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(71) Applicant (for all designated States except US):
RAQUALIA PHARMA INC. [JP/JP]; 2, Aza 5-gochi, Taketoyo-cho, Chita-gun, Aichi, 4702341 (JP).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **YAMAGISHI, Tatsuya** [JP/JP]; c/o RAQUALIA PHARMA INC., 2, Aza 5-gochi, Taketoyo-cho, Chita-gun, Aichi, 4702341 (JP). **ARANO, Yoshimasa** [JP/JP]; c/o RAQUALIA PHARMA INC., 2, Aza 5-gochi, Taketoyo-cho, Chita-gun, Aichi, 4702341 (JP). **MORITA, Mikio** [JP/JP]; c/o RAQUALIA PHARMA INC., 2, Aza 5-gochi, Taketoyo-cho, Chita-gun, Aichi, 4702341 (JP). **INOUE, Tadashi** [JP/JP]; c/o RAQUALIA PHARMA INC., 2, Aza 5-gochi, Taketoyo-cho, Chita-gun, Aichi, 4702341 (JP).(74) Agent: **IWATANI, Ryo**; KEIHAN Dojima Bldg. 3F, 1-31, Dojima 2-chome, Kita-ku, Osaka-shi, Osaka, 5300003 (JP).

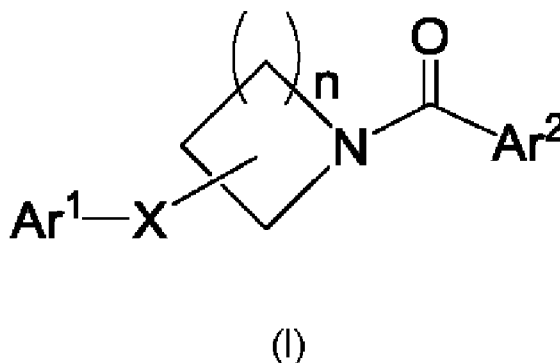
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(54) Title: ARYL CARBOXAMIDE DERIVATIVES AS TTX-S BLOCKERS



(57) **Abstract:** The present invention relates to aryl carboxamide derivatives of formula (I), wherein Ar¹ is phenyl; Ar² is aryl; n is 1-4; X is -O-, -S-, -SO- or -SO₂-, a prodrug thereof or a pharmaceutically acceptable salt thereof, which have blocking activities of voltage gated sodium channels as the TTX-S channels, and which are useful in the treatment or prevention of such disorders and diseases as pain in which voltage gated sodium channels are involved. The invention also relates to pharmaceutical compositions comprising these compounds and the use of these compounds and compositions in the prevention or treatment of such diseases as pain in which voltage gated sodium channels are involved.



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Description

Title of Invention: ARYL CARBOXAMIDE DERIVATIVES AS TTX-S BLOCKERS

Technical Field

[0001] The present invention relates to aryl carboxamide derivatives compounds which are tetrodotoxin-sensitive (TTX-S) blockers over the $\text{Na}_{\text{V}1.5}$ channel, and which are useful in the treatment or prevention of neurological and psychiatric disorders and diseases in which TTX-S channels are involved. The invention also relates to pharmaceutical compositions comprising these compounds and the use of these compounds and compositions in the prevention or treatment of such diseases in which TTX-S sodium channels are involved.

Background Art

[0002] The aryl carboxamide derivatives of the present invention are sodium channel blockers and have a number of therapeutic applications, particularly in the treatment of pain.

More particularly, the aryl carboxamide derivatives of the invention are selective tetrodotoxin-sensitive (TTX-S) blockers. In the discussion that follows, the invention is exemplified by reference to the inhibition of $\text{Na}_{\text{V}1.3}$ or $\text{Na}_{\text{V}1.7}$ channel as the TTX-S channels. They show the affinity for $\text{Na}_{\text{V}1.3}$ or $\text{Na}_{\text{V}1.7}$ channel which is significantly greater than their affinity for $\text{Na}_{\text{V}1.5}$ channel as the tetrodotoxin-resistant (TTX-R) sodium channels. Aryl carboxamide derivatives of the invention show good selectivity for the $\text{Na}_{\text{V}1.3}$ or $\text{Na}_{\text{V}1.7}$ channel as compared with $\text{Na}_{\text{V}1.5}$ channel.

[0003] The rat $\text{Na}_{\text{V}1.3}$ channel and the human $\text{Na}_{\text{V}1.3}$ channel have been cloned in 1988 and 1998/2000 respectively (FEBS Lett. 228 (1), 187-194, 1988; J. Mol. Neurosci., 10 (1), 67-70, 1998; Eur. J. Neurosci. 12 (12), 4281-4289, 2000). The $\text{Na}_{\text{V}1.3}$ channel was formerly known as brain type III sodium channel. $\text{Na}_{\text{V}1.3}$ is present at relatively high levels in the nervous system of rat embryos but is barely detectable in adult rats. $\text{Na}_{\text{V}1.3}$ is up-regulated following axotomy in the Spinal Nerve Ligation (SNL), Chronic Constriction Injury (CCI), and diabetic neuropathy models (J Neurophysiol 82, 2776-2785, 1999. J. A. Black et al.; Ann Neurol 52, 786-792, 2002. M.J. Craner et al.; Pain 83, 591-600, 1999. S. Dib-Hajj et al.; J Biol Chem 279, 29341-29350, 2004. S. Hong et al.; Mol Brain Res 95, 153-161, 2001. C.H. Kim et al.). The up-regulation of $\text{Na}_{\text{V}1.3}$ channel contributes to rapidly repriming sodium current in small dorsal root ganglion (DRG) neurons (J Neurophysiol 82, 2776-2785, 1999. J.A. Black et al.). These observations suggest that $\text{Na}_{\text{V}1.3}$ may make a key contribution to neuronal hyperexcitability.

- [0004] In order to validate the contribution of $\text{Na}_{\text{v}1.3}$ sodium channel in the pain states, specific antisense oligonucleotides (ASO) were used in animal pain models. $\text{Na}_{\text{v}1.3}$ sodium channel ASO treatment significantly attenuated pain-related behaviors after CCI operation (J. Neurosci. 24, 4832-4839, 2004, Hains, B.C. et al.). These findings suggest that $\text{Na}_{\text{v}1.3}$ sodium channel antagonist is useful to treat neuropathic pain conditions.
- [0005] The $\text{Na}_{\text{v}1.7}$ channel appears to be the best 'validated' pain target. The most exciting findings with respect to $\text{Na}_{\text{v}1.7}$ have come from human genetic studies. Cox et al. (Nature 444, 894-898, 2006) discovered SCN9A mutations that cause a loss of $\text{Na}_{\text{v}1.7}$ function in three families from Pakistan. Their observations link loss of $\text{Na}_{\text{v}1.7}$ function with a congenital inability to experience pain, adding to the evidence indicating $\text{Na}_{\text{v}1.7}$ channel as an essential participant in human nociception.
- [0006] By contrast, Gain-of-function mutations have also been described that lead to enhanced pain, for example, Primary Erythralgia in one case and Paroxysmal Extreme Pain Disorder in another. These gain-of-function mutations in patients led to different types of gating changes in $\text{Na}_{\text{v}1.7}$ sodium currents and, interestingly, different degrees of effectiveness of specific sodium channel blocking drugs. The implication from these findings is that a selective $\text{Na}_{\text{v}1.7}$ blocker may be an effective treatment for pain in man.
- [0007] A local anaesthetic lidocaine and a volatile anaesthetic halothane are known to act on both TTX-R and TTX-S sodium channels with poor selectivity and low potency (IC_{50} values range from 50 μM to 10 mM). These anaesthetics at high systemic concentrations could cause devastating side effects, e.g., paralysis and cardiac arrest. However, systemic administration of lidocaine at low concentrations is effective to treat chronic pain (Trends in Pharm. Sci 22, 27-31, 2001, Baker, M.D. et al.). In rats, application of a very low dose of TTX to the DRG of the injured segment of the L5 spinal nerve significantly reduces mechanical allodynic behavior (Brain Res 871, 98-103, 2000, Lyu, Y.S. et al.). This suggests that TTX-S subtypes of sodium channels play an important role in maintaining allodynic behaviors in an animal model of neuropathic pain.
- [0008] The $\text{Na}_{\text{v}1.5}$ channel is also a member of TTX-resistant sodium channels. The $\text{Na}_{\text{v}1.5}$ channel is almost exclusively expressed in cardiac tissue and has been shown to underlie a variety of cardiac arrhythmias and conduction disorders.

Summary of Invention

- [0009] It is an objective of the invention to provide new TTX-S blockers that are good drug candidates. Preferred compounds should bind potently to the TTX-S ($\text{Na}_{\text{v}1.3}$ and $\text{Na}_{\text{v}1.7}$) channels whilst showing little affinity for other sodium channels, particularly the $\text{Na}_{\text{v}1.5}$

channel. They should be well absorbed from the gastrointestinal tract, be metabolically stable and possess favorable pharmacokinetic properties. They should be non-toxic and demonstrate few side-effects. Furthermore, the ideal drug candidate will exist in a physical form that is stable, non-hygroscopic and easily formulated.

[0010] In particular, the aryl carboxamide derivatives of the present invention are selective for the TTX-S channels over the $\text{Na}_{\text{v}1.5}$ channel, leading to improvements in the side-effect profile.

The aryl carboxamide derivatives of the present invention are therefore useful in the treatment of a wide range of disorders, particularly pain, acute pain, chronic pain, neuropathic pain, inflammatory pain, visceral pain, nociceptive pain including post-surgical pain, and mixed pain types involving the viscera, gastrointestinal tract, cranial structures, musculoskeletal system, spine, urogenital system, cardiovascular system and CNS, including cancer pain, back and orofacial pain.

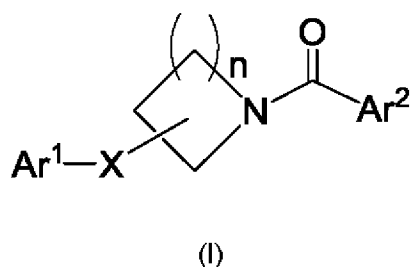
[0011] Other conditions that may be treated with the aryl carboxamide derivatives of the present invention include multiple sclerosis, neurodegenerative disorders, irritable bowel syndrome, osteoarthritis, rheumatoid arthritis, neuropathological disorders, functional bowel disorders, inflammatory bowel diseases, pain associated with dysmenorrhea, pelvic pain, cystitis, pancreatitis, migraine, cluster and tension headaches, diabetic neuropathy, peripheral neuropathic pain, sciatica, fibromyalgia Crohn's disease, epilepsy or epileptic conditions, bipolar depression, tachyarrhythmias, mood disorder, bipolar disorder, psychiatric disorders such as anxiety and depression, myotonia, arrhythmia, movement disorders, neuroendocrine disorders, ataxia, incontinence, visceral pain, trigeminal neuralgia, herpetic neuralgia, general neuralgia, postherpetic neuralgia, radicular pain, sciatica, back pain, head or neck pain, severe or intractable pain, breakthrough pain, postsurgical pain, stroke, cancer pain, seizure disorder and causalgia.

[0012] Although WO 2003/037274 discloses pyrazol amide compounds which have sodium channel blocking activities, the phenoxy group is not included in the patent. WO 2003/084948 also discloses compounds which have sodium channel blocking activities. The compounds of the invention, which are represented by the formula $\text{A}^1\text{-X}^1\text{-X}^2\text{-Z}^1\text{-X}^3\text{-X}^4\text{-A}^2$ in claim 1, involve an extremely large number of compounds. However the compounds which are disclosed in the meaning of Article 5 of the PCT and are supported by the description in the meaning of Article 6 of the PCT are limited to an extremely small part of the compounds claimed. Especially an amide moiety is formally included in the said broad formula in claim 1, but neither actual working examples nor embodiments in the specification. In addition, the representative compound, Example 198 (3-((4-(phenoxy)methyl)piperidin-1-yl)methyl)pyrazin-2(1H)-one), in WO 2003/084948 showed >30 μM and 15 μM against $\text{Na}_{\text{v}1.3}$ and $\text{Na}_{\text{v}1.7}$, re-

spectively in FRET Assay (Method A) described in the present patent application, whereas the compounds of this invention showed <5 microM.

- [0013] The compounds of this invention characterized by having phenoxy, phenylthio, phenylsulfoxy, or phenylsulfonyl group and amide group are novel, and are quite different from the prior arts. In addition the compounds of this invention with an amide group greatly contribute improving the selectivity for the Na_{v1.3} or Na_{v1.7} channel as compared with Na_{v1.5} channel. Furthermore the compounds with an amide group surprisingly reduced the dofetilide binding activities, which reduce the risk of cardiovascular adverse events.
- [0014] Structurally close compounds are disclosed in WO 2002/34718, WO 2006/010967, US 2007/0027163, WO 2007/082079 and WO2009/105722, which are not for sodium channel blockers of this invention but for quite different biological targets. Particularly although WO 2007/082079 discloses 4-pyridyl compounds as protein kinase inhibitors, the 4-pyridyl compounds of this invention with terminal chloro, trifluoromethyl, trifluoromethoxy, trifluoroethoxy or ethoxy phenyl ring showed excellent sodium channel blocking activities.
- [0015] With respect to other compounds disclosed in the art, the compounds of the present invention may show less toxicity, good absorption, distribution, good solubility, less plasma protein binding, less drug-drug interaction, good metabolic stability, reduced inhibitory activity at HERG channel, and reduced QT prolongation.
- [0016] The present invention is directed to aryl carboxamide derivatives compounds which are TTX-S blockers over the Na_{v1.5} channel, and which are useful in the treatment or prevention of neurological and psychiatric disorders and diseases in which TTX-S channels are involved. The invention is also directed to pharmaceutical compositions comprising these compounds and the use of these compounds and compositions in the prevention or treatment of such diseases in which TTX-S sodium channels are involved.
- [0017] [1] The present invention provides a use of a compound of the following formula (I) for the manufacture of a medicament for the treatment of a condition or disorder in which TTX-S channel blockers are involved:

[Chem.1]



wherein

[0018] Ar¹ is phenyl which may be optionally substituted with 1 to 5 substituents independently selected from the group consisting of

(1) halogen, (2) C₁-C₄ alkyl-O_i-, (3) C₃-C₈ cycloalkyl-O_i-, (4) C₁-C₄ haloalkyl-O_i-, (5) hydroxy, (6) C₃-C₈ cycloalkyl-C₁-C₄ alkyl-O_i-, (7) C₁-C₄ alkylthio, (8) nitro, (9) R¹N(R²)-C₀₋₄ alkyl-O_i- (10) cyano, (11) hydroxy C₁-C₄ alkyl-O_i-, (12) C₁-C₄ alkyl-O-C₁-C₄ alkyl-O_i-, (13) C₁-C₄ alkylsulfonyl, (14) R¹N(R²)-SO₂-C₀₋₄ alkyl-O_i-, (15) C₁-C₄ alkyl C(=O)-, (16) HO-C(=O)-, (17) C₁-C₄ alkyl-O-C(=O)-, (18) R¹N(R²)C(=O)-C₀₋₄ alkyl-O_i-, (19) C₁-C₄ alkyl-SO₂-NH-C₀₋₄ alkyl-O_i-, (20) R¹-O_i-C(=O)N(R²)-C₀₋₄ alkyl-O_k-, (21) NH₂(HN=)C-, (22) NH₂C(=O)NH-, (23) 5 to 10 membered aryl-O_i-C₀-C₄ alkyl-O_k-; wherein said aryl may be optionally substituted with 1 to 5 substituents independently selected from the group consisting of hydroxy, halogen, C₁-C₄ alkyl, C₁-C₄ alkoxy, hydroxy C₁-C₄ alkyl, amino C₁-C₄ alkyl, C₁-C₄ haloalkyl, C₁-C₄ haloalkoxy, C₃-C₇ cycloalkyl C₀₋₆ alkyl, amino, C₁-C₄ alkylamino, di(C₁-C₄ alkyl)amino, C₁-C₄ alkylthio, C₁-C₄ alkylsulfonyl, R¹N(R²)C(=O)-, C₁-C₄ alkyl-SO₂-NH-, and nitro; and (24) heterocyclic group-O_i-C₀-C₄ alkyl-O_k-; wherein said heterocyclic group may be optionally substituted with 1 to 5 substituents independently selected from the group consisting of hydroxy, halogen, C₁-C₄ alkyl, C₁-C₄ alkoxy, hydroxy C₁-C₄ alkyl, amino C₁-C₄ alkyl, C₁-C₄ haloalkyl, C₁-C₄ haloalkoxy, C₃-C₇ cycloalkyl C₀₋₆ alkyl, amino, C₁-C₄ alkylamino, di(C₁-C₄ alkyl)amino, C₁-C₄ alkylthio, C₁-C₄ alkylsulfonyl, R¹N(R²)C(=O)-, C₁-C₄ alkyl-SO₂-NH-, and nitro;

[0019] Ar² is aryl which may be optionally substituted with 1 to 5 substituents independently selected from the group consisting of

(1) halogen, (2) C₁-C₄ alkyl-O_i-, (3) C₃-C₈ cycloalkyl-O_i-, (4) C₁-C₄ haloalkyl-O_i-, (5) hydroxy, (6) C₃-C₈ cycloalkyl-C₁-C₄ alkyl-O_i-, (7) C₁-C₄ alkylthio, (8) nitro, (9) R¹N(R²)-C₀₋₄ alkyl-O_i- (10) cyano, (11) hydroxy C₁-C₄ alkyl-O_i-, (12) C₁-C₄ alkyl-O-C₁-C₄ alkyl-O_i-, (13) C₁-C₄ alkylsulfonyl, (14) R¹N(R²)-SO₂-C₀₋₄ alkyl-O_i-, (15) C₁-C₄ alkyl C(=O)-, (16) HO-C(=O)-, (17) C₁-C₄ alkyl-O-C(=O)-, (18) R¹N(R²)C(=O)-C₀₋₄ alkyl-O_i-, (19) C₁-C₄ alkyl-SO₂-NH-C₀₋₄ alkyl-O_i-, (20) R¹-O_i-C(=O)N(R²)-C₀₋₄ alkyl-O_k-, (21) NH₂(HN=)C-, (22) NH₂C(=O)NH-, (23) 5 to 10 membered aryl-O_i-C₀-C₄ alkyl-O_k-; wherein said aryl may be optionally substituted with 1 to 5 substituents independently selected from the group consisting of hydroxy, halogen, C₁-C₄ alkyl, C₁-C₄ alkoxy, hydroxy C₁-C₄ alkyl, amino C₁-C₄ alkyl, C₁-C₄ haloalkyl, C₁-C₄ haloalkoxy, C₃-C₇ cycloalkyl C₀₋₆ alkyl, amino, C₁-C₄ alkylamino, di(C₁-C₄ alkyl)amino, C₁-C₄ alkylthio, C₁-C₄ alkylsulfonyl, R¹N(R²)C(=O)-, C₁-C₄ alkyl-SO₂-NH-, and nitro; and (24) heterocyclic group-O_i-C₀-C₄ alkyl-O_k-; wherein said heterocyclic group may be optionally substituted with 1 to 5 substituents independently selected from the group consisting of hydroxy, halogen, C₁-C₄ alkyl, C₁-C₄ alkoxy, hydroxy C₁-C₄ alkyl, amino C₁-C₄ alkyl, C₁-C₄ haloalkyl, C₁-C₄ haloalkoxy, C₃-C₇ cycloalkyl C₀₋₆ alkyl, amino, C₁-C₄

alkylamino, di(C₁-C₄ alkyl)amino, C₁-C₄ alkylthio, C₁-C₄ alkylsulfonyl, R¹N(R²)C(=O)-, C₁-C₄ alkyl-SO₂-NH-, and nitro;

[0020] n is 1, 2, 3 or 4;

i is 0 or 1;

k is 0 or 1;

[0021] R¹ and R² are independently selected from the group consisting of:

(1) hydrogen, (2) C₁₋₆ alkyl, (3) hydroxy C₁-C₄ alkyl, (4) C₁-C₄ alkoxy C₁-C₄ alkyl, (5) amino C₁-C₄ alkyl, (6) C₁-C₄ haloalkyl, (7) C₁-C₄ haloalkoxy, (8) C₃₋₆ alkenyl, (9) C₃₋₈ cycloalkyl C₀₋₆ alkyl, (10) phenyl, which is unsubstituted or substituted with R³, and (11) 5 to 10 membered aryl C₀-C₄ alkyl; wherein said aryl may be optionally substituted with 1 to 5 substituents independently selected from the group consisting of hydroxy, halogen, C₁-C₄ alkyl, C₁-C₄ alkoxy, hydroxy C₁-C₄ alkyl, amino C₁-C₄ alkyl, C₁-C₄ haloalkyl, C₁-C₄ haloalkoxy, C₃₋₇ cycloalkyl C₀₋₆ alkyl, amino, C₁-C₄ alkylamino, di(C₁-C₄ alkyl)amino, C₁-C₄ alkylthio, and nitro;

or R¹ and R² taken together with the nitrogen atom to which they are attached form a 3 to 8 membered ring, where the ring may contain one to four heteroatom(s) independently selected from nitrogen, oxygen, and sulfur; where the ring may be saturated or partially saturated or unsaturated; and the ring is unsubstituted or substituted one or more substituents selected from R³;

[0022] R³ is selected from the group consisting of:

(1) hydroxy, (2) halogen, (3) C₁₋₆ alkyl, (4) -C₃₋₈ cycloalkyl, (5) -O-C₁₋₆ alkyl, (6) -O(C=O)-C₁₋₆ alkyl, (7) -NH-C₁₋₆ alkyl, (8) phenyl, (9) heterocyclic group, (10) -CO₂H, and (11) -CN;

[0023] X is -O-, -S-, -SO-, or -SO₂-;

or a prodrug thereof or a pharmaceutically acceptable salt thereof, each as described herein, for the manufacture of a medicament for the treatment of a condition or disorder mediated by TTX-S channel; in particular, Na_{v1.3} channels blocking activity. In order to use the compounds of formula (I), prodrugs thereof, and pharmaceutically acceptable salts thereof in therapy, they will normally be formulated into a pharmaceutical composition in accordance with standard pharmaceutical practice.

[0024] [2] This invention provides the use of a compound as described in formula (I) wherein Ar² is aryl selected from

benzofuranyl, benzofurazanyl, benzimidazolonyl, benzoimidazolyl, benzoisothiazolyl, benzoisoxazolyl, benzothiadiazolyl, benzothiazolyl, benzoxadiazolyl, benzoxazolonyl, benzoxazolyl, benzothiophenyl, benzotriazolyl, chromanyl, cinnolinyl, 2,3-dioxoindolyl, furanyl, furopyridyl, fuopyrrolyl, imidazolyl, imidazopyrazinyl, imidazopyridinyl, imidazopyrimidinyl, imidazothiazolyl, indazolyl, indolinyl, indolyl, isochromanyl, isoquinolyl, isoxazolopyridyl, isoxazolyl,

isothiazolyl, naphthyridinyl, oxadiazolyl, oxazolyl, 2-oxoindolyl, oxoisindolyl, phthalazyl, pyrazolyl, pyrazolopyridyl, pyrazolopyrimidinyl, pyrazinyl, pyridopyrimidinyl, pyridyl, pyrimidyl, pyridazinyl, pyrrolopyridyl, pyrrolyl, quinazolyl, quinolyl, quinoxalyl, thiazolyl, thiophenyl, thienopyrazinyl, thienopyrazolyl, thienopyridyl, thienopyrrolyl, triazolopyrimidinyl, triazolyl, 3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazinyl, 1-methyl-4-oxo-1,4-dihydroquinolyl, 2-oxo-1,2-dihydropyridyl, 4-oxo-1,4-dihydropyrimidinyl, 2-oxo-1,2-dihydroquinolyl, 4-oxo-4H-pyrido[1,2-a]pyrimidinyl, 2-oxo-2,5,6,7-tetrahydro-1H-cyclopentapyridyl, 4,5,6,7-tetrahydro-indazolyl, 4-oxo-1,4-dihydro-1,8-naphthyridyl, and 5,6,7,8-tetrahydro-1,6-naphthyridyl;

and the other descriptors are the same as in the definition described in [1]; or a prodrug thereof or a pharmaceutically acceptable salt thereof.

- [0025] [3] The present invention also provides the use as described in [1] or [2], wherein the condition or disorder is selected from the group consisting of: pain, acute pain, chronic pain, neuropathic pain, inflammatory pain, visceral pain, nociceptive pain, multiple sclerosis, neurodegenerative disorder, irritable bowel syndrome, osteoarthritis, rheumatoid arthritis, neuropathological disorders, functional bowel disorders, inflammatory bowel diseases, pain associated with dysmenorrhea, pelvic pain, cystitis, pancreatitis, migraine, cluster and tension headaches, diabetic neuropathy, peripheral neuropathic pain, sciatica, fibromyalgia Crohn's disease, epilepsy or epileptic conditions, bipolar depression, tachyarrhythmias, mood disorder, bipolar disorder, psychiatric disorders such as anxiety and depression, myotonia, arrhythmia, movement disorders, neuroendocrine disorders, ataxia, incontinence, visceral pain, trigeminal neuralgia, herpetic neuralgia, general neuralgia, postherpetic neuralgia, radicular pain, sciatica, back pain, head or neck pain, severe or intractable pain, breakthrough pain, postsurgical pain, stroke, cancer pain, seizure disorder and causalgia; and combinations thereof.

- [0026] [4] The present invention provides a compound of formula (I) as described in [1] wherein

Ar¹ is phenyl which may be optionally substituted with 1 to 5 substituents independently selected from the group consisting of

(1) halogen, (2) C₁-C₄ alkyl-O_i-, (3) C₃-C₈ cycloalkyl-O_i-, (4) C₁-C₄ haloalkyl-O_i-, (5) hydroxy, (6) C₃-C₈ cycloalkyl-C₁-C₄ alkyl-O_i-, (7) C₁-C₄ alkylthio, (8) nitro, (9) R¹N(R²)-C₀₋₄ alkyl-O_i-, (10) cyano, (11) hydroxy C₁-C₄ alkyl-O_i-, (12) C₁-C₄ alkyl-O-C₁-C₄ alkyl-O_i-, (13) C₁-C₄ alkylsulfonyl, (14) R¹N(R²)-SO₂-C₀₋₄ alkyl-O_i-, (15) C₁-C₄ alkyl C(=O)-, (16) HO-C(=O)-, (17) C₁-C₄ alkyl-O-C(=O)-, (18) R¹N(R²)C(=O)-C₀₋₄ alkyl-O_i-, (19) C₁-C₄ alkyl-SO₂-NH-C₀₋₄ alkyl-O_i-, (20) R¹-O_i-C(=O)N(R²)-C₀₋₄ alkyl-O_k-, (21) NH₂(HN=C)-, (22) NH₂C(=O)NH-, (23) 5 to 10 membered aryl-O_i-C₀-C₄ alkyl-O_k-;

wherein said aryl may be optionally substituted with 1 to 5 substituents independently selected from the group consisting of hydroxy, halogen, C₁-C₄ alkyl, C₁-C₄ alkoxy, hydroxy C₁-C₄ alkyl, amino C₁-C₄ alkyl, C₁-C₄ haloalkyl, C₁-C₄ haloalkoxy, C₃-C₇ cycloalkyl C₀₋₆ alkyl, amino, C₁-C₄ alkylamino, di(C₁-C₄ alkyl)amino, C₁-C₄ alkylthio, C₁-C₄ alkylsulfonyl, R¹N(R²)C(=O)-, C₁-C₄ alkyl-SO₂-NH-, and nitro; and (24) heterocyclic group-O_i-C₀-C₄ alkyl-O_k-; wherein said heterocyclic group may be optionally substituted with 1 to 5 substituents independently selected from the group consisting of hydroxy, halogen, C₁-C₄ alkyl, C₁-C₄ alkoxy, hydroxy C₁-C₄ alkyl, amino C₁-C₄ alkyl, C₁-C₄ haloalkyl, C₁-C₄ haloalkoxy, C₃-C₇ cycloalkyl C₀₋₆ alkyl, amino, C₁-C₄ alkylamino, di(C₁-C₄ alkyl)amino, C₁-C₄ alkylthio, C₁-C₄ alkylsulfonyl, R¹N(R²)C(=O)-, C₁-C₄ alkyl-SO₂-NH-, and nitro;

[0027] Ar² is selected from; 3-benzofuranyl, 4-benzofuranyl, 5-benzofuranyl, 6-benzofuranyl, 7-benzofuranyl, benzofurazanyl, benzimidazolonyl, 3-benzoimidazolyl, 4-benzoimidazolyl, 5-benzoimidazolyl, 6-benzoimidazolyl, 7-benzoimidazolyl, benzoisothiazolyl, benzoisoxazolyl, benzothiadiazolyl, 3-benzothiazolyl, 4-benzothiazolyl, 5-benzothiazolyl, 6-benzothiazolyl, 7-benzothiazolyl, benzoxadiazolyl, benzoxazolonyl, 3-benzoxazolyl, 4-benzoxazolyl, 5-benzoxazolyl, 6-benzoxazolyl, 7-benzoxazolyl, 3-benzothiophenyl, 4-benzothiophenyl, 5-benzothiophenyl, 6-benzothiophenyl, 7-benzothiophenyl, benzotriazolyl, chromanyl, cinnoliny, 2,3-dioxoindolyl, furanyl, furopyridyl, furopyrryl, imidazolyl, imidazopyrazinyl, imidazopyridinyl, imidazopyrimidinyl, imidazothiazolyl, indazolyl, indoliny, 4-indolyl, 5-indolyl, 6-indolyl, 7-indolyl, isochromanyl, isoquinolyl, isoxazolopyridyl, isoxazolyl, isothiazolyl, naphthyridinyl, oxadiazolyl, oxazolyl, 2-oxoindolyl, oxoisindolyl, phthalazyl, pyrazolyl, pyrazolopyridyl, pyrazolopyrimidinyl, pyrazinyl, pyridopyrimidinyl, 2-pyridyl, 3-pyridyl, 5-pyridyl, 6-pyridyl, pyrimidyl, pyridazinyl, pyrrolopyridyl, pyrrolyl, quinazoliny, quinolyl, quinoxaliny, thiazolyl, thiophenyl, thienopyrazinyl, thienopyrazolyl, thienopyridyl, thienopyrryl, triazolopyrimidinyl, triazolyl, 3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazinyl, 1-methyl-4-oxo-1,4-dihydroquinolyl, 4-oxo-1,4-dihydropyrimidyl, 2-oxo-1,2-dihydroquinolyl, 4-oxo-4H-pyrido[1,2-a]pyrimidinyl, 2-oxo-2,5,6,7-tetrahydro-1H-cyclopentapyridyl, 4,5,6,7-tetrahydro-indazolyl, 4-oxo-1,4-dihydro-1,8-naphthyridyl, and 5,6,7,8-tetrahydro-1,6-naphthyridyl

[0028] wherein said 3-benzofuranyl, 4-benzofuranyl, 5-benzofuranyl, 6-benzofuranyl, 7-benzofuranyl, benzofurazanyl, benzimidazolonyl, 3-benzoimidazolyl, 4-benzoimidazolyl, 5-benzoimidazolyl, 6-benzoimidazolyl, 7-benzoimidazolyl, benzoisothiazolyl, benzoisoxazolyl, benzothiadiazolyl, 3-benzothiazolyl, 4-benzothiazolyl, 5-benzothiazolyl, 6-benzothiazolyl, 7-benzothiazolyl, benzoxadiazolyl, benzox-

azolonyl, 3-benzoxazolyl, 4-benzoxazolyl, 5-benzoxazolyl, 6-benzoxazolyl, 7-benzoxazolyl, 3-benzothiophenyl, 4-benzothiophenyl, 5-benzothiophenyl, 6-benzothiophenyl, 7-benzothiophenyl, benzotriazolyl, chromanyl, cinnolonyl, 2,3-dioxindolyl, furanyl, furopyridyl, furopyrrolyl, imidazolyl, imidazopyrazinyl, imidazopyridinyl, imidazopyrimidinyl, imidazothiazolyl, indazolyl, indolonyl, 4-indolyl, 5-indolyl, 6-indolyl, 7-indolyl, isochromanyl, isoquinolyl, isoxazolopyridyl, isoxazolyl, isothiazolyl, naphthyridinyl, oxadiazolyl, oxazolyl, 2-oxindolyl, oxoisindolyl, phthalazyl, pyrazolyl, pyrazolopyridyl, pyrazolopyrimidinyl, pyrazinyl, pyridopyrimidinyl, 2-pyridyl, 3-pyridyl, 5-pyridyl, 6-pyridyl, pyrimidyl, pyridazinyl, pyrrolopyridyl, pyrrolyl, quinazoliny, quinoxaliny, thiazolyl, thiophenyl, thienopyrazinyl, thienopyrazolyl, thienopyridyl, thienopyrrolyl, triazolopyrimidinyl, triazolyl, 3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazinyl, 1-methyl-4-oxo-1,4-dihydroquinolyl, 4-oxo-1,4-dihydropyrimidyl, 2-oxo-1,2-dihydroquinolyl, 4-oxo-4H-pyrido[1,2-a]pyrimidyl, 2-oxo-2,5,6,7-tetrahydro-1H-cyclopentapyridyl, 4,5,6,7-tetrahydro-indazolyl, 4-oxo-1,4-dihydro-1,8-naphthyridyl, and 5,6,7,8-tetrahydro-1,6-naphthyridyl may be optionally substituted with 1 to 5 substituents independently selected from the group consisting of

(1) halogen, (2) C₁-C₄ alkyl-O_i-, (3) C₃-C₈ cycloalkyl-O_i-, (4) C₁-C₄ haloalkyl-O_i-, (5) hydroxy, (6) C₃-C₈ cycloalkyl-C₁-C₄ alkyl-O_i-, (7) C₁-C₄ alkylthio, (8) nitro, (9) R¹N(R²)-C₀₋₄ alkyl-O_i-, (10) cyano, (11) hydroxy C₁-C₄ alkyl-O_i-, (12) C₁-C₄ alkyl-O-C₁-C₄ alkyl-O_i-, (13) C₁-C₄ alkylsulfonyl, (14) R¹N(R²)-SO₂-C₀₋₄ alkyl-O_i-, (15) C₁-C₄ alkyl C(=O)-, (16) HO-C(=O)-, (17) C₁-C₄ alkyl-O-C(=O)-, (18) R¹N(R²)C(=O)-C₀₋₄ alkyl-O_i-, (19) C₁-C₄ alkyl-SO₂-NH-C₀₋₄ alkyl-O_i-, (20) R¹-O_i-C(=O)N(R²)-C₀₋₄ alkyl-O_k-, (21) NH₂(HN=C)-, (22) NH₂C(=O)NH-, (23) 5 to 10 membered aryl-O_i-C₀-C₄ alkyl-O_k-; wherein said aryl may be optionally substituted with 1 to 5 substituents independently selected from the group consisting of hydroxy, halogen, C₁-C₄ alkyl, C₁-C₄ alkoxy, hydroxy C₁-C₄ alkyl, amino C₁-C₄ alkyl, C₁-C₄ haloalkyl, C₁-C₄ haloalkoxy, C₃-C₇ cycloalkyl C₀₋₆ alkyl, amino, C₁-C₄ alkylamino, di(C₁-C₄ alkyl)amino, C₁-C₄ alkylthio, C₁-C₄ alkylsulfonyl, R¹N(R²)C(=O)-, C₁-C₄ alkyl-SO₂-NH-, and nitro; and (24) heterocyclic group-O_i-C₀-C₄ alkyl-O_k-; wherein said heterocyclic group may be optionally substituted with 1 to 5 substituents independently selected from the group consisting of hydroxy, halogen, C₁-C₄ alkyl, C₁-C₄ alkoxy, hydroxy C₁-C₄ alkyl, amino C₁-C₄ alkyl, C₁-C₄ haloalkyl, C₁-C₄ haloalkoxy, C₃-C₇ cycloalkyl C₀₋₆ alkyl, amino, C₁-C₄ alkylamino, di(C₁-C₄ alkyl)amino, C₁-C₄ alkylthio, C₁-C₄ alkylsulfonyl, R¹N(R²)C(=O)-, C₁-C₄ alkyl-SO₂-NH-, and nitro;

[0029] said quinolyl may be optionally substituted with 1 to 4 substituents independently selected from the group consisting of

(1) halogen, (2) C₁-C₄ alkyl-O_i-, (3) C₃-C₈ cycloalkyl-O_i-, (4) C₁-C₄ haloalkyl-O_i-, (5) 2-hydroxyl, (6) 3-hydroxyl, (7) 5-hydroxyl, (8) 6-hydroxyl, (9) 7-hydroxyl, (10) 8-hydroxyl, (11) C₃-C₈ cycloalkyl-C₁-C₄ alkyl-O_i-, (12) C₁-C₄ alkylthio, (13) nitro, (14) R¹N(R²)-C₀₋₄ alkyl-O_i- (15) cyano, (16) hydroxy C₁-C₄ alkyl-O_i-, (17) C₁-C₄ alkyl-O-C₁-C₄ alkyl-O_i-, (18) C₁-C₄ alkylsulfonyl, (19) R¹N(R²)-SO₂-C₀₋₄ alkyl-O_i-, (20) C₁-C₄ alkyl C(=O)-, (21) HO-C(=O)-, (22) C₁-C₄ alkyl-O-C(=O)-, (23) R¹N(R²)C(=O)-C₀₋₄ alkyl-O_i-, (24) C₁-C₄ alkyl-SO₂-NH-C₀₋₄ alkyl-O_i-, (25) R¹-O_i-C(=O)N(R²)-C₀₋₄ alkyl-O_k-, (26) NH₂(HN=C)-, (27) NH₂C(=O)NH-, (28) 5 to 10 membered aryl-O_i-C₀₋₄ alkyl-O_k-; wherein said aryl may be optionally substituted with 1 to 5 substituents independently selected from the group consisting of hydroxy, halogen, C₁-C₄ alkyl, C₁-C₄ alkoxy, hydroxy C₁-C₄ alkyl, amino C₁-C₄ alkyl, C₁-C₄ haloalkyl, C₁-C₄ haloalkoxy, C₃-C₇ cycloalkyl C₀₋₆ alkyl, amino, C₁-C₄ alkylamino, di(C₁-C₄ alkyl)amino, C₁-C₄ alkylthio, C₁-C₄ alkylsulfonyl, R¹N(R²)C(=O)-, C₁-C₄ alkyl-SO₂-NH-, and nitro; and (29) heterocyclic group-O_i-C₀₋₄ alkyl-O_k-; wherein said heterocyclic group may be optionally substituted with 1 to 5 substituents independently selected from the group consisting of hydroxy, halogen, C₁-C₄ alkyl, C₁-C₄ alkoxy, hydroxy C₁-C₄ alkyl, amino C₁-C₄ alkyl, C₁-C₄ haloalkyl, C₁-C₄ haloalkoxy, C₃-C₇ cycloalkyl C₀₋₆ alkyl, amino, C₁-C₄ alkylamino, di(C₁-C₄ alkyl)amino, C₁-C₄ alkylthio, C₁-C₄ alkylsulfonyl, R¹N(R²)C(=O)-, C₁-C₄ alkyl-SO₂-NH-, and nitro;

[0030] n is 1, 2, 3, or 4;

i is 0 or 1;

k is 0 or 1;

[0031] R¹ and R² are independently selected from the group consisting of:

(1) hydrogen, (2) C₁₋₆ alkyl, (3) hydroxy C₁-C₄ alkyl, (4) C₁-C₄ alkoxy C₁-C₄ alkyl, (5) amino C₁-C₄ alkyl, (6) C₁-C₄ haloalkyl, (7) C₁-C₄ haloalkoxy, (8) C₃₋₆ alkenyl, (9) C₃₋₈ cycloalkyl C₀₋₆ alkyl, (10) phenyl, which is unsubstituted or substituted with R³, and (11) 5 to 10 membered aryl C₀₋₄ alkyl; wherein said aryl may be optionally substituted with 1 to 5 substituents independently selected from the group consisting of hydroxy, halogen, C₁-C₄ alkyl, C₁-C₄ alkoxy, hydroxy C₁-C₄ alkyl, amino C₁-C₄ alkyl, C₁-C₄ haloalkyl, C₁-C₄ haloalkoxy, C₃-C₇ cycloalkyl C₀₋₆ alkyl, amino, C₁-C₄ alkylamino, di(C₁-C₄ alkyl)amino, C₁-C₄ alkylthio, and nitro;

or R¹ and R² taken together with the nitrogen atom to which they are attached form a 3 to 8 membered ring, where the ring may contain one to four heteroatom(s) independently selected from nitrogen, oxygen, and sulfur; where the ring may be saturated or partially saturated or unsaturated; and the ring is unsubstituted or substituted one or more substituents selected from R³;

[0032] R³ is selected from the group consisting of:

(1) hydroxy, (2) halogen, (3) C₁₋₆ alkyl, (4) -C₃₋₈ cycloalkyl, (5) -O-C₁₋₆ alkyl, (6) -

O(C=O)-C₁₋₆ alkyl, (7) -NH-C₁₋₆ alkyl, (8) phenyl, (9) heterocyclic group, (10) -CO₂H, and (11) -CN;

[0033] X is -O-, -S-, -SO-, or -SO₂-;

or a prodrug thereof or a pharmaceutically acceptable salt thereof.

[0034] [5] The present invention provides a compound of formula (I) as described in [1] wherein

Ar¹ is phenyl which is substituted with chloro, trifluoromethyl, trifluoromethoxy, trifluoroethoxy or ethoxy; and which may be substituted with 1 to 2 substituents independently selected from:

(1) halogen, (2) C₁-C₄ alkyl-O_i-, (3) C₃-C₈ cycloalkyl-O_i-, (4) C₁-C₄ haloalkyl-O_i-, (5) hydroxy, (6) C₃-C₈ cycloalkyl-C₁-C₄ alkyl-O_i-, (7) C₁-C₄ alkylthio, (8) nitro, (9) R¹N(R²)-C₀₋₄ alkyl-O_i-, (10) cyano, (11) hydroxy C₁-C₄ alkyl-O_i-, (12) C₁-C₄ alkyl-O-C₁-C₄ alkyl-O_i-, (13) C₁-C₄ alkylsulfonyl, (14) R¹N(R²)-SO₂-C₀₋₄ alkyl-O_i-, (15) C₁-C₄ alkyl C(=O)-, (16) HO-C(=O)-, (17) C₁-C₄ alkyl-O-C(=O)-, (18) R¹N(R²)C(=O)-C₀₋₄ alkyl-O_i-, (19) C₁-C₄ alkyl-SO₂-NH-C₀₋₄ alkyl-O_i-, (20) R¹-O_i-C(=O)N(R²)-C₀₋₄ alkyl-O_k-, (21) NH₂(HN=)C-, (22) NH₂C(=O)NH-, (23) 5 to 10 membered aryl-O_i-C₀-C₄ alkyl-O_k-; wherein said aryl may be optionally substituted with 1 to 5 substituents independently selected from the group consisting of hydroxy, halogen, C₁-C₄ alkyl, C₁-C₄ alkoxy, hydroxy C₁-C₄ alkyl, amino C₁-C₄ alkyl, C₁-C₄ haloalkyl, C₁-C₄ haloalkoxy, C₃-C₇ cycloalkyl C₀₋₆ alkyl, amino, C₁-C₄ alkylamino, di(C₁-C₄ alkyl)amino, C₁-C₄ alkylthio, C₁-C₄ alkylsulfonyl, R¹N(R²)C(=O)-, C₁-C₄ alkyl-SO₂-NH-, and nitro; and (24) heterocyclic group-O_i-C₀-C₄ alkyl-O_k-; wherein said heterocyclic group may be optionally substituted with 1 to 5 substituents independently selected from the group consisting of hydroxy, halogen, C₁-C₄ alkyl, C₁-C₄ alkoxy, hydroxy C₁-C₄ alkyl, amino C₁-C₄ alkyl, C₁-C₄ haloalkyl, C₁-C₄ haloalkoxy, C₃-C₇ cycloalkyl C₀₋₆ alkyl, amino, C₁-C₄ alkylamino, di(C₁-C₄ alkyl)amino, C₁-C₄ alkylthio, C₁-C₄ alkylsulfonyl, R¹N(R²)C(=O)-, C₁-C₄ alkyl-SO₂-NH-, and nitro;

[0035] Ar² is 4-pyridyl which may be optionally substituted with 1 to 5 substituents independently selected from the group consisting of

(1) halogen, (2) C₁-C₄ alkyl-O_i-, (3) C₃-C₈ cycloalkyl-O_i-, (4) C₁-C₄ haloalkyl-O_i-, (5) hydroxy, (6) C₃-C₈ cycloalkyl-C₁-C₄ alkyl-O_i-, (7) C₁-C₄ alkylthio, (8) nitro, (9) R¹N(R²)-C₀₋₄ alkyl-O_i-, (10) cyano, (11) hydroxy C₁-C₄ alkyl-O_i-, (12) C₁-C₄ alkyl-O-C₁-C₄ alkyl-O_i-, (13) C₁-C₄ alkylsulfonyl, (14) R¹N(R²)-SO₂-C₀₋₄ alkyl-O_i-, (15) C₁-C₄ alkyl C(=O)-, (16) HO-C(=O)-, (17) C₁-C₄ alkyl-O-C(=O)-, (18) R¹N(R²)C(=O)-C₀₋₄ alkyl-O_i-, (19) C₁-C₄ alkyl-SO₂-NH-C₀₋₄ alkyl-O_i-, (20) R¹-O_i-C(=O)N(R²)-C₀₋₄ alkyl-O_k-, (21) NH₂(HN=)C-, (22) NH₂C(=O)NH-, (23) 5 to 10 membered aryl-O_i-C₀-C₄ alkyl-O_k-; wherein said aryl may be optionally substituted with 1 to 5 substituents independently selected from the group consisting of hydroxy, halogen, C₁-C₄ alkyl, C₁-C₄ alkoxy,

hydroxy C₁-C₄ alkyl, amino C₁-C₄ alkyl, C₁-C₄ haloalkyl, C₁-C₄ haloalkoxy, C₃-C₇ cycloalkyl C₀₋₆ alkyl, amino, C₁-C₄ alkylamino, di(C₁-C₄ alkyl)amino, C₁-C₄ alkylthio, C₁-C₄ alkylsulfonyl, R¹N(R²)C(=O)-, C₁-C₄ alkyl-SO₂-NH-, and nitro; and (24) heterocyclic group-O_i-C₀-C₄ alkyl-O_k-; wherein said heterocyclic group may be optionally substituted with 1 to 5 substituents independently selected from the group consisting of hydroxy, halogen, C₁-C₄ alkyl, C₁-C₄ alkoxy, hydroxy C₁-C₄ alkyl, amino C₁-C₄ alkyl, C₁-C₄ haloalkyl, C₁-C₄ haloalkoxy, C₃-C₇ cycloalkyl C₀₋₆ alkyl, amino, C₁-C₄ alkylamino, di(C₁-C₄ alkyl)amino, C₁-C₄ alkylthio, C₁-C₄ alkylsulfonyl, R¹N(R²)C(=O)-, C₁-C₄ alkyl-SO₂-NH-, and nitro;

[0036] n is 1, 2, 3, or 4;

i is 0 or 1;

k is 0 or 1;

[0037] R¹ and R² are independently selected from the group consisting of:

(1) hydrogen, (2) C₁₋₆ alkyl, (3) hydroxy C₁-C₄ alkyl, (4) C₁-C₄ alkoxy C₁-C₄ alkyl, (5) amino C₁-C₄ alkyl, (6) C₁-C₄ haloalkyl, (7) C₁-C₄ haloalkoxy, (8) C₃₋₆ alkenyl, (9) C₃₋₈ cycloalkyl C₀₋₆ alkyl, (10) phenyl, which is unsubstituted or substituted with R³, and (11) 5 to 10 membered aryl C₀-C₄ alkyl; wherein said aryl may be optionally substituted with 1 to 5 substituents independently selected from the group consisting of hydroxy, halogen, C₁-C₄ alkyl, C₁-C₄ alkoxy, hydroxy C₁-C₄ alkyl, amino C₁-C₄ alkyl, C₁-C₄ haloalkyl, C₁-C₄ haloalkoxy, C₃-C₇ cycloalkyl C₀₋₆ alkyl, amino, C₁-C₄ alkylamino, di(C₁-C₄ alkyl)amino, C₁-C₄ alkylthio, and nitro;

or R¹ and R² taken together with the nitrogen atom to which they are attached form a 3 to 8 membered ring, where the ring may contain one to four heteroatom(s) independently selected from nitrogen, oxygen, and sulfur; where the ring may be saturated or partially saturated or unsaturated; and the ring is unsubstituted or substituted one or more substituents selected from R³;

[0038] R³ is selected from the group consisting of:

(1) hydroxy, (2) halogen, (3) C₁₋₆ alkyl, (4) -C₃₋₈ cycloalkyl, (5) -O-C₁₋₆ alkyl, (6) -O(C=O)-C₁₋₆ alkyl, (7) -NH-C₁₋₆ alkyl, (8) phenyl, (9) heterocyclic group, (10) -CO₂H, and (11) -CN;

[0039] X is -O-, -S-, -SO-, or -SO₂-;

or a prodrug thereof or a pharmaceutically acceptable salt thereof.

[0040] [6] Suitable individual compounds of the invention are:

(4-(4-chlorophenoxy)piperidin-1-yl)(8-hydroxyquinolin-2-yl)methanone;

(4-(2-chlorophenoxy)piperidin-1-yl)(8-hydroxyquinolin-2-yl)methanone;

(4-(3-chlorophenoxy)piperidin-1-yl)(8-hydroxyquinolin-2-yl)methanone;

(8-hydroxyquinolin-2-yl)(4-(o-tolyloxy)piperidin-1-yl)methanone;

(8-hydroxyquinolin-2-yl)(4-(m-tolyloxy)piperidin-1-yl)methanone;

(8-hydroxyquinolin-2-yl)(4-(p-tolyloxy)piperidin-1-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(quinolin-2-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(4-hydroxyquinolin-2-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(quinolin-6-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(quinolin-3-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(isoquinolin-3-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(1,6-naphthyridin-2-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(isoquinolin-1-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(quinolin-4-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(6-(2,2,2-trifluoroethoxy)pyridin-3-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(6-methylpyridin-2-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(3,5-difluoropyridin-2-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(5-methylpyridin-3-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(quinoxalin-6-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(6-phenoxy pyridin-3-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(quinolin-8-yl)methanone;
benzo[c]isoxazol-3-yl(4-(4-chlorophenoxy)piperidin-1-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(1-isopropyl-1H-benzo[d][1,2,3]triazol-5-yl)methanone;
none;
(4-(4-chlorophenoxy)piperidin-1-yl)(5-fluoro-1H-indol-2-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(6-fluoro-1H-indol-2-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(5-isobutylisoxazol-3-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(2-methyl-5-phenylfuran-3-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(3-(2-methylthiazol-4-yl)phenyl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(5-methoxy-1H-indol-2-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(1H-indol-4-yl)methanone;
(3-(1H-pyrazol-1-yl)phenyl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone;
(4-(1H-1,2,4-triazol-1-yl)phenyl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(5-methyl-2-phenyl-2H-1,2,3-triazol-4-yl)methanone;
ne;
(4-(4-chlorophenoxy)piperidin-1-yl)(4,5-dichloroisothiazol-3-yl)methanone;
benzofuran-2-yl(4-(4-chlorophenoxy)piperidin-1-yl)methanone;
benzo[b]thiophen-2-yl(4-(4-chlorophenoxy)piperidin-1-yl)methanone;
(8-hydroxyquinolin-2-yl)(4-(2-methoxyphenoxy)piperidin-1-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(4-methyl-2-phenylpyrimidin-5-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(6-phenylpyrimidin-4-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(4-methoxyquinolin-2-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(quinoxalin-2-yl)methanone;

benzo[d]thiazol-6-yl(4-(4-chlorophenoxy)piperidin-1-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(1H-indol-3-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(1H-indol-2-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(1-methyl-1H-indol-3-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(1-methyl-1H-indol-2-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(2,3-dimethyl-1H-indol-5-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(1H-indol-6-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(2-methyl-1H-benzo[d]imidazol-5-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(imidazo[1,2-a]pyridin-2-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(2-methylimidazo[1,2-a]pyridin-3-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(5-methyl-1-phenyl-1H-pyrazol-4-yl)methanone;
(4-(tert-butyl)phenyl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(4-chlorophenyl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(4-fluorophenyl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(3-(5-fluoro-1H-benzo[d]imidazol-2-yl)phenyl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(3-(1-methyl-1H-benzo[d]imidazol-2-yl)phenyl)methanone;
(4-(2-fluorophenoxy)piperidin-1-yl)(8-hydroxyquinolin-2-yl)methanone;
(4-(3-fluorophenoxy)piperidin-1-yl)(8-hydroxyquinolin-2-yl)methanone;
(4-(4-fluorophenoxy)piperidin-1-yl)(8-hydroxyquinolin-2-yl)methanone;
(8-hydroxyquinolin-2-yl)(4-(3-methoxyphenoxy)piperidin-1-yl)methanone;
2-((1-(8-hydroxyquinoline-2-carbonyl)piperidin-4-yl)oxy)benzonitrile;
4-((1-(8-hydroxyquinoline-2-carbonyl)piperidin-4-yl)oxy)benzonitrile;
3-((1-(8-hydroxyquinoline-2-carbonyl)piperidin-4-yl)oxy)benzonitrile;
(4-(4-chlorophenoxy)piperidin-1-yl)(8-methoxyquinolin-2-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(1-methyl-1H-indol-7-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(1-methyl-1H-indol-4-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(1,8-naphthyridin-2-yl)methanone;
(8-hydroxyquinolin-2-yl)(4-phenoxy)piperidin-1-yl)methanone;
(8-hydroxyquinolin-2-yl)(4-(2-(trifluoromethyl)phenoxy)piperidin-1-yl)methanone;
(8-hydroxyquinolin-2-yl)(4-(3-(trifluoromethyl)phenoxy)piperidin-1-yl)methanone;
(5-(tert-butyl)isoxazol-3-yl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(5-phenylisoxazol-3-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(5-cyclopropylisoxazol-3-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(3,5-dimethylisoxazol-4-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(1-methyl-1H-indazol-3-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(2-methyl-2H-indazol-3-yl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(cinnolin-4-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(2-methyl-4-phenylpyrimidin-5-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(6-methylpyridin-3-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(pyridin-4-yl)methanone;
[1,2,4]triazolo[1,5-a]pyrimidin-2-yl(4-(4-chlorophenoxy)piperidin-1-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(1,2,3-trimethyl-1H-indol-5-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(1-methyl-1H-indol-6-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(2-methylthiazol-4-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(6-methoxypyridin-3-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(2-phenoxy-pyridin-3-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(1H-indol-7-yl)methanone;
7-(4-(4-chlorophenoxy)piperidine-1-carbonyl)indoline-2,3-dione;
(4-(4-chlorophenoxy)piperidin-1-yl)(3-methylpyridin-2-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(6-hydroxypyridin-2-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(2,4-dimethylthiazol-5-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(5-methyl-1,3,4-oxadiazol-2-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(1H-indazol-3-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(4,5,6,7-tetrahydro-1H-indazol-3-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(6-methoxypyridin-2-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(2-methyl-4,5,6,7-tetrahydro-2H-indazol-3-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(isoquinolin-4-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(4-methylpyridin-2-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(6-methoxyquinolin-2-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(6-methoxy-2-methylquinolin-3-yl)methanone;
(3-(4-chlorophenoxy)azetidin-1-yl)(8-hydroxyquinolin-2-yl)methanone;
benzo[d]isoxazol-3-yl(4-(4-chlorophenoxy)piperidin-1-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(2-(trifluoromethyl)-1H-benzo[d]imidazol-5-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(1,5-naphthyridin-2-yl)methanone;
(3-(4-chlorophenoxy)pyrrolidin-1-yl)(8-hydroxyquinolin-2-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(2-methyl-6-phenylpyridin-3-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(1,5-dimethyl-1H-indol-3-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(5-fluoro-1-methyl-1H-indol-3-yl)methanone;
(5-chloro-1-methyl-1H-indol-3-yl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(5-methoxy-1-methyl-1H-indol-3-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(1,6-dimethyl-1H-indol-3-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(6-fluoro-1-methyl-1H-indol-3-yl)methanone;

(6-chloro-1-methyl-1H-indol-3-yl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(6-methoxy-1-methyl-1H-indol-3-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(5-fluoro-1-methyl-1H-indol-2-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(5-methoxy-1-methyl-1H-indol-2-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(3-fluorophenyl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(p-tolyl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(4-methoxyphenyl)methanone;
4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)benzonitrile;
(4-(4-chlorophenoxy)piperidin-1-yl)(6-methylimidazo[1,2-a]pyridin-2-yl)methanone;
(6-chloroimidazo[1,2-a]pyridin-2-yl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(2-methylpyridin-3-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(4-isopropoxyphenyl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(4-(trifluoromethoxy)phenyl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(4-(methylsulfonyl)phenyl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(3-methoxyphenyl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(pyridin-2-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(5-methylisoxazol-3-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(oxazol-4-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(4-methylthiazol-5-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(5-methylpyrazin-2-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(6-fluoro-1-methyl-1H-indol-2-yl)methanone;
4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-N,N-dimethylbenzenesulfonamide;
4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)benzamide;
(4-(4-chlorophenoxy)piperidin-1-yl)(5-fluoro-1H-indazol-3-yl)methanone;
(5-chloro-1H-indazol-3-yl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone;
(6-chloro-1H-indazol-3-yl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(4-(2-hydroxypropan-2-yl)phenyl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(2,6-dimethoxypyridin-3-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(6-methoxy-1-methyl-1H-indol-2-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(1-methyl-5-(trifluoromethoxy)-1H-indol-2-yl)methanone;
2-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-1-methyl-1H-indole-5-carbonitrile;
(4-(4-chlorophenoxy)piperidin-1-yl)(1-methyl-5-(methylsulfonyl)-1H-indol-2-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(4-methylpyridin-3-yl)methanone;
3-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-5,6-dimethylpyridin-2(1H)-one;
(4-(4-chlorophenoxy)piperidin-1-yl)(quinolin-5-yl)methanone;
(4-(4-fluorophenoxy)piperidin-1-yl)(2-methyl-2H-indazol-3-yl)methanone;

(4-(4-fluorophenoxy)piperidin-1-yl)(6-methoxypyridin-3-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(3-methoxy-4-methylphenyl)methanone;
(5-chloro-4-methoxythiophen-3-yl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone;
(4-phenoxy)piperidin-1-yl(quinolin-8-yl)methanone;
(4-(4-fluorophenoxy)piperidin-1-yl)(imidazo[1,2-a]pyridin-2-yl)methanone;
(4-(4-fluorophenoxy)piperidin-1-yl)(quinolin-8-yl)methanone;
(6-aminopyridin-3-yl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone;
(5-bromopyridin-3-yl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone;
(5-bromopyridin-2-yl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone;
1-(4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)phenyl)ethanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(3,4-dimethoxyphenyl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(isoquinolin-5-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(phenyl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(m-tolyl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(2-methoxyphenyl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(3-(trifluoromethoxy)phenyl)methanone;
(1H-benzo[d]imidazol-5-yl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(1,5-dimethyl-1H-pyrazol-3-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(1,3-dimethyl-1H-pyrazol-5-yl)methanone;
(3-(tert-butyl)-1-methyl-1H-pyrazol-5-yl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(1-methyl-5-(trifluoromethyl)-1H-pyrazol-3-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(1-(4-methoxyphenyl)-5-methyl-1H-pyrazol-4-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(1-(2-methoxyphenyl)-1H-pyrazol-4-yl)methanone;
;
(4-(4-chlorophenoxy)piperidin-1-yl)(3,5-dimethyl-1H-pyrazol-4-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(1H-1,2,4-triazol-3-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(5-isopropyl-1H-pyrazol-3-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(imidazo[2,1-b]thiazol-6-yl)methanone;
(4-(3-methoxyphenoxy)piperidin-1-yl)(quinolin-8-yl)methanone;
imidazo[1,2-a]pyridin-2-yl(4-(3-methoxyphenoxy)piperidin-1-yl)methanone;
(4-(3-fluorophenoxy)piperidin-1-yl)(quinolin-8-yl)methanone;
(4-(3-fluorophenoxy)piperidin-1-yl)(imidazo[1,2-a]pyridin-2-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(5-chloropyridin-3-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(5-methoxypyridin-3-yl)methanone;
3-(4-(4-chlorophenoxy)piperidine-1-carbonyl)benzotrile;

(4-(4-chlorophenoxy)piperidin-1-yl)(2-ethoxypyridin-3-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(2-methoxypyridin-4-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(isoquinolin-8-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(2-methylthiazol-5-yl)methanone;
 (4-((4-chlorophenyl)thio)piperidin-1-yl)(quinolin-8-yl)methanone;
 (4-((4-chlorophenyl)thio)piperidin-1-yl)(6-methylpyridin-3-yl)methanone;
 (4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(quinolin-8-yl)methanone;
 1-(3-((1-(quinoline-8-carbonyl)piperidin-4-yl)oxy)phenyl)ethanone;
 (4-(3,5-dimethoxyphenoxy)piperidin-1-yl)(quinolin-8-yl)methanone;
 quinolin-8-yl(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(3-methylisoxazol-5-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(1-isopropyl-1H-pyrazol-4-yl)methanone;
 5-(4-(4-chlorophenoxy)piperidine-1-carbonyl)picolinonitrile;
 (4-(4-chlorophenoxy)piperidin-1-yl)(2-hydroxyquinolin-4-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(5-(trifluoromethyl)-1H-pyrazol-3-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(5-cyclopropyl-1H-pyrazol-3-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(5-(2-methoxyphenyl)-1H-pyrazol-3-yl)methanone
 ;
 (4-(4-chlorophenoxy)piperidin-1-yl)(3-isopropyl-1-methyl-1H-pyrazol-5-yl)methanone
 ;
 (4-(4-chlorophenoxy)piperidin-1-yl)(3-ethyl-1-methyl-1H-pyrazol-5-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(1-ethyl-3-methyl-1H-pyrazol-5-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(2-methyloxazol-4-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(thieno[3,2-b]pyridin-2-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(imidazo[1,2-a]pyridin-6-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(1-methyl-1H-indazol-6-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(6-(trifluoromethoxy)-1H-indazol-3-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(1-methyl-6-(trifluoromethoxy)-1H-indazol-3-yl)
 methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(2,4-dimethyloxazol-5-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(5-methoxypyridin-2-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(imidazo[1,2-a]pyridin-7-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(imidazo[1,2-a]pyrazin-2-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(2-methyl-2H-indazol-6-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(6-(pyrrolidin-1-yl)pyridin-2-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(5-(pyrrolidin-1-yl)pyridin-2-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(4-fluoro-3-methoxyphenyl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(4-methyl-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazi

n-7-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(6-(piperidin-1-yl)pyridin-3-yl)methanone;
3-(4-(4-chlorophenoxy)piperidine-1-carbonyl)quinolin-2(1H)-one;
(4-(4-chlorophenoxy)piperidin-1-yl)(imidazo[1,2-a]pyridin-8-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(pyrazolo[1,5-a]pyridin-7-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(4-(trifluoromethyl)pyridin-3-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(1-methyl-1H-imidazol-2-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(1-(2-(trifluoromethyl)phenyl)-1H-imidazol-2-yl)methanone;
3-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-1-methylquinolin-4(1H)-one;
(3-(4-chlorophenoxy)azetidin-1-yl)(quinolin-8-yl)methanone;
(3-(4-chlorophenoxy)azetidin-1-yl)(6-methylpyridin-3-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(pyrimidin-4-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(5-chloropyridin-2-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(2-methoxyquinolin-4-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(5-hydroxypyridin-3-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(6-(trifluoromethyl)pyridin-3-yl)methanone;
(5-aminopyridin-3-yl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(imidazo[1,2-a]pyrimidin-2-yl)methanone;
N-(5-(4-(4-chlorophenoxy)piperidine-1-carbonyl)pyridin-3-yl)acetamide;
(4-(4-chlorophenoxy)piperidin-1-yl)(chroman-6-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(1-methyl-1H-pyrazolo[3,4-b]pyridin-3-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(1-methyl-1H-indol-5-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(3-(pyridin-2-yloxy)phenyl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(1-methyl-1H-benzo[d]imidazol-5-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(4-((tetrahydro-2H-pyran-4-yl)oxy)phenyl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(pyrazolo[1,5-a]pyridin-2-yl)methanone;
1-(3-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-1H-pyrazol-5-yl)ethanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(1,3,5-trimethyl-1H-pyrazol-4-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(1H-pyrrolo[2,3-b]pyridin-2-yl)methanone;
4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-1-methylquinolin-2(1H)-one;
5-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-1H-benzo[d]imidazol-2(3H)-one;
(4-(4-chlorophenoxy)piperidin-1-yl)(5-methoxypyrazin-2-yl)methanone;
5-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-1,3-dimethyl-1H-benzo[d]imidazol-2(3H)-one;
(4-(4-chlorophenoxy)piperidin-1-yl)(1-methyl-1H-imidazol-4-yl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(2-phenyl-1H-imidazol-4-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(1,3-dimethyl-1H-pyrazol-4-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(1,5-dimethyl-1H-pyrazol-4-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(3-isobutyl-1-methyl-1H-pyrazol-5-yl)methanone;
 (4-chloro-5-methyl-1H-pyrazol-3-yl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone;
 3-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-1-isopropyl-6,7-dihydro-1H-cyclopenta
 [b]pyridin-2(5H)-one;
 5-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-2-methoxybenzonitrile;
 (4-(4-chlorophenoxy)piperidin-1-yl)(2-isopropylthiazol-4-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(5,6-dimethoxy-1H-indol-2-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(2,7-dimethylpyrazolo[1,5-a]pyrimidin-6-yl)metha
 none;
 (4-(4-chlorophenoxy)piperidin-1-yl)(1H-pyrrolo[2,3-b]pyridin-3-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(1-methyl-1H-pyrrolo[2,3-b]pyridin-2-yl)methano
 ne;
 (4-(4-chlorophenoxy)piperidin-1-yl)(5,6-dimethoxy-1-methyl-1H-indol-2-yl)methanon
 e;
 (4-(4-chlorophenoxy)piperidin-1-yl)(1-methyl-1H-pyrrolo[2,3-b]pyridin-3-yl)methano
 ne;
 3-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-1-isopropyl-4-methylquinolin-2(1H)-on
 e;
 (4-(4-chlorophenoxy)piperidin-1-yl)(4-methyl-4H-furo[3,2-b]pyrrol-5-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(4-methyl-4H-thieno[3,2-b]pyrrol-5-yl)methanone
 ;
 (4-(4-chlorophenoxy)piperidin-1-yl)(1,3-dimethyl-1H-thieno[2,3-c]pyrazol-5-yl)metha
 none;
 2-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-6,7-dihydropyrido[3,2,1-ij]quinolin-3(5
 H)-one;
 5-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-1H-pyrrolo[3,2,1-ij]quinolin-4(2H)-one
 ;
 3-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-1-ethyl-7-methyl-1,8-naphthyridin-4(1
 H)-one;
 (4-(4-chlorophenoxy)piperidin-1-yl)(isoquinolin-6-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(5-methylpyridin-2-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(5-(2,2,2-trifluoroethoxy)pyridin-3-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(3-methylisoxazolo[5,4-b]pyridin-5-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(1,3,6-trimethyl-1H-pyrazolo[3,4-b]pyridin-4-yl)m
 ethanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(thieno[2,3-b]pyridin-2-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(thieno[2,3-b]pyrazin-6-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(pyrazolo[1,5-a]pyrimidin-3-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(2-(pyrrolidin-1-yl)pyrimidin-5-yl)methanone;
(1H-benzo[d]imidazol-4-yl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone;
benzo[d][1,2,3]thiadiazol-7-yl(4-(4-chlorophenoxy)piperidin-1-yl)methanone;
3-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-1-methylquinolin-2(1H)-one;
(4-(4-chlorophenoxy)piperidin-1-yl)(1-methyl-1H-benzo[d]imidazol-2-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(pyrazolo[1,5-a]pyrimidin-2-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(2-methoxypyrimidin-5-yl)methanone;
(1H-benzo[d][1,2,3]triazol-4-yl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(6-methylimidazo[2,1-b]thiazol-5-yl)methanone;
benzo[c][1,2,5]thiadiazol-4-yl(4-(4-chlorophenoxy)piperidin-1-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(1-(2-methoxyethyl)-1H-indol-5-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(1-(2-methoxyethyl)-1H-indol-6-yl)methanone;
(3-amino-1-methyl-1H-pyrazol-5-yl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(5-cyclopropyl-1-methyl-1H-pyrazol-3-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(3-cyclopropyl-1-methyl-1H-pyrazol-5-yl)methanone;
1-benzyl-3-(4-(4-chlorophenoxy)piperidine-1-carbonyl)pyridin-2(1H)-one;
(1-benzyl-1H-pyrazol-4-yl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(1-(2-methoxyethyl)-1H-indol-2-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(1-(2-methoxyethyl)-1H-indol-4-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(3,6-dimethylisoxazolo[5,4-b]pyridin-4-yl)methanone;
4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-1-methylpyridin-2(1H)-one;
3-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-4H-pyrido[1,2-a]pyrimidin-4-one;
3-(4-(4-chlorophenoxy)piperidine-1-carbonyl)isoquinolin-1(2H)-one;
(4-(4-chlorophenoxy)piperidin-1-yl)(2-(3,5-dimethyl-1H-pyrazol-4-yl)phenyl)methanone;
benzo[c][1,2,5]oxadiazol-5-yl(4-(4-chlorophenoxy)piperidin-1-yl)methanone;
(6-aminopyridin-2-yl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone;
3-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-1,6-dimethylpyridin-2(1H)-one;
(4-(4-chlorophenoxy)piperidin-1-yl)(3-propoxypyridin-2-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(6-((tetrahydro-2H-pyran-4-yl)oxy)pyridin-3-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(6-((tetrahydro-2H-pyran-4-yl)oxy)pyridin-2-yl)methanone;

ethanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(5-((tetrahydro-2H-pyran-4-yl)oxy)pyridin-3-yl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(3-hydroxy-4-methoxyphenyl)methanone;

(4-chloro-2-hydroxyphenyl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(4-hydroxy-3-methylphenyl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(6-morpholinopyridin-2-yl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(2-morpholinopyridin-4-yl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(1-methyl-3-(trifluoromethyl)-1H-pyrazol-5-yl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(2-hydroxy-4-(trifluoromethyl)phenyl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(3-hydroxy-4-methylphenyl)methanone;

tert-butyl

((2-(4-(4-chlorophenoxy)piperidine-1-carbonyl)pyridin-4-yl)methyl)carbamate;

(4-(aminomethyl)pyridin-2-yl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone;

N-((2-(4-(4-chlorophenoxy)piperidine-1-carbonyl)pyridin-4-yl)methyl)pivalamide;

N-((2-(4-(4-chlorophenoxy)piperidine-1-carbonyl)pyridin-4-yl)methyl)-4-fluorobenzamide;

N-((2-(4-(4-chlorophenoxy)piperidine-1-carbonyl)pyridin-4-yl)methyl)-4-fluorobenzenesulfonamide;

tert-butyl

2-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-7,8-dihydro-1,6-naphthyridine-6(5H)-carboxylate;

(4-(4-chlorophenoxy)piperidin-1-yl)(6-(methylsulfonyl)-5,6,7,8-tetrahydro-1,6-naphthyridin-2-yl)methanone;

N-(tert-butyl)-4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)benzamide;

N-(tert-butyl)-4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-N-methylbenzamide;

4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-N-(2,2,2-trifluoroethyl)benzamide;

(4-(4-chlorophenoxy)piperidin-1-yl)(4-(2-methoxyethoxy)phenyl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(4-(2-hydroxyethoxy)phenyl)methanone;

N-(4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)benzyl)pivalamide;

4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)picolinamide;

(4-(4-chlorophenoxy)piperidin-1-yl)(5-morpholinopyridin-3-yl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(6-(piperidin-1-yl)pyrimidin-4-yl)methanone;

(3-(1H-imidazol-1-yl)phenyl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone;

(2-(1H-pyrazol-1-yl)phenyl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(2-(2-methyl-1H-imidazol-1-yl)phenyl)methanone

;

(4-(4-chlorophenoxy)piperidin-1-yl)(2-(3-methyl-1,2,4-oxadiazol-5-yl)phenyl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(3-methyl-1H-pyrazol-5-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(6-(piperidine-1-carbonyl)pyridin-2-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(2-hydroxy-4-methoxyphenyl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(4-hydroxy-3-methoxyphenyl)methanone;
N-(5-chloro-2-(4-(4-chlorophenoxy)piperidine-1-carbonyl)phenyl)methanesulfonamide;
N-(4-chloro-2-(4-(4-chlorophenoxy)piperidine-1-carbonyl)phenyl)methanesulfonamide;
(4-(4-chlorophenoxy)piperidin-1-yl)(2'-(hydroxymethyl)-[1,1'-biphenyl]-4-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(2'-(methylsulfonyl)-[1,1'-biphenyl]-4-yl)methanone;
(3-chloro-4-hydroxyphenyl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone;
3-(tert-butyl)-5-(4-(4-chlorophenoxy)piperidine-1-carbonyl)benzamide;
3-(tert-butyl)-5-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-N,N-dimethylbenzamide;
(3-(tert-butyl)-5-(4-(4-chlorophenoxy)piperidine-1-carbonyl)phenyl)(morpholino)methanone;
4'-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-[1,1'-biphenyl]-3-carboxamide;
(4-(4-chlorophenoxy)piperidin-1-yl)(1-(2-morpholinoethyl)-1H-indol-5-yl)methanone;
2-(5-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-1H-indol-1-yl)-N,N-dimethylacetamide;
(4-(4-chlorophenoxy)piperidin-1-yl)(1-(2-hydroxyethyl)-1H-indol-5-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(4-morpholinopyridin-2-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(4-(piperidin-1-yl)pyridin-2-yl)methanone;
2-(3-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-1H-indol-1-yl)-N,N-dimethylacetamide;
(4-(4-chlorophenoxy)piperidin-1-yl)(1-(2-hydroxyethyl)-1H-indol-3-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(1-(2-morpholinoethyl)-1H-indol-3-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(1-(2-(piperidin-1-yl)ethyl)-1H-indol-3-yl)methanone;
2-(4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)phenyl)-2-methylpropanenitrile;
(4-(4-chlorophenoxy)piperidin-1-yl)(3-fluoro-4-hydroxyphenyl)methanone;
2-chloro-5-(4-(4-chlorophenoxy)piperidine-1-carbonyl)benzenesulfonamide;
4'-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-[1,1'-biphenyl]-4-carboxamide;
4'-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-[1,1'-biphenyl]-2-carboxamide;
(5-chloro-2-hydroxyphenyl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(2-hydroxy-4-methylphenyl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(5-fluoro-2-hydroxyphenyl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(2-hydroxy-3-methylphenyl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(2-hydroxy-3-isopropylphenyl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(2-hydroxy-6-methoxyphenyl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(2-fluoro-6-hydroxyphenyl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(3-hydroxy-2-methylphenyl)methanone;
 (2-chloro-4-hydroxyphenyl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(2-fluoro-4-hydroxyphenyl)methanone;
 N-(4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-2-methylphenyl)methanesulfonamide;
 (4-(4-chlorophenoxy)piperidin-1-yl)(4-fluoro-3-hydroxyphenyl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(2-hydroxy-5-methylphenyl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(2-hydroxy-3-methoxyphenyl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(4-fluoro-2-hydroxyphenyl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(3,5-dihydroxyphenyl)methanone;
 N-(3-(4-(4-chlorophenoxy)piperidine-1-carbonyl)phenyl)acetamide;
 (4-(4-chlorophenoxy)piperidin-1-yl)(1-((4-hydroxytetrahydro-2H-pyran-4-yl)methyl)-1H-indol-5-yl)methanone;
 (1-(2-aminoethyl)-1H-indol-5-yl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone;
 N-(2-(5-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-1H-indol-1-yl)ethyl)acetamide;
 N-(2-(5-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-1H-indol-1-yl)ethyl)methanesulfonamide;
 2-(5-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-1H-indol-1-yl)-1-morpholinoethanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(3'-(methylsulfonyl)-[1,1'-biphenyl]-4-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(3'-(hydroxymethyl)-[1,1'-biphenyl]-4-yl)methanone;
 N-(4'-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-[1,1'-biphenyl]-2-yl)methanesulfonamide;
 N-(4'-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-[1,1'-biphenyl]-3-yl)methanesulfonamide;
 4'-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-N-methyl-[1,1'-biphenyl]-3-carboxamide;
 4'-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-N,N-dimethyl-[1,1'-biphenyl]-3-carboxamide;
 (4-(4-chlorophenoxy)piperidin-1-yl)(3'-(morpholine-4-carbonyl)-[1,1'-biphenyl]-4-yl)

methanone;

(4-chloro-3-hydroxyphenyl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone;

N-(5-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-2-methylphenyl)methanesulfonamide;

1-(3-(4-(4-chlorophenoxy)piperidine-1-carbonyl)phenyl)ethanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(1-(2-hydroxyethyl)-2-methyl-1H-benzo[d]imidazol-5-yl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(6-ethoxypyridin-2-yl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(4-hydroxy-7-methyl-1,8-naphthyridin-3-yl)methanone;

N-(6-(4-(4-chlorophenoxy)piperidine-1-carbonyl)pyridin-2-yl)acetamide;

N-(4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)pyridin-2-yl)acetamide;

N-(5-(4-(4-chlorophenoxy)piperidine-1-carbonyl)pyridin-2-yl)acetamide;

(4-(4-chlorophenoxy)piperidin-1-yl)(3-hydroxypyridin-2-yl)methanone;

(4-bromo-1-methoxynaphthalen-2-yl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone;

6-(4-(4-chlorophenoxy)piperidine-1-carbonyl)isoindolin-1-one;

(4-(4-chlorophenoxy)piperidin-1-yl)(quinoxalin-5-yl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(1,6-naphthyridin-5-yl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(4-hydroxyphenyl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(4-ethoxy-2-hydroxyphenyl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(3-hydroxyphenyl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(2-hydroxyphenyl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(4-hydroxy-3,5-dimethoxyphenyl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(4-hydroxy-2-methylphenyl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(5-hydroxy-2-methylphenyl)methanone;

(3-chloro-2-hydroxyphenyl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(3-fluoro-2-hydroxyphenyl)methanone;

2-(5-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-2-methylphenoxy)acetamide;

2-(2-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-5-methylphenoxy)acetamide;

(4-(4-chlorophenoxy)piperidin-1-yl)(2,6-dihydroxyphenyl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(2-fluoro-3-hydroxyphenyl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(2-fluoro-5-hydroxyphenyl)methanone;

(2-chloro-5-hydroxyphenyl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone;

(3-(tert-butyl)-1-methyl-1H-pyrazol-5-yl)(4-(4-fluorophenoxy)piperidin-1-yl)methanone;

(4-fluoro-3-methoxyphenyl)(4-(4-fluorophenoxy)piperidin-1-yl)methanone;

(4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(2-methyl-2H-indazol-3-yl)methanone;

(4-(4-fluorophenoxy)piperidin-1-yl)(4-fluorophenyl)methanone;

(5-(tert-butyl)isoxazol-3-yl)(4-(4-fluorophenoxy)piperidin-1-yl)methanone;
(4-(4-fluorophenoxy)piperidin-1-yl)(1-methyl-5-(trifluoromethyl)-1H-pyrazol-3-yl)methanone;
(4-(4-fluorophenoxy)piperidin-1-yl)(1-methyl-1H-indazol-3-yl)methanone;
(4-(4-fluorophenoxy)piperidin-1-yl)(quinoxalin-2-yl)methanone;
(4-(4-fluorophenoxy)piperidin-1-yl)(4-methoxyquinolin-2-yl)methanone;
(4-(4-fluorophenoxy)piperidin-1-yl)(6-methoxyquinolin-2-yl)methanone;
(4-(4-fluorophenoxy)piperidin-1-yl)(isoquinolin-1-yl)methanone;
(4-(4-fluorophenoxy)piperidin-1-yl)(isoquinolin-4-yl)methanone;
(4-(4-fluorophenoxy)piperidin-1-yl)(quinolin-4-yl)methanone;
(5-aminopyridin-2-yl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone;
(6-(tert-butyl)pyridin-3-yl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone;
(6-(tert-butyl)pyridin-3-yl)(4-(4-fluorophenoxy)piperidin-1-yl)methanone;
N-(6-(4-(4-chlorophenoxy)piperidine-1-carbonyl)pyridin-3-yl)acetamide;
(6-methylpyridin-3-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
(1,3-dimethyl-1H-pyrazol-5-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
(3,5-dimethylisoxazol-4-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
;
(6-hydroxypyridin-2-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
(3-methylpyridin-2-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
(5-methoxypyridin-3-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
(5-aminopyridin-3-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
(6-methoxypyridin-3-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
4-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)picolinamide;
(3-methylisoxazol-5-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
(2-methylthiazol-5-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
(1-methyl-1H-imidazol-4-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
(2-hydroxy-6-methoxyphenyl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
(2,4-dimethylthiazol-5-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
(2-methyl-2H-indazol-3-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
;
(2-methyl-2H-indazol-6-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
;
imidazo[1,2-a]pyridin-8-yl(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
(1,8-naphthyridin-2-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;

(1,5-naphthyridin-2-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
 (2-hydroxyquinolin-4-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
 1,6-dimethyl-3-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)pyridin-2(1H)-
 one;
 benzo[d]thiazol-6-yl(4-(4-fluorophenoxy)piperidin-1-yl)methanone;
 (4-(4-fluorophenoxy)piperidin-1-yl)(2-methyl-1H-benzo[d]imidazol-5-yl)methanone;
 (4-(4-fluorophenoxy)piperidin-1-yl)(1-methyl-1H-benzo[d]imidazol-5-yl)methanone;
 (4-(4-fluorophenoxy)piperidin-1-yl)(5-methoxypyridin-2-yl)methanone;
 (4-(4-fluorophenoxy)piperidin-1-yl)(4-methyl-2-phenylpyrimidin-5-yl)methanone;
 (4-(4-fluorophenoxy)piperidin-1-yl)(1-methyl-1H-benzo[d]imidazol-2-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(6-ethoxypyridin-3-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(6-(dimethylamino)pyridin-3-yl)methanone;
 (4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(quinolin-2-yl)methanone;
 (4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(quinolin-3-yl)methanone;
 (4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(5-methyl-1-phenyl-1H-pyrazol-4-yl)methanone;
 (4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(4-methoxyquinolin-2-yl)methanone;
 (4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(6-ethoxypyridin-2-yl)methanone;
 (6-methoxypyridin-2-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
 (5-methoxypyrazin-2-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
 (2-hydroxy-3-methoxyphenyl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
 (2-methyloxazol-4-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
 (4-(2-hydroxypropan-2-yl)phenyl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
 (6-ethoxypyridin-2-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
 (1H-benzo[d]imidazol-6-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
 imidazo[1,2-a]pyrazin-2-yl(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
 ;
 (4-hydroxy-7-methyl-1,8-naphthyridin-3-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
 N-(4-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)pyridin-2-yl)acetamide;
 N-(6-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)pyridin-2-yl)acetamide;
 (4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(p-tolyl)methanone;
 (4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(4-methoxyphenyl)methanone;
 (4-chlorophenyl)(4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)methanone;
 (4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(1,5-naphthyridin-2-yl)methanone;

(4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(6-methoxy-1-methyl-1H-indol-2-yl)methanone;
 quinolin-8-yl(4-((3-(trifluoromethyl)phenyl)sulfonyl)piperidin-1-yl)methanone;
 quinolin-8-yl(4-tosylpiperidin-1-yl)methanone;
 (4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(isoquinolin-3-yl)methanone;
 4-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)benzamide;
 3-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)benzamide;
 3-(4-(4-chlorophenoxy)piperidine-1-carbonyl)benzamide;
 3-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-N-methylbenzamide;
 4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-N-methylbenzamide;
 (4-hydroxyquinolin-2-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
 (3-hydroxyquinoxalin-2-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
 ;
 (6-(hydroxymethyl)pyridin-2-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
 (1-(2-hydroxyethyl)-2-methyl-1H-benzo[d]imidazol-5-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
 (2-hydroxy-6-methylpyridin-4-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
 1-methyl-4-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)pyridin-2(1H)-one;
 ;
 (2-hydroxy-6-methylpyridin-3-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
 3-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)quinolin-2(1H)-one;
 (1H-1,2,4-triazol-3-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
 2-cyclopropyl-6-methyl-5-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)pyridin-4(1H)-one;
 5,6-dimethyl-3-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)pyridin-2(1H)-one;
 (4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)(1,3,6-trimethyl-1H-pyrazolo[3,4-b]pyridin-4-yl)methanone;
 4-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)-1H-benzo[d]imidazol-2(3H)-one;
 (4-(4-chloro-2-methoxyphenoxy)piperidin-1-yl)(quinolin-8-yl)methanone;
 1-(5-chloro-2-((1-(quinoline-8-carbonyl)piperidin-4-yl)oxy)phenyl)ethanone;
 5-chloro-2-((1-(quinoline-8-carbonyl)piperidin-4-yl)oxy)benzonitrile;
 (4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(quinoxalin-2-yl)methanone;
 (4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(6-methoxyquinolin-2-yl)methanone;

(4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(4-methyl-2-phenylpyrimidin-5-yl)methanone;
 (4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(6-(pyrrolidin-1-yl)pyridin-2-yl)methanone;
 (5-(tert-butyl)isoxazol-3-yl)(4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)methanone;
 (4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(6-(2,2,2-trifluoroethoxy)pyridin-3-yl)methanone;
 (4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(1-methyl-1H-indol-5-yl)methanone;
 (4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(1-methyl-1H-indol-2-yl)methanone;
 (4-(3-fluorophenoxy)piperidin-1-yl)(4-fluorophenyl)methanone;
 (4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(1-methyl-1H-indol-6-yl)methanone;
 3-(4-(3-(trifluoromethyl)phenoxy)piperidine-1-carbonyl)benzamide;
 4-(4-(3-(trifluoromethyl)phenoxy)piperidine-1-carbonyl)benzamide;
 4-(4-(3-(trifluoromethyl)phenoxy)piperidine-1-carbonyl)picolinamide;
 (4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(2-methoxyquinolin-4-yl)methanone;
 (4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(6-phenoxy-pyridin-3-yl)methanone;
 3-(4-((4-chlorophenyl)sulfonyl)piperidine-1-carbonyl)quinolin-2(1H)-one;
 3-(4-((4-chlorophenyl)sulfonyl)piperidine-1-carbonyl)-1-methylquinolin-2(1H)-one;
 (4-(4-fluorophenoxy)piperidin-1-yl)(5-methyl-1-phenyl-1H-pyrazol-4-yl)methanone;
 4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-N-(2-methoxyethyl)-N-methylbenzamide;
 4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-N-(2-methoxyethyl)benzamide;
 4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-N-(1-((1-hydroxycyclohexyl)methyl)piperidin-4-yl)benzamide;
 (S)-4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-N-(2-hydroxy-1-phenylethyl)benzamide;
 (S)-4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-N-(2-hydroxy-2-phenylethyl)benzamide;
 (S)-4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-N-(1-hydroxy-3-phenylpropan-2-yl)benzamide;
 (S)-N-(1-amino-1-oxo-3-phenylpropan-2-yl)-4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)benzamide;
 (4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(1-methyl-1H-indol-4-yl)methanone;
 4-(4-((4-chlorophenyl)thio)piperidine-1-carbonyl)picolinamide;
 6-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)picolinamide;
 4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-N-(2-oxo-2-phenylethyl)benzamide;
 (2-(methylsulfonyl)phenyl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
 ;

(3-(methylsulfonyl)phenyl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone
;
(4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(5-fluoro-1-methyl-1H-indol-2-yl)methanone;
(4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(6-fluoro-1-methyl-1H-indol-2-yl)methanone;
(4-(3-ethoxyphenoxy)piperidin-1-yl)(quinolin-8-yl)methanone;
(4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(3-(2-methylthiazol-4-yl)phenyl)methanone;
N-methyl-3-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)benzamide;
3-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)benzenesulfonamide;
4-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)benzenesulfonamide;
(4-(4-fluorophenoxy)piperidin-1-yl)(1,5-naphthyridin-2-yl)methanone;
(4-(4-fluorophenoxy)piperidin-1-yl)(quinolin-2-yl)methanone;
(4-(3-fluorophenoxy)piperidin-1-yl)(4-methoxyquinolin-2-yl)methanone;
(1H-benzo[d][1,2,3]triazol-7-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
2-(2-(4-(4-chlorophenoxy)piperidine-1-carbonyl)phenoxy)acetamide;
2-(4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)phenoxy)acetamide;
2-(2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenoxy)acetamide;
2-(3-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenoxy)acetamide;
2-(4-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenoxy)acetamide;
(8-hydroxyquinolin-2-yl)(4-((3-(trifluoromethoxy)phenyl)sulfonyl)piperidin-1-yl)methanone;
quinolin-8-yl(4-((3-(trifluoromethoxy)phenyl)sulfonyl)piperidin-1-yl)methanone;
quinolin-2-yl(4-((3-(trifluoromethoxy)phenyl)sulfonyl)piperidin-1-yl)methanone;
(4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(5-phenylisoxazol-3-yl)methanone;
(6-methoxyquinolin-2-yl)(4-((3-(trifluoromethoxy)phenyl)sulfonyl)piperidin-1-yl)methanone;
(5-methyl-2-phenyl-2H-1,2,3-triazol-4-yl)(4-((3-(trifluoromethoxy)phenyl)sulfonyl)piperidin-1-yl)methanone;
(5-fluoro-1-methyl-1H-indol-2-yl)(4-((3-(trifluoromethoxy)phenyl)sulfonyl)piperidin-1-yl)methanone;
(6-fluoro-1-methyl-1H-indol-2-yl)(4-((3-(trifluoromethoxy)phenyl)sulfonyl)piperidin-1-yl)methanone;
(4-hydroxyquinolin-8-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
(1,8-naphthyridin-4-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
(1,6-naphthyridin-8-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;

[1,2,4]triazolo[1,5-a]pyrimidin-2-yl(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
 (5-methyl-1H-pyrazol-3-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
 ;
 2-chloro-5-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)benzenesulfonamide;
 ;
 (S)-3-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-N-(2-hydroxy-2-phenylethyl)benzamide;
 (S)-3-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-N-(2-hydroxy-1-phenylethyl)benzamide;
 (S)-3-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-N-(1-hydroxy-3-phenylpropan-2-yl)benzamide;
 (S)-N-(1-amino-1-oxo-3-phenylpropan-2-yl)-3-(4-(4-chlorophenoxy)piperidine-1-carbonyl)benzamide;
 (4-((3-ethoxyphenyl)sulfonyl)piperidin-1-yl)(8-hydroxyquinolin-2-yl)methanone;
 (4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(4-methyl-2-phenylthiazol-5-yl)methanone;
 ;
 (4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(2-phenylthiazol-4-yl)methanone;
 (4-chloro-2-(methylsulfonyl)phenyl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
 (5-fluoro-2-(methylsulfonyl)phenyl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
 N,N-dimethyl-4-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)benzenesulfonamide;
 N-(2-(4-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenoxy)ethyl)acetamide;
 (2-phenyl-1H-imidazol-5-yl)(4-((3-(trifluoromethoxy)phenyl)sulfonyl)piperidin-1-yl)methanone;
 (3-(2-methylthiazol-4-yl)phenyl)(4-((3-(trifluoromethoxy)phenyl)sulfonyl)piperidin-1-yl)methanone;
 N-(4-(4-(3-ethoxyphenoxy)piperidine-1-carbonyl)pyridin-2-yl)acetamide;
 (4-(3-ethoxyphenoxy)piperidin-1-yl)(2-(methylsulfonyl)phenyl)methanone;
 3-(4-(3-ethoxyphenoxy)piperidine-1-carbonyl)benzenesulfonamide;
 N-(6-(4-(3-ethoxyphenoxy)piperidine-1-carbonyl)pyridin-2-yl)acetamide;
 (4-(3-ethoxyphenoxy)piperidin-1-yl)(2-methyl-2H-indazol-3-yl)methanone;
 (4-(3-ethoxyphenoxy)piperidin-1-yl)(1,5-naphthyridin-2-yl)methanone;
 (8-hydroxyquinolin-2-yl)(4-((4-(trifluoromethoxy)phenyl)sulfonyl)piperidin-1-yl)methanone;

quinolin-8-yl(4-((4-(trifluoromethoxy)phenyl)sulfonyl)piperidin-1-yl)methanone;
 quinolin-2-yl(4-((4-(trifluoromethoxy)phenyl)sulfonyl)piperidin-1-yl)methanone;
 N-(3-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenyl)methanesulfonamide;
 (2-(ethylsulfonyl)phenyl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
 (3-fluoro-4-(methylsulfonyl)phenyl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
 ethyl
 (4-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)pyridin-2-yl)carbamate;
 2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)thiazole-4-carboxamide;
 N,N-dimethyl-2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)benzenesulfonamide;
 (4-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenyl)methanesulfonamide;
 4-methoxy-3-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)benzenesulfonamide;
 2-((2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)pyridin-3-yl)oxy)acetamide;
 (4-(aminomethyl)pyridin-2-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
 N-((2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)pyridin-4-yl)methyl)methanesulfonamide;
 ethyl
 ((2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)pyridin-4-yl)methyl)carbamate;
 N-(2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)benzyl)acetamide;
 N-(2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)benzyl)methanesulfonamide;
 ethyl 2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)benzylcarbamate;
 (2-(methylsulfonyl)phenyl)(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidin-1-yl)methanone;
 N-(4-(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidine-1-carbonyl)pyridin-2-yl)acetamide;
 4-(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidine-1-carbonyl)picolinamide;
 3-(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidine-1-carbonyl)benzamide;
 3-(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidine-1-carbonyl)benzenesulfonamide;
 2-(2-(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidine-1-carbonyl)phenoxy)acetamide;
 quinolin-8-yl(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidin-1-yl)methanone;

(1,5-naphthyridin-2-yl)(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidin-1-yl)methanone
 ;
 (2-methyl-2H-indazol-3-yl)(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidin-1-yl)methanone;
 (1,3-dimethyl-1H-pyrazol-5-yl)(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidin-1-yl)methanone;
 N-(6-(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidine-1-carbonyl)pyridin-2-yl)acetamide;
 4-(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidine-1-carbonyl)benzamide;
 (3,5-dimethylisoxazol-4-yl)(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidin-1-yl)methanone;
 (3-(methylsulfonyl)phenyl)(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidin-1-yl)methanone;
 (1,6-naphthyridin-8-yl)(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidin-1-yl)methanone
 ;
 (3-methyl-1H-pyrazol-5-yl)(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidin-1-yl)methanone;
 2-(3-(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidine-1-carbonyl)phenoxy)acetamide;
 (5-((tetrahydro-2H-pyran-4-yl)oxy)pyridin-3-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
 1-(3-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenyl)urea;
 1-(4-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenyl)urea;
 (1H-1,2,4-triazol-3-yl)(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidin-1-yl)methanone;
 (4-(3-ethoxyphenoxy)piperidin-1-yl)(3-(methylsulfonyl)phenyl)methanone;
 (4-(3-ethoxyphenoxy)piperidin-1-yl)(3-methyl-1H-pyrazol-5-yl)methanone;
 N,N-dimethyl-3-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)benzenesulfonamide;
 N-(2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenyl)methanesulfonamide;
 (6-aminopyridin-2-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
 2-(methyl(3-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)benzyl)amino)acetamide;
 2-(methyl(4-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)benzyl)amino)acetamide;
 N,N-dimethyl-2-(2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenoxy)acetamide;
 (1,3-dimethyl-1H-pyrazol-5-yl)(4-(3-(trifluoromethyl)phenoxy)piperidin-1-yl)methanone;

(2-(methylsulfonyl)phenyl)(4-(3-(trifluoromethyl)phenoxy)piperidin-1-yl)methanone;
 N-(6-(4-(3-(trifluoromethyl)phenoxy)piperidine-1-carbonyl)pyridin-2-yl)acetamide;
 3-(4-(3-(trifluoromethyl)phenoxy)piperidine-1-carbonyl)benzenesulfonamide;
 (3,5-dimethylisoxazol-4-yl)(4-(3-(trifluoromethyl)phenoxy)piperidin-1-yl)methanone;
 (1,6-naphthyridin-8-yl)(4-(3-(trifluoromethyl)phenoxy)piperidin-1-yl)methanone;
 (3-methyl-1H-pyrazol-5-yl)(4-(3-(trifluoromethyl)phenoxy)piperidin-1-yl)methanone;
 2-(2-(4-(3-(trifluoromethyl)phenoxy)piperidine-1-carbonyl)phenoxy)acetamide;
 2-(4-(4-(3-(trifluoromethyl)phenoxy)piperidine-1-carbonyl)phenoxy)acetamide;
 2-(3-(4-(3-(trifluoromethyl)phenoxy)piperidine-1-carbonyl)phenoxy)acetamide;
 (1H-1,2,4-triazol-3-yl)(4-(3-(trifluoromethyl)phenoxy)piperidin-1-yl)methanone;
 N-(2-(2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenoxy)ethyl)acetamide;
 N-(2-(2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenoxy)ethyl)methanesulfonamide;
 ethyl
 (2-(2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenoxy)ethyl)carbamate;
 N-(2-(2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenoxy)ethyl)cyclopropane-1,1-dicarboxamide;
 (3-(2-aminoethoxy)phenyl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
 ;
 N-(2-(3-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenoxy)ethyl)acetamide;
 N-(2-(3-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenoxy)ethyl)methanesulfonamide;
 ethyl
 (2-(3-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenoxy)ethyl)carbamate;
 N-(2-(3-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenoxy)ethyl)cyclopropane-1,1-dicarboxamide;
 N-(3-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)pyridin-2-yl)acetamide;
 N-(1-methyl-5-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)-1H-pyrazol-3-yl)acetamide;
 (2-(ethylsulfonyl)phenyl)(4-(3-(trifluoromethyl)phenoxy)piperidin-1-yl)methanone;
 (4-(3-ethoxyphenoxy)piperidin-1-yl)(2-(ethylsulfonyl)phenyl)methanone;
 (2-(ethylsulfonyl)phenyl)(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidin-1-yl)methanone;
 N-(2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)pyridin-3-yl)acetamide;

2-(4-(4-(3-chlorophenoxy)piperidine-1-carbonyl)phenoxy)acetamide;
 2-(2-(4-((4-chlorophenyl)thio)piperidine-1-carbonyl)phenoxy)acetamide;
 2-(3-(4-((4-chlorophenyl)thio)piperidine-1-carbonyl)phenoxy)acetamide;
 (4-((4-chlorophenyl)thio)piperidin-1-yl)(2-(methylsulfonyl)phenyl)methanone;
 2-(methyl(2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)benzyl)amino)acetamide;
 1-morpholino-2-(2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenoxy)ethanone;
 1-(piperidin-1-yl)-2-(2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenoxy)ethanone;
 (2-(2-methoxyethoxy)phenyl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
 (3-(methylsulfonyl)phenyl)(4-(3-(trifluoromethyl)phenoxy)piperidin-1-yl)methanone;
 (4-(3-chlorophenoxy)piperidin-1-yl)(3-(methylsulfonyl)phenyl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(3-(methylsulfonyl)phenyl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(2-(ethylsulfonyl)phenyl)methanone;
 N,N-dimethyl-3-(4-(3-(trifluoromethyl)phenoxy)piperidine-1-carbonyl)benzenesulfonamide;
 3-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-N,N-dimethylbenzenesulfonamide;
 N,N-dimethyl-3-(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidine-1-carbonyl)benzenesulfonamide;
 N,N-dimethyl-2-(4-(3-(trifluoromethyl)phenoxy)piperidine-1-carbonyl)benzenesulfonamide;
 2-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-N,N-dimethylbenzenesulfonamide;
 N,N-dimethyl-2-(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidine-1-carbonyl)benzenesulfonamide;
 (4-(3-(2-methoxyethoxy)phenoxy)piperidin-1-yl)(quinolin-8-yl)methanone;
 (4-(3-(2-methoxyethoxy)phenoxy)piperidin-1-yl)(quinolin-2-yl)methanone;
 (4-(3-(2-methoxyethoxy)phenoxy)piperidin-1-yl)(2-methyl-2H-indazol-3-yl)methanone;
 2-((2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenyl)thio)acetamide;
 2-((2-(4-(4-chlorophenoxy)piperidine-1-carbonyl)phenyl)thio)acetamide;
 4-(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidine-1-carbonyl)-1H-benzo[d]imidazol-2(3H)-one;
 (4-(3-ethoxyphenoxy)piperidin-1-yl)(1-methyl-1H-benzo[d]imidazol-2-yl)methanone;
 (4-(3-fluorophenoxy)piperidin-1-yl)(1-methyl-1H-benzo[d]imidazol-2-yl)methanone;
 (1H-pyrrolo[2,3-b]pyridin-2-yl)(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidin-1-yl)methanone;

(4-(3-ethoxyphenoxy)piperidin-1-yl)(1H-pyrrolo[2,3-b]pyridin-2-yl)methanone;
(1H-pyrrolo[2,3-b]pyridin-2-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
(4-(3-ethoxyphenoxy)piperidin-1-yl)(1-methyl-1H-pyrazolo[3,4-b]pyridin-3-yl)methanone;
(4-(3-ethoxyphenoxy)piperidin-1-yl)(1H-pyrrolo[2,3-b]pyridin-3-yl)methanone;
(4-(3-ethoxyphenoxy)piperidin-1-yl)(pyrazolo[1,5-a]pyrimidin-3-yl)methanone;
(1,3-dimethyl-1H-thieno[2,3-c]pyrazol-5-yl)(4-(3-ethoxyphenoxy)piperidin-1-yl)methanone;
(4-(3-fluorophenoxy)piperidin-1-yl)(4-methyl-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)methanone;
(3,5-dimethyl-1H-pyrazol-4-yl)(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidin-1-yl)methanone;
N-(2-hydroxyethyl)-N-methyl-2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)benzenesulfonamide;
N-(2-methoxyethyl)-N-methyl-2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)benzenesulfonamide;
(2-(morpholinosulfonyl)phenyl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
2-(N-methyl-2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenylsulfonamido)acetamide;
N-methyl-3-(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidine-1-carbonyl)benzenesulfonamide;
3-(4-(3-ethoxyphenoxy)piperidine-1-carbonyl)-N-methylbenzenesulfonamide;
N-methyl-3-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)benzenesulfonamide;
(1,5-naphthyridin-2-yl)(4-(3-(trifluoromethyl)phenoxy)piperidin-1-yl)methanone;
3-(4-((4-chlorophenyl)thio)piperidine-1-carbonyl)benzenesulfonamide;
(4-((4-chlorophenyl)thio)piperidin-1-yl)(1,5-naphthyridin-2-yl)methanone;
N-(6-(4-((4-chlorophenyl)thio)piperidine-1-carbonyl)pyridin-2-yl)acetamide;
(4-((4-chlorophenyl)thio)piperidin-1-yl)(1,6-naphthyridin-8-yl)methanone;
2-(4-(4-(3,4-difluorophenoxy)piperidine-1-carbonyl)phenoxy)acetamide;
(4-(3,4-difluorophenoxy)piperidin-1-yl)(1,5-naphthyridin-2-yl)methanone;
2-(4-(4-(2,4-difluorophenoxy)piperidine-1-carbonyl)phenoxy)acetamide;
N-(4-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)pyridin-2-yl)pivalamide;
(2-(1H-imidazol-1-yl)pyridin-4-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
N-(4-(4-(3-ethoxyphenoxy)piperidine-1-carbonyl)pyridin-2-yl)pivalamide;

1-(3-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenyl)pyrrolidin-2-one;
 1-(3-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenyl)imidazolidin-2-one;
 and
 (5-amino-1H-pyrazol-3-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
 or a prodrug thereof or a pharmaceutically acceptable salt thereof.

- [0041] [7] More suitable individual compounds of the invention are:
- (4-(4-chlorophenoxy)piperidin-1-yl)(quinoxalin-6-yl)methanone;
 - (4-(4-chlorophenoxy)piperidin-1-yl)(quinolin-8-yl)methanone;
 - (4-(1H-1,2,4-triazol-1-yl)phenyl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone;
 - (4-(4-chlorophenoxy)piperidin-1-yl)(3,5-dimethylisoxazol-4-yl)methanone;
 - (4-(4-chlorophenoxy)piperidin-1-yl)(2-methyl-2H-indazol-3-yl)methanone;
 - (4-(4-chlorophenoxy)piperidin-1-yl)(6-methylpyridin-3-yl)methanone;
 - (4-(4-chlorophenoxy)piperidin-1-yl)(6-methoxypyridin-3-yl)methanone;
 - (4-(4-chlorophenoxy)piperidin-1-yl)(3-methylpyridin-2-yl)methanone;
 - (4-(4-chlorophenoxy)piperidin-1-yl)(2,4-dimethylthiazol-5-yl)methanone;
 - (4-(4-chlorophenoxy)piperidin-1-yl)(4,5,6,7-tetrahydro-1H-indazol-3-yl)methanone;
 - (4-(4-chlorophenoxy)piperidin-1-yl)(6-methoxypyridin-2-yl)methanone;
 - (4-(4-chlorophenoxy)piperidin-1-yl)(2-methyl-4,5,6,7-tetrahydro-2H-indazol-3-yl)methanone;
 - (4-(4-chlorophenoxy)piperidin-1-yl)(1,5-naphthyridin-2-yl)methanone;
 - 4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)benzamide;
 - (4-(4-chlorophenoxy)piperidin-1-yl)(4-(2-hydroxypropan-2-yl)phenyl)methanone;
 - (4-(4-chlorophenoxy)piperidin-1-yl)(quinolin-5-yl)methanone;
 - (4-(4-fluorophenoxy)piperidin-1-yl)(2-methyl-2H-indazol-3-yl)methanone;
 - (4-phenoxy)piperidin-1-yl)(quinolin-8-yl)methanone;
 - (4-(4-fluorophenoxy)piperidin-1-yl)(quinolin-8-yl)methanone;
 - (4-(4-chlorophenoxy)piperidin-1-yl)(phenyl)methanone;
 - (1H-benzo[d]imidazol-5-yl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone;
 - (4-(4-chlorophenoxy)piperidin-1-yl)(1,3-dimethyl-1H-pyrazol-5-yl)methanone;
 - (4-(3-methoxyphenoxy)piperidin-1-yl)(quinolin-8-yl)methanone;
 - (4-(3-fluorophenoxy)piperidin-1-yl)(quinolin-8-yl)methanone;
 - (4-(4-chlorophenoxy)piperidin-1-yl)(2-methylthiazol-5-yl)methanone;
 - 1-(3-((1-(quinoline-8-carbonyl)piperidin-4-yl)oxy)phenyl)ethanone;
 - (4-(4-chlorophenoxy)piperidin-1-yl)(3-methylisoxazol-5-yl)methanone;
 - (4-(4-chlorophenoxy)piperidin-1-yl)(1-isopropyl-1H-pyrazol-4-yl)methanone;
 - (4-(4-chlorophenoxy)piperidin-1-yl)(3-isopropyl-1-methyl-1H-pyrazol-5-yl)methanone;
 - (4-(4-chlorophenoxy)piperidin-1-yl)(3-ethyl-1-methyl-1H-pyrazol-5-yl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(imidazo[1,2-a]pyrazin-2-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(4-methyl-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(pyrazolo[1,5-a]pyridin-7-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(1-methyl-1H-imidazol-2-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(1-methyl-1H-imidazol-4-yl)methanone;
(4-chloro-5-methyl-1H-pyrazol-3-yl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(4-methyl-4H-furo[3,2-b]pyrrol-5-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(pyrazolo[1,5-a]pyrimidin-3-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(2-(pyrrolidin-1-yl)pyrimidin-5-yl)methanone;
(1H-benzo[d][1,2,3]triazol-4-yl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone;
3-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-1,6-dimethylpyridin-2(1H)-one;
(4-(4-chlorophenoxy)piperidin-1-yl)(1-methyl-3-(trifluoromethyl)-1H-pyrazol-5-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(4-(2-hydroxyethoxy)phenyl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(2-hydroxy-4-methoxyphenyl)methanone;
2-(3-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-1H-indol-1-yl)-N,N-dimethylacetamide;
(4-(4-chlorophenoxy)piperidin-1-yl)(3-fluoro-4-hydroxyphenyl)methanone;
2-chloro-5-(4-(4-chlorophenoxy)piperidine-1-carbonyl)benzenesulfonamide;
(4-(4-chlorophenoxy)piperidin-1-yl)(2-hydroxy-6-methoxyphenyl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(2-fluoro-4-hydroxyphenyl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(4-fluoro-3-hydroxyphenyl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(2-hydroxy-3-methoxyphenyl)methanone;
N-(3-(4-(4-chlorophenoxy)piperidine-1-carbonyl)phenyl)acetamide;
(4-(4-chlorophenoxy)piperidin-1-yl)(1-((4-hydroxytetrahydro-2H-pyran-4-yl)methyl)-1H-indol-5-yl)methanone;
N-(6-(4-(4-chlorophenoxy)piperidine-1-carbonyl)pyridin-2-yl)acetamide;
N-(4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)pyridin-2-yl)acetamide;
(4-(4-chlorophenoxy)piperidin-1-yl)(1,6-naphthyridin-5-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(3-hydroxyphenyl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(2-fluoro-3-hydroxyphenyl)methanone;
(3-(tert-butyl)-1-methyl-1H-pyrazol-5-yl)(4-(4-fluorophenoxy)piperidin-1-yl)methanone;
(4-fluoro-3-methoxyphenyl)(4-(4-fluorophenoxy)piperidin-1-yl)methanone;
(4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(2-methyl-2H-indazol-3-yl)methanone;
(4-(4-fluorophenoxy)piperidin-1-yl)(1-methyl-1H-indazol-3-yl)methanone;
(4-(4-fluorophenoxy)piperidin-1-yl)(4-methoxyquinolin-2-yl)methanone;

(4-(4-fluorophenoxy)piperidin-1-yl)(isoquinolin-1-yl)methanone;
 (5-aminopyridin-2-yl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone;
 (1,3-dimethyl-1H-pyrazol-5-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
 (3,5-dimethylisoxazol-4-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
 ;
 (3-methylpyridin-2-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
 4-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)picolinamide;
 (1-methyl-1H-imidazol-4-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
 (2-hydroxy-6-methoxyphenyl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
 (2,4-dimethylthiazol-5-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
 (2-methyl-2H-indazol-3-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
 ;
 1,6-dimethyl-3-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)pyridin-2(1H)-one;
 benzo[d]thiazol-6-yl(4-(4-fluorophenoxy)piperidin-1-yl)methanone;
 (4-(4-fluorophenoxy)piperidin-1-yl)(1-methyl-1H-benzo[d]imidazol-2-yl)methanone;
 (2-methyloxazol-4-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
 N-(4-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)pyridin-2-yl)acetamide;
 N-(6-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)pyridin-2-yl)acetamide;
 3-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)benzamide;
 (6-(hydroxymethyl)pyridin-2-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
 5,6-dimethyl-3-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)pyridin-2(1H)-one;
 4-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)-1H-benzo[d]imidazol-2(3H)-one;
 (4-(4-chloro-2-methoxyphenoxy)piperidin-1-yl)(quinolin-8-yl)methanone;
 3-(4-(3-(trifluoromethyl)phenoxy)piperidine-1-carbonyl)benzamide;
 4-(4-(3-(trifluoromethyl)phenoxy)piperidine-1-carbonyl)picolinamide;
 (4-(4-fluorophenoxy)piperidin-1-yl)(5-methyl-1-phenyl-1H-pyrazol-4-yl)methanone;
 4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-N-(2-methoxyethyl)-N-methylbenzamide;
 (S)-4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-N-(2-hydroxy-2-phenylethyl)benzamide;
 4-(4-((4-chlorophenyl)thio)piperidine-1-carbonyl)picolinamide;

6-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)picolinamide;
 (2-(methylsulfonyl)phenyl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone
 ;
 (4-(3-ethoxyphenoxy)piperidin-1-yl)(quinolin-8-yl)methanone;
 N-methyl-3-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)benzamide;
 3-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)benzenesulfonamide;
 4-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)benzenesulfonamide;
 (4-(4-fluorophenoxy)piperidin-1-yl)(1,5-naphthyridin-2-yl)methanone;
 (4-(4-fluorophenoxy)piperidin-1-yl)(quinolin-2-yl)methanone;
 (4-(3-fluorophenoxy)piperidin-1-yl)(4-methoxyquinolin-2-yl)methanone;
 (1H-benzo[d][1,2,3]triazol-7-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
 2-(2-(4-(4-chlorophenoxy)piperidine-1-carbonyl)phenoxy)acetamide;
 2-(2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenoxy)acetamide;
 (4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(5-phenylisoxazol-3-yl)methanone;
 (4-hydroxyquinolin-8-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
 (1,8-naphthyridin-4-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
 (1,6-naphthyridin-8-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
 [1,2,4]triazolo[1,5-a]pyrimidin-2-yl(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
 (5-methyl-1H-pyrazol-3-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone
 ;
 2-chloro-5-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)benzenesulfonamide;
 (S)-3-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-N-(2-hydroxy-2-phenylethyl)benzamide;
 (S)-N-(1-amino-1-oxo-3-phenylpropan-2-yl)-3-(4-(4-chlorophenoxy)piperidine-1-carbonyl)benzamide;
 (4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(2-phenylthiazol-4-yl)methanone;
 (5-fluoro-2-(methylsulfonyl)phenyl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
 N,N-dimethyl-4-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)benzenesulfonamide;
 N-(2-(4-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenoxy)ethyl)acetamide;
 N-(4-(4-(3-ethoxyphenoxy)piperidine-1-carbonyl)pyridin-2-yl)acetamide;
 3-(4-(3-ethoxyphenoxy)piperidine-1-carbonyl)benzenesulfonamide;
 N-(6-(4-(3-ethoxyphenoxy)piperidine-1-carbonyl)pyridin-2-yl)acetamide;

(4-(3-ethoxyphenoxy)piperidin-1-yl)(1,5-naphthyridin-2-yl)methanone;
 quinolin-8-yl(4-((4-(trifluoromethoxy)phenyl)sulfonyl)piperidin-1-yl)methanone;
 quinolin-2-yl(4-((4-(trifluoromethoxy)phenyl)sulfonyl)piperidin-1-yl)methanone;
 (2-(ethylsulfonyl)phenyl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
 2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)thiazole-4-carboxamide;
 (4-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenyl)methanesulfonamide;
 4-methoxy-3-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)benzenesulfonamide;
 2-((2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)pyridin-3-yl)oxy)acetamide;
 (4-(aminomethyl)pyridin-2-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
 N-((2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)pyridin-4-yl)methyl)methanesulfonamide;
 ethyl
 ((2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)pyridin-4-yl)methyl)carbamate;
 N-(2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)benzyl)acetamide;
 N-(2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)benzyl)methanesulfonamide;
 (2-(methylsulfonyl)phenyl)(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidin-1-yl)methanone;
 N-(4-(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidine-1-carbonyl)pyridin-2-yl)acetamide;
 4-(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidine-1-carbonyl)picolinamide;
 3-(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidine-1-carbonyl)benzamide;
 2-(2-(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidine-1-carbonyl)phenoxy)acetamide;
 (1,5-naphthyridin-2-yl)(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidin-1-yl)methanone;
 ;
 (2-methyl-2H-indazol-3-yl)(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidin-1-yl)methanone;
 (1,3-dimethyl-1H-pyrazol-5-yl)(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidin-1-yl)methanone;
 N-(6-(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidine-1-carbonyl)pyridin-2-yl)acetamide;
 4-(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidine-1-carbonyl)benzamide;
 (3,5-dimethylisoxazol-4-yl)(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidin-1-yl)metha

none;
 (3-(methylsulfonyl)phenyl)(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidin-1-yl)methanone;
 (1,6-naphthyridin-8-yl)(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidin-1-yl)methanone;
 ;
 (3-methyl-1H-pyrazol-5-yl)(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidin-1-yl)methanone;
 2-(3-(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidine-1-carbonyl)phenoxy)acetamide;
 1-(4-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenyl)urea;
 (1H-1,2,4-triazol-3-yl)(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidin-1-yl)methanone;
 (4-(3-ethoxyphenoxy)piperidin-1-yl)(3-(methylsulfonyl)phenyl)methanone;
 (4-(3-ethoxyphenoxy)piperidin-1-yl)(3-methyl-1H-pyrazol-5-yl)methanone;
 N,N-dimethyl-3-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)benzenesulfonamide;
 N-(2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenyl)methanesulfonamide;
 (6-aminopyridin-2-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
 N,N-dimethyl-2-(2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenoxy)acetamide;
 (1,3-dimethyl-1H-pyrazol-5-yl)(4-(3-(trifluoromethyl)phenoxy)piperidin-1-yl)methanone;
 (2-(methylsulfonyl)phenyl)(4-(3-(trifluoromethyl)phenoxy)piperidin-1-yl)methanone;
 N-(6-(4-(3-(trifluoromethyl)phenoxy)piperidine-1-carbonyl)pyridin-2-yl)acetamide;
 3-(4-(3-(trifluoromethyl)phenoxy)piperidine-1-carbonyl)benzenesulfonamide;
 (3,5-dimethylisoxazol-4-yl)(4-(3-(trifluoromethyl)phenoxy)piperidin-1-yl)methanone;
 (1,6-naphthyridin-8-yl)(4-(3-(trifluoromethyl)phenoxy)piperidin-1-yl)methanone;
 (3-methyl-1H-pyrazol-5-yl)(4-(3-(trifluoromethyl)phenoxy)piperidin-1-yl)methanone;
 2-(2-(4-(3-(trifluoromethyl)phenoxy)piperidine-1-carbonyl)phenoxy)acetamide;
 2-(3-(4-(3-(trifluoromethyl)phenoxy)piperidine-1-carbonyl)phenoxy)acetamide;
 (1H-1,2,4-triazol-3-yl)(4-(3-(trifluoromethyl)phenoxy)piperidin-1-yl)methanone;
 N-(2-(2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenoxy)ethyl)methanesulfonamide;
 N-(2-(2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenoxy)ethyl)cyclopropane-1,1-dicarboxamide;
 N-(2-(3-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenoxy)ethyl)methanesulfonamide;
 N-(3-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)pyridin-2-yl)acetamide;
 N-(1-methyl-5-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)-1H-pyrazol-3-

yl)acetamide;
(2-(ethylsulfonyl)phenyl)(4-(3-(trifluoromethyl)phenoxy)piperidin-1-yl)methanone;
(2-(ethylsulfonyl)phenyl)(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidin-1-yl)methanone;
N-(2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)pyridin-3-yl)acetamide;
(3-(methylsulfonyl)phenyl)(4-(3-(trifluoromethyl)phenoxy)piperidin-1-yl)methanone;
(4-(3-chlorophenoxy)piperidin-1-yl)(3-(methylsulfonyl)phenyl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(3-(methylsulfonyl)phenyl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(2-(ethylsulfonyl)phenyl)methanone;
N,N-dimethyl-3-(4-(3-(trifluoromethyl)phenoxy)piperidine-1-carbonyl)benzenesulfonamide;
3-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-N,N-dimethylbenzenesulfonamide;
(4-(3-(2-methoxyethoxy)phenoxy)piperidin-1-yl)(quinolin-8-yl)methanone;
(4-(3-(2-methoxyethoxy)phenoxy)piperidin-1-yl)(quinolin-2-yl)methanone;
(4-(3-(2-methoxyethoxy)phenoxy)piperidin-1-yl)(2-methyl-2H-indazol-3-yl)methanone;
2-((2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenyl)thio)acetamide;
2-((2-(4-(4-chlorophenoxy)piperidine-1-carbonyl)phenyl)thio)acetamide;
4-(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidine-1-carbonyl)-1H-benzo[d]imidazol-2(3H)-one;
(4-(3-ethoxyphenoxy)piperidin-1-yl)(1-methyl-1H-benzo[d]imidazol-2-yl)methanone;
(4-(3-fluorophenoxy)piperidin-1-yl)(1-methyl-1H-benzo[d]imidazol-2-yl)methanone;
(4-(3-ethoxyphenoxy)piperidin-1-yl)(1-methyl-1H-pyrazolo[3,4-b]pyridin-3-yl)methanone;
(4-(3-ethoxyphenoxy)piperidin-1-yl)(pyrazolo[1,5-a]pyrimidin-3-yl)methanone;
(4-(3-fluorophenoxy)piperidin-1-yl)(4-methyl-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)methanone;
(3,5-dimethyl-1H-pyrazol-4-yl)(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidin-1-yl)methanone;
N-(2-hydroxyethyl)-N-methyl-2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)benzenesulfonamide;
(2-(morpholinosulfonyl)phenyl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
2-(N-methyl-2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenylsulfonamido)acetamide;
N-methyl-3-(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidine-1-carbonyl)benzenesulfonamide;
3-(4-(3-ethoxyphenoxy)piperidine-1-carbonyl)-N-methylbenzenesulfonamide;

N-methyl-3-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)benzenesulfonamide;

4-((4-chlorophenyl)thio)piperidin-1-yl)(1,5-naphthyridin-2-yl)methanone;

N-(6-(4-((4-chlorophenyl)thio)piperidine-1-carbonyl)pyridin-2-yl)acetamide;

2-(4-(4-(3,4-difluorophenoxy)piperidine-1-carbonyl)phenoxy)acetamide;

(4-(3,4-difluorophenoxy)piperidin-1-yl)(1,5-naphthyridin-2-yl)methanone;

2-(4-(4-(2,4-difluorophenoxy)piperidine-1-carbonyl)phenoxy)acetamide;

N-(4-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)pyridin-2-yl)pivalamide;

and

(5-amino-1H-pyrazol-3-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;

or a prodrug thereof or a pharmaceutically acceptable salt thereof.

[0042] [8] The present invention provides a method for the treatment of a condition or disorder in which TTX-S channel blockers are involved, in a mammalian subject, including a human, which comprises administering to a mammal in need of such treatment a therapeutically effective amount of the compound or the prodrug thereof or the pharmaceutically acceptable salt thereof, as described in any one of [1] to [7].

[0043] [9] The present invention provides the method as described in [8], wherein said condition or disorder is selected from the group consisting of: pain, acute pain, chronic pain, neuropathic pain, inflammatory pain, visceral pain, nociceptive pain, multiple sclerosis, neurodegenerative disorder, irritable bowel syndrome, osteoarthritis, rheumatoid arthritis, neuropathological disorders, functional bowel disorders, inflammatory bowel diseases, pain associated with dysmenorrhea, pelvic pain, cystitis, pancreatitis, migraine, cluster and tension headaches, diabetic neuropathy, peripheral neuropathic pain, sciatica, fibromyalgia Crohn's disease, epilepsy or epileptic conditions, bipolar depression, tachyarrhythmias, mood disorder, bipolar disorder, psychiatric disorders such as anxiety and depression, myotonia, arrhythmia, movement disorders, neuroendocrine disorders, ataxia, incontinence, visceral pain, trigeminal neuralgia, herpetic neuralgia, general neuralgia, postherpetic neuralgia, radicular pain, sciatica, back pain, head or neck pain, severe or intractable pain, breakthrough pain, postsurgical pain, stroke, cancer pain, seizure disorder and causalgia; and combinations thereof.

[0044] [10] The present invention provides a pharmaceutical composition comprising the compound or the prodrug thereof or the pharmaceutically acceptable salt thereof, as described in any one of [4] to [7], together with a pharmaceutically acceptable carrier.

[0045] [11] The present invention provides a pharmaceutical composition as described in [10], further comprising another pharmacologically active agent.

[0046] [12] The present invention provides a compound of formula (I) described in [1] or a prodrug thereof or a pharmaceutically acceptable salt, solvate or composition thereof

for use in the treatment of a condition or disorder in which TTX-S channel blockers are involved.

[0047] [13] Also, the present invention provides a process for preparing a pharmaceutical composition, the process comprising mixing a compound described in any one of [4] to [7] or a prodrug thereof or a pharmaceutically acceptable salt thereof and a pharmaceutically acceptable carrier or excipient.

[0048] [14] Also, the present invention provides an intermediate in a process for preparing a compound of formula (I) or a prodrug thereof or a pharmaceutically acceptable salt thereof.

[0049] Examples of conditions or disorders mediated by TTX-S channels blocking activity include, but are not limited to, TTX-S channels related diseases. The compounds of the present invention show the TTX-S channels blocking activity. The compounds of the present invention may show less toxicity, good absorption, distribution, good solubility, less protein binding affinity other than TTX-S channels, less drug-drug interaction, and good metabolic stability.

Description of Embodiments

[0050] As appreciated by those of skill in the art, "halogen" or "halo" as used herein are intended to include fluoro, chloro, bromo and iodo. Similarly, C₁₋₆, as in C₁₋₆ alkyl is defined to identify the group as having 1, 2, 3, 4, 5 or 6 carbons in a linear or branched arrangement, such that C₁₋₈ alkyl specifically includes methyl, ethyl, n-propyl, isopropyl, n-butyl, iso-butyl, tert-butyl, pentyl, and hexyl. Similarly, C₂₋₆ alkenyl is defined to identify the group as having 2, 3, 4, 5 or 6 carbons which incorporates at least one double bond, which may be in a E- or a Z- arrangement. A group which is designated as being independently substituted with substituents may be independently substituted with multiple numbers of such substituents.

[0051] The term "alkenyl", as used herein, means a hydrocarbon radical having at least one double bond including, but not limited to, ethenyl, propenyl, 1-butenyl, 2-butenyl and the like.

[0052] The term "cycloalkyl", as used herein, means a mono- or bicyclic ring, but not limited to, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, norboranyl, and adamantyl groups and the like.

[0053] The term "aryl", as used herein, means mono- or bi-carbocyclic or mono- or bi-heterocyclic group which may contain 0-4 heteroatoms selected from O, N and S, but not limited to, phenyl, naphthyl, benzofuranyl, benzofurazanyl, benzimidazolonyl, benzoimidazolyl, benzoisothiazolyl, benzoisoxazolyl, benzothiadiazolyl, benzothiazolyl, benzoxadiazolyl, benzoxazolonyl, benzoxazolyl, benzothiophenyl, benzotriazolyl, carbazolyl, carbolinyl, chromanyl, cinnolinyl, 2,3-dioxoindolyl, furanyl, frazanyl,

furopyridyl, furopyrrolyl, imidazolyl, imidazopyrazinyl, imidazopyridinyl, imidazopyrimidinyl, imidazothiazolyl, indazolyl, indolazinyl, indolynyl, indolyl, isobenzofuranyl, isochromanyl, isoindolyl, isoquinolyl, isoxazolopyridyl, isoxazolynyl, isoxazolyl, isothiazolyl, naphthyridinyl, oxazolynyl, oxadiazolyl, oxazolyl, oxetanyl, 2-oxoindolyl, oxoisoindolyl, phthalazyl, pyrazolyl, pyrazolopyridyl, pyrazolopyrimidinyl, pyrazinyl, pyridyl, pyrimidyl, pyridazinyl, pyridopyrimidinyl, pyrrolopyridyl, pyrrolyl, quinazolynyl, quinolyl, quinoxalynyl, tetrazolopyridyl, tetrazolyl, thiadiazoleyl, thiazolyl, thiophenyl, thienopyrazinyl, thienopyrazolyl, thienopyridyl, thienopyrrolyl, triazolopyrimidinyl, triazolyl, 4-oxo-1,4-dihydroquinolyl, 2-oxo-1,2-dihydropyridyl, 4-oxo-1,4-dihydropyrimidyl, 2-oxo-1,2-dihydroquinolyl, 4-oxo-4H-pyrido[1,2-a]pyrimidyl, 4-oxo-1,4-dihydro-1,8-naphthyridyl, and N-oxides thereof, and wherein the saturated heterocyclic moieties include tetrahydrothienyl, 3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazinyl, 2-oxo-2,5,6,7-tetrahydro-1H-cyclopentapyridyl, 4,5,6,7-tetrahydro-indazolyl, 5,6,7,8-tetrahydro-1,6-naphthyridyl, and N-oxides thereof and S-oxides thereof and the said rings which are fully or partially saturated and the like.

- [0054] The term "heterocyclic group" as used herein includes both unsaturated and saturated heterocyclic moieties, wherein the unsaturated heterocyclic moieties include benzofuranyl, benzofurazanyl, benzimidazolonyl, benzoimidazolyl, benzoisothiazolyl, benzoisoxazolyl, benzothiadiazolyl, benzothiazolyl, benzoxadiazolyl, benzoxazolonyl, benzoxazolyl, benzothiophenyl, benzotriazolyl, carbazolyl, carbolinyl, chromanyl, cinnolynyl, 2,3-dioxoindolyl, furanyl, frazanyl, furopyridyl, furopyrrolyl, imidazolyl, imidazopyrazinyl, imidazopyridinyl, imidazopyrimidinyl, imidazothiazolyl, indazolyl, indolazinyl, indolynyl, indolyl, isobenzofuranyl, isochromanyl, isoindolyl, isoquinolyl, isoxazolopyridyl, isoxazolynyl, isoxazolyl, isothiazolyl, naphthyridinyl, oxazolynyl, oxadiazolyl, oxazolyl, oxetanyl, 2-oxoindolyl, oxoisoindolyl, phthalazyl, pyrazolyl, pyrazolopyridyl, pyrazolopyrimidinyl, pyrazinyl, pyridyl, pyrimidyl, pyridazinyl, pyridopyrimidinyl, pyrrolopyridyl, pyrrolyl, quinazolynyl, quinolyl, quinoxalynyl, tetrazolopyridyl, tetrazolyl, thiadiazoleyl, thiazolyl, thiophenyl, thienopyrazinyl, thienopyrazolyl, thienopyridyl, thienopyrrolyl, triazolopyrimidinyl, triazolyl, 4-oxo-1,4-dihydroquinolyl, 2-oxo-1,2-dihydropyridyl, 4-oxo-1,4-dihydropyrimidyl, 2-oxo-1,2-dihydroquinolyl, 4-oxo-4H-pyrido[1,2-a]pyrimidyl, 4-oxo-1,4-dihydro-1,8-naphthyridyl, and N-oxides thereof, and wherein the saturated heterocyclic moieties include azetidynyl, 1,4-dioxanyl, hexahydroazepinyl, piperazinyl, piperidinyl, pyridin-2-onyl, pyrrolidinyl, morpholynyl, tetrahydrofuranyl, thiomorpholynyl, triazolopyrimidyl, tetrahydrothienyl, 3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazinyl, 2-oxo-2,5,6,7-tetrahydro-1H-cyclopentapyridyl, 4,5,6,7-tetrahydro-indazolyl,

5,6,7,8-tetrahydro-1,6-naphthyridyl, and N-oxides thereof and S-oxides thereof.

[0055] The term "C₀", as used herein, means direct bond.

[0056] The term "protecting group", as used herein, means a amino or carboxyl protecting group which is selected from typical amino or carboxyl protecting groups described in *Protective Groups in Organic Synthesis* edited by T. W. Greene et al. (John Wiley & Sons, 2007).

[0057] The term "treating" and "treatment", as used herein, refers to curative, palliative and prophylactic treatment, including reversing, alleviating, inhibiting the progress of, or preventing the disorder or condition to which such term applies, or one or more symptoms of such disorder or condition.

[0058] As used herein, the article "a" or "an" refers to both the singular and plural form of the object to which it refers unless indicated otherwise.

[0059] Included within the scope of the "compounds of the invention" are all salts, solvates, hydrates, complexes, polymorphs, prodrugs, radiolabeled derivatives, stereoisomers and optical isomers of the compounds of formula (I).

[0060] The compounds of formula (I) can form acid addition salts thereof. It will be appreciated that for use in medicine the salts of the compounds of formula (I) should be pharmaceutically acceptable. Suitable pharmaceutically acceptable salts will be apparent to those skilled in the art and include those described in *J. Pharm. Sci.*, 1977, 66, 1-19, such as acid addition salts formed with inorganic acids e.g. hydrochloric, hydrobromic, sulfuric, nitric or phosphoric acid; and organic acids e.g. succinic, maleic, formic, acetic, trifluoroacetic, propionic, fumaric, citric, tartaric, benzoic, p-toluenesulfonic, methanesulfonic or naphthalenesulfonic acid. Certain of the compounds of formula (I) may form acid addition salts with one or more equivalents of the acid. The present invention includes within its scope all possible stoichiometric and non-stoichiometric forms. In addition, certain compounds containing an acidic function such as a carboxy can be isolated in the form of their inorganic salt in which the counter ion can be selected from sodium, potassium, lithium, calcium, magnesium and the like, as well as from organic bases.

[0061] Also within the scope of the invention are so-called "prodrugs" of the compounds of formula (I). Thus certain derivatives of compounds of formula (I) which may have little or no pharmacological activity themselves can, when administered into or onto the body, be converted into compounds of formula (I) having the desired activity, for example, by hydrolytic cleavage. Such derivatives are referred to as "prodrugs". Further information on the use of prodrugs may be found in *Pro-drugs as Novel Delivery Systems*, Vol. 14, ACS Symposium Series (T Higuchi and W Stella) and *Bioreversible Carriers in Drug Design*, Pergamon Press, 1987 (ed. E B Roche, American Pharmaceutical Association).

[0062] Prodrugs in accordance with the invention can, for example, be produced by replacing appropriate functionalities present in the compounds of formula (I) with certain moieties known to those skilled in the art as 'pro-moieties' as described, for example, in Design of Prodrugs by H Bundgaard (Elsevier, 1985). Some examples of prodrugs in accordance with the invention include:

(i) where the compound of formula (I) contains an alcohol functionality (-OH), compounds wherein the hydroxy group is replaced with a moiety convertible in vivo into the hydroxy group. Said moiety convertible in vivo into the hydroxy group means a moiety transformable in vivo into a hydroxyl group by e.g. hydrolysis and/or by an enzyme, e.g. an esterase. Examples of said moiety include, but are not limited to, ester and ether groups which may be hydrolyzed easily in vivo. Preferred are the moieties replaced the hydrogen of hydroxy group with acyloxyalkyl, 1-(alkoxycarbonyloxy)alkyl, phthalidyl and acyloxyalkyloxycarbonyl such as pivaloyloxymethyloxycarbonyl.

(ii) where the compound of the formula (I) contains an amino group, an amide derivative prepared by reacting with a suitable acid halide or a suitable acid anhydride is exemplified as a prodrug. A particularly preferred amide derivative as a prodrug is -NHCO(CH₂)₂OCH₃, -NHCOCH(NH₂)CH₃ or the like.

[0063] Further examples of replacement groups in accordance with the foregoing examples and examples of other prodrug types may be found in the aforementioned references.

[0064] The compounds of formula (I) and salts thereof may be prepared in crystalline or non-crystalline form, and, if crystalline, may optionally be hydrated or solvated. This invention includes within its scope stoichiometric hydrates or solvates as well as compounds containing variable amounts of water and/or solvent.

[0065] Salts and solvates having non-pharmaceutically acceptable counter-ions or associated solvents are within the scope of the present invention, for example, for use as intermediates in the preparation of other compounds of formula (I) and their pharmaceutically acceptable salts.

[0066] The compounds of formula (I) may have polymorphs in crystalline form, which are within the scope of the present invention.

[0067] Additionally, the compounds of formula (I) may be administered as prodrugs. As used herein, a "prodrug" of a compound of formula (I) is a functional derivative of the compound which, upon administration to a patient, eventually liberates the compound of formula (I) in vivo. Administration of a compound of formula (I) as a prodrug may enable the skilled artisan to do one or more of the following: (a) modify the onset of action of the compound in vivo; (b) modify the duration of action of the compound in vivo; (c) modify the transportation or distribution of the compound in vivo; (d) modify the solubility of the compound in vivo; and (e) overcome a side effect or other

difficulty encountered with the compound. Typical functional derivatives used to prepare prodrugs include modifications of the compound that are chemically or enzymatically cleaved in vivo. Such modifications, which include the preparation of phosphates, amides, esters, thioesters, carbonates, and carbamates, are well known to those skilled in the art.

[0068] In certain of the compounds of formula (I), there may be some chiral carbon atoms. In such cases, compounds of formula (I) exist as stereoisomers. The invention extends to all optical isomers such as stereoisomeric forms of the compounds of formula (I) including enantiomers, diastereoisomers and mixtures thereof, such as racemates. The different stereoisomeric forms may be separated or resolved one from the other by conventional methods or any given isomer may be obtained by conventional stereoselective or asymmetric syntheses.

[0069] Certain of the compounds herein can exist in various tautomeric forms and it is to be understood that the invention encompasses all such tautomeric forms.

[0070] The invention also includes isotopically-labeled compounds, which are identical to those described herein, but for the fact that one or more atoms are replaced by an atom having an atomic mass or mass number different from the atomic mass or mass number usually found in nature. Examples of isotopes that can be incorporated into compounds of the invention include isotopes of hydrogen, carbon, nitrogen, oxygen, phosphorous, fluorine, iodine, and chlorine, such as ^2H , ^3H , ^{11}C , ^{13}C , ^{14}C , ^{18}F , ^{123}I and ^{125}I . Compounds of the invention that contain the aforementioned isotopes and/or other isotopes of other atoms are within the scope of the present invention. Isotopically-labeled compounds of the present invention, for example those into which radioactive isotopes such as ^3H , ^{14}C are incorporated, are useful in drug and/or substrate tissue distribution assays. Tritiated, i.e., ^3H , and carbon-14, i.e., ^{14}C , isotopes are particularly preferred for their ease of preparation and detectability. ^{11}C and ^{18}F isotopes are particularly useful in PET (positron emission tomography), and ^{125}I isotopes are particularly useful in SPECT (single photon emission computerized tomography), all useful in brain imaging. Further, substitution with heavier isotopes such as deuterium, i.e., ^2H , can afford certain therapeutic advantages resulting from greater metabolic stability, for example increased in vivo half-life or reduced dosage requirements and, hence, may be preferred in some circumstances. Isotopically labeled compounds of the invention can generally be prepared by carrying out the procedures disclosed in the Schemes and/or in the Examples below, then substituting a readily available isotopically labeled reagent for a non-isotopically labeled reagent.

[0071] The compounds of formula (I), being $\text{Na}_{\text{v}1.3}$ channel blockers, are potentially useful in the treatment of a range of disorders. The treatment of pain, particularly chronic, inflammatory, neuropathic, nociceptive and visceral pain, is a preferred use.

- [0072] Physiological pain is an important protective mechanism designed to warn of danger from potentially injurious stimuli from the external environment. The system operates through a specific set of primary sensory neurones and is activated by noxious stimuli via peripheral transducing mechanisms (see Millan, 1999, *Prog. Neurobiol.*, 57, 1-164 for a review). These sensory fibres are known as nociceptors and are characteristically small diameter axons with slow conduction velocities. Nociceptors encode the intensity, duration and quality of noxious stimulus and by virtue of their topographically organised projection to the spinal cord, the location of the stimulus. The nociceptors are found on nociceptive nerve fibres of which there are two main types, A-delta fibres (myelinated) and C fibres (non-myelinated). The activity generated by nociceptor input is transferred, after complex processing in the dorsal horn, either directly, or via brain stem relay nuclei, to the ventrobasal thalamus and then on to the cortex, where the sensation of pain is generated.
- [0073] Pain may generally be classified as acute or chronic. Acute pain begins suddenly and is short-lived (usually in twelve weeks or less). It is usually associated with a specific cause such as a specific injury and is often sharp and severe. It is the kind of pain that can occur after specific injuries resulting from surgery, dental work, a strain or a sprain. Acute pain does not generally result in any persistent psychological response. In contrast, chronic pain is long-term pain, typically persisting for more than three months and leading to significant psychological and emotional problems. Common examples of chronic pain are neuropathic pain (e.g. painful diabetic neuropathy, postherpetic neuralgia), carpal tunnel syndrome, back pain, headache, cancer pain, arthritic pain and chronic post-surgical pain.
- [0074] When a substantial injury occurs to body tissue, via disease or trauma, the characteristics of nociceptor activation are altered and there is sensitisation in the periphery, locally around the injury and centrally where the nociceptors terminate. These effects lead to a heightened sensation of pain. In acute pain these mechanisms can be useful, in promoting protective behaviours which may better enable repair processes to take place. The normal expectation would be that sensitivity returns to normal once the injury has healed. However, in many chronic pain states, the hypersensitivity far outlasts the healing process and is often due to nervous system injury. This injury often leads to abnormalities in sensory nerve fibres associated with maladaptation and aberrant activity (Woolf & Salter, 2000, *Science*, 288, 1765-1768).
- [0075] Clinical pain is present when discomfort and abnormal sensitivity feature among the patient's symptoms. Patients tend to be quite heterogeneous and may present with various pain symptoms. Such symptoms include: 1) spontaneous pain which may be dull, burning, or stabbing; 2) exaggerated pain responses to noxious stimuli (hyperalgesia); and 3) pain produced by normally innocuous stimuli (allodynia - Meyer

et al., 1994, Textbook of Pain, 13-44). Although patients suffering from various forms of acute and chronic pain may have similar symptoms, the underlying mechanisms may be different and may, therefore, require different treatment strategies. Pain can also therefore be divided into a number of different subtypes according to differing pathophysiology, including nociceptive, inflammatory and neuropathic pain.

[0076] Nociceptive pain is induced by tissue injury or by intense stimuli with the potential to cause injury. Pain afferents are activated by transduction of stimuli by nociceptors at the site of injury and activate neurons in the spinal cord at the level of their termination. This is then relayed up the spinal tracts to the brain where pain is perceived (Meyer et al., 1994, Textbook of Pain, 13-44). The activation of nociceptors activates two types of afferent nerve fibres. Myelinated A-delta fibres transmit rapidly and are responsible for sharp and stabbing pain sensations, whilst unmyelinated C fibres transmit at a slower rate and convey a dull or aching pain. Moderate to severe acute nociceptive pain is a prominent feature of pain from central nervous system trauma, strains/sprains, burns, myocardial infarction and acute pancreatitis, post-operative pain (pain following any type of surgical procedure), posttraumatic pain, renal colic, cancer pain and back pain. Cancer pain may be chronic pain such as tumour related pain (e.g. bone pain, headache, facial pain or visceral pain) or pain associated with cancer therapy (e.g. postchemotherapy syndrome, chronic postsurgical pain syndrome or post radiation syndrome). Cancer pain may also occur in response to chemotherapy, immunotherapy, hormonal therapy or radiotherapy. Back pain may be due to herniated or ruptured intervertebral discs or abnormalities of the lumbar facet joints, sacroiliac joints, paraspinal muscles or the posterior longitudinal ligament. Back pain may resolve naturally but in some patients, where it lasts over 12 weeks, it becomes a chronic condition which can be particularly debilitating.

[0077] Neuropathic pain is currently defined as pain initiated or caused by a primary lesion or dysfunction in the nervous system. Nerve damage can be caused by trauma and disease and thus the term 'neuropathic pain' encompasses many disorders with diverse aetiologies. These include, but are not limited to, peripheral neuropathy, diabetic neuropathy, post herpetic neuralgia, trigeminal neuralgia, back pain, cancer neuropathy, HIV neuropathy, phantom limb pain, carpal tunnel syndrome, central post-stroke pain and pain associated with chronic alcoholism, hypothyroidism, uremia, multiple sclerosis, spinal cord injury, Parkinson's disease, epilepsy and vitamin deficiency. Neuropathic pain is pathological as it has no protective role. It is often present well after the original cause has dissipated, commonly lasting for years, significantly decreasing a patient's quality of life (Woolf and Mannion, 1999, Lancet, 353, 1959-1964). The symptoms of neuropathic pain are difficult to treat, as they are often heterogeneous even between patients with the same disease (Woolf & Decosterd,

1999, Pain Supp., 6, S141-S147; Woolf and Mannion, 1999, Lancet, 353, 1959-1964). They include spontaneous pain, which can be continuous, and paroxysmal or abnormal evoked pain, such as hyperalgesia (increased sensitivity to a noxious stimulus) and allodynia (sensitivity to a normally innocuous stimulus).

[0078] The inflammatory process is a complex series of biochemical and cellular events, activated in response to tissue injury or the presence of foreign substances, which results in swelling and pain (Levine and Taiwo, 1994, Textbook of Pain, 45-56). Arthritic pain is the most common inflammatory pain. Rheumatoid disease is one of the commonest chronic inflammatory conditions in developed countries and rheumatoid arthritis is a common cause of disability. The exact aetiology of rheumatoid arthritis is unknown, but current hypotheses suggest that both genetic and microbiological factors may be important (Grennan & Jayson, 1994, Textbook of Pain, 397-407). It has been estimated that almost 16 million Americans have symptomatic osteoarthritis (OA) or degenerative joint disease, most of whom are over 60 years of age, and this is expected to increase to 40 million as the age of the population increases, making this a public health problem of enormous magnitude (Houge & Mersfelder, 2002, Ann Pharmacother., 36, 679-686; McCarthy et al., 1994, Textbook of Pain, 387-395). Most patients with osteoarthritis seek medical attention because of the associated pain. Arthritis has a significant impact on psychosocial and physical function and is known to be the leading cause of disability in later life. Ankylosing spondylitis is also a rheumatic disease that causes arthritis of the spine and sacroiliac joints. It varies from intermittent episodes of back pain that occur throughout life to a severe chronic disease that attacks the spine, peripheral joints and other body organs.

[0079] Another type of inflammatory pain is visceral pain which includes pain associated with inflammatory bowel disease (IBD). Visceral pain is pain associated with the viscera, which encompass the organs of the abdominal cavity. These organs include the sex organs, spleen and part of the digestive system. Pain associated with the viscera can be divided into digestive visceral pain and non-digestive visceral pain. Commonly encountered gastrointestinal (GI) disorders that cause pain include functional bowel disorder (FBD) and inflammatory bowel disease (IBD). These GI disorders include a wide range of disease states that are currently only moderately controlled, including, in respect of FBD, gastro-esophageal reflux, dyspepsia, irritable bowel syndrome (IBS) and functional abdominal pain syndrome (FAPS), and, in respect of IBD, Crohn's disease, ileitis and ulcerative colitis, all of which regularly produce visceral pain. Other types of visceral pain include the pain associated with dysmenorrhea, cystitis and pancreatitis and pelvic pain.

[0080] It should be noted that some types of pain have multiple aetiologies and thus can be classified in more than one area, e.g. back pain and cancer pain have both nociceptive

and neuropathic components.

[0081] Other types of pain include:

- pain resulting from musculo-skeletal disorders, including myalgia, fibromyalgia, spondylitis, sero-negative (non-rheumatoid) arthropathies, non-articular rheumatism, dystrophinopathy, glycogenolysis, polymyositis and pyomyositis;

- heart and vascular pain, including pain caused by angina, myocardial infarction, mitral stenosis, pericarditis, Raynaud's phenomenon, scleredoma and skeletal muscle ischemia;

- head pain, such as migraine (including migraine with aura and migraine without aura), cluster headache, tension-type headache mixed headache and headache associated with vascular disorders; and

- orofacial pain, including dental pain, otic pain, burning mouth syndrome and temporomandibular myofascial pain.

[0082] The aryl carboxamide derivatives of formula (I) are also expected to be useful in the treatment of multiple sclerosis.

[0083] The invention also relates to therapeutic use of the aryl carboxamide derivatives of formula (I) as agents for treating or relieving the symptoms of neurodegenerative disorders. Such neurodegenerative disorders include, for example, Alzheimer's disease, Huntington's disease, Parkinson's disease, and Amyotrophic Lateral Sclerosis. The present invention also covers treating neurodegenerative disorders termed acute brain injury. These include but are not limited to: stroke, head trauma, and asphyxia. Stroke refers to a cerebral vascular disease and may also be referred to as a cerebral vascular accident (CVA) and includes acute thromboembolic stroke. Stroke includes both focal and global ischemia. Also, included are transient cerebral ischemic attacks and other cerebral vascular problems accompanied by cerebral ischemia. These vascular disorders may occur in a patient undergoing carotid endarterectomy specifically or other cerebrovascular or vascular surgical procedures in general, or diagnostic vascular procedures including cerebral angiography and the like. Other incidents are head trauma, spinal cord trauma, or injury from general anoxia, hypoxia, hypoglycemia, hypotension as well as similar injuries seen during procedures from embole, hyperfusion, and hypoxia. The instant invention would be useful in a range of incidents, for example, during cardiac bypass surgery, in incidents of intracranial hemorrhage, in perinatal asphyxia, in cardiac arrest, and status epilepticus.

[0084] A skilled physician will be able to determine the appropriate situation in which subjects are susceptible to or at risk of, for example, stroke as well as suffering from stroke for administration by methods of the present invention.

[0085] TTX-S sodium channels have been implicated in a wide range of biological functions. This has suggested a potential role for these receptors in a variety of disease

processes in humans or other species. The compounds of the present invention have utility in treating, preventing, ameliorating, controlling or reducing the risk of a variety of neurological and psychiatric disorders associated with TTX-S sodium channels, including one or more of the following conditions or diseases: pain, acute pain, chronic pain, neuropathic pain, inflammatory pain, visceral pain, nociceptive pain, multiple sclerosis, neurodegenerative disorder, irritable bowel syndrome, osteoarthritis, rheumatoid arthritis, neuropathological disorders, functional bowel disorders, inflammatory bowel diseases, pain associated with dysmenorrhea, pelvic pain, cystitis, pancreatitis, migraine, cluster and tension headaches, diabetic neuropathy, peripheral neuropathic pain, sciatica, fibromyalgia Crohn's disease, epilepsy or epileptic conditions, bipolar depression, tachyarrhythmias, mood disorder, bipolar disorder, psychiatric disorders such as anxiety and depression, myotonia, arrhythmia, movement disorders, neuroendocrine disorders, ataxia, incontinence, visceral pain, trigeminal neuralgia, herpetic neuralgia, general neuralgia, postherpetic neuralgia, radicular pain, sciatica, back pain, head or neck pain, severe or intractable pain, breakthrough pain, postsurgical pain, stroke, cancer pain, seizure disorder and causalgia.

[0086] The dosage of active ingredient in the compositions of this invention may be varied, however, it is necessary that the amount of the active ingredient be such that a suitable dosage form is obtained. The active ingredient may be administered to patients (animals and human) in need of such treatment in dosages that will provide optimal pharmaceutical efficacy.

[0087] The selected dosage depends upon the desired therapeutic effect, on the route of administration, and on the duration of the treatment. The dose will vary from patient to patient depending upon the nature and severity of disease, the patient's weight, special diets then being followed by a patient, concurrent medication, and other factors which those skilled in the art will recognize.

[0088] For administration to human patients, the total daily dose of the compounds of the invention is typically in the range 0.1 mg to 1000 mg depending, of course, on the mode of administration. For example, oral administration may require a total daily dose of from 1 mg to 1000 mg, while an intravenous dose may only require from 0.1 mg to 100 mg. The total daily dose may be administered in single or divided doses and may, at the physician's discretion, fall outside of the typical range given herein.

[0089] These dosages are based on an average human subject having a weight of about 60kg to 70kg. The physician will readily be able to determine doses for subjects whose weight falls outside this range, such as infants and the elderly.

[0090] For the avoidance of doubt, references herein to "treatment" include references to curative, palliative and prophylactic treatment.

[0091] In one embodiment, the dosage range will be about 0.5 mg to 500 mg per patient per

day; in another embodiment about 0.5 mg to 200 mg per patient per day; in another embodiment about 1 mg to 100 mg per patient per day; and in another embodiment about 5 mg to 50 mg per patient per day; in yet another embodiment about 1 mg to 30 mg per patient per day. Pharmaceutical compositions of the present invention may be provided in a solid dosage formulation such as comprising about 0.5 mg to 500 mg active ingredient, or comprising about 1 mg to 250 mg active ingredient. The pharmaceutical composition may be provided in a solid dosage formulation comprising about 1 mg, 5 mg, 10mg, 25 mg, 50 mg, 100 mg, 200 mg or 250 mg active ingredient. For oral administration, the compositions may be provided in the form of tablets containing 1.0 to 1000 milligrams of the active ingredient, such as 1, 5, 10, 15, 20, 25, 50, 75, 100, 150, 200, 250, 300, 400, 500, 600, 750, 800, 900, and 1000 milligrams of the active ingredient for the symptomatic adjustment of the dosage to the patient to be treated. The compounds may be administered on a regimen of 1 to 4 times per day, such as once or twice per day.

[0092] The compounds of the present invention may be used in combination with one or more other drugs in the treatment, prevention, control, amelioration, or reduction of risk of diseases or conditions for which compounds of the present invention or the other drugs may have utility, where the combination of the drugs together are safer or more effective than either drug alone. Such other drug(s) may be administered, by a route and in an amount commonly used therefore, contemporaneously or sequentially with a compound of the present invention. When a compound of the present invention is used contemporaneously with one or more other drugs, a pharmaceutical composition in unit dosage form containing such other drugs and the compound of the present invention is envisioned. However, the combination therapy may also include therapies in which the compound of the present invention and one or more other drugs are administered on different overlapping schedules. It is also contemplated that when used in combination with one or more other active ingredients, the compounds of the present invention and the other active ingredients may be used in lower doses than when each is used singly.

[0093] Accordingly, the pharmaceutical compositions of the present invention include those that contain one or more other active ingredients, in addition to a compound of the present invention. The above combinations include combinations of a compound of the present invention not only with one other active compound, but also with two or more other active compounds.

[0094] Likewise, compounds of the present invention may be used in combination with other drugs that are used in the prevention, treatment, control, amelioration, or reduction of risk of the diseases or conditions for which compounds of the present invention are useful. Such other drugs may be administered, by a route and in an

amount commonly used therefore, contemporaneously or sequentially with a compound of the present invention. When a compound of the present invention is used contemporaneously with one or more other drugs, a pharmaceutical composition containing such other drugs in addition to the compound of the present invention is envisioned. Accordingly, the pharmaceutical compositions of the present invention include those that also contain one or more other active ingredients, in addition to a compound of the present invention.

- [0095] The weight ratio of the compound of the present invention to the second active ingredient may be varied and will depend upon the effective dose of each ingredient. Generally, an effective dose of each will be used. Thus, for example, when a compound of the present invention is combined with another agent, the weight ratio of the compound of the present invention to the other agent will generally range from about 1000:1 to about 1:1000, including about 200: 1 to about 1:200. Combinations of a compound of the present invention and other active ingredients will generally also be within the aforementioned range, but in each case, an effective dose of each active ingredient should be used. In such combinations the compound of the present invention and other active agents may be administered separately or in conjunction. In addition, the administration of one element may be prior to, concurrent to, or subsequent to the administration of other agent(s).
- [0096] A TTX-S sodium channels blocker may be usefully combined with another pharmacologically active compound, or with two or more other pharmacologically active compounds, particularly in the treatment of inflammatory, pain and urological diseases or disorders. For example, a TTX-S sodium channels blocker, particularly a compound of formula (I), or a prodrug thereof or a pharmaceutically acceptable salt or solvate thereof, as defined above, may be administered simultaneously, sequentially or separately in combination with one or more agents selected from:
- [0097] - an opioid analgesic, e.g. morphine, heroin, hydromorphone, oxymorphone, levorphanol, levallorphan, methadone, meperidine, fentanyl, cocaine, codeine, dihydrocodeine, oxycodone, hydrocodone, propoxyphene, nalmefene, nalorphine, naloxone, naltrexone, buprenorphine, butorphanol, nalbuphine or pentazocine;
- [0098] - a nonsteroidal antiinflammatory drug (NSAID), e.g. aspirin, diclofenac, diflusal, etodolac, fenbufen, fenoprofen, flufenisal, flurbiprofen, ibuprofen, indomethacin, ketoprofen, ketorolac, meclofenamic acid, mefenamic acid, meloxicam, nabumetone, naproxen, nimesulide, nitroflurbiprofen, olsalazine, oxaprozin, phenylbutazone, piroxicam, sulfasalazine, sulindac, tolmetin or zomepirac;
- [0099] - a barbiturate sedative, e.g. amobarbital, aprobarbital, butabarbital, butabital, mephobarbital, metharbital, methohexital, pentobarbital, phenobarbital, secobarbital, talbutal, theamylal or thiopental;

- a benzodiazepine having a sedative action, e.g. chlordiazepoxide, clorazepate, diazepam, flurazepam, lorazepam, oxazepam, temazepam or triazolam;
 - an H1 antagonist having a sedative action, e.g. diphenhydramine, pyrillamine, promethazine, chlorpheniramine or chlorcyclizine;
 - a sedative such as glutethimide, meprobamate, methaqualone or dichloralphenazone;
 - a skeletal muscle relaxant, e.g. baclofen, carisoprodol, chlorzoxazone, cyclobenzaprine, methocarbamol or orphenadine;
- [0100] - an NMDA receptor antagonist, e.g. dextromethorphan ((+)-3-hydroxy-N-methylmorphinan) or its metabolite dextrophan ((+)-3-hydroxy-N-methylmorphinan), ketamine, memantine, pyrroloquinoline quinine, cis-4-(phosphonomethyl)-2-piperidinecarboxylic acid, budipine, EN-3231 (MorphiDex(registered trademark), a combination formulation of morphine and dextromethorphan), topiramate, neramexane or perzinfotel including an NR2B antagonist, e.g. ifenprodil, traxoprodil or (-)-(R)-6-{2-[4-(3-fluorophenyl)-4-hydroxy-1-piperidinyl]-1-hydroxyethyl-3,4-dihydro-2(1H)-quinolinone;
- [0101] - an alpha-adrenergic, e.g. doxazosin, tamsulosin, clonidine, guanfacine, dexmetatomidine, modafinil, or 4-amino-6,7-dimethoxy-2-(5-methanesulfonamido-1,2,3,4-tetrahydroisoquinol-2-yl)-5-(2-pyridyl) quinazoline;
- a tricyclic antidepressant, e.g. desipramine, imipramine, amitriptyline or nortriptyline;
 - an anticonvulsant, e.g. carbamazepine, lamotrigine, topiramate or valproate;
- [0102] - a tachykinin (NK) antagonist, particularly an NK-3, NK-2 or NK-1 antagonist, e.g. alphaR,9R)-7-[3,5-bis(trifluoromethyl)benzyl]-8,9,10,11-tetrahydro-9-methyl-5-(4-methylphenyl)-7H-[1,4]diazocino[2,1-g][1,7]-naphthyridine-6-13-dione (TAK-637), 5-[[2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy-3-(4-fluorophenyl)-4-morpholinyl]-methyl]-1,2-dihydro-3H-1,2,4-triazol-3-one (MK-869), aprepitant, lanepitant, dapitant or 3-[[2-methoxy-5-(trifluoromethoxy)phenyl]-methylamino]-2-phenylpiperidine (2S,3S);
- a muscarinic antagonist, e.g. oxybutynin, tolterodine, propiverine, trospium chloride, darifenacin, solifenacin, temiverine and ipratropium;
 - a COX-2 selective inhibitor, e.g. celecoxib, rofecoxib, parecoxib, valdecoxib, deracoxib, etoricoxib, or lumiracoxib;
 - a coal-tar analgesic, in particular paracetamol;
- [0103] - a neuroleptic such as droperidol, chlorpromazine, haloperidol, perphenazine, thioridazine, mesoridazine, trifluoperazine, fluphenazine, clozapine, olanzapine, risperidone, ziprasidone, quetiapine, sertindole, aripiprazole, sonopiprazole, blo-

nanserin, iloperidone, perospirone, raclopride, zotepine, bifeprunox, asenapine, lurasidone, amisulpride, balaperidone, palindore, eplivanserin, osanetant, rimonabant, meclinetant, Miraxion(registered trademark) or sarizotan;

- [0104] - a vanilloid receptor agonist (e.g. resiniferatoxin) or antagonist (e.g. capsazepine);
 - a transient receptor potential cation channel subtype (V1, V2, V3, V4, M8, A1) agonists and antagonists;

- a beta-adrenergic such as propranolol;
- a local anaesthetic such as mexiletine;
- a corticosteroid such as dexamethasone;

- [0105] - a 5-HT receptor agonist or antagonist, particularly a 5-HT1B/1D agonist such as eletriptan, sumatriptan, naratriptan, zolmitriptan or rizatriptan;

- a 5-HT2A receptor antagonist such as

R(+)-alpha-(2,3-dimethoxy-phenyl)-1-[2-(4-fluorophenylethyl)]-4-piperidinemethanol (MDL-100907);

- a cholinergic (nicotinic) analgesic, such as ispronicline (TC-1734), (E)-N-methyl-4-(3-pyridinyl)-3-buten-1-amine (RJR-2403), (R)-5-(2-azetidinylmethoxy)-2-chloropyridine (ABT-594) or nicotine;
- Tramadol(registered trademark);

- [0106] - a PDEV inhibitor, such as

5-[2-ethoxy-5-(4-methyl-1-piperazinyl-sulphonyl)phenyl]-1-methyl-3-n-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one (sildenafil),

(6R,12aR)-2,3,6,7,12,12a-hexahydro-2-methyl-6-(3,4-methylenedioxyphenyl)-pyrazin o[2',1':6,1]-pyrido[3,4-b]indole-1,4-dione (IC-351 or tadalafil),

2-[2-ethoxy-5-(4-ethyl-piperazin-1-yl-1-sulphonyl)-phenyl]-5-methyl-7-propyl-3H-imidazo[5,1-f][1,2,4]triazin-4-one (vardenafil),

5-(5-acetyl-2-butoxy-3-pyridinyl)-3-ethyl-2-(1-ethyl-3-azetidiny)-2,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one,

5-(5-acetyl-2-propoxy-3-pyridinyl)-3-ethyl-2-(1-isopropyl-3-azetidiny)-2,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one,

5-[2-ethoxy-5-(4-ethylpiperazin-1-ylsulphonyl)pyridin-3-yl]-3-ethyl-2-[2-methoxyethyl]-2,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one,

4-[(3-chloro-4-methoxybenzyl)amino]-2-[(2S)-2-(hydroxymethyl)pyrrolidin-1-yl]-N-(pyrimidin-2-ylmethyl)pyrimidine-5-carboxamide,

3-(1-methyl-7-oxo-3-propyl-6,7-dihydro-1H-pyrazolo[4,3-d]pyrimidin-5-yl)-N-[2-(1-methylpyrrolidin-2-yl)ethyl]-4-propoxybenzenesulfonamide;

- [0107] - an alpha-2-delta ligand such as gabapentin, pregabalin, 3-methylgabapentin, (1 alpha,3alpha,5alpha)(3-amino-methyl-bicyclo[3.2.0]hept-3-yl)-acetic acid, (3S,5R)-3 aminomethyl-5 methyl-heptanoic acid, (3S,5R)-3 amino-5 methyl-heptanoic acid,

- (3S,5R)-3-amino-5-methyl-octanoic acid, (2S,4S)-4-(3-chlorophenoxy)proline, (2S,4S)-4-(3-fluorobenzyl)-proline, [(1R,5R,6S)-6-(aminomethyl)bicyclo[3.2.0]hept-6-yl]acetic acid, 3-(1-aminomethyl-cyclohexylmethyl)-4H-[1,2,4]oxadiazol-5-one, C-[1-(1H-tetrazol-5-ylmethyl)-cycloheptyl]-methylaniline, (3S,4S)-(1-aminomethyl-3,4-dimethyl-cyclopentyl)-acetic acid, (3S,5R)-3-aminomethyl-5-methyl-octanoic acid, (3S,5R)-3-amino-5-methyl-nonanoic acid, (3S,5R)-3-amino-5-methyl-octanoic acid, (3R,4R,5R)-3-amino-4,5-dimethyl-heptanoic acid and (3R,4R,5R)-3-amino-4,5-dimethyl-octanoic acid;
- a cannabinoid;
 - metabotropic glutamate subtype 1 receptor (mGluR1) antagonist;
- [0108] - a serotonin reuptake inhibitor such as sertraline, sertraline metabolite demethylsertraline, fluoxetine, norfluoxetine (fluoxetine desmethyl metabolite), fluvoxamine, paroxetine, citalopram, citalopram metabolite desmethylcitalopram, escitalopram, d,l-fenfluramine, femoxetine, ifoxetine, cyanodothiepin, litoxetine, dapoxetine, nefazodone, cericlamine and trazodone;
- [0109] - a noradrenaline (norepinephrine) reuptake inhibitor, such as maprotiline, lofepramine, mirtazepine, oxaprotiline, fezolamine, tomoxetine, mianserin, bupropion, bupropion metabolite hydroxybupropion, nomifensine and viloxazine (Vivalan(registered trademark)), especially a selective noradrenaline reuptake inhibitor such as reboxetine, in particular (S,S)-reboxetine;
- [0110] - a dual serotonin-noradrenaline reuptake inhibitor, such as venlafaxine, venlafaxine metabolite O-desmethylvenlafaxine, clomipramine, clomipramine metabolite desmethylclomipramine, duloxetine, milnacipran and imipramine;
- [0111] - an inducible nitric oxide synthase (iNOS) inhibitor such as S-[2-[(1-iminoethyl)amino]ethyl]-L-homocysteine, S-[2-[(1-iminoethyl)-amino]ethyl]-4,4-dioxo-L-cysteine, S-[2-[(1-iminoethyl)amino]ethyl]-2-methyl-L-cysteine, (2S,5Z)-2-amino-2-methyl-7-[(1-iminoethyl)amino]-5-heptenoic acid, 2-[[[(1R,3S)-3-amino-4-hydroxy-1-(5-thiazolyl)butyl]thio]-5-chloro-3-pyridinecarbonitrile; 2-[[[(1R,3S)-3-amino-4-hydroxy-1-(5-thiazolyl)butyl]thio]-4-chlorobenzonitrile, (2S,4R)-2-amino-4-[[2-chloro-5-(trifluoromethyl)phenyl]thio]-5-thiazolebutanol, 2-[[[(1R,3S)-3-amino-4-hydroxy-1-(5-thiazolyl)butyl]thio]-6-(trifluoromethyl)-3-pyridinecarbonitrile, 2-[[[(1R,3S)-3-amino-4-hydroxy-1-(5-thiazolyl)butyl]thio]-5-chlorobenzonitrile, N-[4-[2-(3-chlorobenzylamino)ethyl]phenyl]thiophene-2-carboxamidine, or guanidinoethyldisulfide;
- an acetylcholinesterase inhibitor such as donepezil;

- [0112] - a prostaglandin E2 subtype 4 (EP4) antagonist such as N-[(2-[4-(2-ethyl-4,6-dimethyl-1H-imidazo[4,5-c]pyridin-1-yl)phenyl]ethyl)amino)-carbonyl]-4-methylbenzenesulfonamide or 4-[(1S)-1-({[5-chloro-2-(3-fluorophenoxy)pyridin-3-yl]carbonyl}amino)ethyl]benzoic acid;
 - a leukotriene B4 antagonist; such as 1-(3-biphenyl-4-ylmethyl-4-hydroxy-chroman-7-yl)-cyclopentanecarboxylic acid (CP-105696), 5-[2-(2-Carboxyethyl)-3-[6-(4-methoxyphenyl)-5E-hexenyl]oxyphenoxy]-valeric acid (ONO-4057) or DPC-11870,
 - a 5-lipoxygenase inhibitor, such as zileuton, 6-[(3-fluoro-5-[4-methoxy-3,4,5,6-tetrahydro-2H-pyran-4-yl])phenoxy-methyl]-1-methyl-2-quinolone (ZD-2138), or 2,3,5-trimethyl-6-(3-pyridylmethyl),1,4-benzoquinone (CV-6504);
- [0113] - a sodium channel blocker, such as lidocaine;
 - a 5-HT3 antagonist, such as ondansetron;
 - a chemotherapy drug such as oxaliplatin, 5-fluorouracil, leukovolin, paclitaxel;
 - a calcitonin gene related peptide (CGRP) antagonist;
 - a bradykinin (BK1 and BK2) antagonists;
 - a voltage-gated sodium-dependent channel blockers ($\text{Na}_{v1.3}$, $\text{Na}_{v1.7}$, $\text{Na}_{v1.8}$);
 - a voltage dependent calcium channel blockers (N-type, T-type);
 - a P2X (ion channel type ATP receptor) antagonists;
 - an acid-sensing ion channel (ASIC1a, ASIC3) antagonists;
 and the pharmaceutically acceptable salts and solvates thereof.
- [0114] Such combinations offer significant advantages, including synergistic activity, in therapy.
- [0115] A pharmaceutical composition of the invention, which may be prepared by admixture, suitably at ambient temperature and atmospheric pressure, is usually adapted for oral, parenteral or rectal administration and, as such, may be in the form of tablets, capsules, oral liquid preparations, powders, granules, lozenges, reconstitutable powders, injectable or infusible solutions or suspensions or suppositories. Orally administered compositions are generally preferred. Tablets and capsules for oral administration may be in unit dose form, and may contain conventional excipients, such as binding agents (e.g. pregelatinised maize starch, polyvinylpyrrolidone or hydroxypropyl methylcellulose); fillers (e.g. lactose, microcrystalline cellulose or calcium hydrogen phosphate); tableting lubricants (e.g. magnesium stearate, talc or silica); disintegrants (e.g. potato starch or sodium starch glycolate); and acceptable wetting agents (e.g. sodium lauryl sulphate). The tablets may be coated according to methods well known in normal pharmaceutical practice.

- [0116] Oral liquid preparations may be in the form of, for example, aqueous or oily suspension, solutions, emulsions, syrups or elixirs, or may be in the form of a dry product for reconstitution with water or other suitable vehicle before use. Such liquid preparations may contain conventional additives such as suspending agents (e.g. sorbitol syrup, cellulose derivatives or hydrogenated edible fats), emulsifying agents (e.g. lecithin or acacia), non-aqueous vehicles (which may include edible oils e.g. almond oil, oily esters, ethyl alcohol or fractionated vegetable oils), preservatives (e.g. methyl or propyl-p-hydroxybenzoates or sorbic acid), and, if desired, conventional flavourings or colorants, buffer salts and sweetening agents as appropriate. Preparations for oral administration may be suitably formulated to give controlled release of the active compound or prodrug thereof or pharmaceutically acceptable salt thereof.
- [0117] For parenteral administration, fluid unit dosage forms are prepared utilising a compound of formula (I) or prodrug thereof or pharmaceutically acceptable salt thereof and a sterile vehicle. Formulations for injection may be presented in unit dosage form e.g. in ampoules or in multi-dose, utilising a compound of formula (I) or prodrug thereof or pharmaceutically acceptable salt thereof and a sterile vehicle, optionally with an added preservative. The compositions may take such forms as suspensions, solutions or emulsions in oily or aqueous vehicles, and may contain formulatory agents such as suspending, stabilising and/or dispersing agents. Alternatively, the active ingredient may be in powder form for constitution with a suitable vehicle, e.g. sterile pyrogen-free water, before use. The compound, depending on the vehicle and concentration used, can be either suspended or dissolved in the vehicle. In preparing solutions, the compound can be dissolved for injection and filter sterilised before filling into a suitable vial or ampoule and sealing. Advantageously, adjuvants such as a local anaesthetic, preservatives and buffering agents are dissolved in the vehicle. To enhance the stability, the composition can be frozen after filling into the vial and the water removed under vacuum. Parenteral suspensions are prepared in substantially the same manner, except that the compound is suspended in the vehicle instead of being dissolved, and sterilisation cannot be accomplished by filtration. The compound can be sterilised by exposure to ethylene oxide before suspension in a sterile vehicle. Advantageously, a surfactant or wetting agent is included in the composition to facilitate uniform distribution of the compound.
- [0118] Lotions may be formulated with an aqueous or oily base and will in general also contain one or more emulsifying agents, stabilising agents, dispersing agents, suspending agents, thickening agents, or colouring agents. Drops may be formulated with an aqueous or non-aqueous base also comprising one or more dispersing agents, stabilising agents, solubilising agents or suspending agents. They may also contain a

preservative.

[0119] The compounds of formula (I) or prodrugs thereof or pharmaceutically acceptable salts thereof may also be formulated in rectal compositions such as suppositories or retention enemas, e.g. containing conventional suppository bases such as cocoa butter or other glycerides.

[0120] The compounds of formula (I) or prodrugs thereof or pharmaceutically acceptable salts may also be formulated as depot preparations. Such long acting formulations may be administered by implantation (for example subcutaneously or intramuscularly) or by intramuscular injection. Thus, for example, the compounds of formula (I) or prodrugs thereof or pharmaceutically acceptable salts may be formulated with suitable polymeric or hydrophobic materials (for example as an emulsion in an acceptable oil) or ion exchange resins, or as sparingly soluble derivatives, for example, as a sparingly soluble salt.

[0121] For intranasal administration, the compounds formula (I) or prodrugs thereof or pharmaceutically acceptable salts thereof may be formulated as solutions for administration via a suitable metered or unitary dose device or alternatively as a powder mix with a suitable carrier for administration using a suitable delivery device. Thus compounds of formula (I) or prodrugs thereof or pharmaceutically acceptable salts thereof may be formulated for oral, buccal, parenteral, topical (including ophthalmic and nasal), depot or rectal administration or in a form suitable for administration by inhalation or insufflation (either through the mouth or nose). The compounds of formula (I) or prodrugs thereof or pharmaceutically acceptable salts thereof may be formulated for topical administration in the form of ointments, creams, gels, lotions, pessaries, aerosols or drops (e.g. eye, ear or nose drops). Ointments and creams may, for example, be formulated with an aqueous or oily base with the addition of suitable thickening and/or gelling agents. Ointments for administration to the eye may be manufactured in a sterile manner using sterilized components.

[0122] General Synthesis

[0123] Throughout the instant application, the following abbreviations are used with the following meanings:

DMF: N,N-dimethylformamide

DMSO: Dimethyl sulfoxide

EDC: 1-Ethyl-3-(3-dimethylaminopropyl)carbodiimide Hydrochloride

HOBT: 1-Hydroxybenzotriazole

HBTU: O-(Benzotriazol-1-yl)-N,N,N',N'-tetramethyluronium Hexafluorophosphate

HPLC: High pressure liquid chromatography

LC: liquid chromatography

tR: Retention time

MHz: Megahertz

NMR: Nuclear Magnetic Resonance

TFA: Trifluoroacetic acid

THF: Tetrahydrofuran

TLC: Thin layer chromatography

[0124] The term of "base" is likewise no particular restriction on the nature of the bases used, and any base commonly used in reactions of this type may equally be used here. Examples of such bases include: alkali metal hydroxides, such as lithium hydroxide, sodium hydroxide, potassium hydroxide, and barium hydroxide; alkali metal hydrides, such as lithium hydride, sodium hydride, and potassium hydride; alkali metal alkoxides, such as sodium methoxide, sodium ethoxide, and potassium t-butoxide; alkali metal carbonates, such as lithium carbonate, sodium carbonate, potassium carbonate, and cesium carbonate; alkali metal hydrogencarbonates, such as lithium hydrogencarbonate, sodium hydrogencarbonate, and potassium hydrogencarbonate; amines, such as N-methylmorpholine, triethylamine, tripropylamine, tributylamine, diisopropylethylamine, N-methylpiperidine, pyridine, 4-pyrrolidinopyridine, picoline, 2,6-di(t-butyl)-4-methylpyridine, quinoline, N,N-dimethylaniline, N,N-diethylaniline, 1,5-diazabicyclo[4.3.0]non-5-ene (DBN), 1,4-diazabicyclo[2.2.2]octane (DABCO), 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), lutidine, and colidine; alkali metal amides, such as lithium amide, sodium amide, potassium amide, lithium diisopropyl amide, potassium diisopropyl amide, sodium diisopropyl amide, lithium bis(trimethylsilyl)amide and potassium bis(trimethylsilyl)amide. Of these, triethylamine, diisopropylethylamine, DBU, DBN, DABCO, pyridine, lutidine, colidine, sodium carbonate, sodium hydrogencarbonate, sodium hydroxide, potassium carbonate, potassium hydrogencarbonate, potassium hydroxide, barium hydroxide, and cesium carbonate are preferred.

[0125] The reactions are normally and preferably effected in the presence of inert solvent. There is no particular restriction on the nature of the solvent to be employed, provided that it has no adverse effect on the reaction or the reagents involved and that it can dissolve reagents, at least to some extent. Examples of suitable solvents include, but not limited to: halogenated hydrocarbons, such as dichloromethane, chloroform, carbon tetrachloride, and dichloroethane; ethers, such as diethyl ether, diisopropyl ether, THF, and dioxane; aromatic hydrocarbons, such as benzene, toluene and nitrobenzene; amides, such as, DMF, N,N-dimethylacetamide, and hexamethylphosphoric triamide; amines, such as N-methylmorpholine, triethylamine, tripropylamine, tributylamine, diisopropylethylamine, N-methylpiperidine, pyridine, 4-pyrrolidinopyridine, N,N-dimethylaniline, and N,N-diethylaniline; alcohols, such as methanol, ethanol, propanol, isopropanol, and butanol; nitriles, such as acetonitrile and

benzonitrile; sulfoxides, such as dimethyl sulfoxide (DMSO) and sulfolane; ketones, such as acetone and diethylketone. Of these solvents, including but not limited to DMF, DMSO, THF, diethylether, diisopropylether, dimethoxyethane, acetonitrile, dichloromethane, dichloroethane and chloroform are preferred.

Examples

[0126] The invention is illustrated in the following non-limiting examples in which, unless stated otherwise: all reagents are commercially available, all operations were carried out at room or ambient temperature, that is, in the range of about 18-25 °C; evaporation of solvent was carried out using a rotary evaporator under reduced pressure with a bath temperature of up to about 60 °C; reactions were monitored by thin layer chromatography (tlc) and reaction times are given for illustration only; the structure and purity of all isolated compounds were assured by at least one of the following techniques: tlc (Merck silica gel 60 F₂₅₄ precoated TLC plates or Merck NH₂ F₂₅₄ precoated HPTLC plates), mass spectrometry or NMR. Yields are given for illustrative purposes only. Flash column chromatography was carried out using Merck silica gel 60 (230-400 mesh ASTM) or Fuji Silysia Chromatorex(registered trademark) DU3050 (Amino Type, 30-50 micrometer) or Biotage silica (32-63 mm, KP-Sil) or Biotage amino bounded silica (35-75 mm, KP-NH). The purification of compounds using HPLC (preparative LC-MS) was performed by the following apparatus and conditions.

Apparatus; Waters MS-trigger AutoPurification™ system

Column; Waters XTerra C18, 19X50mm, 5mm particle

Condition A: Methanol or acetonitrile / 0.01%(v/v) ammonia aqueous solution

Condition B: Methanol or acetonitrile / 0.05%(v/v) formic acid aqueous solution

[0127] Low-resolution mass spectral data (ESI) were obtained by the following apparatus and conditions: Apparatus; Waters Alliance HPLC system on ZQ or ZMD mass spectrometer and UV detector. NMR data were determined at 270 MHz (JEOL JNM-LA 270 spectrometer) or 300 MHz (JEOL JNM-LA300) using deuterated chloroform (99.8% D) or dimethylsulfoxide (99.9% D) as solvent unless indicated otherwise, relative to tetramethylsilane (TMS) as internal standard in parts per million (ppm); conventional abbreviations used are: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad, etc. Chemical symbols have their usual meanings; microL (microliter(s)), microg (microgram(s)), M (mol(s) per liter), L(liter(s)), mL (milliliter(s)), g (gram(s)), mg(milligram(s)), mol (moles), mmol (millimoles).

[0128] Conditions for determining HPLC retention time:

[0129] Method A:

Apparatus: Waters ACQUITY Ultra Performance LC with TUV Detector and ZQ mass spectrometer

Column: Waters ACQUITY C18, 2.1 x 100 mm, 1.7 micrometer particle size

Column Temperature: 60 °C

Flow rate: 0.7 mL/min

Run time: 3 min

UV detection: 210 nm

MS detection: ESI positive/negative mode

Mobile phases:

A1: 10 mM Ammonium acetate

B1: acetonitrile

[Table 1]

Gradient program: (QC_neutral_full_3min)

Time (min)	A1(%)	B1(%)
0	95	5
0.1	95	5
1.8	5	95
2.3	95	5

[0130] Method B:

Apparatus: Waters 2795 Alliance HPLC with ZQ 2000 mass spectrometer and 2996 PDA detector

Column: Waters XBridge C18 4.6 x 50 mm, 5 micrometer

Column Temperature: 40 °C

Flow rate: 1.2 mL/min

Run time: 4.5 min

UV detection: 210 - 400 nm scan

MS detection: ESI positive/negative mode

Mobile phases:

A1: H₂O (Milli-Q water)

B1: acetonitrile

C: 1% aq.HCOOH

D: 1% aq.NH₃

[Table 2]

Gradient program: (QC_neutral_4pt5min)

Time (min)	A1(%)	B1(%)	C(%)	D(%)
0	85	10	2.5	2.5
0.2	85	10	2.5	2.5
3.2	0	95	2.5	2.5
3.7	0	95	2.5	2.5
3.71	85	10	2.5	2.5

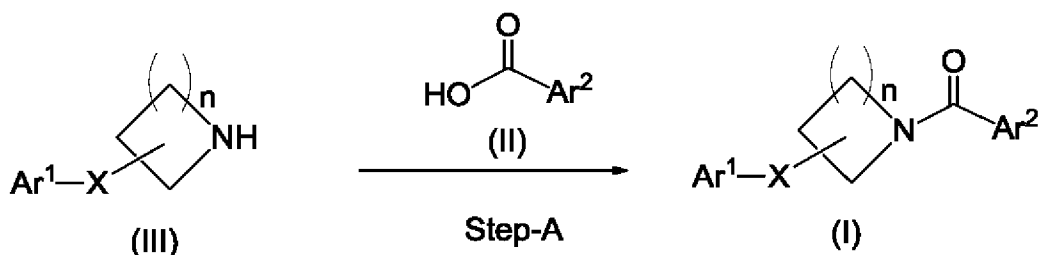
[0131] All of the aryl carboxamide derivatives of the formula (I) can be prepared by the

procedures described in the general methods presented below or by the specific methods described in the Examples section and the Preparations section, or by routine modifications thereof. The present invention also encompasses any one or more of these processes for preparing the aryl carboxamide derivatives of formula (I), in addition to any novel intermediates used therein.

[0132] In the following general methods, descriptors are as previously defined for aryl carboxamide derivatives of the formula (I) unless otherwise stated.

[0133] <Scheme-A>

[Chem.2]



[0134] In Step-A, a compound of formula (I) can be prepared from a compound of formula (III) by amidation with a compound of formula (II) using a suitable condensation agent such as HBTU and EDC-HOBT, preferably under the presence of a base such as triethylamine and N,N-diisopropylethylamine in a suitable solvent such as N,N-dimethylformamide and dichloromethane at a temperature of from about 5 to 60 °C for about 1-24 hours. In addition, a compound of formula (I) can be also prepared from a compound of formula (III) by amidation with an acid chloride prepared from a compound of formula (II) using thionylchloride, preferably under the presence of a base such as triethylamine, pyridine, and N,N-diisopropylethylamine in a suitable solvent such as dichloromethane at a temperature of from about 5 to 40 °C for about 1-24 hours.

[0135] In order to obtain some other compounds of formula (I), the appropriate conversion reaction of the substituents will be used.

[0136] For example, N-acyl / N-sulfonyl / N-alkoxycarbonyl substituted derivative can be prepared from a compound of the corresponding amine with using a suitable acid chloride / sulfonyl chloride / alkyl chloroformate using a suitable base such as pyridine and N,N-diisopropylethylamine, and a suitable solvent such as N,N-dimethylacetamide and dichloromethane at a temperature of from about 5 to 40 °C for about 1-24 hours, respectively. In addition, the corresponding amine for preparation of N-acyl / N-sulfonyl / N-alkoxycarbonyl substituted derivative can be prepared by de-protection of N-tert-butoxycarbonyl group (protecting group) under acidic condition using a suitable agent such as trifluoroacetic acid and a suitable solvent such as dichloromethane at a temperature of from about 5 to 40 °C for about 0.5-12 hours.; N-alkyl substituted

indole derivatives can be prepared from a compound of the corresponding 1H-indole using a suitable alkyl halide, a suitable base such as sodium hydride and a suitable solvent such as N,N-dimethylformamide at a temperature of from about 5 to 120 °C for about 1-24 hours; amide derivatives can be prepared from a compound of the corresponding carboxylic acid and a suitable amine by amidation according to the similar method described in Step-A. In addition, the corresponding carboxylic acid for amidation can be prepared from the ester (protecting group) by hydrolysis using a suitable agent such as aqueous sodium hydroxide solution and a suitable solvent such as methanol, tetrahydrofuran at a temperature of from about 5 to 60 °C for about 1-24 hours.

[0137] All starting materials in the following general syntheses may be commercially available or obtained by conventional methods known to those skilled in the art, otherwise noted in the intermediate synthesis part.

[0138] Intermediate synthesis part (Amine part)

[0139] Intermediate-1: 1-(3-(Piperidin-4-yloxy)phenyl)ethanone hydrochloride

[0140] <Step-1> tert-Butyl 4-(3-acetylphenoxy)piperidine-1-carboxylate

To a stirred solution of tert-butyl 4-hydroxypiperidine-1-carboxylate (4.00 g, 19.9 mmol), 1-(3-hydroxyphenyl)ethanone (2.71 g, 19.9 mmol), and triphenylphosphine (5.73 g, 21.9 mmol) in tetrahydrofuran (100 mL) was added slowly diisopropyl azodicarboxylate (4.25 mL, 21.9 mmol) at 0 °C under Nitrogen. The resulting mixture was stirred at room temperature for 17 hours. The mixture was poured into water (200 mL) and extracted with ethyl acetate (200 mL). The organic layer was washed with water (200 mL) and dried over sodium sulfate. After removal of the solvent, the residue was purified by column chromatography on silica gel eluting with n-hexane / ethyl acetate (4:1) to give 4.70 g (74%) of the title compound as colorless oil.

¹H-NMR (300 MHz, CDCl₃) δ 7.56-7.48 (2H, m), 7.37(1H, t, J = 8.1 Hz), 7.12(1H, ddd, J = 8.1, 2.6, 1.1 Hz), 4.60-4.51 (1H, m), 3.76-3.65 (2H, m), 3.41-3.30 (2H, m), 2.60 (3H, s), 1.99-1.87 (2H, m), 1.83-1.68 (2H, m), 1.47 (9H, s).

[0141] <Step-2> 1-(3-(Piperidin-4-yloxy)phenyl)ethanone hydrochloride

tert-Butyl 4-(3-acetylphenoxy)piperidine-1-carboxylate (4.70 g, 14.7 mmol, Step-1) was dissolved in 4M hydrochloric acid ethyl acetate solution (30 mL). The mixture was stirred at room temperature for 2 hours. After concentration under reduced pressure, the residue was crystallized from diisopropylether to give 3.37 g (89%) of the title compound as a white solid.

¹H-NMR (300 MHz, CDCl₃) δ 9.71 (2H, br.s), 7.61-7.55 (1H, m), 7.51-7.45 (1H, m), 7.41 (1H, t, J = 8.1 Hz), 7.12 (1H, ddd, J = 8.1, 2.6, 1.1 Hz), 4.81-4.72 (1H, m), 3.56-3.23 (4H, m), 2.60 (3H, s), 2.42-2.26 (2H, m), 2.24-2.10 (2H, m), MS (ESI) m/z: 220 (M+H)⁺.

[0142] Intermediate-2: 4-(3-(2,2,2-Trifluoroethoxy)phenoxy)piperidine hydrochloride

[0143] <Step-1> tert-Butyl 4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidine-1-carboxylate

To a stirred solution of tert-butyl 4-(3-hydroxyphenoxy)piperidine-1-carboxylate (2.00 g, 6.82 mmol) and cesium carbonate (4.44 g, 13.6 mmol) in N,N-dimethylformamide (25 mL) was added 2,2,2-trifluoroethyl trifluoromethanesulfonate (1.74 g, 7.50 mmol) at room temperature. After stirring at room temperature for 2 hours, the mixture was poured into water (100 mL) and extracted with ethyl acetate (100 mL). The organic layer was washed with water (100 mL) and dried over sodium sulfate. After removal of the solvent, the residue was purified by column chromatography on silica gel eluting with n-hexane / ethyl acetate (4:1) to give 2.42 g (95%) of the title compound as colorless oil.

¹H-NMR (300 MHz, CDCl₃) δ 7.21 (1H, q, J = 8.8 Hz), 6.63-6.58 (1H, m), 6.55-6.49 (2H, m), 4.50-4.41 (1H, m), 4.33 (2H, q, J = 8.1 Hz), 3.75-3.64 (2H, m), 3.39-3.28 (2H, m), 1.98-1.85 (2H, m), 1.81-1.67 (2H, m), 1.47 (9H, s).

[0144] <Step-2> 4-(3-(2,2,2-Trifluoroethoxy)phenoxy)piperidine hydrochloride

The title compound was prepared in 96% yield (1.94 g, a white solid) from tert-butyl 4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidine-1-carboxylate (2.42 g, 6.44 mmol, Step-1) by the similar manner in Step-2 of Intermediate-1.

¹H-NMR (300 MHz, DMSO-d₆) δ 9.15 (2H, br.s), 7.24 (1H, t, J = 8.1 Hz), 6.75-6.61 (3H, m), 4.74 (2H, q, J = 8.8 Hz), 4.75-4.64 (1H, m), 3.27-3.15 (2H, m), 3.11-2.98 (2H, m), 2.17-2.04 (2H, m), 1.93-1.77 (2H, m), MS (ESI) m/z: 276 (M+H)⁺.

[0145] Intermediate-3: 4-(3-(2-Methoxyethoxy)phenoxy)piperidine hydrochloride

[0146] <Step-1> tert-Butyl 4-(3-(2-methoxyethoxy)phenoxy)piperidine-1-carboxylate

The title compound was prepared in 96% yield (355 mg, colorless syrup) from tert-butyl 4-(3-hydroxyphenoxy)piperidine-1-carboxylate (300 mg, 1.02 mmol) and 1-bromo-2-methoxyethane (171 mg, 1.23 mmol) at a reaction temperature of 60 °C by the similar manner in Step-1 of Intermediate-2.

¹H-NMR (300 MHz, CDCl₃) δ 7.19-7.13 (1H, m), 6.53-6.50 (3H, m), 4.45-4.39 (1H, m), 4.12-4.08 (2H, m), 3.76-3.66 (4H, m), 3.45 (3H, s), 3.35-3.27 (2H, m), 1.96-1.85 (2H, m), 1.79-1.64 (2H, m), 1.47 (9H, s).

[0147] <Step-2> 4-(3-(2-Methoxyethoxy)phenoxy)piperidine hydrochloride

The title compound was prepared in 94% yield (272 mg, a white solid) from tert-butyl 4-(3-(2-methoxyethoxy)phenoxy)piperidine-1-carboxylate (355 mg, 1.01 mmol, Step-1) by the similar manner in Step-2 of Intermediate-1.

¹H-NMR (300 MHz, DMSO-d₆) δ 8.93 (1H, br.s), 7.21-7.15 (1H, m), 6.58-6.53 (3H, m), 4.67-4.62 (1H, m), 4.07-4.04 (2H, m), 3.65-3.62 (2H, m), 3.36 (3H, s), 3.30-3.18 (2H, m), 3.09-3.01 (2H, m), 2.14-2.04 (2H, m), 1.87-1.77 (2H, m), MS (ESI) m/z: 252 (M+H)⁺.

[0148] Intermediate-4: 4-((3-(Trifluoromethoxy)phenyl)sulfonyl)piperidine hydrochloride

[0149] <Step-1> tert-Butyl 4-((3-(trifluoromethoxy)phenyl)thio)piperidine-1-carboxylate

A mixture of tert-butyl 4-((methylsulfonyl)oxy)piperidine-1-carboxylate (1.34 g, 4.79 mmol), 3-(trifluoromethoxy)benzenethiol (1.12 g, 5.75 mmol) and potassium carbonate (1.99 g, 14.4 mmol) in N,N-dimethylformamide (50 mL) at 90 °C for 20 hours. The mixture was poured into water (200 mL) and extracted with ethyl acetate (200 mL). The organic layer was washed with water (200 mL) and dried over sodium sulfate. After removal of the solvent, the residue was purified by column chromatography on silica gel eluting with n-hexane / ethyl acetate (20:1) to give 1.34 g (74%) of the title compound as colorless oil.

¹H-NMR (300 MHz, CDCl₃) δ 7.36-7.25 (3H, m), 7.11-7.09 (1H, m), 3.99-3.95 (2H, m), 3.32-3.22 (1H, m), 2.99-2.92 (2H, m), 1.97-1.91 (2H, m), 1.59-1.48 (2H, m), 1.45 (9H, s)

[0150] <Step-2> tert-Butyl

4-((3-(trifluoromethoxy)phenyl)sulfonyl)piperidine-1-carboxylate

To a stirred solution of tert-butyl 4-((3-(trifluoromethoxy)phenyl)thio)piperidine-1-carboxylate (1.34 g, 3.54 mmol, Step-1) in dichloromethane (30 mL) was added m-chloroperbenzoic acid (1.95 g, 7.79 mmol) at 0 °C. After stirring at 0 °C for 1 hour, the reaction mixture was filtered. The filtrate was washed with saturated sodium thiosulfate aqueous solution (30 mL) and saturated sodium hydrogen carbonate aqueous solution (30 mL). The organic layer was dried over sodium sulfate and concentrated in vacuo. The residue was purified by column chromatography on silica gel eluting with n-hexane / ethyl acetate (3:1) to give 1.35 g (93%) of the title compound as a white solid.

¹H-NMR (300 MHz, CDCl₃) δ 7.82 (1H, dd, J = 7.3, 1.5 Hz), 7.73 (1H, s), 7.66 (1H, t, J = 8.1 Hz), 7.54 (1H, dd, J = 8.1, 1.5 Hz), 4.31-4.18 (2H, m), 3.11-3.01 (1H, m), 2.74-2.60 (2H, m), 2.01-1.97 (2H, m), 1.69-1.55 (2H, m), 1.44 (9H, s).

[0151] <Step-3> 4-((3-(Trifluoromethoxy)phenyl)sulfonyl)piperidine hydrochloride

The title compound was prepared in 96% yield (1.09 g, a white solid) from tert-butyl 4-((3-(trifluoromethoxy)phenyl)sulfonyl)piperidine-1-carboxylate (1.35 g, 3.29 mmol, Step-2) by the similar manner in Step-2 of Intermediate-1.

¹H-NMR (300 MHz, DMSO-d₆) δ 8.95 (1H, br.s), 7.94-7.87 (3H, m), 7.80 (1H, s), 3.80-3.68 (1H, m), 3.40-3.32 (2H, m), 2.90-2.78 (2H, m), 2.04-1.98 (2H, m), 1.83-1.69 (2H, m), MS (ESI) m/z: 310 (M+H)⁺.

[0152] Intermediate-5: 4-((4-(Trifluoromethoxy)phenyl)sulfonyl)piperidine hydrochloride

[0153] <Step-1> tert-Butyl 4-((4-(trifluoromethoxy)phenyl)thio)piperidine-1-carboxylate

The title compound was prepared in 41% yield (0.66 g, colorless oil) from tert-butyl 4-((methylsulfonyl)oxy)piperidine-1-carboxylate (1.20 g, 4.30 mmol) and

4-(trifluoromethoxy)benzenethiol (1.00 g, 5.15 mmol) by the similar manner in Step-1 of Intermediate-4.

¹H-NMR (300 MHz, CDCl₃) δ 7.47-7.40 (2H, m), 7.19-7.13 (2H, m), 4.05-3.89 (2H, m), 3.24-3.13 (1H, m), 2.99-2.85 (2H, m), 1.96-1.86 (2H, m), 1.60-1.48 (2H, m), 1.45 (9H, s), MS (ESI) m/z: 378 (M+H)⁺.

[0154] <Step-2> tert-Butyl

4-((4-(trifluoromethoxy)phenyl)sulfonyl)piperidine-1-carboxylate

The title compound was prepared in 80% yield (578 mg, a white solid) from tert-butyl 4-((4-(trifluoromethoxy)phenyl)thio)piperidine-1-carboxylate (662 mg, 1.75 mmol, Step-1) by the similar manner in Step-2 of Intermediate-4.

¹H-NMR (300 MHz, CDCl₃) δ 7.96-7.89 (2H, m), 7.44-7.38 (2H, m), 4.34-4.15 (2H, m), 3.11-2.99 (1H, m), 2.76-2.55 (2H, m), 2.06-1.91 (2H, m), 1.69-1.52 (2H, m), 1.43 (9H, s).

[0155] <Step-3> 4-((4-(Trifluoromethoxy)phenyl)sulfonyl)piperidine hydrochloride

The title compound was prepared in 99% yield (482 mg, a white solid) from tert-butyl 4-((4-(trifluoromethoxy)phenyl)sulfonyl)piperidine-1-carboxylate (578 mg, 1.41 mmol, Step-2) by the similar manner in Step-2 of Intermediate-1.

¹H-NMR (300 MHz, DMSO-d₆) δ 8.75 (1H, br.s), 8.04-7.99 (2H, m), 7.75-7.68 (2H, m), 3.95-3.60 (1H, m), 3.45-3.26 (2H, m), 2.91-2.79 (2H, m), 2.08-1.96 (2H, m), 1.87-1.64 (2H, m), MS (ESI) m/z: 310 (M+H)⁺.

[0156] Intermediate-6: 4-((3-Ethoxyphenyl)sulfonyl)piperidine hydrochloride

[0157] <Step-1> tert-Butyl 4-((3-ethoxyphenyl)thio)piperidine-1-carboxylate

The title compound was prepared in 67% yield (1.29 g, yellow oil) from tert-butyl 4-((methylsulfonyl)oxy)piperidine-1-carboxylate (1.60 g, 5.73 mmol) and 3-ethoxybenzenethiol (1.06 g, 6.87 mmol) by the similar manner in Step-1 of Intermediate-4.

¹H-NMR (300 MHz, CDCl₃) δ 7.20 (1H, t, J = 8.1 Hz), 7.00-6.94 (2H, m), 6.78 (1H, ddd, J = 8.1, 2.6, 1.1 Hz), 4.02 (2H, q, J = 7.0 Hz), 4.06-3.89 (2H, m), 3.29-3.16 (1H, m), 3.00-2.85 (2H, m), 2.00-1.86 (2H, m), 1.61-1.49 (2H, m), 1.45 (9H, s), 1.42 (3H, t, J = 7.0 Hz), MS (ESI) m/z: 338 (M+H)⁺.

[0158] <Step-2> tert-Butyl 4-((3-ethoxyphenyl)sulfonyl)piperidine-1-carboxylate

The title compound was prepared in 83% yield (1.16 g, a white solid) from tert-butyl 4-((3-ethoxyphenyl)thio)piperidine-1-carboxylate (1.29 g, 3.81 mmol, Step-1) by the similar manner in Step-2 of Intermediate-4.

¹H-NMR (300 MHz, CDCl₃) δ 7.46 (1H, q, J = 8.1 Hz), 7.45-7.39 (1H, m), 7.36-7.32 (1H, m), 7.20-7.14 (1H, m), 4.30-4.15 (2H, m), 4.09 (2H, q, J = 7.0 Hz), 3.12-2.94 (1H, m), 2.75-2.56 (2H, m), 2.05-1.88 (2H, m), 1.70-1.52 (2H, m), 1.45 (3H, t, J = 7.0 Hz), 1.43 (9H, s).

[0159] <Step-3> 4-((3-Ethoxyphenyl)sulfonyl)piperidine hydrochloride

The title compound was prepared in 98% yield (0.95 g, a white solid) from tert-butyl 4-((3-ethoxyphenyl)sulfonyl)piperidine-1-carboxylate (1.16 g, 3.15 mmol, Step-2) by the similar manner in Step-2 of Intermediate-1.

¹H-NMR (300 MHz, DMSO-d₆) δ 7.62 (1H, t, J = 8.1 Hz), 7.44-7.33 (2H, m), 7.30-7.26 (1H, m), 4.13 (2H, q, J = 7.0 Hz), 3.71-3.58 (1H, m), 3.43-3.28 (2H, m), 2.93-2.73 (2H, m), 2.06-1.93 (2H, m), 1.82-1.65 (2H, m), 1.36 (3H, t, J = 7.0 Hz), MS (ESI) m/z: 270 (M+H)⁺.

[0160] Intermediate synthesis part (Carboxylic acid part)

[0161] Intermediate-7: 3-(5-Fluoro-1H-benzo[d]imidazol-2-yl)benzoic acid

A mixture of 3-formylbenzoic acid (500 mg, 3.33 mmol) and 4-fluorobenzene-1,2-diamine (420 mg, 3.33 mmol) in ethanol (10 mL) was refluxed for 5 hours. After cooling to room temperature, the precipitate was collected by filtration and dried to give 311 mg (36%) of the title compound as a brown solid.

MS (ESI) m/z: 257 (M+H)⁺.

[0162] Intermediate-8: 3-(1-Methyl-1H-benzo[d]imidazol-2-yl)benzoic acid

The title compound was prepared in 51% yield (428 g, a slight brown solid) from 3-formylbenzoic acid (500 mg, 3.33 mmol) and N1-methylbenzene-1,2-diamine (407 mg, 3.33 mmol) by the similar manner in Intermediate-7.

MS (ESI) m/z: 253 (M+H)⁺.

[0163] Intermediate-9: 1-(2-Methoxyethyl)-1H-indole-5-carboxylic acid

[0164] <Step-1> Methyl 1-(2-methoxyethyl)-1H-indole-5-carboxylate

To a stirred solution of methyl 1H-indole-5-carboxylate (200 mg, 1.14 mmol) and sodium hydride (60% in oil, 39 mg, 1.71 mmol) in N,N-dimethylformamide (3 mL) was added 1-bromo-2-methoxyethane (190 mg, 1.37 mmol) at room temperature. Then the mixture was stirred at 60 °C for 2 hours. The mixture was poured into water (20 mL) and extracted with ethyl acetate (20 mL). The organic layer was washed with water (20 mL) and dried over sodium sulfate. After removal of the solvent, the residue was purified by column chromatography on silica gel eluting with n-hexane / ethyl acetate (2:1) to give 132 mg (50%) of the title compound as colorless syrup.

MS (ESI) m/z: 234 (M+H)⁺.

[0165] <Step-2> 1-(2-Methoxyethyl)-1H-indole-5-carboxylic acid

A mixture of methyl 1-(2-methoxyethyl)-1H-indole-5-carboxylate (132 mg, 0.57 mmol, Step-1), 2M aqueous sodium hydroxide solution (2 mL), and methanol (2 mL) was stirred at 60 °C for 2 hours. The mixture was acidified with 2M aqueous hydrochloric acid solution, and the organic solvent was concentrated under reduced pressure. The precipitate was collected by filtration and dried to give 118 mg (95%) of the title compound as a white solid.

MS (ESI) m/z: 220 (M+H)⁺.

[0166] Intermediate-10: 1-(2-Methoxyethyl)-1H-indole-6-carboxylic acid

[0167] <Step-1> Methyl 1-(2-methoxyethyl)-1H-indole-6-carboxylate

The title compound was prepared in 30% yield (79 mg, colorless syrup) from methyl 1H-indole-6-carboxylate (200 mg, 1.14 mmol) and 1-bromo-2-methoxyethane (190 mg, 1.37 mmol) by the similar manner in Step-1 of Intermediate-9.

MS (ESI) m/z: 234 (M+H)⁺.

[0168] <Step-2> 1-(2-Methoxyethyl)-1H-indole-6-carboxylic acid

The title compound was prepared in 81% yield (60 mg, a white solid) from methyl 1-(2-methoxyethyl)-1H-indole-6-carboxylate (79 mg, 0.34 mmol, Step-1) by the similar manner in Step-2 of Intermediate-9.

MS (ESI) m/z: 220 (M+H)⁺.

[0169] Intermediate-11: 5-(2,2,2-Trifluoroethoxy)nicotinic acid

[0170] <Step-1> Methyl 5-(2,2,2-trifluoroethoxy)nicotinate

The title compound was prepared in >99% yield (307 mg, a red solid) from methyl 5-hydroxynicotinate (200 mg, 1.31 mmol) by the similar manner in Step-1 of Intermediate-2.

¹H-NMR (300 MHz, CDCl₃) δ 8.91 (1H, d, J = 1.5 Hz), 8.53 (1H, d, J = 2.9 Hz), 7.80 (1H, dd, J = 2.9, 1.5 Hz), 4.44 (2H, q, J = 8.0 Hz), 3.94 (3H, s), MS (ESI) m/z: 236 (M+H)⁺.

[0171] <Step-2> 5-(2,2,2-Trifluoroethoxy)nicotinic acid

The title compound was prepared in 75% yield (233 mg, a white solid) from methyl 5-(2,2,2-trifluoroethoxy)nicotinate (307 mg, 1.31 mmol, Step-1) by the similar manner in Step-2 of Intermediate-9.

¹H-NMR (300 MHz, DMSO-d₆) δ 8.77-8.73 (1H, m), 8.65-8.55 (1H, m), 7.93-7.88 (1H, m), 4.96 (2H, q, J = 8.8 Hz), MS (ESI) m/z: 222 (M+H)⁺.

[0172] Example synthesis part

[0173] Example 1: (4-(4-Chlorophenoxy)piperidin-1-yl)(8-hydroxyquinolin-2-yl)methanone

To a solution of 8-hydroxyquinoline-2-carboxylic acid (15 mg, 0.079 mmol), 4-(4-chlorophenoxy)piperidine (20 mg, 0.096 mmol), and triethylamine (0.044 mL, 0.32 mmol) in DMF was added HBTU (46 mg, 0.12 mol) at room temperature. The reaction mixture was stirred at 60 °C for 2 hours. The mixture was diluted with ethyl acetate (3 mL) and washed with water (1.5 mL). The organic layer was dried over sodium sulfate, and concentrated by N₂-flow. The residue was diluted with methanol and applied onto a strong cation exchange cartridge (BondElute(registered trademark) SCX, 1 g/6 mL, Varian Inc.), and the solid phase matrix was rinsed with methanol (6 mL). The crude mixture was eluted in a collection tube with 1 mol/L ammonia in methanol (6 mL) and concentrated by N₂-flow. The residue was purified by preparative LC-MS to give 6.6 mg (22% yield) of the title compound.

[0174] The following examples, Example 2-102, 104-320, 325, 327-348, 352, 356-383, 389-534, 542-544, 546-577, 582-608, 615-654, 664-725 were prepared according to the procedure similar to that described in Example 1, using the appropriate amino acids and carboxylic acids (see Table 3). In addition, non-basic compounds (e.g., neutral compounds) were purified by silica-gel column chromatography (NH-gel, eluting with ethyl acetate) instead of a strong cation exchange cartridge (BondElute(registered trademark) SCX), and then preparative LC-MS. The reactants were used commercially available material or obtained by conventional methods known to those skilled in the art, otherwise noted in the intermediate synthesis part.

[0175] Example 103: Benzo[d]isoxazol-3-yl(4-(4-chlorophenoxy)piperidin-1-yl)methanone

To a solution of 4-(4-chlorophenoxy)piperidine (26 mg, 0.12 mmol), and N,N-diisopropylethylamine (0.086 mL, 0.49 mmol) in dichloromethane (0.5 mL) was added dropwise a solution of benzo[d]isoxazole-3-carbonyl chloride (22 mg, 0.12 mmol) in dichloromethane (0.5 mL) at room temperature. The reaction mixture was stirred at room temperature for 1 hour. The mixture was diluted with ethyl acetate (3 mL) and washed with water (1.5 mL). The organic layer was dried over sodium sulfate, and concentrated under reduced pressure. The residue was purified by silica-gel column chromatography (NH-gel, eluting with ethyl acetate) and then preparative LC-MS to give 16.3 mg (37% yield) of the title compound.

[0176] Example 321:

(4-(Aminomethyl)pyridin-2-yl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone

[0177] <Step-1>tert-Butyl

((2-(4-(4-chlorophenoxy)piperidine-1-carbonyl)pyridin-4-yl)methyl)carbamate

To a stirred solution of 4-(4-chlorophenoxy)piperidine hydrochloride (98 mg, 0.34 mmol), 4-(((tert-butoxycarbonyl)amino)methyl)picolinic acid (100 mg, 0.34 mmol), and N,N-diisopropylethylamine (0.14 mL, 0.79 mmol) in N,N-dimethylformamide (2 mL) was added HBTU (225 mg, 0.60 mmol) at room temperature. After stirring at 60 °C for 2 hours, the mixture was poured into water (5 mL). This was extracted with ethyl acetate (5 mL) and washed with water (5 mL). The organic layer was dried over sodium sulfate, and concentrated under reduced pressure. The residue was purified by silica-gel column chromatography (NH-gel, eluting with ethyl acetate) to give 177 mg (>99% yield) of the title compound as slight brown syrup.

MS (ESI) m/z: 446 (M+H)⁺.

[0178] <Step-2>

(4-(Aminomethyl)pyridin-2-yl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone

A mixture of tert-butyl ((2-(4-(4-chlorophenoxy)piperidine-1-carbonyl)pyridin-4-yl)methyl)carbamate (165 mg, 0.37 mmol, Step-1), trifluoroacetic acid (2 mL), and dichloromethane (2 mL) was

stirred at room temperature for 1 hour. After removal of the solvent, the residue was purified by a strong cation exchange cartridge (BondElute(registered trademark) SCX) to give 128 mg (>99%) of the title compound as colorless syrup. 25 mg of this material was further purified by preparative LC-MS to give 16.9 mg (68% yield) of the title compound.

[0179] Example 322:

N-((2-(4-(4-Chlorophenoxy)piperidine-1-carbonyl)pyridin-4-yl)methyl)pivalamide

To a stirred solution of (4-(aminomethyl)pyridin-2-yl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone (25 mg, 0.072 mmol, Example 321), N,N-diisopropylethylamine (0.038 mL, 0.22 mmol) in dichloromethane (1 mL) was added pivaloyl chloride (0.011 mL, 0.087 mmol) at room temperature. After stirring at room temperature for 2 hours, the mixture was poured into water (3 mL). This was extracted with ethyl acetate (4 mL) and washed with water (3 mL). The organic layer was dried over sodium sulfate, and concentrated under reduced pressure. The residue was purified by silica-gel column chromatography (NH-gel, eluting with ethyl acetate) and then preparative LC-MS to give 14.0 mg (45% yield) of the title compound.

[0180] Example 323-324 were prepared according to the procedure similar to that described in Example 322, using 4-fluorobenzoyl chloride, 4-fluorobenzenesulfonyl chloride instead of pivaloyl chloride, respectively.

[0181] Example 326 was prepared from Example 325 according to the procedures similar to those described in Step-2 in Example 321 and Example 322, using methanesulfonyl chloride instead of pivaloyl chloride.

[0182] Example 349:

3-(tert-Butyl)-5-(4-(4-chlorophenoxy)piperidine-1-carbonyl)benzamide

[0183] <Step-1> 3-(tert-Butyl)-5-(4-(4-chlorophenoxy)piperidine-1-carbonyl)benzoic acid

To a stirred solution of 4-(4-chlorophenoxy)piperidine hydrochloride (100 mg, 0.40 mmol), 5-(tert-butyl)isophthalic acid (358 mg, 1.61 mmol), and N,N-diisopropylethylamine (0.28 mL, 1.61 mmol) in N,N-dimethylformamide (3 mL) was added HBTU (183 mg, 0.48 mmol) at room temperature. After stirring at 60 °C for 2 hours, the mixture was poured into water (5 mL). This was extracted with ethyl acetate (5 mL) and washed with water (5 mL). The organic layer was dried over sodium sulfate, and concentrated under reduced pressure. The residue was purified by silica-gel column chromatography (eluting with dichloromethane / methanol = 7:1) to give 121 mg (72% yield) of the title compound as a white solid.

MS (ESI) m/z: 416 (M+H)⁺.

[0184] <Step-2> 3-(tert-Butyl)-5-(4-(4-chlorophenoxy)piperidine-1-carbonyl)benzamide

To a stirred solution of

3-(tert-butyl)-5-(4-(4-chlorophenoxy)piperidine-1-carbonyl)benzoic acid (30 mg, 0.072 mmol, Step-1), EDC (21 mg, 0.11 mmol), HOBT (17 mg, 0.11 mmol), and N,N-diisopropylethylamine (0.28 mL, 1.61 mmol) in N,N-dimethylformamide (3 mL) was add 25% ammonium water (1 mL) at room temperature. After stirring at 60 °C for 2 hours, the mixture was poured into water (5 mL). This was extracted with ethyl acetate (5 mL) and washed with water (5 mL). The organic layer was dried over sodium sulfate, and concentrated under reduced pressure. The residue was purified by silica-gel column chromatography (NH-gel, eluting with ethyl acetate) and then preparative LC-MS to give 10.4 mg (35% yield) of the title compound.

[0185] Example 350 and 351 were prepared from

3-(tert-butyl)-5-(4-(4-chlorophenoxy)piperidine-1-carbonyl)benzoic acid (Step-1 of Example 349) according to the procedure similar to that described in Step-2 of Example 349, using 2M dimethylamine THF solution, morpholine instead of 25% ammonium water, respectively.

[0186] Example 353:

(4-(4-Chlorophenoxy)piperidin-1-yl)(1-(2-morpholinoethyl)-1H-indol-5-yl)methanone

[0187] <Step-1> (4-(4-Chlorophenoxy)piperidin-1-yl)(1H-indol-5-yl)methanone

To a stirred solution of 4-(4-chlorophenoxy)piperidine hydrochloride (300 mg, 1.21 mmol), 1H-indole-5-carboxylic acid (195mg, 1.21 mmol), and N,N-diisopropylethylamine (0.85 mL, 4.84 mmol) in N,N-dimethylformamide (10 mL) was add HBTU (688 mg, 1.81 mmol) at room temperature. After stirring at 60 °C for 2 hours, the mixture was poured into water (50 mL). This was extracted with ethyl acetate (50 mL) and washed with water (50 mL). The organic layer was dried over sodium sulfate, and concentrated under reduced pressure. The residue was purified by silica-gel column chromatography (NH-gel, eluting with n-hexane / ethyl acetate = 1/1) to give 403 mg (94% yield) of the title compound as a white solid.

¹H-NMR (300 MHz, CDCl₃) δ 8.52 (1H, br.s), 7.74 (1H, s), 7.38 (1H, d, J = 8.1 Hz), 7.34-7.09 (4H, m), 6.93-6.76 (2H, m), 6.58 (1H, s), 4.64-4.43 (1H, m), 4.05-3.30 (4H, m), 2.14-1.72 (4H, m), MS (ESI) m/z: 355 (M+H)⁺.

[0188] <Step-2>

(4-(4-Chlorophenoxy)piperidin-1-yl)(1-(2-morpholinoethyl)-1H-indol-5-yl)methanone

To a stirred solution of (4-(4-chlorophenoxy)piperidin-1-yl)(1H-indol-5-yl)methanone (30 mg, 0.085 mmol, Step-1) and sodium hydride (60% in oil, 6 mg, 0.25 mmol) in N,N-dimethylformamide (1.5 mL) was added 4-(2-chloroethyl)morpholine hydrochloride (35 mg, 0.19 mmol) at room temperature. Then the mixture was stirred at 70 °C for 2 hours. The mixture was poured into water (20 mL) and extracted with ethyl acetate (20 mL). The organic layer

was washed with water (20 mL), and dried over sodium sulfate. After removal of the solvent, the residue was purified by silica-gel column chromatography (NH-gel, eluting with ethyl acetate) and then preparative LC-MS to give 11.9 mg (30% yield) of the title compound.

[0189] Example 354, 384, and 388 were prepared from (4-(4-chlorophenoxy)piperidin-1-yl)(1H-indol-5-yl)methanone (Step-1 of Example 353) according to the procedure similar to that described in Step-2 of Example 353, using 2-chloro-N,N-dimethylacetamide, 4-(iodomethyl)tetrahydro-2H-pyran-4-ol, and 2-chloro-1-morpholinoethanone instead of 4-(2-chloroethyl)morpholine hydrochloride, respectively.

[0190] Example 355:

(4-(4-Chlorophenoxy)piperidin-1-yl)(1-(2-hydroxyethyl)-1H-indol-5-yl)methanone

To a stirred solution of (4-(4-chlorophenoxy)piperidin-1-yl)(1H-indol-5-yl)methanone (30 mg, 0.085 mmol, Step-1 of Example 353) and sodium hydride (60% in oil, 4 mg, 0.17 mmol) in N,N-dimethylformamide (1.5 mL) was added (2-bromoethoxy)(tert-butyl)dimethylsilane (24 mg, 0.10 mmol) at room temperature. After stirring at room temperature for 2 hours, the mixture was poured into water (20 mL) and extracted with ethyl acetate (20 mL). The organic layer was washed with water (20 mL), and dried over sodium sulfate. After removal of the solvent, the residue was purified by silica-gel column chromatography (NH-gel, eluting with ethyl acetate) to give 43 mg (>99% yield) of (1-(2-((tert-butyldimethylsilyl)oxy)ethyl)-1H-indol-5-yl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone as orange oil. This material was treated with 2M aqueous hydrochloric acid solution (0.4 mL) and tetrahydrofuran (1.5 mL) at room temperature for 1 hour. The mixture was neutralized by saturated sodium hydrogen carbonate aqueous solution and extracted with ethyl acetate (3 mL). The organic layer was dried over sodium sulfate. After removal of the solvent, the residue was purified by silica-gel column chromatography (NH-gel, eluting with ethyl acetate) and then preparative LC-MS to give 7.1 mg (18% yield) of the title compound.

[0191] Example 385:

(1-(2-Aminoethyl)-1H-indol-5-yl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone

[0192] <Step-1> tert-Butyl

(2-(5-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-1H-indol-1-yl)ethyl)carbamate

To a stirred solution of (4-(4-chlorophenoxy)piperidin-1-yl)(1H-indol-5-yl)methanone (80 mg, 0.23 mmol, Step-1 of Example 353) and sodium hydride (60% in oil, 27 mg, 1.13 mmol) in N,N-dimethylformamide (5 mL) was added tert-butyl (2-bromoethyl)carbamate (76

mg, 0.34 mmol) at room temperature. Then the mixture was stirred at 70 °C for 3 hours. The mixture was poured into water (30 mL) and extracted with ethyl acetate (30 mL). The organic layer was washed with water (30 mL), and dried over sodium sulfate. After removal of the solvent, the residue was purified by silica-gel column chromatography (eluting with n-hexane / ethyl acetate = 2/1) to give 112 mg (>99% yield) of the title compound as brown oil.

¹H-NMR (300 MHz, CDCl₃) δ 7.72 (1H, s), 7.37 (1H, d, J = 8.8 Hz), 7.31-7.20 (3H, m), 7.14 (1H, d, J = 3.3 Hz), 6.93-6.86 (2H, d, J = 8.8 Hz), 6.55 (1H, d, J = 3.3 Hz), 4.63-4.46 (2H, m), 4.33-4.24 (2H, m), 3.98-3.75 (1H, m), 3.55-3.43 (2H, m), 2.07-1.61 (6H, m), 1.43 (9H, s), MS (ESI) m/z: 498 (M+H)⁺.

[0193] <Step-2>

(1-(2-Aminoethyl)-1H-indol-5-yl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone

A mixture of tert-butyl (2-(5-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-1H-indol-1-yl)ethyl)carbamate (112 mg, 0.23 mmol, Step-1), trifluoroacetic acid (1.5 mL), and dichloromethane (1.5 mL) was stirred at room temperature for 1 hour. After concentration in vacuo, the residue was purified by a strong cation exchange cartridge (BondElute(registered trademark) SCX) to give 83 mg (83% yield) of the title compound as yellow oil. 13 mg of this material was further purified by preparative LC-MS to give 6.6 mg (51% yield) of the title compound.

[0194] Example 386:

N-(2-(5-(4-(4-Chlorophenoxy)piperidine-1-carbonyl)-1H-indol-1-yl)ethyl)acetamide

To a stirred solution of (1-(2-aminoethyl)-1H-indol-5-yl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone (30 mg, 0.075 mmol, Example 385) and pyridine (1 mL) was added acetic anhydride (0.0085 mL, 0.090 mmol) at room temperature. After stirring at room temperature for 2 hours, the mixture was poured into 1M aqueous hydrochloric acid solution (5 mL). This was extracted with ethyl acetate (5 mL) and washed with saturated sodium hydrogen carbonate aqueous solution (5 mL) and brine (5 mL). The organic layer was dried over sodium sulfate, and concentrated under reduced pressure. The residue was purified by silica-gel column chromatography (NH-gel, eluting with ethyl acetate) and then preparative LC-MS to give 8.9 mg (27% yield) of the title compound.

[0195] Example 387 was prepared from Example 385 according to the procedure similar to that described in Example 386, using methanesulfonyl chloride instead of acetic anhydride.

[0196] Example 535:

4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-N-(2-methoxyethyl)-N-methylbenzamide

[0197] <Step-1> Methyl 4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)benzoate

To a stirred solution of 4-(4-chlorophenoxy)piperidine hydrochloride (250 mg, 1.01 mmol), and triethylamine (0.56 mL, 4.03 mmol) in dichloromethane (10 mL) was added methyl 4-(chlorocarbonyl)benzoate (220 mg, 1.11 mmol) at room temperature. After stirring at room temperature for 2 hours, the mixture was poured into water (30 mL). This was extracted with dichloromethane (30 mL) and washed with water (30 mL). The organic layer was dried over sodium sulfate, and concentrated under reduced pressure. The residue was purified by silica-gel column chromatography (eluting with n-hexane / ethyl acetate = 3 / 1) to give 329 mg (87% yield) of the title compound as a white solid.

¹H-NMR (300 MHz, CDCl₃) δ 8.13-8.07(2H, m), 7.52-7.44 (2H, m), 7.31-7.20 (2H, m), 6.90-6.81 (2H, m), 4.60-4.51 (1H, m), 3.94 (3H, s), 3.97-3.80 (2H, m), 3.68-3.50 (1H, m), 3.40-3.23 (1H, m), 2.11-1.72 (4H, m), MS (ESI) m/z: 374 (M+H)⁺.

[0198] <Step-2> 4-(4-(4-Chlorophenoxy)piperidine-1-carbonyl)benzoic acid

A mixture of methyl methyl 4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)benzoate (329 mg, 0.88 mmol, Step-1), 2M sodium hydroxide aqueous solution (2 mL), tetrahydrofuran (2.5 mL), and methanol (5 mL) was stirred at 50 °C for 1 hour. The mixture was acidified by 1M aqueous hydrochloric acid solution and extracted with ethyl acetate (30 mL). The organic layer was dried over sodium sulfate and concentrated under reduced pressure. The residue was crystallized from diisopropylether to give 265 mg (84% yield) of the title compound as a white solid.

¹H-NMR (300 MHz, DMSO-d₆) δ 8.01-7.93 (2H, m), 7.52-7.45 (2H, m), 7.32-7.24 (2H, m), 7.02-6.94 (2H, m), 4.71-4.49 (1H, m), 4.05-3.63 (2H, m), 3.55-3.37 (1H, m), 3.35-3.08 (1H, m), 2.06-1.80 (2H, m), 1.71-1.47 (2H, m), MS (ESI) m/z: 360 (M+H)⁺.

[0199] <Step-3>

4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-N-(2-methoxyethyl)-N-methylbenzamide

The title compound was prepared in 51% yield (10.1 mg) prepared from 4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)benzoic acid (Step-2) according to the procedure similar to that described in Step-2 of Example 349, using 2-methoxy-N-methylethanamine instead of 25% ammonium water.

[0200] Example 536-541 and 545 were prepared from 4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)benzoic acid (Step-2 of Example 535) according to the procedure similar to that described in Step-2 of Example 349, using 2-methoxyethanamine, 1-((4-aminopiperidin-1-yl)methyl)cyclohexanol, (S)-2-amino-2-phenylethanol, (S)-2-amino-1-phenylethanol, (S)-2-amino-3-phenylpropan-1-ol, (S)-2-amino-3-phenylpropanamide, and

2-amino-1-phenylethanone hydrochloride instead of 25% ammonium water, respectively.

[0201] Example 578:

(S)-3-(4-(4-Chlorophenoxy)piperidine-1-carbonyl)-N-(2-hydroxy-2-phenylethyl)benzamide

[0202] <Step-1> Methyl 3-(4-(4-chlorophenoxy)piperidine-1-carbonyl)benzoate

To a stirred solution of 4-(4-chlorophenoxy)piperidine hydrochloride (200 mg, 0.81 mmol), 3-(methoxycarbonyl)benzoic acid (145 mg, 0.81 mmol), and N,N-diisopropylethylamine (0.56 mL, 3.22 mmol) in N,N-dimethylformamide (4 mL) was added HBTU (458 mg, 1.21 mmol) at room temperature. After stirring at 60 °C for 2 hours, the mixture was poured into water (20 mL). This was extracted with ethyl acetate (20 mL) and washed with water (20 mL). The organic layer was dried over sodium sulfate, and concentrated under reduced pressure. The residue was purified by silica-gel column chromatography (NH-gel, eluting with ethyl acetate) to give 301 mg (>99% yield) of the title compound as yellow syrup.

MS (ESI) m/z: 374 (M+H)⁺.

[0203] <Step-2> 3-(4-(4-Chlorophenoxy)piperidine-1-carbonyl)benzoic acid

A mixture of methyl 3-(4-(4-chlorophenoxy)piperidine-1-carbonyl)benzoate (301 mg, 0.81 mmol, Step-1), 2M sodium hydroxide aqueous solution (2 mL), tetrahydrofuran (2 mL), and methanol (2 mL) was stirred at 60 °C for 2 hours. The mixture was acidified by 2M aqueous hydrochloric acid solution and extracted with ethyl acetate (10 mL). The organic layer was dried over sodium sulfate, and concentrated under reduced pressure to give 270 mg (93% yield) of the title compound as a white solid.

MS (ESI) m/z: 360 (M+H)⁺.

[0204] <Step-3>

(S)-3-(4-(4-Chlorophenoxy)piperidine-1-carbonyl)-N-(2-hydroxy-2-phenylethyl)benzamide

The title compound was prepared in 51% yield (10.1 mg) prepared from 3-(4-(4-chlorophenoxy)piperidine-1-carbonyl)benzoic acid (Step-2) according to the procedure similar to that described in Step-2 of Example 349, using (S)-2-amino-1-phenylethanol instead of 25% ammonium water.

[0205] Example 579-581 were prepared from

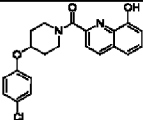
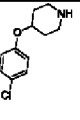
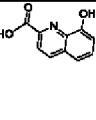
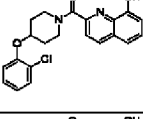
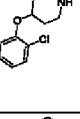
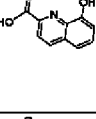
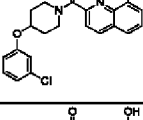
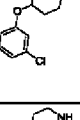
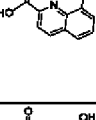
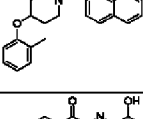
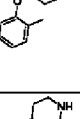
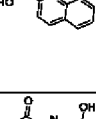
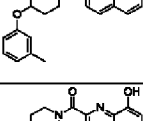
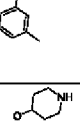
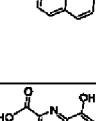
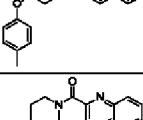
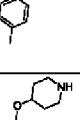
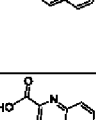
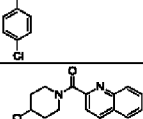
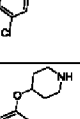
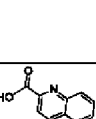
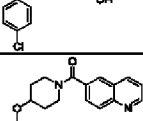
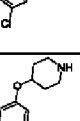
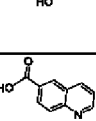
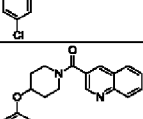
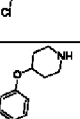
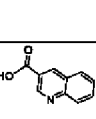
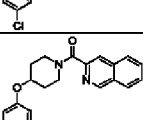
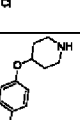
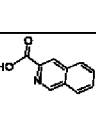
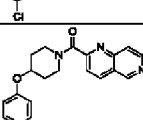
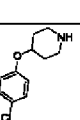
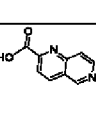
3-(tert-butyl)-5-(4-(4-chlorophenoxy)piperidine-1-carbonyl)benzamide (Step-2 of Example 578) according to the procedure similar to that described in Step-2 of Example 349, using (S)-2-amino-2-phenylethanol, (S)-2-amino-3-phenylpropan-1-ol, and (S)-2-amino-3-phenylpropanamide instead of 25% ammonium water, respectively.

[0206] Example 609 was prepared from 4-(3-(trifluoromethoxy)phenoxy)piperidine hy-

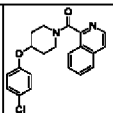
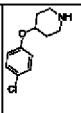
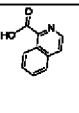
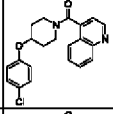
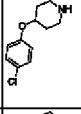
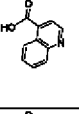
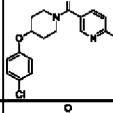
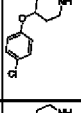
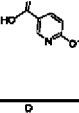
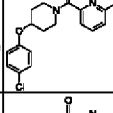
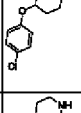
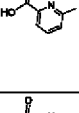
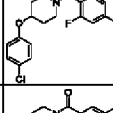
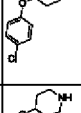
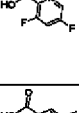
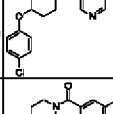
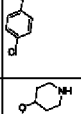
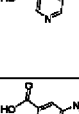
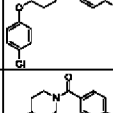
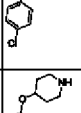
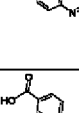
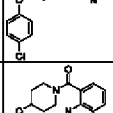
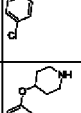
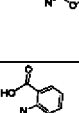
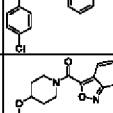
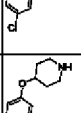
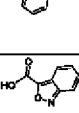
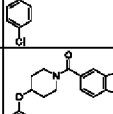
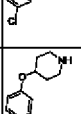
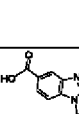
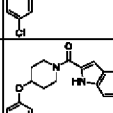
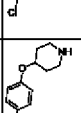
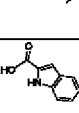
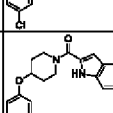
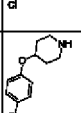
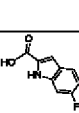
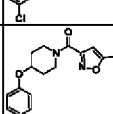
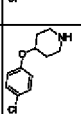
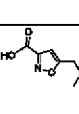
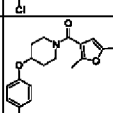
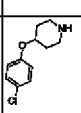
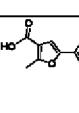
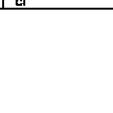
drochloride and 4-(((tert-butoxycarbonyl)amino)methyl)picolinic acid according to the procedures similar to those described in Example 321.

- [0207] Example 610-611 were prepared from Example 609 according to the procedure similar to that described in Example 386, using methanesulfonyl chloride, ethyl chloroformate instead of acetic anhydride, respectively.
- [0208] Example 612 was prepared from 4-(3-(trifluoromethoxy)phenoxy)piperidine hydrochloride and 2-(((tert-butoxycarbonyl)amino)methyl)benzoic acid according to the procedures similar to those described in Example 321 and Example 386.
- [0209] Example 613 and 614 were prepared from 4-(3-(trifluoromethoxy)phenoxy)piperidine hydrochloride and 2-(((tert-butoxycarbonyl)amino)methyl)benzoic acid according to the procedures similar to those described in Example 321 and Example 386, using methanesulfonyl chloride, ethyl chloroformate instead of acetic anhydride, respectively.
- [0210] Example 655 was prepared from 4-(3-(trifluoromethoxy)phenoxy)piperidine hydrochloride and 2-(2-((tert-butoxycarbonyl)amino)ethoxy)benzoic acid according to the procedures similar to those described in Example 321 and Example 386.
- [0211] Example 656-657 were prepared from 4-(3-(trifluoromethoxy)phenoxy)piperidine hydrochloride and 2-(2-((tert-butoxycarbonyl)amino)ethoxy)benzoic acid according to the procedures similar to those described in Example 321 and Example 386, using methanesulfonyl chloride, ethyl chloroformate instead of acetic anhydride, respectively.
- [0212] Example 658 was prepared from 4-(3-(trifluoromethoxy)phenoxy)piperidine hydrochloride and 2-(2-((tert-butoxycarbonyl)amino)ethoxy)benzoic acid according to the procedures similar to those described in Example 321 and Step-2 of Example 349, using 1-carbamoylcyclopropanecarboxylic acid.
- [0213] Example 659 was prepared from 4-(3-(trifluoromethoxy)phenoxy)piperidine hydrochloride and 3-(2-((tert-butoxycarbonyl)amino)ethoxy)benzoic acid according to the procedures similar to those described in Example 321.
- [0214] Example 660-663 were prepared from Example 659 according to the procedures similar to those described in Example 655-658, respectively.
- [0215] The observed MS, Retention time and Method by HPLC of all examples are described in Table 3. ¹H-NMR data of Example 21, 80, 92, 191, 403, 451, 561 and 574 are described in Table 4.
- [0216] Table 3

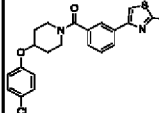
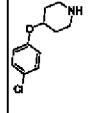
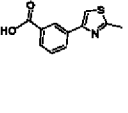
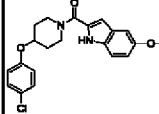
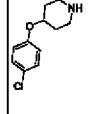
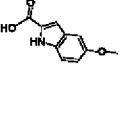
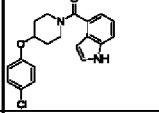
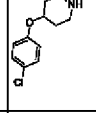
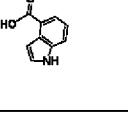
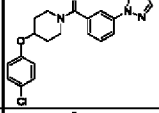
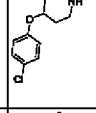
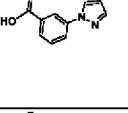
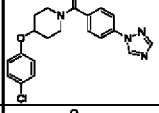
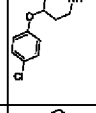
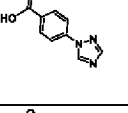
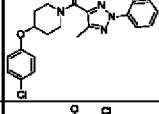
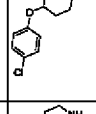
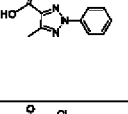
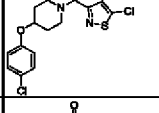
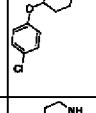
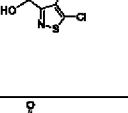
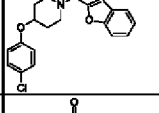
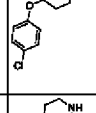
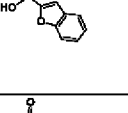
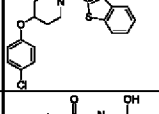
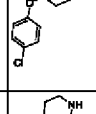
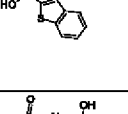
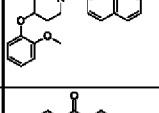
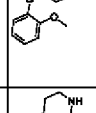
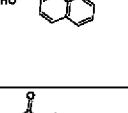
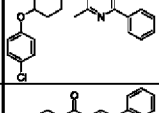
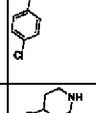
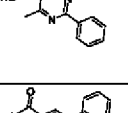
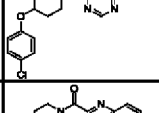
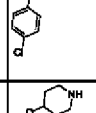
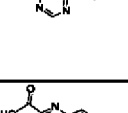
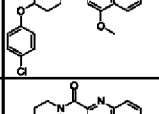
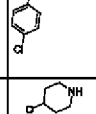
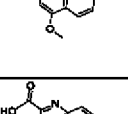
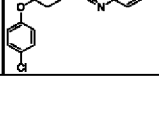
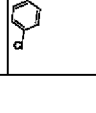
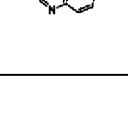
[Table 3-1]

Example	Name	Structure	Structure of amine part	Structure of carboxylic acid part	Observed MS	Retention time	QC Method
Example 1	(4-(4-chlorophenoxy)piperidin-1-yl)(8-hydroxyquinolin-2-yl)methanone				382.9	1.90min	Method A
Example 2	(4-(2-chlorophenoxy)piperidin-1-yl)(8-hydroxyquinolin-2-yl)methanone				382.9	1.87min	Method A
Example 3	(4-(3-chlorophenoxy)piperidin-1-yl)(8-hydroxyquinolin-2-yl)methanone				382.9	1.91min	Method A
Example 4	(8-hydroxyquinolin-2-yl)(4-(o-tolyloxy)piperidin-1-yl)methanone				363	1.89min	Method A
Example 5	(8-hydroxyquinolin-2-yl)(4-(m-tolyloxy)piperidin-1-yl)methanone				363	1.87min	Method A
Example 6	(8-hydroxyquinolin-2-yl)(4-(p-tolyloxy)piperidin-1-yl)methanone				363	1.88min	Method A
Example 7	(4-(4-chlorophenoxy)piperidin-1-yl)(quinolin-2-yl)methanone				366.9	1.92min	Method A
Example 8	(4-(4-chlorophenoxy)piperidin-1-yl)(4-hydroxyquinolin-2-yl)methanone				382.9	1.53min	Method A
Example 9	(4-(4-chlorophenoxy)piperidin-1-yl)(quinolin-6-yl)methanone				366.9	1.73min	Method A
Example 10	(4-(4-chlorophenoxy)piperidin-1-yl)(quinolin-3-yl)methanone				366.9	1.80min	Method A
Example 11	(4-(4-chlorophenoxy)piperidin-1-yl)(isoquinolin-3-yl)methanone				366.9	1.86min	Method A
Example 12	(4-(4-chlorophenoxy)piperidin-1-yl)(1,6-naphthyridin-2-yl)methanone				367.9	1.65min	Method A

[Table 3-2]

Example13	(4-(4-chlorophenoxy)piperidin-1-yl)(isoquinolin-1-yl)methanone				366.9	1.84min	Method A
Example14	(4-(4-chlorophenoxy)piperidin-1-yl)(quinolin-4-yl)methanone				366.9	1.77min	Method A
Example15	(4-(4-chlorophenoxy)piperidin-1-yl)(6-(2,2,2-trifluoroethoxy)pyridin-3-yl)methanone				414.9	1.97min	Method A
Example16	(4-(4-chlorophenoxy)piperidin-1-yl)(6-methylpyridin-2-yl)methanone				331	1.75min	Method A
Example17	(4-(4-chlorophenoxy)piperidin-1-yl)(3,5-difluoropyridin-2-yl)methanone				352.9	1.79min	Method A
Example18	(4-(4-chlorophenoxy)piperidin-1-yl)(5-methylpyridin-3-yl)methanone				331	1.68min	Method A
Example19	(4-(4-chlorophenoxy)piperidin-1-yl)(quinoxalin-6-yl)methanone				367.9	1.69min	Method A
Example20	(4-(4-chlorophenoxy)piperidin-1-yl)(6-phenoxy-pyridin-3-yl)methanone				408.9	1.96min	Method A
Example21	(4-(4-chlorophenoxy)piperidin-1-yl)(quinolin-8-yl)methanone				366.9	1.79min	Method A
Example22	benzo[c]isoxazol-3-yl(4-(4-chlorophenoxy)piperidin-1-yl)methanone				356.9	1.97min	Method A
Example23	(4-(4-chlorophenoxy)piperidin-1-yl)(1-isopropyl-1H-benzod[e][1,2,3]triazol-5-yl)methanone				399	1.83min	Method A
Example24	(4-(4-chlorophenoxy)piperidin-1-yl)(5-fluoro-1H-indol-2-yl)methanone				372.9	1.97min	Method A
Example25	(4-(4-chlorophenoxy)piperidin-1-yl)(6-fluoro-1H-indol-2-yl)methanone				372.9	1.98min	Method A
Example26	(4-(4-chlorophenoxy)piperidin-1-yl)(5-isobutylisoxazol-3-yl)methanone				363	2.07min	Method A
Example27	(4-(4-chlorophenoxy)piperidin-1-yl)(2-methyl-5-phenylfuran-3-yl)methanone				395.9	2.12min	Method A

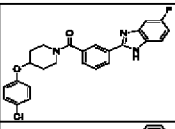
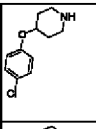
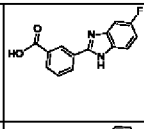
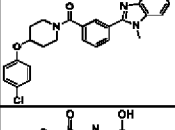
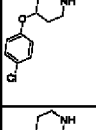
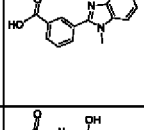
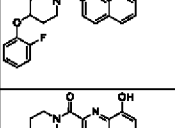
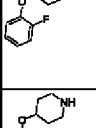
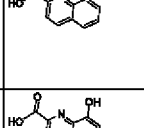
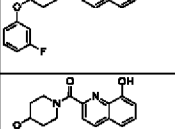
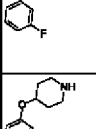
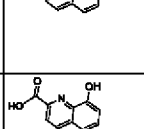
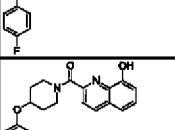
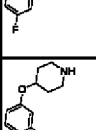
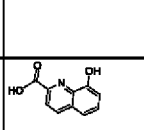
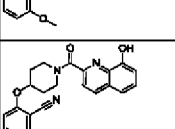
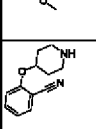
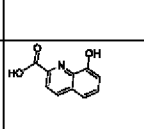
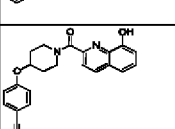
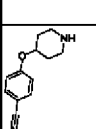
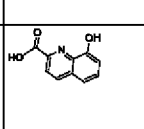
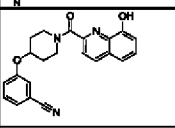
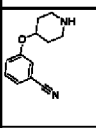
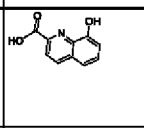
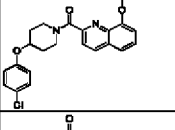
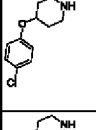
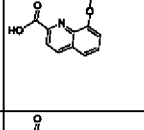
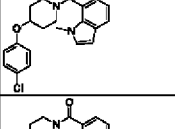
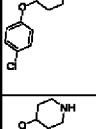
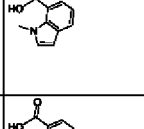
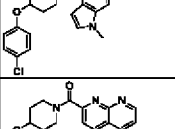
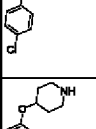
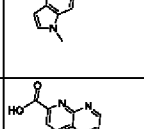
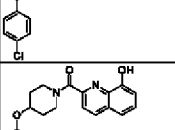
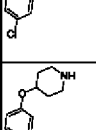
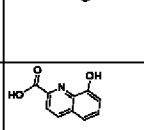
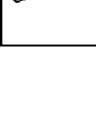
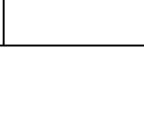
[Table 3-3]

Example 28	(4-(4-chlorophenoxy)piperidin-1-yl)(3-(2-methylthiazol-4-yl)phenyl)methanone				412.9	1.98min	Method A
Example 29	(4-(4-chlorophenoxy)piperidin-1-yl)(5-methoxy-1H-indol-2-yl)methanone				385	1.92min	Method A
Example 30	(4-(4-chlorophenoxy)piperidin-1-yl)(1H-indol-4-yl)methanone				354.9	1.79min	Method A
Example 31	(3-(1H-pyrazol-1-yl)phenyl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone				381.9	1.87min	Method A
Example 32	(4-(1H-1,2,4-triazol-1-yl)phenyl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone				382.9	1.68min	Method A
Example 33	(4-(4-chlorophenoxy)piperidin-1-yl)(5-methyl-2-phenyl-2H-1,2,3-triazol-4-yl)methanone				396.9	2.15min	Method A
Example 34	(4-(4-chlorophenoxy)piperidin-1-yl)(4,5-dichloroisothiazol-3-yl)methanone				390.8	2.05min	Method A
Example 35	benzofuran-2-yl(4-(4-chlorophenoxy)piperidin-1-yl)methanone				355.9	2.02min	Method A
Example 36	benzo[b]thiophen-2-yl(4-(4-chlorophenoxy)piperidin-1-yl)methanone				371.9	2.07min	Method A
Example 37	(8-hydroxyquinolin-2-yl)(2-methoxyphenoxy)piperidin-1-yl)methanone				378.9	1.70min	Method A
Example 38	(4-(4-chlorophenoxy)piperidin-1-yl)(4-methyl-2-phenylpyrimidin-5-yl)methanone				408	2.04min	Method A
Example 39	(4-(4-chlorophenoxy)piperidin-1-yl)(6-phenylpyrimidin-4-yl)methanone				393.9	1.96min	Method A
Example 40	(4-(4-chlorophenoxy)piperidin-1-yl)(4-methoxyquinolin-2-yl)methanone				396.9	1.96min	Method A
Example 41	(4-(4-chlorophenoxy)piperidin-1-yl)(quinoxalin-2-yl)methanone				367.9	1.89min	Method A

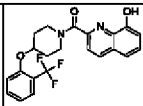
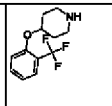
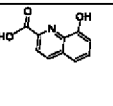
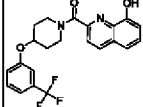
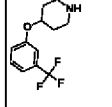
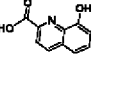
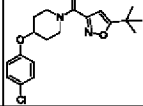
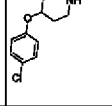
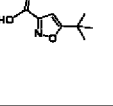
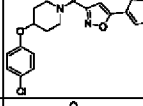
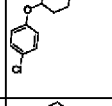
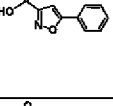
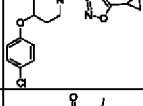
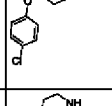
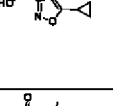
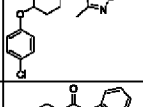
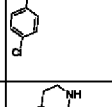
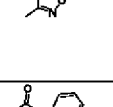
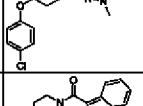
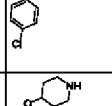
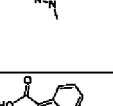
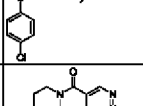
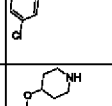
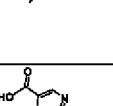
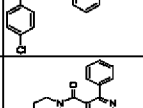
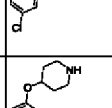
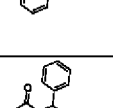
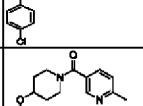
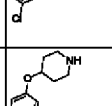
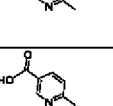
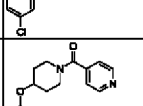
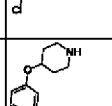
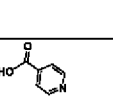
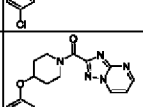
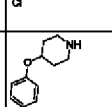
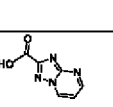
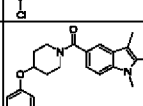
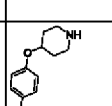
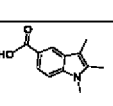
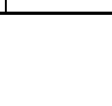
[Table 3-4]

Example42	benzo[d]thiazol-6-yl(4-(4-chlorophenoxy)piperidin-1-yl)methanone				372.9	1.77min	Method A
Example43	(4-(4-chlorophenoxy)piperidin-1-yl)(1H-indol-3-yl)methanone				354.9	1.81min	Method A
Example44	(4-(4-chlorophenoxy)piperidin-1-yl)(1H-indol-2-yl)methanone				354.9	1.97min	Method A
Example45	(4-(4-chlorophenoxy)piperidin-1-yl)(1-methyl-1H-indol-3-yl)methanone				368.9	1.93min	Method A
Example46	(4-(4-chlorophenoxy)piperidin-1-yl)(1-methyl-1H-indol-2-yl)methanone				368.9	2.05min	Method A
Example47	(4-(4-chlorophenoxy)piperidin-1-yl)(2,3-dimethyl-1H-indol-5-yl)methanone				382.9	1.94min	Method A
Example48	(4-(4-chlorophenoxy)piperidin-1-yl)(1H-indol-6-yl)methanone				354.9	1.84min	Method A
Example49	(4-(4-chlorophenoxy)piperidin-1-yl)(2-methyl-1H-benzo[d]imidazol-5-yl)methanone				370	1.54min	Method A
Example50	(4-(4-chlorophenoxy)piperidin-1-yl)(imidazo[1,2-a]pyridin-2-yl)methanone				355.9	1.67min	Method A
Example51	(4-(4-chlorophenoxy)piperidin-1-yl)(2-methylimidazo[1,2-a]pyridin-3-yl)methanone				370	1.69min	Method A
Example52	(4-(4-chlorophenoxy)piperidin-1-yl)(5-methyl-1-phenyl-1H-pyrazol-4-yl)methanone				395.9	1.87min	Method A
Example53	(4-(tert-butyl)phenyl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone				372	2.18min	Method A
Example54	(4-(4-chlorophenoxy)piperidin-1-yl)(4-chlorophenyl)methanone				349.9	2.00min	Method A
Example55	(4-(4-chlorophenoxy)piperidin-1-yl)(4-fluorophenyl)methanone				333.9	1.89min	Method A

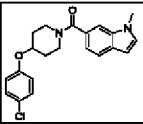
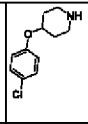
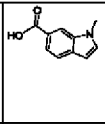
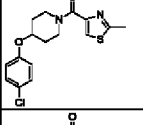
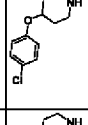
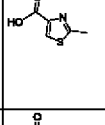
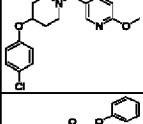
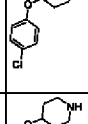
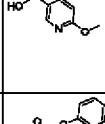
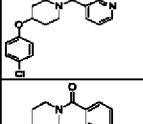
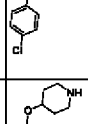
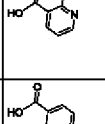
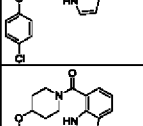
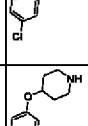
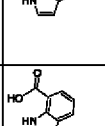
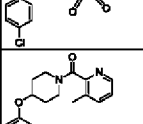
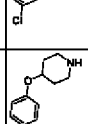
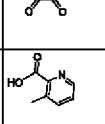
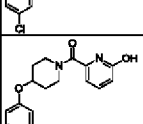
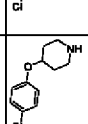
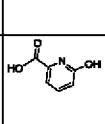
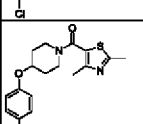
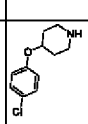
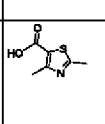
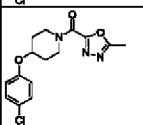
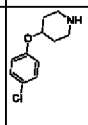
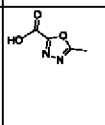
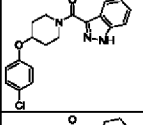
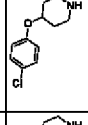
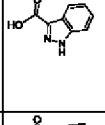
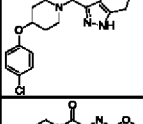
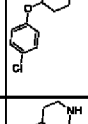
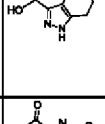
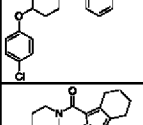
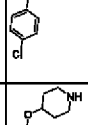
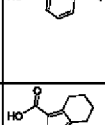
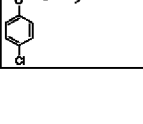
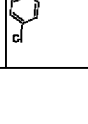
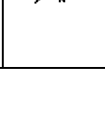
[Table 3-5]

Example56	(4-(4-chlorophenoxy)piperidin-1-yl)(3-(5-fluoro-1H-benz[d]imidazol-2-yl)phenyl)methanone				448.1	1.82min	Method A
Example57	(4-(4-chlorophenoxy)piperidin-1-yl)(3-(1-methyl-1H-benz[d]imidazol-2-yl)phenyl)methanone				446	1.85min	Method A
Example58	(4-(2-fluorophenoxy)piperidin-1-yl)(8-hydroxyquinolin-2-yl)methanone				365.2	1.77min	Method A
Example59	(4-(3-fluorophenoxy)piperidin-1-yl)(8-hydroxyquinolin-2-yl)methanone				365.2	1.79min	Method A
Example60	(4-(4-fluorophenoxy)piperidin-1-yl)(8-hydroxyquinolin-2-yl)methanone				365.2	1.77min	Method A
Example61	(8-hydroxyquinolin-2-yl)(4-(3-methoxyphenoxy)piperidin-1-yl)methanone				377.2	1.75min	Method A
Example62	2-((1-(8-hydroxyquinoline-2-carbonyl)piperidin-4-yl)oxy)benzonitrile				372.2	1.65min	Method A
Example63	4-((1-(8-hydroxyquinoline-2-carbonyl)piperidin-4-yl)oxy)benzonitrile				372.2	1.65min	Method A
Example64	3-((1-(8-hydroxyquinoline-2-carbonyl)piperidin-4-yl)oxy)benzonitrile				372.2	1.69min	Method A
Example65	(4-(4-chlorophenoxy)piperidin-1-yl)(8-methoxyquinolin-2-yl)methanone				396.9	1.85min	Method A
Example66	(4-(4-chlorophenoxy)piperidin-1-yl)(1-methyl-1H-indol-7-yl)methanone				368.9	1.97min	Method A
Example67	(4-(4-chlorophenoxy)piperidin-1-yl)(1-methyl-1H-indol-4-yl)methanone				369	1.91min	Method A
Example68	(4-(4-chlorophenoxy)piperidin-1-yl)(1,8-naphthyridin-2-yl)methanone				367.9	1.59min	Method A
Example69	(8-hydroxyquinolin-2-yl)(4-phenoxypiperidin-1-yl)methanone				347.1	1.76min	Method A

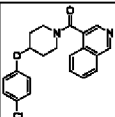
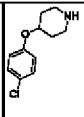
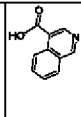
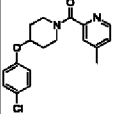
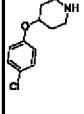
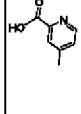
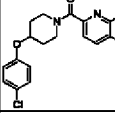
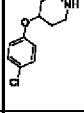
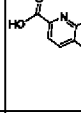
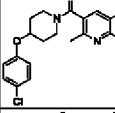
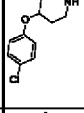
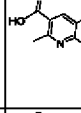
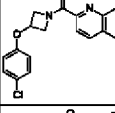
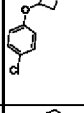
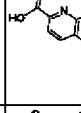
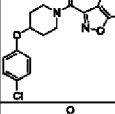
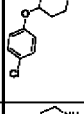
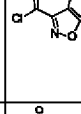
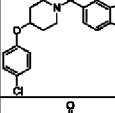
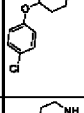
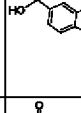
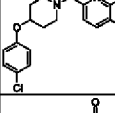
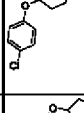
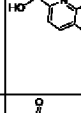
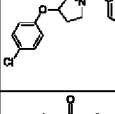
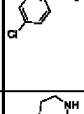
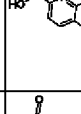
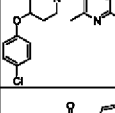
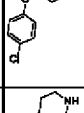
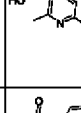
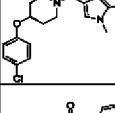
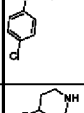
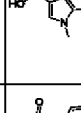
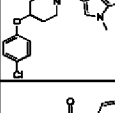
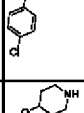
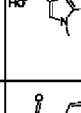
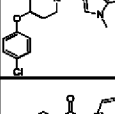
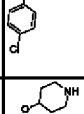
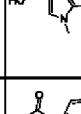
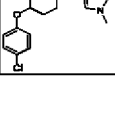
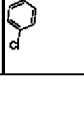
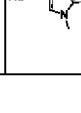
[Table 3-6]

Example70	(8-hydroxyquinolin-2-yl)(4-(2-(trifluoromethyl)phenoxy)piperidin-1-yl)methanone				415.1	1.89min	Method A
Example71	(8-hydroxyquinolin-2-yl)(4-(3-(trifluoromethyl)phenoxy)piperidin-1-yl)methanone				415.1	1.91min	Method A
Example72	(5-(tert-butyl)isoxazol-3-yl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone				362.9	2.06min	Method A
Example73	(4-(4-chlorophenoxy)piperidin-1-yl)(5-phenylisoxazol-3-yl)methanone				382.9	2.04min	Method A
Example74	(4-(4-chlorophenoxy)piperidin-1-yl)(5-cyclopropylisoxazol-3-yl)methanone				347	1.91min	Method A
Example75	(4-(4-chlorophenoxy)piperidin-1-yl)(3,5-dimethylisoxazol-4-yl)methanone				334.9	1.73min	Method A
Example76	(4-(4-chlorophenoxy)piperidin-1-yl)(1-methyl-1H-indazol-3-yl)methanone				370	1.94min	Method A
Example77	(4-(4-chlorophenoxy)piperidin-1-yl)(2-methyl-2H-indazol-3-yl)methanone				370	1.85min	Method A
Example78	(4-(4-chlorophenoxy)piperidin-1-yl)(cinnolin-4-yl)methanone				367.9	1.68min	Method A
Example79	(4-(4-chlorophenoxy)piperidin-1-yl)(2-methyl-4-phenylpyrimidin-5-yl)methanone				408	1.86min	Method A
Example80	(4-(4-chlorophenoxy)piperidin-1-yl)(6-methylpyridin-3-yl)methanone				330.9	1.65min	Method A
Example81	(4-(4-chlorophenoxy)piperidin-1-yl)pyridin-4-yl)methanone				316.9	1.59min	Method A
Example82	[1,2,4]triazolo[1,5-a]pyrimidin-2-yl(4-(4-chlorophenoxy)piperidin-1-yl)methanone				357.9	1.52min	Method A
Example83	(4-(4-chlorophenoxy)piperidin-1-yl)(1,2,3-trimethyl-1H-indol-5-yl)methanone				396.9	2.06min	Method A

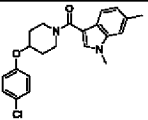
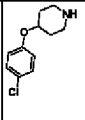
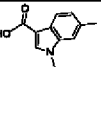
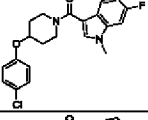
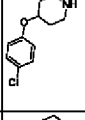
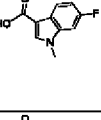
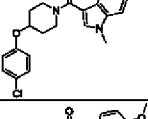
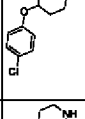
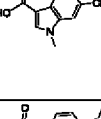
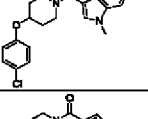
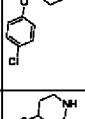
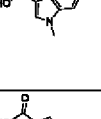
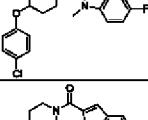
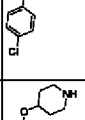
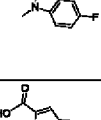
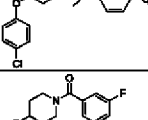
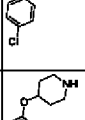
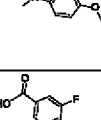
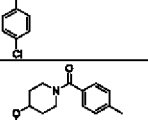
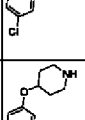
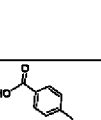
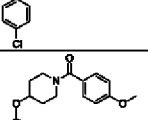
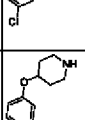
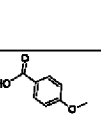
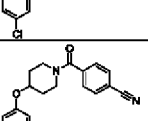
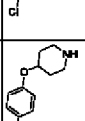
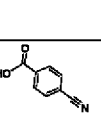
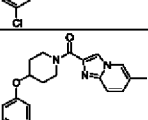
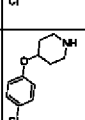
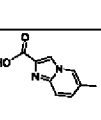
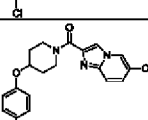
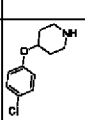
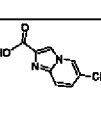
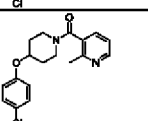
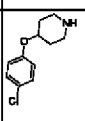
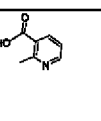
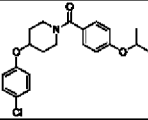
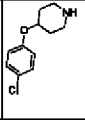
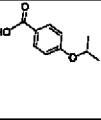
[Table 3-7]

Example 84	(4-(4-chlorophenoxy)piperidin-1-yl)(1-methyl-1H-indol-6-yl)methanone				368.9	1.93min	Method A
Example 85	(4-(4-chlorophenoxy)piperidin-1-yl)(2-methylthiazol-4-yl)methanone				336.9	1.75min	Method A
Example 86	(4-(4-chlorophenoxy)piperidin-1-yl)(6-methoxypyridin-3-yl)methanone				347	1.79min	Method A
Example 87	(4-(4-chlorophenoxy)piperidin-1-yl)(2-phenoxypyridin-3-yl)methanone				408.9	1.93min	Method A
Example 88	(4-(4-chlorophenoxy)piperidin-1-yl)(1H-indol-7-yl)methanone				353.1	1.94min	Method A
Example 89	7-(4-(4-chlorophenoxy)piperidin-1-carbonyl)indoline-2,3-dione				383.1	1.68min	Method A
Example 90	(4-(4-chlorophenoxy)piperidin-1-yl)(3-methylpyridin-2-yl)methanone				330.9	1.70min	Method A
Example 91	(4-(4-chlorophenoxy)piperidin-1-yl)(6-hydroxypyridin-2-yl)methanone				331.1	1.48min	Method A
Example 92	(4-(4-chlorophenoxy)piperidin-1-yl)(2,4-dimethylthiazol-5-yl)methanone				350.9	1.76min	Method A
Example 93	(4-(4-chlorophenoxy)piperidin-1-yl)(5-methyl-1,3,4-oxadiazol-2-yl)methanone				321.9	1.69min	Method A
Example 94	(4-(4-chlorophenoxy)piperidin-1-yl)(1H-indazol-3-yl)methanone				354.1	1.79min	Method A
Example 95	(4-(4-chlorophenoxy)piperidin-1-yl)(4,5,6,7-tetrahydro-1H-indazol-3-yl)methanone				358.1	1.79min	Method A
Example 96	(4-(4-chlorophenoxy)piperidin-1-yl)(6-methoxypyridin-2-yl)methanone				347	1.90min	Method A
Example 97	(4-(4-chlorophenoxy)piperidin-1-yl)(2-methyl-4,5,6,7-tetrahydro-2H-indazol-3-yl)methanone				373.9	1.88min	Method A

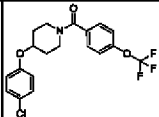
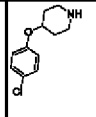
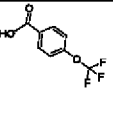
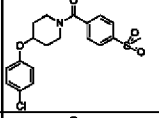
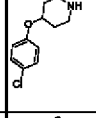
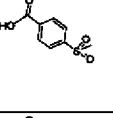
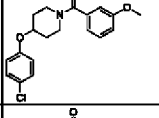
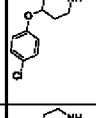
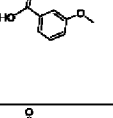
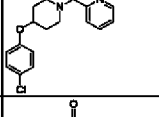
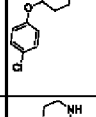
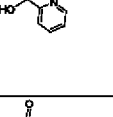
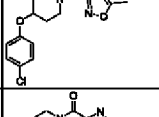
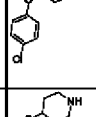
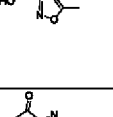
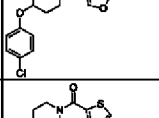
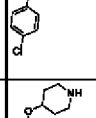
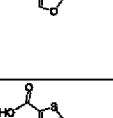
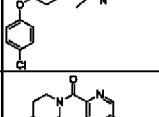
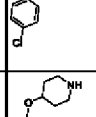
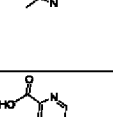
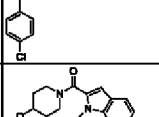
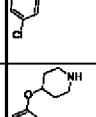
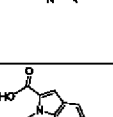
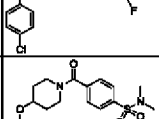
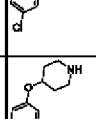
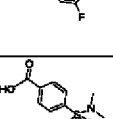
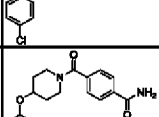
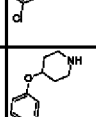
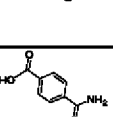
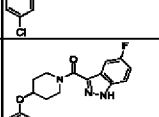
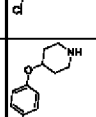
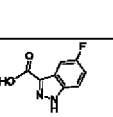
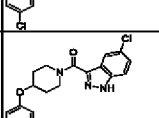
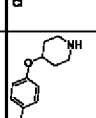
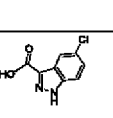
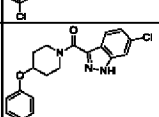
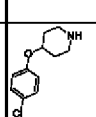
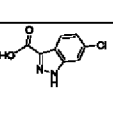
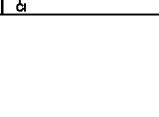
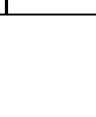
[Table 3-8]

Example 98	(4-(4-chlorophenoxy)piperidin-1-yl)(isoquinolin-4-yl)methanone				366.9	1.77 min	Method A
Example 99	(4-(4-chlorophenoxy)piperidin-1-yl)(4-methylpyridin-2-yl)methanone				330.9	1.73 min	Method A
Example 100	(4-(4-chlorophenoxy)piperidin-1-yl)(6-methoxyquinolin-2-yl)methanone				396.9	1.91 min	Method A
Example 101	(4-(4-chlorophenoxy)piperidin-1-yl)(6-methoxy-2-methylquinolin-3-yl)methanone				410.9	1.82 min	Method A
Example 102	(3-(4-chlorophenoxy)azetidin-1-yl)(8-hydroxyquinolin-2-yl)methanone				353.1	1.83 min	Method A
Example 103	benzo[d]isoxazol-3-yl(4-(4-chlorophenoxy)piperidin-1-yl)methanone				356.9	1.99 min	Method A
Example 104	(4-(4-chlorophenoxy)piperidin-1-yl)(2-(trifluoromethyl)-1H-benzof[d]imidazol-5-yl)methanone				422.1	1.73 min	Method A
Example 105	(4-(4-chlorophenoxy)piperidin-1-yl)(1,5-naphthyridin-2-yl)methanone				367.9	1.68 min	Method A
Example 106	(3-(4-chlorophenoxy)pyrrolidin-1-yl)(8-hydroxyquinolin-2-yl)methanone				367.1	1.82 min	Method A
Example 107	(4-(4-chlorophenoxy)piperidin-1-yl)(2-methyl-6-phenylpyridin-3-yl)methanone				407	2.04 min	Method A
Example 108	(4-(4-chlorophenoxy)piperidin-1-yl)(1,5-dimethyl-1H-indol-3-yl)methanone				382.9	2.01 min	Method A
Example 109	(4-(4-chlorophenoxy)piperidin-1-yl)(5-fluoro-1-methyl-1H-indol-3-yl)methanone				386.9	1.94 min	Method A
Example 110	(5-chloro-1-methyl-1H-indol-3-yl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone				402.9	2.03 min	Method A
Example 111	(4-(4-chlorophenoxy)piperidin-1-yl)(5-methoxy-1-methyl-1H-indol-3-yl)methanone				399	1.90 min	Method A

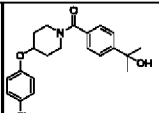
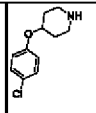
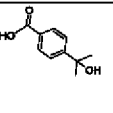
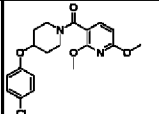
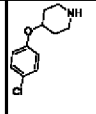
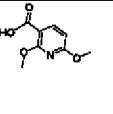
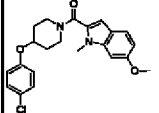
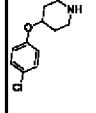
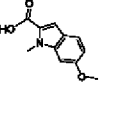
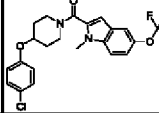
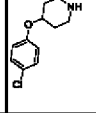
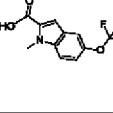
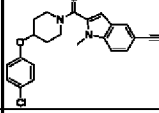
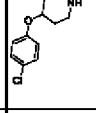
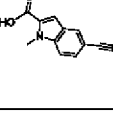
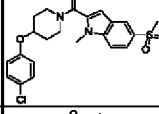
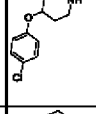
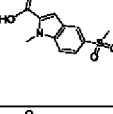
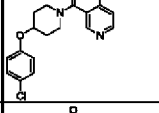
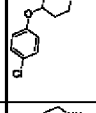
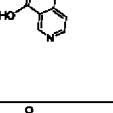
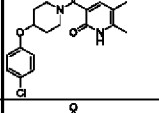
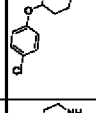
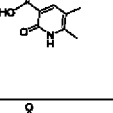
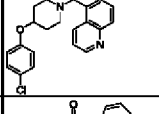
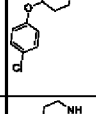
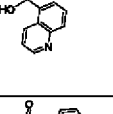
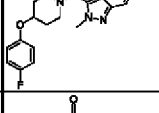
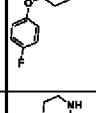
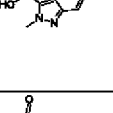
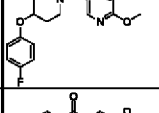
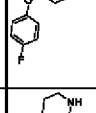
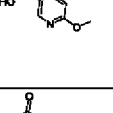
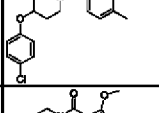
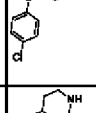
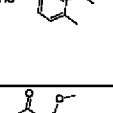
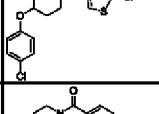
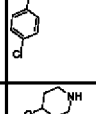
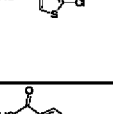
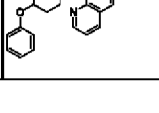
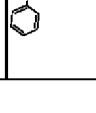
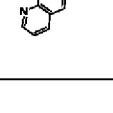
[Table 3-9]

Example 112	(4-(4-chlorophenoxy)piperidin-1-yl)(1,6-dimethyl-1H-indol-3-yl)methanone				382.9	2.02min	Method A
Example 113	(4-(4-chlorophenoxy)piperidin-1-yl)(6-fluoro-1-methyl-1H-indol-3-yl)methanone				386.9	1.95min	Method A
Example 114	(6-chloro-1-methyl-1H-indol-3-yl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone				402.9	2.04min	Method A
Example 115	(4-(4-chlorophenoxy)piperidin-1-yl)(6-methoxy-1-methyl-1H-indol-3-yl)methanone				399	1.90min	Method A
Example 116	(4-(4-chlorophenoxy)piperidin-1-yl)(5-fluoro-1-methyl-1H-indol-2-yl)methanone				386.9	2.04min	Method A
Example 117	(4-(4-chlorophenoxy)piperidin-1-yl)(5-methoxy-1-methyl-1H-indol-2-yl)methanone				399	2.00min	Method A
Example 118	(4-(4-chlorophenoxy)piperidin-1-yl)(3-fluorophenyl)methanone				334	1.91min	Method A
Example 119	(4-(4-chlorophenoxy)piperidin-1-yl)(p-tolyl)methanone				330	1.97min	Method A
Example 120	(4-(4-chlorophenoxy)piperidin-1-yl)(4-methoxyphenyl)methanone				345.9	1.88min	Method A
Example 121	4-(4-(4-chlorophenoxy)piperidin-1-carbonyl)benzonitrile				340.9	1.81min	Method A
Example 122	(4-(4-chlorophenoxy)piperidin-1-yl)(6-methylimidazo[1,2-a]pyridin-2-yl)methanone				369.9	1.75min	Method A
Example 123	(6-chloroimidazo[1,2-a]pyridin-2-yl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone				389.8	1.81min	Method A
Example 124	(4-(4-chlorophenoxy)piperidin-1-yl)(2-methylpyridin-3-yl)methanone				330.9	1.62min	Method A
Example 125	(4-(4-chlorophenoxy)piperidin-1-yl)(4-isopropoxyphenyl)methanone				373.9	2.03min	Method A

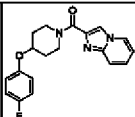
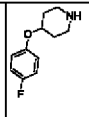
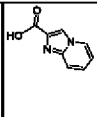
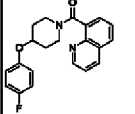
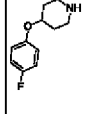
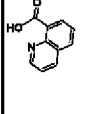
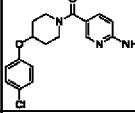
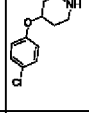
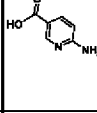
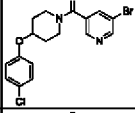
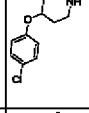
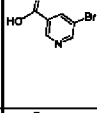
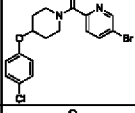
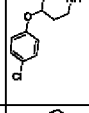
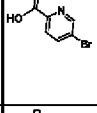
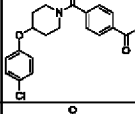
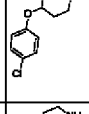
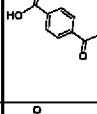
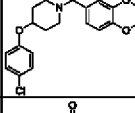
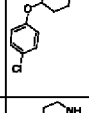
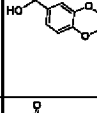
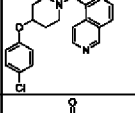
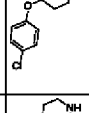
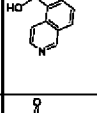
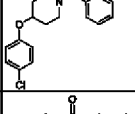
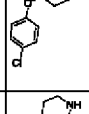
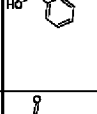
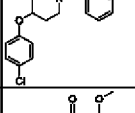
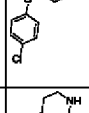
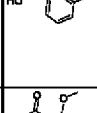
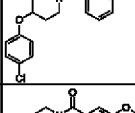
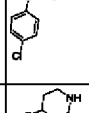
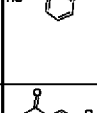
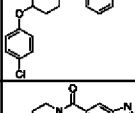
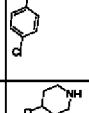
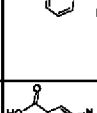
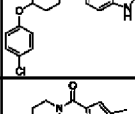
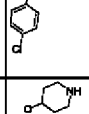
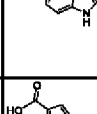
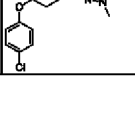
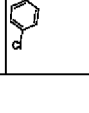
[Table 3-10]

Example 126	(4-(4-chlorophenoxy)piperidin-1-yl)(4-(trifluoromethoxy)phenyl)methanone				399.9	2.04 min	Method A
Example 127	(4-(4-chlorophenoxy)piperidin-1-yl)(4-(methylsulfonyl)phenyl)methanone				393.8	1.68 min	Method A
Example 128	(4-(4-chlorophenoxy)piperidin-1-yl)(3-methoxyphenyl)methanone				345.9	1.89 min	Method A
Example 129	(4-(4-chlorophenoxy)piperidin-1-yl)(pyridin-2-yl)methanone				316.9	1.66 min	Method A
Example 130	(4-(4-chlorophenoxy)piperidin-1-yl)(5-methylisoxazol-3-yl)methanone				320.9	1.81 min	Method A
Example 131	(4-(4-chlorophenoxy)piperidin-1-yl)(oxazol-4-yl)methanone				306.9	1.64 min	Method A
Example 132	(4-(4-chlorophenoxy)piperidin-1-yl)(4-methylthiazol-5-yl)methanone				336.9	1.69 min	Method A
Example 133	(4-(4-chlorophenoxy)piperidin-1-yl)(5-methylpyrazin-2-yl)methanone				332	1.68 min	Method A
Example 134	(4-(4-chlorophenoxy)piperidin-1-yl)(6-fluoro-1-methyl-1H-indol-2-yl)methanone				386.9	2.05 min	Method A
Example 135	4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-N,N-dimethylbenzenesulfonamide				422.9	1.80 min	Method A
Example 136	4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)benzamide				357.1	1.53 min	Method A
Example 137	(4-(4-chlorophenoxy)piperidin-1-yl)(5-fluoro-1H-indazol-3-yl)methanone				372.1	1.83 min	Method A
Example 138	(5-chloro-1H-indazol-3-yl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone				388.1	1.92 min	Method A
Example 139	(6-chloro-1H-indazol-3-yl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone				388.1	1.91 min	Method A

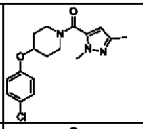
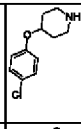
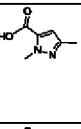
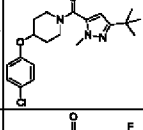
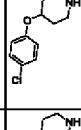
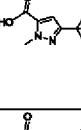
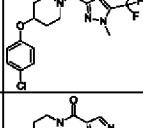
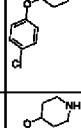
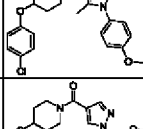
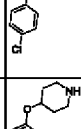
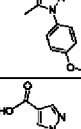
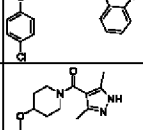
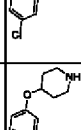
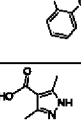
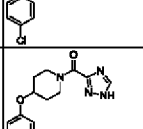
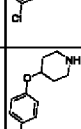
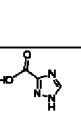
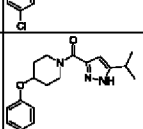
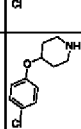
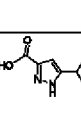
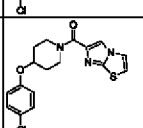
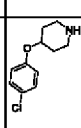
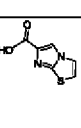
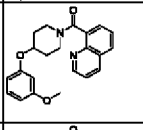
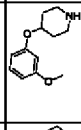
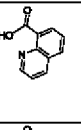
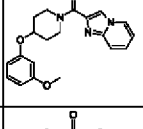
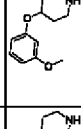
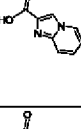
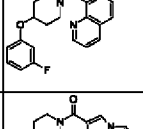
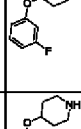
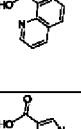
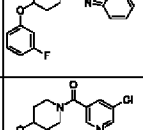
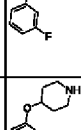
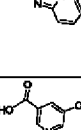
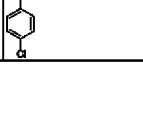
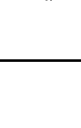
[Table 3-11]

Example 140	(4-(4-chlorophenoxy)piperidin-1-yl)(4-(2-hydroxypropan-2-yl)phenyl)methanone				373.9	1.75min	Method A
Example 141	(4-(4-chlorophenoxy)piperidin-1-yl)(2,6-dimethoxypyridin-3-yl)methanone				376.9	1.93min	Method A
Example 142	(4-(4-chlorophenoxy)piperidin-1-yl)(6-methoxy-1-methyl-1H-indol-2-yl)methanone				398.9	2.01min	Method A
Example 143	(4-(4-chlorophenoxy)piperidin-1-yl)(1-methyl-5-(trifluoromethoxy)-1H-indol-2-yl)methanone				452.9	2.16min	Method A
Example 144	2-(4-(4-chlorophenoxy)piperidin-1-carbonyl)-1-methyl-1H-indole-5-carbonitrile				394	1.92min	Method A
Example 145	(4-(4-chlorophenoxy)piperidin-1-yl)(1-methyl-5-(methylsulfonyl)-1H-indol-2-yl)methanone				446.9	1.76min	Method A
Example 146	(4-(4-chlorophenoxy)piperidin-1-yl)(4-methylpyridin-3-yl)methanone				330.9	1.63min	Method A
Example 147	3-(4-(4-chlorophenoxy)piperidin-1-carbonyl)-5,6-dimethylpyridin-2(1H)-one				359.1	1.51min	Method A
Example 148	(4-(4-chlorophenoxy)piperidin-1-yl)(quinolin-5-yl)methanone				366.9	1.72min	Method A
Example 149	(4-(4-fluorophenoxy)piperidin-1-yl)(2-methyl-2H-indazol-3-yl)methanone				353.9	1.72min	Method A
Example 150	(4-(4-fluorophenoxy)piperidin-1-yl)(6-methoxypyridin-3-yl)methanone				330.9	1.65min	Method A
Example 151	(4-(4-chlorophenoxy)piperidin-1-yl)(3-methoxy-4-methylphenyl)methanone				359.9	2.01min	Method A
Example 152	(5-chloro-4-methoxythiophen-3-yl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone				385.8	1.99min	Method A
Example 153	(4-phenoxy)piperidin-1-yl)(quinolin-8-yl)methanone				333	1.65min	Method A

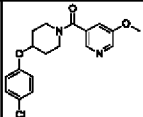
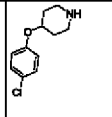
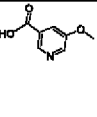
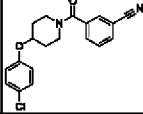
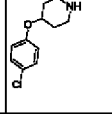
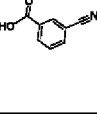
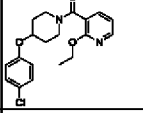
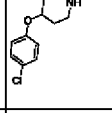
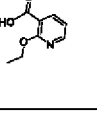
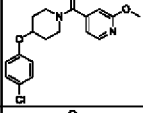
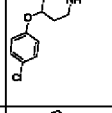
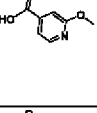
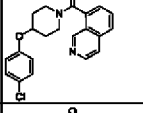
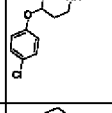
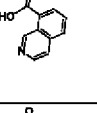
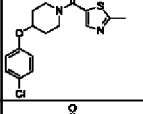
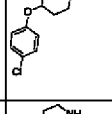
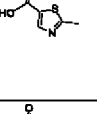
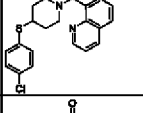
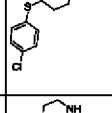
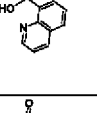
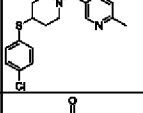
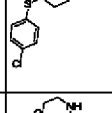
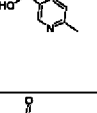
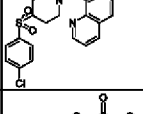
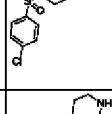
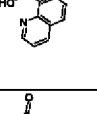
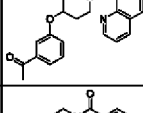
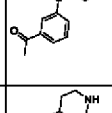
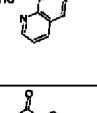
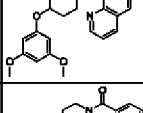
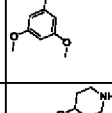
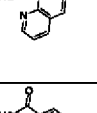
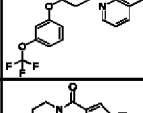
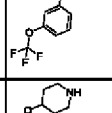
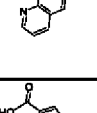
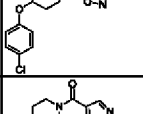
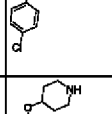
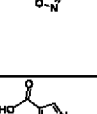
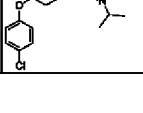
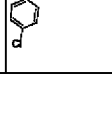
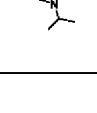
[Table 3-12]

Example 154	(4-(4-fluorophenoxy)piperidin-1-yl)(imidazo[1,2-a]pyridin-2-yl)methanone				339.9	1.53min	Method A
Example 155	(4-(4-fluorophenoxy)piperidin-1-yl)(quinolin-8-yl)methanone				351	1.66min	Method A
Example 156	(6-aminopyridin-3-yl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone				331.9	1.53min	Method A
Example 157	(5-bromopyridin-3-yl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone				394.8	1.85min	Method A
Example 158	(5-bromopyridin-2-yl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone				394.8	1.92min	Method A
Example 159	1-(4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)phenyl)ethanone				357.9	1.83min	Method A
Example 160	(4-(4-chlorophenoxy)piperidin-1-yl)(3,4-dimethoxyphenyl)methanone				375.8	1.82min	Method A
Example 161	(4-(4-chlorophenoxy)piperidin-1-yl)(isoquinolin-5-yl)methanone				366.8	1.73min	Method A
Example 162	(4-(4-chlorophenoxy)piperidin-1-yl)(phenyl)methanone				315.9	1.92min	Method A
Example 163	(4-(4-chlorophenoxy)piperidin-1-yl)(m-tolyl)methanone				329.9	2.02min	Method A
Example 164	(4-(4-chlorophenoxy)piperidin-1-yl)(2-methoxyphenyl)methanone				345.9	1.92min	Method A
Example 165	(4-(4-chlorophenoxy)piperidin-1-yl)(3-(trifluoromethoxy)phenyl)methanone				399.8	2.10min	Method A
Example 166	(1H-benzod[imidazol-5-yl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone				354.1	1.54min	Method A
Example 167	(4-(4-chlorophenoxy)piperidin-1-yl)(1,5-dimethyl-1H-pyrazol-3-yl)methanone				333.9	1.72min	Method A

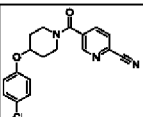
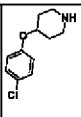
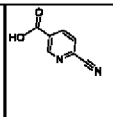
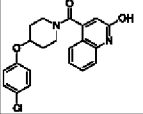
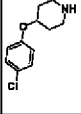
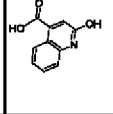
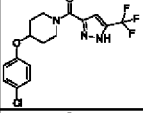
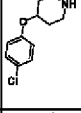
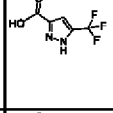
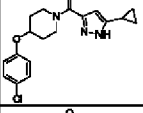
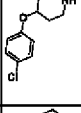
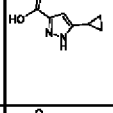
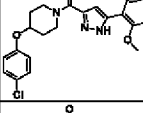
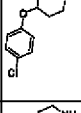
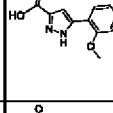
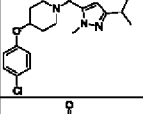
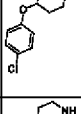
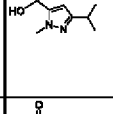
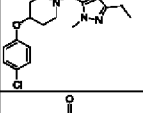
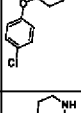
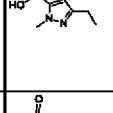
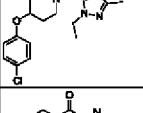
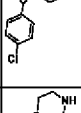
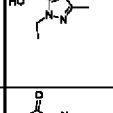
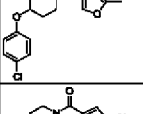
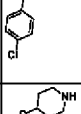
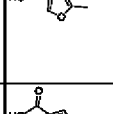
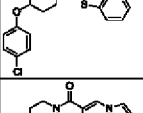
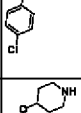
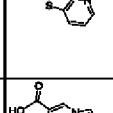
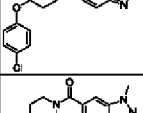
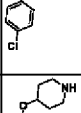
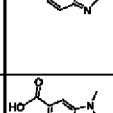
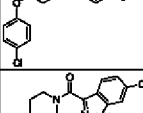
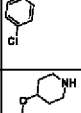
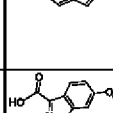
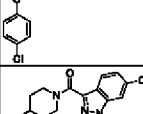
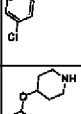
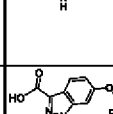
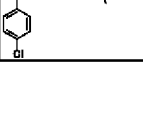
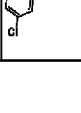
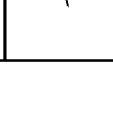
[Table 3-13]

Example 168	(4-(4-chlorophenoxy)piperidin-1-yl)(1,3-dimethyl-1H-pyrazol-5-yl)methanone				333.9	1.73min	Method A
Example 169	(3-(tert-butyl)-1-methyl-1H-pyrazol-5-yl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone				375.9	2.02min	Method A
Example 170	(4-(4-chlorophenoxy)piperidin-1-yl)(1-methyl-5-(trifluoromethyl)-1H-pyrazol-3-yl)methanone				387.8	1.96min	Method A
Example 171	(4-(4-chlorophenoxy)piperidin-1-yl)(1-(4-methoxyphenyl)-5-methyl-1H-pyrazol-4-yl)methanone				425.9	1.88min	Method A
Example 172	(4-(4-chlorophenoxy)piperidin-1-yl)(1-(2-methoxyphenyl)-1H-pyrazol-4-yl)methanone				411.8	1.89min	Method A
Example 173	(4-(4-chlorophenoxy)piperidin-1-yl)(3,5-dimethyl-1H-pyrazol-4-yl)methanone				332.1	1.54min	Method A
Example 174	(4-(4-chlorophenoxy)piperidin-1-yl)(1H-1,2,4-triazol-3-yl)methanone				305	1.47min	Method A
Example 175	(4-(4-chlorophenoxy)piperidin-1-yl)(5-isopropyl-1H-pyrazol-3-yl)methanone				346.1	1.77min	Method A
Example 176	(4-(4-chlorophenoxy)piperidin-1-yl)(imidazo[2,1-b]thiazol-6-yl)methanone				361.8	1.71min	Method A
Example 177	(4-(3-methoxyphenoxy)piperidin-1-yl)(quinolin-8-yl)methanone				362.9	1.64min	Method A
Example 178	imidazo[1,2-a]pyridin-2-yl(4-(3-methoxyphenoxy)piperidin-1-yl)methanone				351.9	1.52min	Method A
Example 179	(4-(3-fluorophenoxy)piperidin-1-yl)(quinolin-8-yl)methanone				350.9	1.69min	Method A
Example 180	(4-(3-fluorophenoxy)piperidin-1-yl)(imidazo[1,2-a]pyridin-2-yl)methanone				339.9	1.57min	Method A
Example 181	(4-(4-chlorophenoxy)piperidin-1-yl)(5-chloropyridin-3-yl)methanone				350.9	1.81min	Method A

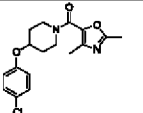
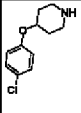
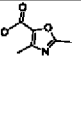
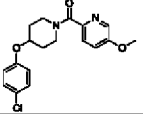
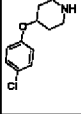
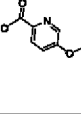
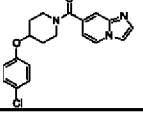
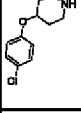
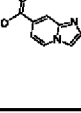
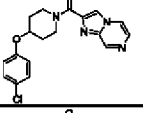
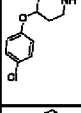
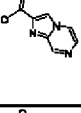
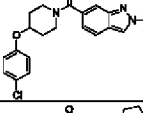
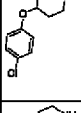
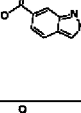
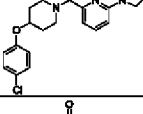
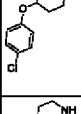
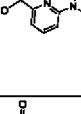
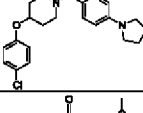
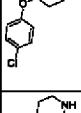
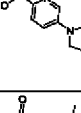
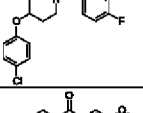
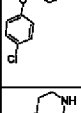
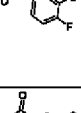
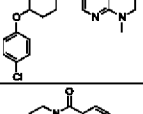
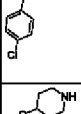
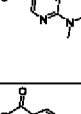
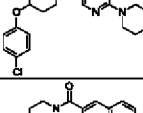
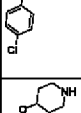
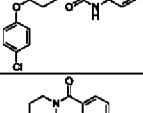
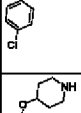
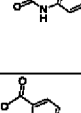
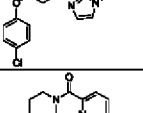
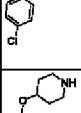
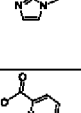
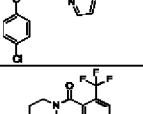
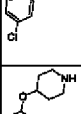
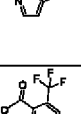
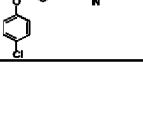
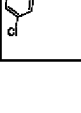
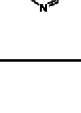
[Table 3-14]

Example 182	(4-(4-chlorophenoxy)piperidin-1-yl)(5-methoxypyridin-3-yl)methanone				346.9	1.69min	Method A
Example 183	3-(4-(4-chlorophenoxy)piperidin-1-carbonyl)benzonitrile				340.9	1.83min	Method A
Example 184	(4-(4-chlorophenoxy)piperidin-1-yl)(2-ethoxypyridin-3-yl)methanone				360.8	1.89min	Method A
Example 185	(4-(4-chlorophenoxy)piperidin-1-yl)(2-methoxypyridin-4-yl)methanone				346.8	1.81min	Method A
Example 186	(4-(4-chlorophenoxy)piperidin-1-yl)(isoquinolin-8-yl)methanone				366.9	1.76min	Method A
Example 187	(4-(4-chlorophenoxy)piperidin-1-yl)(2-methylthiazol-5-yl)methanone				336.9	1.74min	Method A
Example 188	(4-((4-chlorophenyl)thio)piperidin-1-yl)(quinolin-8-yl)methanone				382.8	1.90min	Method A
Example 189	(4-((4-chlorophenyl)thio)piperidin-1-yl)(6-methylpyridin-3-yl)methanone				346.9	1.77min	Method A
Example 190	(4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(quinolin-8-yl)methanone				414.8	1.54min	Method A
Example 191	1-(3-((1-(quinoline-8-carbonyl)piperidin-4-yl)oxy)phenyl)ethanone				374.9	1.54min	Method A
Example 192	(4-(3,5-dimethoxyphenoxy)piperidin-1-yl)(quinolin-8-yl)methanone				392.9	1.65min	Method A
Example 193	quinolin-8-yl(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone				416.9	1.88min	Method A
Example 194	(4-(4-chlorophenoxy)piperidin-1-yl)(3-methylisoxazol-5-yl)methanone				320.9	1.80min	Method A
Example 195	(4-(4-chlorophenoxy)piperidin-1-yl)(1-isopropyl-1H-pyrazol-4-yl)methanone				347.9	1.74min	Method A

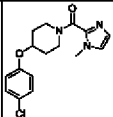
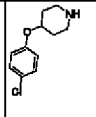
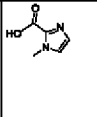
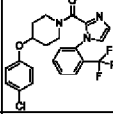
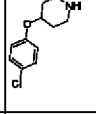
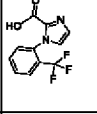
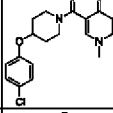
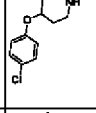
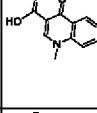
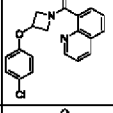
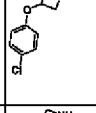
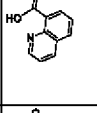
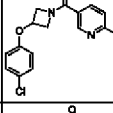
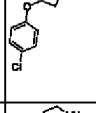
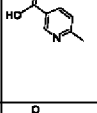
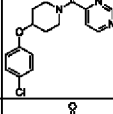
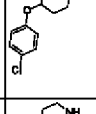
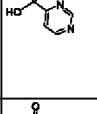
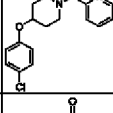
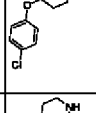
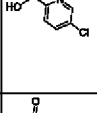
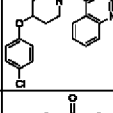
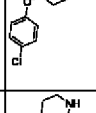
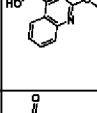
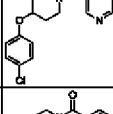
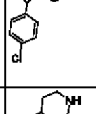
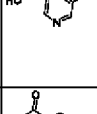
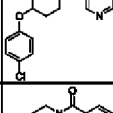
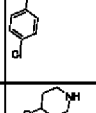
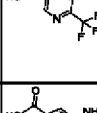
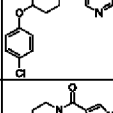
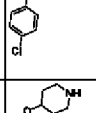
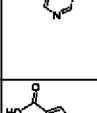
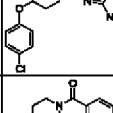
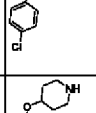
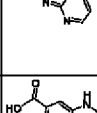
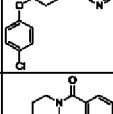
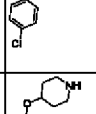
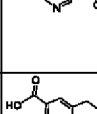
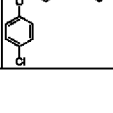
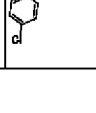
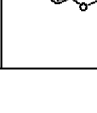
[Table 3-15]

Example 196	5-(4-(4-chlorophenoxy)piperidin-1-carbonyl)picolinonitrile				340	1.76min	Method A
Example 197	(4-(4-(4-chlorophenoxy)piperidin-1-yl)(2-hydroxyquinolin-4-yl)methanone				381.1	1.62min	Method A
Example 198	(4-(4-(4-chlorophenoxy)piperidin-1-yl)(5-(trifluoromethyl)-1H-pyrazol-3-yl)methanone				372	1.86min	Method A
Example 199	(4-(4-(4-chlorophenoxy)piperidin-1-yl)(5-cyclopropyl-1H-pyrazol-3-yl)methanone				344.1	1.72min	Method A
Example 200	(4-(4-(4-chlorophenoxy)piperidin-1-yl)(5-(2-methoxyphenyl)-1H-pyrazol-3-yl)methanone				410.1	1.89min	Method A
Example 201	(4-(4-(4-chlorophenoxy)piperidin-1-yl)(3-isopropyl-1-methyl-1H-pyrazol-5-yl)methanone				361.9	1.93min	Method A
Example 202	(4-(4-(4-chlorophenoxy)piperidin-1-yl)(3-ethyl-1-methyl-1H-pyrazol-5-yl)methanone				347.9	1.84min	Method A
Example 203	(4-(4-(4-chlorophenoxy)piperidin-1-yl)(1-ethyl-3-methyl-1H-pyrazol-5-yl)methanone				347.9	1.82min	Method A
Example 204	(4-(4-(4-chlorophenoxy)piperidin-1-yl)(2-methyloxazol-4-yl)methanone				320.9	1.71min	Method A
Example 205	(4-(4-(4-chlorophenoxy)piperidin-1-yl)(thieno[3,2-b]pyridin-2-yl)methanone				372.8	1.81min	Method A
Example 206	(4-(4-(4-chlorophenoxy)piperidin-1-yl)(imidazo[1,2-a]pyridin-6-yl)methanone				355.8	1.58min	Method A
Example 207	(4-(4-(4-chlorophenoxy)piperidin-1-yl)(1-methyl-1H-indazol-6-yl)methanone				369.8	1.80min	Method A
Example 208	(4-(4-(4-chlorophenoxy)piperidin-1-yl)(6-(trifluoromethoxy)-1H-indazol-3-yl)methanone				438	2.00min	Method A
Example 209	(4-(4-(4-chlorophenoxy)piperidin-1-yl)(1-methyl-6-(trifluoromethoxy)-1H-indazol-3-yl)methanone				453.8	2.14min	Method A

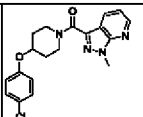
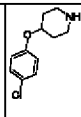
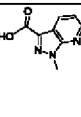
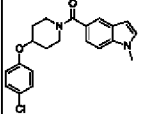
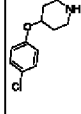
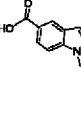
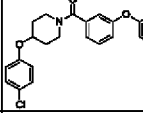
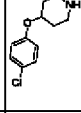
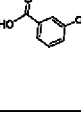
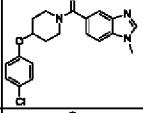
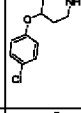
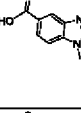
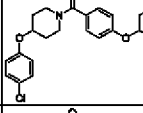
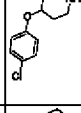
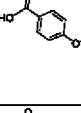
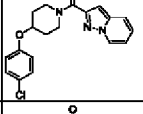
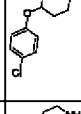
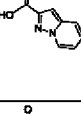
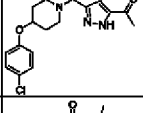
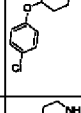
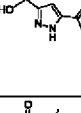
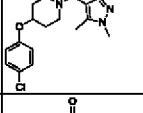
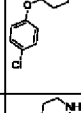
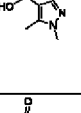
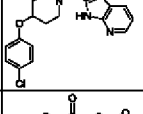
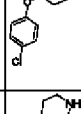
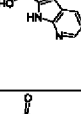
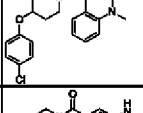
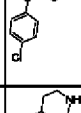
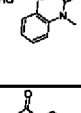
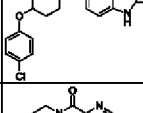
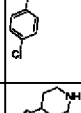
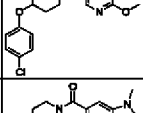
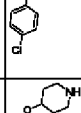
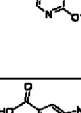
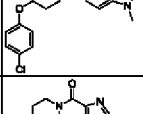
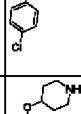
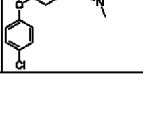
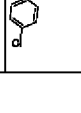
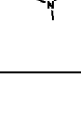
[Table 3-16]

Example 210	(4-(4-chlorophenoxy)piperidin-1-yl)(2,4-dimethyloxazol-5-yl)methanone				334.9	1.73min	Method A
Example 211	(4-(4-chlorophenoxy)piperidin-1-yl)(5-methoxypyridin-2-yl)methanone				346.9	1.75min	Method A
Example 212	(4-(4-chlorophenoxy)piperidin-1-yl)(imidazo[1,2-a]pyridin-7-yl)methanone				355.8	1.58min	Method A
Example 213	(4-(4-chlorophenoxy)piperidin-1-yl)(imidazo[1,2-a]pyrazin-2-yl)methanone				356.8	1.56min	Method A
Example 214	(4-(4-chlorophenoxy)piperidin-1-yl)(2-methyl-2H-indazol-6-yl)methanone				369.8	1.69min	Method A
Example 215	(4-(4-chlorophenoxy)piperidin-1-yl)(6-(pyrrolidin-1-yl)pyridin-2-yl)methanone				385.8	2.07min	Method A
Example 216	(4-(4-chlorophenoxy)piperidin-1-yl)(5-(pyrrolidin-1-yl)pyridin-2-yl)methanone				385.9	1.96min	Method A
Example 217	(4-(4-chlorophenoxy)piperidin-1-yl)(4-fluoro-3-methoxyphenyl)methanone				363.9	1.91min	Method A
Example 218	(4-(4-chlorophenoxy)piperidin-1-yl)(4-methyl-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)methanone				387.9	1.78min	Method A
Example 219	(4-(4-chlorophenoxy)piperidin-1-yl)(6-(piperidin-1-yl)pyridin-3-yl)methanone				399.9	2.05min	Method A
Example 220	3-(4-(4-chlorophenoxy)piperidine-1-carbonyl)quinolin-2(1H)-one				381	1.64min	Method A
Example 221	(4-(4-chlorophenoxy)piperidin-1-yl)(imidazo[1,2-a]pyridin-8-yl)methanone				355.9	1.58min	Method A
Example 222	(4-(4-chlorophenoxy)piperidin-1-yl)(pyrazolo[1,5-a]pyridin-7-yl)methanone				355.8	1.82min	Method A
Example 223	(4-(4-chlorophenoxy)piperidin-1-yl)(4-(trifluoromethyl)pyridin-3-yl)methanone				384.8	1.84min	Method A

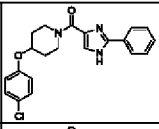
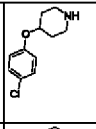
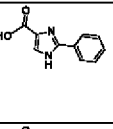
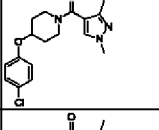
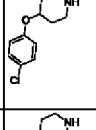
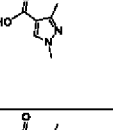
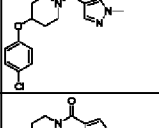
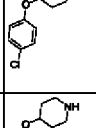
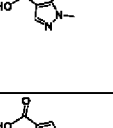
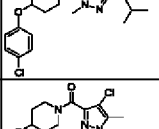
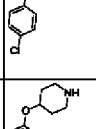
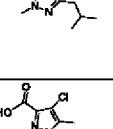
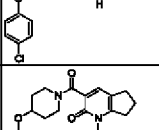
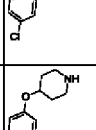
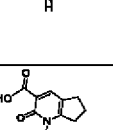
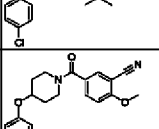
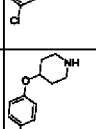
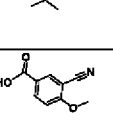
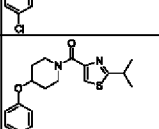
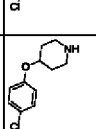
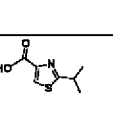
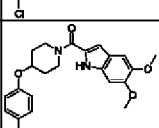
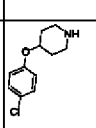
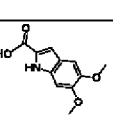
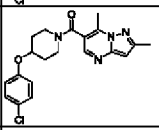
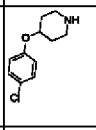
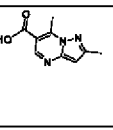
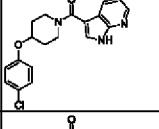
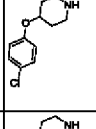
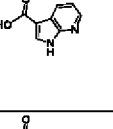
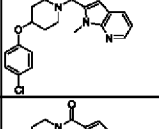
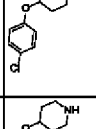
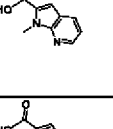
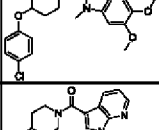
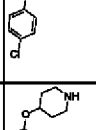
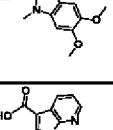
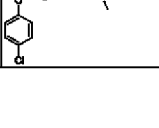
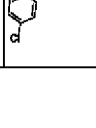
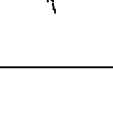
[Table 3-17]

Example224	(4-(4-chlorophenoxy)piperidin-1-yl)(1-methyl-1H-imidazol-2-yl)methanone				319.9	1.62min	Method A
Example225	(4-(4-chlorophenoxy)piperidin-1-yl)(1-(2-(trifluoromethyl)phenyl)-1H-imidazol-2-yl)methanone				449.8	2.00min	Method A
Example226	3-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-1-methylquinolin-4(1H)-one				396.8	1.59min	Method A
Example227	(3-(4-chlorophenoxy)azetidin-1-yl)(quinolin-8-yl)methanone				338.8	1.67min	Method A
Example228	(3-(4-chlorophenoxy)azetidin-1-yl)(6-methylpyridin-3-yl)methanone				302.9	1.57min	Method A
Example229	(4-(4-chlorophenoxy)piperidin-1-yl)(pyrimidin-4-yl)methanone				316.6	1.60min	Method A
Example230	(4-(4-chlorophenoxy)piperidin-1-yl)(5-chloropyridin-2-yl)methanone				350.8	1.90min	Method A
Example231	(4-(4-chlorophenoxy)piperidin-1-yl)(2-methoxyquinolin-4-yl)methanone				396.8	2.05min	Method A
Example232	(4-(4-chlorophenoxy)piperidin-1-yl)(5-hydroxypyridin-3-yl)methanone				331.1	1.52min	Method A
Example233	(4-(4-chlorophenoxy)piperidin-1-yl)(6-(trifluoromethyl)pyridin-3-yl)methanone				384.8	1.90min	Method A
Example234	(5-aminopyridin-3-yl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone				331.9	1.50min	Method A
Example235	(4-(4-chlorophenoxy)piperidin-1-yl)(imidazo[1,2-a]pyrimidin-2-yl)methanone				356.8	1.51min	Method A
Example236	N-(5-(4-(4-chlorophenoxy)piperidine-1-carbonyl)pyridin-3-yl)acetamide				372.1	1.51min	Method A
Example237	(4-(4-chlorophenoxy)piperidin-1-yl)(chroman-6-yl)methanone				371.8	1.97min	Method A

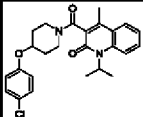
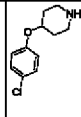
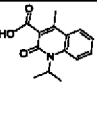
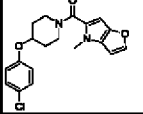
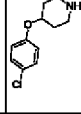
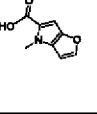
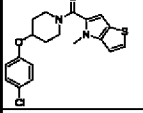
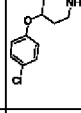
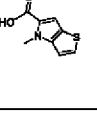
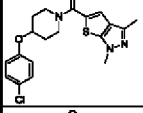
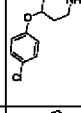
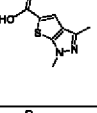
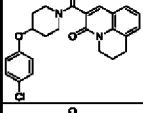
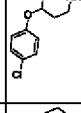
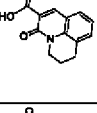
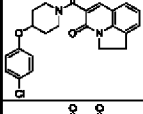
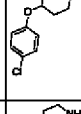
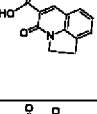
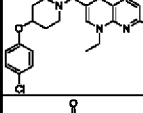
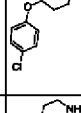
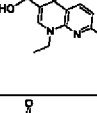
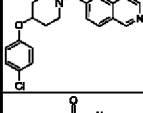
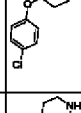
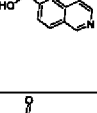
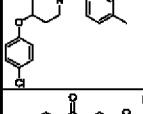
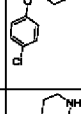
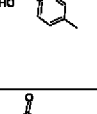
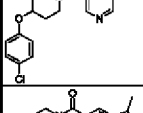
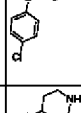
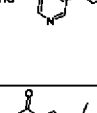
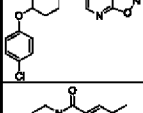
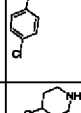
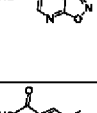
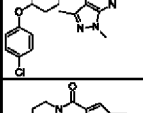
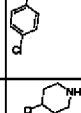
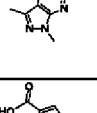
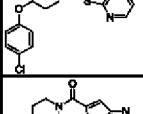
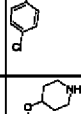
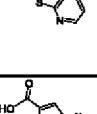
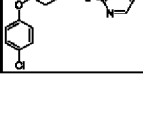
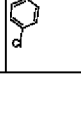
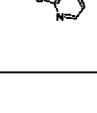
[Table 3-18]

Example238	(4-(4-chlorophenoxy)piperidin-1-yl)(1-methyl-1H-pyrazolo[3,4-b]pyridin-3-yl)methanone				370.8	1.86min	Method A
Example239	(4-(4-chlorophenoxy)piperidin-1-yl)(1-methyl-1H-indol-5-yl)methanone				368.9	1.93min	Method A
Example240	(4-(4-chlorophenoxy)piperidin-1-yl)(3-(pyridin-2-yloxy)phenyl)methanone				408.8	1.94min	Method A
Example241	(4-(4-chlorophenoxy)piperidin-1-yl)(1-methyl-1H-benz[d]imidazol-5-yl)methanone				369.9	1.61min	Method A
Example242	(4-(4-chlorophenoxy)piperidin-1-yl)(4-(tetrahydro-2H-pyran-4-yloxy)phenyl)methanone				415.9	1.90min	Method A
Example243	(4-(4-chlorophenoxy)piperidin-1-yl)(pyrazolo[1,5-a]pyridin-2-yl)methanone				355.9	1.83min	Method A
Example244	1-(3-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-1H-pyrazol-5-yl)ethanone				346.1	1.63min	Method A
Example245	(4-(4-chlorophenoxy)piperidin-1-yl)(1,3,5-trimethyl-1H-pyrazol-4-yl)methanone				347.9	1.63min	Method A
Example246	(4-(4-chlorophenoxy)piperidin-1-yl)(1H-pyrrolo[2,3-b]pyridin-2-yl)methanone				354.1	1.76min	Method A
Example247	4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-1-methylquinolin-2(1H)-one				396.9	1.74min	Method A
Example248	5-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-1H-benz[d]imidazol-2(3H)-one				370.1	1.50min	Method A
Example249	(4-(4-chlorophenoxy)piperidin-1-yl)(5-methoxypyrazin-2-yl)methanone				347.8	1.82min	Method A
Example250	5-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-1,3-dimethyl-1H-benz[d]imidazol-2(3H)-one				399.8	1.68min	Method A
Example251	(4-(4-chlorophenoxy)piperidin-1-yl)(1-methyl-1H-imidazol-4-yl)methanone				319.9	1.53min	Method A

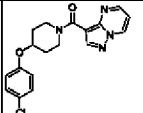
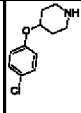
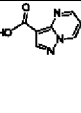
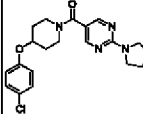
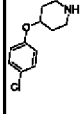
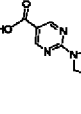
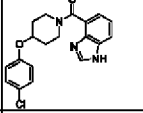
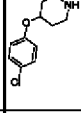
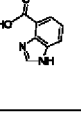
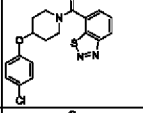
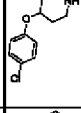
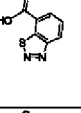
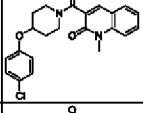
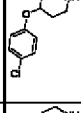
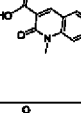
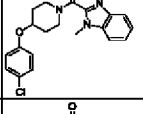
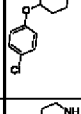
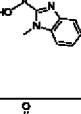
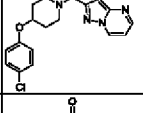
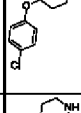
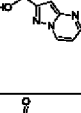
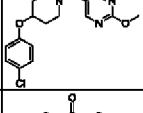
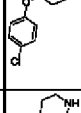
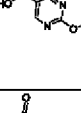
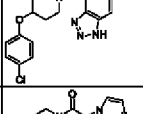
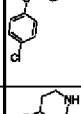
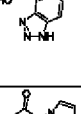
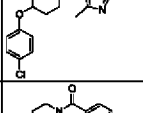
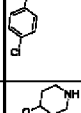
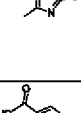
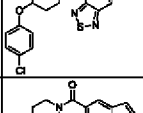
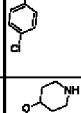
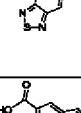
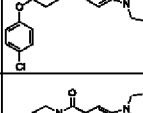
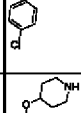
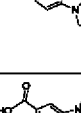
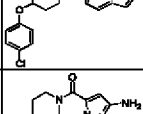
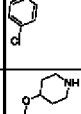
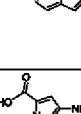
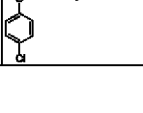
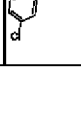
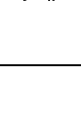
[Table 3-19]

Example252	(4-(4-chlorophenoxy)piperidin-1-yl)(2-phenyl-1H-imidazol-4-yl)methanone				380.1	1.81min	Method A
Example253	(4-(4-chlorophenoxy)piperidin-1-yl)(1,3-dimethyl-1H-pyrazol-4-yl)methanone				333.9	1.60min	Method A
Example254	(4-(4-chlorophenoxy)piperidin-1-yl)(1,5-dimethyl-1H-pyrazol-4-yl)methanone				333.9	1.61min	Method A
Example255	(4-(4-chlorophenoxy)piperidin-1-yl)(3-isobutyl-1-methyl-1H-pyrazol-5-yl)methanone				375.9	2.02min	Method A
Example256	(4-chloro-5-methyl-1H-pyrazol-3-yl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone				352	1.74min	Method A
Example257	3-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-1-isopropyl-6,7-dihydro-1H-cyclopenta[b]pyridin-2(5H)-one				413.1	1.87min	Method A
Example258	5-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-2-methoxybenzonitrile				370.8	1.83min	Method A
Example259	(4-(4-chlorophenoxy)piperidin-1-yl)(2-isopropylthiazol-4-yl)methanone				364.8	2.03min	Method A
Example260	(4-(4-chlorophenoxy)piperidin-1-yl)(5,6-dimethoxy-1H-indol-2-yl)methanone				413.1	1.85min	Method A
Example261	(4-(4-chlorophenoxy)piperidin-1-yl)(2,7-dimethylpyrazolo[1,5-a]pyrimidin-6-yl)methanone				383.1	1.73min	Method A
Example262	(4-(4-chlorophenoxy)piperidin-1-yl)(1H-pyrrolo[2,3-b]pyridin-3-yl)methanone				354.1	1.64min	Method A
Example263	(4-(4-chlorophenoxy)piperidin-1-yl)(1-methyl-1H-pyrrolo[2,3-b]pyridin-2-yl)methanone				369.8	1.87min	Method A
Example264	(4-(4-chlorophenoxy)piperidin-1-yl)(5,6-dimethoxy-1-methyl-1H-indol-2-yl)methanone				428.8	1.92min	Method A
Example265	(4-(4-chlorophenoxy)piperidin-1-yl)(1-methyl-1H-pyrrolo[2,3-b]pyridin-3-yl)methanone				369.8	1.75min	Method A

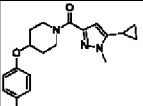
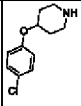
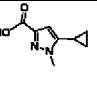
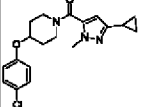
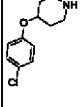
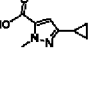
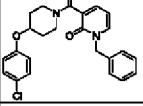
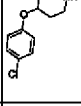
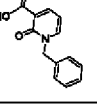
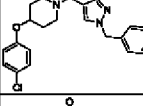
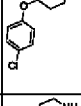
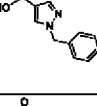
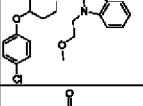
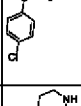
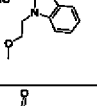
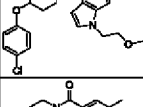
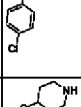
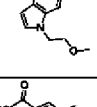
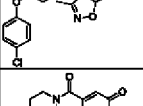
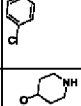
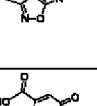
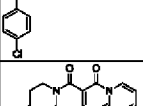
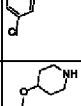
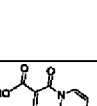
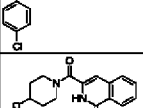
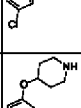
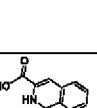
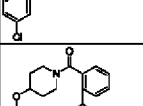
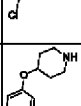
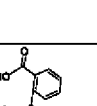
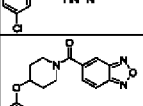
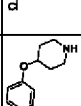
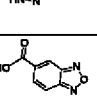
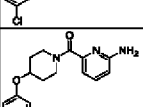
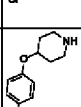
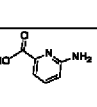
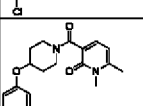
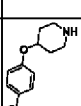
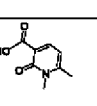
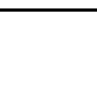
[Table 3-20]

Example 266	3-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-1-isopropyl-4-methylquinolin-2(1H)-one				438.8	1.98min	Method A
Example 267	(4-(4-(4-chlorophenoxy)piperidine-1-yl)(4-methyl-4H-furo[3,2-b]pyrrol-5-yl)methanone				358.9	1.95min	Method A
Example 268	(4-(4-(4-chlorophenoxy)piperidine-1-yl)(4-methyl-4H-thieno[3,2-b]pyrrol-5-yl)methanone				374.8	2.04min	Method A
Example 269	(4-(4-(4-chlorophenoxy)piperidine-1-yl)(1,3-dimethyl-1H-thieno[2,3-c]pyrazol-5-yl)methanone				389.8	1.85min	Method A
Example 270	2-(4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-6,7-dihydropyrido[3,2,1-ij]quinolin-3(5H)-one				422.8	1.85min	Method A
Example 271	5-(4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-1H-pyrrolo[3,2,1-ij]quinolin-4(2H)-one				408.8	1.72min	Method A
Example 272	3-(4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-1-ethyl-7-methyl-1,8-naphthyridin-4(1H)-one				424	1.79min	Method A
Example 273	(4-(4-(4-chlorophenoxy)piperidine-1-yl)(isoquinolin-6-yl)methanone				366.8	1.74min	Method A
Example 274	(4-(4-(4-chlorophenoxy)piperidine-1-yl)(5-methylpyridin-2-yl)methanone				330.9	1.77min	Method A
Example 275	(4-(4-(4-chlorophenoxy)piperidine-1-yl)(5-(2,2,2-trifluoroethoxy)pyridin-3-yl)methanone				414.8	1.84min	Method A
Example 276	(4-(4-(4-chlorophenoxy)piperidine-1-yl)(3-methylisoxazolo[5,4-b]pyridin-5-yl)methanone				371.8	1.77min	Method A
Example 277	(4-(4-(4-chlorophenoxy)piperidine-1-yl)(1,3,6-trimethyl-1H-pyrazolo[3,4-b]pyridin-4-yl)methanone				398.8	1.79min	Method A
Example 278	(4-(4-(4-chlorophenoxy)piperidine-1-yl)(thieno[2,3-b]pyridin-2-yl)methanone				372.8	1.86min	Method A
Example 279	(4-(4-(4-chlorophenoxy)piperidine-1-yl)(thieno[2,3-b]pyrazin-6-yl)methanone				373.8	1.82min	Method A

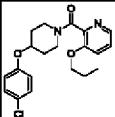
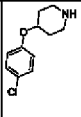
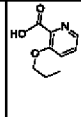
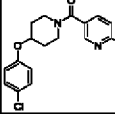
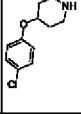
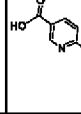
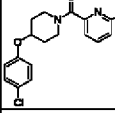
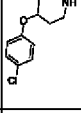
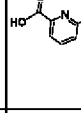
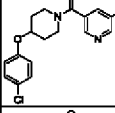
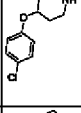
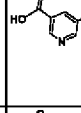
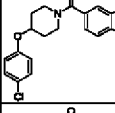
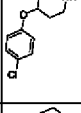
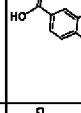
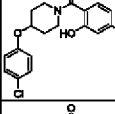
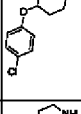
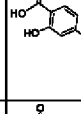
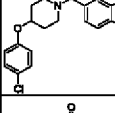
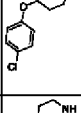
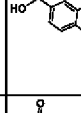
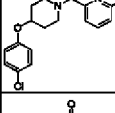
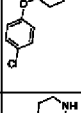
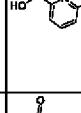
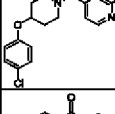
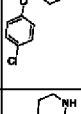
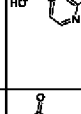
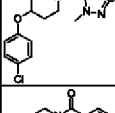
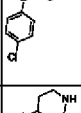
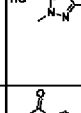
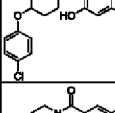
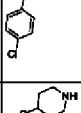
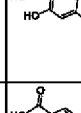
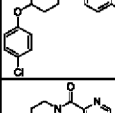
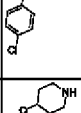
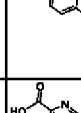
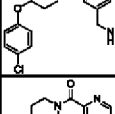
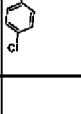
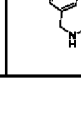
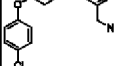
[Table 3-21]

Example 280	(4-(4-chlorophenoxy)piperidin-1-yl)(pyrazolo[1,5-a]pyrimidin-3-yl)methanone				356.8	1.60min	Method A
Example 281	(4-(4-chlorophenoxy)piperidin-1-yl)(2-(pyrrolidin-1-yl)pyrimidin-5-yl)methanone				386.9	1.83min	Method A
Example 282	(1H-benzo[d]imidazol-4-yl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone				354	1.57min	Method A
Example 283	benzo[d][1,2,3]thiadiazol-7-yl(4-(4-chlorophenoxy)piperidin-1-yl)methanone				373.8	1.95min	Method A
Example 284	3-(4-(4-chlorophenoxy)piperidin-1-carbonyl)-1-methylquinolin-2(1H)-one				396.8	1.77min	Method A
Example 285	(4-(4-chlorophenoxy)piperidin-1-yl)(1-methyl-1H-benzo[d]imidazol-2-yl)methanone				369.9	1.84min	Method A
Example 286	(4-(4-chlorophenoxy)piperidin-1-yl)(pyrazolo[1,5-a]pyrimidin-2-yl)methanone				355.1	1.65min	Method A
Example 287	(4-(4-chlorophenoxy)piperidin-1-yl)(2-methoxypyrimidin-5-yl)methanone				347.8	1.68min	Method A
Example 288	(1H-benzo[d][1,2,3]triazol-4-yl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone				355	1.60min	Method A
Example 289	(4-(4-chlorophenoxy)piperidin-1-yl)(6-methylimidazo[2,1-b]thiazol-5-yl)methanone				375.8	1.72min	Method A
Example 290	benzo[c][1,2,5]thiadiazol-4-yl(4-(4-chlorophenoxy)piperidin-1-yl)methanone				373.8	1.88min	Method A
Example 291	(4-(4-chlorophenoxy)piperidin-1-yl)(1-(2-methoxyethyl)-1H-indol-5-yl)methanone				412.8	1.93min	Method A
Example 292	(4-(4-chlorophenoxy)piperidin-1-yl)(1-(2-methoxyethyl)-1H-indol-6-yl)methanone				412.8	1.96min	Method A
Example 293	(3-amino-1-methyl-1H-pyrazol-5-yl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone				334.9	1.51min	Method A

[Table 3-22]

Example294	(4-(4-chlorophenoxy)piperidin-1-yl)(3-cyclopropyl-1-methyl-1H-pyrazol-3-yl)methanone				359.9	1.86min	Method A
Example295	(4-(4-chlorophenoxy)piperidin-1-yl)(3-cyclopropyl-1-methyl-1H-pyrazol-5-yl)methanone				359.9	1.86min	Method A
Example296	1-benzyl-3-(4-(4-chlorophenoxy)piperidine-1-carbonyl)pyridin-2(1H)-one				422.8	1.79min	Method A
Example297	(1-benzyl-1H-pyrazol-4-yl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone				395.9	1.85min	Method A
Example298	(4-(4-chlorophenoxy)piperidin-1-yl)(1-(2-methoxyethyl)-1H-indol-2-yl)methanone				412.8	2.09min	Method A
Example299	(4-(4-chlorophenoxy)piperidin-1-yl)(1-(2-methoxyethyl)-1H-indol-4-yl)methanone				412.8	1.93min	Method A
Example300	(4-(4-chlorophenoxy)piperidin-1-yl)(3,6-dimethylisoxazolo[5,4-b]pyridin-4-yl)methanone				384	1.84min	Method A
Example301	4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-1-methylpyridin-2(1H)-one				346.8	1.49min	Method A
Example302	3-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-4H-pyrido[1,2-a]pyrimidin-4-one				383.8	1.57min	Method A
Example303	3-(4-(4-chlorophenoxy)piperidine-1-carbonyl)isoquinolin-1(2H)-one				381	1.73min	Method A
Example304	(4-(4-chlorophenoxy)piperidin-1-yl)(2-(3,5-dimethyl-1H-pyrazol-4-yl)phenyl)methanone				408	1.73min	Method A
Example305	benzo[c][1,2,5]oxadiazol-5-yl(4-(4-chlorophenoxy)piperidin-1-yl)methanone				357.8	1.89min	Method A
Example306	(6-aminopyridin-2-yl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone				329.9	1.59min	Method A
Example307	3-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-1,6-dimethylpyridin-2(1H)-one				359	1.55min	Method A

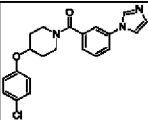
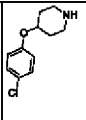
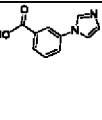
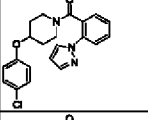
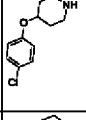
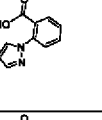
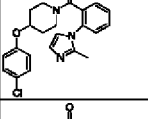
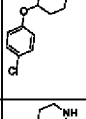
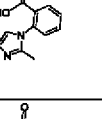
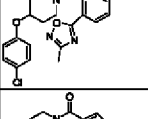
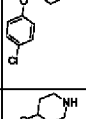
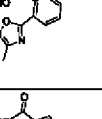
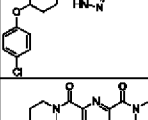
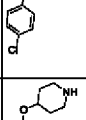
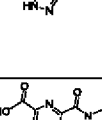
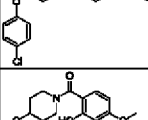
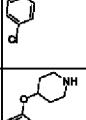
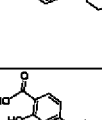
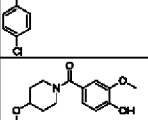
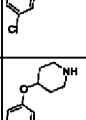
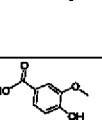
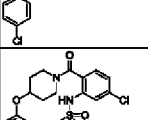
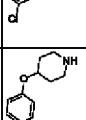
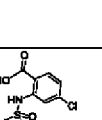
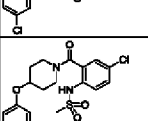
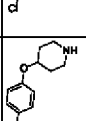
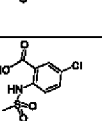
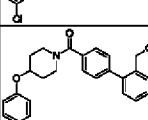
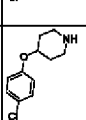
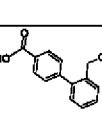
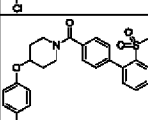
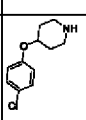
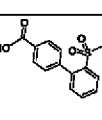
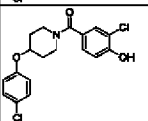
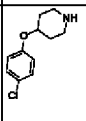
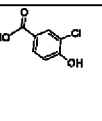
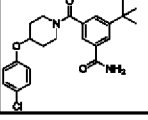
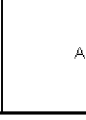
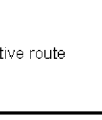
[Table 3-23]

Example308	(4-(4-chlorophenoxy)piperidin-1-yl)(3-propoxypyridin-2-yl)methanone				374.8	1.84min	Method A
Example309	(4-(4-chlorophenoxy)piperidin-1-yl)(6-((tetrahydro-2H-pyran-4-yl)oxy)pyridin-3-yl)methanone				416.8	1.86min	Method A
Example310	(4-(4-chlorophenoxy)piperidin-1-yl)(5-((tetrahydro-2H-pyran-4-yl)oxy)pyridin-2-yl)methanone				416.8	1.90min	Method A
Example311	(4-(4-chlorophenoxy)piperidin-1-yl)(5-((tetrahydro-2H-pyran-4-yl)oxy)pyridin-3-yl)methanone				416.8	1.71min	Method A
Example312	(4-(4-chlorophenoxy)piperidin-1-yl)(3-hydroxy-4-methoxyphenyl)methanone				360	1.70min	Method A
Example313	(4-chloro-2-hydroxyphenyl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone				364	1.88min	Method A
Example314	(4-(4-chlorophenoxy)piperidin-1-yl)(4-hydroxy-3-methylphenyl)methanone				344	1.76min	Method A
Example315	(4-(4-chlorophenoxy)piperidin-1-yl)(6-morpholinopyridin-2-yl)methanone				401.9	1.84min	Method A
Example316	(4-(4-chlorophenoxy)piperidin-1-yl)(2-morpholinopyridin-4-yl)methanone				401.9	1.77min	Method A
Example317	(4-(4-chlorophenoxy)piperidin-1-yl)(1-methyl-3-(trifluoromethyl)-1H-pyrazol-5-yl)methanone				387.8	1.97min	Method A
Example318	(4-(4-chlorophenoxy)piperidin-1-yl)(2-hydroxy-4-(trifluoromethyl)phenyl)methanone				398	1.91min	Method A
Example319	(4-(4-chlorophenoxy)piperidin-1-yl)(3-hydroxy-4-methylphenyl)methanone				344.1	1.81min	Method A
Example320	tert-butyl ((2-(4-(4-chlorophenoxy)piperidine-1-carbonyl)pyridin-4-yl)methyl)carbamate				444.1	1.83min	Method A
Example321	(4-(aminomethyl)pyridin-2-yl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone		Alternative route		345.9	1.39min	Method A

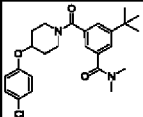
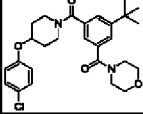
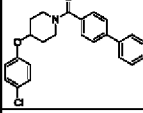
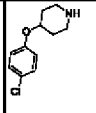
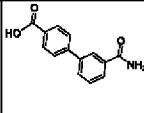
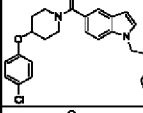
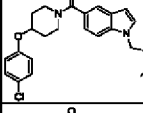
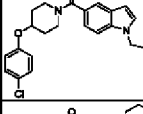
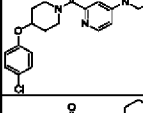
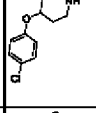
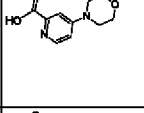
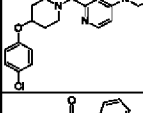
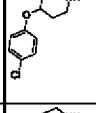
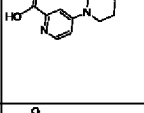
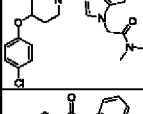
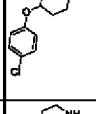
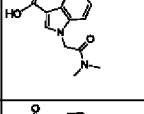
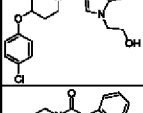
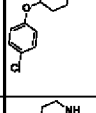
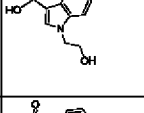
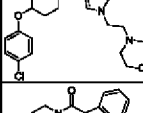
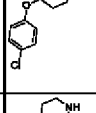
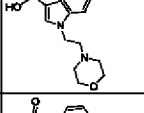
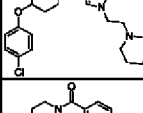
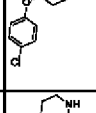
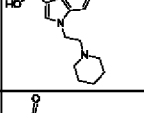
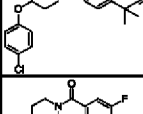
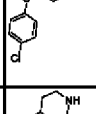
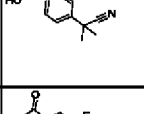
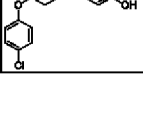
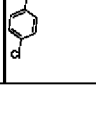
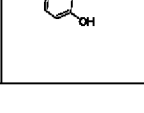
[Table 3-24]

Example322	N-((2-(4-(4-chlorophenoxy)piperidine-1-carbonyl)pyridin-4-yl)methyl)pivalamide		Alternative route	428.1	1.89min	Method A
Example323	N-((2-(4-(4-chlorophenoxy)piperidine-1-carbonyl)pyridin-4-yl)methyl)-4-fluorobenzamide		Alternative route	466.1	1.73min	Method A
Example324	N-((2-(4-(4-chlorophenoxy)piperidine-1-carbonyl)pyridin-4-yl)methyl)-4-fluorobenzenesulfonamide		Alternative route	502	1.79min	Method A
Example325	tert-butyl 2-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-7,8-dihydro-1,6-naphthyridine-6(5H)-carboxylate			471.9	1.99min	Method A
Example326	(4-(4-chlorophenoxy)piperidin-1-yl)(6-(methylsulfonyl)-5,6,7,8-tetrahydro-1,6-naphthyridin-2-yl)methanone		Alternative route	448.1	1.65min	Method A
Example327	N-(tert-butyl)-4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)benzamide			413.1	1.87min	Method A
Example328	N-(tert-butyl)-4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-N-methylbenzamide			428.9	1.94min	Method A
Example329	4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-N-(2,2,2-trifluoroethyl)benzamide			439	1.79min	Method A
Example330	(4-(4-chlorophenoxy)piperidin-1-yl)(4-(2-methoxyethoxy)phenyl)methanone			389.9	1.86min	Method A
Example331	(4-(4-chlorophenoxy)piperidin-1-yl)(4-(2-hydroxyethoxy)phenyl)methanone			375.8	1.65min	Method A
Example332	N-(4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)benzyl)pivalamide			427.1	1.82min	Method A
Example333	4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)picolinamide			358.1	1.55min	Method A
Example334	(4-(4-chlorophenoxy)piperidin-1-yl)(5-morpholinopyridin-3-yl)methanone			401.9	1.64min	Method A
Example335	(4-(4-chlorophenoxy)piperidin-1-yl)(6-(piperidin-1-yl)pyrimidin-4-yl)methanone			400.9	1.90min	Method A

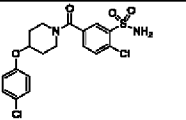
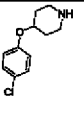
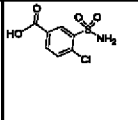
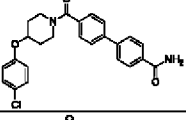
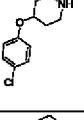
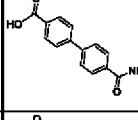
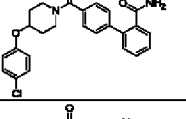
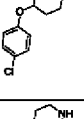
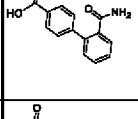
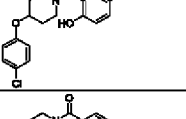
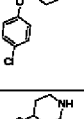
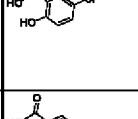
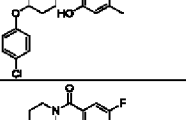
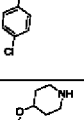
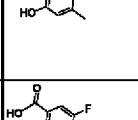
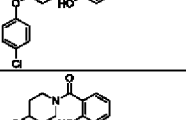
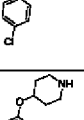
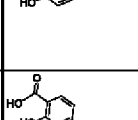
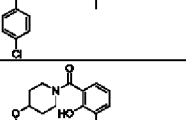
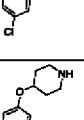
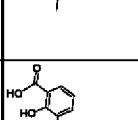
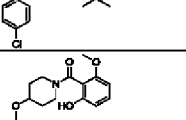
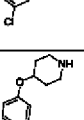
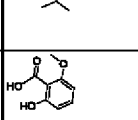
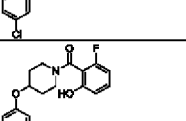
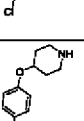
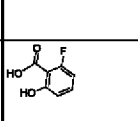
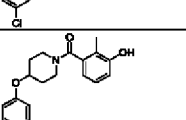
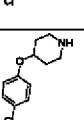
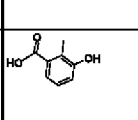
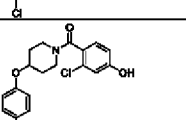
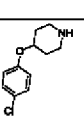
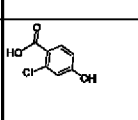
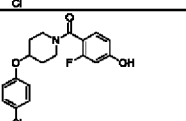
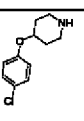
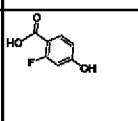
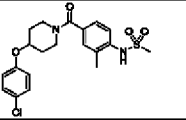
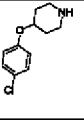
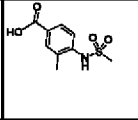
[Table 3-25]

Example336	(3-(1H-imidazol-1-yl)phenyl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone				381.9	1.68min	Method A
Example337	(2-(1H-pyrazol-1-yl)phenyl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone				381.9	1.87min	Method A
Example338	(4-(4-chlorophenoxy)piperidin-1-yl)(2-(2-methyl-1H-imidazol-1-yl)phenyl)methanone				395.9	1.68min	Method A
Example339	(4-(4-chlorophenoxy)piperidin-1-yl)(2-(3-methyl-1,2,4-oxadiazol-5-yl)phenyl)methanone				397.9	1.90min	Method A
Example340	(4-(4-chlorophenoxy)piperidin-1-yl)(3-methyl-1H-pyrazol-5-yl)methanone				318.1	1.61min	Method A
Example341	(4-(4-chlorophenoxy)piperidin-1-yl)(6-(piperidine-1-carbonyl)pyridin-2-yl)methanone				427.9	1.76min	Method A
Example342	(4-(4-chlorophenoxy)piperidin-1-yl)(2-hydroxy-4-methoxyphenyl)methanone				360	1.83min	Method A
Example343	(4-(4-chlorophenoxy)piperidin-1-yl)(4-hydroxy-3-methoxyphenyl)methanone				360	1.70min	Method A
Example344	N-(5-chloro-2-(4-(4-chlorophenoxy)piperidine-1-carbonyl)phenyl)methanesulfonamide				440.9	1.87min	Method A
Example345	N-(4-chloro-2-(4-(4-chlorophenoxy)piperidine-1-carbonyl)phenyl)methanesulfonamide				440.9	1.88min	Method A
Example346	(4-(4-chlorophenoxy)piperidin-1-yl)(2'-(hydroxymethyl)-[1,1'-biphenyl]-4-yl)methanone				421.8	1.89min	Method A
Example347	(4-(4-chlorophenoxy)piperidin-1-yl)(2'-(methylsulfonyl)-[1,1'-biphenyl]-4-yl)methanone				469.7	1.88min	Method A
Example348	(3-chloro-4-hydroxyphenyl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone				364	1.77min	Method A
Example349	3-(tert-butyl)-5-(4-(4-chlorophenoxy)piperidine-1-carbonyl)benzamide		Alternative route		413.1	1.84min	Method A

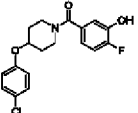
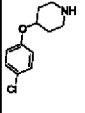
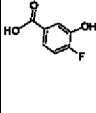
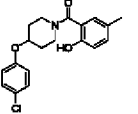
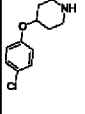
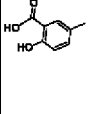
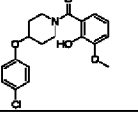
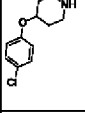
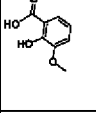
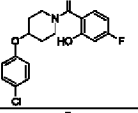
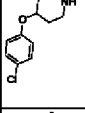
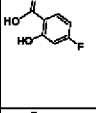
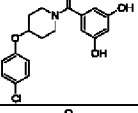
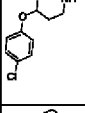
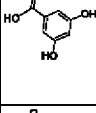
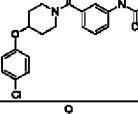
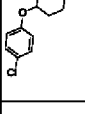
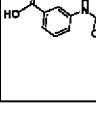
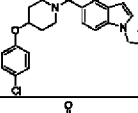
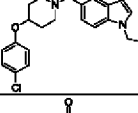
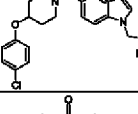
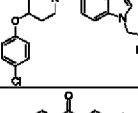
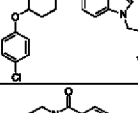
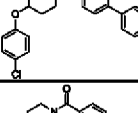
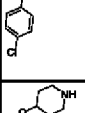
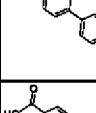
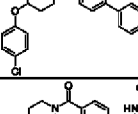
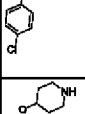
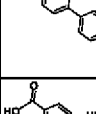
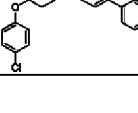
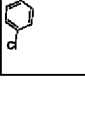
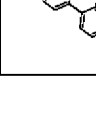
[Table 3-26]

Example350	3-(tert-butyl)-5-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-N,N-dimethylbenzamide		Alternative route	442.9	1.95min	Method A
Example351	(3-(tert-butyl)-5-(4-(4-chlorophenoxy)piperidine-1-carbonyl)phenyl)(morpholino)methanone		Alternative route	484.8	1.93min	Method A
Example352	4'-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-[1,1'-biphenyl]-3-carboxamide		 	433	1.73min	Method A
Example353	(4-(4-chlorophenoxy)piperidin-1-yl)(1-(2-morpholinoethyl)-1H-indol-5-yl)methanone		Alternative route	467.8	1.85min	Method A
Example354	2-(5-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-1H-indol-1-yl)-N,N-dimethylacetamide		Alternative route	439.8	1.73min	Method A
Example355	(4-(4-chlorophenoxy)piperidin-1-yl)(1-(2-hydroxyethyl)-1H-indol-5-yl)methanone		Alternative route	397	1.72min	Method A
Example356	(4-(4-chlorophenoxy)piperidin-1-yl)(4-morpholinopyridin-2-yl)methanone		 	400	1.64min	Method A
Example357	(4-(4-chlorophenoxy)piperidin-1-yl)(4-(piperidin-1-yl)pyridin-2-yl)methanone		 	399.8	1.90min	Method A
Example358	2-(3-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-1H-indol-1-yl)-N,N-dimethylacetamide		 	438.1	1.76min	Method A
Example359	(4-(4-chlorophenoxy)piperidin-1-yl)(1-(2-hydroxyethyl)-1H-indol-3-yl)methanone		 	398.8	1.76min	Method A
Example360	(4-(4-chlorophenoxy)piperidin-1-yl)(1-(2-morpholinoethyl)-1H-indol-3-yl)methanone		 	467.8	1.90min	Method A
Example361	(4-(4-chlorophenoxy)piperidin-1-yl)(1-(2-(piperidin-1-yl)ethyl)-1H-indol-3-yl)methanone		 	465.9	2.12min	Method A
Example362	2-(4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)phenyl)-2-methylpropanenitrile		 	382.8	1.96min	Method A
Example363	(4-(4-chlorophenoxy)piperidin-1-yl)(3-fluoro-4-hydroxyphenyl)methanone		 	348	1.70min	Method A

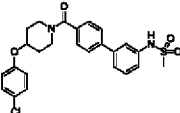
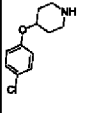
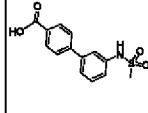
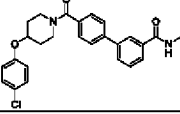
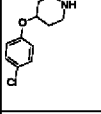
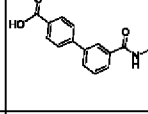
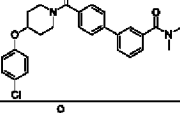
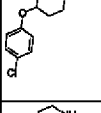
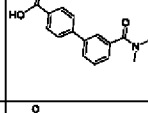
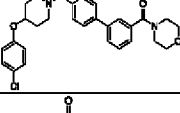
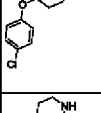
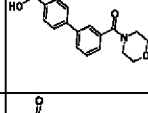
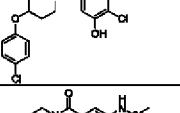
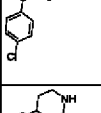
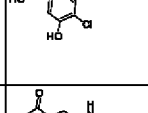
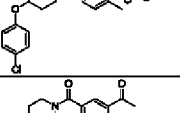
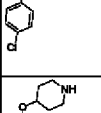
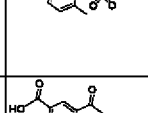
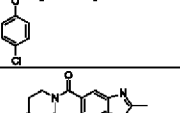
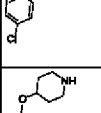
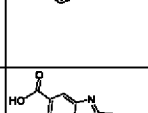
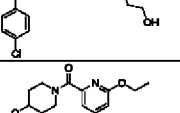
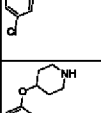
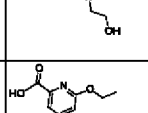
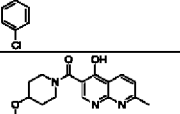
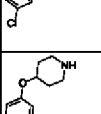
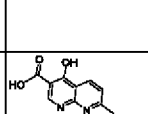
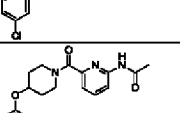
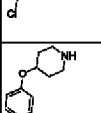
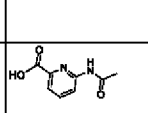
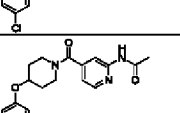
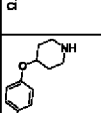
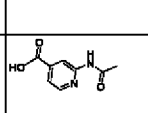
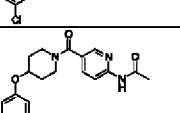
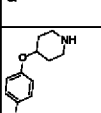
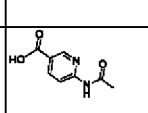
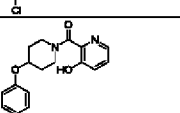
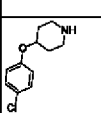
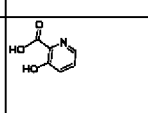
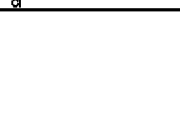
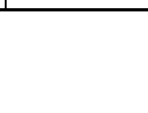
[Table 3-27]

Example364	2-chloro-5-(4-(4-chlorophenoxy)piperidine-1-carbonyl)benzenesulfonamide				427	1.70min	Method A
Example365	4'-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-[1,1'-biphenyl]-4-carboxamide				433.1	1.74min	Method A
Example366	4'-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-[1,1'-biphenyl]-2-carboxamide				433	1.76min	Method A
Example367	(5-chloro-2-hydroxyphenyl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone				364	1.92min	Method A
Example368	(4-(4-chlorophenoxy)piperidin-1-yl)(2-hydroxy-4-methylphenyl)methanone				344.1	1.92min	Method A
Example369	(4-(4-chlorophenoxy)piperidin-1-yl)(5-fluoro-2-hydroxyphenyl)methanone				348	1.83min	Method A
Example370	(4-(4-chlorophenoxy)piperidin-1-yl)(2-hydroxy-3-methylphenyl)methanone				346.1	3.45min	Method B
Example371	(4-(4-chlorophenoxy)piperidin-1-yl)(2-hydroxy-3-isopropylphenyl)methanone				374.1	3.82min	Method B
Example372	(4-(4-chlorophenoxy)piperidin-1-yl)(2-hydroxy-6-methoxyphenyl)methanone				362.1	2.97min	Method B
Example373	(4-(4-chlorophenoxy)piperidin-1-yl)(2-fluoro-6-hydroxyphenyl)methanone				348.2	3.02min	Method B
Example374	(4-(4-chlorophenoxy)piperidin-1-yl)(3-hydroxy-2-methylphenyl)methanone				344.2	3.02min	Method B
Example375	(2-chloro-4-hydroxyphenyl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone				364.1	3.02min	Method B
Example376	(4-(4-chlorophenoxy)piperidin-1-yl)(2-fluoro-4-hydroxyphenyl)methanone				348.2	2.95min	Method B
Example377	N-(4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-2-methylphenyl)methanesulfonamide				421.2	2.93min	Method B

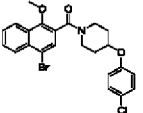
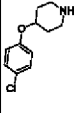
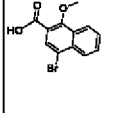
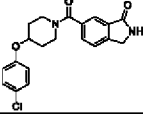
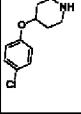
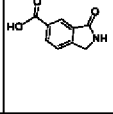
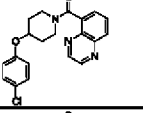
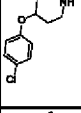
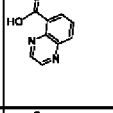
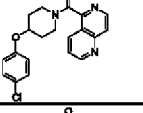
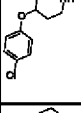
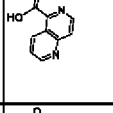
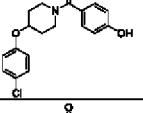
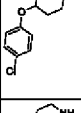
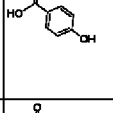
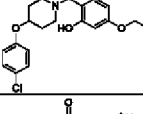
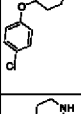
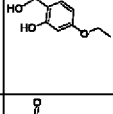
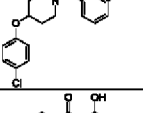
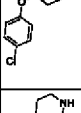
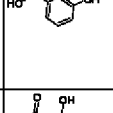
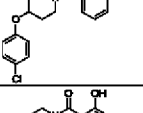
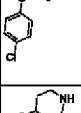
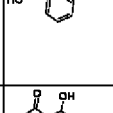
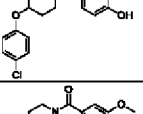
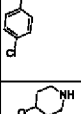
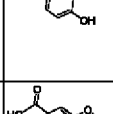
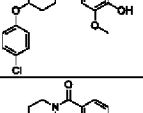
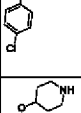
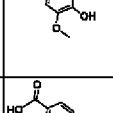
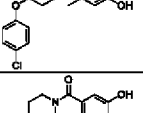
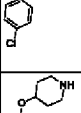
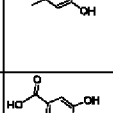
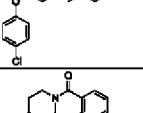
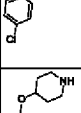
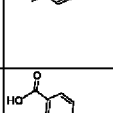
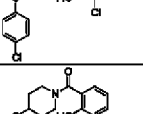
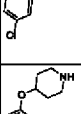
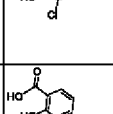
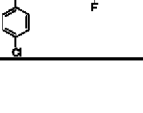
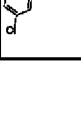
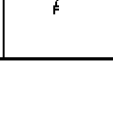
[Table 3-28]

Example378	(4-(4-chlorophenoxy)piperidin-1-yl)(4-fluoro-3-hydroxyphenyl)methanone				348.1	1.73min	Method A
Example379	(4-(4-chlorophenoxy)piperidin-1-yl)(2-hydroxy-5-methylphenyl)methanone				344.1	1.84min	Method A
Example380	(4-(4-chlorophenoxy)piperidin-1-yl)(2-hydroxy-3-methoxyphenyl)methanone				360.1	1.77min	Method A
Example381	(4-(4-chlorophenoxy)piperidin-1-yl)(4-fluoro-2-hydroxyphenyl)methanone				348.1	1.80min	Method A
Example382	(4-(4-chlorophenoxy)piperidin-1-yl)(3,5-dihydroxyphenyl)methanone				346	1.55min	Method A
Example383	N-(3-(4-(4-chlorophenoxy)piperidine-1-carbonyl)phenyl)acetamide				371.1	1.66min	Method A
Example384	(4-(4-chlorophenoxy)piperidin-1-yl)(1-((4-hydroxytetrahydro-2H-pyran-4-yl)methyl)-1H-indol-5-yl)methanone		Alternative route		467	1.75min	Method A
Example385	(1-(2-aminoethyl)-1H-indol-5-yl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone		Alternative route		397.8	1.57min	Method A
Example386	N-(2-(5-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-1H-indol-1-yl)ethyl)acetamide		Alternative route		438.1	1.67min	Method A
Example387	N-(2-(5-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-1H-indol-1-yl)ethyl)methanesulfonamide		Alternative route		474	1.74min	Method A
Example388	2-(5-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-1H-indol-1-yl)-1-morpholinoethanone		Alternative route		480	1.72min	Method A
Example389	(4-(4-chlorophenoxy)piperidin-1-yl)(3-(methylsulfonyl)-[1,1'-biphenyl]-4-yl)methanone				469.7	1.87min	Method A
Example390	(4-(4-chlorophenoxy)piperidin-1-yl)(3'-(hydroxymethyl)-[1,1'-biphenyl]-4-yl)methanone				419.9	1.86min	Method A
Example391	N-(4'-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-[1,1'-biphenyl]-2-yl)methanesulfonamide				483	1.88min	Method A

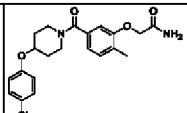
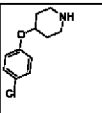
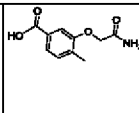
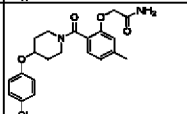
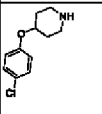
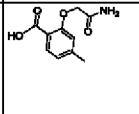
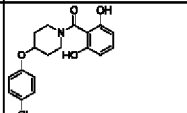
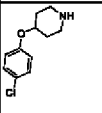
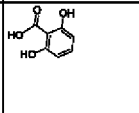
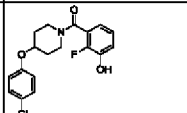
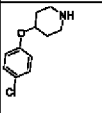
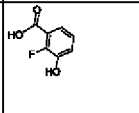
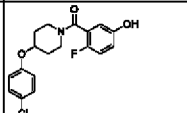
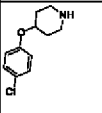
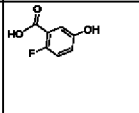
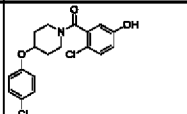
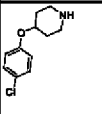
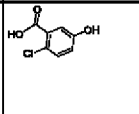
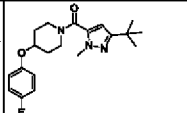
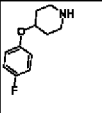
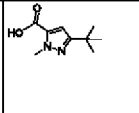
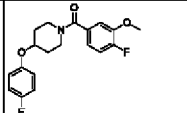
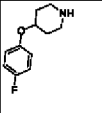
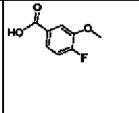
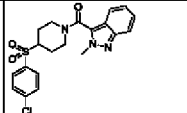
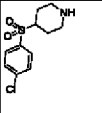
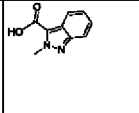
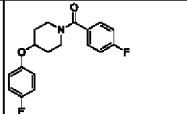
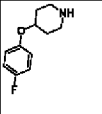
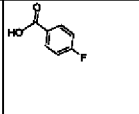
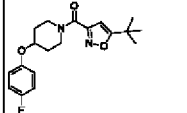
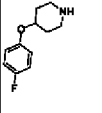
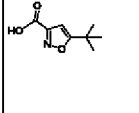
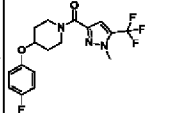
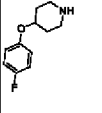
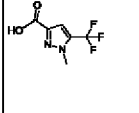
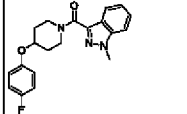
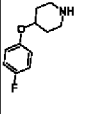
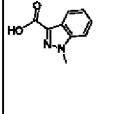
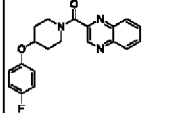
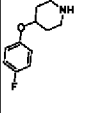
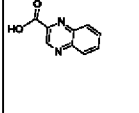
[Table 3-29]

Example392	N-{4'-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-[1,1'-biphenyl]-3-yl}methanesulfonamide				483	1.86min	Method A
Example393	4'-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-N-methyl-[1,1'-biphenyl]-3-carboxamide				447	1.80min	Method A
Example394	4'-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-N,N-dimethyl-[1,1'-biphenyl]-3-carboxamide				462.8	1.86min	Method A
Example395	(4-(4-chlorophenoxy)piperidin-1-yl)(3'-(morpholine-4-carbonyl)-[1,1'-biphenyl]-4-yl)methanone				504.8	1.84min	Method A
Example396	(4-chloro-3-hydroxyphenyl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone				364	1.81min	Method A
Example397	N-(5-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-2-methylphenyl)methanesulfonamide				421	1.73min	Method A
Example398	1-(3-(4-(4-chlorophenoxy)piperidine-1-carbonyl)phenyl)ethanone				357.8	1.82min	Method A
Example399	(4-(4-chlorophenoxy)piperidin-1-yl)(1-(2-hydroxyethyl)-2-methyl-1H-benzo[d]imidazol-5-yl)methanone				413.8	1.52min	Method A
Example400	(4-(4-chlorophenoxy)piperidin-1-yl)(6-ethoxypyridin-2-yl)methanone				360.8	1.99min	Method A
Example401	(4-(4-chlorophenoxy)piperidin-1-yl)(4-hydroxy-7-methyl-1,8-naphthyridin-3-yl)methanone				396	1.52min	Method A
Example402	N-(6-(4-(4-chlorophenoxy)piperidine-1-carbonyl)pyridin-2-yl)acetamide				372	1.65min	Method A
Example403	N-(4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)pyridin-2-yl)acetamide				372	1.60min	Method A
Example404	N-(5-(4-(4-chlorophenoxy)piperidine-1-carbonyl)pyridin-2-yl)acetamide				372	1.60min	Method A
Example405	(4-(4-chlorophenoxy)piperidin-1-yl)(3-hydroxypyridin-2-yl)methanone				331	1.65min	Method A

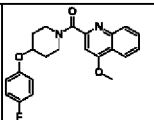
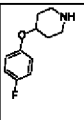
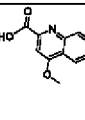
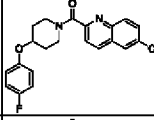
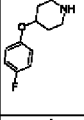
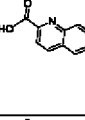
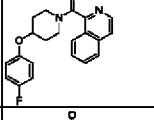
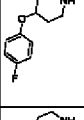
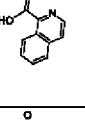
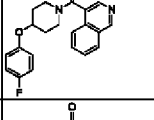
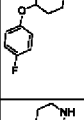
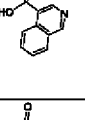
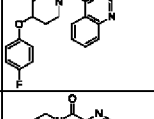
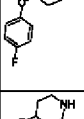
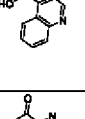
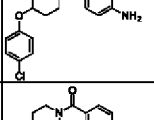
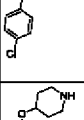
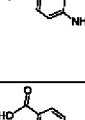
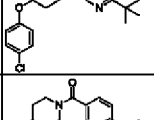
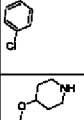
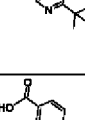
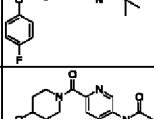
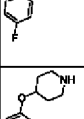
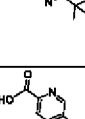
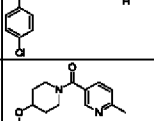
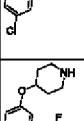
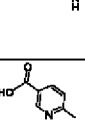
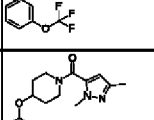
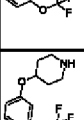
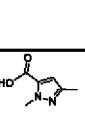
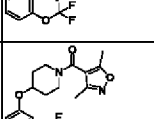
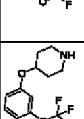
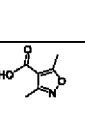
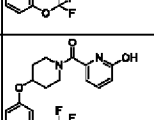
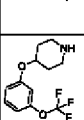
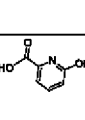
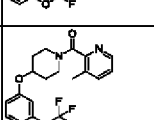
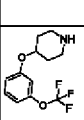
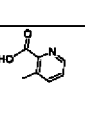
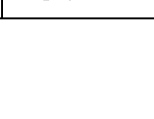
[Table 3-30]

Example406	(4-bromo-1-methoxynaphthalen-2-yl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone				473.7	2.25min	Method A
Example407	6-(4-(4-chlorophenoxy)piperidin-1-carbonyl)isoindolin-1-one				369.1	1.55min	Method A
Example408	(4-(4-chlorophenoxy)piperidin-1-yl)(quinoxalin-5-yl)methanone				367.8	1.70min	Method A
Example409	(4-(4-chlorophenoxy)piperidin-1-yl)(1,6-naphthyridin-5-yl)methanone				366.6	1.65min	Method A
Example410	(4-(4-chlorophenoxy)piperidin-1-yl)(4-hydroxyphenyl)methanone				330.1	1.67min	Method A
Example411	(4-(4-chlorophenoxy)piperidin-1-yl)(4-ethoxy-2-hydroxyphenyl)methanone				374.1	1.92min	Method A
Example412	(4-(4-chlorophenoxy)piperidin-1-yl)(3-hydroxyphenyl)methanone				330.1	1.70min	Method A
Example413	(4-(4-chlorophenoxy)piperidin-1-yl)(2-hydroxyphenyl)methanone				330.1	1.75min	Method A
Example414	(4-(4-chlorophenoxy)piperidin-1-yl)(2,4-dihydroxyphenyl)methanone				346.1	1.62min	Method A
Example415	(4-(4-chlorophenoxy)piperidin-1-yl)(4-hydroxy-3,5-dimethoxyphenyl)methanone				390.1	1.69min	Method A
Example416	(4-(4-chlorophenoxy)piperidin-1-yl)(4-hydroxy-2-methylphenyl)methanone				344.1	1.71min	Method A
Example417	(4-(4-chlorophenoxy)piperidin-1-yl)(5-hydroxy-2-methylphenyl)methanone				344.1	1.75min	Method A
Example418	(3-chloro-2-hydroxyphenyl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone				364	1.88min	Method A
Example419	(4-(4-chlorophenoxy)piperidin-1-yl)(3-fluoro-2-hydroxyphenyl)methanone				348.1	1.76min	Method A

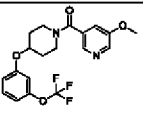
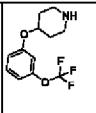
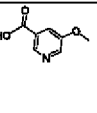
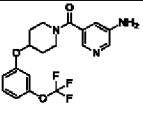
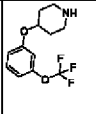
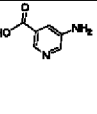
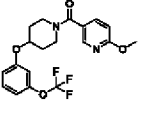
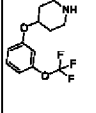
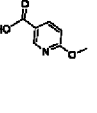
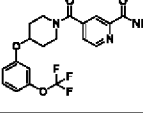
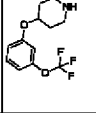
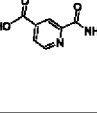
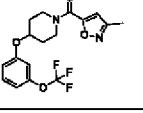
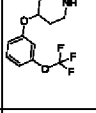
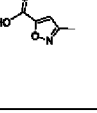
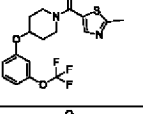
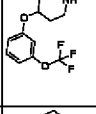
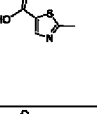
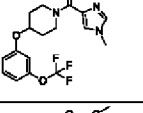
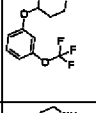
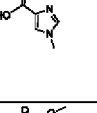
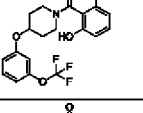
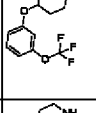
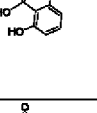
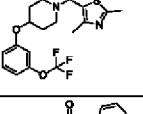
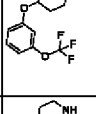
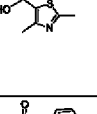
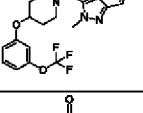
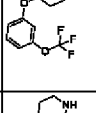
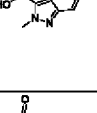
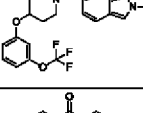
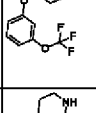
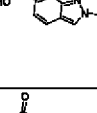
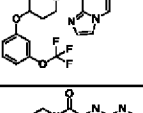
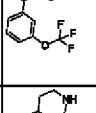
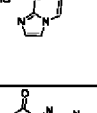
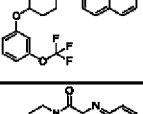
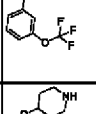
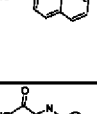
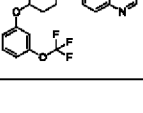
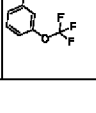
[Table 3-31]

Example420	2-(5-(4-(4-chlorophenoxy)piperidin-1-carbonyl)-2-methylphenoxy)acetamide				401.1	1.68min	Method A
Example421	2-(2-(4-(4-chlorophenoxy)piperidin-1-carbonyl)-5-methylphenoxy)acetamide				401.1	1.72min	Method A
Example422	(4-(4-chlorophenoxy)piperidin-1-yl)(2,6-dihydroxyphenyl)methanone				346.1	1.54min	Method A
Example423	(4-(4-chlorophenoxy)piperidin-1-yl)(2-fluoro-3-hydroxyphenyl)methanone				348	1.71min	Method A
Example424	(4-(4-chlorophenoxy)piperidin-1-yl)(2-fluoro-5-hydroxyphenyl)methanone				348	1.75min	Method A
Example425	(2-chloro-5-hydroxyphenyl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone				364	1.80min	Method A
Example426	(3-(tert-butyl)-1-methyl-1H-pyrazol-5-yl)(4-(4-fluorophenoxy)piperidin-1-yl)methanone				359.9	1.90min	Method A
Example427	(4-(4-fluoro-3-methoxyphenyl)(4-(4-fluorophenoxy)piperidin-1-yl)methanone				347.8	1.79min	Method A
Example428	(4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(2-methyl-2H-indazol-3-yl)methanone				416	1.61min	Method A
Example429	(4-(4-fluorophenoxy)piperidin-1-yl)(4-fluorophenyl)methanone				317.9	1.78min	Method A
Example430	(5-(tert-butyl)isoxazol-3-yl)(4-(4-fluorophenoxy)piperidin-1-yl)methanone				346.9	1.97min	Method A
Example431	(4-(4-fluorophenoxy)piperidin-1-yl)(1-methyl-5-(trifluoromethyl)-1H-pyrazol-3-yl)methanone				371.8	1.84min	Method A
Example432	(4-(4-fluorophenoxy)piperidin-1-yl)(1-methyl-1H-indazol-3-yl)methanone				353.9	1.83min	Method A
Example433	(4-(4-fluorophenoxy)piperidin-1-yl)(quinoxalin-2-yl)methanone				351.8	1.77min	Method A

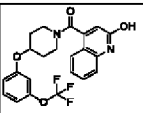
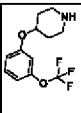
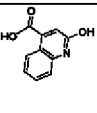
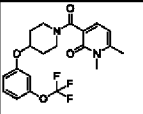
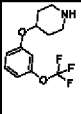
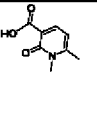
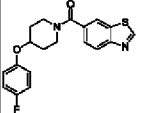
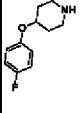
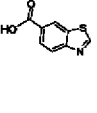
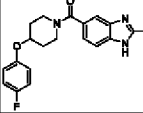
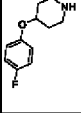
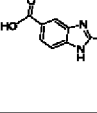
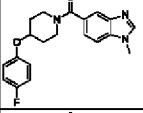
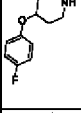
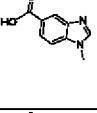
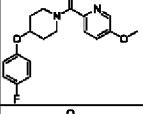
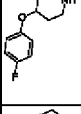
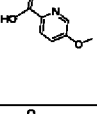
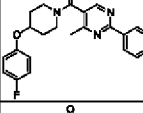
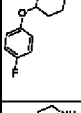
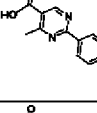
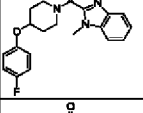
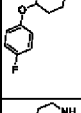
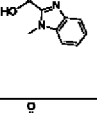
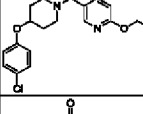
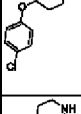
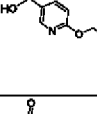
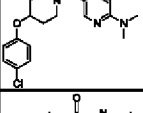
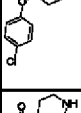
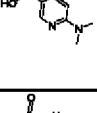
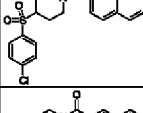
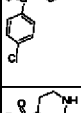
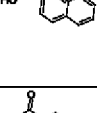
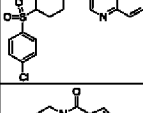
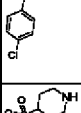
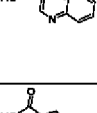
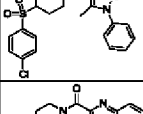
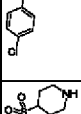
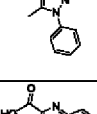
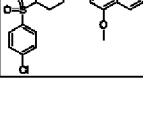
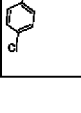
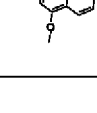
[Table 3-32]

Example434	(4-(4-fluorophenoxy)piperidin-1-yl)(4-methoxyquinolin-2-yl)methanone				380.8	1.85min	Method A
Example435	(4-(4-fluorophenoxy)piperidin-1-yl)(6-methoxyquinolin-2-yl)methanone				380.8	1.81min	Method A
Example436	(4-(4-fluorophenoxy)piperidin-1-yl)(isoquinolin-1-yl)methanone				350.9	1.72min	Method A
Example437	(4-(4-fluorophenoxy)piperidin-1-yl)(isoquinolin-4-yl)methanone				350.9	1.65min	Method A
Example438	(4-(4-fluorophenoxy)piperidin-1-yl)(quinolin-4-yl)methanone				350.9	1.65min	Method A
Example439	(5-aminopyridin-2-yl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone				330.1	1.55min	Method A
Example440	(6-(tert-butyl)pyridin-3-yl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone				373.1	2.00min	Method A
Example441	(6-(tert-butyl)pyridin-3-yl)(4-(4-fluorophenoxy)piperidin-1-yl)methanone				357.1	1.88min	Method A
Example442	N-(6-(4-(4-chlorophenoxy)piperidin-1-carbonyl)pyridin-3-yl)acetamide				372.1	1.54min	Method A
Example443	(6-methylpyridin-3-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone				381	1.76min	Method A
Example444	(1,3-dimethyl-1H-pyrazol-5-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone				384	1.81min	Method A
Example445	(3,5-dimethylisoxazol-4-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone				383.3	1.83min	Method A
Example446	(6-hydroxypyridin-2-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone				381.1	1.59min	Method A
Example447	(3-methylpyridin-2-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone				381	1.79min	Method A

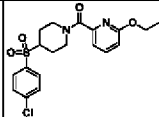
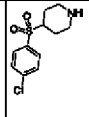
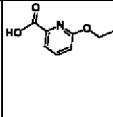
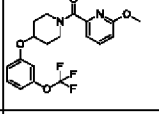
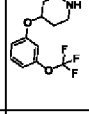
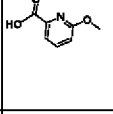
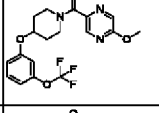
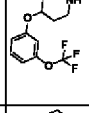
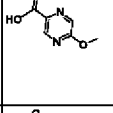
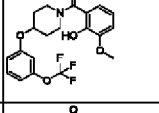
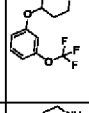
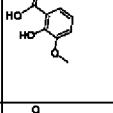
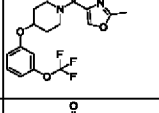
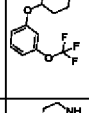
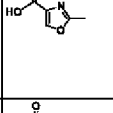
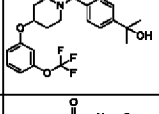
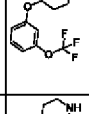
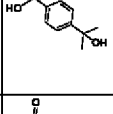
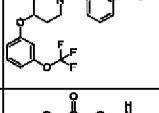
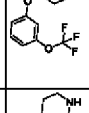
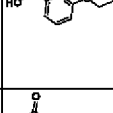
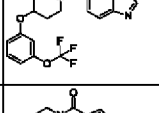
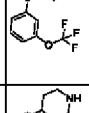
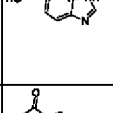
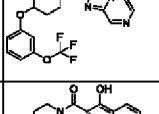
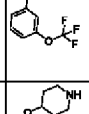
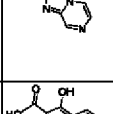
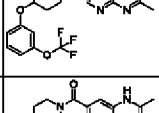
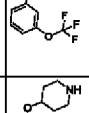
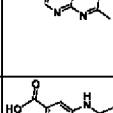
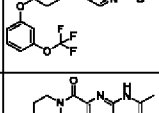
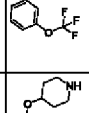
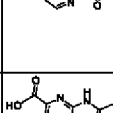
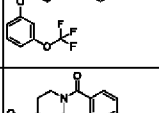
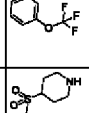
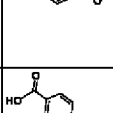
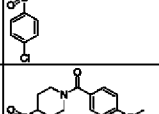
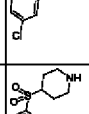
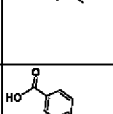
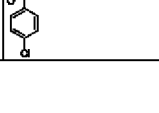
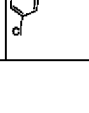
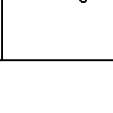
[Table 3-33]

Example448	(5-methoxypyridin-3-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone				397	1.76min	Method A
Example449	(5-aminopyridin-3-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone				380.2	1.60min	Method A
Example450	(6-methoxypyridin-3-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone				397	1.88min	Method A
Example451	4-(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-carbonyl)picolinamide				408.1	1.65min	Method A
Example452	(3-methylisoxazol-5-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone				371.1	1.86min	Method A
Example453	(2-methylthiazol-5-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone				387	1.81min	Method A
Example454	(1-methyl-1H-imidazol-4-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone				370	1.64min	Method A
Example455	(2-hydroxy-6-methoxyphenyl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone				410.1	1.78min	Method A
Example456	(2,4-dimethylthiazol-5-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone				401	1.84min	Method A
Example457	(2-methyl-2H-indazol-3-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone				420.1	1.93min	Method A
Example458	(2-methyl-2H-indazol-6-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone				420.1	1.77min	Method A
Example459	imidazo[1,2-a]pyridin-8-yl(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone				406	1.68min	Method A
Example460	(1,8-naphthyridin-2-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone				418	1.70min	Method A
Example461	(1,5-naphthyridin-2-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone				418	1.78min	Method A

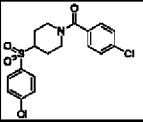
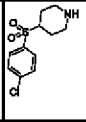
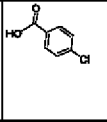
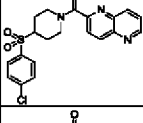
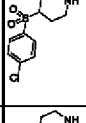
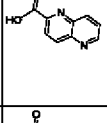
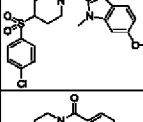
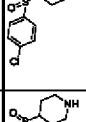
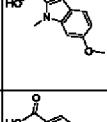
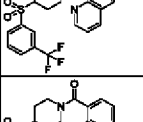
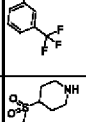
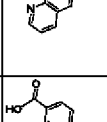
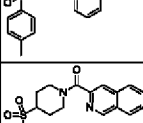
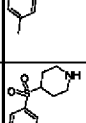
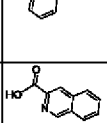
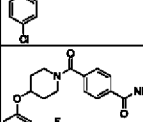
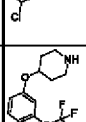
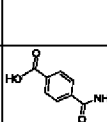
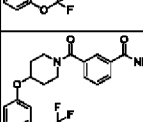
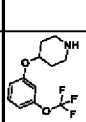
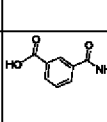
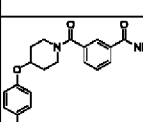
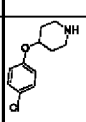
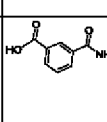
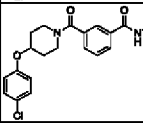
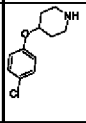
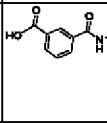
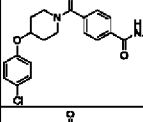
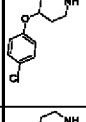
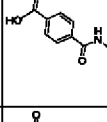
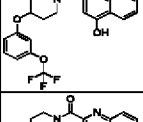
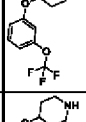
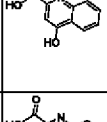
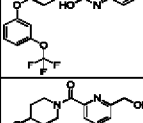
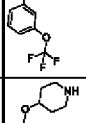
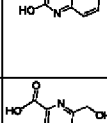
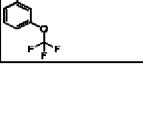
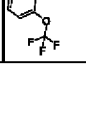
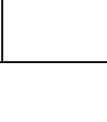
[Table 3-34]

Example 462	(2-hydroxyquinolin-4-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone				431.1	1.71 min	Method A
Example 463	1,6-dimethyl-3-(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)-2-(1H)-one				409.2	1.65 min	Method A
Example 464	benzo[d]thiazol-6-yl(4-(4-fluorophenoxy)piperidin-1-yl)methanone				355.3	1.65 min	Method A
Example 465	(4-(4-fluorophenoxy)piperidin-1-yl)(2-methyl-1H-benzo[d]imidazol-5-yl)methanone				352.2	1.44 min	Method A
Example 466	(4-(4-fluorophenoxy)piperidin-1-yl)(1-methyl-1H-benzo[d]imidazol-5-yl)methanone				354.1	1.50 min	Method A
Example 467	(4-(4-fluorophenoxy)piperidin-1-yl)(5-methoxypyridin-2-yl)methanone				331.1	1.62 min	Method A
Example 468	(4-(4-fluorophenoxy)piperidin-1-yl)(4-methyl-2-phenylpyrimidin-5-yl)methanone				390.2	1.93 min	Method A
Example 469	(4-(4-fluorophenoxy)piperidin-1-yl)(1-methyl-1H-benzo[d]imidazol-2-yl)methanone				354.1	1.71 min	Method A
Example 470	(4-(4-chlorophenoxy)piperidin-1-yl)(6-ethoxypyridin-3-yl)methanone				361.1	1.90 min	Method A
Example 471	(4-(4-chlorophenoxy)piperidin-1-yl)(6-(dimethylamino)pyridin-3-yl)methanone				360.1	1.80 min	Method A
Example 472	(4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(quinolin-2-yl)methanone				413.5	1.65 min	Method A
Example 473	(4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(quinolin-3-yl)methanone				413.2	1.57 min	Method A
Example 474	(4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(5-methyl-1-phenyl-1H-pyrazol-4-yl)methanone				444.1	1.64 min	Method A
Example 475	(4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(4-methoxyquinolin-2-yl)methanone				445.1	1.71 min	Method A

[Table 3-35]

Example476	(4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(6-ethoxypyridin-2-yl)methanone				407.1	1.70min	Method A
Example477	(6-methoxypyridin-2-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone				397.1	1.95min	Method A
Example478	(5-methoxypyrazin-2-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone				398.1	1.89min	Method A
Example479	(2-hydroxy-3-methoxyphenyl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone				410.3	1.83min	Method A
Example480	(2-methyloxazol-4-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone				371.1	1.80min	Method A
Example481	(4-(2-hydroxypropan-2-yl)phenyl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone				424.2	1.83min	Method A
Example482	(6-ethoxypyridin-2-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone				411.2	2.03min	Method A
Example483	(1H-benzo[d]imidazol-6-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone				404.3	1.62min	Method A
Example484	imidazo[1,2-a]pyrazin-2-yl(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone				405.1	1.66min	Method A
Example485	(4-hydroxy-7-methyl-1,8-naphthyridin-3-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone				446.3	1.62min	Method A
Example486	N-(4-(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-carbonyl)pyridin-2-yl)acetamide				422.3	1.70min	Method A
Example487	N-(6-(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-carbonyl)pyridin-2-yl)acetamide				422.3	1.74min	Method A
Example488	(4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(p-tolyl)methanone				376.1	1.71min	Method A
Example489	(4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(4-methoxyphenyl)methanone				394.1	1.63min	Method A

[Table 3-36]

Example490	(4-chlorophenyl){4-[(4-chlorophenyl)sulfonyl]piperidin-1-yl}methanone				396.2	1.74min	Method A
Example491	(4-[(4-chlorophenyl)sulfonyl]piperidin-1-yl){1,5-naphthyridin-2-yl}methanone				413.9	1.45min	Method A
Example492	(4-[(4-chlorophenyl)sulfonyl]piperidin-1-yl){6-methoxy-1-methyl-1H-indol-2-yl}methanone				445.9	1.77min	Method A
Example493	quinolin-8-yl{4-[(3-(trifluoromethyl)phenyl)sulfonyl]piperidin-1-yl}methanone				449	1.60min	Method A
Example494	quinolin-8-yl{4-tosylpiperidin-1-yl}methanone				393.3	1.49min	Method A
Example495	(4-[(4-chlorophenyl)sulfonyl]piperidin-1-yl){isoquinolin-3-yl}methanone				415	1.61min	Method A
Example496	4-{4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl}benzamide				407.3	1.64min	Method A
Example497	3-{4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl}benzamide				407.2	1.65min	Method A
Example498	3-{4-(4-chlorophenoxy)piperidine-1-carbonyl}benzamide				357.2	1.56min	Method A
Example499	3-{4-(4-chlorophenoxy)piperidine-1-carbonyl}-N-methylbenzamide				371.2	1.62min	Method A
Example500	4-{4-(4-chlorophenoxy)piperidine-1-carbonyl}-N-methylbenzamide				371.2	1.60min	Method A
Example501	(4-hydroxyquinolin-2-yl){4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl}methanone				431.3	1.63min	Method A
Example502	(3-hydroxyquinoxalin-2-yl){4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl}methanone				432.3	1.74min	Method A
Example503	(6-(hydroxymethyl)pyridin-2-yl){4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl}methanone				395.3	1.64min	Method A

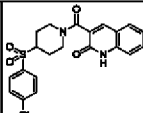
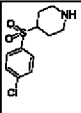
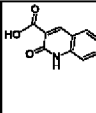
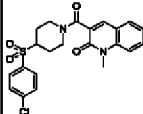
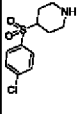
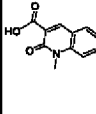
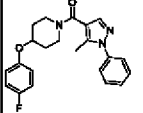
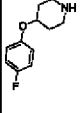
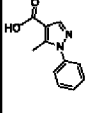
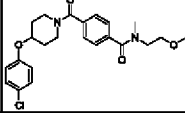
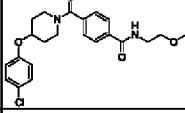
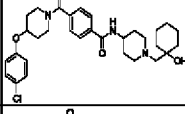
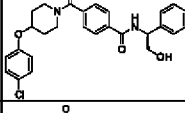
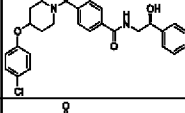
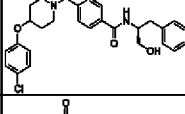
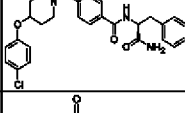
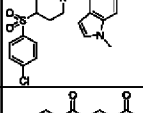
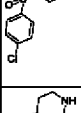
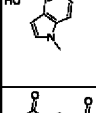
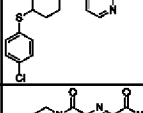
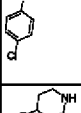
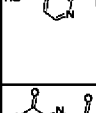
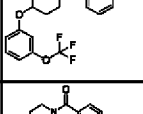
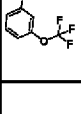
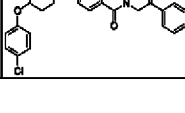
[Table 3-37]

Example504	(1-(2-hydroxyethyl)-2-methyl-1H-benzo[d]imidazol-5-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone				464.1	1.60min	Method A
Example505	(2-hydroxy-6-methylpyridin-4-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone				395.3	1.57min	Method A
Example506	1-methyl-4-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)pyridin-2(1H)-one				395.4	1.59min	Method A
Example507	(2-hydroxy-6-methylpyridin-3-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone				395.3	1.56min	Method A
Example508	3-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)quinolin-2(1H)-one				431.3	1.72min	Method A
Example509	(1H-1,2,4-triazol-3-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone				355.3	1.57min	Method A
Example510	2-cyclopropyl-6-methyl-5-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)pyrimidin-4(1H)-one				436.3	1.64min	Method A
Example511	5,6-dimethyl-3-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)pyridin-2(1H)-one				409.3	1.62min	Method A
Example512	(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)(1,3,6-trimethyl-1H-pyrazolo[3,4-b]pyridin-4-yl)methanone				449.1	1.86min	Method A
Example513	4-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)-1H-benzo[d]imidazol-2(3H)-one				420.2	1.65min	Method A
Example514	(4-(4-chloro-2-methoxyphenoxy)piperidin-1-yl)(quinolin-8-yl)methanone				397.1	1.74min	Method A
Example515	1-(5-chloro-2-((1-(quinoline-8-carbonyl)piperidin-4-yl)oxy)phenyl)ethanone				409.1	1.72min	Method A
Example516	5-chloro-2-((1-(quinoline-8-carbonyl)piperidin-4-yl)oxy)benzonitrile				392.1	1.71min	Method A
Example517	(4-(4-chlorophenyl)sulfonyl)piperidin-1-yl)(quinoxalin-2-yl)methanone				416	1.63min	Method A

[Table 3-38]

Example 518	4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(6-methoxyquinolin-2-yl)methanone				445	1.68min	Method A
Example 519	4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(4-methyl-2-phenylpyrimidin-5-yl)methanone				454.2	1.80min	Method A
Example 520	4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(6-(pyrrolidin-1-yl)pyridin-2-yl)methanone				434.1	1.77min	Method A
Example 521	(5-(tert-butyl)isoxazol-3-yl)(4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)methanone				411.1	1.83min	Method A
Example 522	4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(6-(2,2,2-trifluoroethoxy)pyridin-3-yl)methanone				461.1	1.76min	Method A
Example 523	4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(1-methyl-1H-indol-5-yl)methanone				417	1.67min	Method A
Example 524	4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(1-methyl-1H-indol-2-yl)methanone				415.1	1.80min	Method A
Example 525	4-(3-(3-fluorophenoxy)piperidin-1-yl)(4-fluorophenyl)methanone				318.1	1.81min	Method A
Example 526	4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(1-methyl-1H-indol-6-yl)methanone				417	1.70min	Method A
Example 527	3-(4-(3-(trifluoromethyl)phenoxy)piperidine-1-carbonyl)benzamide				391.3	1.61min	Method A
Example 528	4-(4-(3-(trifluoromethyl)phenoxy)piperidine-1-carbonyl)benzamide				391.3	1.60min	Method A
Example 529	4-(4-(3-(trifluoromethyl)phenoxy)piperidine-1-carbonyl)picolinamide				392.2	1.61min	Method A
Example 530	4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(2-methoxyquinolin-4-yl)methanone				443.3	1.76min	Method A
Example 531	4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(6-phenoxypyridin-3-yl)methanone				455.3	1.75min	Method A

[Table 3-39]

Example532	3-((4-(4-chlorophenyl)sulfonyl)piperidine-1-carbonyl)quinolin-2(1H)-one				429.2	1.44min	Method A
Example533	3-((4-(4-chlorophenyl)sulfonyl)piperidine-1-carbonyl)-1-methylquinolin-2(1H)-one				445.1	1.55min	Method A
Example534	(4-(4-fluorophenoxy)piperidin-1-yl)(5-methyl-1-phenyl-1H-pyrazol-4-yl)methanone				380.1	1.76min	Method A
Example535	4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-N-(2-methoxyethyl)-N-methylbenzamide		Alternative route		431.1	1.69min	Method A
Example536	4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-N-(2-methoxyethyl)benzamide		Alternative route		415.3	1.64min	Method A
Example537	4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-N-(1-(1-hydroxycyclohexyl)methyl)piperidin-4-ylbenzamide		Alternative route		552.4	1.78min	Method A
Example538	(S)-4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-N-(2-hydroxy-1-phenylethyl)benzamide		Alternative route		477.4	1.72min	Method A
Example539	(S)-4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-N-(2-hydroxy-2-phenylethyl)benzamide		Alternative route		477.3	1.73min	Method A
Example540	(S)-4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-N-(1-hydroxy-3-phenylpropan-2-yl)benzamide		Alternative route		491.4	1.75min	Method A
Example541	(S)-N-(1-amino-1-oxo-3-phenylpropan-2-yl)-4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)benzamide		Alternative route		504.3	1.70min	Method A
Example542	(4-((4-(4-chlorophenyl)sulfonyl)piperidin-1-yl)(1-methyl-1H-indol-4-yl)methanone				417.1	1.66min	Method A
Example543	4-(4-(4-chlorophenylthio)piperidine-1-carbonyl)picolinamide				374.3	1.64min	Method A
Example544	6-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)picolinamide				410.1	1.65min	Method A
Example545	4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-N-(2-oxo-2-phenylethyl)benzamide		Alternative route		475.3	1.80min	Method A

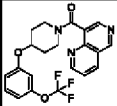
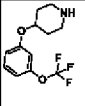
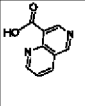
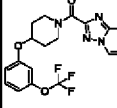
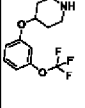
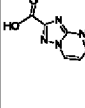
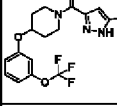
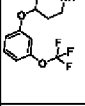
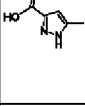
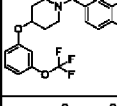
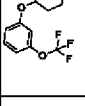
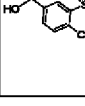
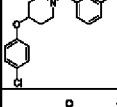
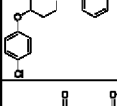
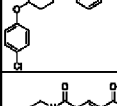
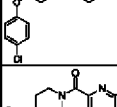
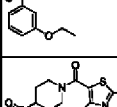
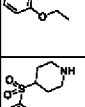
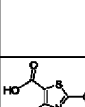
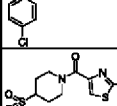
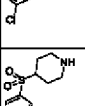
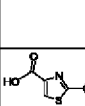
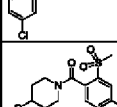
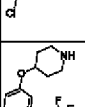
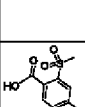
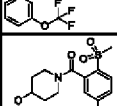
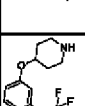
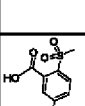
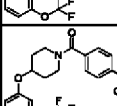
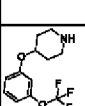
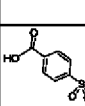
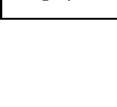
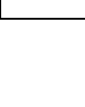
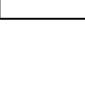
[Table 3-40]

Example546	(2-(methylsulfonyl)phenyl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone				444.1	1.83min	Method A
Example547	(3-(methylsulfonyl)phenyl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone				442.3	1.75min	Method A
Example548	(4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(5-fluoro-1-methyl-1H-indol-2-yl)methanone				433.3	1.78min	Method A
Example549	(4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(6-fluoro-1-methyl-1H-indol-2-yl)methanone				433.3	1.79min	Method A
Example550	(4-(3-ethoxyphenoxy)piperidin-1-yl)(quinolin-8-yl)methanone				377.2	1.74min	Method A
Example551	(4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(3-(2-methylthiazol-4-yl)phenyl)methanone				461.1	1.71min	Method A
Example552	N-methyl-3-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)benzamide				421.3	1.69min	Method A
Example553	3-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)benzenesulfonamide				443.3	1.70min	Method A
Example554	4-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)benzenesulfonamide				443.3	1.68min	Method A
Example555	(4-(4-fluorophenoxy)piperidin-1-yl)(1,5-naphthyridin-2-yl)methanone				352.2	1.56min	Method A
Example556	(4-(4-fluorophenoxy)piperidin-1-yl)(quinolin-2-yl)methanone				351.1	1.78min	Method A
Example557	(4-(3-fluorophenoxy)piperidin-1-yl)(4-methoxyquinolin-2-yl)methanone				381.2	1.85min	Method A
Example558	(1H-benzo[d][1,2,3-triazol-7-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone				405.3	1.67min	Method A
Example559	2-(2-(4-(4-chlorophenoxy)piperidine-1-carbonyl)phenoxy)acetamide				387.4	1.63min	Method A

[Table 3-41]

Example580	2-(4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)phenoxy)acetamide				387.4	1.57min	Method A
Example581	2-(2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenoxy)acetamide				437.3	1.71min	Method A
Example582	2-(3-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenoxy)acetamide				437.4	1.67min	Method A
Example583	2-(4-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenoxy)acetamide				437.4	1.65min	Method A
Example584	(8-hydroxyquinolin-2-yl)(4-(3-(trifluoromethoxy)phenyl)sulfonyl)piperidine-1-yl)methanone				479.3	1.73min	Method A
Example585	quinolin-8-yl(4-(3-(trifluoromethoxy)phenyl)sulfonyl)piperidine-1-yl)methanone				463.9	1.63min	Method A
Example586	quinolin-2-yl(4-(3-(trifluoromethoxy)phenyl)sulfonyl)piperidine-1-yl)methanone				463.3	1.73min	Method A
Example587	(4-(4-(4-chlorophenyl)sulfonyl)piperidine-1-yl)(5-phenylisoxazol-3-yl)methanone				431.1	1.80min	Method A
Example588	(6-methoxyquinolin-2-yl)(4-(3-(trifluoromethoxy)phenyl)sulfonyl)piperidine-1-yl)methanone				493.3	1.73min	Method A
Example589	(5-methyl-2-phenyl-2H-1,2,3-triazol-4-yl)(4-(3-(trifluoromethoxy)phenyl)sulfonyl)piperidine-1-yl)methanone				493.5	1.92min	Method A
Example570	(5-fluoro-1-methyl-1H-indol-2-yl)(4-(3-(trifluoromethoxy)phenyl)sulfonyl)piperidine-1-yl)methanone				483.4	1.85min	Method A
Example571	(6-fluoro-1-methyl-1H-indol-2-yl)(4-(3-(trifluoromethoxy)phenyl)sulfonyl)piperidine-1-yl)methanone				483.4	1.86min	Method A
Example572	(4-hydroxyquinolin-8-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-yl)methanone				431.4	1.62min	Method A
Example573	(1,8-naphthyridin-4-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-yl)methanone				418.2	1.64min	Method A

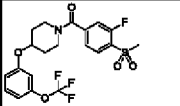
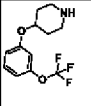
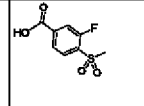
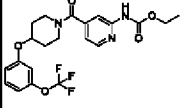
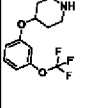
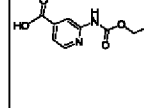
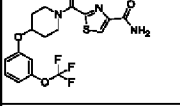
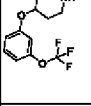
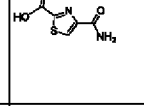
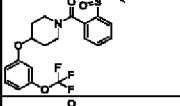
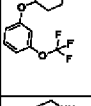
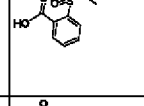
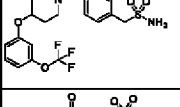
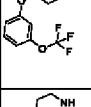
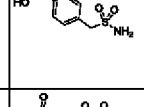
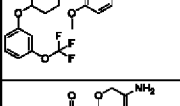
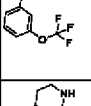
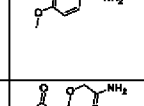
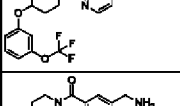
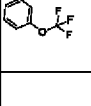
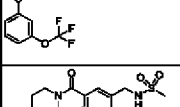
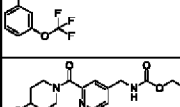
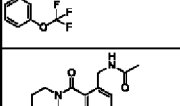
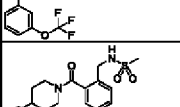
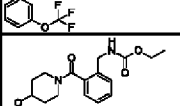
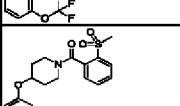
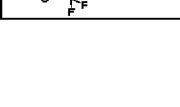
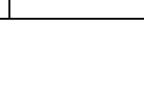
[Table 3-42]

Example574	(1,6-naphthyridin-8-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone				418.2	1.67min	Method A
Example575	[1,2,4]triazolo[1,5-a]pyrimidin-2-yl(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone				406.4	1.62min	Method A
Example576	(5-methyl-1H-pyrazol-3-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone				368.4	1.69min	Method A
Example577	2-chloro-5-(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-carbonyl)benzenesulfonamide				477.3	1.75min	Method A
Example578	(S)-3-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-N-(2-hydroxy-2-phenylethyl)benzamide		Alternative route		477.4	1.72min	Method A
Example579	(S)-3-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-N-(2-hydroxy-1-phenylethyl)benzamide		Alternative route		477.4	1.72min	Method A
Example580	(S)-3-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-N-(1-hydroxy-3-phenylpropan-2-yl)benzamide		Alternative route		491.4	1.75min	Method A
Example581	(S)-N-(1-amino-1-oxo-3-phenylpropan-2-yl)-3-(4-(4-chlorophenoxy)piperidine-1-carbonyl)benzamide		Alternative route		504.5	1.70min	Method A
Example582	(4-((3-ethoxyphenyl)sulfonyl)piperidin-1-yl)(8-hydroxyquinolin-2-yl)methanone				439.4	1.64min	Method A
Example583	(4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(4-methyl-2-phenylthiazol-5-yl)methanone				459.1	1.80min	Method A
Example584	(4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(2-phenylthiazol-4-yl)methanone				447.1	1.81min	Method A
Example585	(4-chloro-2-(methylsulfonyl)phenyl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone				478.1	1.95min	Method A
Example586	(5-fluoro-2-(methylsulfonyl)phenyl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone				460.4	1.87min	Method A
Example587	N,N-dimethyl-4-(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-carbonyl)benzenesulfonamide				473.2	1.86min	Method A

[Table 3-43]

Example588	N-(2-(4-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenoxy)ethyl)acetamide				465.4	1.69min	Method A
Example589	(2-phenyl-1H-imidazol-5-yl)(4-(3-(trifluoromethoxy)phenyl)sulfonyl)piperidin-1-yl)methanone				478.3	1.64min	Method A
Example590	(3-(2-methylthiazol-4-yl)phenyl)(4-(3-(trifluoromethoxy)phenyl)sulfonyl)piperidin-1-yl)methanone				509.2	1.79min	Method A
Example591	N-(4-(4-(3-ethoxyphenoxy)piperidine-1-carbonyl)pyridin-2-yl)acetamide				382.5	1.55min	Method A
Example592	(4-(3-ethoxyphenoxy)piperidin-1-yl)(2-(methylsulfonyl)phenyl)methanone				404.2	1.71min	Method A
Example593	3-(4-(3-ethoxyphenoxy)piperidine-1-carbonyl)benzenesulfonamide				403.4	1.56min	Method A
Example594	N-(6-(4-(3-ethoxyphenoxy)piperidine-1-carbonyl)pyridin-2-yl)acetamide				382.5	1.59min	Method A
Example595	(4-(3-ethoxyphenoxy)piperidin-1-yl)(2-methyl-2H-indazol-3-yl)methanone				380.2	1.80min	Method A
Example596	(4-(3-ethoxyphenoxy)piperidin-1-yl)(1,5-naphthyridin-2-yl)methanone				378.2	1.63min	Method A
Example597	(8-hydroxyquinolin-2-yl)(4-(4-(trifluoromethoxy)phenyl)sulfonyl)piperidin-1-yl)methanone				479.4	1.73min	Method A
Example598	quinolin-8-yl(4-(4-(trifluoromethoxy)phenyl)sulfonyl)piperidin-1-yl)methanone				463.5	1.63min	Method A
Example599	quinolin-2-yl(4-(4-(trifluoromethoxy)phenyl)sulfonyl)piperidin-1-yl)methanone				463.3	1.73min	Method A
Example600	N-(3-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenyl)methanesulfonamide				457.4	1.75min	Method A
Example601	(2-(ethylsulfonyl)phenyl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone				458.2	1.88min	Method A

[Table 3-44]

Example602	(3-fluoro-4-(methylsulfonyl)phenyl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone				462.1	1.80min	Method A
Example603	ethyl 4-(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-carbonyl)pyridin-2-yl)carbamate				452.4	1.83min	Method A
Example604	2-(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-carbonyl)thiazole-4-carboxamide				414.4	1.69min	Method A
Example605	N,N-dimethyl-2-(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-carbonyl)benzenesulfonamide				473.3	1.89min	Method A
Example606	4-(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-carbonyl)phenylmethanesulfonamide				457.4	1.67min	Method A
Example607	4-methoxy-3-(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-carbonyl)benzenesulfonamide				473.4	1.69min	Method A
Example608	2-((2-(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-carbonyl)pyridin-3-yl)oxy)acetamide				438.4	1.56min	Method A
Example609	4-(aminomethyl)pyridin-2-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone		Alternative route		396.2	1.52min	Method A
Example610	N-(2-(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-carbonyl)pyridin-4-yl)methylmethanesulfonamide		Alternative route		472.4	1.63min	Method A
Example611	ethyl ((2-(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-carbonyl)pyridin-4-yl)methyl)carbamate		Alternative route		466.5	1.74min	Method A
Example612	N-(2-(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-carbonyl)benzyl)acetamide		Alternative route		437.3	1.71min	Method A
Example613	N-(2-(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-carbonyl)benzyl)methanesulfonamide		Alternative route		471.4	1.78min	Method A
Example614	ethyl 2-(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-carbonyl)benzylcarbamate		Alternative route		467.3	1.89min	Method A
Example615	(2-(methylsulfonyl)phenyl)(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidin-1-yl)methanone				458.3	1.76min	Method A

[Table 3-45]

Example616	N-(4-(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidine-1-carbonyl)pyridin-2-yl)acetamide				436.5	1.61min	Method A
Example617	4-(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidine-1-carbonyl)picolinamide				422.5	1.57min	Method A
Example618	3-(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidine-1-carbonyl)benzamide				421.4	1.57min	Method A
Example619	3-(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidine-1-carbonyl)benzenesulfonamide				457.4	1.63min	Method A
Example620	2-(2-(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidine-1-carbonyl)phenoxy)acetamide				451.5	1.64min	Method A
Example621	quinolin-8-yl(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidine-1-yl)methanone				431.3	1.77min	Method A
Example622	(1,5-naphthyridin-2-yl)(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidine-1-yl)methanone				432.3	1.69min	Method A
Example623	(2-methyl-2H-indazol-3-yl)(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidine-1-yl)methanone				434.3	1.83min	Method A
Example624	(1,3-dimethyl-1H-pyrazol-5-yl)(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidine-1-yl)methanone				398.3	1.72min	Method A
Example625	N-(6-(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidine-1-carbonyl)pyridin-2-yl)acetamide				436.5	1.65min	Method A
Example626	4-(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidine-1-carbonyl)benzamide				421.4	1.56min	Method A
Example627	(3,5-dimethylisoxazol-4-yl)(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidine-1-yl)methanone				399.2	1.74min	Method A
Example628	(3-(methylsulfonyl)phenyl)(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidine-1-yl)methanone				456.5	1.69min	Method A
Example629	(1,6-naphthyridin-8-yl)(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidine-1-yl)methanone				432.3	1.60min	Method A

[Table 3-46]

Example630	(3-methyl-1H-pyrazol-5-yl)(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidin-1-yl)methanone				382.5	1.62min	Method A
Example631	2-(3-(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidin-1-carbonyl)phenoxy)acetamide				451.5	1.60min	Method A
Example632	(5-(tetrahydro-2H-pyran-4-yl)oxy)pyridin-3-yl(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone				467.3	1.77min	Method A
Example633	1-(3-(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-carbonyl)phenyl)urea				422.4	1.63min	Method A
Example634	1-(4-(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-carbonyl)phenyl)urea				422.4	1.61min	Method A
Example635	(1H-1,2,4-triazol-3-yl)(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidin-1-yl)methanone				369.4	1.51min	Method A
Example636	(4-(3-ethoxyphenoxy)piperidin-1-yl)(3-(methylsulfonyl)phenyl)methanone				404.3	1.65min	Method A
Example637	(4-(3-ethoxyphenoxy)piperidin-1-yl)(3-methyl-1H-pyrazol-5-yl)methanone				328.5	1.56min	Method A
Example638	N,N-dimethyl-3-(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-carbonyl)benzenesulfonamide				473.3	1.86min	Method A
Example639	N-(2-(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-carbonyl)phenyl)methanesulfonamide				457.4	1.82min	Method A
Example640	(6-aminopyridin-2-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone				380.4	1.68min	Method A
Example641	2-(methyl(3-(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-carbonyl)benzyl)amino)acetamide				466.3	1.72min	Method A
Example642	2-(methyl(4-(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-carbonyl)benzyl)amino)acetamide				464.5	1.71min	Method A
Example643	N,N-dimethyl-2-(2-(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-carbonyl)phenoxy)acetamide				467.3	1.77min	Method A

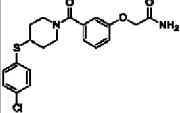
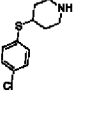
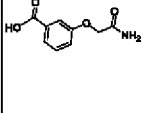
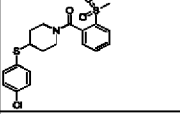
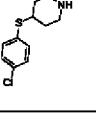
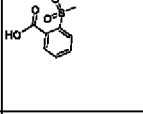
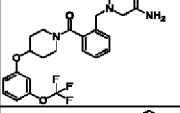
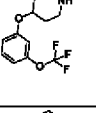
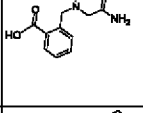
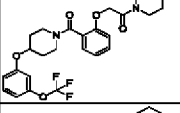
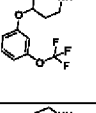
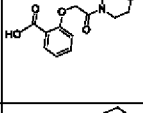
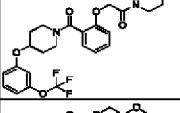
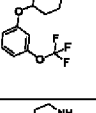
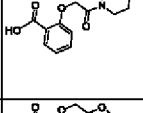
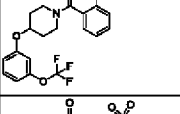
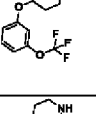
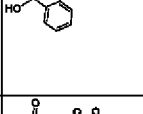
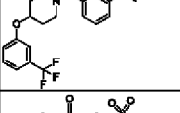
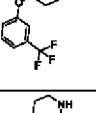
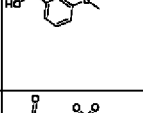
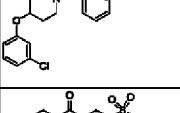
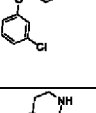
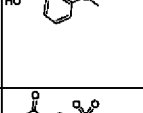
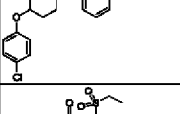
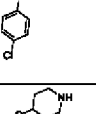
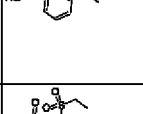
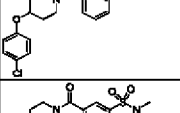
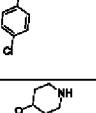
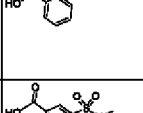
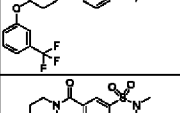
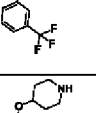
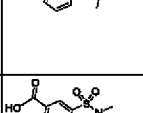
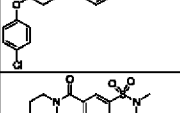
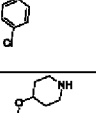
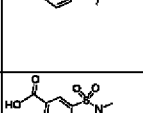
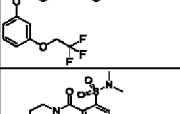
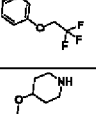
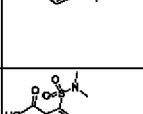
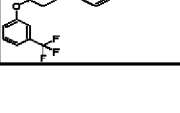
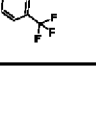
[Table 3-47]

Example644	(1,3-dimethyl-1H-pyrazol-5-yl)(4-(3-(trifluoromethyl)phenoxy)piperidin-1-yl)methanone				368.2	1.75min	Method A
Example645	(2-(methylsulfonyl)phenyl)(4-(3-(trifluoromethyl)phenoxy)piperidin-1-yl)methanone				428.1	1.79min	Method A
Example646	N-(6-(4-(3-(trifluoromethyl)phenoxy)piperidine-1-carbonyl)pyridin-2-yl)acetamide				406.4	1.67min	Method A
Example647	3-(4-(3-(trifluoromethyl)phenoxy)piperidine-1-carbonyl)benzenesulfonamide				427.3	1.64min	Method A
Example648	(3,5-dimethylisoxazol-4-yl)(4-(3-(trifluoromethyl)phenoxy)piperidin-1-yl)methanone				367.3	1.77min	Method A
Example649	(1,6-naphthyridin-8-yl)(4-(3-(trifluoromethyl)phenoxy)piperidin-1-yl)methanone				402.2	1.62min	Method A
Example650	(3-methyl-1H-pyrazol-5-yl)(4-(3-(trifluoromethyl)phenoxy)piperidin-1-yl)methanone				352.4	1.64min	Method A
Example651	2-(2-(4-(3-(trifluoromethyl)phenoxy)piperidine-1-carbonyl)phenoxy)acetamide				421.4	1.65min	Method A
Example652	2-(4-(4-(3-(trifluoromethyl)phenoxy)piperidine-1-carbonyl)phenoxy)acetamide				421.4	1.60min	Method A
Example653	2-(3-(4-(3-(trifluoromethyl)phenoxy)piperidine-1-carbonyl)phenoxy)acetamide				421.4	1.62min	Method A
Example654	(1H-1,2,4-triazol-3-yl)(4-(3-(trifluoromethyl)phenoxy)piperidin-1-yl)methanone				339.3	1.51min	Method A
Example655	N-(2-(2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenoxy)ethyl)acetamide		Alternative route		467.2	1.73min	Method A
Example656	N-(2-(2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenoxy)ethyl)methanesulfonamide		Alternative route		501.3	1.80min	Method A
Example657	ethyl 2-(2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenoxy)ethyl)carbamate		Alternative route		497.2	1.90min	Method A

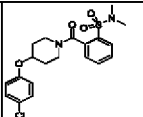
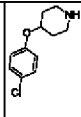
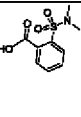
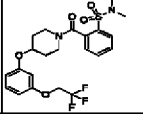
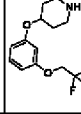
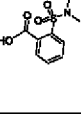
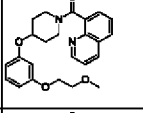
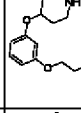
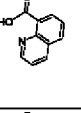
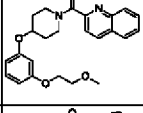
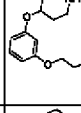
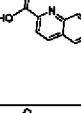
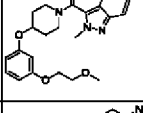
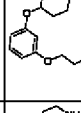
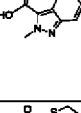
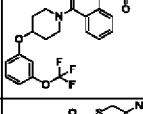
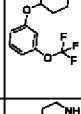
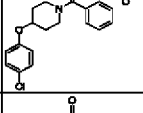
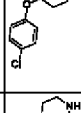
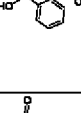
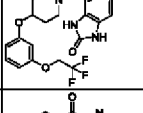
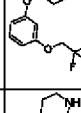
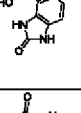
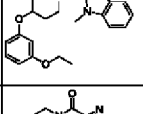
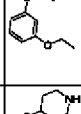
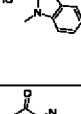
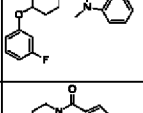
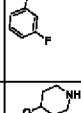
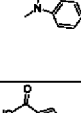
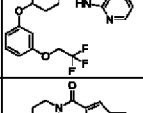
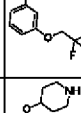
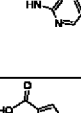
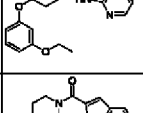
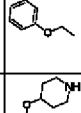
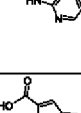
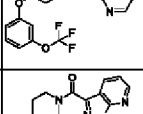
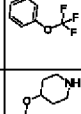
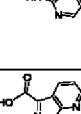
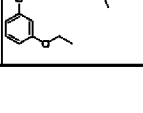
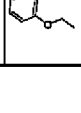
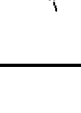
[Table 3-48]

Example658	N-(2-(2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenoxy)ethyl)cyclopropane-1,1-dicarboxamide		Alternative route		534.4	1.72min	Method A
Example659	(3-(2-aminoethoxy)phenyl)(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-yl)methanone		Alternative route		425.2	1.62min	Method A
Example660	N-(2-(3-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenoxy)ethyl)acetamide		Alternative route		467.2	1.72min	Method A
Example661	N-(2-(3-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenoxy)ethyl)methanesulfonamide		Alternative route		503.1	1.77min	Method A
Example662	ethyl (2-(3-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenoxy)ethyl)carbamate		Alternative route		497.2	1.88min	Method A
Example663	N-(2-(3-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenoxy)ethyl)cyclopropane-1,1-dicarboxamide		Alternative route		536.2	1.69min	Method A
Example664	N-(3-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)pyridin-2-yl)acetamide				424.1	1.61min	Method A
Example665	N-(1-methyl-5-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)-1H-pyrazol-3-yl)acetamide				427.1	1.62min	Method A
Example666	(2-(ethylsulfonyl)phenyl)(4-(3-(trifluoromethyl)phenoxy)piperidine-1-yl)methanone				442.1	1.85min	Method A
Example667	(4-(3-ethoxyphenoxy)piperidine-1-yl)(2-(ethylsulfonyl)phenyl)methanone				418.1	1.77min	Method A
Example668	(2-(ethylsulfonyl)phenyl)(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidine-1-yl)methanone				472.1	1.80min	Method A
Example669	N-(2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)pyridin-3-yl)acetamide				424.1	1.65min	Method A
Example670	2-(4-(4-(3-chlorophenoxy)piperidine-1-carbonyl)phenoxy)acetamide				389.1	1.57min	Method A
Example671	2-(2-(4-(4-chlorophenylthio)piperidine-1-carbonyl)phenoxy)acetamide				405.1	1.70min	Method A

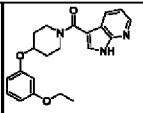
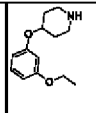
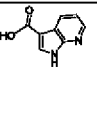
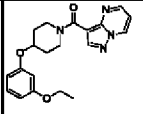
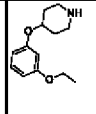
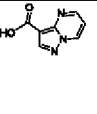
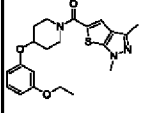
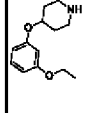
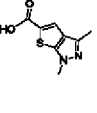
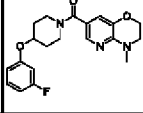
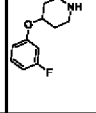
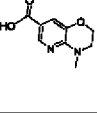
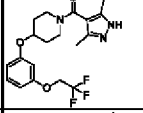
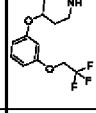
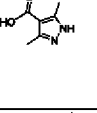
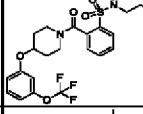
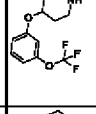
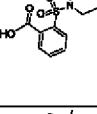
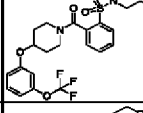
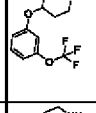
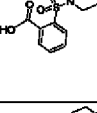
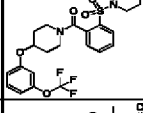
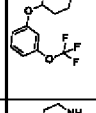
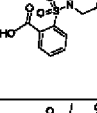
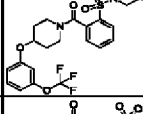
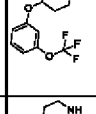
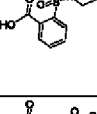
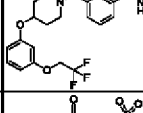
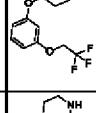
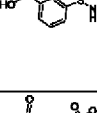
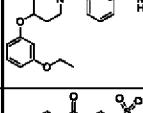
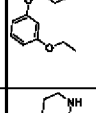
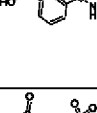
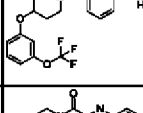
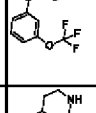
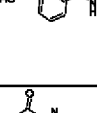
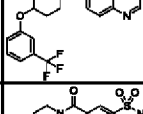
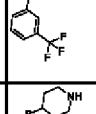
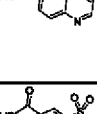
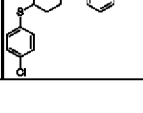
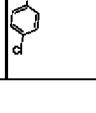
[Table 3-49]

Example672	2-(3-(4-(4-chlorophenyl)thio)piperidine-1-carbonyl)phenoxy)acetamide				405.1	1.67min	Method A
Example673	{4-(4-chlorophenyl)thio}piperidin-1-yl}{2-(methylsulfonyl)phenyl}methanone				410.1	1.84min	Method A
Example674	2-(methyl{2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)benzyl}amino)acetamide				466.2	1.77min	Method A
Example675	1-morpholino-2-(2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenoxy)ethanone				509.2	1.76min	Method A
Example676	1-(piperidin-1-yl)-2-(2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenoxy)ethanone				507.2	1.91min	Method A
Example677	(2-(2-methoxyethoxy)phenyl){4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl}methanone				440.1	1.92min	Method A
Example678	{3-(methylsulfonyl)phenyl}{4-(3-(trifluoromethyl)phenoxy)piperidin-1-yl}methanone				428.1	1.72min	Method A
Example679	{4-(3-chlorophenoxy)piperidin-1-yl}{3-(methylsulfonyl)phenyl}methanone				394.1	1.69min	Method A
Example680	{4-(4-chlorophenoxy)piperidin-1-yl}{3-(methylsulfonyl)phenyl}methanone				394.1	1.69min	Method A
Example681	{4-(4-chlorophenoxy)piperidin-1-yl}{2-(ethylsulfonyl)phenyl}methanone				408.2	1.82min	Method A
Example682	N,N-dimethyl-3-{4-(3-(trifluoromethyl)phenoxy)piperidine-1-carbonyl}benzenesulfonamide				457.2	1.83min	Method A
Example683	3-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-N,N-dimethylbenzenesulfonamide				423.1	1.80min	Method A
Example684	N,N-dimethyl-3-{4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidine-1-carbonyl}benzenesulfonamide				487.2	1.79min	Method A
Example685	N,N-dimethyl-2-{4-(3-(trifluoromethyl)phenoxy)piperidine-1-carbonyl}benzenesulfonamide				457.2	1.86min	Method A

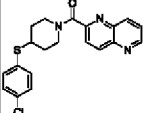
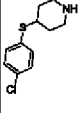
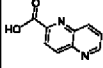
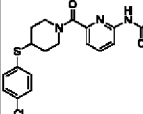
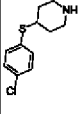
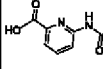
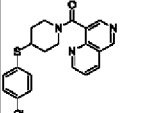
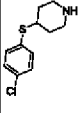
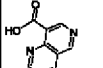
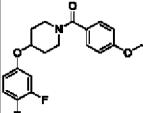
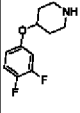
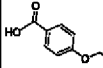
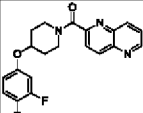
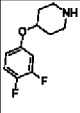
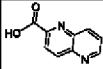
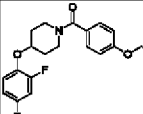
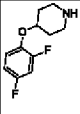
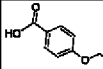
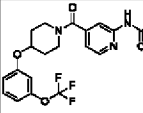
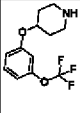
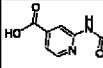
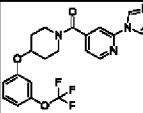
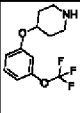
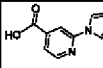
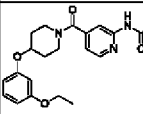
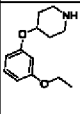
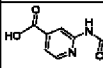
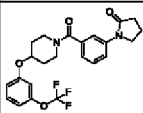
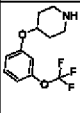
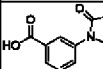
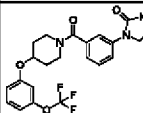
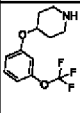
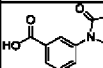
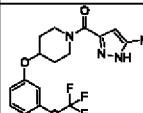
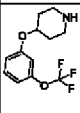
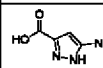
[Table 3-50]

Example686	2-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-N,N-dimethylbenzenesulfonamide				423.1	1.83min	Method A
Example687	N,N-dimethyl-2-(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidine-1-carbonyl)benzenesulfonamide				487.2	1.81min	Method A
Example688	4-(3-(2-methoxyethoxy)phenoxy)piperidine-1-yl)(quinolin-8-yl)methanone				407.2	1.59min	Method A
Example689	4-(3-(2-methoxyethoxy)phenoxy)piperidine-1-yl)(quinolin-2-yl)methanone				407.2	1.71min	Method A
Example690	4-(3-(2-methoxyethoxy)phenoxy)piperidine-1-yl)(2-methyl-2H-indazol-3-yl)methanone				410.2	1.67min	Method A
Example691	2-((2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenyl)thio)acetamide				455.1	1.71min	Method A
Example692	2-((2-(4-(4-chlorophenoxy)piperidine-1-carbonyl)phenyl)thio)acetamide				405.1	1.64min	Method A
Example693	4-(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidine-1-carbonyl)-1H-benz[d]imidazol-2(3H)-one				436.2	1.58min	Method A
Example694	4-(3-(3-ethoxyphenoxy)piperidine-1-yl)(1-methyl-1H-benz[d]imidazol-2-yl)methanone				380.3	1.78min	Method A
Example695	4-(3-(3-fluorophenoxy)piperidine-1-yl)(1-methyl-1H-benz[d]imidazol-2-yl)methanone				354.3	1.72min	Method A
Example696	(1H-pyrrolo[2,3-b]pyridin-2-yl)(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidine-1-yl)methanone				420.2	1.74min	Method A
Example697	4-(3-(3-ethoxyphenoxy)piperidine-1-yl)(1H-pyrrolo[2,3-b]pyridin-2-yl)methanone				366.2	1.71min	Method A
Example698	(1H-pyrrolo[2,3-b]pyridin-2-yl)(4-(3-(3-(trifluoromethoxy)phenoxy)piperidine-1-yl)methanone				406.1	1.82min	Method A
Example699	4-(3-(3-ethoxyphenoxy)piperidine-1-yl)(1-methyl-1H-pyrazolo[3,4-b]pyridin-3-yl)methanone				381.2	1.78min	Method A

[Table 3-51]

Example 700	(4-(3-ethoxyphenoxy)piperidin-1-yl)(1H-pyrrolo[2,3-b]pyridin-3-yl)methanone				366.2	1.58min	Method A
Example 701	(4-(3-ethoxyphenoxy)piperidin-1-yl)(pyrazolo[1,5-a]pyrimidin-3-yl)methanone				367.2	1.55min	Method A
Example 702	(1,3-dimethyl-1H-thieno[2,3-c]pyrazol-5-yl)(4-(3-ethoxyphenoxy)piperidin-1-yl)methanone				400.2	1.78min	Method A
Example 703	(4-(3-fluorophenoxy)piperidin-1-yl)(4-methyl-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)methanone				372.2	1.66min	Method A
Example 704	(3,5-dimethyl-1H-pyrazol-4-yl)(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidin-1-yl)methanone				398.2	1.56min	Method A
Example 705	N-(2-hydroxyethyl)-N-methyl-2-(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-carbonyl)benzenesulfonamide				503.2	1.78min	Method A
Example 706	N-(2-methoxyethyl)-N-methyl-2-(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-carbonyl)benzenesulfonamide				517.2	1.91min	Method A
Example 707	(2-(morpholinosulfonyl)phenyl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone				515.2	1.88min	Method A
Example 708	2-(N-methyl-2-(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-carbonyl)phenylsulfonamido)acetamide				516.2	1.72min	Method A
Example 709	N-methyl-3-(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidin-1-carbonyl)benzenesulfonamide				473.2	1.70min	Method A
Example 710	3-(4-(3-ethoxyphenoxy)piperidin-1-carbonyl)-N-methylbenzenesulfonamide				419.2	1.66min	Method A
Example 711	N-methyl-3-(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-carbonyl)benzenesulfonamide				459.2	1.77min	Method A
Example 712	(1,5-naphthyridin-2-yl)(4-(3-(trifluoromethyl)phenoxy)piperidin-1-yl)methanone				402.2	1.73min	Method A
Example 713	3-(4-(4-chlorophenylthio)piperidin-1-carbonyl)benzenesulfonamide				411.1	1.69min	Method A

[Table 3-52]

Example 714	(4-((4-chlorophenyl)thio)piperidin-1-yl)(1,5-naphthyridin-2-yl)methanone				384.1	1.77min	Method A
Example 715	N-(6-(4-((4-chlorophenyl)thio)piperidine-1-carbonyl)pyridin-2-yl)acetamide				390.1	1.71min	Method A
Example 716	(4-((4-chlorophenyl)thio)piperidin-1-yl)(1,6-naphthyridin-8-yl)methanone				384.1	1.66min	Method A
Example 717	2-(4-(4-(3,4-difluorophenoxy)piperidine-1-carbonyl)phenoxy)acetamide				391.2	1.49min	Method A
Example 718	(4-(3,4-difluorophenoxy)piperidin-1-yl)(1,5-naphthyridin-2-yl)methanone				370.2	1.61min	Method A
Example 719	2-(4-(4-(2,4-difluorophenoxy)piperidine-1-carbonyl)phenoxy)acetamide				391.2	1.48min	Method A
Example 720	N-(4-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)pyridin-2-yl)pivalamide				464.5	1.92min	Method A
Example 721	(2-(1H-imidazol-1-yl)pyridin-4-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone				433.2	1.72min	Method A
Example 722	N-(4-(4-(3-ethoxyphenoxy)piperidine-1-carbonyl)pyridin-2-yl)pivalamide				424.5	1.82min	Method A
Example 723	1-(3-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenyl)pyrrolidin-2-one				449.1	1.81min	Method A
Example 724	1-(3-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenyl)imidazolidin-2-one				448.3	1.72min	Method A
Example 725	(5-amino-1H-pyrazol-3-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone				371.1	1.54min	Method A

[0217]

[Table 4]

Example	¹ H-NMR data (300Mz, CDCl ₃)
Example21	δ 8.98–8.93 (1H, m), 8.18 (1H, d, J = 8.4 Hz), 7.87–7.85 (1H, m), 7.70–7.67 (1H, m), 7.60–7.55 (1H, m), 7.46–7.42 (1H, m), 7.24–7.21 (2H, m), 6.85–6.83 (2H, m), 4.57–4.50 (1H, m), 4.16–3.96 (2H, m), 3.48–3.35 (1H, m), 3.17–3.04 (1H, m), 2.28–1.48 (4H, m)
Example80	δ 8.57 (1H, d, J = 1.5 Hz), 7.67 (1H, dd, J = 8.1, 2.2 Hz), 7.28–7.21 (3H, m), 6.88–6.83 (2H, m), 4.59–4.52 (1H, m), 3.94–3.32 (4H, m), 2.60 (3H, s), 2.08–1.70 (4H, m)
Example92	δ 7.28–7.21 (2H, m), 6.89–6.82 (2H, m), 4.58–4.50 (1H, m), 3.82–3.51 (4H, m), 2.68 (3H, s), 2.41 (3H, s), 2.01–1.79 (4H, m)
Example191	δ 8.99–8.95 (1H, m), 8.20–8.16 (1H, m), 7.88 (1H, d, J = 1.5 Hz), 7.86–7.84 (1H, m), 7.70–7.34 (5H, m), 7.14–7.10 (1H, m), 4.71–4.64 (1H, m), 4.20–3.96 (2H, m), 3.51–3.36 (1H, m), 3.20–3.05 (1H, m), 2.59 (3H, s), 2.32–1.56 (4H, m)
Example403	δ 8.33 (1H, d, J = 5.1 Hz), 8.23 (1H, s), 8.16 (1H, s), 7.26–7.20 (2H, m), 7.08–7.05 (1H, m), 6.87–6.81 (2H, m), 4.60–4.53 (1H, m), 3.97–3.74 (2H, m), 3.67–3.55 (1H, m), 3.91–3.76 (1H, m), 2.22 (3H, s), 2.09–1.75 (4H, m)
Example451	δ 8.68 (1H, d, J = 4.4 Hz), 8.19 (1H, s), 7.85 (1H, br.s), 7.50 (1H, dd, J = 5.1, 1.5 Hz), 7.33–7.27 (1H, m), 6.86–6.77 (3H, m), 5.72 (1H, br.s), 4.68–4.59 (1H, m), 4.02–3.77 (2H, m), 3.67–3.52 (1H, m), 3.39–3.28 (1H, m), 2.12–1.78 (4H, m)
Example561	δ 7.91–7.74 (1H, m), 7.45–7.20 (3H, m), 7.11–7.00 (2H, m), 6.90–6.75 (3H, m), 5.52 (1H, br.s), 4.76–4.55 (3H, m), 4.08–3.77 (2H, m), 3.67–3.55 (1H, m), 3.42–3.31 (1H, m), 2.10–1.76 (4H, m)
Example574	δ 9.32(1H, s), 9.20–9.13 (1H, m), 8.77 (1H, d, J = 1.5 Hz), 8.39–8.32 (1H, m), 7.61(1H, dd, J = 8.4, 4.0 Hz), 7.28 (1H, t, J = 8.4 Hz), 6.89–6.73 (3H, m), 4.66–4.56 (1H, m), 4.19–3.96 (2H, m), 3.55–3.41 (1H, m), 3.25–3.09 (1H, m), 2.29–1.76 (4H, m)

[0218] Pharmacological assays

[0219] In vitro activities against human voltage gated sodium channels

The inhibitory activities of compounds against voltage gated sodium channels were determined by methodology well known in the art.

The ability of the aryl substituted carboxamid derivatives of the formula (I) to inhibit the Na_{v1.3}, Na_{v1.7} and Na_{v1.5} channels was measured by Fluorescence Resonance Energy Transfer (FRET) assay and electrophysiology assay described below.

[0220] FRET Assay (Method A)

This screen was used to determine the effects of compounds on human Na_{v1.3}, human Na_{v1.7}, and human Na_{v1.5} channels, utilising the cell imaging technology by Hamamatsu Photonics's Functional Drug Screening System (FDSS). The change of membrane potential was monitored with fluorescent membrane potential dye pair, oxonol (DiSBAC2(3)) and coumarin (CC2-DMPE), using FRET technology.

[0221] Cell Maintenance:

Each HEK293 cells expressing human Na_{v1.3} channels and HEK293 cells expressing human Na_{v1.5} channels were grown in T225 flasks, in a 5% CO₂ humidified incubator to about 80% confluence. Media composition consisted of Dulbecco's Modified Eagle Medium (high glucose), 10% fetal calf serum (FCS), 100 units/ml Penicillin, 100

microgram/ml Streptomycin and 500 microgram/ml Geneticine.

CHO cells expressing human Na_{v1.7} channels were grown in T225 flasks, in a 5% CO₂ humidified incubator to about 80% confluence. Media composition consisted of HAM/F12 with Glutamax I, 10% FCS, 100 units/ml Penicillin and 100 microgram/ml Hygromycin.

[0222] Protocol:

- Seeded each cell lines (1.5×10^4 cells/well) into poly-D-lysine coated 384-well plates prior to experimentation.
- Incubated at 37°C in 5% CO₂ for 24 hours.
- Washed each well with buffer #1 (140 mM NaCl, 4.5 mM KCl, 10 mM D-Glucose, 2 mM CaCl₂, 1 mM MgCl₂, 10 mM HEPES, pH 7.4 adjusted with NaOH) twice.
- Added 1st loading solution containing 5 microM CC2-DMPE and 0.02 % Pluronic F-127 in buffer #1.
- Incubated the plate at room temperature in dark for 0.5 hours.
- Washed each well with buffer #2 (160 mM Choline, 10 mM D-Glucose, 0.1 mM CaCl₂, 1 mM MgCl₂, 10 mM HEPES, pH 7.4 adjusted with KOH) twice.
- Added 2nd loading solution containing 15 microM DiSBAC2(3), 0.5 mM VABSC-1, 10 microM veratridine and 0.004 % Pluronic F-127 in buffer #2.
- Added compound solutions into the assay plate for 30 minutes under the dark at room temperature.
- Measured the activity by FDSS.

[0223] The data were analyzed and reported as normalized ratios of intensities measured in the 465 nm and 575 nm channels. The process of calculating these ratios was performed as follows:

"FI465B" = the mean of fluorescence intensity as baseline (before Na⁺ ligand addition) at 465nm

"FI575B" = the mean of fluorescence intensity as baseline (before Na⁺ ligand addition) at 575nm

"FI465Max" = maximum fluorescence intensity at 465nm after Na⁺ stimulation

"FI575Min" = minimum fluorescence intensity at 575nm after Na⁺ stimulation

"FR" = fluorescence ratio = (FI465Max/FI575Min)-(FI465B/FI575B)

[Math.1]

$$\text{Inhibition (\%)} = 100 - \frac{(\text{FR of each well}) - (\text{median FR in positive controls})}{(\text{median FR in negative controls}) - (\text{median FR in negative controls})} \times 100$$

This analysis was performed using a computerized specific program designed for FDSS generated data. Fluorescence ratio values were plotted using XLfit to determine an IC₅₀ value for each compound.

[0224] All tested compounds in this assay showed less than about 5 microM against either

Na_{v1.3} or Na_{v1.7} in the above assays. Preferable compounds showed less than about 1 microM against either Na_{v1.3} or Na_{v1.7} in the above assays. In addition, all tested compounds showed higher IC₅₀ values in Na_{v1.5} FRET Assay than IC₅₀ values in Na_{v1.3} or Na_{v1.7} FRET Assay.

Especially, Example 1, 2, 3, 4, 5, 6, 7, 9, 10, 11, 13, 14, 15, 16, 20, 21, 22, 26, 27, 28, 30, 31, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 45, 46, 47, 48, 49, 50, 52, 53, 54, 55, 57, 58, 59, 60, 61, 65, 66, 67, 69, 70, 71, 72, 73, 74, 76, 77, 78, 79, 80, 83, 84, 86, 87, 88, 92, 94, 95, 96, 97, 98, 100, 103, 104, 107, 109, 112, 113, 114, 115, 116, 117, 118, 119, 120, 122, 123, 125, 126, 128, 134, 137, 139, 141, 142, 143, 144, 151, 152, 159, 163, 168, 169, 170, 171, 172, 175, 176, 183, 185, 186, 188, 189, 190, 193, 197, 199, 200, 205, 207, 211, 212, 215, 216, 217, 218, 219, 220, 222, 226, 230, 231, 232, 233, 237, 238, 239, 240, 241, 242, 243, 246, 252, 256, 257, 258, 259, 263, 265, 266, 267, 268, 269, 270, 271, 278, 283, 284, 285, 290, 291, 292, 294, 296, 297, 298, 299, 303, 305, 312, 313, 314, 315, 318, 319, 320, 323, 324, 325, 328, 329, 330, 336, 337, 338, 339, 340, 342, 343, 345, 347, 348, 350, 353, 354, 355, 357, 360, 361, 362, 363, 367, 368, 369, 370, 371, 374, 375, 376, 378, 379, 380, 381, 382, 385, 389, 396, 398, 400, 401, 406, 410, 411, 412, 413, 414, 416, 417, 418, 419, 421, 423, 424, 434, 435, 440, 450, 451, 455, 459, 460, 461, 463, 470, 471, 472, 477, 478, 479, 481, 482, 483, 484, 485, 486, 487, 492, 493, 495, 496, 508, 512, 513, 514, 518, 520, 522, 539, and 540 of the invention have an IC₅₀ less than about 1 microM in the Na_{v1.3} or Na_{v1.7} FRET Assay.

[0225] FRET Assay (Method B)

This screen was used to determine the effects of compounds on human Na_{v1.3}, human Na_{v1.7}, and human Na_{v1.5} channels, utilising electrical field stimulation (EFS) system in 96-well plate format on FDSS (Hamamatsu Photonics) platform. The change of membrane potential was monitored with FRET dye pair, oxonol (DiSBAC2(3)) and coumarin (CC2-DMPE).

[0226] Cell Maintenance:

Each HEK293 cells expressing human Na_{v1.3} channels and HEK293 cells expressing human Na_{v1.5} channels were grown in T225 flasks, in a 5% CO₂ humidified incubator to about 80% confluence. Media composition consisted of Dulbecco's Modified Eagle Medium (high glucose), 10% FCS, 100 units/ml Penicillin, 100 microgram/ml Streptomycin and 500 microgram/ml Geneticine.

CHO cells expressing human Na_{v1.7} channels were grown in T225 flasks, in a 5% CO₂ humidified incubator to about 80% confluence. Media composition consisted of HAM/F12 with Glutamax I, 10% FCS, 100 units/ml Penicillin and 100 microgram/ml Hygromycin.

[0227] Protocol:

- Seeded each cell lines (1 x 10⁵ cells/well) into poly-D-lysine coated 96-well plates

prior to experimentation.

- Incubated at 37°C in 5% CO₂ for 24 hours.
- Washed each well with assay buffer (140 mM NaCl, 4.5 mM KCl, 10 mM D-Glucose, 2 mM CaCl₂, 1 mM MgCl₂, 10 mM HEPES, pH 7.4 adjusted with NaOH) twice.
- Added 1st loading solution containing 10 microM CC2-DMPE and 0.06 % Pluronic F-127 in assay buffer.
- Incubated the plate at room temperature in dark for 1 hour.
- Removed 1st loading solution and added 2nd loading solution containing 15 microM DiSBAC2(3), 0.555 mM VABSC-1 and 0.004 % Pluronic F-127 in assay buffer.
- Placed the plate under the dark at room temperature for 25 minutes.
- Added compound solutions into the assay plate.
- Set the assay plate in FDSS and placed an EFS device on the plate.
- Measured EFS-induced fluorescent response by FDSS.

[0228] The data were analyzed and reported as normalized ratios of intensities measured at 440 nm. The process of calculating these ratios was performed as follows:

[Math.2]

FIR = Fluorescence Integration Ratio = the integral of the ratio normalized by baseline (before EFS)

$$\% \text{ inhibition} = \left\{ 1 - \frac{(\text{FIR of each well} - \text{median FIR in } 100 \% \text{ Inh.})}{(\text{median FIR in } 0 \% \text{ Inh.} - \text{median FIR in } 100 \% \text{ Inh.})} \right\} \times 100$$

This analysis was performed using a computerized specific program designed for FDSS generated data. Fluorescence ratio values were plotted using XLfit to determine an IC₅₀ value for each compound.

[0229] All tested compounds in this assay showed less than about 5 microM against either Na_{v1.3} or Na_{v1.7} in the above assays. Preferable compounds showed less than about 3 microM against either Na_{v1.3} or Na_{v1.7} in the above assays.

Especially, Example 1, 21, 52, 90, 105, 136, 168, 187, 195, 331, 364, 395, 403, 404, 409, 434, 444, 445, 447, 450, 451, 454, 455, 456, 457, 463, 464, 469, 477, 478, 480, 482, 485, 486, 487, 503, 509, 513, 530, 546, 550, 553, 556, 557, 558, 560, 561, 562, 563, 564, 566, 567, 568, 570, 571, 574, 575, 576, 577, 578, 590, 593, 597, 599, 601, 602, 604, 605, 606, 609, 611, 612, 614, 615, 616, 617, 618, 619, 620, 621, 622, 623, 624, 625, 627, 628, 629, 630, 631, 636, 638, 639, 640, 641, 642, 643, 645, 648, 649, 650, 652, 654, 655, 656, 657, 658, 659, 660, 661, 662, 663, 665, 666, 667, 668, 669, 670, 671, 673, 674, 675, 676, 677, 678, 680, 681, 684, 685, 686, 687, 691, 693, 696, 697, 698, 699, 700, 702, 705, 707, 709, 710, 711, 712, 714, 715, 716, 720, 721, 723, and 725 of the invention have an IC₅₀ less than about 3 microM in the Na_{v1.3} or Na_{v1.7} EFS-FRET Assay. In addition, all tested compounds showed higher IC₅₀ values in Na

$v_{1.5}$ FRET Assay than IC_{50} values in $Na_{v1.3}$ or $Na_{v1.7}$ FRET Assay.

[0230] Electrophysiology assay

Whole cell patch clamp recording was used to assess the efficacy or selectivity of Na channel blocker on human $Na_{v1.3}$ (hSCN3A) expressing HEK293 cells or human $Na_{v1.7}$ (hSCN9A) expressing CHO cells. Human $Na_{v1.3}$ expressing HEK293 cells were grown in growth media which comprised: DMEM, 10% heat-inactivated FBS (Hyclone Laboratories Inc), 100 microgram/ml Penicillin/100U/ml Streptomycin, 150 microgram/ml Zeocin, 3 microgram/ml Geneticin. Human $Na_{v1.7}$ expressing CHO cells were grown in growth media which comprised: HAM/F-12, 9% heat-inactivated FBS (Hyclone Laboratories Inc), 100 microgram/ml Penicillin/100U/ml Streptomycin, 100 microgram/ml Hygromycin.

Na channel expressing cells were dissociated by 0.05% Trypsine-EDTA, and then seeded on cover glass for 24-48hr.

[0231] Glass pipettes were pulled to a tip diameter of 1-2 micrometer on a pipette puller. The pipettes were filled with the intracellular solution and a chloridized silver wire was inserted along its length, which was then connected to the headstage of the voltage-clamp amplifier (Axon Instruments or HEKA elektronik). The extracellular recording solution consists of (mM): 140 NaCl, 5 KCl, 2 $CaCl_2$, 1 $MgCl_2$, 10 HEPES, 10 Glucose, pH 7.4 adjusted with NaOH. The internal solution consists of (mM): 120 CsF, 15 NaCl, 10 EGTA, 10 HEPES, pH 7.2 adjusted with CsOH; Upon insertion of the pipette tip into the bath, the pipette resistance was noted (acceptable range is between 1-3 megaohm). The junction potential between the pipette and bath solutions was zeroed on the amplifier. After establishing the whole-cell configuration, approximately 10 minutes were allowed for the pipette solution to equilibrate within the cell before beginning recording. Currents were lowpass filtered between 2-5 kHz and digitally sampled at 10 kHz.

[0232] The normalized steady-state inactivation curve was constructed using 2sec (for vehicle) or 60sec (for drugs) conditioning pulse to different potentials followed immediately by the test pulse to -10 mV. Peak currents were plotted as fraction of the maximum current at the conditioning potentials ranging from -120 mV to -40 mV for $Na_{v1.3}$ and from -130 mV to -60 mV for $Na_{v1.7}$. $V_{1/2}$ or k values were estimated from Boltzmann fits. The affinity of drugs to resting state of Na channels ($K_{resting}$ or K_r) was assessed by 30 msec test pulse from a negative holding potential of -120 or -130 mV, where virtually all channels are in the resting state. K_r value was calculated by a conventional 1:1 binding model:

$$K_{resting} (K_r) = \{ [drug] I_{max, drug} / (I_{max, control} - I_{max, drug}) \}$$

where $K_{resting}$ ($=K_r$) is a dissociation constant for the resting state and [drug] is compound concentration. $I_{max, control}$ and $I_{max, drug}$ are peak currents in the absence and

presence of compound, respectively.

- [0233] The affinity of drug to inactivated state of Na channels (K_{inact} or K_i) was estimated from the shift of the availability curve by compound. Interaction of the compound with the channel on inactivated state was evaluated by the following equation:

[Math.3]

$$K_{\text{inact}} (K_i) = \{[\text{drug}] / ((1 + [\text{drug}] / K_r) * \exp(-\Delta V / k) - 1)\}$$

where K_{inact} ($=K_i$) is a dissociation constant for the inactivated state. ΔV is the compound-induced voltage shift of half maximal voltage of Boltzmann curve and k is the slop factor on presense of compound.

- [0234] All tested compounds of the invention showed potent activities in this model.

- [0235] In vivo assay

- [0236] Chronic constriction injury (CCI)-induced static allodynia

Male Sprague-Dawley rats weighing 210-240 g were purchased from Charles River Japan, Inc. (Kanagawa, Japan). Animals were housed in groups of two per cage under a 12-h light/dark cycle (lights on at 07:00) with access to food and water ad libitum. CCI surgery was performed according to the method of Bennett GJ and Xie YK (Pain 1988, 33: 87-107). Animals were anesthetized with intraperitoneal injection of pento-barbital sodium. The left common sciatic nerve was exposed at the level of the middle of the thigh, freed of adhering tissue, and four ligatures were loosely tied around it by using 4-0 silk thread (Ethicon Inc., Brussels, Belgium) with approximately 1 mm apart. The incision was sutured, and the rats were allowed to recover. Sham operation was performed in the same manner except of sciatic nerve ligation. After 2 to 3 weeks, static allodynia was assessed using von Frey hairs (VFHs; North Coast Medical Inc., San Jose, CA) as described by Field MJ et al. (Pain 1999, 83: 303-311). The animals were placed in grid bottom cages and allowed to acclimate for at least 30 min prior to the start of experiment. VFHs in ascending order of force (0.16, 0.4, 0.6, 1, 1.4, 2, 4, 6, 8, 10, 15 and 26 g) were applied to the plantar surface of the operated hind paw. Each VFH was applied to the paw for 6 sec, or until a withdrawal response occurred. Once a withdrawal response was happened, the paw was re-tested starting with the next descending VFH until no response occurred. The lowest amount of force required to elicit a response was defined as paw withdrawal threshold (PWT) in g. Animals showing <2 g of PWT in CCI were selected for evaluation and randomized to be nearly equal across all groups. The compounds of the invention or their vehicles were administered systemically. PWT was measured at the appropriated time after compound administration.

All tested compounds of the invention showed potent activities in this model.

- [0237] Complete Freund's Adjuvant (CFA)-induced thermal hyperalgesia

Male Sprague-Dawley rats weighing 200-250 g were purchased from Charles River Japan, Inc. (Kanagawa, Japan). Animals were housed under a 12-h light/dark cycle (lights on at 07:00) with access to food and water ad libitum. CFA-induced thermal hyperalgesia was assessed using the plantar test apparatus (Ugo Basile, Varese, Italy) as described by Hargreaves K et al. (Pain 1988, 32: 77-88). Animals were placed in an apparatus consisting of individual testing box on an elevated glass table and allowed to acclimate for at least 10 min. Following habituation, a mobile radiant heat source was located under the table and heat stimulation was applied to the plantar surface of the right hind paw. The latency to remove its hind paw was defined as paw withdrawal latency (PWL) in sec. The cut-off point was set at 30 sec to prevent tissue damage. CFA was prepared at a concentration of 200 microg/100 microl of Mycobacterium tuberculosis H37 RA (Difco Laboratories Inc.) in liquid paraffin and injected intraplantarly with a 100 microl of CFA into the right hind paw. PWL was measured before and 2 days after CFA injection. Animals showing decrease of the PWL on day 2 were selected for evaluation and randomized to be nearly equal across all groups. The compounds of the invention or their vehicles were administered systemically. PWL was measured at the appropriated time after compound administration. All tested compounds of the invention showed potent activities in this model.

[0238] Human dofetilide binding assay

Human HERG transfected HEK293S cells were prepared and grown in-house. The collected cells were suspended in 50 mM Tris-HCl (pH 7.4 at 4°C) and homogenized using a hand held Polytron PT 1200 disruptor set at full power for 20 sec on ice. The homogenates were centrifuged at 48,000 x g at 4°C for 20 min. The pellets were then resuspended, homogenized, and centrifuged once more in the same manner. The final pellets were resuspended in an appropriate volume of 50 mM Tris-HCl, 10 mM KCl, 1 mM MgCl₂ (pH 7.4 at 4°C), homogenized, aliquoted and stored at -80°C until use. An aliquot of membrane fractions was used for protein concentration determination using BCA protein assay kit (PIERCE) and ARVOsx plate reader (Wallac). Binding assays were conducted in a total volume of 30 microL in 384-well plates. The activity was measured by PHERAstar (BMG LABTECH) using fluorescence polarization technology. Ten microL of test compounds were incubated with 10 microL of fluorescence ligand (6 nM Cy3B tagged dofetilide derivative) and 10 microL of membrane homogenate (6 microg protein) for 120 minutes at room temperature. Nonspecific binding was determined by 10 microM E4031 at the final concentration.

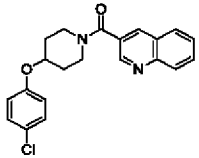
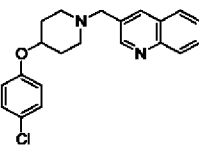
[0239] Examples showed higher IC₅₀ values in human dofetilide binding than IC₅₀ values in Na_{v1.3} or Na_{v1.7} FRET Assay (Method A and/or B). The high IC₅₀ values in human dofetilide binding activities lead to reducing the risk of cardiovascular adverse events.

As shown in the following table, the Example 10, which has amide group, is as good

as the Example 726, which does not have amide group, in Na_v1.7 FRET assay. However in IC₅₀ value in the human dofetilide assay, the example 10 is much preferable to the example 270.

Example 726 was prepared from 4-(4-chlorophenoxy)piperidine and quinoline-3-carbaldehyde by reductive amination with sodium triacetoxyborohydride.

[0240] [Table 5]

Example	Structure of Example (I)	IC ₅₀ in the Na _v 1.7 FRET Assay (μM)	IC ₅₀ in the Human dofetilide binding Assay (μM)
10		0.36	7.91
726		0.47	0.28

[0241] Metabolic stability assay:

Half-life in human liver microsomes (HLM)

Test compounds (1 microM) were incubated with 3.3 mM MgCl₂ and 0.78 mg/mL HLM (HL101) or 0.74 mg/mL HLM (Gentest UltraPool 150) in 100 mM potassium phosphate buffer (pH 7.4) at 37°C on the 96-deep well plate. The reaction mixture was split into two groups, a non-P450 and a P450 group. NADPH was only added to the reaction mixture of the P450 group. (NADPH generation system was also used instead of NADPH.) An aliquot of samples of P450 group was collected at 0, 10, 30, and 60 min time point, where 0 min time point indicated the time when NADPH was added into the reaction mixture of P450 group. An aliquot of samples of non-P450 group was collected at -10 and 65 min time point. Collected aliquots were extracted with acetonitrile solution containing an internal standard. The precipitated protein was spun down in centrifuge (2000 rpm, 15 min). The compound concentration in supernatant was measured by LC/MS/MS system.

[0242] The half-life value was obtained by plotting the natural logarithm of the peak area ratio of compounds/ internal standard versus time. The slope of the line of best fit through the points yields the rate of metabolism (k). This was converted to a half-life value using following equations: Half-life = ln 2/k

The compounds of this invention showed preferable stability, which show the above-mentioned practical use.

[0243] Drug-drug interaction assay

This method essentially involves determining the percent inhibition of metabolites

formation from probes (Tacrine (Sigma A3773-1G) 2 microM, Dextromethorphan (Sigma D-9684) 5 microM, Diclofenac (Sigma D-6899-10G) 5 microM, and Midazolam(ULTRAFINE UC-429) 2 microM) at 3 microM of the each compound.

[0244] More specifically, the assay is carried out as follows. The compounds (60 microM, 10 microL) were pre-incubated in 170 microL of mixture including 0.1 mg protein/mL human liver microsomes, 100 mM potassium phosphate buffer (pH 7.4), 1 mM MgCl₂ and probes as substrate for 5min. Reaction was started by adding a 20 microL of 10mM NADPH (20 microL of NADPH generating system, which consist of 10 mM NADP⁺, 50 mM DL-Isocitric acid and 10 U/ml Isocitric Dehydrogenase, was also used). The assay plate was incubated at 37 °C. Acetonitril was added to the incubate solution at appropriate time (e.g. 8 min).

The metabolites'concentration in the supernatant was measured by LC/MS/MS system.

The degree of drug drug interaction was interpreted based on generation % of metabolites in the presence or absence of test compound.

The compounds of this invention showed preferable results, which show the above-mentioned practical use.

[0245] Plasma protein binding assay

Plasma protein binding of the test compound (1 microM) was measured by the method of equilibrium dialysis using 96-well plate type equipment. HTD96a(registered trademark), regenerated cellulose membranes (molecular weight cut-off 12,000-14,000, 22 mm x 120 mm) were soaked for over night in distilled water, then for 15 minutes in 30% ethanol, and finally for 20 minutes in dialysis buffer (Dulbecco's phosphate buffered saline, pH7.4). Frozen plasma of human, Sprague-Dawley rats, and Beagle dogs were used. The dialysis equipment was assembled and added 150 microL of compound-fortified plasma to one side of each well and 150 microL of dialysis buffer to the other side of each well. After 4 hours incubation at 37 °C for 150 r.p.m, aliquots of plasma and buffer were sampled. The compound in plasma and buffer were extracted with 300 microL of acetonitrile containing internal standard compounds for analysis. The concentration of the compound was determined with LC/MS/MS analysis.

The fraction of the compound unbound was calculated by the following equation (A) or (B):

[Math.4]

$$(A) f_u = 1 - \{ ([\text{plasma}]_{\text{eq}} - [\text{buffer}]_{\text{eq}}) / ([\text{plasma}]_{\text{eq}}) \}$$

wherein [plasma]_{eq} and [buffer]_{eq} are the concentrations of the compound in plasma and buffer, respectively.

[Math.5]

$$(B) \quad fu(\%) = \frac{Cb / Cis, b \times 4}{Cp / Cis, p \times \frac{4}{3}} \times 100$$

wherein Cp is the peak area of the compound in plasma sample;

Cis,p is the peak area of the internal standard in plasma sample;

Cb is the peak area of the compound in buffer sample;

Cis,b is the peak area of the internal standard in buffer sample;

4 and 4/3 is the reciprocal of the dilution rate in plasma and buffer, respectively.

The compounds of this invention showed preferable plasma protein binding, which show the above-mentioned practical use.

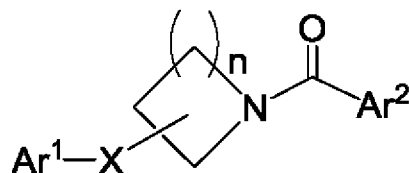
[0246] All publications, including but not limited to, issued patents, patent applications, and journal articles, cited in this application are each herein incorporated by reference in their entirety. Although the invention has been described above with reference to the disclosed embodiments, those skilled in the art will readily appreciate that the specific experiments detailed are only illustrative of the invention. It should be understood that various modifications can be made without departing from the spirit of the invention. Accordingly, the invention is limited only by the following claims.

Claims

[Claim 1]

A use of a compound of the following formula (I) for the manufacture of a medicament for the treatment of a condition or disorder in which TTX-S channel blockers are involved:

[Chem.3]



(I)

wherein

Ar¹ is phenyl which may be optionally substituted with 1 to 5 substituents independently selected from the group consisting of

(1) halogen, (2) C₁-C₄ alkyl-O-, (3) C₃-C₈ cycloalkyl-O-, (4) C₁-C₄ haloalkyl-O-, (5) hydroxy, (6) C₃-C₈ cycloalkyl-C₁-C₄ alkyl-O-, (7) C₁-C₄ alkylthio, (8) nitro, (9) R¹N(R²)-C₀₋₄ alkyl-O-, (10) cyano, (11) hydroxy C₁-C₄ alkyl-O-, (12) C₁-C₄ alkyl-O-C₁-C₄ alkyl-O-, (13) C₁-C₄ alkylsulfonyl, (14) R¹N(R²)-SO₂-C₀₋₄ alkyl-O-, (15) C₁-C₄ alkyl C(=O)-, (16) HO-C(=O)-, (17) C₁-C₄ alkyl-O-C(=O)-, (18) R¹N(R²)C(=O)-C₀₋₄ alkyl-O-, (19) C₁-C₄ alkyl-SO₂-NH-C₀₋₄ alkyl-O-, (20) R¹-O_i-C(=O)N(R²)-C₀₋₄ alkyl-O_k-, (21) NH₂(HN=)C-, (22) NH₂C(=O)NH-, (23) 5 to 10 membered aryl-O_i-C₀-C₄ alkyl-O_k-; wherein said aryl may be optionally substituted with 1 to 5 substituents independently selected from the group consisting of hydroxy, halogen, C₁-C₄ alkyl, C₁-C₄ alkoxy, hydroxy C₁-C₄ alkyl, amino C₁-C₄ alkyl, C₁-C₄ haloalkyl, C₁-C₄ haloalkoxy, C₃-C₇ cycloalkyl C₀₋₆ alkyl, amino, C₁-C₄ alkylamino, di(C₁-C₄ alkyl)amino, C₁-C₄ alkylthio, C₁-C₄ alkylsulfonyl, R¹N(R²)C(=O)-, C₁-C₄ alkyl-SO₂-NH-, and nitro; and (24) heterocyclic group-O_i-C₀-C₄ alkyl-O_k-; wherein said heterocyclic group may be optionally substituted with 1 to 5 substituents independently selected from the group consisting of hydroxy, halogen, C₁-C₄ alkyl, C₁-C₄ alkoxy, hydroxy C₁-C₄ alkyl, amino C₁-C₄ alkyl, C₁-C₄ haloalkyl, C₁-C₄ haloalkoxy, C₃-C₇ cycloalkyl C₀₋₆ alkyl, amino, C₁-C₄ alkylamino, di(C₁-C₄ alkyl)amino, C₁-C₄ alkylthio, C₁-C₄ alkylsulfonyl, R¹N(R²)C(=O)-, C₁-C₄ alkyl-SO₂-NH-, and nitro;

Ar² is aryl which may be optionally substituted with 1 to 5 substituents

independently selected from the group consisting of

(1) halogen, (2) C₁-C₄ alkyl-O_i-, (3) C₃-C₈ cycloalkyl-O_i-, (4) C₁-C₄ haloalkyl-O_i-, (5) hydroxy, (6) C₃-C₈ cycloalkyl-C₁-C₄ alkyl-O_i-, (7) C₁-C₄ alkylthio, (8) nitro, (9) R¹N(R²)-C₀₋₄ alkyl-O_i-, (10) cyano, (11) hydroxy C₁-C₄ alkyl-O_i-, (12) C₁-C₄ alkyl-O-C₁-C₄ alkyl-O_i-, (13) C₁-C₄ alkylsulfonyl, (14) R¹N(R²)-SO₂-C₀₋₄ alkyl-O_i-, (15) C₁-C₄ alkyl C(=O)-, (16) HO-C(=O)-, (17) C₁-C₄ alkyl-O-C(=O)-, (18) R¹N(R²)C(=O)-C₀₋₄ alkyl-O_i-, (19) C₁-C₄ alkyl-SO₂-NH-C₀₋₄ alkyl-O_i-, (20) R¹-O_i-C(=O)N(R²)-C₀₋₄ alkyl-O_k-, (21) NH₂(HN=)C-, (22) NH₂C(=O)NH-, (23) 5 to 10 membered aryl-O_i-C₀-C₄ alkyl-O_k-; wherein said aryl may be optionally substituted with 1 to 5 substituents independently selected from the group consisting of hydroxy, halogen, C₁-C₄ alkyl, C₁-C₄ alkoxy, hydroxy C₁-C₄ alkyl, amino C₁-C₄ alkyl, C₁-C₄ haloalkyl, C₁-C₄ haloalkoxy, C₃-C₇ cycloalkyl C₀₋₆ alkyl, amino, C₁-C₄ alkylamino, di(C₁-C₄ alkyl)amino, C₁-C₄ alkylthio, C₁-C₄ alkylsulfonyl, R¹N(R²)C(=O)-, C₁-C₄ alkyl-SO₂-NH-, and nitro; and (24) heterocyclic group-O_i-C₀-C₄ alkyl-O_k-; wherein said heterocyclic group may be optionally substituted with 1 to 5 substituents independently selected from the group consisting of hydroxy, halogen, C₁-C₄ alkyl, C₁-C₄ alkoxy, hydroxy C₁-C₄ alkyl, amino C₁-C₄ alkyl, C₁-C₄ haloalkyl, C₁-C₄ haloalkoxy, C₃-C₇ cycloalkyl C₀₋₆ alkyl, amino, C₁-C₄ alkylamino, di(C₁-C₄ alkyl)amino, C₁-C₄ alkylthio, C₁-C₄ alkylsulfonyl, R¹N(R²)C(=O)-, C₁-C₄ alkyl-SO₂-NH-, and nitro;

n is 1, 2, 3, or 4;

i is 0 or 1;

k is 0 or 1;

R¹ and R² are independently selected from the group consisting of:

(1) hydrogen, (2) C₁₋₆ alkyl, (3) hydroxy C₁-C₄ alkyl, (4) C₁-C₄ alkoxy C₁-C₄ alkyl, (5) amino C₁-C₄ alkyl, (6) C₁-C₄ haloalkyl, (7) C₁-C₄ haloalkoxy, (8) C₃₋₆ alkenyl, (9) C₃₋₈ cycloalkyl C₀₋₆ alkyl, (10) phenyl, which is unsubstituted or substituted with R³, and (11) 5 to 10 membered aryl C₀-C₄ alkyl; wherein said aryl may be optionally substituted with 1 to 5 substituents independently selected from the group consisting of hydroxy, halogen, C₁-C₄ alkyl, C₁-C₄ alkoxy, hydroxy C₁-C₄ alkyl, amino C₁-C₄ alkyl, C₁-C₄ haloalkyl, C₁-C₄ haloalkoxy, C₃-C₇ cycloalkyl C₀₋₆ alkyl, amino, C₁-C₄ alkylamino, di(C₁-C₄ alkyl)amino, C₁-C₄ alkylthio, and nitro;

or R¹ and R² taken together with the nitrogen atom to which they are

attached form a 3 to 8 membered ring, where the ring may contain one to four heteroatom(s) independently selected from nitrogen, oxygen, and sulfur; where the ring may be saturated or partially saturated or unsaturated; and the ring is unsubstituted or substituted one or more substituents selected from R³;

R³ is selected from the group consisting of:

(1) hydroxy, (2) halogen, (3) C₁₋₆ alkyl, (4) -C₃₋₈ cycloalkyl, (5) -O-C₁₋₆ alkyl, (6) -O(C=O)-C₁₋₆ alkyl, (7) -NH-C₁₋₆ alkyl, (8) phenyl, (9) heterocyclic group, (10) -CO₂H, and (11) -CN;

X is -O-, -S-, -SO-, or -SO₂-;

or a prodrug thereof or a pharmaceutically acceptable salt thereof.

[Claim 2]

The use as claimed in claim 1,

wherein Ar² is aryl selected from

benzofuranyl, benzofurazanyl, benzimidazolonyl, benzoimidazolyl, benzoisothiazolyl, benzoisoxazolyl, benzothiadiazolyl, benzothiazolyl, benzoxadiazolyl, benzoxazolonyl, benzoxazolyl, benzothiophenyl, benzotriazolyl, chromanyl, cinnolyl, 2,3-dioxoindolyl, furanyl, furopyridyl, furopyrryl, imidazolyl, imidazopyrazinyl, imidazopyridinyl, imidazopyrimidinyl, imidazothiazolyl, indazolyl, indolyl, isochromanyl, isoquinolyl, isoxazolopyridyl, isoxazolyl, isothiazolyl, naphthyridinyl, oxadiazolyl, oxazolyl, 2-oxoindolyl, oxoisoindolyl, phthalazyl, pyrazolyl, pyrazolopyridyl, pyrazolopyrimidinyl, pyrazinyl, pyridopyrimidinyl, pyridyl, pyrimidyl, pyridazinyl, pyrrolopyridyl, pyrrolyl, quinazolinyl, quinolyl, quinoxalinyl, thiazolyl, thiophenyl, thienopyrazinyl, thienopyrazolyl, thienopyridyl, thienopyrryl, triazolopyrimidinyl, triazolyl, 3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazinyl, 1-methyl-4-oxo-1,4-dihydroquinolyl, 2-oxo-1,2-dihydropyridyl, 4-oxo-1,4-dihydropyrimidinyl, 2-oxo-1,2-dihydroquinolyl, 4-oxo-4H-pyrido[1,2-a]pyrimidinyl, 2-oxo-2,5,6,7-tetrahydro-1H-cyclopentapyridyl, 4,5,6,7-tetrahydro-indazolyl, 4-oxo-1,4-dihydro-1,8-naphthyridyl, and 5,6,7,8-tetrahydro-1,6-naphthyridyl.

[Claim 3]

The use as claimed in claim 1 or claim 2, wherein the condition or disorder is selected from the group consisting of: pain, acute pain, chronic pain, neuropathic pain, inflammatory pain, visceral pain, nociceptive pain, multiple sclerosis, neurodegenerative disorder, irritable bowel syndrome, osteoarthritis, rheumatoid arthritis, neuropathological

disorders, functional bowel disorders, inflammatory bowel diseases, pain associated with dysmenorrhea, pelvic pain, cystitis, pancreatitis, migraine, cluster and tension headaches, diabetic neuropathy, peripheral neuropathic pain, sciatica, fibromyalgia Crohn's disease, epilepsy or epileptic conditions, bipolar depression, tachyarrhythmias, mood disorder, bipolar disorder, psychiatric disorders such as anxiety and depression, myotonia, arrhythmia, movement disorders, neuroendocrine disorders, ataxia, incontinence, visceral pain, trigeminal neuralgia, herpetic neuralgia, general neuralgia, postherpetic neuralgia, radicular pain, sciatica, back pain, head or neck pain, severe or intractable pain, breakthrough pain, postsurgical pain, stroke, cancer pain, seizure disorder and causalgia; and combinations thereof.

[Claim 4]

A compound of formula (I) as described in claim 1 wherein

Ar¹ is phenyl which may be optionally substituted with 1 to 5 substituents independently selected from the group consisting of

(1) halogen, (2) C₁-C₄ alkyl-O_i-, (3) C₃-C₈ cycloalkyl-O_i-, (4) C₁-C₄ haloalkyl-O_i-, (5) hydroxy, (6) C₃-C₈ cycloalkyl-C₁-C₄ alkyl-O_i-, (7) C₁-C₄ alkylthio, (8) nitro, (9) R¹N(R²)-C₀₋₄ alkyl-O_i-, (10) cyano, (11) hydroxy C₁-C₄ alkyl-O_i-, (12) C₁-C₄ alkyl-O-C₁-C₄ alkyl-O_i-, (13) C₁-C₄ alkylsulfonyl, (14) R¹N(R²)-SO₂-C₀₋₄ alkyl-O_i-, (15) C₁-C₄ alkyl C(=O)-, (16) HO-C(=O)-, (17) C₁-C₄ alkyl-O-C(=O)-, (18) R¹N(R²)C(=O)-C₀₋₄ alkyl-O_i-, (19) C₁-C₄ alkyl-SO₂-NH-C₀₋₄ alkyl-O_i-, (20) R¹-O_i-C(=O)N(R²)-C₀₋₄ alkyl-O_k-, (21) NH₂(HN=C)-, (22) NH₂C(=O)NH-, (23) 5 to 10 membered aryl-O_i-C₀-C₄ alkyl-O_k-; wherein said aryl may be optionally substituted with 1 to 5 substituents independently selected from the group consisting of hydroxy, halogen, C₁-C₄ alkyl, C₁-C₄ alkoxy, hydroxy C₁-C₄ alkyl, amino C₁-C₄ alkyl, C₁-C₄ haloalkyl, C₁-C₄ haloalkoxy, C₃-C₇ cycloalkyl C₀₋₆ alkyl, amino, C₁-C₄ alkylamino, di(C₁-C₄ alkyl)amino, C₁-C₄ alkylthio, C₁-C₄ alkylsulfonyl, R¹N(R²)C(=O)-, C₁-C₄ alkyl-SO₂-NH-, and nitro; and (24) heterocyclic group-O_i-C₀-C₄ alkyl-O_k-; wherein said heterocyclic group may be optionally substituted with 1 to 5 substituents independently selected from the group consisting of hydroxy, halogen, C₁-C₄ alkyl, C₁-C₄ alkoxy, hydroxy C₁-C₄ alkyl, amino C₁-C₄ alkyl, C₁-C₄ haloalkyl, C₁-C₄ haloalkoxy, C₃-C₇ cycloalkyl C₀₋₆ alkyl, amino, C₁-C₄ alkylamino, di(C₁-C₄ alkyl)amino, C₁-C₄ alkylthio, C₁-C₄ alkylsulfonyl, R¹N(R²)C(=O)-, C₁-C₄ alkyl-SO₂-

NH-, and nitro;

Ar² is selected from; 3-benzofuranyl, 4-benzofuranyl, 5-benzofuranyl, 6-benzofuranyl, 7-benzofuranyl, benzofurazanyl, benzimidazolonyl, 3-benzoimidazolyl, 4-benzoimidazolyl, 5-benzoimidazolyl, 6-benzoimidazolyl, 7-benzoimidazolyl, benzoisothiazolyl, benzoisoxazolyl, benzothiadiazolyl, 3-benzothiazolyl, 4-benzothiazolyl, 5-benzothiazolyl, 6-benzothiazolyl, 7-benzothiazolyl, benzoxadiazolyl, benzoxazolonyl, 3-benzoxazolyl, 4-benzoxazolyl, 5-benzoxazolyl, 6-benzoxazolyl, 7-benzoxazolyl, 3-benzothiophenyl, 4-benzothiophenyl, 5-benzothiophenyl, 6-benzothiophenyl, 7-benzothiophenyl, benzotriazolyl, chromanyl, cinnolinyl, 2,3-dioxoindolyl, furanyl, furopyridyl, furopyrryl, imidazolyl, imidazopyrazinyl, imidazopyridinyl, imidazopyrimidinyl, imidazothiazolyl, indazolyl, indolinyl, 4-indolyl, 5-indolyl, 6-indolyl, 7-indolyl, isochromanyl, isoquinolyl, isoxazolopyridyl, isoxazolyl, isothiazolyl, naphthyridinyl, oxadiazolyl, oxazolyl, 2-oxoindolyl, oxoisoindolyl, phthalazyl, pyrazolyl, pyrazolopyridyl, pyrazolopyrimidinyl, pyrazinyl, pyridopyrimidinyl, 2-pyridyl, 3-pyridyl, 5-pyridyl, 6-pyridyl, pyrimidyl, pyridazinyl, pyrrolopyridyl, pyrrolyl, quinazolinyl, quinolyl, quinoxalinyl, thiazolyl, thiophenyl, thienopyrazinyl, thienopyrazolyl, thienopyridyl, thienopyrryl, triazolopyrimidinyl, triazolyl, 3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazinyl, 1-methyl-4-oxo-1,4-dihydroquinolyl, 4-oxo-1,4-dihydropyrimidyl, 2-oxo-1,2-dihydroquinolyl, 4-oxo-4H-pyrido[1,2-a]pyrimidyl, 2-oxo-2,5,6,7-tetrahydro-1H-cyclopentapyridyl, 4,5,6,7-tetrahydro-indazolyl, 4-oxo-1,4-dihydro-1,8-naphthyridyl, and 5,6,7,8-tetrahydro-1,6-naphthyridyl

wherein said 3-benzofuranyl, 4-benzofuranyl, 5-benzofuranyl, 6-benzofuranyl, 7-benzofuranyl, benzofurazanyl, benzimidazolonyl, 3-benzoimidazolyl, 4-benzoimidazolyl, 5-benzoimidazolyl, 6-benzoimidazolyl, 7-benzoimidazolyl, benzoisothiazolyl, benzoisoxazolyl, benzothiadiazolyl, 3-benzothiazolyl, 4-benzothiazolyl, 5-benzothiazolyl, 6-benzothiazolyl, 7-benzothiazolyl, benzoxadiazolyl, benzoxazolonyl, 3-benzoxazolyl, 4-benzoxazolyl, 5-benzoxazolyl, 6-benzoxazolyl, 7-benzoxazolyl, 3-benzothiophenyl, 4-benzothiophenyl, 5-benzothiophenyl, 6-benzothiophenyl, 7-benzothiophenyl, benzotriazolyl, chromanyl, cinnolinyl, 2,3-dioxoindolyl, furanyl, furopyridyl, furopyrryl, imidazolyl, imida-

zopyrazinyl, imidazopyridinyl, imidazopyrimidinyl, imidazothiazolyl, indazolyl, indolinyl, 4-indolyl, 5-indolyl, 6-indolyl, 7-indolyl, isochromanyl, isoquinolyl, isoxazolopyridyl, isoxazolyl, isothiazolyl, naphthyridinyl, oxadiazolyl, oxazolyl, 2-oxoindolyl, oxoisindolyl, phthalazyl, pyrazolyl, pyrazolopyridyl, pyrazolopyrimidinyl, pyrazinyl, pyridopyrimidinyl, 2-pyridyl, 3-pyridyl, 5-pyridyl, 6-pyridyl, pyrimidyl, pyridazinyl, pyrrolopyridyl, pyrrolyl, quinazolinyl, quinoxalinyl, thiazolyl, thiophenyl, thienopyrazinyl, thienopyrazolyl, thienopyridyl, thienopyrrolyl, triazolopyrimidinyl, triazolyl, 3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazinyl, 1-methyl-4-oxo-1,4-dihydroquinolyl, 4-oxo-1,4-dihydropyrimidinyl, 2-oxo-1,2-dihydroquinolyl, 4-oxo-4H-pyrido[1,2-a]pyrimidinyl, 2-oxo-2,5,6,7-tetrahydro-1H-cyclopentapyridyl, 4,5,6,7-tetrahydro-indazolyl, 4-oxo-1,4-dihydro-1,8-naphthyridyl, and 5,6,7,8-tetrahydro-1,6-naphthyridyl may be optionally substituted with 1 to 5 substituents independently selected from the group consisting of (1) halogen, (2) C₁-C₄ alkyl-O_i-, (3) C₃-C₈ cycloalkyl-O_i-, (4) C₁-C₄ haloalkyl-O_i-, (5) hydroxy, (6) C₃-C₈ cycloalkyl-C₁-C₄ alkyl-O_i-, (7) C₁-C₄ alkylthio, (8) nitro, (9) R¹N(R²)-C₀₋₄ alkyl-O_i-, (10) cyano, (11) hydroxy C₁-C₄ alkyl-O_i-, (12) C₁-C₄ alkyl-O-C₁-C₄ alkyl-O_i-, (13) C₁-C₄ alkylsulfonyl, (14) R¹N(R²)-SO₂-C₀₋₄ alkyl-O_i-, (15) C₁-C₄ alkyl C(=O)-, (16) HO-C(=O)-, (17) C₁-C₄ alkyl-O-C(=O)-, (18) R¹N(R²)C(=O)-C₀₋₄ alkyl-O_i-, (19) C₁-C₄ alkyl-SO₂-NH-C₀₋₄ alkyl-O_i-, (20) R¹-O_i-C(=O)N(R²)-C₀₋₄ alkyl-O_k-, (21) NH₂(HN=C)-, (22) NH₂C(=O)NH-, (23) 5 to 10 membered aryl-O_i-C₀-C₄ alkyl-O_k-; wherein said aryl may be optionally substituted with 1 to 5 substituents independently selected from the group consisting of hydroxy, halogen, C₁-C₄ alkyl, C₁-C₄ alkoxy, hydroxy C₁-C₄ alkyl, amino C₁-C₄ alkyl, C₁-C₄ haloalkyl, C₁-C₄ haloalkoxy, C₃-C₇ cycloalkyl C₀₋₆ alkyl, amino, C₁-C₄ alkylamino, di(C₁-C₄ alkyl)amino, C₁-C₄ alkylthio, C₁-C₄ alkylsulfonyl, R¹N(R²)C(=O)-, C₁-C₄ alkyl-SO₂-NH-, and nitro; and (24) heterocyclic group-O_i-C₀-C₄ alkyl-O_k-; wherein said heterocyclic group may be optionally substituted with 1 to 5 substituents independently selected from the group consisting of hydroxy, halogen, C₁-C₄ alkyl, C₁-C₄ alkoxy, hydroxy C₁-C₄ alkyl, amino C₁-C₄ alkyl, C₁-C₄ haloalkyl, C₁-C₄ haloalkoxy, C₃-C₇ cycloalkyl C₀₋₆ alkyl, amino, C₁-C₄ alkylamino, di(C₁-C₄ alkyl)amino, C₁-C₄ alkylthio, C₁-C₄ alkylsulfonyl, R¹N(R²)C(=O)-, C₁-C₄ alkyl-SO₂-NH-, and nitro;

said quinolyl may be optionally substituted with 1 to 4 substituents independently selected from the group consisting of

(1) halogen, (2) C₁-C₄ alkyl-O_i-, (3) C₃-C₈ cycloalkyl-O_i-, (4) C₁-C₄ haloalkyl-O_i-, (5) 2-hydroxyl, (6) 3-hydroxyl, (7) 5-hydroxyl, (8) 6-hydroxyl, (9) 7-hydroxyl, (10) 8-hydroxyl, (11) C₃-C₈ cycloalkyl-C₁-C₄ alkyl-O_i-, (12) C₁-C₄ alkylthio, (13) nitro, (14) R¹N(R²)-C₀₋₄ alkyl-O_i-, (15) cyano, (16) hydroxy C₁-C₄ alkyl-O_i-, (17) C₁-C₄ alkyl-O-C₁-C₄ alkyl-O_i-, (18) C₁-C₄ alkylsulfonyl, (19) R¹N(R²)-SO₂-C₀₋₄ alkyl-O_i-, (20) C₁-C₄ alkyl C(=O)-, (21) HO-C(=O)-, (22) C₁-C₄ alkyl-O-C(=O)-, (23) R¹N(R²)C(=O)-C₀₋₄ alkyl-O_i-, (24) C₁-C₄ alkyl-SO₂-NH-C₀₋₄ alkyl-O_i-, (25) R¹-O_i-C(=O)N(R²)-C₀₋₄ alkyl-O_k-, (26) NH₂(HN=)C-, (27) NH₂ C(=O)NH-, (28) 5 to 10 membered aryl-O_i-C₀-C₄ alkyl-O_k-; wherein said aryl may be optionally substituted with 1 to 5 substituents independently selected from the group consisting of hydroxy, halogen, C₁-C₄ alkyl, C₁-C₄ alkoxy, hydroxy C₁-C₄ alkyl, amino C₁-C₄ alkyl, C₁-C₄ haloalkyl, C₁-C₄ haloalkoxy, C₃-C₇ cycloalkyl C₀₋₆ alkyl, amino, C₁-C₄ alkylamino, di(C₁-C₄ alkyl)amino, C₁-C₄ alkylthio, C₁-C₄ alkylsulfonyl, R¹N(R²)C(=O)-, C₁-C₄ alkyl-SO₂-NH-, and nitro; and (29) heterocyclic group-O_i-C₀-C₄ alkyl-O_k-; wherein said heterocyclic group may be optionally substituted with 1 to 5 substituents independently selected from the group consisting of hydroxy, halogen, C₁-C₄ alkyl, C₁-C₄ alkoxy, hydroxy C₁-C₄ alkyl, amino C₁-C₄ alkyl, C₁-C₄ haloalkyl, C₁-C₄ haloalkoxy, C₃-C₇ cycloalkyl C₀₋₆ alkyl, amino, C₁-C₄ alkylamino, di(C₁-C₄ alkyl)amino, C₁-C₄ alkylthio, C₁-C₄ alkylsulfonyl, R¹N(R²)C(=O)-, C₁-C₄ alkyl-SO₂-NH-, and nitro;

n is 1, 2, 3, or 4;

i is 0 or 1;

k is 0 or 1;

R¹ and R² are independently selected from the group consisting of:

(1) hydrogen, (2) C₁₋₆ alkyl, (3) hydroxy C₁-C₄ alkyl, (4) C₁-C₄ alkoxy C₁-C₄ alkyl, (5) amino C₁-C₄ alkyl, (6) C₁-C₄ haloalkyl, (7) C₁-C₄ haloalkoxy, (8) C₃₋₆ alkenyl, (9) C₃₋₈ cycloalkyl C₀₋₆ alkyl, (10) phenyl, which is unsubstituted or substituted with R³, and (11) 5 to 10 membered aryl C₀-C₄ alkyl; wherein said aryl may be optionally substituted with 1 to 5 substituents independently selected from the group consisting of hydroxy, halogen, C₁-C₄ alkyl, C₁-C₄ alkoxy, hydroxy C₁-C₄ alkyl, amino C₁-C₄ alkyl, C₁-C₄ haloalkyl, C₁-C₄ haloalkoxy, C₃-C₇ cycloalkyl C₀₋₆ alkyl, amino, C₁-C₄ alkylamino, di(C₁-C₄ alkyl)amino, C

₁-C₄ alkylthio, and nitro;

or R¹ and R² taken together with the nitrogen atom to which they are attached form a 3 to 8 membered ring, where the ring may contain one to four heteroatom(s) independently selected from nitrogen, oxygen, and sulfur; where the ring may be saturated or partially saturated or unsaturated; and the ring is unsubstituted or substituted one or more substituents selected from R³;

R³ is selected from the group consisting of:

(1) hydroxy, (2) halogen, (3) C₁₋₆ alkyl, (4) -C₃₋₈ cycloalkyl, (5) -O-C₁₋₆ alkyl, (6) -O(C=O)-C₁₋₆ alkyl, (7) -NH-C₁₋₆ alkyl, (8) phenyl, (9) heterocyclic group, (10) -CO₂H, and (11) -CN;

X is -O-, -S-, -SO-, or -SO₂-;

or a prodrug thereof or a pharmaceutically acceptable salt thereof.

[Claim 5]

A compound of formula (I) as described in claim 1

wherein

Ar¹ is phenyl which is substituted with chloro, trifluoromethyl, trifluoromethoxy, trifluoroethoxy or ethoxy; and which may be substituted with 1 to 2 substituents independently selected from:

(1) halogen, (2) C₁-C₄ alkyl-O_i-, (3) C₃-C₈ cycloalkyl-O_i-, (4) C₁-C₄ haloalkyl-O_i-, (5) hydroxy, (6) C₃-C₈ cycloalkyl-C₁-C₄ alkyl-O_i-, (7) C₁-C₄ alkylthio, (8) nitro, (9) R¹N(R²)-C₀₋₄ alkyl-O_i-, (10) cyano, (11) hydroxy C₁-C₄ alkyl-O_i-, (12) C₁-C₄ alkyl-O-C₁-C₄ alkyl-O_i-, (13) C₁-C₄ alkylsulfonyl, (14) R¹N(R²)-SO₂-C₀₋₄ alkyl-O_i-, (15) C₁-C₄ alkyl C(=O)-, (16) HO-C(=O)-, (17) C₁-C₄ alkyl-O-C(=O)-, (18) R¹N(R²)C(=O)-C₀₋₄ alkyl-O_i-, (19) C₁-C₄ alkyl-SO₂-NH-C₀₋₄ alkyl-O_i-, (20) R¹-O_i-C(=O)N(R²)-C₀₋₄ alkyl-O_k-, (21) NH₂(HN=)C-, (22) NH₂C(=O)NH-, (23) 5 to 10 membered aryl-O_i-C₀-C₄ alkyl-O_k-; wherein said aryl may be optionally substituted with 1 to 5 substituents independently selected from the group consisting of hydroxy, halogen, C₁-C₄ alkyl, C₁-C₄ alkoxy, hydroxy C₁-C₄ alkyl, amino C₁-C₄ alkyl, C₁-C₄ haloalkyl, C₁-C₄ haloalkoxy, C₃-C₇ cycloalkyl C₀₋₆ alkyl, amino, C₁-C₄ alkylamino, di(C₁-C₄ alkyl)amino, C₁-C₄ alkylthio, C₁-C₄ alkylsulfonyl, R¹N(R²)C(=O)-, C₁-C₄ alkyl-SO₂-NH-, and nitro; and (24) heterocyclic group-O_i-C₀-C₄ alkyl-O_k-; wherein said heterocyclic group may be optionally substituted with 1 to 5 substituents independently selected from the group consisting of hydroxy, halogen, C₁-C₄ alkyl, C₁-C₄ alkoxy, hydroxy C₁-C₄ alkyl, amino C₁-C₄ alkyl, C₁-C₄ haloalkyl, C₁-C₄ haloalkoxy, C₃-C₇ cycloalkyl C₀₋₆ alkyl, amino, C₁-C₄ alkylamino, di(C₁-C₄ alkyl)amino, C

$_1$ -C₄ alkylthio, C₁-C₄ alkylsulfonyl, R¹N(R²)C(=O)-, C₁-C₄ alkyl-SO₂-NH-, and nitro;

Ar² is 4-pyridyl which may be optionally substituted with 1 to 5 substituents independently selected from the group consisting of

(1) halogen, (2) C₁-C₄ alkyl-O_i-, (3) C₃-C₈ cycloalkyl-O_i-, (4) C₁-C₄ haloalkyl-O_i-, (5) hydroxy, (6) C₃-C₈ cycloalkyl-C₁-C₄ alkyl-O_i-, (7) C₁-C₄ alkylthio, (8) nitro, (9) R¹N(R²)-C₀₋₄ alkyl-O_i-, (10) cyano, (11) hydroxy C₁-C₄ alkyl-O_i-, (12) C₁-C₄ alkyl-O-C₁-C₄ alkyl-O_i-, (13) C₁-C₄ alkylsulfonyl, (14) R¹N(R²)-SO₂-C₀₋₄ alkyl-O_i-, (15) C₁-C₄ alkyl C(=O)-, (16) HO-C(=O)-, (17) C₁-C₄ alkyl-O-C(=O)-, (18) R¹N(R²)C(=O)-C₀₋₄ alkyl-O_i-, (19) C₁-C₄ alkyl-SO₂-NH-C₀₋₄ alkyl-O_i-, (20) R¹-O_i-C(=O)N(R²)-C₀₋₄ alkyl-O_k-, (21) NH₂(HN=)C-, (22) NH₂C(=O)NH-, (23) 5 to 10 membered aryl-O_i-C₀-C₄ alkyl-O_k-; wherein said aryl may be optionally substituted with 1 to 5 substituents independently selected from the group consisting of hydroxy, halogen, C₁-C₄ alkyl, C₁-C₄ alkoxy, hydroxy C₁-C₄ alkyl, amino C₁-C₄ alkyl, C₁-C₄ haloalkyl, C₁-C₄ haloalkoxy, C₃-C₇ cycloalkyl C₀₋₆ alkyl, amino, C₁-C₄ alkylamino, di(C₁-C₄ alkyl)amino, C₁-C₄ alkylthio, C₁-C₄ alkylsulfonyl, R¹N(R²)C(=O)-, C₁-C₄ alkyl-SO₂-NH-, and nitro; and (24) heterocyclic group-O_i-C₀-C₄ alkyl-O_k-; wherein said heterocyclic group may be optionally substituted with 1 to 5 substituents independently selected from the group consisting of hydroxy, halogen, C₁-C₄ alkyl, C₁-C₄ alkoxy, hydroxy C₁-C₄ alkyl, amino C₁-C₄ alkyl, C₁-C₄ haloalkyl, C₁-C₄ haloalkoxy, C₃-C₇ cycloalkyl C₀₋₆ alkyl, amino, C₁-C₄ alkylamino, di(C₁-C₄ alkyl)amino, C₁-C₄ alkylthio, C₁-C₄ alkylsulfonyl, R¹N(R²)C(=O)-, C₁-C₄ alkyl-SO₂-NH-, and nitro;

n is 1, 2, 3, or 4;

i is 0 or 1;

k is 0 or 1;

R¹ and R² are independently selected from the group consisting of:

(1) hydrogen, (2) C₁₋₆ alkyl, (3) hydroxy C₁-C₄ alkyl, (4) C₁-C₄ alkoxy C₁-C₄ alkyl, (5) amino C₁-C₄ alkyl, (6) C₁-C₄ haloalkyl, (7) C₁-C₄ haloalkoxy, (8) C₃₋₆ alkenyl, (9) C₃₋₈ cycloalkyl C₀₋₆ alkyl, (10) phenyl, which is unsubstituted or substituted with R³, and (11) 5 to 10 membered aryl C₀-C₄ alkyl; wherein said aryl may be optionally substituted with 1 to 5 substituents independently selected from the group consisting of hydroxy, halogen, C₁-C₄ alkyl, C₁-C₄ alkoxy, hydroxy C₁-C₄ alkyl, amino C₁-C₄ alkyl, C₁-C₄ haloalkyl, C₁-C₄ haloalkoxy, C₃-C₇

cycloalkyl C₀₋₆ alkyl, amino, C₁₋₄ alkylamino, di(C₁₋₄ alkyl)amino, C₁₋₄ alkylthio, and nitro;

or R¹ and R² taken together with the nitrogen atom to which they are attached form a 3 to 8 membered ring, where the ring may contain one to four heteroatom(s) independently selected from nitrogen, oxygen, and sulfur; where the ring may be saturated or partially saturated or unsaturated; and the ring is unsubstituted or substituted one or more substituents selected from R³;

R³ is selected from the group consisting of:

(1) hydroxy, (2) halogen, (3) C₁₋₆ alkyl, (4) -C₃₋₈ cycloalkyl, (5) -O-C₁₋₆ alkyl, (6) -O(C=O)-C₁₋₆ alkyl, (7) -NH-C₁₋₆ alkyl, (8) phenyl, (9) heterocyclic group, (10) -CO₂H, and (11) -CN;

X is -O-, -S-, -SO-, or -SO₂-;

or a prodrug thereof or a pharmaceutically acceptable salt thereof.

[Claim 6]

A compound which is selected from:

(4-(4-chlorophenoxy)piperidin-1-yl)(8-hydroxyquinolin-2-yl)methanone;

(4-(2-chlorophenoxy)piperidin-1-yl)(8-hydroxyquinolin-2-yl)methanone;

(4-(3-chlorophenoxy)piperidin-1-yl)(8-hydroxyquinolin-2-yl)methanone;

(8-hydroxyquinolin-2-yl)(4-(o-tolyloxy)piperidin-1-yl)methanone;

(8-hydroxyquinolin-2-yl)(4-(m-tolyloxy)piperidin-1-yl)methanone;

(8-hydroxyquinolin-2-yl)(4-(p-tolyloxy)piperidin-1-yl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(quinolin-2-yl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(4-hydroxyquinolin-2-yl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(quinolin-6-yl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(quinolin-3-yl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(isoquinolin-3-yl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(1,6-naphthyridin-2-yl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(isoquinolin-1-yl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(quinolin-4-yl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(6-(2,2,2-trifluoroethoxy)pyridin-3-yl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(6-methylpyridin-2-yl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(3,5-difluoropyridin-2-yl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(5-methylpyridin-3-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(quinoxalin-6-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(6-phenoxy-pyridin-3-yl)methanone;
;
(4-(4-chlorophenoxy)piperidin-1-yl)(quinolin-8-yl)methanone;
benzo[c]isoxazol-3-yl(4-(4-chlorophenoxy)piperidin-1-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(1-isopropyl-1H-benzo[d][1,2,3]triazol-5-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(5-fluoro-1H-indol-2-yl)methanone;
;
(4-(4-chlorophenoxy)piperidin-1-yl)(6-fluoro-1H-indol-2-yl)methanone;
;
(4-(4-chlorophenoxy)piperidin-1-yl)(5-isobutylisoxazol-3-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(2-methyl-5-phenylfuran-3-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(3-(2-methylthiazol-4-yl)phenyl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(5-methoxy-1H-indol-2-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(1H-indol-4-yl)methanone;
(3-(1H-pyrazol-1-yl)phenyl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone;
(4-(1H-1,2,4-triazol-1-yl)phenyl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(5-methyl-2-phenyl-2H-1,2,3-triazol-4-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(4,5-dichloroisothiazol-3-yl)methanone;
benzofuran-2-yl(4-(4-chlorophenoxy)piperidin-1-yl)methanone;
benzo[b]thiophen-2-yl(4-(4-chlorophenoxy)piperidin-1-yl)methanone;
(8-hydroxyquinolin-2-yl)(4-(2-methoxyphenoxy)piperidin-1-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(4-methyl-2-phenylpyrimidin-5-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(6-phenylpyrimidin-4-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(4-methoxyquinolin-2-yl)methanone

e;
(4-(4-chlorophenoxy)piperidin-1-yl)(quinoxalin-2-yl)methanone;
benzo[d]thiazol-6-yl(4-(4-chlorophenoxy)piperidin-1-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(1H-indol-3-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(1H-indol-2-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(1-methyl-1H-indol-3-yl)methanone;
e;
(4-(4-chlorophenoxy)piperidin-1-yl)(1-methyl-1H-indol-2-yl)methanone;
e;
(4-(4-chlorophenoxy)piperidin-1-yl)(2,3-dimethyl-1H-indol-5-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(1H-indol-6-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(2-methyl-1H-benzo[d]imidazol-5-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(imidazo[1,2-a]pyridin-2-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(2-methylimidazo[1,2-a]pyridin-3-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(5-methyl-1-phenyl-1H-pyrazol-4-yl)methanone;
(4-(tert-butyl)phenyl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(4-chlorophenyl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(4-fluorophenyl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(3-(5-fluoro-1H-benzo[d]imidazol-2-yl)phenyl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(3-(1-methyl-1H-benzo[d]imidazol-2-yl)phenyl)methanone;
(4-(2-fluorophenoxy)piperidin-1-yl)(8-hydroxyquinolin-2-yl)methanone;
e;
(4-(3-fluorophenoxy)piperidin-1-yl)(8-hydroxyquinolin-2-yl)methanone;
e;
(4-(4-fluorophenoxy)piperidin-1-yl)(8-hydroxyquinolin-2-yl)methanone;
e;
(8-hydroxyquinolin-2-yl)(4-(3-methoxyphenoxy)piperidin-1-yl)methanone;
2-((1-(8-hydroxyquinoline-2-carbonyl)piperidin-4-yl)oxy)benzonitrile;
4-((1-(8-hydroxyquinoline-2-carbonyl)piperidin-4-yl)oxy)benzonitrile;
3-((1-(8-hydroxyquinoline-2-carbonyl)piperidin-4-yl)oxy)benzonitrile;

(4-(4-chlorophenoxy)piperidin-1-yl)(8-methoxyquinolin-2-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(1-methyl-1H-indol-7-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(1-methyl-1H-indol-4-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(1,8-naphthyridin-2-yl)methanone;
(8-hydroxyquinolin-2-yl)(4-phenoxy piperidin-1-yl)methanone;
(8-hydroxyquinolin-2-yl)(4-(2-(trifluoromethyl)phenoxy)piperidin-1-yl)methanone;
(8-hydroxyquinolin-2-yl)(4-(3-(trifluoromethyl)phenoxy)piperidin-1-yl)methanone;
(5-(tert-butyl)isoxazol-3-yl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(5-phenylisoxazol-3-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(5-cyclopropylisoxazol-3-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(3,5-dimethylisoxazol-4-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(1-methyl-1H-indazol-3-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(2-methyl-2H-indazol-3-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(cinnolin-4-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(2-methyl-4-phenylpyrimidin-5-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(6-methylpyridin-3-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(pyridin-4-yl)methanone;
[1,2,4]triazolo[1,5-a]pyrimidin-2-yl(4-(4-chlorophenoxy)piperidin-1-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(1,2,3-trimethyl-1H-indol-5-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(1-methyl-1H-indol-6-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(2-methylthiazol-4-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(6-methoxypyridin-3-yl)methanone;
;
(4-(4-chlorophenoxy)piperidin-1-yl)(2-phenoxy pyridin-3-yl)methanone

;

(4-(4-chlorophenoxy)piperidin-1-yl)(1H-indol-7-yl)methanone;

7-(4-(4-chlorophenoxy)piperidine-1-carbonyl)indoline-2,3-dione;

(4-(4-chlorophenoxy)piperidin-1-yl)(3-methylpyridin-2-yl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(6-hydroxypyridin-2-yl)methanone

;

(4-(4-chlorophenoxy)piperidin-1-yl)(2,4-dimethylthiazol-5-yl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(5-methyl-1,3,4-oxadiazol-2-yl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(1H-indazol-3-yl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(4,5,6,7-tetrahydro-1H-indazol-3-yl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(6-methoxypyridin-2-yl)methanone

;

(4-(4-chlorophenoxy)piperidin-1-yl)(2-methyl-4,5,6,7-tetrahydro-2H-indazol-3-yl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(isoquinolin-4-yl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(4-methylpyridin-2-yl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(6-methoxyquinolin-2-yl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(6-methoxy-2-methylquinolin-3-yl)methanone;

(3-(4-chlorophenoxy)azetidin-1-yl)(8-hydroxyquinolin-2-yl)methanone

;

benzo[d]isoxazol-3-yl(4-(4-chlorophenoxy)piperidin-1-yl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(2-(trifluoromethyl)-1H-benzo[d]imidazol-5-yl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(1,5-naphthyridin-2-yl)methanone;

(3-(4-chlorophenoxy)pyrrolidin-1-yl)(8-hydroxyquinolin-2-yl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(2-methyl-6-phenylpyridin-3-yl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(1,5-dimethyl-1H-indol-3-yl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(5-fluoro-1-methyl-1H-indol-3-yl)methanone;

(5-chloro-1-methyl-1H-indol-3-yl)(4-(4-chlorophenoxy)piperidin-1-yl)

methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(5-methoxy-1-methyl-1H-indol-3-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(1,6-dimethyl-1H-indol-3-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(6-fluoro-1-methyl-1H-indol-3-yl)methanone;
(6-chloro-1-methyl-1H-indol-3-yl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(6-methoxy-1-methyl-1H-indol-3-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(5-fluoro-1-methyl-1H-indol-2-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(5-methoxy-1-methyl-1H-indol-2-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(3-fluorophenyl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(p-tolyl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(4-methoxyphenyl)methanone;
4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)benzonitrile;
(4-(4-chlorophenoxy)piperidin-1-yl)(6-methylimidazo[1,2-a]pyridin-2-yl)methanone;
(6-chloroimidazo[1,2-a]pyridin-2-yl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(2-methylpyridin-3-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(4-isopropoxyphenyl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(4-(trifluoromethoxy)phenyl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(4-(methylsulfonyl)phenyl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(3-methoxyphenyl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(pyridin-2-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(5-methylisoxazol-3-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(oxazol-4-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(4-methylthiazol-5-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(5-methylpyrazin-2-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(6-fluoro-1-methyl-1H-indol-2-yl)methanone;
4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-N,N-dimethylbenzenesulfonyl

lfonamide;
4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)benzamide;
(4-(4-chlorophenoxy)piperidin-1-yl)(5-fluoro-1H-indazol-3-yl)methanone;
(5-chloro-1H-indazol-3-yl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone;
(6-chloro-1H-indazol-3-yl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(4-(2-hydroxypropan-2-yl)phenyl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(2,6-dimethoxypyridin-3-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(6-methoxy-1-methyl-1H-indol-2-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(1-methyl-5-(trifluoromethoxy)-1H-indol-2-yl)methanone;
2-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-1-methyl-1H-indole-5-carbonitrile;
(4-(4-chlorophenoxy)piperidin-1-yl)(1-methyl-5-(methylsulfonyl)-1H-indol-2-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(4-methylpyridin-3-yl)methanone;
3-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-5,6-dimethylpyridin-2(1H)-one;
(4-(4-chlorophenoxy)piperidin-1-yl)(quinolin-5-yl)methanone;
(4-(4-fluorophenoxy)piperidin-1-yl)(2-methyl-2H-indazol-3-yl)methanone;
(4-(4-fluorophenoxy)piperidin-1-yl)(6-methoxypyridin-3-yl)methanone;
;
(4-(4-chlorophenoxy)piperidin-1-yl)(3-methoxy-4-methylphenyl)methanone;
(5-chloro-4-methoxythiophen-3-yl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone;
(4-phenoxy)piperidin-1-yl)(quinolin-8-yl)methanone;
(4-(4-fluorophenoxy)piperidin-1-yl)(imidazo[1,2-a]pyridin-2-yl)methanone;
(4-(4-fluorophenoxy)piperidin-1-yl)(quinolin-8-yl)methanone;
(6-aminopyridin-3-yl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone;
(5-bromopyridin-3-yl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone;

(5-bromopyridin-2-yl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone;
1-(4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)phenyl)ethanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(3,4-dimethoxyphenyl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(isoquinolin-5-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(phenyl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(m-tolyl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(2-methoxyphenyl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(3-(trifluoromethoxy)phenyl)methanone;
(1H-benzo[d]imidazol-5-yl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(1,5-dimethyl-1H-pyrazol-3-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(1,3-dimethyl-1H-pyrazol-5-yl)methanone;
(3-(tert-butyl)-1-methyl-1H-pyrazol-5-yl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(1-methyl-5-(trifluoromethyl)-1H-pyrazol-3-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(1-(4-methoxyphenyl)-5-methyl-1H-pyrazol-4-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(1-(2-methoxyphenyl)-1H-pyrazol-4-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(3,5-dimethyl-1H-pyrazol-4-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(1H-1,2,4-triazol-3-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(5-isopropyl-1H-pyrazol-3-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(imidazo[2,1-b]thiazol-6-yl)methanone;
(4-(3-methoxyphenoxy)piperidin-1-yl)(quinolin-8-yl)methanone;
imidazo[1,2-a]pyridin-2-yl(4-(3-methoxyphenoxy)piperidin-1-yl)methanone;
(4-(3-fluorophenoxy)piperidin-1-yl)(quinolin-8-yl)methanone;
(4-(3-fluorophenoxy)piperidin-1-yl)(imidazo[1,2-a]pyridin-2-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(5-chloropyridin-3-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(5-methoxypyridin-3-yl)methanone

;

3-(4-(4-chlorophenoxy)piperidine-1-carbonyl)benzonitrile;

(4-(4-chlorophenoxy)piperidin-1-yl)(2-ethoxypyridin-3-yl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(2-methoxypyridin-4-yl)methanone

;

(4-(4-chlorophenoxy)piperidin-1-yl)(isoquinolin-8-yl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(2-methylthiazol-5-yl)methanone;

(4-((4-chlorophenyl)thio)piperidin-1-yl)(quinolin-8-yl)methanone;

(4-((4-chlorophenyl)thio)piperidin-1-yl)(6-methylpyridin-3-yl)methanone;

(4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(quinolin-8-yl)methanone;

1-(3-((1-(quinoline-8-carbonyl)piperidin-4-yl)oxy)phenyl)ethanone;

(4-(3,5-dimethoxyphenoxy)piperidin-1-yl)(quinolin-8-yl)methanone;

quinolin-8-yl(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(3-methylisoxazol-5-yl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(1-isopropyl-1H-pyrazol-4-yl)methanone;

5-(4-(4-chlorophenoxy)piperidine-1-carbonyl)picolinonitrile;

(4-(4-chlorophenoxy)piperidin-1-yl)(2-hydroxyquinolin-4-yl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(5-(trifluoromethyl)-1H-pyrazol-3-yl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(5-cyclopropyl-1H-pyrazol-3-yl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(5-(2-methoxyphenyl)-1H-pyrazol-3-yl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(3-isopropyl-1-methyl-1H-pyrazol-5-yl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(3-ethyl-1-methyl-1H-pyrazol-5-yl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(1-ethyl-3-methyl-1H-pyrazol-5-yl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(2-methylloxazol-4-yl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(thieno[3,2-b]pyridin-2-yl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(imidazo[1,2-a]pyridin-6-yl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(1-methyl-1H-indazol-6-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(6-(trifluoromethoxy)-1H-indazol-3-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(1-methyl-6-(trifluoromethoxy)-1H-indazol-3-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(2,4-dimethyloxazol-5-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(5-methoxypyridin-2-yl)methanone;
 ;
 (4-(4-chlorophenoxy)piperidin-1-yl)(imidazo[1,2-a]pyridin-7-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(imidazo[1,2-a]pyrazin-2-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(2-methyl-2H-indazol-6-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(6-(pyrrolidin-1-yl)pyridin-2-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(5-(pyrrolidin-1-yl)pyridin-2-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(4-fluoro-3-methoxyphenyl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(4-methyl-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(6-(piperidin-1-yl)pyridin-3-yl)methanone;
 3-(4-(4-chlorophenoxy)piperidine-1-carbonyl)quinolin-2(1H)-one;
 (4-(4-chlorophenoxy)piperidin-1-yl)(imidazo[1,2-a]pyridin-8-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(pyrazolo[1,5-a]pyridin-7-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(4-(trifluoromethyl)pyridin-3-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(1-methyl-1H-imidazol-2-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(1-(2-(trifluoromethyl)phenyl)-1H-imidazol-2-yl)methanone;
 3-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-1-methylquinolin-4(1H)

-one;
 (3-(4-chlorophenoxy)azetidin-1-yl)(quinolin-8-yl)methanone;
 (3-(4-chlorophenoxy)azetidin-1-yl)(6-methylpyridin-3-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(pyrimidin-4-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(5-chloropyridin-2-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(2-methoxyquinolin-4-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(5-hydroxypyridin-3-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(6-(trifluoromethyl)pyridin-3-yl)methanone;
 (5-aminopyridin-3-yl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(imidazo[1,2-a]pyrimidin-2-yl)methanone;
 N-(5-(4-(4-chlorophenoxy)piperidine-1-carbonyl)pyridin-3-yl)acetamide;
 (4-(4-chlorophenoxy)piperidin-1-yl)(chroman-6-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(1-methyl-1H-pyrazolo[3,4-b]pyridin-3-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(1-methyl-1H-indol-5-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(3-(pyridin-2-yloxy)phenyl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(1-methyl-1H-benzo[d]imidazol-5-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(4-((tetrahydro-2H-pyran-4-yl)oxy)phenyl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(pyrazolo[1,5-a]pyridin-2-yl)methanone;
 1-(3-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-1H-pyrazol-5-yl)ethanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(1,3,5-trimethyl-1H-pyrazol-4-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(1H-pyrrolo[2,3-b]pyridin-2-yl)methanone;
 4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-1-methylquinolin-2(1H)-one;
 5-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-1H-benzo[d]imidazol-2(

3H)-one;
 (4-(4-chlorophenoxy)piperidin-1-yl)(5-methoxypyrazin-2-yl)methanone;
 5-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-1,3-dimethyl-1H-benzodimidazol-2(3H)-one;
 (4-(4-chlorophenoxy)piperidin-1-yl)(1-methyl-1H-imidazol-4-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(2-phenyl-1H-imidazol-4-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(1,3-dimethyl-1H-pyrazol-4-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(1,5-dimethyl-1H-pyrazol-4-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(3-isobutyl-1-methyl-1H-pyrazol-5-yl)methanone;
 (4-chloro-5-methyl-1H-pyrazol-3-yl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone;
 3-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-1-isopropyl-6,7-dihydro-1H-cyclopenta[b]pyridin-2(5H)-one;
 5-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-2-methoxybenzonitrile;
 (4-(4-chlorophenoxy)piperidin-1-yl)(2-isopropylthiazol-4-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(5,6-dimethoxy-1H-indol-2-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(2,7-dimethylpyrazolo[1,5-a]pyrimidin-6-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(1H-pyrrolo[2,3-b]pyridin-3-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(1-methyl-1H-pyrrolo[2,3-b]pyridin-2-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(5,6-dimethoxy-1-methyl-1H-indol-2-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(1-methyl-1H-pyrrolo[2,3-b]pyridin-3-yl)methanone;
 3-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-1-isopropyl-4-methylquinolin-2(1H)-one;
 (4-(4-chlorophenoxy)piperidin-1-yl)(4-methyl-4H-furo[3,2-b]pyrrol-5-yl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(4-methyl-4H-thieno[3,2-b]pyrrol-5-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(1,3-dimethyl-1H-thieno[2,3-c]pyrazol-5-yl)methanone;
 2-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-6,7-dihydropyrido[3,2,1-ij]quinolin-3(5H)-one;
 5-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-1H-pyrrolo[3,2,1-ij]quinolin-4(2H)-one;
 3-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-1-ethyl-7-methyl-1,8-naphthyridin-4(1H)-one;
 (4-(4-chlorophenoxy)piperidin-1-yl)(isoquinolin-6-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(5-methylpyridin-2-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(5-(2,2,2-trifluoroethoxy)pyridin-3-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(3-methylisoxazolo[5,4-b]pyridin-5-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(1,3,6-trimethyl-1H-pyrazolo[3,4-b]pyridin-4-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(thieno[2,3-b]pyridin-2-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(thieno[2,3-b]pyrazin-6-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(pyrazolo[1,5-a]pyrimidin-3-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(2-(pyrrolidin-1-yl)pyrimidin-5-yl)methanone;
 (1H-benzo[d]imidazol-4-yl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone;
 benzo[d][1,2,3]thiadiazol-7-yl(4-(4-chlorophenoxy)piperidin-1-yl)methanone;
 3-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-1-methylquinolin-2(1H)-one;
 (4-(4-chlorophenoxy)piperidin-1-yl)(1-methyl-1H-benzo[d]imidazol-2-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(pyrazolo[1,5-a]pyrimidin-2-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(2-methoxypyrimidin-5-yl)methanone;

(1H-benzo[d][1,2,3]triazol-4-yl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(6-methylimidazo[2,1-b]thiazol-5-yl)methanone;

benzo[c][1,2,5]thiadiazol-4-yl(4-(4-chlorophenoxy)piperidin-1-yl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(1-(2-methoxyethyl)-1H-indol-5-yl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(1-(2-methoxyethyl)-1H-indol-6-yl)methanone;

(3-amino-1-methyl-1H-pyrazol-5-yl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(5-cyclopropyl-1-methyl-1H-pyrazol-3-yl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(3-cyclopropyl-1-methyl-1H-pyrazol-5-yl)methanone;

1-benzyl-3-(4-(4-chlorophenoxy)piperidine-1-carbonyl)pyridin-2(1H)-one;

(1-benzyl-1H-pyrazol-4-yl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(1-(2-methoxyethyl)-1H-indol-2-yl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(1-(2-methoxyethyl)-1H-indol-4-yl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(3,6-dimethylisoxazolo[5,4-b]pyridin-4-yl)methanone;

4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-1-methylpyridin-2(1H)-one;

3-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-4H-pyrido[1,2-a]pyrimidin-4-one;

3-(4-(4-chlorophenoxy)piperidine-1-carbonyl)isoquinolin-1(2H)-one;

(4-(4-chlorophenoxy)piperidin-1-yl)(2-(3,5-dimethyl-1H-pyrazol-4-yl)phenyl)methanone;

benzo[c][1,2,5]oxadiazol-5-yl(4-(4-chlorophenoxy)piperidin-1-yl)methanone;

(6-aminopyridin-2-yl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone;

3-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-1,6-dimethylpyridin-2(1H)-one;

(4-(4-chlorophenoxy)piperidin-1-yl)(3-propoxypyridin-2-yl)methanone
 ;
 (4-(4-chlorophenoxy)piperidin-1-yl)(6-((tetrahydro-2H-pyran-4-yl)oxy)
 pyridin-3-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(6-((tetrahydro-2H-pyran-4-yl)oxy)
 pyridin-2-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(5-((tetrahydro-2H-pyran-4-yl)oxy)
 pyridin-3-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(3-hydroxy-4-methoxyphenyl)meth
 anone;
 (4-chloro-2-hydroxyphenyl)(4-(4-chlorophenoxy)piperidin-1-yl)methan
 one;
 (4-(4-chlorophenoxy)piperidin-1-yl)(4-hydroxy-3-methylphenyl)metha
 none;
 (4-(4-chlorophenoxy)piperidin-1-yl)(6-morpholinopyridin-2-yl)methan
 one;
 (4-(4-chlorophenoxy)piperidin-1-yl)(2-morpholinopyridin-4-yl)methan
 one;
 (4-(4-chlorophenoxy)piperidin-1-yl)(1-methyl-3-(trifluoromethyl)-1H-
 pyrazol-5-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(2-hydroxy-4-(trifluoromethyl)phe
 nyl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(3-hydroxy-4-methylphenyl)metha
 none;
 tert-butyl
 ((2-(4-(4-chlorophenoxy)piperidine-1-carbonyl)pyridin-4-yl)methyl)car
 bamate;
 (4-(aminomethyl)pyridin-2-yl)(4-(4-chlorophenoxy)piperidin-1-yl)met
 hanone;
 N-((2-(4-(4-chlorophenoxy)piperidine-1-carbonyl)pyridin-4-yl)methyl)
 pivalamide;
 N-((2-(4-(4-chlorophenoxy)piperidine-1-carbonyl)pyridin-4-yl)methyl)
 -4-fluorobenzamide;
 N-((2-(4-(4-chlorophenoxy)piperidine-1-carbonyl)pyridin-4-yl)methyl)
 -4-fluorobenzenesulfonamide;
 tert-butyl
 2-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-7,8-dihydro-1,6-naphthy
 ridine-6(5H)-carboxylate;

(4-(4-chlorophenoxy)piperidin-1-yl)(6-(methylsulfonyl)-5,6,7,8-tetrahydro-1,6-naphthyridin-2-yl)methanone;
N-(tert-butyl)-4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)benzamide;
;
N-(tert-butyl)-4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-N-methyl benzamide;
4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-N-(2,2,2-trifluoroethyl)benzamide;
(4-(4-chlorophenoxy)piperidin-1-yl)(4-(2-methoxyethoxy)phenyl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(4-(2-hydroxyethoxy)phenyl)methanone;
N-(4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)benzyl)pivalamide;
4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)picolinamide;
(4-(4-chlorophenoxy)piperidin-1-yl)(5-morpholinopyridin-3-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(6-(piperidin-1-yl)pyrimidin-4-yl)methanone;
(3-(1H-imidazol-1-yl)phenyl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone;
(2-(1H-pyrazol-1-yl)phenyl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(2-(2-methyl-1H-imidazol-1-yl)phenyl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(2-(3-methyl-1,2,4-oxadiazol-5-yl)phenyl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(3-methyl-1H-pyrazol-5-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(6-(piperidine-1-carbonyl)pyridin-2-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(2-hydroxy-4-methoxyphenyl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(4-hydroxy-3-methoxyphenyl)methanone;
N-(5-chloro-2-(4-(4-chlorophenoxy)piperidine-1-carbonyl)phenyl)methanesulfonamide;
N-(4-chloro-2-(4-(4-chlorophenoxy)piperidine-1-carbonyl)phenyl)methanesulfonamide;

(4-(4-chlorophenoxy)piperidin-1-yl)(2'-(hydroxymethyl)-[1,1'-biphenyl]-4-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(2'-(methylsulfonyl)-[1,1'-biphenyl]-4-yl)methanone;
(3-chloro-4-hydroxyphenyl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone;
3-(tert-butyl)-5-(4-(4-chlorophenoxy)piperidine-1-carbonyl)benzamide;
3-(tert-butyl)-5-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-N,N-dimethylbenzamide;
(3-(tert-butyl)-5-(4-(4-chlorophenoxy)piperidine-1-carbonyl)phenyl)(morpholino)methanone;
4'-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-[1,1'-biphenyl]-3-carboxamide;
(4-(4-chlorophenoxy)piperidin-1-yl)(1-(2-morpholinoethyl)-1H-indol-5-yl)methanone;
2-(5-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-1H-indol-1-yl)-N,N-dimethylacetamide;
(4-(4-chlorophenoxy)piperidin-1-yl)(1-(2-hydroxyethyl)-1H-indol-5-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(4-morpholinopyridin-2-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(4-(piperidin-1-yl)pyridin-2-yl)methanone;
2-(3-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-1H-indol-1-yl)-N,N-dimethylacetamide;
(4-(4-chlorophenoxy)piperidin-1-yl)(1-(2-hydroxyethyl)-1H-indol-3-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(1-(2-morpholinoethyl)-1H-indol-3-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(1-(2-(piperidin-1-yl)ethyl)-1H-indol-3-yl)methanone;
2-(4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)phenyl)-2-methylpropanenitrile;
(4-(4-chlorophenoxy)piperidin-1-yl)(3-fluoro-4-hydroxyphenyl)methanone;
2-chloro-5-(4-(4-chlorophenoxy)piperidine-1-carbonyl)benzenesulfonamide;
4'-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-[1,1'-biphenyl]-4-carbo

xamide;

4'-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-[1,1'-biphenyl]-2-carboxamide;

(5-chloro-2-hydroxyphenyl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(2-hydroxy-4-methylphenyl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(5-fluoro-2-hydroxyphenyl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(2-hydroxy-3-methylphenyl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(2-hydroxy-3-isopropylphenyl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(2-hydroxy-6-methoxyphenyl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(2-fluoro-6-hydroxyphenyl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(3-hydroxy-2-methylphenyl)methanone;

(2-chloro-4-hydroxyphenyl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(2-fluoro-4-hydroxyphenyl)methanone;

N-(4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-2-methylphenyl)methanesulfonamide;

(4-(4-chlorophenoxy)piperidin-1-yl)(4-fluoro-3-hydroxyphenyl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(2-hydroxy-5-methylphenyl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(2-hydroxy-3-methoxyphenyl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(4-fluoro-2-hydroxyphenyl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(3,5-dihydroxyphenyl)methanone;

N-(3-(4-(4-chlorophenoxy)piperidine-1-carbonyl)phenyl)acetamide;

(4-(4-chlorophenoxy)piperidin-1-yl)(1-((4-hydroxytetrahydro-2H-pyran-4-yl)methyl)-1H-indol-5-yl)methanone;

(1-(2-aminoethyl)-1H-indol-5-yl)(4-(4-chlorophenoxy)piperidin-1-yl)m

ethanone;

N-(2-(5-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-1H-indol-1-yl)ethyl)acetamide;

N-(2-(5-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-1H-indol-1-yl)ethyl)methanesulfonamide;

2-(5-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-1H-indol-1-yl)-1-morpholinoethanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(3'-(methylsulfonyl)-[1,1'-biphenyl]-4-yl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(3'-(hydroxymethyl)-[1,1'-biphenyl]-4-yl)methanone;

N-(4'-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-[1,1'-biphenyl]-2-yl)methanesulfonamide;

N-(4'-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-[1,1'-biphenyl]-3-yl)methanesulfonamide;

4'-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-N-methyl-[1,1'-biphenyl]-3-carboxamide;

4'-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-N,N-dimethyl-[1,1'-biphenyl]-3-carboxamide;

(4-(4-chlorophenoxy)piperidin-1-yl)(3'-(morpholine-4-carbonyl)-[1,1'-biphenyl]-4-yl)methanone;

(4-chloro-3-hydroxyphenyl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone;

N-(5-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-2-methylphenyl)methanesulfonamide;

1-(3-(4-(4-chlorophenoxy)piperidine-1-carbonyl)phenyl)ethanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(1-(2-hydroxyethyl)-2-methyl-1H-benzo[d]imidazol-5-yl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(6-ethoxypyridin-2-yl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(4-hydroxy-7-methyl-1,8-naphthyridin-3-yl)methanone;

N-(6-(4-(4-chlorophenoxy)piperidine-1-carbonyl)pyridin-2-yl)acetamide;

N-(4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)pyridin-2-yl)acetamide;

N-(5-(4-(4-chlorophenoxy)piperidine-1-carbonyl)pyridin-2-yl)acetamide;

(4-(4-chlorophenoxy)piperidin-1-yl)(3-hydroxypyridin-2-yl)methanone

;

(4-bromo-1-methoxynaphthalen-2-yl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone;

6-(4-(4-chlorophenoxy)piperidine-1-carbonyl)isoindolin-1-one;

(4-(4-chlorophenoxy)piperidin-1-yl)(quinoxalin-5-yl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(1,6-naphthyridin-5-yl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(4-hydroxyphenyl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(4-ethoxy-2-hydroxyphenyl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(3-hydroxyphenyl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(2-hydroxyphenyl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(4-hydroxy-3,5-dimethoxyphenyl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(4-hydroxy-2-methylphenyl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(5-hydroxy-2-methylphenyl)methanone;

(3-chloro-2-hydroxyphenyl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(3-fluoro-2-hydroxyphenyl)methanone;

2-(5-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-2-methylphenoxy)acetamide;

2-(2-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-5-methylphenoxy)acetamide;

(4-(4-chlorophenoxy)piperidin-1-yl)(2,6-dihydroxyphenyl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(2-fluoro-3-hydroxyphenyl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(2-fluoro-5-hydroxyphenyl)methanone;

(2-chloro-5-hydroxyphenyl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone;

(3-(tert-butyl)-1-methyl-1H-pyrazol-5-yl)(4-(4-fluorophenoxy)piperidin-1-yl)methanone;

(4-fluoro-3-methoxyphenyl)(4-(4-fluorophenoxy)piperidin-1-yl)methanone;

(4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(2-methyl-2H-indazol-3-yl)methanone;

(4-(4-fluorophenoxy)piperidin-1-yl)(4-fluorophenyl)methanone;
(5-(tert-butyl)isoxazol-3-yl)(4-(4-fluorophenoxy)piperidin-1-yl)methanone;
(4-(4-fluorophenoxy)piperidin-1-yl)(1-methyl-5-(trifluoromethyl)-1H-pyrazol-3-yl)methanone;
(4-(4-fluorophenoxy)piperidin-1-yl)(1-methyl-1H-indazol-3-yl)methanone;
(4-(4-fluorophenoxy)piperidin-1-yl)(quinoxalin-2-yl)methanone;
(4-(4-fluorophenoxy)piperidin-1-yl)(4-methoxyquinolin-2-yl)methanone;
(4-(4-fluorophenoxy)piperidin-1-yl)(6-methoxyquinolin-2-yl)methanone;
(4-(4-fluorophenoxy)piperidin-1-yl)(isoquinolin-1-yl)methanone;
(4-(4-fluorophenoxy)piperidin-1-yl)(isoquinolin-4-yl)methanone;
(4-(4-fluorophenoxy)piperidin-1-yl)(quinolin-4-yl)methanone;
(5-aminopyridin-2-yl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone;
(6-(tert-butyl)pyridin-3-yl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone;
(6-(tert-butyl)pyridin-3-yl)(4-(4-fluorophenoxy)piperidin-1-yl)methanone;
N-(6-(4-(4-chlorophenoxy)piperidine-1-carbonyl)pyridin-3-yl)acetamide;
(6-methylpyridin-3-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
(1,3-dimethyl-1H-pyrazol-5-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
(3,5-dimethylisoxazol-4-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
(6-hydroxypyridin-2-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
(3-methylpyridin-2-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
(5-methoxypyridin-3-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
(5-aminopyridin-3-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
(6-methoxypyridin-3-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;

4-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)picolinamide
 ;
 (3-methylisoxazol-5-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)
)methanone;
 (2-methylthiazol-5-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)
 methanone;
 (1-methyl-1H-imidazol-4-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidi
 n-1-yl)methanone;
 (2-hydroxy-6-methoxyphenyl)(4-(3-(trifluoromethoxy)phenoxy)piperid
 in-1-yl)methanone;
 (2,4-dimethylthiazol-5-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1
 -yl)methanone;
 (2-methyl-2H-indazol-3-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-
 1-yl)methanone;
 (2-methyl-2H-indazol-6-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-
 1-yl)methanone;
 imidazo[1,2-a]pyridin-8-yl(4-(3-(trifluoromethoxy)phenoxy)piperidin-1
 -yl)methanone;
 (1,8-naphthyridin-2-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)
 methanone;
 (1,5-naphthyridin-2-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)
 methanone;
 (2-hydroxyquinolin-4-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-
 yl)methanone;
 1,6-dimethyl-3-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl
)pyridin-2(1H)-one;
 benzo[d]thiazol-6-yl(4-(4-fluorophenoxy)piperidin-1-yl)methanone;
 (4-(4-fluorophenoxy)piperidin-1-yl)(2-methyl-1H-benzo[d]imidazol-5-
 yl)methanone;
 (4-(4-fluorophenoxy)piperidin-1-yl)(1-methyl-1H-benzo[d]imidazol-5-
 yl)methanone;
 (4-(4-fluorophenoxy)piperidin-1-yl)(5-methoxypyridin-2-yl)methanone
 ;
 (4-(4-fluorophenoxy)piperidin-1-yl)(4-methyl-2-phenylpyrimidin-5-yl)
 methanone;
 (4-(4-fluorophenoxy)piperidin-1-yl)(1-methyl-1H-benzo[d]imidazol-2-
 yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(6-ethoxypyridin-3-yl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(6-(dimethylamino)pyridin-3-yl)methanone;
 (4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(quinolin-2-yl)methanone;
 (4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(quinolin-3-yl)methanone;
 (4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(5-methyl-1-phenyl-1H-pyrazol-4-yl)methanone;
 (4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(4-methoxyquinolin-2-yl)methanone;
 (4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(6-ethoxypyridin-2-yl)methanone;
 (6-methoxypyridin-2-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
 (5-methoxypyrazin-2-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
 (2-hydroxy-3-methoxyphenyl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
 (2-methyloxazol-4-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
 (4-(2-hydroxypropan-2-yl)phenyl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
 (6-ethoxypyridin-2-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
 (1H-benzo[d]imidazol-6-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
 imidazo[1,2-a]pyrazin-2-yl(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
 (4-hydroxy-7-methyl-1,8-naphthyridin-3-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
 N-(4-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)pyridin-2-yl)acetamide;
 N-(6-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)pyridin-2-yl)acetamide;
 (4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(p-tolyl)methanone;
 (4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(4-methoxyphenyl)methanone;
 (4-chlorophenyl)(4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)methanone;
 (4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(1,5-naphthyridin-2-yl)met

hanone;

(4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(6-methoxy-1-methyl-1H-indol-2-yl)methanone;

quinolin-8-yl(4-((3-(trifluoromethyl)phenyl)sulfonyl)piperidin-1-yl)methanone;

quinolin-8-yl(4-tosylpiperidin-1-yl)methanone;

(4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(isoquinolin-3-yl)methanone;

4-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)benzamide;

3-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)benzamide;

3-(4-(4-chlorophenoxy)piperidine-1-carbonyl)benzamide;

3-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-N-methylbenzamide;

4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-N-methylbenzamide;

(4-hydroxyquinolin-2-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;

(3-hydroxyquinoxalin-2-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;

(6-(hydroxymethyl)pyridin-2-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;

(1-(2-hydroxyethyl)-2-methyl-1H-benzo[d]imidazol-5-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;

(2-hydroxy-6-methylpyridin-4-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;

1-methyl-4-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)pyridin-2(1H)-one;

(2-hydroxy-6-methylpyridin-3-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;

3-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)quinolin-2(1H)-one;

(1H-1,2,4-triazol-3-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;

2-cyclopropyl-6-methyl-5-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)pyrimidin-4(1H)-one;

5,6-dimethyl-3-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)pyridin-2(1H)-one;

(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)(1,3,6-trimethyl-1H-pyrazolo[3,4-b]pyridin-4-yl)methanone;

4-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)-1H-benzo[d]

imidazol-2(3H)-one;
 (4-(4-chloro-2-methoxyphenoxy)piperidin-1-yl)(quinolin-8-yl)methanone;
 1-(5-chloro-2-((1-(quinoline-8-carbonyl)piperidin-4-yl)oxy)phenyl)ethanone;
 5-chloro-2-((1-(quinoline-8-carbonyl)piperidin-4-yl)oxy)benzonitrile;
 (4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(quinoxalin-2-yl)methanone;
 (4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(6-methoxyquinolin-2-yl)methanone;
 (4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(4-methyl-2-phenylpyrimidin-5-yl)methanone;
 (4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(6-(pyrrolidin-1-yl)pyridin-2-yl)methanone;
 (5-(tert-butyl)isoxazol-3-yl)(4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)methanone;
 (4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(6-(2,2,2-trifluoroethoxy)pyridin-3-yl)methanone;
 (4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(1-methyl-1H-indol-5-yl)methanone;
 (4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(1-methyl-1H-indol-2-yl)methanone;
 (4-(3-fluorophenoxy)piperidin-1-yl)(4-fluorophenyl)methanone;
 (4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(1-methyl-1H-indol-6-yl)methanone;
 3-(4-(3-(trifluoromethyl)phenoxy)piperidine-1-carbonyl)benzamide;
 4-(4-(3-(trifluoromethyl)phenoxy)piperidine-1-carbonyl)benzamide;
 4-(4-(3-(trifluoromethyl)phenoxy)piperidine-1-carbonyl)picolinamide;
 (4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(2-methoxyquinolin-4-yl)methanone;
 (4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(6-phenoxy-pyridin-3-yl)methanone;
 3-(4-((4-chlorophenyl)sulfonyl)piperidine-1-carbonyl)quinolin-2(1H)-one;
 3-(4-((4-chlorophenyl)sulfonyl)piperidine-1-carbonyl)-1-methylquinolin-2(1H)-one;
 (4-(4-fluorophenoxy)piperidin-1-yl)(5-methyl-1-phenyl-1H-pyrazol-4-yl)methanone;

4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-N-(2-methoxyethyl)-N-methylbenzamide;
 4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-N-(2-methoxyethyl)benzamide;
 4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-N-(1-((1-hydroxycyclohexyl)methyl)piperidin-4-yl)benzamide;
 (S)-4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-N-(2-hydroxy-1-phenylethyl)benzamide;
 (S)-4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-N-(2-hydroxy-2-phenylethyl)benzamide;
 (S)-4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-N-(1-hydroxy-3-phenylpropan-2-yl)benzamide;
 (S)-N-(1-amino-1-oxo-3-phenylpropan-2-yl)-4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)benzamide;
 (4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(1-methyl-1H-indol-4-yl)methanone;
 4-(4-((4-chlorophenyl)thio)piperidine-1-carbonyl)picolinamide;
 6-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)picolinamide;
 ;
 4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-N-(2-oxo-2-phenylethyl)benzamide;
 (2-(methylsulfonyl)phenyl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
 (3-(methylsulfonyl)phenyl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
 (4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(5-fluoro-1-methyl-1H-indol-2-yl)methanone;
 (4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(6-fluoro-1-methyl-1H-indol-2-yl)methanone;
 (4-(3-ethoxyphenoxy)piperidin-1-yl)(quinolin-8-yl)methanone;
 (4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(3-(2-methylthiazol-4-yl)phenyl)methanone;
 N-methyl-3-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)benzamide;
 3-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)benzenesulfonamide;
 4-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)benzenesulfonamide;

(4-(4-fluorophenoxy)piperidin-1-yl)(1,5-naphthyridin-2-yl)methanone;
 (4-(4-fluorophenoxy)piperidin-1-yl)(quinolin-2-yl)methanone;
 (4-(3-fluorophenoxy)piperidin-1-yl)(4-methoxyquinolin-2-yl)methanone;
 (1H-benzo[d][1,2,3]triazol-7-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
 2-(2-(4-(4-chlorophenoxy)piperidine-1-carbonyl)phenoxy)acetamide;
 2-(4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)phenoxy)acetamide;
 2-(2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenoxy)acetamide;
 2-(3-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenoxy)acetamide;
 2-(4-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenoxy)acetamide;
 (8-hydroxyquinolin-2-yl)(4-((3-(trifluoromethoxy)phenyl)sulfonyl)piperidin-1-yl)methanone;
 quinolin-8-yl(4-((3-(trifluoromethoxy)phenyl)sulfonyl)piperidin-1-yl)methanone;
 quinolin-2-yl(4-((3-(trifluoromethoxy)phenyl)sulfonyl)piperidin-1-yl)methanone;
 (4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(5-phenylisoxazol-3-yl)methanone;
 (6-methoxyquinolin-2-yl)(4-((3-(trifluoromethoxy)phenyl)sulfonyl)piperidin-1-yl)methanone;
 (5-methyl-2-phenyl-2H-1,2,3-triazol-4-yl)(4-((3-(trifluoromethoxy)phenyl)sulfonyl)piperidin-1-yl)methanone;
 (5-fluoro-1-methyl-1H-indol-2-yl)(4-((3-(trifluoromethoxy)phenyl)sulfonyl)piperidin-1-yl)methanone;
 (6-fluoro-1-methyl-1H-indol-2-yl)(4-((3-(trifluoromethoxy)phenyl)sulfonyl)piperidin-1-yl)methanone;
 (4-hydroxyquinolin-8-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
 (1,8-naphthyridin-4-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
 (1,6-naphthyridin-8-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
 [1,2,4]triazolo[1,5-a]pyrimidin-2-yl(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;

(5-methyl-1H-pyrazol-3-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
 2-chloro-5-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)benzenesulfonamide;
 (S)-3-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-N-(2-hydroxy-2-phenylethyl)benzamide;
 (S)-3-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-N-(2-hydroxy-1-phenylethyl)benzamide;
 (S)-3-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-N-(1-hydroxy-3-phenylpropan-2-yl)benzamide;
 (S)-N-(1-amino-1-oxo-3-phenylpropan-2-yl)-3-(4-(4-chlorophenoxy)piperidine-1-carbonyl)benzamide;
 (4-((3-ethoxyphenyl)sulfonyl)piperidin-1-yl)(8-hydroxyquinolin-2-yl)methanone;
 (4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(4-methyl-2-phenylthiazol-5-yl)methanone;
 (4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(2-phenylthiazol-4-yl)methanone;
 (4-chloro-2-(methylsulfonyl)phenyl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
 (5-fluoro-2-(methylsulfonyl)phenyl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
 N,N-dimethyl-4-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)benzenesulfonamide;
 N-(2-(4-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenoxy)ethyl)acetamide;
 (2-phenyl-1H-imidazol-5-yl)(4-((3-(trifluoromethoxy)phenyl)sulfonyl)piperidin-1-yl)methanone;
 (3-(2-methylthiazol-4-yl)phenyl)(4-((3-(trifluoromethoxy)phenyl)sulfonyl)piperidin-1-yl)methanone;
 N-(4-(4-(3-ethoxyphenoxy)piperidine-1-carbonyl)pyridin-2-yl)acetamide;
 (4-(3-ethoxyphenoxy)piperidin-1-yl)(2-(methylsulfonyl)phenyl)methanone;
 3-(4-(3-ethoxyphenoxy)piperidine-1-carbonyl)benzenesulfonamide;
 N-(6-(4-(3-ethoxyphenoxy)piperidine-1-carbonyl)pyridin-2-yl)acetamide;
 (4-(3-ethoxyphenoxy)piperidin-1-yl)(2-methyl-2H-indazol-3-yl)methanone

one;

(4-(3-ethoxyphenoxy)piperidin-1-yl)(1,5-naphthyridin-2-yl)methanone;
(8-hydroxyquinolin-2-yl)(4-((4-(trifluoromethoxy)phenyl)sulfonyl)piperidin-1-yl)methanone;

quinolin-8-yl(4-((4-(trifluoromethoxy)phenyl)sulfonyl)piperidin-1-yl)methanone;

quinolin-2-yl(4-((4-(trifluoromethoxy)phenyl)sulfonyl)piperidin-1-yl)methanone;

N-(3-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenyl)methanesulfonamide;

(2-(ethylsulfonyl)phenyl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;

(3-fluoro-4-(methylsulfonyl)phenyl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;

ethyl

(4-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)pyridin-2-yl)carbamate;

2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)thiazole-4-carboxamide;

N,N-dimethyl-2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)benzenesulfonamide;

(4-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenyl)methanesulfonamide;

4-methoxy-3-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)benzenesulfonamide;

2-((2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)pyridin-3-yl)oxy)acetamide;

(4-(aminomethyl)pyridin-2-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;

N-((2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)pyridin-4-yl)methyl)methanesulfonamide;

ethyl

((2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)pyridin-4-yl)methyl)carbamate;

N-(2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)benzyl)acetamide;

N-(2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)benzyl)methanesulfonamide;

ethyl

2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)benzylcarbamate;

(2-(methylsulfonyl)phenyl)(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidin-1-yl)methanone;

N-(4-(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidine-1-carbonyl)pyridin-2-yl)acetamide;

4-(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidine-1-carbonyl)picolinamide;

3-(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidine-1-carbonyl)benzamide;

3-(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidine-1-carbonyl)benzenesulfonamide;

2-(2-(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidine-1-carbonyl)phenoxy)acetamide;

quinolin-8-yl(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidin-1-yl)methanone;

(1,5-naphthyridin-2-yl)(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidin-1-yl)methanone;

(2-methyl-2H-indazol-3-yl)(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidin-1-yl)methanone;

(1,3-dimethyl-1H-pyrazol-5-yl)(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidin-1-yl)methanone;

N-(6-(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidine-1-carbonyl)pyridin-2-yl)acetamide;

4-(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidine-1-carbonyl)benzamide;

(3,5-dimethylisoxazol-4-yl)(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidin-1-yl)methanone;

(3-(methylsulfonyl)phenyl)(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidin-1-yl)methanone;

(1,6-naphthyridin-8-yl)(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidin-1-yl)methanone;

(3-methyl-1H-pyrazol-5-yl)(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidin-1-yl)methanone;

2-(3-(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidine-1-carbonyl)phenoxy)acetamide;

(5-((tetrahydro-2H-pyran-4-yl)oxy)pyridin-3-yl)(4-(3-(trifluoromethox

y)phenoxy)piperidin-1-yl)methanone;
 1-(3-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenyl)ur
 ea;
 1-(4-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenyl)ur
 ea;
 (1H-1,2,4-triazol-3-yl)(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidin-1
 -yl)methanone;
 (4-(3-ethoxyphenoxy)piperidin-1-yl)(3-(methylsulfonyl)phenyl)methan
 one;
 (4-(3-ethoxyphenoxy)piperidin-1-yl)(3-methyl-1H-pyrazol-5-yl)methan
 one;
 N,N-dimethyl-3-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbony
 l)benzenesulfonamide;
 N-(2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenyl)m
 ethanesulfonamide;
 (6-aminopyridin-2-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)
 methanone;
 2-(methyl(3-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)be
 nzyl)amino)acetamide;
 2-(methyl(4-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)be
 nzyl)amino)acetamide;
 N,N-dimethyl-2-(2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carb
 onyl)phenoxy)acetamide;
 (1,3-dimethyl-1H-pyrazol-5-yl)(4-(3-(trifluoromethyl)phenoxy)piperidi
 n-1-yl)methanone;
 (2-(methylsulfonyl)phenyl)(4-(3-(trifluoromethyl)phenoxy)piperidin-1-
 yl)methanone;
 N-(6-(4-(3-(trifluoromethyl)phenoxy)piperidine-1-carbonyl)pyridin-2-y
 l)acetamide;
 3-(4-(3-(trifluoromethyl)phenoxy)piperidine-1-carbonyl)benzenesulfon
 amide;
 (3,5-dimethylisoxazol-4-yl)(4-(3-(trifluoromethyl)phenoxy)piperidin-1-
 yl)methanone;
 (1,6-naphthyridin-8-yl)(4-(3-(trifluoromethyl)phenoxy)piperidin-1-yl)
 methanone;
 (3-methyl-1H-pyrazol-5-yl)(4-(3-(trifluoromethyl)phenoxy)piperidin-1-
 yl)methanone;
 2-(2-(4-(3-(trifluoromethyl)phenoxy)piperidine-1-carbonyl)phenoxy)ac

etamide;

2-(4-(4-(3-(trifluoromethyl)phenoxy)piperidine-1-carbonyl)phenoxy)acetamide;

2-(3-(4-(3-(trifluoromethyl)phenoxy)piperidine-1-carbonyl)phenoxy)acetamide;

(1H-1,2,4-triazol-3-yl)(4-(3-(trifluoromethyl)phenoxy)piperidin-1-yl)methanone;

N-(2-(2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenoxy)ethyl)acetamide;

N-(2-(2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenoxy)ethyl)methanesulfonamide;

ethyl

(2-(2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenoxy)ethyl)carbamate;

N-(2-(2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenoxy)ethyl)cyclopropane-1,1-dicarboxamide;

(3-(2-aminoethoxy)phenyl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;

N-(2-(3-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenoxy)ethyl)acetamide;

N-(2-(3-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenoxy)ethyl)methanesulfonamide;

ethyl

(2-(3-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenoxy)ethyl)carbamate;

N-(2-(3-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenoxy)ethyl)cyclopropane-1,1-dicarboxamide;

N-(3-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)pyridin-2-yl)acetamide;

N-(1-methyl-5-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)-1H-pyrazol-3-yl)acetamide;

(2-(ethylsulfonyl)phenyl)(4-(3-(trifluoromethyl)phenoxy)piperidin-1-yl)methanone;

(4-(3-ethoxyphenoxy)piperidin-1-yl)(2-(ethylsulfonyl)phenyl)methanone;

(2-(ethylsulfonyl)phenyl)(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidin-1-yl)methanone;

N-(2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)pyridin-3

-yl)acetamide;
 2-(4-(4-(3-chlorophenoxy)piperidine-1-carbonyl)phenoxy)acetamide;
 2-(2-(4-((4-chlorophenyl)thio)piperidine-1-carbonyl)phenoxy)acetamide;
 2-(3-(4-((4-chlorophenyl)thio)piperidine-1-carbonyl)phenoxy)acetamide;
 (4-((4-chlorophenyl)thio)piperidin-1-yl)(2-(methylsulfonyl)phenyl)methanone;
 2-(methyl(2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)benzyl)amino)acetamide;
 1-morpholino-2-(2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenoxy)ethanone;
 1-(piperidin-1-yl)-2-(2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenoxy)ethanone;
 (2-(2-methoxyethoxy)phenyl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
 (3-(methylsulfonyl)phenyl)(4-(3-(trifluoromethyl)phenoxy)piperidin-1-yl)methanone;
 (4-(3-chlorophenoxy)piperidin-1-yl)(3-(methylsulfonyl)phenyl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(3-(methylsulfonyl)phenyl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(2-(ethylsulfonyl)phenyl)methanone;
 N,N-dimethyl-3-(4-(3-(trifluoromethyl)phenoxy)piperidine-1-carbonyl)benzenesulfonamide;
 3-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-N,N-dimethylbenzenesulfonamide;
 N,N-dimethyl-3-(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidine-1-carbonyl)benzenesulfonamide;
 N,N-dimethyl-2-(4-(3-(trifluoromethyl)phenoxy)piperidine-1-carbonyl)benzenesulfonamide;
 2-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-N,N-dimethylbenzenesulfonamide;
 N,N-dimethyl-2-(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidine-1-carbonyl)benzenesulfonamide;
 (4-(3-(2-methoxyethoxy)phenoxy)piperidin-1-yl)(quinolin-8-yl)methanone;

(4-(3-(2-methoxyethoxy)phenoxy)piperidin-1-yl)(quinolin-2-yl)methanone;

(4-(3-(2-methoxyethoxy)phenoxy)piperidin-1-yl)(2-methyl-2H-indazol-3-yl)methanone;

2-((2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenyl)thio)acetamide;

2-((2-(4-(4-chlorophenoxy)piperidine-1-carbonyl)phenyl)thio)acetamide;

4-(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidine-1-carbonyl)-1H-benzodimidazol-2(3H)-one;

(4-(3-ethoxyphenoxy)piperidin-1-yl)(1-methyl-1H-benzodimidazol-2-yl)methanone;

(4-(3-fluorophenoxy)piperidin-1-yl)(1-methyl-1H-benzodimidazol-2-yl)methanone;

(1H-pyrrolo[2,3-b]pyridin-2-yl)(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidin-1-yl)methanone;

(4-(3-ethoxyphenoxy)piperidin-1-yl)(1H-pyrrolo[2,3-b]pyridin-2-yl)methanone;

(1H-pyrrolo[2,3-b]pyridin-2-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;

(4-(3-ethoxyphenoxy)piperidin-1-yl)(1-methyl-1H-pyrazolo[3,4-b]pyridin-3-yl)methanone;

(4-(3-ethoxyphenoxy)piperidin-1-yl)(1H-pyrrolo[2,3-b]pyridin-3-yl)methanone;

(4-(3-ethoxyphenoxy)piperidin-1-yl)(pyrazolo[1,5-a]pyrimidin-3-yl)methanone;

(1,3-dimethyl-1H-thieno[2,3-c]pyrazol-5-yl)(4-(3-ethoxyphenoxy)piperidin-1-yl)methanone;

(4-(3-fluorophenoxy)piperidin-1-yl)(4-methyl-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)methanone;

(3,5-dimethyl-1H-pyrazol-4-yl)(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidin-1-yl)methanone;

N-(2-hydroxyethyl)-N-methyl-2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)benzenesulfonamide;

N-(2-methoxyethyl)-N-methyl-2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)benzenesulfonamide;

(2-(morpholinosulfonyl)phenyl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;

2-(N-methyl-2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenylsulfonamido)acetamide;
 N-methyl-3-(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidine-1-carbonyl)benzenesulfonamide;
 3-(4-(3-ethoxyphenoxy)piperidine-1-carbonyl)-N-methylbenzenesulfonamide;
 N-methyl-3-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)benzenesulfonamide;
 (1,5-naphthyridin-2-yl)(4-(3-(trifluoromethyl)phenoxy)piperidin-1-yl)methanone;
 3-(4-((4-chlorophenyl)thio)piperidine-1-carbonyl)benzenesulfonamide;
 (4-((4-chlorophenyl)thio)piperidin-1-yl)(1,5-naphthyridin-2-yl)methanone;
 N-(6-(4-((4-chlorophenyl)thio)piperidine-1-carbonyl)pyridin-2-yl)acetamide;
 (4-((4-chlorophenyl)thio)piperidin-1-yl)(1,6-naphthyridin-8-yl)methanone;
 2-(4-(4-(3,4-difluorophenoxy)piperidine-1-carbonyl)phenoxy)acetamide;
 (4-(3,4-difluorophenoxy)piperidin-1-yl)(1,5-naphthyridin-2-yl)methanone;
 2-(4-(4-(2,4-difluorophenoxy)piperidine-1-carbonyl)phenoxy)acetamide;
 N-(4-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)pyridin-2-yl)pivalamide;
 (2-(1H-imidazol-1-yl)pyridin-4-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
 N-(4-(4-(3-ethoxyphenoxy)piperidine-1-carbonyl)pyridin-2-yl)pivalamide;
 1-(3-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenyl)piperidin-2-one;
 1-(3-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenyl)imidazolidin-2-one; and
 (5-amino-1H-pyrazol-3-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
 or a prodrug thereof or a pharmaceutically acceptable salt thereof.

[Claim 7]

A compound which is selected from:

(4-(4-chlorophenoxy)piperidin-1-yl)(quinoxalin-6-yl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(quinolin-8-yl)methanone;
 (4-(1H-1,2,4-triazol-1-yl)phenyl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(3,5-dimethylisoxazol-4-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(2-methyl-2H-indazol-3-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(6-methylpyridin-3-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(6-methoxypyridin-3-yl)methanone;
 ;
 (4-(4-chlorophenoxy)piperidin-1-yl)(3-methylpyridin-2-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(2,4-dimethylthiazol-5-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(4,5,6,7-tetrahydro-1H-indazol-3-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(6-methoxypyridin-2-yl)methanone;
 ;
 (4-(4-chlorophenoxy)piperidin-1-yl)(2-methyl-4,5,6,7-tetrahydro-2H-indazol-3-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(1,5-naphthyridin-2-yl)methanone;
 4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)benzamide;
 (4-(4-chlorophenoxy)piperidin-1-yl)(4-(2-hydroxypropan-2-yl)phenyl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(quinolin-5-yl)methanone;
 (4-(4-fluorophenoxy)piperidin-1-yl)(2-methyl-2H-indazol-3-yl)methanone;
 (4-phenoxy)piperidin-1-yl)(quinolin-8-yl)methanone;
 (4-(4-fluorophenoxy)piperidin-1-yl)(quinolin-8-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(phenyl)methanone;
 (1H-benzo[d]imidazol-5-yl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(1,3-dimethyl-1H-pyrazol-5-yl)methanone;
 (4-(3-methoxyphenoxy)piperidin-1-yl)(quinolin-8-yl)methanone;
 (4-(3-fluorophenoxy)piperidin-1-yl)(quinolin-8-yl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(2-methylthiazol-5-yl)methanone;
 1-(3-((1-(quinoline-8-carbonyl)piperidin-4-yl)oxy)phenyl)ethanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(3-methylisoxazol-5-yl)methanone;

(4-(4-chlorophenoxy)piperidin-1-yl)(1-isopropyl-1H-pyrazol-4-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(3-isopropyl-1-methyl-1H-pyrazol-5-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(3-ethyl-1-methyl-1H-pyrazol-5-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(imidazo[1,2-a]pyrazin-2-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(4-methyl-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(pyrazolo[1,5-a]pyridin-7-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(1-methyl-1H-imidazol-2-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(1-methyl-1H-imidazol-4-yl)methanone;
(4-chloro-5-methyl-1H-pyrazol-3-yl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(4-methyl-4H-furo[3,2-b]pyrrol-5-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(pyrazolo[1,5-a]pyrimidin-3-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(2-(pyrrolidin-1-yl)pyrimidin-5-yl)methanone;
(1H-benzo[d][1,2,3]triazol-4-yl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone;
3-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-1,6-dimethylpyridin-2(1H)-one;
(4-(4-chlorophenoxy)piperidin-1-yl)(1-methyl-3-(trifluoromethyl)-1H-pyrazol-5-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(4-(2-hydroxyethoxy)phenyl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(2-hydroxy-4-methoxyphenyl)methanone;
2-(3-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-1H-indol-1-yl)-N,N-dimethylacetamide;
(4-(4-chlorophenoxy)piperidin-1-yl)(3-fluoro-4-hydroxyphenyl)methanone;

2-chloro-5-(4-(4-chlorophenoxy)piperidine-1-carbonyl)benzenesulfonamide;
(4-(4-chlorophenoxy)piperidin-1-yl)(2-hydroxy-6-methoxyphenyl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(2-fluoro-4-hydroxyphenyl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(4-fluoro-3-hydroxyphenyl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(2-hydroxy-3-methoxyphenyl)methanone;
N-(3-(4-(4-chlorophenoxy)piperidine-1-carbonyl)phenyl)acetamide;
(4-(4-chlorophenoxy)piperidin-1-yl)(1-((4-hydroxytetrahydro-2H-pyran-4-yl)methyl)-1H-indol-5-yl)methanone;
N-(6-(4-(4-chlorophenoxy)piperidine-1-carbonyl)pyridin-2-yl)acetamide;
N-(4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)pyridin-2-yl)acetamide;
(4-(4-chlorophenoxy)piperidin-1-yl)(1,6-naphthyridin-5-yl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(3-hydroxyphenyl)methanone;
(4-(4-chlorophenoxy)piperidin-1-yl)(2-fluoro-3-hydroxyphenyl)methanone;
(3-(tert-butyl)-1-methyl-1H-pyrazol-5-yl)(4-(4-fluorophenoxy)piperidin-1-yl)methanone;
(4-fluoro-3-methoxyphenyl)(4-(4-fluorophenoxy)piperidin-1-yl)methanone;
(4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(2-methyl-2H-indazol-3-yl)methanone;
(4-(4-fluorophenoxy)piperidin-1-yl)(1-methyl-1H-indazol-3-yl)methanone;
(4-(4-fluorophenoxy)piperidin-1-yl)(4-methoxyquinolin-2-yl)methanone;
(4-(4-fluorophenoxy)piperidin-1-yl)(isoquinolin-1-yl)methanone;
(5-aminopyridin-2-yl)(4-(4-chlorophenoxy)piperidin-1-yl)methanone;
(1,3-dimethyl-1H-pyrazol-5-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
(3,5-dimethylisoxazol-4-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
(3-methylpyridin-2-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)

methanone;

4-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)picolinamide
;

(1-methyl-1H-imidazol-4-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;

(2-hydroxy-6-methoxyphenyl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;

(2,4-dimethylthiazol-5-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;

(2-methyl-2H-indazol-3-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;

1,6-dimethyl-3-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)pyridin-2(1H)-one;

benzo[d]thiazol-6-yl(4-(4-fluorophenoxy)piperidin-1-yl)methanone;

(4-(4-fluorophenoxy)piperidin-1-yl)(1-methyl-1H-benzo[d]imidazol-2-yl)methanone;

(2-methyloxazol-4-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;

N-(4-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)pyridin-2-yl)acetamide;

N-(6-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)pyridin-2-yl)acetamide;

3-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)benzamide;

(6-(hydroxymethyl)pyridin-2-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;

5,6-dimethyl-3-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)pyridin-2(1H)-one;

4-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)-1H-benzo[d]imidazol-2(3H)-one;

(4-(4-chloro-2-methoxyphenoxy)piperidin-1-yl)(quinolin-8-yl)methanone;

3-(4-(3-(trifluoromethyl)phenoxy)piperidine-1-carbonyl)benzamide;

4-(4-(3-(trifluoromethyl)phenoxy)piperidine-1-carbonyl)picolinamide;

(4-(4-fluorophenoxy)piperidin-1-yl)(5-methyl-1-phenyl-1H-pyrazol-4-yl)methanone;

4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-N-(2-methoxyethyl)-N-methylbenzamide;

(S)-4-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-N-(2-hydroxy-2-phe

nylethyl)benzamide;
 4-(4-((4-chlorophenyl)thio)piperidine-1-carbonyl)picolinamide;
 6-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)picolinamide
 ;
 (2-(methylsulfonyl)phenyl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
 (4-(3-ethoxyphenoxy)piperidin-1-yl)(quinolin-8-yl)methanone;
 N-methyl-3-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)benzamide;
 3-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)benzenesulfonamide;
 4-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)benzenesulfonamide;
 (4-(4-fluorophenoxy)piperidin-1-yl)(1,5-naphthyridin-2-yl)methanone;
 (4-(4-fluorophenoxy)piperidin-1-yl)(quinolin-2-yl)methanone;
 (4-(3-fluorophenoxy)piperidin-1-yl)(4-methoxyquinolin-2-yl)methanone;
 (1H-benzo[d][1,2,3]triazol-7-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
 2-(2-(4-(4-chlorophenoxy)piperidine-1-carbonyl)phenoxy)acetamide;
 2-(2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenoxy)acetamide;
 (4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(5-phenylisoxazol-3-yl)methanone;
 (4-hydroxyquinolin-8-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
 (1,8-naphthyridin-4-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
 (1,6-naphthyridin-8-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
 [1,2,4]triazolo[1,5-a]pyrimidin-2-yl(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
 (5-methyl-1H-pyrazol-3-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
 2-chloro-5-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)benzenesulfonamide;
 (S)-3-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-N-(2-hydroxy-2-phenylethyl)benzamide;

(S)-N-(1-amino-1-oxo-3-phenylpropan-2-yl)-3-(4-(4-chlorophenoxy)piperidine-1-carbonyl)benzamide;
 (4-((4-chlorophenyl)sulfonyl)piperidin-1-yl)(2-phenylthiazol-4-yl)methanone;
 (5-fluoro-2-(methylsulfonyl)phenyl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
 N,N-dimethyl-4-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)benzenesulfonamide;
 N-(2-(4-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenoxy)ethyl)acetamide;
 N-(4-(4-(3-ethoxyphenoxy)piperidine-1-carbonyl)pyridin-2-yl)acetamide;
 3-(4-(3-ethoxyphenoxy)piperidine-1-carbonyl)benzenesulfonamide;
 N-(6-(4-(3-ethoxyphenoxy)piperidine-1-carbonyl)pyridin-2-yl)acetamide;
 (4-(3-ethoxyphenoxy)piperidin-1-yl)(1,5-naphthyridin-2-yl)methanone;
 quinolin-8-yl(4-((4-(trifluoromethoxy)phenyl)sulfonyl)piperidin-1-yl)methanone;
 quinolin-2-yl(4-((4-(trifluoromethoxy)phenyl)sulfonyl)piperidin-1-yl)methanone;
 (2-(ethylsulfonyl)phenyl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
 2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)thiazole-4-carboxamide;
 (4-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenyl)methanesulfonamide;
 4-methoxy-3-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)benzenesulfonamide;
 2-((2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)pyridin-3-yl)oxy)acetamide;
 (4-(aminomethyl)pyridin-2-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
 N-((2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)pyridin-4-yl)methyl)methanesulfonamide;
 ethyl
 ((2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)pyridin-4-yl)methyl)carbamate;
 N-(2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)benzyl)ac

etamide;

N-(2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)benzyl)methanesulfonamide;

(2-(methylsulfonyl)phenyl)(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidine-1-yl)methanone;

N-(4-(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidine-1-carbonyl)pyridin-2-yl)acetamide;

4-(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidine-1-carbonyl)picolinamide;

3-(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidine-1-carbonyl)benzamide;

2-(2-(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidine-1-carbonyl)phenoxy)acetamide;

(1,5-naphthyridin-2-yl)(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidine-1-yl)methanone;

(2-methyl-2H-indazol-3-yl)(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidine-1-yl)methanone;

(1,3-dimethyl-1H-pyrazol-5-yl)(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidine-1-yl)methanone;

N-(6-(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidine-1-carbonyl)pyridin-2-yl)acetamide;

4-(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidine-1-carbonyl)benzamide;

(3,5-dimethylisoxazol-4-yl)(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidine-1-yl)methanone;

(3-(methylsulfonyl)phenyl)(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidine-1-yl)methanone;

(1,6-naphthyridin-8-yl)(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidine-1-yl)methanone;

(3-methyl-1H-pyrazol-5-yl)(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidine-1-yl)methanone;

2-(3-(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidine-1-carbonyl)phenoxy)acetamide;

1-(4-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenyl)urea;

(1H-1,2,4-triazol-3-yl)(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidine-1-yl)methanone;

(4-(3-ethoxyphenoxy)piperidine-1-yl)(3-(methylsulfonyl)phenyl)methan

one;
 (4-(3-ethoxyphenoxy)piperidin-1-yl)(3-methyl-1H-pyrazol-5-yl)methanone;
 one;
 N,N-dimethyl-3-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)benzenesulfonamide;
 N-(2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenyl)methanesulfonamide;
 (6-aminopyridin-2-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
 N,N-dimethyl-2-(2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenoxy)acetamide;
 (1,3-dimethyl-1H-pyrazol-5-yl)(4-(3-(trifluoromethyl)phenoxy)piperidin-1-yl)methanone;
 (2-(methylsulfonyl)phenyl)(4-(3-(trifluoromethyl)phenoxy)piperidin-1-yl)methanone;
 N-(6-(4-(3-(trifluoromethyl)phenoxy)piperidine-1-carbonyl)pyridin-2-yl)acetamide;
 3-(4-(3-(trifluoromethyl)phenoxy)piperidine-1-carbonyl)benzenesulfonamide;
 (3,5-dimethylisoxazol-4-yl)(4-(3-(trifluoromethyl)phenoxy)piperidin-1-yl)methanone;
 (1,6-naphthyridin-8-yl)(4-(3-(trifluoromethyl)phenoxy)piperidin-1-yl)methanone;
 (3-methyl-1H-pyrazol-5-yl)(4-(3-(trifluoromethyl)phenoxy)piperidin-1-yl)methanone;
 2-(2-(4-(3-(trifluoromethyl)phenoxy)piperidine-1-carbonyl)phenoxy)acetamide;
 2-(3-(4-(3-(trifluoromethyl)phenoxy)piperidine-1-carbonyl)phenoxy)acetamide;
 (1H-1,2,4-triazol-3-yl)(4-(3-(trifluoromethyl)phenoxy)piperidin-1-yl)methanone;
 N-(2-(2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenoxy)ethyl)methanesulfonamide;
 N-(2-(2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenoxy)ethyl)cyclopropane-1,1-dicarboxamide;
 N-(2-(3-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenoxy)ethyl)methanesulfonamide;
 N-(3-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)pyridin-2-

-yl)acetamide;
 N-(1-methyl-5-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)-1H-pyrazol-3-yl)acetamide;
 (2-(ethylsulfonyl)phenyl)(4-(3-(trifluoromethyl)phenoxy)piperidin-1-yl)methanone;
 (2-(ethylsulfonyl)phenyl)(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidin-1-yl)methanone;
 N-(2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)pyridin-3-yl)acetamide;
 (3-(methylsulfonyl)phenyl)(4-(3-(trifluoromethyl)phenoxy)piperidin-1-yl)methanone;
 (4-(3-chlorophenoxy)piperidin-1-yl)(3-(methylsulfonyl)phenyl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(3-(methylsulfonyl)phenyl)methanone;
 (4-(4-chlorophenoxy)piperidin-1-yl)(2-(ethylsulfonyl)phenyl)methanone;
 N,N-dimethyl-3-(4-(3-(trifluoromethyl)phenoxy)piperidine-1-carbonyl)benzenesulfonamide;
 3-(4-(4-chlorophenoxy)piperidine-1-carbonyl)-N,N-dimethylbenzenesulfonamide;
 (4-(3-(2-methoxyethoxy)phenoxy)piperidin-1-yl)(quinolin-8-yl)methanone;
 (4-(3-(2-methoxyethoxy)phenoxy)piperidin-1-yl)(quinolin-2-yl)methanone;
 (4-(3-(2-methoxyethoxy)phenoxy)piperidin-1-yl)(2-methyl-2H-indazol-3-yl)methanone;
 2-((2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenyl)thio)acetamide;
 2-((2-(4-(4-chlorophenoxy)piperidine-1-carbonyl)phenyl)thio)acetamide;
 4-(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidine-1-carbonyl)-1H-benzo[d]imidazol-2(3H)-one;
 (4-(3-ethoxyphenoxy)piperidin-1-yl)(1-methyl-1H-benzo[d]imidazol-2-yl)methanone;
 (4-(3-fluorophenoxy)piperidin-1-yl)(1-methyl-1H-benzo[d]imidazol-2-yl)methanone;
 (4-(3-ethoxyphenoxy)piperidin-1-yl)(1-methyl-1H-pyrazolo[3,4-b]pyri

din-3-yl)methanone;
 (4-(3-ethoxyphenoxy)piperidin-1-yl)(pyrazolo[1,5-a]pyrimidin-3-yl)methanone;
 (4-(3-fluorophenoxy)piperidin-1-yl)(4-methyl-3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazin-7-yl)methanone;
 (3,5-dimethyl-1H-pyrazol-4-yl)(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidin-1-yl)methanone;
 N-(2-hydroxyethyl)-N-methyl-2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)benzenesulfonamide;
 (2-(morpholinosulfonyl)phenyl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
 2-(N-methyl-2-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)phenylsulfonamido)acetamide;
 N-methyl-3-(4-(3-(2,2,2-trifluoroethoxy)phenoxy)piperidine-1-carbonyl)benzenesulfonamide;
 3-(4-(3-ethoxyphenoxy)piperidine-1-carbonyl)-N-methylbenzenesulfonamide;
 N-methyl-3-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)benzenesulfonamide;
 (4-((4-chlorophenyl)thio)piperidin-1-yl)(1,5-naphthyridin-2-yl)methanone;
 N-(6-(4-((4-chlorophenyl)thio)piperidine-1-carbonyl)pyridin-2-yl)acetamide;
 2-(4-(4-(3,4-difluorophenoxy)piperidine-1-carbonyl)phenoxy)acetamide;
 (4-(3,4-difluorophenoxy)piperidin-1-yl)(1,5-naphthyridin-2-yl)methanone;
 2-(4-(4-(2,4-difluorophenoxy)piperidine-1-carbonyl)phenoxy)acetamide;
 N-(4-(4-(3-(trifluoromethoxy)phenoxy)piperidine-1-carbonyl)pyridin-2-yl)pivalamide; and
 (5-amino-1H-pyrazol-3-yl)(4-(3-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone;
 or a prodrug thereof or a pharmaceutically acceptable salt thereof.

[Claim 8]

A method for the treatment of a condition or disorder in which TTX-S channel blockers are involved, in a mammalian subject, including a human, which comprises administering to a mammal in need of such treatment a therapeutically effective amount of the compound or the

prodrug thereof or the pharmaceutically acceptable salt thereof, as claimed in any one of claims 1 to 7.

[Claim 9]

The method as claimed in claim 8, wherein said condition or disorder is selected from the group consisting of: pain, acute pain, chronic pain, neuropathic pain, inflammatory pain, visceral pain, nociceptive pain, multiple sclerosis, neurodegenerative disorder, irritable bowel syndrome, osteoarthritis, rheumatoid arthritis, neuropathological disorders, functional bowel disorders, inflammatory bowel diseases, pain associated with dysmenorrhea, pelvic pain, cystitis, pancreatitis, migraine, cluster and tension headaches, diabetic neuropathy, peripheral neuropathic pain, sciatica, fibromyalgia Crohn's disease, epilepsy or epileptic conditions, bipolar depression, tachyarrhythmias, mood disorder, bipolar disorder, psychiatric disorders such as anxiety and depression, myotonia, arrhythmia, movement disorders, neuroendocrine disorders, ataxia, incontinence, visceral pain, trigeminal neuralgia, herpetic neuralgia, general neuralgia, postherpetic neuralgia, radicular pain, sciatica, back pain, head or neck pain, severe or intractable pain, breakthrough pain, postsurgical pain, stroke, cancer pain, seizure disorder and causalgia; and combinations thereof.

[Claim 10]

A pharmaceutical composition comprising the compound or the prodrug thereof or the pharmaceutically acceptable salt thereof, as claimed in any one of claims 4 to 7, and a pharmaceutically acceptable carrier.

[Claim 11]

A pharmaceutical composition as claimed in claim 10, further comprising another pharmacologically active agent.

[Claim 12]

A compound of formula (I) as described in claim 1 or a prodrug thereof or a pharmaceutically acceptable salt, solvate or composition thereof for use in the treatment of a condition or disorder in which TTX-S channel blockers are involved.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/JP2010/006723

A. CLASSIFICATION OF SUBJECT MATTER		
Int.Cl. See extra sheet		
According to International Patent Classification (IPC) or to both national classification and IPC		
B. FIELDS SEARCHED		
Minimum documentation searched (classification system followed by classification symbols)		
Int.Cl. See extra sheet		
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Published examined utility model applications of Japan 1922-1996 Published unexamined utility model applications of Japan 1971-2010 Registered utility model specifications of Japan 1996-2010 Published registered utility model applications of Japan 1994-2010		
Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) CAplus/REGISTRY (STN)		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2008/118758 A1 (ICAGEN, INC.) 2008.10.02, Abstract; CLAIMS; p.1, Table A; p.93, [0317]-p.94, [0319]; p.139-141; p.146; p.150 & JP 2010-522242 A & US 2009/0143358 A1 & EP 1995241 A1 & DE 602008000809 D & UY 30978 A & CL 8352008 A & PA 8773501 A & AR 65824 A & CA 2681572 A & AT 461177 T & ES 2340640 T & PE 2372009 A	1-7, 10-12
X A	WO 2009/105722 A1 (IRM LLC) 2009.08.27, Abstract; CLAIMS; p.27; p.28; p.30 & AU 2009217282 A	1-5, 10-12 6, 7
☒ Further documents are listed in the continuation of Box C. ☐ See patent family annex.		
* Special categories of cited documents: "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier application or patent but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art "&" document member of the same patent family		
Date of the actual completion of the international search 13.12.2010		Date of mailing of the international search report 21.12.2010
Name and mailing address of the ISA/JP Japan Patent Office 3-4-3, Kasumigaseki, Chiyoda-ku, Tokyo 100-8915, Japan		Authorized officer Koichi SESHITA Telephone No. +81-3-3581-1101 Ext. 3492

INTERNATIONAL SEARCH REPORT

International application No.

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C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X A	WO 2007/014851 A2 (F.HOFFMANN-LA ROCHE AG) 2007.02.08, Abstract; Claims; p.50 & US 2007/0027163 A1 & US 2010/0222357 A & EP 1917255 A & WO 2007/014851 A2 & AR 57086 A & NO 20080316 A & CA 2616937 A & KR 10-2008-0027897 A & CN 101277945 A & BRA PI0614692 & NZ 564550 A & ZA 200800523 A & IL 188928 D	1-5, 10-12 6, 7
X A	WO 2006/010967 A1 (RICHTER GEDEON VEGYESZETI GYAR RT.) 2006.02.02, Abstract; claims; p.15, Example 7,8; p.16, Example 10 & JP 2008-508250 A & US 2009/0012118 A1 & EP 1771436 A & HU 401525 A & CA 2574167 A & NO 20071111 A & KR 10-2007-0043965 A & CN 1989127 A & BRA PI0513912 & ZA 200700321 A & AP 200603842 D & EA 200700364 A & IL 179487 D & HU 401525 D0	1-5, 10-12 6, 7
X A	WO 01/34718 A1 (RICHTER GEDEON VEGYESZETI GYAR RT.) 2002.05.02, Abstract; claims; p.31-38, Example 44,52,54,71 & EP 1099740 A1 & AU 1015201 A	1-5, 10-12 6, 7
X A	WO 2009/112845 A1 (THE UNIVERSITY OF EDINBURGH) 2009.09.17, Abstract; CLAIMS; p.124, EE-5 & AU 2009224017 A	1-5, 10-12 6, 7
X A	WO 2009/098576 A1 (PFIZER INC.) 2009.08.13, Abstract; CLAIMS; p.69; p.73; p.74-78, p.80; p.83; p.p.86; p.89; p.92 & US 2009/0197859 A1 & CA 2714232 A & UY 31632 A & PA 8815001 A & PE 13792009 A & AR 70343 A	4, 5, 10, 11 1-3, 6, 7, 12
X A	WO 2009/093032 A1 (ASTRAZENECA AB) 2009.07.30, Abstract; Claims; p.47; p.49 & US 2009/0192156 A1 & EP 2231638 A & AU 2009207498 A & CA 2708175 A & MX 2010006364 A & UY 31603 A & PE 13352009 A & AR 70221 A	4, 5, 10, 11 1-3, 6, 7, 12

INTERNATIONAL SEARCH REPORT

International application No.

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C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X A	WO 2009/051244 A1 (TAKEDA PHARMACEUTICAL COMPANY LIMITED)2009.04.23, Abstract; Claims; p.132-148; p.150; p.151 & EP 2202223 A1	4, 5, 10, 11 1-3, 6, 7, 12
X A	WO 2009/023179 A2 (GENELABS TECHNOLOGIES, INC.) 2009.02.19, Abstract; CLAIMS; p.137 & EP 2202223 A1	4, 5, 10, 11 1-3, 6, 7, 12
X A	EP 2065369 A1 (Astellas Pharma Inc.)2007.08.22, Abstract; Claims; p.67,[0171] & WO 2008/023720 A1 & CA 2665804 A	4, 5, 10, 11 1-3, 6, 7, 12
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X A	WO 2007/097470 A2 (TAKEDA PHARMACEUTICAL COMPANY IMITED) 2007.08.30, Abstract; Claims; p.406 & JP 2009-527459 A & US 2010/0234351 A & EP 1987037 A	4, 5, 10, 11 1-3, 6, 7, 12
X A	WO 2006/136402 A1 (DEVELOGEN AKTIEN-GESELLSCHAFT) 2006.12.28, Abstract; Claims; p.110, Compound 214a, 215a & JP 2008-543898 A & US 2010/0143341 A & EP 1899353 A & CA 2655799 A	4, 5, 10, 11 1-3, 6, 7, 12
X A	WO 2005/105760 A1 (TAKEDA PHARMACEUTICAL COMPANY LIMITED) 2005.11.10, Abstract; CLAIMS; p.111, Example 124 & JP 2007-535488 A & US 2008/0027050 A1 & EP 1740551 A & CA 2564085 A & NO 20065537 A & KR 10-2007-0008709 A & CN 1976907 A & BRA PI0510305 & ZA 200609259 A	4, 5, 10, 11 1-3, 6, 7, 12

INTERNATIONAL SEARCH REPORT

International application No.

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C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X A	WO 2004/043924 A1 (ASTRAZENECA AB) 2004.05.27, Abstract; Claims; p.89, Example 2.169 & JP 2006-513261 A & US 2006/0035938 A1 & EP 1562902 A & DE 60305061 D & DE 60305061 T & IS 7867 A & BRA PI0316081 & SE 203348 D & CA 2504766 A & BR 316081 A & NO 20052818 A & AT 325096 T & DK 1562902 T & HK 1079200 A & PT 1562902 E & NZ 539787 A & NZ 539787 A & ES 2262029 T & PL 376957 A & KR 10-2005-0086516 A & CN 1711243 A & RU 2328486 C & SI 1562902 T & ZA 200503710 A & AU 2003276802 B & AR 42024 A	4, 5, 10, 11 1-3, 6, 7, 12
X A	WO 01/21598 A1 (ASTRAZANCA AB) 2001.03.29, Abstract; CLAIMS; p.17, No.127 & JP 2003-509501 A & EP 1218358 A & DE 60030741 D & DE 60030741 T & AU 7031500 A & AT 339406 T & ES 2270867 T	4, 5, 10, 11 1-3, 6, 7, 12
X A	WO 98/58934 A1 (SOCIETE DE CONSEILS DE RECHERCHES ET D'APPLICATIONS SCIENTIFIQUES) 1998.12.30, Abstract; REVENDICATIONS; p.82, Example 20 & JP 2002-507965 A & US 2002/0007062 A1 & US 2002/0045753 A1 & US 2003/0078420 A1 & US 2005/0043397 A1 & US 2005/0187272 A1 & US 2008/0182993 A1 & US 6335445 B1 & US 2002/0042511 A1 & EP 991654 A & DE 69830584 D & DE 69830584 T & FR 2764889 A & FR 2764889 A1 & AU 8218998 A & NO 996208 A & BR 9810197 A & PL 337499 A & SK 179699 A & HU 2425 A & NZ 501656 A & CA 2294809 A & HK 1030218 A & ZA 9805392 A & CZ 9904597 A & TR 9903175 T & TW 422842 B & IL 133223 D & AU 737964 B & AT 297935 T & DK 991654 T & ES 2244068 T & PT 991654 E & KR 10-2005-0098970 A & CN 1264385 A & RU 2202543 C	4, 5, 10, 11 1-3, 6, 7, 12
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INTERNATIONAL SEARCH REPORT

International application No.

PCT/JP2010/006723

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X A	GB 2310660 A (Merck & Co Inc) 1997.09.03, Abstract; CLAIMS; p.43, Example 16 & GB 9704025 D0	4, 5, 10, 11 1-3, 6, 7, 12
X A	WO 95/02405 A1 (MERCK & CO., INC.) 1995.01.26, Abstract; CLAIMS; p.331 & JP 9-500134 A & EP 714299 A & DE 69430483 D & AU 7513294 A & AT 216580 T & CA 2166975 A & AU 691829 B	4, 5, 10, 11 1-3, 6, 7, 12
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X A	EP 0304888 A1 (Eisai Co., Ltd.) 1989.03.01, Abstract; Claims; p.31 & JP 1-52756 A & JP 1-52752 A & JP 1-52717 A & US 4977165 A & US 5082850 A & US 5162347 A & US 5246946 A & DE 3875866 A & DE 3875866 T & AT 82263 T & NO 883750 A & PH 25458 A & CA 1263658 A & DK 470488 A & HU 48587 A & ES 2045044 T & GR 3006380 T & KR 10-1991-0002581 B & NO 883750 A0	4, 5, 10, 11 1-3, 6, 7, 12
X A	EP 0270074 A2 (HOECHST AKTIENGESELLSCHAFT) 1987.06.08, Abstract; Patentensprüche; p.14, Beispiel Nr7,9 & JP 63-145277 A & US 4889864 A & DE 3641343 A & PL 269186 A & PT 86271 A & AU 8198987 A & BR 8706535 A & CS 8708724 A & DD 264607 A & DK 633287 A & HU 46688 A & IL 84663 A & ZA 8709043 A & IL 84663 D & IE 328087 L & CN 87108072 A & AU 598066 B & DK 633287 A0	4, 5, 10, 11 1-3, 6, 7, 12

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C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
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X A	EP 0194112 A1 (A.H. ROBINS COMPANY, INCORPORATED) 1986.09.10, Abstract; Claims; p.24, Example 38 & JP 61-210031 A & JP 61-205254 A & US 4956359 A & US 5068231 A & US 5151418 A & US 5183902 A & DE 3671369 D & AT 52915 E & AT 52915 T & NZ 215313 A & PH 25455 A & PT 82117 A & AU 5388786 A & FI 860847 A & CY 1724 A & DK 90086 A & IE 58943 B & & ZA 8601215 A & GR 860531 A & AU 599312 B & DK 90086 A0	4, 5, 10, 11 1-3, 6, 7, 12
X A	GHOSH, P. et al, Comparative QSAR studies of nitrofuranyl amide derivatives using theoretical structural properties, Molecular Simulation, 2009, Vol.35, No.14-15, p.1185-1200 Abstract; p.1187, N-3	4, 5, 10, 11 1-3, 6, 7, 12
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X A	BORZA, I. et al, Kynurenic acid amides as novel NR2B selective NMDA receptor antagonists, Bioorganic & Medicinal Chemistry Letters, 2007, Vol.17, No.2, p.406-409 Abstract; p.408, Table 1	4, 5, 10, 11 1-3, 6, 7, 12

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Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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X A	WO 2008/029084 A2 (SYNGENTA LIMITED) 2008.03.13, Abstract; Claims; p.99,#1956 & GB 617575 D & GB 617575 D0 & AR 62640 A & CL 25822007 A	4, 5 1-3, 6, 7, 10-12
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PX PA	WO 2010/050461 A1 (MITSUBISHI TANABE PHARMA CORPORATION) 2010.05.06, Abstract; Claims; p.51,[0217]; p.105,[0454]; p.180,#51-55; p.245,[1092] (No Family)	1-3, 12 4-7, 10, 11
PX PA	WO 2010/124112 A1 (JANSSEN PHARMACEUTICA NV) 2010.10.28, Abstract; claims; p.246-247, Cpd 440,442 & 444 (No Family)	1, 2, 12 3-7, 10, 11
PX PA	WO 2010/124116 A1 (JANSSEN PHARMACEUTICA NV) 2010.10.28, Abstract; claims; p.248-249, Cpd 440,442 & 444 (No Family)	1, 2, 12 3-7, 10, 11
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C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
PX PA	WO 2010/124119 A1 (JANSSEN PHARMACEUTICA NV) 2010.10.28, Abstract; claims; p.252-253, Cpd 440,442 & 444 (No Family)	1, 2, 12 3-7, 10, 11
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CLASSIFICATION OF SUBJECT MATTER

A61K31/445(2006.01) i, A61K31/435(2006.01) i, A61K31/44(2006.01) i,
A61K31/4525(2006.01) i, A61K31/4535(2006.01) i, A61K31/454(2006.01) i,
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A61P1/00(2006.01) i, A61P1/18(2006.01) i, A61P9/00(2006.01) i,
A61P9/06(2006.01) i, A61P13/00(2006.01) i, A61P13/10(2006.01) i,
A61P15/00(2006.01) i, A61P19/02(2006.01) i, A61P21/02(2006.01) i,
A61P25/00(2006.01) i, A61P25/04(2006.01) i, A61P25/06(2006.01) i,
A61P25/08(2006.01) i, A61P25/14(2006.01) i, A61P25/16(2006.01) i,
A61P25/18(2006.01) i, A61P25/20(2006.01) i, A61P25/22(2006.01) i,
A61P25/28(2006.01) i, A61P29/00(2006.01) i, A61P35/00(2006.01) i,
A61P43/00(2006.01) i, C07D211/46(2006.01) i, C07D401/06(2006.01) i,
C07D401/10(2006.01) i, C07D401/12(2006.01) i, C07D401/14(2006.01) i,
C07D405/06(2006.01) i, C07D405/12(2006.01) i, C07D405/14(2006.01) i,
C07D409/06(2006.01) i, C07D413/06(2006.01) i, C07D417/06(2006.01) i,
C07D417/10(2006.01) i, C07D455/04(2006.01) i, C07D471/04(2006.01) i,
C07D471/06(2006.01) i, C07D487/04(2006.01) i, C07D491/048(2006.01) i,
C07D495/04(2006.01) i, C07D498/04(2006.01) i, C07D513/04(2006.01) i

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Minimum documentation searched

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Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 8, 9
because they relate to subject matter not required to be searched by this Authority, namely:
The subject-matter of claim 8 and 9 relates to [a method for treatment of the human body by surgery or therapy], which does not require an intentional search by the International Searching Authority in accordance with PCT Article 17(2)(a)(i) and [Rule 39.1(iv)].
2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ No protest accompanied the payment of additional search fees.