-[1,1'-bifenil]-4-il)metanon;

(3-(2-(4-klór-benzil)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-fluor-fenil)metanon;

(3-(2-(4-klór-benzil)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(tiofén-2-il)fenil)metanon;

(4-fluor-fenil)(3-(2-(p-tolil)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(4-(tiofén-2-il)fenil)(3-(2-(p-tolil)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

[1,1`-bifenil]-4-il(3-(2-(p-tolil)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(4-fluor-fenil)(3-(2-(tiofén-2-il)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(4-(tiofén-2-il)fenil)(3-(2-(tiofén-2-il)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

[1,1'-bifenil]-4-il(3-(2-(tiofén-2-il)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(4'-fluor-[1,1'-bifenil]-4-il)(3-(2-(tiofén-2-il)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(3-(2-(((4-klór-fenil)szulfonil)metil)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(tiofén-2-il)fenil)metanon;

[1,1'-bifenil]-4-il(3-(2-(((4-klór-fenil)szulfonil)metil)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(3-(2-(((4-klór-fenil)szulfonil)metil)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4'-fluor-[1,1'-bifenil]-4-il)metanon;

(4-fluor-fenil)(3-(2-(2-metoxi-fenil)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(3-(2-(2-metoxi-fenil)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(tiofén-2-il)fenil)metanon;

[1,1'-bifenil]-4-il(3-(2-(2-metoxi-fenil)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

[1,1'-bifenil]-4-il(3-(3-(4-fluor-fenil)-1,2,4-oxadiazol-5-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(4'-fluor-[1,1'-bifenil]-4-il)(3-(3-(4-fluor-fenil)-1,2,4-oxadiazol-5-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(4-fluor-fenil)(3-(2-(3-fluor-fenil)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(3-(2-(3-fluor-fenil)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(tiofén-2-il)fenil)metanon;

(4-fluor-fenil)(3-(2-izopropiltiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(3-(3-(4-fluor-fenil)-1,2,4-oxadiazol-5-il)-8-metil-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(tiofén-2-il)fenil)metanon;

(3-(3-fenil-1,2,4-tiadiazol-5-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(tiofén-2-il)fenil)metanon;

(4-fluor-fenil)(3-(3-fenil-1,2,4-tiadiazol-5-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(3-(2-(4-bróm-fenil)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(tiofén-2-il)fenil)metanon;

(3-(2-(4-bróm-fenil)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-fluor-fenil)metanon;

(3-(2-(4-fluor-fenil)tiazol-4-il)-8-metil-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(5-metil-tiofén-2-il)fenil)metanon;

4-(3-(2-(4-fluor-fenil)tiazol-4-il)-8-metil-5,6,7,8-tetrahidro-[1,2,4]triazol[4,3-a]pirazin-7-karbonil)benzonitrile;

[1,1'-bifenil]-4-il(3-(3-fenil-1,2,4-oxadiazol-5-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;ű

(4-fluor-fenil)(3-(2-(piridin-4-il)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(3-(2-(kinolin-2-il)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(tiofén-2-il)fenil)metanon;

(3-(1-metil-3-fenil-1H-pirazol-5-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(tiofén-2-il)fenil)metanon;

(3-(2-(4-(dimetil-amino)fenil)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-fluor-fenil)metanon;

(3-(1-metil-5-fenil-1H-pirazol-3-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(tiofén-2-il)fenil)metanon;

(4'-fluor-[1,1'-bifenil]-4-il)(3-(3-fenil-1,2,4-oxadiazol-5-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(3-(2-(piridin-2-il)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(tiofén-2-il)fenil)metanon;

(4-fluor-fenil)(3-(1-metil-3-fenil-1H-pirazol-5-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(3-(2-(pirimidin-2-il)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(tiofén-2-il)fenil)metanon;

(S)-(8-metil-3-(2-morfolino-tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(tiofén-2-il)fenil)metanon;

(3-(2-(piridin-4-il)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(tiofén-2-il)fenil)metanon;

(3-(2-(4-(dimetil-amino)fenil)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(tiofén-2-il)fenil)metanon;

(4-fluor-fenil)(3-(2-(piridin-2-il)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

fenil(3-(piridin-2-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(3-(piridin-2-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(p-tolil)metanon;

(S)-(3-(2-(4-fluor-fenil)tiazol-4-il)-8-metil-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(2-metil-tiofén-3-il)fenil)metanon;

(R)-(3-(2-(4-fluor-fenil)tiazol-4-il)-8-metil-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(2-metil-tiofén-3-il)fenil)metanon;

(3-(2-(pirazin-2-il)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(tiofén-2-il)fenil)metanon;

4-(4-(7-(4-(tiofén-2-il)benzoil)-5,6,7,8-tetrahidro-[1,2,4]triazol[4,3-a]pirazin-3-il)tiazol-2-il)benzonitril;

(4-fluor-fenil)(3-(2-(pirazin-2-il)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(4-fluor-fenil)(3-(1-metil-5-fenil-1H-pirazol-3-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(3-(2-(4-morfolino-fenil)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(tiofén-2-il)fenil)metanon;

(4-fluor-fenil)(3-(2-(4-morfolino-fenil)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(3-(2-(4-(4-metil-piperazin-1-il)fenil)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(tiofén-2-il)fenil)metanon;

(4-fluor-fenil)(3-(2-(4-(4-metil-piperazin-1-il)fenil)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(3-(2-(4-(piperidin-1-il)fenil)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(tiofén-2-il)fenil)metanon;

(4-fluor-fenil)(3-(2-(4-(piperidin-1-il)fenil)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(3-(2-(4-(pirrolidin-1-il)fenil)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(tiofén-2-il)fenil)metanon;

(4-fluor-fenil)(3-(2-(4-(pirrolidin-1-il)fenil)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(3-(2-(piperidin-1-il)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(tiofén-2-il)fenil)metanon;

(3-(2-(pirrolidin-1-il)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(tiofén-2-il)fenil)metanon;

(4-fluor-fenil)(3-(2-(pirrolidin-1-il)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(3-(2-(4-metil-piperazin-1-il)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(tiofén-2-il)fenil)metanon;

(4-fluor-fenil)(3-(2-(4-metil-piperazin-1-il)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(3-(1-metil-2-fenil-1H-imidazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(tiofén-2-il)fenil)metanon;

(4-(dimetil-amino)fenil)(3-(2-(4-fluor-fenil)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(3-(1-(2-metoxi-etil)-3-fenil-1H-pirazol-5-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(tiofén-2-il)fenil)metanon;

(4-fluor-fenil)(3-(1-(2-metoxi-etil)-3-fenil-1H-pirazol-5-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(3-(2-izobutil-tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(tiofén-2-il)fenil)metanon;

(3-(2-(2-(2-metoxi-etil)morfolino)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(tiofén-2-il)fenil)metanon;

(3-(2-(4,4-difluor-piperidin-1-il)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-fluor-fenil)metanon;

(4-fluor-fenil)(3-(2-izobutil-tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(3-(2-(2,5-dimetil-morfolino)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(tiofén-2-il)fenil)metanon;

(3-(2-(2-hidroxi-fenil)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(tiofén-2-il)fenil)metanon;

(3-(2-(4,4-difluor-piperidin-1-il)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(tiofén-2-il)fenil)metanon;

(3-(2-(2,6-dimetil-morfolino)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(tiofén-2-il)fenil)metanon;

(3-(2-(2,2-dimetil-morfolino)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(tiofén-2-il)fenil)metanon;

(3-(3-fenil-1H-pirazol-5-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(tiofén-2-il)fenil)metanon;

(3-(2-(4-fluor-fenil)tiazol-4-il)-8-metil-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(3-metil-tiofén-2-il)fenil)metanon;

(4-fluor-fenil)(3-(3-fenil-1H-pirazol-5-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(R)-(3-(2-(4-fluor-fenil)tiazol-4-il)-8-metil-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(3-metil-tiofén-2-il)fenil)metanon;

(4-fluor-fenil)(3-(2-(2-hidroxi-fenil)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(S)-(3-(2-(4-fluor-fenil)tiazol-4-il)-8-metil-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(3-metil-tiofén-2-il)fenil)metanon;

(3-(2-(2-metil-morfolino)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(tiofén-2-il)fenil)metanon;

(3-(2-(4,4-dimetil-piperidin-1-il)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(tiofén-2-il)fenil)metanon;

(3-(5-metil-tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(tiofén-2-il)fenil)metanon;

(3-(2-(4,4-dimetil-piperidin-1-il)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-fluor-fenil)metanon;

(4-fluor-fenil)(3-(2-(2-(metoxi-metil)piperidin-1-il)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(4-fluor-fenil)(8-metil-3-(6-metil-piridin-2-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(3-(2-(2-(metoxi-metil)piperidin-1-il)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(tiofén-2-il)fenil)metanon;

terc-butil (2-(2-(4-(7-(4-(tiofén-2-il)benzoil)-5,6,7,8-tetrahidro-[1,2,4]triazol[4,3-a]pirazin-3-il)tiazol-2-il)fenoxi)etil)karbamát;

(3-(2-(2-(2-hidroxi-etoxi)fenil)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(tiofén-2-il)fenil)metanon;

(3-(2-(2-(2-amino-etoxi)fenil)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(tiofén-2-il)fenil)metanon;

N-(4-(4-(7-(4-(tiofén-2-il)benzoil)-5,6,7,8-tetrahidro-[1,2,4]triazol[4,3-a]pirazin-3-il)tiazol-2-il)fenil)metán-szulfonamid;

(3-(1-(2-hidroxi-etil)-3-fenil-1H-pirazol-5-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(tiofén-2-il)fenil)metanon;

(3-(1-(2-hidroxi-etil)-5-fenil-1H-pirazol-3-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(tiofén-2-il)fenil)metanon;

[1,1`-bifenil]-4-il(8-metil-3-(6-metil-piridin-2-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(8-metil-3-(6-metil-piridin-2-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(tiofén-2-il)fenil)metanon;

(3-(2-(2,4-difluor-fenil)-5-metil-tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(tiofén-2-il)fenil)metanon;

(3-(2-(3-(dimetil-amino)fenil)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(tiofén-2-il)fenil)metanon;

(3-(2-(3-(dimetil-amino)fenil)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-fluor-fenil)metanon;

N-(3-(4-(7-(4-(tiofén-2-il)benzoil)-5,6,7,8-tetrahidro-[1,2,4]triazol[4,3-a]pirazin-3-il)tiazol-2-il)fenil)metán-szulfonamid;

N-(2-(4-(7-(4-(tiofén-2-il)benzoil)-5,6,7,8-tetrahidro-[1,2,4]triazol[4,3-a]pirazin-3-il)tiazol-2-il)fenil)metán-szulfonamid;

(3-(4-klór-fenil)-1H-pirazol-5-il)(3-(2-(4-fluor-fenil)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(3-(4-klór-fenil)-1-metil-1H-pirazol-5-il)(3-(2-(4-fluor-fenil)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(3-(3,4-diklór-fenil)-1-metil-1H-pirazol-5-il)(3-(2-(4-fluor-fenil)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

(5-(4-klór-fenil)-1-metil-1H-pirazol-3-il)(3-(2-(4-fluor-fenil)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)metanon;

terc-butil (2-(3-fenil-5-(7-(4-(tiofén-2-il)benzoil)-5,6,7,8-tetrahidro-[1,2,4]triazol[4,3-a]pirazin-3-il)-1H-pirazol-1-il)etil)karbamát;

terc-butil (2-(5-fenil-3-(7-(4-(tiofén-2-il)benzoil)-5,6,7,8-tetrahidro-[1,2,4]triazol[4,3-a]pirazin-3-il)-1H-pirazol-1-il)etil)karbamát;

(3-(2-(2-bróm-fenil)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(tiofén-2-il)fenil)metanon;

(3-(2-(3-bróm-fenil)tiazol-4-il)-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(tiofén-2-il)fenil)metanon;

2-(4-(7-(4-(tiofén-2-il)benzoil)-5,6,7,8-tetrahidro-[1,2,4]triazol[4,3-a]pirazin-3-il)tiazol-2-il)benzonitril;

3-(4-(7-(4-(tiofén-2-il)benzoil)-5,6,7,8-tetrahidro-[1,2,4]triazol[4,3-a]pirazin-3-il)tiazol-2-il)benzonitril;

(3-(2-(4-fluor-fenil)tiazol-4-il)-8-metil-5,6-dihidro-[1,2,4]triazol[4,3-a]pirazin-7(8H)-il)(4-(2-metil-tiofén-3-il)fenil)metanon;

és azok gyógyászatilag elfogadható sói és szolvátjai.

13. Gyógyászati készítmény, amely tartalmazza a következőket: egy az 1.-től 12.-ig igénypontok bármelyike szerinti vegyületet vagy annak egy gyógyászatilag elfogadható sóját vagy szolvátját és legalább egy gyógyászatilag elfogadható hordozót, hígítót, excipienst (segédanyagot) és/vagy adjuvánst.

14. Gyógyszer, amely tartalmazza a következőket: egy az 1.-től 12.-ig igénypontok bármelyike szerinti vegyületet vagy annak egy gyógyászatilag elfogadható sóját vagy szolvátját.

15. Vegyület az 1.-től 12.-ig igénypontok bármelyike szerint vagy annak egy gyógyászatilag elfogadható sója vagy szolvátja, alkalmazás céljából a következőknek a kezelésére és/vagy megelőzésére: depresszió, anxietás, pszichózis, skizofrénia, pszichotikus zavarok, bipoláris zavarok, kognitív zavarok, Parkinson-kór, Alzheimer-kór, figyelemhiányos hiperaktivitás rendellenesség (ADHD), fájdalom, görcs, elhízás (obezitás), gyulladásos betegségek, amelyek magukban foglalják a következőket: irritábilis bél szindróma és gyulladásos bélzavarok, hányás, preeklampszia, légutakkal kapcsolatos betegségek, amelyek magukban foglalják a következőket: krónikus obstruktív tüdőbetegség, asztma, légúti túlérzékenység, hörgőszűkület és köhögés, reprodukciós zavarok és nemi hormonfüggő betegségek, amelyek magukban foglalják, de nem kizárólagosan, a következőket: jóindulatú prosztata hiperplázia (megnagyobbodás) (BPH), metasztázisos prosztata karcinóma, hererák, mellrák (emlőrák), androgén-függő akne, férfias androgén alopécia (férfias típusú hajhullás), endometriózis, abnormális pubertás (angolul: „abnormal puberty"), méhfibrózis, hormonfüggő rákok, hiperandrogenizmus, hirszutizmus (túlzott szőrnövekedés), virilizáció, policisztás ovárium szindróma (PCOS), HAIR-AN szindróma (hiperandrogenizmus, inzulin rezisztencia és acanthosis nigricans (akantózis nigrikánsz)), ovariális hyperthecosis (angolul: „ovarian hyperthecosis") (HAIR-AN, amely a luteinizált téka sejtek hiperpláziájával jár az ovariális strómában), magas intraovariális (petefészken belüli) androgén koncentrációk más megnyilvánulásai (például follikuláris érés gátlása, atrézia (angolul: „atresia"), anovuláció, diszmenorrea (fájdalmas menstruáció), diszfunkcionális méhvérzés, meddőség), nőgyógyászati rendellenességek, meddőség és androgéntermelő tumor (virilizáló ovariális (petefészek) vagy mellékvese tumor).

16. Vegyület az 1.-től 12.-ig igénypontok bármelyike szerint vagy annak egy gyógyászatilag elfogadható sója vagy szolvátja, alkalmazás céljából az LH-emelkedés szupressziójára mesterséges megtermékenyítés során egy páciensnél.

17. Vegyület az 1.-től 12.-ig igénypontok bármelyike szerint vagy annak egy gyógyászatilag elfogadható sója vagy szolvátja, alkalmazás céljából a következők okozására: hím kasztráció (ivartalanítás) vagy a nemi vágy gátlása férfiaknál.