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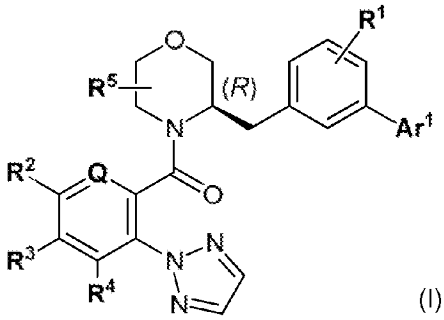
(54) **Title**: 2-(1,2,3-TRIAZOL-2-YL)BENZAMIDE AND 3-(1,2,3-TRIAZOL-2-YL)PICOLINAMIDE DERIVATIVES AS OREXIN RECEPTOR ANTAGONISTS



(I)

(57) **Abstract**: The present invention relates to 2-(1,2,3-triazol-2-yl)benzamide and 3-(1,2,3-triazol-2- yl)picolinamide derivatives of formula (I) Formula (I) wherein Ar^1, Q, and R^1 to R^5 are as described in the description, to their preparation, to pharmaceutically acceptable salts thereof, and to their use as pharmaceuticals, to pharmaceutical compositions containing one or more compounds of formula (I), and especially to their use as orexin receptor antagonists.

2-(1,2,3-TRIAZOL-2-YL)BENZAMIDE AND 3-(1,2,3-TRIAZOL-2-YL)PICOLINAMIDE DERIVATIVES AS OREXIN RECEPTOR ANTAGONISTS

The present invention relates to novel 2-(1,2,3-triazol-2-yl)benzamide and 3-(1,2,3-triazol-2-yl)picolinamide derivatives of formula (I) and their use as pharmaceuticals. The invention also concerns related aspects including processes for the preparation of the compounds, pharmaceutical compositions containing one or more compounds of formula (I), and their use as orexin receptor antagonists, especially as orexin-1 receptor antagonists.

Orexins (orexin A or OX-A and orexin B or OX-B) are neuropeptides found in 1998 by two research groups, orexin A is a 33 amino acid peptide and orexin B is a 28 amino acid peptide (Sakurai T. *et al.*, Cell, **1998**, 92, 573-585). Orexins are produced in discrete neurons of the lateral hypothalamus and bind to the G-protein-coupled receptors (OX_1 and OX_2 receptors). The orexin-1 receptor (OX_1) is selective for OX-A, and the orexin-2 receptor (OX_2) is capable to bind OX-A as well as OX-B. Orexin receptor antagonists are a novel type of nervous system or psychotropic drugs. Their mode of action in animals and humans involves either blockade of both orexin-1 and orexin-2 receptor (dual antagonists), or individual and selective blockade of either the orexin-1 or the orexin-2 receptor (selective antagonists) in the brain. Orexins were initially found to stimulate food consumption in rats suggesting a physiological role for these peptides as mediators in the central feedback mechanism that regulates feeding behaviour (Sakurai T. *et al.*, Cell, **1998**, 92, 573-585).

On the other hand, orexin neuropeptides and orexin receptors play an essential and central role in regulating circadian vigilance states. In the brain, orexin neurons collect sensory input about internal and external states and send short intrahypothalamic axonal projections as well as long projections to many other brain regions. The particular distribution of orexin fibers and receptors in basal forebrain, limbic structures and brainstem regions - areas related to the regulation of waking, sleep and emotional reactivity- suggests that orexins exert essential functions as regulators of behavioral arousal; by activating wake-promoting cell firing, orexins contribute to orchestrate all brain arousal systems that regulate circadian activity, energy balance and emotional reactivity. This role opens large therapeutic opportunities for medically addressing numerous mental health disorders possibly relating to orexinergic dysfunctions [see for example: Tsujino N and Sakurai T, "Orexin/hypocretin: a neuropeptide at the interface of sleep, energy homeostasis, and reward systems.", Pharmacol Rev. **2009**, 61:162-176; and Carter ME et al., "The brain hypocretins and their receptors: mediators of allostatic arousal.", Curr Op Pharmacol. **2009**, 9: 39-45] that are described in the following sections. It was also observed that orexins regulate states of sleep and wakefulness opening potentially novel therapeutic approaches to insomnia and other sleep disorders (Chemelli R.M. *et al.*, Cell, **1999**, 98, 437-451).

Human memory is comprised of multiple systems that have different operating principles and different underlying neuronal substrates. The major distinction is between the capacity for conscious, declarative memory and a set of unconscious, non-declarative memory abilities. Declarative memory is further subdivided into semantic and episodic memory. Non-declariative memory is further subdivided into priming and perceptual learning, procedural memory for skills and habits, associative and non-associative learning, and some others. While semantic memory refers to the general knowledge about the world, episodic memory is autobiographical memory of events. Procedural memories refer to the ability to perform skill-based operations, as e.g. motor skills. Long-term memory is established during a multiple stage process through gradual changes involving diverse brain structures, beginning with learning, or memory acquisition, or formation. Subsequently, consolidation of what has been learned may stabilize memories. When long-term memories are retrieved, they may return to a labile state in which original content may be updated, modulated or disrupted. Subsequently, reconsolidation may again stabilize memories. At a late stage, long-term memory may be resistant to disruption. Long-term memory is conceptually and anatomically different from working memory, the latter of which is the capacity to maintain temporarily a limited amount of information in mind. Behavioural research has suggested that the human brain consolidates long-term memory at certain key time intervals. The initial phase of memory consolidation may occur in the first few minutes after we are exposed to a new idea or learning experience. The next, and possibly most important phase, may occur over a longer period of time, such as during sleep; in fact, certain consolidation processes have been suggested to be sleep-dependent [R. Stickgold et al., Sleep-dependent memory consolidation; Nature **2005**, 437, 1272-1278]. Learning and memory processes are believed to be fundamentally affected in a variety of neurological and mental disorders, such as e.g. mental retardation, Alzheimer's disease or depression. Indeed, memory loss or impairment of memory acquisition is a significant feature of such diseases, and no effective therapy to prevent this detrimental process has emerged yet.

In addition, both anatomical and functional evidence from in vitro and in vivo studies suggest an important positive interaction of the endogenous orexin system with reward pathways of the brain [Aston-Jones G et al., Brain Res **2010**, 1314, 74-90; Sharf R et al., Brain Res **2010**, 1314, 130-138]. Selective pharmacological OXR-1 blockade reduced cue- and stress-induced reinstatement of cocaine seeking [Boutrel B, et al., "Role for hypocretin in mediating stress-induced reinstatement of cocaine-seeking behavior." Proc Natl Acad Sci **2005**, 102(52), 19168-19173; Smith RJ et al., "Orexin/hypocretin signaling at the orexin 1 receptor regulates cue-elicited cocaine-seeking." Eur J Neurosci **2009**, 30(3), 493-503; Smith RJ et al., "Orexin/hypocretin is necessary for context-driven cocaine-seeking." Neuropharmacology 2010, 58(1), 179-184], cue-induced reinstatement of alcohol seeking [Lawrence AJ et al., Br J Pharmacol **2006**, 148(6), 752-759] and nicotine self-administration [Hollander JA et al., Proc Natl Acad Sci **2008**, 105(49), 19480-19485; LeSage MG et al., Psychopharmacology **2010**, 209(2), 203-212]. Orexin-1 receptor antagonism also attenuated the expression of amphetamine- and cocaine-induced CPP [Gozzi A et al., PLoS One **2011**, 6(1), e16406; Hutcheson DM et al., Behav Pharmacol **2011**, 22(2), 173-181], and reduced the expression or development of locomotor sensitization to amphetamine and cocaine [Borgland SL et al., Neuron **2006**, 49(4), 589-601; Quarta D et al., "The orexin-1 receptor antagonist SB-334867 reduces amphetamine-evoked dopamine outflow in the shell of the nucleus accumbens and decreases the expression of amphetamine sensitization." Neurochem Int **2010**, 56(1), 11-15].

The effect of a drug to diminish addictions may be modelled in normal or particularly sensitive mammals used as animal models [see for example Spealman et al, Pharmacol. Biochem. Behav. **1999**, *64*, 327-336; or T.S. Shippenberg, G.F. Koob, "Recent advances in animal models of drug addiction" in Neuropsychopharmacology: The fifth generation of progress; K.L.Davis, D. Charney, J.T.Doyle, C. Nemeroff (eds.) **2002**; chapter 97, pages 1381-1397].

Several converging lines of evidence furthermore demonstrate a direct role of the orexin system as modulator of the acute stress response. For instance, stress (i.e. psychological stress or physical stress) is associated with increased arousal and vigilance which in turn is controlled by orexins [Sutcliffe, JG et al., Nat Rev Neurosci **2002***,* 3(5), 339-349]. Orexin neurons are likely to be involved in the coordinated regulation of behavioral and physiological responses in stressful environments [Y. Kayaba et al., Am. J. Physiol. Regul. Integr. Comp. Physiol. **2003,** 285:R581-593]. Hypocretin/orexin contributes to the expression of some but not all forms of stress and arousal [Furlong T M et al., Eur J Neurosci **2009**, 30(8), 1603-1614]. Stress response may lead to dramatic, usually time-limited physiological, psychological and behavioural changes that may affect appetite, metabolism and feeding behavior [Chrousos, GP et al., *JAMA* **1992***,* 267(9), 1244-1252]. The acute stress response may include behavioural, autonomic and endocrinological changes, such as promoting heightened vigilance, decreased libido, increased heart rate and blood pressure, or a redirection of blood flow to fuel the muscles, heart and the brain [Majzoub, JA et al., European Journal of Endocrinology **2006***,* 155 (suppl_1) S71-S76].

As outlined above the orexin system regulates homeostatic functions such as sleep-wake cycle, energy balance, emotions and reward. Orexins are also involved in mediating the acute behavioral and autonomous nervous system response to stress [Zhang Wet al., "Multiple components of the defense response depend on orexin: evidence from orexin knockout mice and orexin neuron-ablated mice." Auton Neurosci **2006**, 126-127, 139-145]. Mood disorders including all types of depression and bipolar disorder are characterized by disturbed “mood” and feelings, as well as by sleeping problems (insomnia as well as hypersomnia), changes in appetite or weight and reduced pleasure and loss of interest in daily or once enjoyed activities [Liu X et al., Sleep **2007**, 30(1): 83-90]. Thus, there is a strong rationale that disturbances in the orexin system may contribute to the symptoms of mood disorders. Evidence in humans, for instance, exists that depressed patients show blunted diurnal variation in CSF orexin levels [Salomon RM et al., Biol Psychiatry **2003**, 54(2), 96-104]. In rodent models of depression, orexins were also shown to be involved. Pharmacological induction of a depressive behavioral state in rats, for instance, revealed an association with increased hypothalamic orexin levels [Feng P et al., J Psychopharmacol **2008**, 22(7): 784-791]. A chronic stress model of depression in mice also demonstrated an association of molecular orexin system disturbances with depressed behavioral states and a reversal of these molecular changes by antidepressant treatment [Nollet et al., NeuroPharm **2011**, 61(1-2):336-46].

The orexin system is also involved in stress-related appetitive/reward seeking behaviour (Berridge CW et al., Brain Res **2009**, 1314, 91-102). In certain instances, a modulatory effect on stress may be complementary to an effect on appetitive/reward seeking behaviour as such. For instance, an OX_1 selective orexin receptor antagonist was able to prevent footshock stress induced reinstatement of cocaine seeking behaviour [Boutrel, B et al., Proc Natl Acad Sci **2005***,* 102(52), 19168-19173]. In addition, stress is also known to play an integral part in withdrawal which occurs during cessation of drug taking (Koob, GF et al., Curr Opin Investig Drugs **2010**, 11(1), 63-71).

Orexins have been found to increase food intake and appetite [Tsujino, N, Sakurai, T, Pharmacol Rev **2009***,* 61(2) 162-176]. As an additional environmental factor, stress can contribute to binge eating behaviour, and lead to obesity [Adam, TC et al. Physiol Be*hav* **2007***,* 91(4) 449-458]. Animal models that are clinically relevant models of binge eating in humans are described for example in W. Foulds Mathes et al.; Appetite **2009**, 52, 545–553.

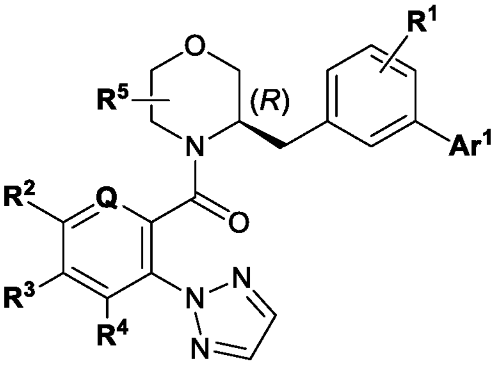
A number of recent studies report that orexins may play a role into several other important functions relating to arousal, especially when an organism must respond to unexpected stressors and challenges in the environment [Tsujino N and Sakurai T. Pharmacol Rev. **2009**, 61:162-176; Carter ME, Borg JS and deLecea L., Curr Op Pharmacol. **2009**, 9: 39-45; C Boss, C Brisbare-Roch, F Jenck, Journal of Medicinal Chemistry **2009**, 52: 891-903]. The orexin system interacts with neural networks that regulate emotion, reward and energy homeostasis to maintain proper vigilance states. Dysfunctions in its function may thus relate to many mental health disorders in which vigilance, arousal, wakefulness or attention is disturbed.

The compound (2R)-2-{(1S)-6,7-dimethoxy-1-[2-(4-trifluoromethyl-phenyl)-ethyl]-3,4-dihydro-1H-isoquinolin-2-yl}-*N*-methyl-2-phenyl-acetamide (WO2005/118548), a dual orexin receptor antagonist, showed clinical efficacy in humans when tested for the indication primary insomnia. In the rat, the compound has been shown to decrease alertness, characterized by decreases in both active wake and locomotion; and to dose-dependently increase the time spent in both REM and NREM sleep [Brisbare et al., Nature Medicine **2007**, *13*, 150-155]. The compound further attenuated cardiovascular responses to conditioned fear and novelty exposure in rats [Furlong T M et al., Eur J Neurosci **2009**, 30(8), 1603-1614]. It is also active in an animal model of conditioned fear: the rat fear-potentiated startle paradigm (WO2009/047723) which relates to emotional states of fear and anxiety diseases such as anxieties including phobias and post traumatic stress disorders (PTSDs). In addition, intact declarative and non-declarative learning and memory has been demonstrated in rats treated with this compound [WO2007/105177, H Dietrich, F Jenck, Psychopharmacology **2010**, 212, 145-154]. Said compound furthermore decreased brain levels of amyloid-beta (Aβ) as well as Aβ plaque deposition after acute sleep restriction in amyloid precursor protein transgenic mice [JE Kang et al., "Amyloid-beta dynamics are regulated by orexin and the sleep-wake cycle.", Science **2009**, 326(5955): 1005-1007]. The accumulation of the Aβ in the brain extracellular space is hypothesized to be a critical event in the pathogenesis of Alzheimer's disease. The so-called and generally known "amyloid cascade hypothesis" links Aβ to Alzheimer's disease and, thus, to the cognitive dysfunction, expressed as impairment of learning and memory. The compound has also been shown to induce antidepressant-like activity in a mouse model of depression, when administered chronically [Nollet et al., NeuroPharm **2011**, 61(1-2):336-46]. Moreover, the compound has been shown to attenuate the natural activation induced by orexin A in fasted hungry rats exposed to food odors [MJ Prud'homme et al., Neuroscience **2009**, 162(4), 1287-1298]. The compound also displayed pharmacological activity in a rat model of nicotine self-administration [LeSage MG et al., Psychopharmacology **2010**, 209(2), 203-212]. Another dual orexin receptor antagonist, N-biphenyl-2-yl-1-{[(1-methyl-1H-benzimidazol-2-yl)sulfanyl]acetyl}-L-prolinamide inhibited nicotine-reinstatement for a conditioned reinforcer and reduced behavioral (locomotor sensitization) and molecular (transcriptional responses) changes induced by repeated amphetamine administration in rodents [Winrow et al., Neuropharmacology **2009**, 58(1),185-94].

WO2003/002559 discloses N-aroyl cyclic amine derivatives encompassing morpholine derivatives as orexin receptor antagonists. A particular pyrrolidine derived orexin-1 selective compound within the scope of WO2003/002559 is disclosed in Langmead et. al, Brit. J. Pharmacol. **2004**, 141, 340-346: 1-(5-(2-fluoro-phenyl)-2-methyl-thiazol-4-yl)-1-[(S)-2-(5-phenyl-[1,3,4]oxadiazol-2-ylmethyl)-pyrrolidin-1-yl)-methanone. The present compounds are different from the compounds disclosed in WO2003/002559 in view of the particular 2-(1,2,3-triazol-2-yl)benzamide and 3-(1,2,3-triazol-2-yl)picolinamide moiety and notably in view of the present particular benzyl substituent in position 3 of the morpholine moiety.

The present invention provides novel 2-(1,2,3-triazol-2-yl)benzamide and 3-(1,2,3-triazol-2-yl)picolinamide derivatives, which are non-peptide antagonists of human orexin receptors, especially the orexin-1 receptor. These compounds are in particular of potential use in the treatment of disorders relating to orexinergic dysfunctions, comprising especially anxiety disorders, addiction disorders, mood disorders, or appetite disorders, as well as cognitive dysfunctions or sleep disorders. The compounds of the present invention may notably be useful to treat mental health diseases or disorders relating to dysfunctions of the orexin 1 receptor.

In one aspect, the invention provides a compound of formula (I)



Formula (I)

wherein

Ar^1 represents a 5- or 6-membered heteroaryl selected from the group consisting of pyrrolyl, pyrazolyl, triazolyl, oxazolyl, thiazolyl, oxadiazolyl, thiophenyl, pyridinyl, pyrimidinyl, pyrazinyl, and pyridazinyl; wherein said heteroaryl is unsubstituted, mono-, or di-substituted, wherein the substituents are independently selected from the group consisting of (C_{1-4})alkyl, (C_{1-4})alkoxy, halogen, cyano, (C_{1-3})fluoroalkyl, and (C_{1-3})fluoroalkoxy;

R^1 represents one optional substituent selected from (C_{1-4})alkyl, (C_{1-4})alkoxy, hydroxy, and halogen;

R^2 represents hydrogen, (C_{1-4})alkyl, (C_{1-4})alkoxy, halogen, or cyano;

R^3 represents hydrogen, (C_{1-4})alkyl, (C_{1-4})alkoxy, (C_{1-3})fluoroalkyl, or halogen;

R^4 represents hydrogen, (C_{1-4})alkyl, (C_{1-3})fluoroalkyl, or halogen;

R^5 represents one optional substituent on any ring carbon atom of the morpholine ring, wherein said substituent independently is methyl or ethyl; and

Q represents C**R^6**; or, in case **R^2** is (C_{1-4})alkyl or (C_{1-4})alkoxy, **Q** represents C**R^6** or N; wherein **R^6** represents hydrogen, fluoro or methyl;

or a pharmaceutically acceptable salt thereof.

In another aspect, the invention provides a pharmaceutical composition comprising, as active principle, one or more compounds of the invention, or a pharmaceutically acceptable salt thereof, and at least one therapeutically inert excipient.

In another aspect, the invention provides a compound of the invention, or a pharmaceutically acceptable salt thereof, for use as a medicament.

In another aspect, the invention provides a compound of the invention, or a pharmaceutically acceptable salt thereof, when used in the prevention or treatment of a disease selected from the group consisting of anxiety disorders, addiction disorders, mood disorders, and appetite disorders.

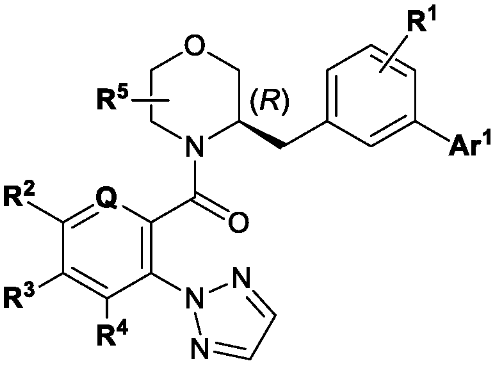
In another aspect, the invention provides use of a compound of the invention, or of a pharmaceutically acceptable salt thereof, in the preparation of a medicament for the prevention or treatment of a disease selected from the group consisting of anxiety disorders, addiction disorders, mood disorders, and appetite disorders.

In another aspect, the invention provides a method of treatment of a disease selected from the group consisting anxiety disorders, addiction disorders, mood disorders, and appetite disorders; comprising administering to a patient an effective amount of a compound of the invention, in free or pharmaceutically acceptable salt form.

In this specification where reference has been made to patent specifications, other external documents, or other sources of information, this is generally for the purpose of providing a context for discussing the features of the invention. Unless specifically stated otherwise, reference to such external documents is not to be construed as an admission that such documents, or such sources of information, in any jurisdiction, are prior art, or form part of the common general knowledge in the art.

The term “comprising” as used in this specification and claims means “consisting at least in part of”. When interpreting statements in this specification and claims which include the term “comprising”, other features besides the features prefaced by this term in each statement can also be present. Related terms such as “comprise” and “comprised” are to be interpreted in similar manner.

1) A first disclosure relates to compounds of the formula (I)



Formula (I)

wherein

Ar^1 represents a 5- or 6-membered heteroaryl selected from the group consisting of pyrrolyl, pyrazolyl, triazolyl, oxazolyl, thiazolyl, oxadiazolyl, thiophenyl, pyridinyl, pyrimidinyl, pyrazinyl, and pyridazinyl; wherein said heteroaryl is unsubstituted, mono-, or di-substituted, wherein the substituents are independently selected from the group consisting of (C_{1-4})alkyl, (C_{1-4})alkoxy, halogen, cyano, (C_{1-3})fluoroalkyl, and (C_{1-3})fluoroalkoxy;

R^1 represents one optional substituent selected from (C_{1-4})alkyl, (C_{1-4})alkoxy, hydroxy, and halogen;

R^2 represents hydrogen, (C_{1-4})alkyl, (C_{1-4})alkoxy, halogen, or cyano;

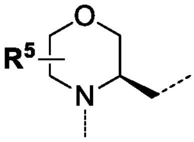
R^3 represents hydrogen, (C_{1-4})alkyl, (C_{1-4})alkoxy, (C_{1-3})fluoroalkyl, or halogen;

R^4 represents hydrogen, (C_{1-4})alkyl, (C_{1-3})fluoroalkyl, or halogen;

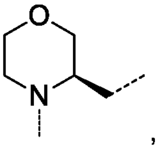
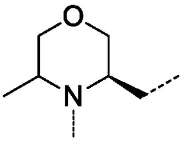
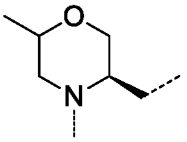
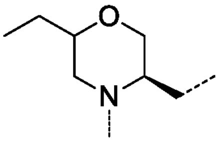
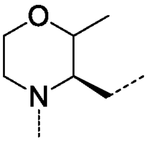
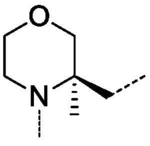
R^5 represents one optional substituent on any ring carbon atom of the morpholine ring, wherein said substituent independently is methyl or ethyl; and

Q represents CR^6; or, in case **R^2** is (C_{1-4})alkyl or (C_{1-4})alkoxy, **Q** represents CR^6 or N; wherein **R^6** represents hydrogen, fluoro or methyl.

2) A second disclosure relates to compounds according to disclosure 1), wherein the morpholine ring of the compounds of formula (I):



is a ring selected from the group consisting of:

, , , , , and ;

Ar^1 represents a 5- or 6-membered heteroaryl selected from the group consisting of pyrrolyl, pyrazolyl, triazolyl, oxazolyl, thiazolyl, oxadiazolyl, thiophenyl, pyridinyl, pyrimidinyl, pyrazinyl, and pyridazinyl; wherein said heteroaryl is unsubstituted or mono-substituted with (C_{1-4})alkyl (especially unsubstituted, or in case said heteroaryl is pyrimidinyl, optionally mono-substituted with methyl);

R^1 represents one optional substituent selected from methyl, methoxy, hydroxy, and halogen;

R^2 represents hydrogen, methyl, methoxy, halogen, or cyano;

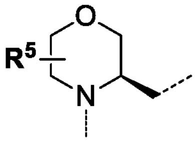
R^3 represents hydrogen, methyl, methoxy, trifluoroalkyl, or halogen;

R^4 represents hydrogen, methyl, trifluoroalkyl, or halogen;

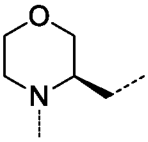
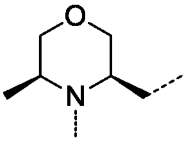
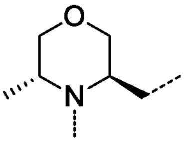
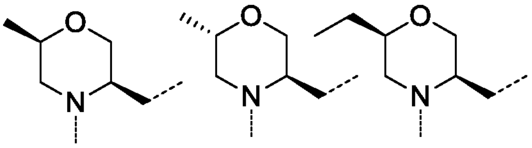
Q represents CR^6; or, in case **R**^{2} is methyl, **Q** represents CR^6 or N; wherein

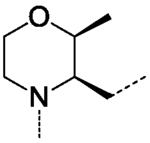
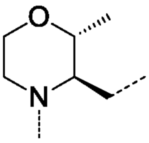
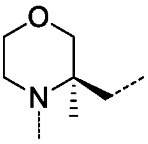
R^6 represents hydrogen, fluoro or methyl.

3) A further disclosure relates to compounds according to disclosures 1) or 2), wherein the morpholine ring of the compounds of formula (I):

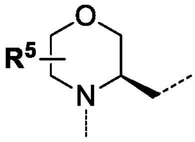


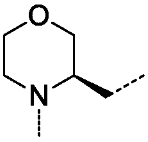
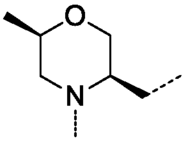
is a ring selected from the group consisting of:

,  , ,

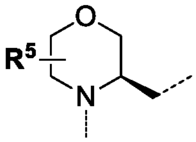
 , and .

4) Another disclosure relates to compounds according to disclosures 1) or 2), wherein the morpholine ring of the compounds of formula (I):

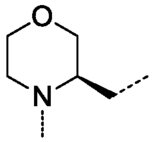


represents , or .

5) A further disclosure relates to compounds according to disclosures 1) or 2), wherein the morpholine ring of the compounds of formula (I):

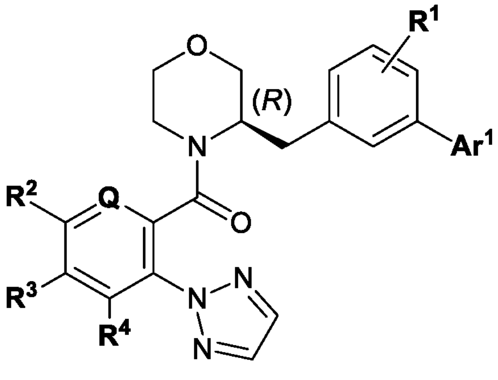


represents



.

6) Another disclosure relates to compounds of formula (I) according to disclosure 1) which are also compounds of the formula (II)



Formula (II)

wherein

Ar^1 represents a 5- or 6-membered heteroaryl selected from the group consisting of pyrrolyl, pyrazolyl, triazolyl, oxazolyl, thiazolyl, oxadiazolyl, thiophenyl, pyridinyl, pyrimidinyl, pyrazinyl, and pyridazinyl; wherein said heteroaryl is unsubstituted, mono-, or di-substituted, wherein the substituents are independently selected from the group consisting of (C_{1-4})alkyl, (C_{1-4})alkoxy, halogen, cyano, (C_{1-3})fluoroalkyl, and (C_{1-3})fluoroalkoxy;

R^1 represents one optional substituent selected from (C_{1-4})alkyl, (C_{1-4})alkoxy, and halogen;

R^2 represents hydrogen, (C_{1-4})alkyl, (C_{1-4})alkoxy, halogen, or cyano;

R^3 represents hydrogen, (C_{1-4})alkyl, (C_{1-4})alkoxy, or halogen;

R^4 represents hydrogen, or halogen;

Q represents CH; or, in case **R^2** is (C_{1-4})alkyl or (C_{1-4})alkoxy, **Q** represents CH, CF or N.

7) Another disclosure relates to compounds according to any one of disclosures 1) to 6), wherein **Ar^1** represents pyrrol-1-yl, pyrazol-1-yl, [1,2,3]triazol-1-yl, [1,2,3]triazol-2-yl, [1,2,4]triazol-1-yl, oxazol-2-yl, thiazol-2-yl, [1,2,4]oxadiazol-3-yl, thiophen-2-yl, pyridin-2-yl, pyridin-3-yl, pyridin-4-yl, pyrimidin-2-yl, pyrazin-2-yl, and pyridazin-3-yl, which groups are unsubstituted or mono-substituted with (C_{1-4})alkyl (especially methyl)).

8) Another disclosure relates to compounds according to any one of disclosures 1) to 6), wherein **Ar**^{1} represents pyrrol-1-yl, pyrazol-1-yl, [1,2,3]triazol-2-yl, oxazol-2-yl, thiophen-2-yl, pyridin-2-yl, pyridin-3-yl, pyrimidin-2-yl, pyrazin-2-yl, and pyridazin-3-yl, which groups are unsubstituted or mono-substituted, wherein the substituents are independently selected from (C$_{1-4}$)alkyl.

9) Another disclosure relates to compounds according to any one of disclosures 1) to 6), wherein **Ar**^{1} represents a 5- or 6-membered heteroaryl selected from the group consisting of pyrrolyl, pyrazolyl, triazolyl, oxadiazolyl, thiophenyl, 2-pyridinyl, pyrimidinyl, pyrazinyl, and pyridazinyl; wherein said heteroaryl is unsubstituted, or in case said heteroaryl is pyrimidinyl, optionally mono-substituted with methyl.

10) Another disclosure relates to compounds according to any one of disclosures 1) to 6), wherein **Ar**^{1} represents a 5- or 6-membered heteroaryl selected from the group consisting of pyrazolyl, triazolyl, oxadiazolyl, and pyrimidinyl; wherein said heteroaryl is unsubstituted, or in case said heteroaryl is pyrimidinyl, optionally mono-substituted with methyl.

11) Another disclosure relates to compounds according to any one of disclosures 1) to 6), wherein **Ar**^{1} represents pyrrol-1-yl, pyrazol-1-yl, [1,2,3]triazol-2-yl, [1,2,4]oxadiazol-3-yl, thiophen-2-yl, pyridin-2-yl, pyrimidin-2-yl, pyrazin-2-yl, and pyridazin-3-yl, which groups are unsubstituted, or in case of pyrimidin-2-yl, optionally mono-substituted with methyl.

12) A preferred disclosure relates to compounds according to any one of disclosures 1) to 6), wherein **Ar**^{1} represents pyrazol-1-yl, [1,2,3]triazol-2-yl, [1,2,4]oxadiazol-3-yl, and pyrimidin-2-yl, which groups are unsubstituted, or in case of pyrimidin-2-yl, optionally mono-substituted with methyl.

13) Another preferred disclosure relates to compounds according to any one of disclosures 1) to 6), wherein **Ar**^{1} represents unsubstituted [1,2,4]oxadiazol-3-yl, or unsubstituted [1,2,3]triazol-2-yl.

14) Another disclosure relates to compounds according to any one of disclosures 1) to 6), wherein **Ar**^{1} represents unsubstituted pyrazol-1-yl, or unsubstituted [1,2,3]triazol-2-yl.

15) Another preferred disclosure relates to compounds according to any one of disclosures 1) to 6), wherein **Ar**^{1} represents unsubstituted [1,2,3]triazol-2-yl.

16) Another disclosure relates to compounds according to any one of disclosures 1) to 15), wherein **R**^{1} is absent, or **R**^{1} represents (C$_{1-4}$)alkoxy (especially methoxy).

17) Another disclosure relates to compounds according to any one of disclosures 1) to 15), wherein **R**^{1} is absent, or **R**^{1} represents methoxy in position 4 of the phenyl ring (i.e. in *para*

position to the point of attachment of the $-CH_2-$ group which links the phenyl ring to the rest of the molecule and *ortho* to the point of attachment of Ar^1).

18) Another disclosure relates to compounds according to any one of disclosures 1) to 15), wherein **R**^{1} is absent; or **R**^{1} represents halogen (especially fluoro or chloro) in position 2 or 3 of the phenyl ring; or **R**^{1} represents methyl in position 2, 3, or 4 of the phenyl ring; or **R**^{1} represents methoxy in position 4 of the phenyl ring [it being understood that the point of attachment of the $-CH_2-$ group which links the phenyl ring to the rest of the molecule is position 1, and the point of attachment of Ar^1 is in position 5 of the phenyl ring].

19) Another disclosure relates to compounds according to any one of disclosures 1) to 15), wherein **R**^{1} is absent, or **R**^{1} represents halogen (especially fluoro or chloro) in position 2 of the phenyl ring (i.e. in *para* position to the point of attachment of Ar^1).

20) Another disclosure relates to compounds according to any one of disclosures 1) to 19), wherein **R**^{2} represents hydrogen, methyl, methoxy, cyano, fluoro, or chloro; **R**^{3} represents hydrogen, methyl, methoxy, or fluoro; **R**^{4} represent hydrogen, or fluoro; and **Q** represents C**R**^{6}; or, in case **R**^{2} is methyl, **Q** represents CH; or, in case **R**^{2} is (C_{1-4})alkyl or (C_{1-4})alkoxy, **Q** represents CH, or N.

21) A preferred disclosure relates to compounds according to any one of disclosures 1) to 5), or 7) to 19); wherein **R**^{2} represents hydrogen, methyl, methoxy, cyano, fluoro, or chloro; **R**^{3} represents hydrogen, methyl, trifluoromethyl, fluoro, or chloro; **R**^{4} represent hydrogen, methyl, trifluoromethyl, or fluoro; and **Q** represents C**R**^{6}; or, in case **R**^{2} is methyl, **Q** represents C**R**^{6} or N; wherein **R**^{6} represents hydrogen, fluoro or methyl.

22) Another disclosure relates to compounds according to any one of disclosures 1) to 19), wherein **R**^{2} represents hydrogen, methyl, methoxy, cyano, fluoro, or chloro.

23) Another disclosure relates to compounds according to any one of disclosures 1) to 19) or 21), wherein **R**^{2} represents hydrogen, fluoro, or chloro.

24) Another disclosure relates to compounds according to any one of disclosures 1) to 5), 7) to 19), 21) or 23), wherein **R**^{3} represents hydrogen, methyl, trifluoromethyl, or chloro.

25) Another disclosure relates to compounds according to any one of disclosures 1) to 19), or 22), wherein **R**^{3} represents hydrogen, methyl, methoxy, or fluoro.

26) Another disclosure relates to compounds according to any one of disclosures 1) to 5), 7) to 19), 21), 23), or 24), wherein **R**^{4} represents hydrogen or methyl.

27) Another disclosure relates to compounds according to any one of disclosures 1) to 19), 22) or 25), wherein **R**^{4} represents hydrogen, or fluoro.

28) Another disclosure relates to compounds according to any one of disclosures 1) to 19), wherein **R**^{2}, **R**^{3} and **R**^{4} represent hydrogen; or **R**^{2} represents methyl, and **R**^{3} and **R**^{4} represent hydrogen; or **R**^{2} represents methoxy, and **R**^{3} and **R**^{4} represent hydrogen; or **R**^{2} represents chloro, and **R**^{3} and **R**^{4} represent hydrogen; or **R**^{3} represents methyl, and **R**^{2} and **R**^{4} represent hydrogen; or **R**^{2} and **R**^{3} represent methyl, and **R**^{4} represents hydrogen; or **R**^{2} represents methoxy, **R**^{3} represents methyl or methoxy, and **R**^{4} represents hydrogen.

29) Another disclosure relates to compounds according to any one of disclosures 1) to 28), wherein **Q** represents CH; or, in case **R**^{2} is (C_{1-4})alkyl or (C_{1-4})alkoxy, **Q** represents CH, or N.

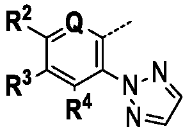
30) Another disclosure relates to compounds according to any one of disclosures 1) to 28), wherein **R**^{2} is methyl and **Q** represents N.

31) Another disclosure relates to compounds according to any one of disclosures 1) to 5), 7) to 19), 21), 23), 24), or 26), wherein **Q** represents C**R**^{6}; wherein **R**^{6} represents hydrogen, fluoro or methyl.

32) A preferred disclosure relates to compounds according to any one of disclosures 1) to 28), wherein **Q** represents CH.

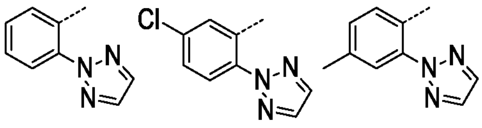
33) Another preferred disclosure relates to compounds according to any one of disclosures 1) to 5), or 7) to 19), wherein **R**^{2} represents hydrogen or chloro; **R**^{3} represents hydrogen, chloro, methyl or trifluoromethyl, **R**^{4} represent hydrogen or methyl; and **Q** represents CH.

34) Another preferred disclosure relates to compounds according to any one of the disclosures 1) to 5), or 7) to 19), wherein the group



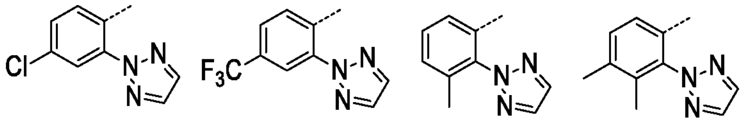
is a group independently selected from the following groups A) to F):

A)



;

B)



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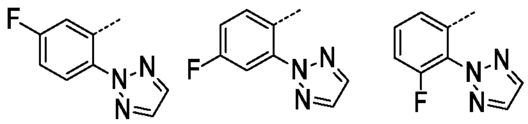
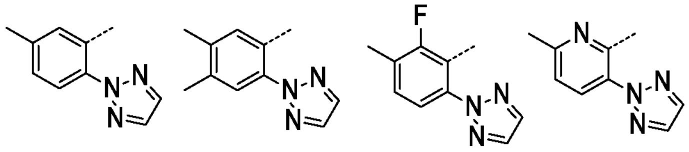
C)



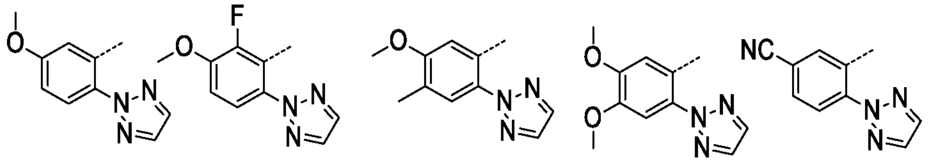
;

D)



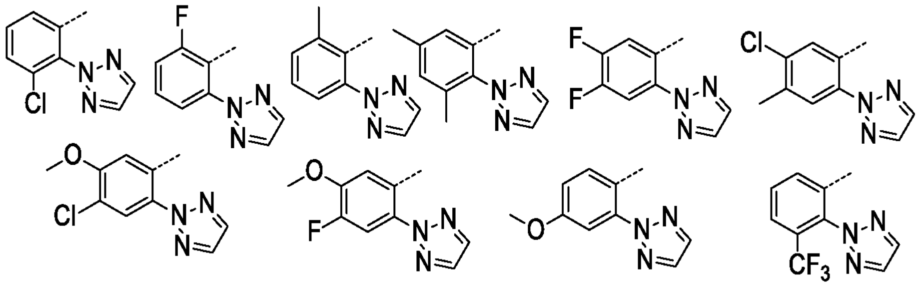
;

E)



;

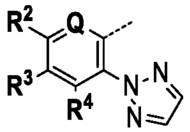
F)



;

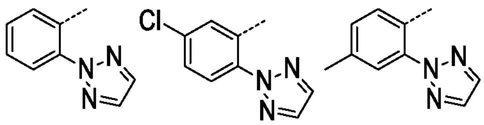
wherein each of the above groups A) to F) form a particular sub-disclosure.

35) Another preferred disclosure relates to compounds according to any one of the disclosures 1) to 5), or 7) to 19), wherein the group



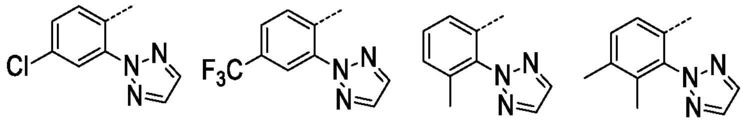
is a group selected from the group consisting of the following groups A) and B):

A)



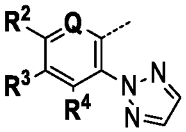
;

B)

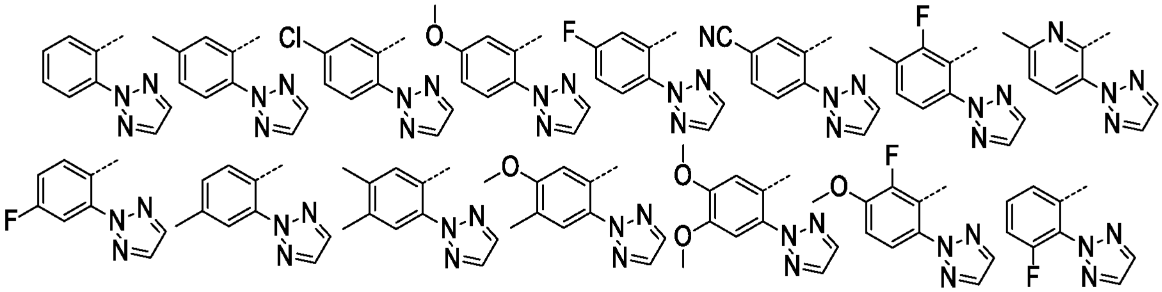


;

wherein the groups A) and B) each form a particular sub-disclosure36) Another disclosure relates to compounds according to any one of the disclosures 1) to 19) wherein the group

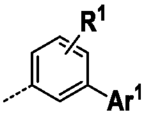


is a group selected from the group consisting of:



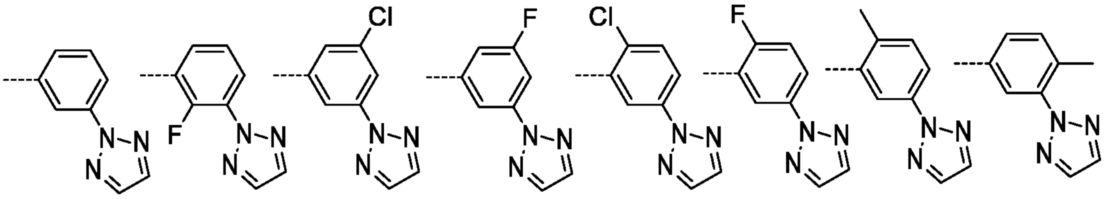
.

37) Another disclosure relates to compounds according to any one of the disclosures 1) to 5), or 20) to 36), wherein the group



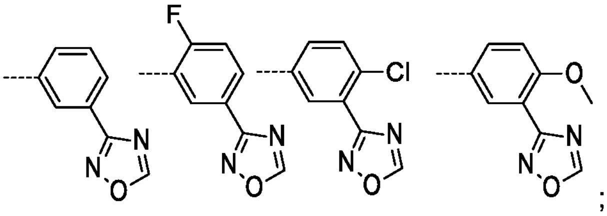
is a group independently selected from the following groups A) to H):

A)



;

B)



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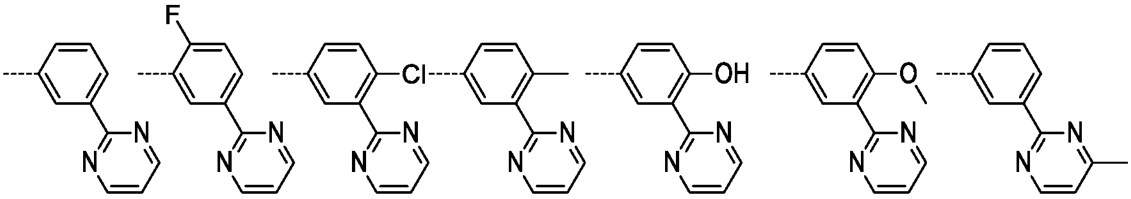
C)



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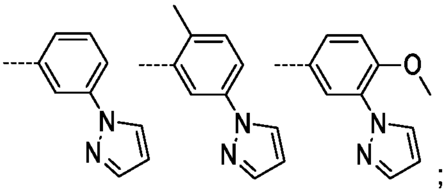
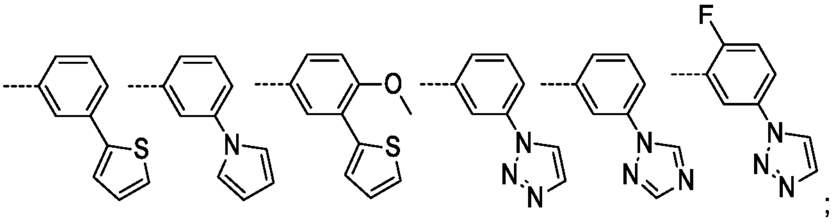
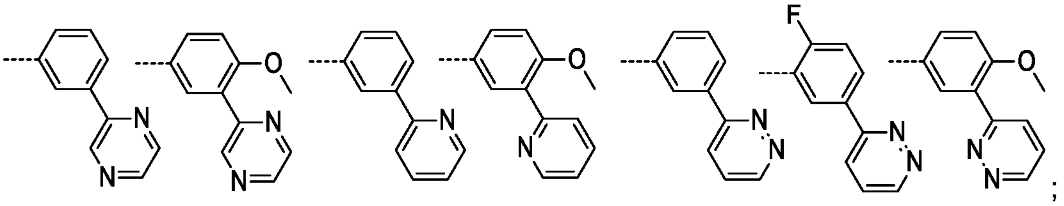
D)



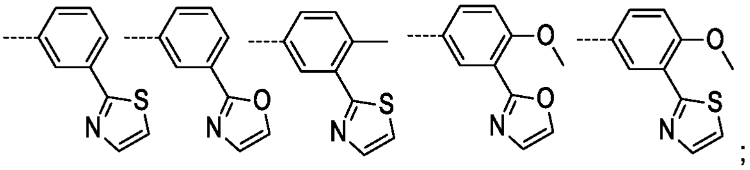
E)



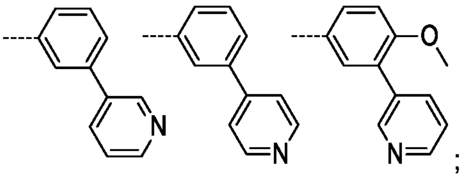
F)



G)

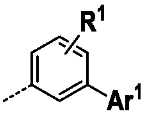


H)



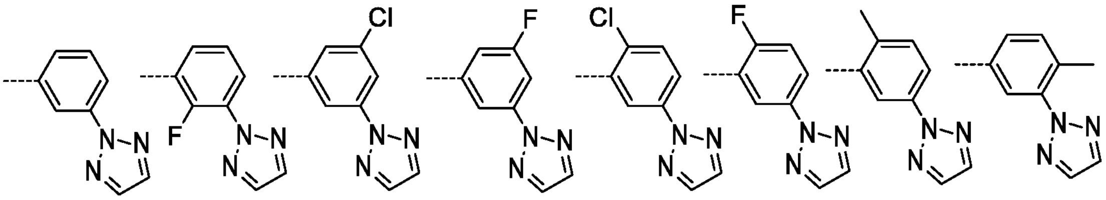
wherein the groups A) to F), and especially the groups A) to D), each form a preferred sub-disclosure.

38) Another disclosure relates to compounds according to any one of the disclosures 1) to 6), or 20) to 36), wherein the group



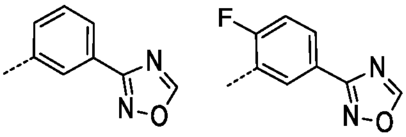
is a group independently selected from the group consisting of any one the following groups A), B) and C):

A)



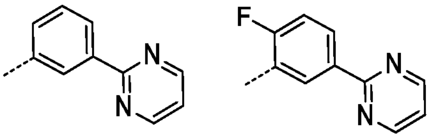
;

B)



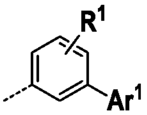
;

C)



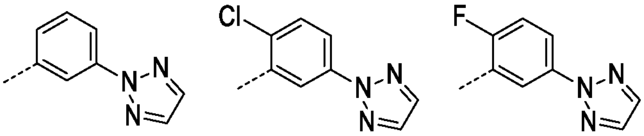
.

39) A preferred disclosure relates to compounds according to any one of the disclosures 1) to 6), or 20) to 36), wherein the group



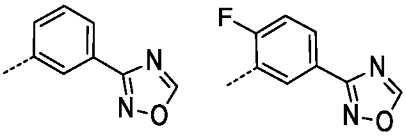
is a group independently selected from the group consisting of any one the following groups A), B) and C):

A)



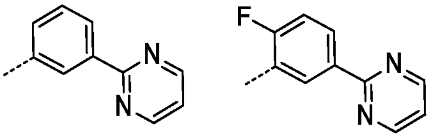
;

B)



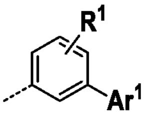
;

C)



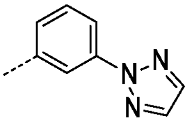
.

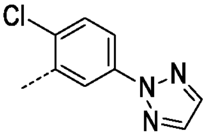
40) Another preferred disclosure relates to compounds according to any one of the disclosures 1) to 6), or 20) to 36), wherein the group

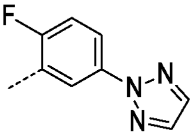


is a group selected from the group consisting of the following groups A) and B):

A)

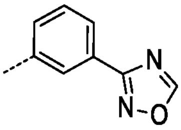


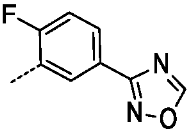




; and

B)





.

41) Herein described are compounds of the formula (I) as defined in disclosure 1), compounds of the formula (II) as defined in disclosure 6); or such compounds further limited by the characteristics of any one of disclosures 2) to 40), under consideration of their respective dependencies; pharmaceutically acceptable salts thereof; and the use of such compounds as medicaments especially in the treatment of mental health disorders relating to orexinergic dysfunctions, which disorders are as defined below and which are especially selected from anxiety disorders, addiction disorders, mood disorders, and appetite disorders. For avoidance of any doubt, especially the following disclosures relating to the compounds of formula (I) and (II) are thus possible and intended and herewith specifically disclosed in individualized form:

2+1, 5+1, 7+1, 7+2+1, 7+5+1, 12+1, 12+2+1, 12+5+1, 13+1, 13+2+1, 13+5+1, 15+1, 15+2+1, 15+5+1, 19+1, 19+2+1, 19+5+1, 19+7+1, 19+7+2+1, 19+7+5+1, 19+12+1, 19+12+2+1, 19+12+5+1, 19+13+1, 19+13+2+1, 19+13+5+1, 19+15+1, 19+15+2+1, 19+15+5+1, 21+1, 21+2+1, 21+5+1, 21+7+1, 21+7+2+1, 21+7+5+1, 21+12+1, 21+12+2+1, 21+12+5+1, 21+13+1, 21+13+2+1, 21+13+5+1, 21+15+1, 21+15+2+1, 21+15+5+1, 21+19+1, 21+19+2+1, 21+19+5+1, 21+19+7+1, 21+19+7+2+1, 21+19+7+5+1, 21+19+12+1, 21+19+12+2+1, 21+19+12+5+1, 21+19+13+1, 21+19+13+2+1, 21+19+13+5+1, 21+19+15+1, 21+19+15+2+1, 21+19+15+5+1, 32+1, 32+2+1, 32+5+1, 32+7+1, 32+7+2+1, 32+7+5+1, 32+12+1, 32+12+2+1, 32+12+5+1, 32+13+1, 32+13+2+1, 32+13+5+1, 32+15+1, 32+15+2+1, 32+15+5+1, 32+19+1, 32+19+2+1, 32+19+5+1, 32+19+7+1, 32+19+7+2+1, 32+19+7+5+1, 32+19+12+1, 32+19+12+2+1, 32+19+12+5+1, 32+19+13+1, 32+19+13+2+1, 32+19+13+5+1, 32+19+15+1, 32+19+15+2+1, 32+19+15+5+1, 32+21+1, 32+21+2+1, 32+21+5+1, 32+21+7+1, 32+21+7+2+1, 32+21+7+5+1, 32+21+12+1, 32+21+12+2+1, 32+21+12+5+1, 32+21+13+1, 32+21+13+2+1, 32+21+13+5+1, 32+21+15+1, 32+21+15+2+1, 32+21+15+5+1, 32+21+19+1, 32+21+19+2+1, 32+21+19+5+1, 32+21+19+7+1, 32+21+19+7+2+1, 32+21+19+7+5+1, 32+21+19+12+1, 32+21+19+12+2+1, 32+21+19+12+5+1, 32+21+19+13+1, 32+21+19+13+2+1, 32+21+19+13+5+1, 32+21+19+15+1, 32+21+19+15+2+1, 32+21+19+15+5+1, 33+1, 33+2+1, 33+5+1, 33+7+1, 33+7+2+1, 33+7+5+1, 33+12+1, 33+12+2+1, 33+12+5+1, 33+13+1, 33+13+2+1, 33+13+5+1, 33+15+1, 33+15+2+1, 33+15+5+1, 33+19+1, 33+19+2+1, 33+19+5+1, 33+19+7+1, 33+19+7+2+1, 33+19+7+5+1, 33+19+12+1, 33+19+12+2+1, 33+19+12+5+1, 33+19+13+1, 33+19+13+2+1, 33+19+13+5+1, 33+19+15+1, 33+19+15+2+1, 33+19+15+5+1, 34+1, 34+2+1, 34+5+1, 34+7+1, 34+7+2+1, 34+7+5+1, 34+12+1, 34+12+2+1, 34+12+5+1, 34+13+1, 34+13+2+1, 34+13+5+1, 34+15+1, 34+15+2+1, 34+15+5+1, 34+19+1, 34+19+2+1, 34+19+5+1, 34+19+7+1, 34+19+7+2+1, 34+19+7+5+1, 34+19+12+1, 34+19+12+2+1, 34+19+12+5+1, 34+19+13+1, 34+19+13+2+1, 34+19+13+5+1, 34+19+15+1, 34+19+15+2+1, 34+19+15+5+1, 35+1, 35+2+1, 35+5+1, 35+7+1, 35+7+2+1, 35+7+5+1, 35+12+1, 35+12+2+1, 35+12+5+1, 35+13+1, 35+13+2+1, 35+13+5+1, 35+15+1, 35+15+2+1, 35+15+5+1, 35+19+1, 35+19+2+1, 35+19+5+1, 35+19+7+1, 35+19+7+2+1, 35+19+7+5+1, 35+19+12+1, 35+19+12+2+1, 35+19+12+5+1, 35+19+13+1, 35+19+13+2+1, 35+19+13+5+1, 35+19+15+1, 35+19+15+2+1, 35+19+15+5+1;

37+1, 37+2+1, 37+5+1, 37+21+1, 37+21+2+1, 37+21+5+1, 37+32+1, 37+32+2+1, 37+32+5+1, 37+33+1, 37+33+2+1, 37+33+5+1, 37+34+1, 37+34+2+1, 37+34+5+1, 37+35+1, 37+35+2+1, 37+35+5+1, 38+1, 38+2+1, 38+5+1, 38+21+1, 38+21+2+1, 38+21+5+1, 38+32+1, 38+32+2+1, 38+32+5+1, 38+33+1, 38+33+2+1, 38+33+5+1, 38+34+1, 38+34+2+1, 38+34+5+1, 38+35+1, 38+35+2+1, 38+35+5+1, 40+1, 40+2+1, 40+5+1, 40+21+1, 40+21+2+1, 40+21+5+1, 40+32+1, 40+32+2+1, 40+32+5+1, 40+33+1, 40+33+2+1, 40+33+5+1, 40+34+1, 40+34+2+1, 40+34+5+1, 40+35+1, 40+35+2+1, 40+35+5+1;

6+1, 7+6+1, 14+6+1, 20+6+1, 20+7+6+1, 20+14+6+1, 22+6+1, 22+7+6+1, 22+14+6+1, 25+6+1, 25+7+6+1, 25+14+6+1, 25+22+6+1, 25+22+7+6+1, 25+22+14+6+1, 27+6+1, 27+7+6+1, 27+14+6+1, 27+22+6+1, 27+22+7+6+1, 27+22+14+6+1, 27+25+6+1, 27+25+7+6+1, 27+25+14+6+1, 27+25+22+6+1, 27+25+22+7+6+1, 27+25+22+14+6+1, 28+6+1, 28+7+6+1, 28+14+6+1, 32+6+1, 32+7+6+1, 32+14+6+1, 32+22+6+1, 32+22+7+6+1, 32+22+14+6+1, 32+25+6+1, 32+25+7+6+1, 32+25+14+6+1, 32+25+22+6+1, 32+25+22+7+6+1, 32+25+22+14+6+1, 32+27+6+1, 32+27+7+6+1, 32+27+14+6+1, 32+27+22+6+1, 32+27+22+7+6+1, 32+27+22+14+6+1, 32+27+25+6+1, 32+27+25+7+6+1, 32+27+25+14+6+1, 32+27+25+22+6+1, 32+27+25+22+7+6+1, 32+27+25+22+14+6+1, 32+28+6+1, 32+28+7+6+1, 32+28+14+6+1, 36+6+1, 36+7+6+1, 36+14+6+1.

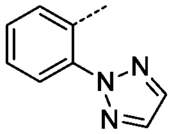
In the list above the numbers refer to the disclosures according to their numbering provided hereinabove whereas "+" indicates the dependency from another disclosure. The different individualized disclosures are separated by commas. In other words, "40+35+5+1" for example refers to disclosure 40) depending on disclosure 35), depending on disclosure 5), depending on disclosure 1), i.e. disclosure "40+35+5+1" corresponds to the compounds of disclosure 1) further limited by all the features of the disclosures 5), 35), and 40).

The compounds of formula (I) and (II) contain at least one stereogenic center which is situated in position 3 of the morpholine moiety. It is understood that the absolute configuration of said chiral center is as depicted in formula (I) and (II), i.e. it is in absolute (*R*) configuration.

In addition, the compounds of formula (I) (especially compounds of formula (I) in case R^5 is other than hydrogen) and (II) may contain one or more stereogenic or asymmetric centers, such as one or more asymmetric carbon atoms. The compounds of formula (I) and (II) may thus be present as mixtures of stereoisomers or preferably as pure stereoisomers. Mixtures of stereoisomers may be separated in a manner known to a person skilled in the art.

The present invention also includes isotopically labelled, especially ^2H (deuterium) labelled compounds of formula (I) and (II), which compounds are identical to the compounds of formula (I) and (II) except that one or more atoms have each been replaced by an atom having the same atomic number but an atomic mass different from the atomic mass usually found in nature. Isotopically labelled, especially ^2H (deuterium) labelled compounds of formula (I) and (II) and salts thereof are within the scope of the present invention. Substitution of hydrogen with the heavier isotope ^2H (deuterium) may lead to greater metabolic stability, resulting e.g. in increased *in-vivo* half-life or reduced dosage requirements, or may lead to reduced inhibition of cytochrome P450 enzymes, resulting e.g. in an improved safety profile. In one embodiment of the invention, the compounds of formula (I) and (II) are not isotopically labelled, or they are labelled only with one or more deuterium atoms. In a sub-embodiment, the compounds of formula (I) and (II) are not isotopically labelled at all. Isotopically labelled compounds of formula (I) and (II) may be prepared in analogy to the methods described hereinafter, but using the appropriate isotopic variation of suitable reagents or starting materials.

In this patent application, a dotted line shows the point of attachment of the radical drawn. For example, the radical drawn below



represents a 2-([1,2,3]triazol-2-yl)-phenyl group.

Where the plural form is used for compounds, salts, pharmaceutical compositions, diseases and the like, this is intended to mean also a single compound, salt, or the like.

Any reference to compounds of formula (I) or (II) is to be understood as referring also to the salts (and especially the pharmaceutically acceptable salts) of such compounds, as appropriate and expedient.

The term "pharmaceutically acceptable salts" refers to non-toxic, inorg. or organic acid and/or base addition salts. Reference can be made to "Salt selection for basic drugs", *Int. J. Pharm.* (1986), **33**, 201-217.

Definitions provided herein are intended to apply uniformly to the compounds of formula (I) and (II) as defined in any one of disclosures 1) to 41), and, *mutatis mutandis*, throughout the description and the claims unless an otherwise expressly set out definition provides a broader or narrower definition. It is well understood that a definition or preferred definition of a term defines and may replace the respective term independently of (and in combination with) any definition or preferred definition of any or all other terms as defined herein.

The term “halogen” means fluorine, chlorine, or bromine, preferably fluorine or chlorine.

The term “alkyl”, used alone or in combination, refers to a saturated straight or branched chain alkyl group containing one to six carbon atoms. The term “(C_{x-y})alkyl” (x and y each being an integer), refers to an alkyl group as defined before, containing x to y carbon atoms. For example a (C_{1-4})alkyl group contains from one to four carbon atoms. Examples of alkyl groups are methyl, ethyl, propyl, isopropyl, n-butyl, isobutyl, sec.-butyl and tert.-butyl. Preferred are methyl and ethyl. Most preferred is methyl.

The term “alkoxy”, used alone or in combination, refers to an alkyl-O- group wherein the alkyl group is as defined before. The term “(C_{x-y})alkoxy” (x and y each being an integer) refers to an alkoxy group as defined before containing x to y carbon atoms. For example a (C_{1-4})alkoxy group means a group of the formula (C_{1-4})alkyl-O- in which the term “(C_{1-4})alkyl” has the previously given significance. Examples of alkoxy groups are methoxy, ethoxy, n-propoxy, isopropoxy, n-butoxy, isobutoxy, sec.-butoxy and tert.-butoxy. Preferred are ethoxy and especially methoxy.

The term "fluoroalkyl” refers to an alkyl group as defined before containing one to three carbon atoms in which one or more (and possibly all) hydrogen atoms have been replaced with fluorine. The term “(C_{x-y})fluoroalkyl” (x and y each being an integer) refers to a fluoroalkyl group as defined before containing x to y carbon atoms. For example a (C_{1-3})fluoroalkyl group contains from one to three carbon atoms in which one to seven hydrogen atoms have been replaced with fluorine. Representative examples of fluoroalkyl groups include trifluoromethyl, 2-fluoroethyl, 2,2-difluoroethyl and 2,2,2-trifluoroethyl. Preferred are (C_1)fluoroalkyl groups such as trifluoromethyl.

The term "fluoroalkoxy" refers to an alkoxy group as defined before containing one to three carbon atoms in which one or more (and possibly all) hydrogen atoms have been replaced with fluorine. The term "(C_{x-y})fluoroalkoxy" (x and y each being an integer) refers to a fluoroalkoxy group as defined before containing x to y carbon atoms. For example a (C_{1-3})fluoroalkoxy group contains from one to three carbon atoms in which one to seven hydrogen atoms have been replaced with fluorine. Representative examples of fluoroalkoxy groups include trifluoromethoxy, difluoromethoxy, 2-fluoroethoxy, 2,2-difluoroethoxy and 2,2,2-trifluoroethoxy. Preferred are (C_1)fluoroalkoxy groups such as trifluoromethoxy and difluoromethoxy.

Particular examples of **Ar^1** representing a
"5- or 6-membered heteroaryl selected from the group consisting of pyrrolyl, pyrazolyl, triazolyl, oxazolyl, thiazolyl, oxadiazolyl, thiophenyl, pyridinyl, pyrimidinyl, pyrazinyl, and pyridazinyl; wherein said heteroaryl is unsubstituted, mono-, or di-substituted, wherein the substituents are independently selected from the group consisting of (C_{1-4})alkyl, (C_{1-4})alkoxy, halogen, cyano, (C_{1-3})fluoroalkyl, and (C_{1-3})fluoroalkoxy"
are notably pyrrolyl (in particular pyrrol-1-yl), pyrazolyl (in particular pyrazol-1-yl), triazolyl (in particular [1,2,3]triazol-1-yl, [1,2,3]triazol-2-yl, [1,2,4]triazol-1-yl), oxazolyl (in particular oxazol-2-yl), thiazolyl (in particular thiazol-2-yl), oxadiazolyl (in particular [1,2,4]oxadiazol-3-yl), thiophenyl (in particular thiophen-2-yl), pyridinyl (in particular pyridin-2-yl, pyridin-3-yl, pyridin-4-yl), pyrimidinyl (in particular pyrimidin-2-yl), pyrazinyl (in particular pyrazin-2-yl), and pyridazinyl (in particular pyridazin-3-yl). In a sub-disclosure, particular examples are pyrrol-1-yl, pyrazol-1-yl, [1,2,3]triazol-2-yl, oxazol-2-yl, thiophen-2-yl, pyridin-2-yl, pyridin-3-yl, pyrimidin-2-yl, pyrazin-2-yl, and pyridazin-3-yl. In a further sub-disclosure, particular examples are pyrazol-1-yl, and especially [1,2,3]triazol-2-yl. The above mentioned groups may be unsubstituted or substituted as explicitly defined. Notably, they are unsubstituted, mono-, or di-substituted, wherein the substituents are independently selected from (C_{1-4})alkyl. In a sub-disclosure, the above mentioned groups are unsubstituted or mono-substituted with (C_{1-4})alkyl (especially methyl). In a further sub-disclosure, the above mentioned groups are unsubstituted, or, in the case of pyrimidinyl groups, unsubstituted or mono-substituted with (C_{1-4})alkyl (especially methyl).

42) A further disclosure relates to particular compounds of formula (I) according to disclosure 1) which are selected from the following compounds:

[(R)-3-(3-[1,2,4]Oxadiazol-3-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone;

(5-Methyl-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-[1,2,4]oxadiazol-3-yl-benzyl)-morpholin-4-yl]-methanone;

[(R)-3-(4-Methoxy-3-pyridin-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(R)-3-(4-Methoxy-3-pyridin-3-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(R)-3-(4-Methoxy-3-pyrimidin-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone;
[(R)-3-(4-Methoxy-3-pyrazin-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone;
[(R)-3-(4-Methoxy-3-pyridazin-3-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone;
[(R)-3-(4-Methoxy-3-thiazol-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone;
[(R)-3-(4-Methoxy-3-oxazol-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone;
[(R)-3-(4-Methoxy-3-thiophen-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone;
(5-Methyl-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone;
[(R)-3-(3-[1,2,3]Triazol-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone;
[(S)-3-(3-[1,2,3]Triazol-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone;
[(R)-3-(4-Methoxy-3-pyrazol-1-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone;
(5-Methyl-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-[1,2,3]triazol-1-yl-benzyl)-morpholin-4-yl]-methanone;
[(R)-3-(3-Pyrazol-1-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone;
(5-Methyl-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-pyrimidin-2-yl-benzyl)-morpholin-4-yl]-methanone;
[(R)-3-(3-Pyrimidin-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone;
(5-Methyl-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-pyrazol-1-yl-benzyl)-morpholin-4-yl]-methanone;
(5-Fluoro-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-pyrazol-1-yl-benzyl)-morpholin-4-yl]-methanone;
(2-Fluoro-3-methyl-6-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-pyrazol-1-yl-benzyl)-morpholin-4-yl]-methanone;
(4-Methyl-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-pyrazol-1-yl-benzyl)-morpholin-4-yl]-methanone;
(5-Methyl-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-[1,2,4]triazol-1-yl-benzyl)-morpholin-4-yl]-methanone;
(5-Methyl-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-pyridin-2-yl-benzyl)-morpholin-4-yl]-methanone;
(5-Methyl-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-pyridin-3-yl-benzyl)-morpholin-4-yl]-methanone;
(5-Fluoro-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone;
(4-Methyl-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone;
(5-Methyl-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-pyridin-4-yl-benzyl)-morpholin-4-yl]-methanone;
(2-Fluoro-3-methyl-6-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone;
(5-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone;
4-[1,2,3]Triazol-2-yl-3-[(R)-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholine-4-carbonyl]-benzonitrile;
(5-Methoxy-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone;
(2-Fluoro-3-methoxy-6-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone;
(4,5-Dimethoxy-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone;
(4,5-Dimethyl-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone;
(4-Fluoro-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone;
(5-Methoxy-4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone;
(5-Methyl-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-pyrrol-1-yl-benzyl)-morpholin-4-yl]-methanone;
{(R)-3-[3-(4-Methyl-pyrimidin-2-yl)-benzyl]-morpholin-4-yl}-(5-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;
{(R)-3-[3-(4-Methyl-pyrimidin-2-yl)-benzyl]-morpholin-4-yl}-(2-[1,2,3]triazol-2-yl-phenyl)-methanone;

(5-Methyl-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-pyrazin-2-yl-benzyl)-morpholin-4-yl]-methanone;
[(R)-3-(3-Oxazol-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone;
(5-Methyl-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-thiazol-2-yl-benzyl)-morpholin-4-yl]-methanone;
[(R)-3-(3-Thiazol-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone;
(5-Methyl-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-thiophen-2-yl-benzyl)-morpholin-4-yl]-methanone;
[(R)-3-(3-Thiophen-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone;
(5-Methyl-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-pyridazin-3-yl-benzyl)-morpholin-4-yl]-methanone;
[(R)-3-(3-Pyridazin-3-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone;
(2-Fluoro-3-methyl-6-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-pyrimidin-2-yl-benzyl)-morpholin-4-yl]-methanone;
(5-Methoxy-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-pyrimidin-2-yl-benzyl)-morpholin-4-yl]-methanone;
(5-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-pyrimidin-2-yl-benzyl)-morpholin-4-yl]-methanone;
(6-Methyl-3-[1,2,3]triazol-2-yl-pyridin-2-yl)-[(R)-3-(3-pyrazol-1-yl-benzyl)-morpholin-4-yl]-methanone;
(6-Methyl-3-[1,2,3]triazol-2-yl-pyridin-2-yl)-[(R)-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone; and
(3-Fluoro-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone.

43) In addition to the above-listed compounds, further particular compounds of formula (I) according to disclosure 1) are selected from the group consisting of:

[(R)-3-(4-Hydroxy-3-pyrimidin-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone;
[(R)-3-(2-Fluoro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(5-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;
[(R)-3-(2-Fluoro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone;
[(R)-3-(4-Methoxy-3-[1,2,4]oxadiazol-3-yl-benzyl)-morpholin-4-yl]-(5-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;
[(R)-3-(4-Methoxy-3-[1,2,4]oxadiazol-3-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone;
[(R)-3-(4-Methoxy-3-[1,2,4]oxadiazol-3-yl-benzyl)-morpholin-4-yl]-(4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;
(4-Fluoro-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(4-methoxy-3-[1,2,4]oxadiazol-3-yl-benzyl)-morpholin-4-yl]-methanone;
[(R)-3-(2-Fluoro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;
[(R)-3-(4-Methoxy-3-[1,2,4]oxadiazol-3-yl-benzyl)-morpholin-4-yl]-(2-methyl-6-[1,2,3]triazol-2-yl-phenyl)-methanone;
(3-Methyl-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone;
[(R)-3-(4-Methyl-3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(5-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;
[(R)-3-(4-Methyl-3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone;
[(R)-3-(4-Methyl-3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;
[(3R,5R)-3-Methyl-5-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone;
[(3R,5R)-3-Methyl-5-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(3R,5R)-3-Methyl-5-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(3-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(3S,5R)-3-Methyl-5-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(3S,5R)-3-Methyl-5-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(3-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(3S,5R)-3-Methyl-5-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(5-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

(4,5-Dimethyl-2-[1,2,3]triazol-2-yl-phenyl)-[(3S,5R)-3-methyl-5-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone;

(3,5-Dimethyl-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone;

[(R)-3-(3-[1,2,3]Triazol-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-4-trifluoromethyl-phenyl)-methanone;

(4-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone;

(4-Fluoro-5-methoxy-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone;

(4,5-Dimethyl-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(4-methyl-3-[1,2,4]oxadiazol-3-yl-benzyl)-morpholin-4-yl]-methanone;

(4,5-Difluoro-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-[1,2,4]oxadiazol-3-yl-benzyl)-morpholin-4-yl]-methanone;

(4-Methyl-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-[1,2,4]oxadiazol-3-yl-benzyl)-morpholin-4-yl]-methanone;

(3-Fluoro-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-[1,2,4]oxadiazol-3-yl-benzyl)-morpholin-4-yl]-methanone;

(3-Methyl-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-[1,2,4]oxadiazol-3-yl-benzyl)-morpholin-4-yl]-methanone;

(5-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-[1,2,4]oxadiazol-3-yl-benzyl)-morpholin-4-yl]-methanone;

(4,5-Dimethyl-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-[1,2,4]oxadiazol-3-yl-benzyl)-morpholin-4-yl]-methanone;

(4-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-[1,2,4]oxadiazol-3-yl-benzyl)-morpholin-4-yl]-methanone;

[(R)-3-(3-[1,2,4]Oxadiazol-3-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-4-trifluoromethyl-phenyl)-methanone;

(5-Fluoro-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-[1,2,4]oxadiazol-3-yl-benzyl)-morpholin-4-yl]-methanone;

(3,5-Dimethyl-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-[1,2,4]oxadiazol-3-yl-benzyl)-morpholin-4-yl]-methanone;

[(R)-3-(4-Chloro-3-[1,2,4]oxadiazol-3-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone;

(4,5-Difluoro-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone;

(3,4-Dimethyl-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone;

(4-Methoxy-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone;

(3,4-Dimethyl-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(2-fluoro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone;

[(R)-3-(2-Fluoro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(4-methoxy-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(2S,5R)-2-Methyl-5-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(2R,5R)-2-Methyl-5-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(3-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

(4,5-Dimethyl-2-[1,2,3]triazol-2-yl-phenyl)-[(2R,5R)-2-methyl-5-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone;

(3,4-Dimethyl-2-[1,2,3]triazol-2-yl-phenyl)-[(2R,5R)-2-methyl-5-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone;

[(2R,5R)-2-Methyl-5-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(2R,5R)-2-Methyl-5-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(R)-3-Methyl-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(5-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

(5-Chloro-4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone;

(4-Chloro-5-methoxy-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone;

[(R)-3-(3-Chloro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(R)-3-(3-Chloro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(3-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

(3-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone;

[(2R,5R)-2-Methyl-5-(3-pyrimidin-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(2R,5R)-2-Methyl-5-(3-pyrimidin-2-yl-benzyl)-morpholin-4-yl]-(5-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(2R,5R)-2-Methyl-5-(3-pyrimidin-2-yl-benzyl)-morpholin-4-yl]-(4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(2R,5R)-2-Methyl-5-(3-pyrimidin-2-yl-benzyl)-morpholin-4-yl]-(3-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

(3,4-Dimethyl-2-[1,2,3]triazol-2-yl-phenyl)-[(2R,5R)-2-methyl-5-(3-pyrimidin-2-yl-benzyl)-morpholin-4-yl]-methanone;

(5-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[(2R,5R)-2-methyl-5-(3-pyrimidin-2-yl-benzyl)-morpholin-4-yl]-methanone;

(4-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[(2R,5R)-2-methyl-5-(3-pyrimidin-2-yl-benzyl)-morpholin-4-yl]-methanone;

[(2R,5R)-5-(2-Fluoro-5-[1,2,3]triazol-2-yl-benzyl)-2-methyl-morpholin-4-yl]-(5-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(2R,5R)-5-(2-Fluoro-5-[1,2,3]triazol-2-yl-benzyl)-2-methyl-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(2R,5R)-5-(2-Fluoro-5-[1,2,3]triazol-2-yl-benzyl)-2-methyl-morpholin-4-yl]-(4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(2R,5R)-5-(2-Fluoro-5-[1,2,3]triazol-2-yl-benzyl)-2-methyl-morpholin-4-yl]-(3-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(R)-3-(2-Methyl-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(5-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(R)-3-(2-Chloro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(R)-3-(2-Methyl-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(R)-3-(2-Chloro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(3-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(R)-3-(2-Methyl-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(R)-3-(2-Methyl-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(3-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(R)-3-(2-Chloro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(5-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(R)-3-(2-Chloro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(R)-3-(2-Fluoro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(3-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

(4,5-Dimethyl-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(2-fluoro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone;

(5-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(2-fluoro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone;

(4-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(2-fluoro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone;

[(R)-3-(2-Fluoro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(5-methoxy-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

(2-Fluoro-3-methyl-6-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(2-fluoro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone;

(2-Fluoro-3-methoxy-6-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(2-fluoro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone;

[(R)-3-(2-Fluoro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(5-methoxy-4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

(3-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(2-fluoro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone;

[(R)-3-(2-Fluoro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(2-fluoro-6-[1,2,3]triazol-2-yl-phenyl)-methanone;

(4,5-Difluoro-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(2-fluoro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone;

[(R)-3-(2-Fluoro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-4-trifluoromethyl-phenyl)-methanone;

(4-Chloro-5-methoxy-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(2-fluoro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone;

[(2R,5R)-5-(2-Fluoro-5-[1,2,3]triazol-1-yl-benzyl)-2-methyl-morpholin-4-yl]-(5-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(2R,5R)-5-(2-Fluoro-5-[1,2,3]triazol-1-yl-benzyl)-2-methyl-morpholin-4-yl]-(4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(2R,5R)-2-Ethyl-5-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(5-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(2R,5R)-2-Ethyl-5-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(2R,5R)-2-Ethyl-5-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(R)-3-(3-Fluoro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(R)-3-(3-Fluoro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(2R,5R)-5-(2-Fluoro-5-pyrimidin-2-yl-benzyl)-2-methyl-morpholin-4-yl]-(5-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(2R,5R)-5-(2-Fluoro-5-pyrimidin-2-yl-benzyl)-2-methyl-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(2R,5R)-5-(2-Fluoro-5-pyrimidin-2-yl-benzyl)-2-methyl-morpholin-4-yl]-(4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(2R,5R)-5-(2-Fluoro-5-pyrimidin-2-yl-benzyl)-2-methyl-morpholin-4-yl]-(3-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

(3,4-Dimethyl-2-[1,2,3]triazol-2-yl-phenyl)-[(2R,5R)-5-(2-fluoro-5-pyrimidin-2-yl-benzyl)-2-methyl-morpholin-4-yl]-methanone;

(5-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[(2R,5R)-5-(2-fluoro-5-pyrimidin-2-yl-benzyl)-2-methyl-morpholin-4-yl]-methanone;

(4-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[(2R,5R)-5-(2-fluoro-5-pyrimidin-2-yl-benzyl)-2-methyl-morpholin-4-yl]-methanone;

(3-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[(2R,5R)-5-(2-fluoro-5-pyrimidin-2-yl-benzyl)-2-methyl-morpholin-4-yl]-methanone;

[(R)-3-(2-Fluoro-5-pyrimidin-2-yl-benzyl)-morpholin-4-yl]-(5-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(R)-3-(2-Fluoro-5-pyrimidin-2-yl-benzyl)-morpholin-4-yl]-(4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(R)-3-(2-Fluoro-5-pyrimidin-2-yl-benzyl)-morpholin-4-yl]-(3-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

(3,4-Dimethyl-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(2-fluoro-5-pyrimidin-2-yl-benzyl)-morpholin-4-yl]-methanone;

(5-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(2-fluoro-5-pyrimidin-2-yl-benzyl)-morpholin-4-yl]-methanone;

(4-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(2-fluoro-5-pyrimidin-2-yl-benzyl)-morpholin-4-yl]-methanone;

(3-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(2-fluoro-5-pyrimidin-2-yl-benzyl)-morpholin-4-yl]-methanone;

[(2S,3R)-2-Methyl-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(5-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(2S,3R)-2-Methyl-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(2S,3R)-2-Methyl-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(3-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(2R,5R)-5-(2-Fluoro-5-pyridazin-3-yl-benzyl)-2-methyl-morpholin-4-yl]-(4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(R)-3-(2-Fluoro-5-pyridazin-3-yl-benzyl)-morpholin-4-yl]-(4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(2R,3R)-2-Methyl-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(5-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(2R,3R)-2-Methyl-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(R)-3-(2-Chloro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(3,4-dimethyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(R)-3-(2-Chloro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(4-chloro-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(R)-3-(2-Chloro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(3-chloro-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

(3-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[(2R,5R)-2-methyl-5-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone;

(3-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[(2R,5R)-5-(2-fluoro-5-[1,2,3]triazol-2-yl-benzyl)-2-methyl-morpholin-4-yl]-methanone;

[(R)-3-(2-Fluoro-5-[1,2,4]oxadiazol-3-yl-benzyl)-morpholin-4-yl]-(5-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(R)-3-(2-Fluoro-5-[1,2,4]oxadiazol-3-yl-benzyl)-morpholin-4-yl]-(4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

(5-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(2-fluoro-5-[1,2,4]oxadiazol-3-yl-benzyl)-morpholin-4-yl]-methanone;

[(R)-3-(2-Fluoro-5-[1,2,4]oxadiazol-3-yl-benzyl)-morpholin-4-yl]-(3-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

(4-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(2-fluoro-5-[1,2,4]oxadiazol-3-yl-benzyl)-morpholin-4-yl]-methanone;

(4,5-Dimethyl-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(2-fluoro-5-[1,2,4]oxadiazol-3-yl-benzyl)-morpholin-4-yl]-methanone;

(3-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(2-fluoro-5-[1,2,4]oxadiazol-3-yl-benzyl)-morpholin-4-yl]-methanone;

(3,4-Dimethyl-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(2-fluoro-5-[1,2,4]oxadiazol-3-yl-benzyl)-morpholin-4-yl]-methanone;

[(R)-3-(3-[1,2,3]Triazol-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-3-trifluoromethyl-phenyl)-methanone;

[(R)-3-(2-Fluoro-3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

(5-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[(2R,5R)-2-methyl-5-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone;

(4-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[(2R,5R)-2-methyl-5-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone;

(5-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[(2R,5R)-5-(2-fluoro-5-[1,2,3]triazol-2-yl-benzyl)-2-methyl-morpholin-4-yl]-methanone;

(4-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[(2R,5R)-5-(2-fluoro-5-[1,2,3]triazol-2-yl-benzyl)-2-methyl-morpholin-4-yl]-methanone;

[(R)-3-(2-Methyl-5-pyrazol-1-yl-benzyl)-morpholin-4-yl]-(5-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(R)-3-(2-Methyl-5-pyrazol-1-yl-benzyl)-morpholin-4-yl]-(4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(R)-3-(2-Methyl-5-pyrazol-1-yl-benzyl)-morpholin-4-yl]-(3-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

(4-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(2-methyl-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone;

[(R)-3-(4-Methyl-3-pyrimidin-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(R)-3-(4-Methyl-3-thiazol-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone; and

[(R)-3-(4-Chloro-3-pyrimidin-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone.

44) A further disclosure relates to particular compounds of formula (I) according to disclosure 1) are selected from the group consisting of:

(4-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone;

(4-Methyl-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone;

[(R)-3-(3-[1,2,3]Triazol-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-4-trifluoromethyl-phenyl)-methanone;

(4-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(2-fluoro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone;

(3,4-Dimethyl-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone;

[(R)-3-(2-Chloro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(R)-3-(2-Fluoro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(R)-3-(3-[1,2,4]Oxadiazol-3-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-4-trifluoromethyl-phenyl)-methanone;

(5-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone;
(3-Methyl-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone;
(3,4-Dimethyl-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(2-fluoro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone;
[(R)-3-(3-[1,2,3]Triazol-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone; and
[(2R,5R)-5-(2-Fluoro-5-[1,2,3]triazol-2-yl-benzyl)-2-methyl-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone.

The compounds of formula (I) and (II) according to any one of disclosures 1) to 44) and their pharmaceutically acceptable salts can be used as medicaments, e.g. in the form of pharmaceutical compositions for enteral (such especially oral) or parenteral administration (including topical application or inhalation).

The production of the pharmaceutical compositions can be effected in a manner which will be familiar to any person skilled in the art (see for example Remington, *The Science and Practice of Pharmacy*, 21st Edition (2005), Part 5, “Pharmaceutical Manufacturing” [published by Lippincott Williams & Wilkins]) by bringing the described compounds of formula (I) or their pharmaceutically acceptable salts, optionally in combination with other therapeutically valuable substances, into a galenical administration form together with suitable, non-toxic, inert, therapeutically compatible solid or liquid carrier materials and, if desired, usual pharmaceutical adjuvants.

Described herein is a method for the prevention or treatment of a disease or disorder mentioned herein comprising administering to a subject a pharmaceutically active amount of a compound of formula (I) and (II) according to any one of disclosures 1) to 44).

In a preferred disclosure of the invention, the administered amount is comprised between 1 mg and 1000 mg per day, particularly between 5 mg and 500 mg per day, more particularly between 25 mg and 400 mg per day, especially between 50 mg and 200 mg per day.

For avoidance of any doubt, if compounds are described as useful for the prevention or treatment of certain diseases, such compounds are likewise suitable for use in the preparation of a medicament for the prevention or treatment of said diseases.

The compounds of formula (I) and (II) according to any one of disclosures 1) to 44) are useful for the prevention or treatment of disorders relating to orexinergic dysfunctions.

Such disorders relating to orexinergic dysfunctions are diseases or disorders where an antagonist of a human orexin receptor is required, notably mental health diseases or disorders relating to orexinergic dysfunctions, notably of the orexin 1 receptor. The above mentioned disorders may in particular be defined as comprising anxiety disorders, addiction disorders, mood disorders, or appetite disorders, as well as cognitive dysfunctions or sleep disorders. Especially, the above mentioned disorders comprise anxiety disorders, addiction disorders and mood disorders, notably anxiety disorders and addiction disorders.

In addition, further disorders relating to orexinergic dysfunctions are selected from treating, controlling, ameliorating or reducing the risk of epilepsy, including absence epilepsy; treating or controlling pain, including neuropathic pain; treating or controlling Parkinson's disease; treating or controlling psychosis including acute mania and bipolar disorder; treating or controlling stroke, particularly ischemic or haemorrhagic stroke; blocking an emetic response i.e. nausea and vomiting; and treating or controlling agitation, in isolation or co-morbid with another medical condition.

Anxiety disorders can be distinguished by the primary object or specificity of threat, ranging from rather diffuse as in generalized anxiety disorder, to circumscribed as encountered in phobic anxieties (PHOBs) or post-traumatic stress disorders (PTSDs). Anxiety disorders may, thus, be defined as comprising generalized anxiety disorders (GAD), obsessive compulsive disorders (OCDs), acute stress disorders, posttraumatic stress disorders (PTSDs), panic anxiety disorders (PADs) including panic attacks, phobic anxieties (PHOBs), specific phobia, social phobia (social anxiety disorder), avoidance, somatoform disorders including hypochondriasis, separation anxiety disorder, anxiety disorders due to a general medical condition, and substance induced anxiety disorders. In a sub-disclosure, particular examples of circumscribed threat induced anxiety disorders are phobic anxieties or post-traumatic stress disorders. Anxiety disorders especially include generalized anxiety disorders, post-traumatic stress disorders, obsessive compulsive disorders, panic attacks, phobic anxieties, and avoidance.

Addiction disorders may be defined as addictions to one or more rewarding stimuli, notably to one rewarding stimulus. Such rewarding stimuli may be of either natural or synthetic origin. Examples of such rewarding stimuli are substances / drugs {of either natural or synthetic origin; such as cocaine, amphetamines, opiates [of natural or (semi-)synthetic origin such as morphine or heroin], cannabis, ethanol, mescaline, nicotine, and the like}, which substances / drugs may be consumed alone or in combination; or other rewarding stimuli {of either natural origin (such as food, sweet, fat, or sex, and the like), or synthetic origin [such as gambling, or internet/IT (such as immoderate gaming, or inappropriate involvement in online social networking sites or blogging), and the like]}. In a sub-embodiment, addiction disorders relating to psychoactive substance use, abuse, seeking and reinstatement are defined as all types of psychological or physical addictions and their related tolerance and dependence components. Substance-related addiction disorders especially include substance use disorders such as substance dependence, substance craving and substance abuse;

substance-induced disorders such as substance intoxication, substance withdrawal, and substance-induced delirium. The expression "prevention or treatment of addictions" (i.e. preventive or curative treatment of patients who have been diagnosed as having an addiction, or as being at risk of developing addictions) refers to diminishing addictions, notably diminishing the onset of addictions, to weakening their maintenance, to facilitating withdrawal, to facilitating abstinence, or to attenuating, decreasing or preventing the occurrence of reinstatement of addiction (especially to diminishing the onset of addictions, to facilitating withdrawal, or to attenuating, decreasing or preventing the occurrence of reinstatement of addiction).

Mood disorders include major depressive episode, manic episode, mixed episode and hypomanic episode; depressive disorders including major depressive disorder, dysthymic disorders; bipolar disorders including bipolar I disorder, bipolar II disorder (recurrent major depressive episodes with hypomanic episodes), cyclothymic disorder; mood disorders including mood disorder due to a general medical condition (including the subtypes with depressive features, with major depressive-like episode, with manic features, and with mixed features), substance-induced mood disorder (including the subtypes with depressive features, with manic features, and with mixed features). Such mood disorders are especially major depressive episode, major depressive disorder, mood disorder due to a general medical condition; and substance-induced mood disorder.

Appetite disorders comprise eating disorders and drinking disorders. Eating disorders may be defined as comprising eating disorders associated with excessive food intake and complications associated therewith; anorexias; compulsive eating disorders; obesity (due to any cause, whether genetic or environmental); obesity-related disorders including overeating and obesity observed in Type 2 (non-insulin-dependent) diabetes patients; bulimias including bulimia nervosa; cachexia; and binge eating disorder. Particular eating disorders comprise metabolic dysfunction; dysregulated appetite control; compulsive obesities; bulimia or anorexia nervosa. In a sub-embodiment, eating disorders may be defined as especially comprising anorexia nervosa, bulimia, cachexia, binge eating disorder, or compulsive obesities. Drinking disorders include polydipsias in psychiatric disorders and all other types of excessive fluid intake. Pathologically modified food intake may result from disturbed appetite (attraction or aversion for food); altered energy balance (intake vs. expenditure); disturbed perception of food quality (high fat or carbohydrates, high palatability); disturbed food availability (unrestricted diet or deprivation) or disrupted water balance.

Cognitive dysfunctions include deficits in attention, learning and especially memory functions occurring transiently or chronically in psychiatric, neurologic, neurodegenerative, cardiovascular and immune disorders, and also occurring transiently or chronically in the normal, healthy, young, adult, or especially aging population. Cognitive dysfunctions especially relate to the enhancement or maintenance of memory in patients who have been diagnosed as having, or being at risk of developing, diseases or disorders in which diminished memory (notably declarative or procedural) is a symptom [in particular dementias such as frontotemporal dementia, or dementia with Lewy bodies, or (especially) Alzheimer's disease]. Especially, the term "prevention or treatment of cognitive dysfunctions" relates to the enhancement or maintenance of memory in patients who have a clinical manifestation of a cognitive dysfunction, especially expressed as a deficit of declarative memory, linked to dementias such as frontotemporal dementia, or dementia with Lewy bodies, or (especially) Alzheimer's disease. Furthermore, the term "prevention or treatment of cognitive dysfunctions" also relates to improving memory consolidation in any of the above mentioned patient populations.

Sleep disorders comprise dyssomnias, parasomnias, sleep disorders associated with a general medical condition and substance-induced sleep disorders. In particular, dyssomnias include intrinsic sleep disorders (especially insomnias, breathing-related sleep disorders, periodic limb movement disorder, and restless leg syndrome), extrinsic sleep disorders, and circadian-rythm sleep disorders. Dyssomnias notably include insomnia, primary insomnia, idiopathic insomnia, insomnias associated with depression, emotional/mood disorders, aging, Alzheimer's disease or cognitive impairment; REM sleep interruptions; breathing-related sleep disorders; sleep apnea; periodic limb movement disorder (nocturnal myoclonus), restless leg syndrome, circadian rhythm sleep disorder; shift work sleep disorder; and jet-lag syndrome. Parasomnias include arousal disorders and sleep-wake transition disorders; notably parasomnias include nightmare disorder, sleep terror disorder, and sleepwalking disorder. Sleep disorders associated with a general medical condition are in particular sleep disorders associated with diseases such as mental disorders, neurological disorders, neuropathic pain, and heart and lung diseases. Substance-induced sleep disorders include especially the subtypes insomnia type, parasomnia type and mixed type, and notably include conditions due to drugs which cause reductions in REM sleep as a side effect. Sleep disorders especially include all types of insomnias, sleep-related dystonias; restless leg syndrome; sleep apneas; jet-lag syndrome; shift work sleep disorder, delayed or advanced sleep phase syndrome, or insomnias related to psychiatric disorders. In addition, sleep disorders further include sleep disorders associated with aging; intermittent treatment of chronic insomnia; situational transient insomnia (new environment, noise) or short-term insomnia due to stress; grief; pain or illness.

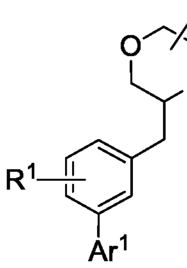
In the context of the present invention, it is to be understood that, in case certain environmental conditions such as stress or fear (wherein stress may be of social origin (e.g. social stress) or of physical origin (e.g. physical stress), including stress caused by fear) facilitate or precipitate any of the disorders or diseases as defined before, the present compounds may be particularly useful for the treatment of such environmentally conditioned disorder or disease.

The present invention also relates to the compounds of formula (I) and (II), and/or to pharmaceutical compositions comprising, as active principle, one or more compounds of formula (I) and / or (II) for use in the treatment of the above-mentioned disorders relating to orexinergic dysfunctions, in combination with one or more further pharmaceutically active ingredients.

Preparation of compounds of formula (I):

The compounds of formula (I) can be prepared by the methods given below, by the methods given in the experimental part below or by analogous methods. Optimum reaction conditions may vary with the particular reactants or solvents used, but such conditions can be determined by a person skilled in the art by routine optimisation procedures. In some cases the final product may be further modified, for example, by manipulation of substituents to give a new final product. These manipulations may include, but are not limited to, reduction, oxidation, alkylation, acylation, and hydrolysis reactions which are commonly known to those skilled in the art. In some cases the order of carrying out the following reaction schemes, and/or reaction steps, may be varied to facilitate the reaction or to avoid unwanted reaction products.

Compounds of formula (I) of the present invention can be prepared according to the general sequence of reactions outlined below wherein Q, Ar^1, R^1, R^2, R^3, R^4 and R^5 are as defined for formula (I).



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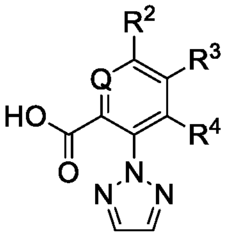

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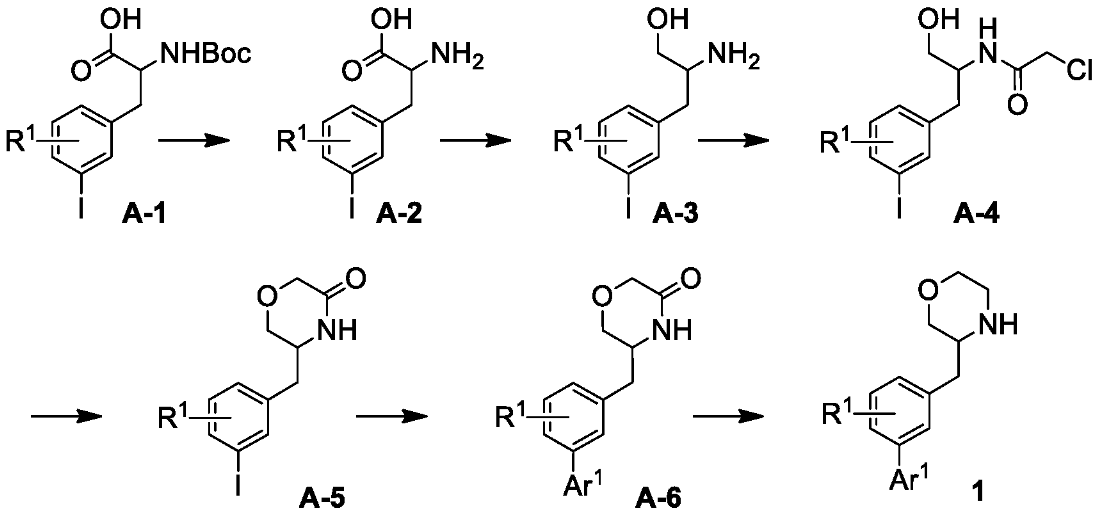
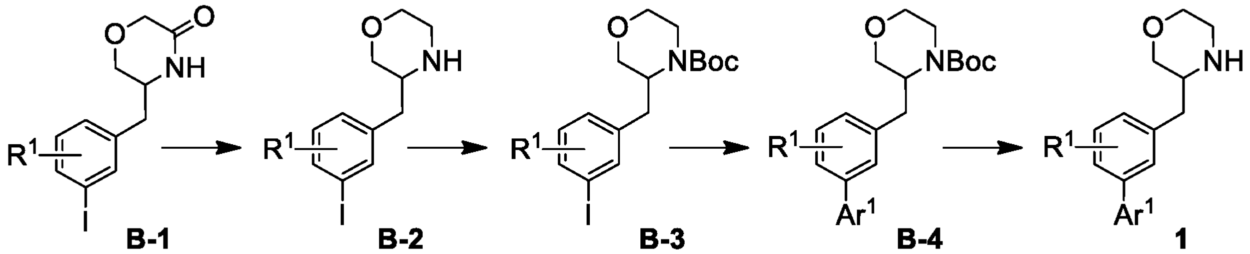
Compounds of formula (I) are prepared by reaction of an amine of Structure **1**, or a salt such as a hydrochloride salt thereof, with an acid of Structure **2** in the presence of an amide-coupling reagent such as TBTU, HATU, EDC, DCC or PyBOP and a base like DIPEA or TEA in a solvent such as MeCN or DMF. Alternatively, coupling can be achieved via the corresponding acid chloride of Structure **2**, prepared conventionally using a chlorinating reagent like oxalyl chloride or thionyl chloride.

Compounds of Structure **1** may be prepared by one of the synthetic pathways described below.



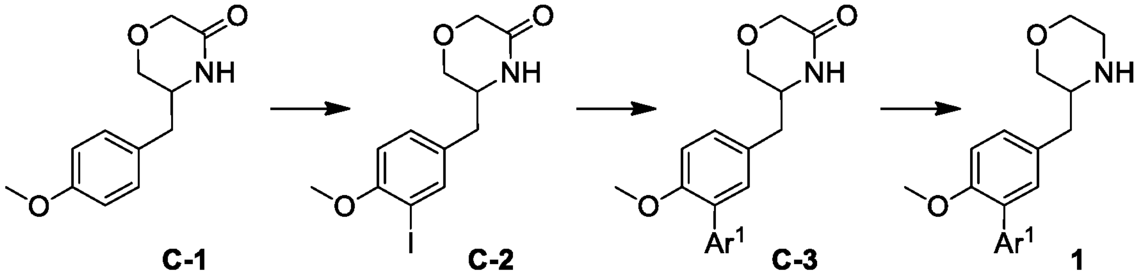
Reaction Scheme A

Compounds of Structure **1** may be prepared in analogy to the procedure described in WO2008047109 and as illustrated in Reaction Scheme A. A Boc-protected iodophenyl alanine derivative **A-1**, racemic or enantiomerically enriched, either commercially available or prepared following the procedure described by Greenspan *et al.* in J. Med. Chem. **2001**, *44*, 4524-4534, can be Boc-deprotected by treatment with 4M HCl in dioxane or with TFA to give the corresponding iodophenyl alanine as its HCl or TFA salt **A-2**. Iodophenyl alanine **A-2**, racemic or enantiomerically enriched, either commercially available or prepared as described above can be reduced with borane in a solvent like THF to furnish the corresponding amino alcohol **A-3**. Acylation of **A-3** with chloroacetyl chloride furnishes amide **A-4** which upon treatment with a base like sodium hydride or potassium *tert*butoxide in a solvent like THF affords morpholinone **A-5**. Arylation of **A-5** can be accomplished under metal catalysed conditions employing for example copper, palladium or zinc catalysts to give intermediates of type **A-6**. Alternatively, conversion of **A-5** into it's corresponding boronic acid or ester followed by a Suzuki reaction gives intermediates of type **A-6**. Reduction of **A-6** with borane in a solvent like THF furnishes compounds of Structure **1**.



Reaction Scheme B

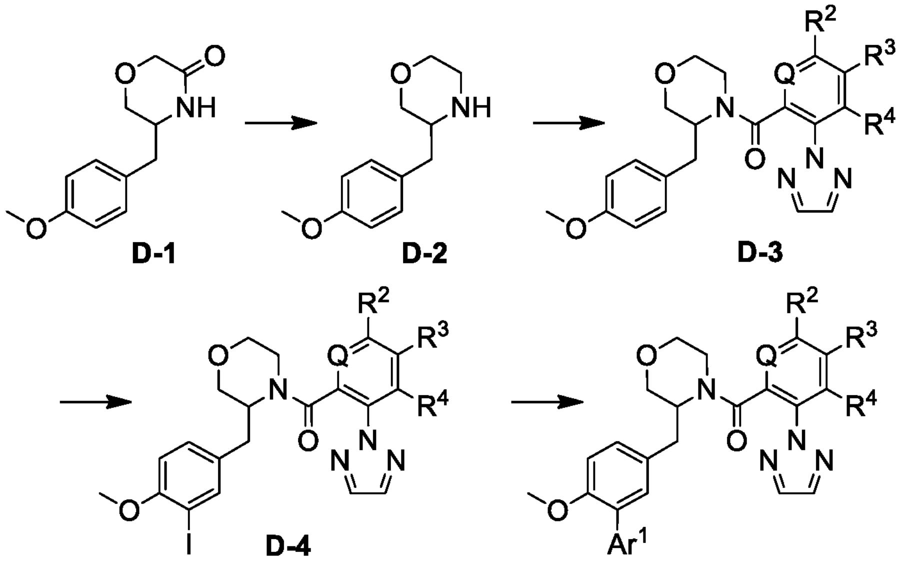
Compounds of Structure **1** may also be prepared as illustrated in Reaction Scheme B. Reduction of morpholinone **B-1** with borane in a solvent like THF gives the corresponding morpholine **B-2** which can be boc-protected under standard conditions to furnish intermediates of type **B-3**. Arylation of **B-3** can be achieved by following one of several methods. For example, under metal catalysed conditions as described above, or alternatively, conversion of **B-3** into it's corresponding boronic pinacol ester by treatment with bis(pinacolato) diboron in a solvent like DMSO followed by a Suzuki reaction. Intermediates of type **B-3** can also be converted into their corresponding cyano derivatives by treatment with zinc cyanide under palladium catalysed conditions in a solvent like 1,4-dioxane followed by treatment with hydroxylamine and subsequent ring closure in trimethyl orthoformate to give intermediates of type **B-4** where Ar^1 is a 1,2,4-oxadiazole. Boc-deprotection of **B-4** by treatment with 4M HCl in dioxane or with TFA leads to compounds of Structure **1**.



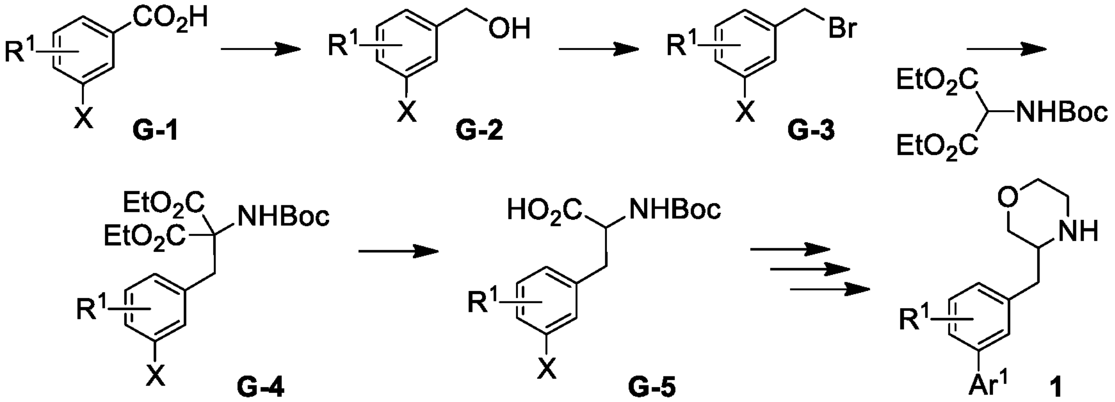
Reaction Scheme C

Compounds of Structure **1** may also be prepared as illustrated in Reaction Scheme C. Intermediate **C-1** can be prepared from *p*-methoxyphenyl alanine in analogy to the sequence of reactions described in Reaction Scheme A. Iodination of morpholinone **C-1** with NIS in the presence of an acid like triflic acid in a solvent like DCM or MeCN gives the corresponding morpholinone **C-2**. Arylation of **C-2** can be accomplished under metal catalysed conditions employing for example copper or palladium catalysts to give intermediates of type **C-3**. Alternatively, conversion of **C-2** into it's corresponding boronic pinacol ester by treatment with bis(pinacolato) diboron in a solvent like DMSO followed by a Suzuki reaction with the appropriate aryl halide furnishes intermediates of type **C-3**. Reduction of **C-3** with borane in a solvent like THF furnishes compounds of Structure **1**.

Final compounds of the present invention may be prepared as illustrated in Reaction Scheme D. For example, intermediate **D-1** can be prepared from *p*-methoxyphenyl alanine in analogy to the sequence of reactions described in Reaction Scheme A. Reduction of morpholinone **D-1** with borane in a solvent like THF gives the corresponding morpholine **D-2**. Reaction of **D-2** with an acid of Structure **2** in the presence of an amide-coupling reagent such as TBTU, HATU or EDC, and a base like DIPEA or TEA in a solvent such as MeCN or DMF furnishes intermediates of type **D-3**. Iodination of **D-3** in the presence of an acid like triflic acid in a solvent like DCM or MeCN gives intermediates of type **D-4**. Arylation of **D-4** can be accomplished under metal catalysed conditions employing for example copper or palladium catalysts to give final compounds. Alternatively, conversion of **D-4** into it's corresponding boronic pinacol ester by treatment with bis(pinacolato) diboron in a solvent like DMSO followed by a Suzuki reaction with the appropriate aryl halide furnishes final compounds.

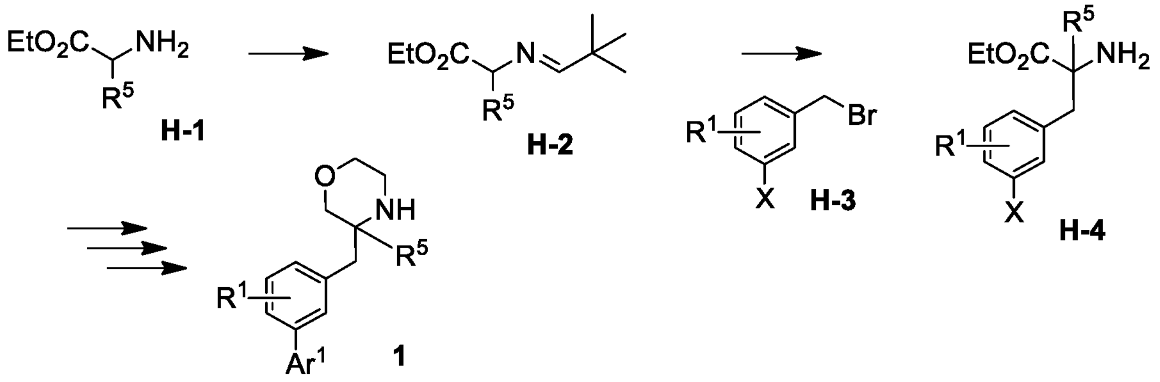


Reaction Scheme D



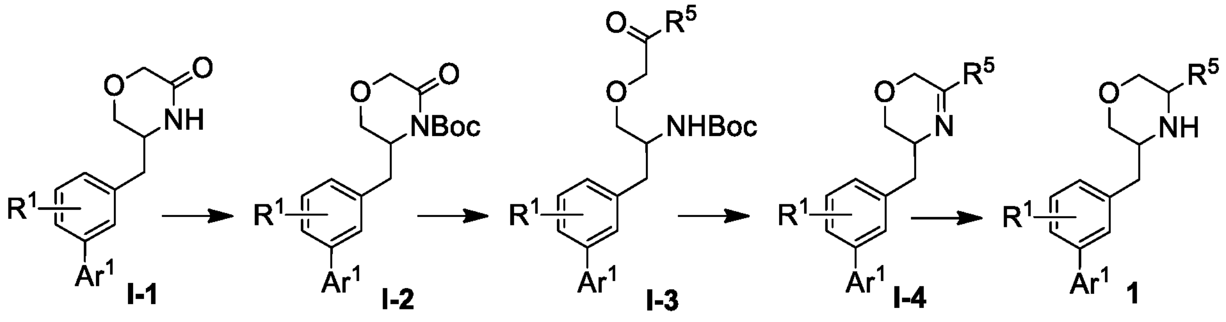
Reaction Scheme G

Compounds of Structure **1** may also be prepared as illustrated in Reaction Scheme G. Reduction of commercially available *m*-halobenzoic acid (X = Br or I) **G-1** with borane in a solvent like THF gives the corresponding benzyl alcohol **G-2** which can be brominated under standard conditions with phosphorus tribromide in a solvent like DCM to furnish benzyl bromides of type **G-3**. Subsequent Boc-aminomalonate alkylation chemistry with benzyl bromide **G-3** as described by Greenspan *et al.* in J. Med. Chem. **2001**, *44*, 4524-4534, furnishes Boc-protected halophenyl alanine derivative **G-5.** Conversion of **G-5** into compounds of Structure **1** can be accomplished by following the sequence of transformations as described in Reaction Scheme A.



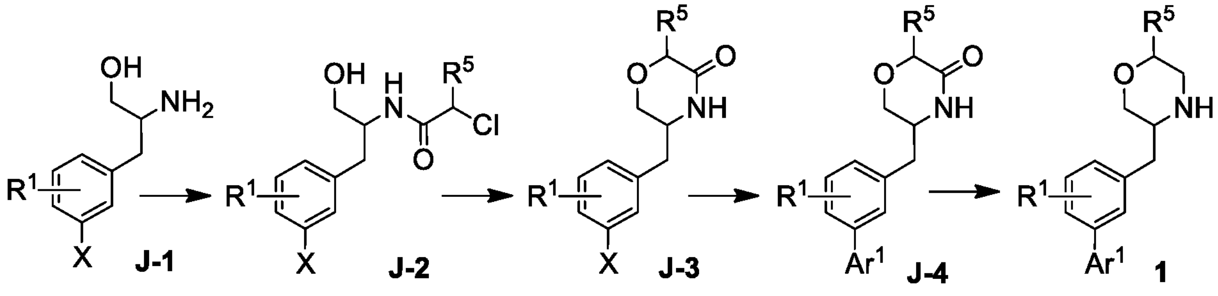
Reaction Scheme H

Compounds of Structure **1** may also be prepared as illustrated in Reaction Scheme H. Reaction of commercially available α-aminoester **H-1** with trimethylacetaldehyde in a solvent like DCM in the presence of a dehydrating agent like $MgSO_4$ gives the corresponding imine **H-2**. Alkylation of **H-2** with benzyl bromides **H-3**, prepared as described in Reaction Scheme G, in a solvent like toluene gives after imine hydrolysis intermediates of type **H-4**. Conversion of **H-4** into compounds of Structure **1** can be accomplished by following the sequence of transformations as described in Reaction Scheme A.



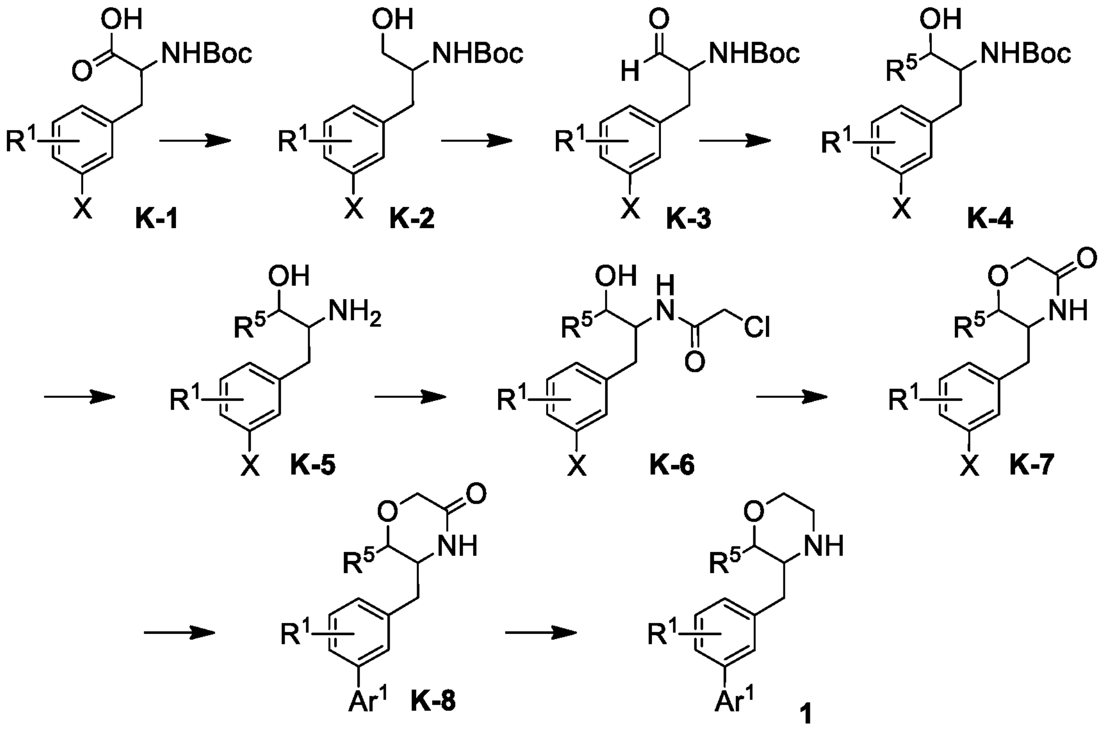
Reaction Scheme I

Compounds of Structure **1** may also be prepared as illustrated in Reaction Scheme I. Intermediate **I-1**, prepared according to Reaction Schemes A, C or G can be Boc-protected following the procedure described by Terashima *et al.* in Tetrahedron, **1994**, *50*, 6221-6238 to give Boc-morpholinone **I-2**. Reaction of **I-2** with an appropriate alkyl-metal reagent like alkyl lithium reagents in a solvent like THF at a temperature of -78°C gives the ring-opened ketone **I-3**. Boc-deprotection of **I-3** by treatment with 4M HCl in dioxane or with TFA leads to cyclic imines of type **I-4** that can be subsequently reduced with $NaBH_4$ in a solvent like MeOH to furnish compounds of Structure **1**.



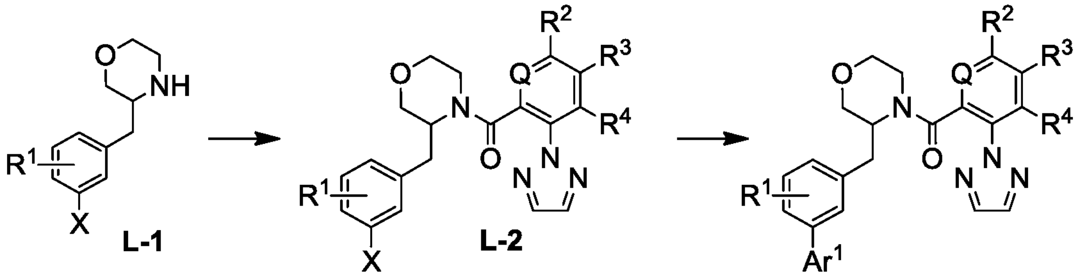
Reaction Scheme J

Compounds of Structure **1** may also be prepared as illustrated in Reaction Scheme J. In analogy to the procedure desribed by Kazmierski *et al.* in Bioorg. Med. Chem. Lett. **2006**, *16*, 5226-5230, amino alcohol **J-1**, prepared according to Reaction Scheme A can be acylated with chloroacetyl chloride derivatives to furnish amide **J-2** which upon treatment with a base like sodium hydride or potassium *tert*butoxide in a solvent like THF affords morpholinone **J-3** as a single *cis*-diastereomer. Arylation of **J-3** can be accomplished under metal catalysed conditions employing for example copper, palladium or zinc catalysts to give intermediates of type **J-4**. Alternatively, conversion of **J-3** into it's corresponding boronic acid or ester followed by a Suzuki reaction gives intermediates of type **J-4**. Reduction of **J-4** with borane in a solvent like THF furnishes compounds of Structure **1**.



Reaction Scheme K

Compounds of Structure **1** may also be prepared as illustrated in Reaction Scheme K. A Boc-protected halophenyl alanine derivative (X = Br or I) **K-1**, racemic or enantiomerically enriched, either commercially available or prepared as illustrated in Reaction Scheme G can be reduced with $NaBH_4$ via its mixed anhydride in a solvent like THF to afford Boc-protected amino alcohol **K-2**. Dess-Martin oxidation of **K-2** gives the corresponding aldehyde **K-3** which can be alkylated with an alkyl zinc or magnesium reagent to give the 2° alcohol **K-4**. Boc-deprotection of **K-4** by treatment with 4M HCl in dioxane or with TFA leads to the amino alcohol **K-5** which can be converted into compounds of Structure **1** by following the sequence of transformations described above in Reaction Scheme A.



Reaction Scheme L

Final compounds of the present invention may also be prepared as illustrated in Reaction Scheme L. For example, intermediate **L-1** (X = Br or I), prepared according to Reaction Scheme B can be coupled with an acid of Structure **2** in the presence of an amide-coupling reagent such as TBTU, HATU or EDC, and a base like DIPEA or TEA in a solvent such as

MeCN or DMF to furnish intermediates of type **L-2**. Arylation of **L-2** can be accomplished under metal catalysed conditions employing for example copper or palladium catalysts to give final compounds. Alternatively, conversion of **L-2** into it's corresponding boronic pinacol ester by treatment with bis(pinacolato) diboron in a solvent like DMSO followed by a Suzuki reaction with the appropriate aryl halide furnishes final compounds.

Carboxylic acid derivatives of Structure **2** are well known in the art and can be especially prepared following the procedures reported in WO2008069997, WO2008008517, WO2010048012, WO2010063662, WO2010063663, WO2011050198, WO2011050200 and WO2011050202. In addition, they may be prepared in analogy to the methods given in the experimental part.

Whenever the compounds of formula (I) are obtained in the form of mixtures of enantiomers, the enantiomers can be separated using methods known to one skilled in the art: e.g. by formation and separation of diastereomeric salts or by HPLC over a chiral stationary phase such as a Regis Whelk-O1(R,R) (10 μm) column, a Daicel ChiralCel OD-H (5-10 μm) column, or a Daicel ChiralPak IA (10 μm), IC (5 μm) or AD-H (5 μm) column. Typical conditions of chiral HPLC are an isocratic mixture of eluent A (EtOH, in presence or absence of an amine such as triethylamine or diethylamine) and eluent B (heptane), at a flow rate of 0.8 to 150 mL/min.

The following examples are provided to illustrate the invention. These examples are illustrative only and should not be construed as limiting the invention in any way.

Experimental Part

I. Chemistry

All temperatures are stated in °C. Commercially available starting materials were used as received without further purification. Unless otherwise specified, all reactions were carried out in oven-dried glassware under an atmosphere of nitrogen. Compounds were purified by flash column chromatography on silica gel or by preparative HPLC. Compounds described in the invention are characterised by LC-MS data (retention time t_R is given in min; molecular weight obtained from the mass spectrum is given in g/mol) using the conditions listed below. In cases where compounds of the present invention appear as a mixture of conformational isomers, particularly visible in their LC-MS spectra, the retention time of the most abundant conformer is given.

LC-MS with acidic conditions

Method A: Agilent 1100 series with mass spectrometry detection (MS: Finnigan single quadrupole). Column: Zorbax SB-aq (3.5 μm, 4.6 x 50 mm). Conditions: MeCN [eluent A];

water + 0.04% TFA [eluent B]. Gradient: 95% B → 5% B over 1.5 min (flow: 4.5 mL/min). Detection: UV/Vis + MS.

Method B: Agilent 1100 series with mass spectrometry detection (MS: Finnigan single quadrupole). Column: Waters XBridge C18 (2.5 μm, 4.6 x 30 mm). Conditions: MeCN [eluent A]; water + 0.04% TFA [eluent B]. Gradient: 95% B → 5% B over 1.5 min (flow: 4.5 mL/min). Detection: UV/Vis + MS.

LC-MS with basic conditions

Method C: Agilent 1100 series with mass spectrometry detection (MS: Finnigan single quadrupole). Column: Zorbax Extend C18 (5 μm, 4.6 x 50 mm). Conditions: MeCN [eluent A]; 13 mmol/L NH_3 in water [eluent B]. Gradient: 95% B → 5% B over 1.5 min (flow: 4.5 mL/min). Detection: UV/Vis + MS.

Method D: Agilent 1100 series with mass spectrometry detection (MS: Finnigan single quadrupole). Column: Waters XBridge C18 (5 μm, 4.6 x 50 mm). Conditions: MeCN [eluent A]; 13 mmol/L NH_3 in water [eluent B]. Gradient: 95% B → 5% B over 1.5 min (flow: 4.5 mL/min). Detection: UV/Vis + MS.

Preparative HPLC with acidic conditions

Method E: Column: Waters XBridge (10 μm, 75 x 30 mm). Conditions: MeCN [eluent A]; water + 0.5% HCOOH [eluent B]; Gradient: 90% B → 5% B over 6.4 min (flow: 75 mL/min). Detection: UV/Vis + MS.

Preparative HPLC with basic conditions

Method F: Column: Waters XBridge (10 μm, 75 x 30 mm). Conditions: MeCN [eluent A]; water + 0.5% NH_4OH (25% aq.) [eluent B]; Gradient: 90% B → 5% B over 6.5 min (flow: 75 mL/min). Detection: UV/Vis + MS.

Preparative HPLC for chiral separations

Final compounds that are obtained in racemic form are separated into their enantiomers using the following conditions:column:(*R*,*R*)Whelk-01 21x250 mm, 5 μM,15% MeCN in MTBE + 0.1% DEA (flow: 16 mL/min). Detection: UV/Vis.

Abbreviations (as used hereinbefore or hereinafter):

acac	acetylacetonate
aq.	aqueous
atm	atmosphere
BSA	bovine serum albumin
Boc	butyloxycarbonyl

CDI	carbonyl diimidazole
d	days
dba	dibenzylidene acetone
DCC	dicyclohexyl carbodiimide
DCM	dichloromethane
DEA	diethylamine
DIPEA	diisopropyl-ethylamine, Hünig's base, ethyl-diisopropylamine
DMAP	4-dimethylaminopyridne
DMCDA	trans-*N*,*N*'-dimethylcyclohexane-1,2-diamine
DMF	dimethylformamide
DMP	Dess-Martin periodinane
DMSO	dimethylsulfoxide
dppf	1,1'-bis(diphenylphosphino)ferrocene
EDC	N-(3-dimethylaminopropyl)-N'-ethyl-carbodiimide
eq.	equivalent(s)
Et	ethyl
Et_2O	diethyl ether
EtOAc	ethyl acetate
Ex.	example(s)
h	hour(s)
HBTU	O-(benzotriazol-1-yl)-N,N,N',N'-tetramethyluronium hexafluorophosphate
HOBt	1-hydroxybenzotriazole
HPLC	high performance liquid chromatography
HV	high vacuum conditions
^{i}Bu	isobutyl
^{i}Pr	isopropyl
KO^{t}Bu	potassium *tert*-butoxide
LC-MS	liquid chromatography – mass spectrometry
Lit.	Literature
Me	methyl
MeCN	acetonitrile
MeOH	methanol
MeLi	methyl lithium
MTBE	methyl-*tert*butyl ether
min	minute(s)

NaOAc	sodium acetate
^{n}BuLi	n-butyl-lithium
NIS	N-iodo succinimide
^{n}Pr	n-propyl
OAc	acetate
Pd(dppf)Cl$_2$·DCM	[1,1'-bis(diphenylphosphino)-ferrocene]dichloropalladium (II) complex with dichloromethane
Ph	phenyl
PPh$_3$	triphenyl phosphine
prep.	Preparative
PyBOP	benzotriazol-1-yl-oxy-tris-pyrrolidino-phosphonium-hexafluoro-phosphate
rac	racemic
RT	room temperature
s	second(s)
sat.	saturated
soln.	solution
TBTU	2-(1H-benzotriazole-1-yl)-1,2,3,3-tetramethyluronium tetrafluoroborate
TEA	triethylamine
TFA	trifluoroacetic acid
TFAA	trifluoroacetic anhydride
THF	tetrahydrofuran
TLC	thin layer chromatography
TMS	trimethylsilyl
t$_R$	retention time

General method A for the synthesis of 3-benzyl morpholines of Structure 1

(*R*)-2-Amino-3-(3-iodo-phenyl)-propionic acid hydrochloride (A-7)

A solution of Boc-3-iodo-D-phenylalanine (5 g, 12.8 mmol, available from Matrix Scientific and 3BSC) in 4M HCl in dioxane (63.9 mL, 256 mmol) under argon was stirred at RT for 15h. The resulting suspension was filtered, washed with Et$_2$O and dried *in vacuo* to give the title compound as a white solid. LC-MS B: t$_R$ = 0.42 min; [M+H]$^+$ = 291.98.

(*R*)-2-Amino-3-(3-iodo-phenyl)-propan-1-ol (A-8)

Borane.THF complex 1M soln. (197 mL, 0.197 mol) was added dropwise to a 0°C suspension of (*R*)-2-amino-3-(3-iodo-phenyl)-propionic acid hydrochloride **A-7** (21.5 g, 65.8 mmol) in THF (200 mL) under argon and after complete addition the reaction mixture was heated to 70°C for 2h. The reaction mixture was cooled to 0°C and quenched with MeOH and after stirring for 5 min the reaction mixture was evaporated *in vacuo*. The residue was partitioned between 2M aq. HCl and MeOH and stirred for 30 min before being concentrated *in vacuo*. The remaining aqueous phase was diluted with additional water and extracted once with DCM. The layers were separated and the organic phase was re-washed with 2M aq. HCl before being discarded. The acidic aq. phases were combined and basified with 5M aq. NaOH and extracted with DCM (3x). The combined organic extracts were dried over Na_2SO_4, filtered and evaporated *in vacuo* to give the title compound as a cream solid that was used further without purification. LC-MS B: t_R = 0.45 min; $[M+H]^+$ = 278.03.

2-Chloro-*N*-[(*R*)-1-hydroxymethyl-2-(3-iodo-phenyl)-ethyl]-acetamide (A-9)

Chloroacetylchloride (1.05 mL, 13.1 mmol) was added dropwise to a 0°C solution of (*R*)-2-amino-3-(3-iodo-phenyl)-propan-1-ol **A-8** (3.03 g, 10.9 mmol) and Et_3N (1.98 mL, 14.2 mmol) in THF (50 mL) under argon and the resulting suspension was warmed to RT and stirred for 30 min. The reaction mixture was cooled back to 0°C before being quenched with water and concentrated *in vacuo*. The remaining aq. phase was extracted with EtOAc (2x) and the combined organic extracts were washed with brine, dried over Na_2SO_4, filtered and evaporated *in vacuo* to give the title compound as a cream solid that was used further without purification. LC-MS B: t_R = 0.71 min; $[M(^{35}Cl)+H]^+$ = 353.75.

(*R*)-5-(3-Iodo-benzyl)-morpholin-3-one (A-10)

NaH 60% Dispersion in mineral oil (0.93 g, 23.2 mmol) was added portionwise to a 0°C solution of 2-chloro-*N*-[(*R*)-1-hydroxymethyl-2-(3-iodo-phenyl)-ethyl]-acetamide **A-9** (3.72 g, 10.5 mmol) in THF (100 mL) under argon and the resulting suspension was warmed to RT and stirred for 1h. The reaction mixture was cooled back to 0°C before being quenched with water and concentrated *in vacuo*. The remaining aqueous phase was extracted with DCM (3x) and the combined organic extracts were washed with brine, dried over Na_2SO_4, filtered and evaporated *in vacuo* to give the crude product that was purified by flash chromatography (eluting with a gradient of 50% to 100% EtOAc in hexane) to give the title compound as a white solid. LC-MS B: t_R = 0.72 min; $[M+H+MeCN]^+$ = 359.01; ^1H NMR ($CDCl_3$) δ_H: 7.64 (d, J = 7.9 Hz, 1 H), 7.59 (s, 1 H), 7.18 (m, 1 H), 7.10 (t, J = 7.7 Hz, 1 H), 6.25 (s, 1 H), 4.20 (s, 2 H), 3.91 (dd, J_1 = 11.7 Hz, J_2 = 3.7 Hz, 1 H), 3.76 (m, 1 H), 3.60 (dd, J_1 = 11.7 Hz, J_2 = 6.1 Hz, 1 H), 2.87 (dd, J_1 = 13.6 Hz, J_2 = 6.0 Hz, 1 H), 2.72 (dd, J_1 = 13.6 Hz, J_2 = 8.5 Hz, 1 H).

(*R*)-5-(3-Pyrazol-1-yl-benzyl)-morpholin-3-one (A-11)

A mixture of (*R*)-5-(3-iodo-benzyl)-morpholin-3-one **A-10** (1.0 g, 3.15 mmol), pyrazole (322 mg, 4.73 mmol), K_2CO_3 (872 mg, 6.31 mmol), copper(I) chloride (31 mg, 0.32 mmol) and L-proline (73 mg, 0.63 mmol) in DMF (8 mL) was heated under argon to 110°C for 24h. The reaction mixture was cooled to RT and partitioned between water and DCM before being filtered through a celite plug. The layers were separated and the aqueous phase was re-extracted with DCM (2x). The combined organic phases were washed with brine, dried over Na_2SO_4, filtered and evaporated *in vacuo* to give the crude product that was purified by flash chromatography (eluting with a gradient of 50% to 100% EtOAc in hexane) to give the title compound as a white solid. LC-MS B: t_R = 0.51 min; $[M+H]^+$ = 257.86.

(*R*)-3-(3-Pyrazol-1-yl-benzyl)-morpholine (A-12)

Borane.THF complex 1M soln. (5.83 mL, 5.83 mmol) was added dropwise to a 0°C solution of (*R*)-5-(3-pyrazol-1-yl-benzyl)-morpholin-3-one **A-11** (500 mg, 1.94 mmol) in THF (7 mL) under argon and after complete addition the reaction mixture was heated to 70°C for 2.5h. The reaction mixture was cooled to 50°C and quenched with MeOH and 2M aq. HCl before being re-heated to 70°C for a further 1h. The reaction mixture was evaporated *in vacuo* and the residue was partitioned between 2M aq. HCl and EtOAC. The layers were separated and the organic phase was re-washed with 2M aq. HCl before being discarded. The acidic aq. phases were combined and basified with 5M aq. NaOH and extracted with EtOAC (3x). The combined organic extracts were dried over Na_2SO_4, filtered and evaporated *in vacuo* to give the title compound as a colourless oil that was used further without purification. LC-MS B: t_R = 0.41 min; $[M+H]^+$ = 244.07.

(*R*)-5-(3-[1,2,3]Triazol-2-yl-benzyl)-morpholin-3-one (A-13) and (*R*)-5-(3-[1,2,3]triazol-1-yl-benzyl)-morpholin-3-one (A-14)

A mixture of (*R*)-5-(3-iodo-benzyl)-morpholin-3-one **A-10** (3.94 g, 12.4 mmol), 1*H*-1,2,3-triazole (1.08 mL, 18.6 mmol), K_2CO_3 (3.43 g, 24.8 mmol), copper(I) chloride (123 mg, 1.24 mmol) and L-proline (286 mg, 2.48 mmol) in DMF (30 mL) was heated under argon to 110°C for 190h. The reaction mixture was cooled to RT and partitioned between water and DCM before being filtered through a celite plug. The layers were separated and the aqueous phase was re-extracted with DCM (2x). The combined organic phases were washed with brine, dried over Na_2SO_4, filtered and evaporated *in vacuo* to give the crude product that was purified by flash chromatography (eluting with a gradient of 50% to 100% EtOAc in hexane) to give the first title compound as a white solid. LC-MS B: t_R = 0.55 min; $[M+H]^+$ = 259.19; ^1H NMR ($CDCl_3$) δ_H: 8.04 (m, 1 H), 7.96 (m, 1 H), 7.85 (s, 2 H), 7.50 (m, 1 H), 7.22 (m, 1 H), 6.19 (s, 1 H), 4.21 (s, 2 H), 3.95 (dd, J_1 = 11.7 Hz, J_2 = 3.7 Hz, 1 H), 3.86 (m, 1 H), 3.64 (m, 1 H), 3.02 (m, 1 H), 2.89 (m, 1 H). Continued elution with 95:5 DCM:MeOH afforded the second title compound as an orange solid. LC-MS B: t_R = 0.43 min; $[M+H]^+$ = 259.20; ^1H NMR ($CDCl_3$) δ_H: 8.04 (s, 1 H), 7.89 (s, 1 H), 7.71 (s, 1 H), 7.65 (m, 1 H), 7.54 (t, J = 7.8 Hz, 1 H), 7.31 (d, J = 7.6 Hz, 1 H), 6.12 (s, 1 H), 4.21 (s, 2 H), 3.95 (dd, J_1 = 11.7 Hz, J_2 = 3.6 Hz, 1 H), 3.85 (m, 1 H), 3.66 (dd, J_1 = 11.7 Hz, J_2 = 5.8 Hz, 1 H), 3.04 (dd, J_1 = 13.6 Hz, J_2 = 5.7 Hz, 1 H), 2.91 (dd, J_1 = 13.6 Hz, J_2 = 8.6 Hz, 1 H).

(*R*)-3-(3-[1,2,3]Triazol-2-yl-benzyl)-morpholine (A-15)

The title compound was prepared from **A-13** in analogy to the procedure described for **A-12**. LC-MS A: t_R = 0.52 min; $[M+H]^+$ = 245.18.

(*R*)-3-(3-[1,2,3]Triazol-1-yl-benzyl)-morpholine (A-16)

The title compound was prepared from **A-14** in analogy to the procedure described for **A-12**. LC-MS A: t_R = 0.46 min; $[M+H]^+$ = 245.18.

(*R*)-5-(3-[1,2,4]Triazol-1-yl-benzyl)-morpholin-3-one (A-17)

The title compound was prepared from **A-10** and 1*H*-1,2,4-triazole in analogy to the procedure described for **A-13**. LC-MS B: t_R = 0.42 min; $[M+H]^+$ = 258.96.

(*R*)-3-(3-[1,2,4]Triazol-1-yl-benzyl)-morpholine (A-18)

The title compound was prepared from **A-17** in analogy to the procedure described for **A-12**. LC-MS B: t_R = 0.34 min; $[M+H]^+$ = 245.08.

(*R*)-5-(3-Pyrrol-1-yl-benzyl)-morpholin-3-one (A-19)

The title compound was prepared from **A-10** and pyrrole in analogy to the procedure described for **A-13**. LC-MS B: t_R = 0.64 min; $[M+H]^+$ = 257.08.

(*R*)-3-(3-Pyrrol-1-yl-benzyl)-morpholine (A-20)

The title compound was prepared from **A-19** in analogy to the procedure described for **A-12**. LC-MS B: t_R = 0.51 min; $[M+H]^+$ = 242.94.

(*S*)-2-Amino-3-(3-iodo-phenyl)-propionic acid hydrochloride (A-21)

The title compound was prepared from Boc-3-iodo-L-phenylalanine (Matrix Scientific) in analogy to the procedure described for **A-7**. LC-MS A: t_R = 0.49 min; $[M+H+MeCN]^+$ = 333.88.

(*S*)-2-Amino-3-(3-iodo-phenyl)-propan-1-ol (A-22)

The title compound was prepared from **A-21** in analogy to the procedure described for **A-8**. LC-MS A: t_R = 0.52 min; $[M+H+MeCN]^+$ = 319.06.

2-Chloro-*N*-[(*S*)-1-hydroxymethyl-2-(3-iodo-phenyl)-ethyl]-acetamide (A-23)

The title compound was prepared from **A-22** in analogy to the procedure described for **A-9**. LC-MS A: t_R = 0.71 min; $[M(^{35}Cl)+H]^+$ = 353.70.

(*S*)-5-(3-Iodo-benzyl)-morpholin-3-one (A-24)

The title compound was prepared from **A-23** in analogy to the procedure described for **A-10**. LC-MS A: t_R = 0.72 min; $[M+H+MeCN]^+$ = 359.01.

(*S*)-5-(3-[1,2,3]Triazol-2-yl-benzyl)-morpholin-3-one (A-25)

The title compound was prepared from **A-24** in analogy to the procedure described for **A-13**. LC-MS A: t_R = 0.65 min; $[M+H]^+$ = 259.18.

(*S*)-3-(3-[1,2,3]Triazol-2-yl-benzyl)-morpholine (A-26)

The title compound was prepared from **A-25** in analogy to the procedure described for **A-12**. LC-MS B: t_R = 0.42 min; $[M+H]^+$ = 245.19.

Listed in Table 1 below are morpholinones of type **A-6** prepared from the corresponding Boc-protected halophenyl alanine derivative **G-5**, in analogy to the sequence of reactions described for **A-13**. In most cases the isolated racemic morpholinone was subsequently separated into its *R*- and *S*-enantiomers by prep. chiral HPLC.

Table 1

No.	Starting material	Intermediate	t_R [min] LC-MS Method	MS-data m/z $[M+H]^+$
A-27	G-30	(*R*)-5-(2-Fluoro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-3-one	0.68 A	277.08
A-28	G-31	(*R*)-5-(2-Chloro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-3-one	0.72 A	(^{35}Cl) 293.07
A-29	G-32	(*R*)-5-(2-Methyl-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-3-one	0.70 A	273.13
A-30	G-33	(*R*)-5-(3-Chloro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-3-one	0.64 B	(^{35}Cl) 293.07
A-31	G-34	*rac*-5-(3-Fluoro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-3-one	0.70 A	277.12
A-32	G-35	*rac*-5-(2-Fluoro-3-[1,2,3]triazol-2-yl-benzyl)-morpholin-3-one	0.50 B	277.21
A-33	G-36	(*R*)-5-(4-Methyl-3-[1,2,3]triazol-2-yl-benzyl)-morpholin-3-one	0.56 B	273.31

Listed in Table 2 below are compounds of Structure 1 prepared from the corresponding intermediates of type **A-6**, in analogy to the procedure described for **A-12**.

Table 2

No.	**Starting material**	**Morpholine 1**	**t_R [min] LC-MS Method**	**MS-data m/z $[M+H]^+$**
A-34	A-27	(*R*)-3-(2-Fluoro-5-[1,2,3]triazol-2-yl-benzyl)-morpholine	0.53 A	263.10
A-35	A-28	(*R*)-3-(2-Chloro-5-[1,2,3]triazol-2-yl-benzyl)-morpholine	0.56 A	(^{35}Cl) 279.10
A-36	A-29	(*R*)-3-(2-Methyl-5-[1,2,3]triazol-2-yl-benzyl)-morpholine	0.56 A	259.18
A-37	A-30	(*R*)-3-(3-Chloro-5-[1,2,3]triazol-2-yl-benzyl)-morpholine	0.58 A	320.09 $[M(^{35}Cl)+H+MeCN]^+$
A-38	A-31	*rac*-3-(3-Fluoro-5-[1,2,3]triazol-2-yl-benzyl)-morpholine	0.54 A	304.13 $[M+H+MeCN]^+$
A-39	A-32	*rac*-3-(2-Fluoro-3-[1,2,3]triazol-2-yl-benzyl)-morpholine	0.39 B	263.22
A-40	A-33	(*R*)-3-(4-Methyl-3-[1,2,3]triazol-2-yl-benzyl)-morpholine	0.44 B	259.02

(*R*)-5-(2-Methyl-5-pyrazol-1-yl-benzyl)-morpholin-3-one (A-41)

The title compound was prepared from **G-32** in analogy to the sequence of reactions described for **A-11** followed by prep. chiral HPLC. LC-MS A: t_R = 0.68 min; $[M+H]^+$ = 272.14.

(*R*)-3-(2-Methyl-5-pyrazol-1-yl-benzyl)-morpholine (A-42)

The title compound was prepared from **A-41** in analogy to the procedure described for **A-12**. LC-MS A: t_R = 0.55 min; $[M+H]^+$ = 257.99.

<u>General method B for the synthesis of 3-benzyl morpholines of Structure 1</u>

(*R*)-3-(3-Iodo-benzyl)-morpholine (B-5)

The title compound was prepared from **A-10** in analogy to the procedure described for **A-13**. LC-MS B: t_R = 0.50 min; $[M+H+MeCN]^+$ = 345.02.

(*R*)-3-(3-Iodo-benzyl)-morpholine-4-carboxylic acid tert-butyl ester (B-6)

A solution of Boc_2O (635 mg, 2.91 mmol) in DCM (4 mL) was added dropwise to a RT solution of (*R*)-3-(3-iodo-benzyl)-morpholine **B-5** (864 mg, 2.85 mmol) and Et_3N (0.4 mL, 2.99 mmol) in DCM (4 mL) under argon and the resulting mixture was stirred for 3h. The reaction mixture was quenched with 1M aq. citric acid and stirred for another 10 min. The layers were separated and the aq. layer was re-extracted once with DCM. The combined organic extracts were washed with 1M aq. citric acid and water (2x), dried over Na_2SO_4, filtered and evaporated *in vacuo* to give the title compound that was used further without purification. LC-MS B: t_R = 0.95 min; $[M-Me]^+$ = 388.82.

(*R*)-3-[3-(4,4,5,5-Tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-morpholine-4-carboxylic acid tert-butyl ester (B-7)

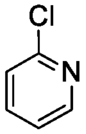
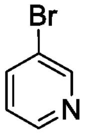
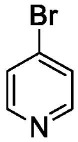
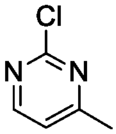
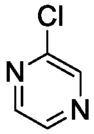
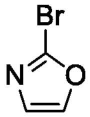
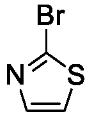
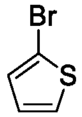
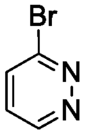
Bis(pinacolato)diboron (732 mg, 2.88 mmol) followed by potassium acetate (772 mg, 7.86 mmol) were added in one portion to a RT solution of (*R*)-3-(3-iodo-benzyl)-morpholine-4-carboxylic acid tert-butyl ester **B-6** (1.06 g, 2.62 mmol) in DMSO (10 mL) and argon was bubbled through the resulting suspension for 1 min. $Pd(dppf)Cl_2 \cdot DCM$ (128 mg, 0.16 mmol) was then added in one portion and the suspension was heated to 80°C for 20 min. The reaction mixture was cooled back to RT, diluted with Et_2O and filtered through a celite plug rinsing with Et_2O and a little MeOH. The volatiles were removed *in vacuo* and the residue was dissolved in Et_2O and washed with water (2x) and sat. aq. NH_4Cl soln. The organic phase was dried over Na_2SO_4, filtered through a second celite plug and evaporated *in vacuo* to give the title compound that was used further without purification. LC-MS B: t_R = 1.01 min; $[M+H-{}^tBu]^+$ = 348.18.

(R)-3-(3-Pyrimidin-2-yl-benzyl)-morpholine-4-carboxylic acid tert-butyl ester (B-8)

2-Bromopyrimidine (43 mg, 0.27 mmol) was added in one portion to a RT solution of (*R*)-3-[3-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-morpholine-4-carboxylic acid tert-butyl ester **B-7** (100 mg, 0.25 mmol) in dioxane (0.76 mL) under argon. EtOH (0.38 mL) was then added followed by 2M aq. Na_2CO_3 (0.38 mL, 0.74 mmol) and argon was bubbled through the resulting suspension for 1 min. $Pd(dppf)Cl_2 \cdot DCM$ (12 mg, 6 mol%) was added in one portion and the resulting mixture was heated to 80°C for 2h. The reaction mixture was cooled to RT, quenched into water and filtered through a celite plug washing with TBME. The layers were separated and the aqueous phase was extracted with TBME (3x). The combined organic extracts were washed with brine, dried over Na_2SO_4, filtered through a second celite plug and evaporated *in vacuo* to give the crude product that was purified by prep. HPLC (method E) to give the title compound as a yellow oil. LC-MS B: t_R = 0.79 min; $[M+H]^+$ = 356.05.

Listed in Table 3 below are intermediates of type **B-4**, prepared from (*R*)-3-[3-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-morpholine-4-carboxylic acid tert-butyl ester **B-7** according to the procedure described for **B-8**.

Table 3

No.	Aryl halide	Intermediate	t_R [min] LC-MS Method	MS-data m/z [M+H]⁺
B-9		(*R*)-3-(3-Pyridin-2-yl-benzyl)-morpholine-4-carboxylic acid tert-butyl ester	0.60 B	355.03
B-10		(*R*)-3-(3-Pyridin-3-yl-benzyl)-morpholine-4-carboxylic acid tert-butyl ester	0.59 B	355.11
B-11		(*R*)-3-(3-Pyridin-4-yl-benzyl)-morpholine-4-carboxylic acid tert-butyl ester	0.57 B	355.14
B-12		(*R*)-3-[3-(4-Methyl-pyrimidin-2-yl)-benzyl]-morpholine-4-carboxylic acid tert-butyl ester	0.85 B	369.51
B-13		(*R*)-3-(3-Pyrazin-2-yl-benzyl)-morpholine-4-carboxylic acid tert-butyl ester	0.77 B	356.03
B-14		(*R*)-3-(3-Oxazol-2-yl-benzyl)-morpholine-4-carboxylic acid tert-butyl ester	0.79 B	345.04
B-15		(*R*)-3-(3-Thiazol-2-yl-benzyl)-morpholine-4-carboxylic acid tert-butyl ester	0.84 B	361.01
B-16		(*R*)-3-(3-Thiophen-2-yl-benzyl)-morpholine-4-carboxylic acid tert-butyl ester	0.97 B	345.00 [M-Me]⁺
B-17		(*R*)-3-(3-Pyridazin-3-yl-benzyl)-morpholine-4-carboxylic acid tert-butyl ester	0.68 B	356.05

Listed in Table 4 below are compounds of Structure 1 prepared from the corresponding intermediates of type **B-4**, in analogy to the procedure described for **A-7**.

Table 4

No.	Starting material	Morpholine 1	t_R [min] LC-MS Method	MS-data m/z $[M+H]^+$
B-18	B-8	(*R*)-3-(3-Pyrimidin-2-yl-benzyl)-morpholine hydrochloride	0.40 B	256.18
B-19	B-9	(*R*)-3-(3-Pyridin-2-yl-benzyl)-morpholine hydrochloride	0.31 B	255.08
B-20	B-10	(*R*)-3-(3-Pyridin-3-yl-benzyl)-morpholine hydrochloride	0.28 B	296.11 $[M+H+MeCN]^+$
B-21	B-11	(*R*)-3-(3-Pyridin-4-yl-benzyl)-morpholine hydrochloride	0.27 B	255.16
B-22	B-12	(*R*)-3-[3-(4-Methyl-pyrimidin-2-yl)-benzyl]-morpholine hydrochloride	0.44 B	270.08
B-23	B-13	(*R*)-3-(3-Pyrazin-2-yl-benzyl)-morpholine hydrochloride	0.39 B	256.07
B-24	B-14	(*R*)-3-(3-Oxazol-2-yl-benzyl)-morpholine hydrochloride	0.41 B	245.08
B-25	B-15	(*R*)-3-(3-Thiazol-2-yl-benzyl)-morpholine hydrochloride	0.45 B	261.19
B-26	B-16	(*R*)-3-(3-Thiophen-2-yl-benzyl)-morpholine hydrochloride	0.56 B	301.19 $[M+H+MeCN]^+$
B-27	B-17	(*R*)-3-(3-Pyridazin-3-yl-benzyl)-morpholine hydrochloride	0.35 B	297.23

[(*R*)-3-(3-Iodo-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone (B-28)

A solution of (*R*)-3-(3-iodo-benzyl)-morpholine **B-5** (100 mg, 0.33 mmol) and DIPEA (57 µL, 0.33 mmol) in DMF (1.5 mL) was added to a RT solution of 2-(2*H*-1,2,3-triazol-2-yl)benzoic acid **E-2** (62 mg, 0.33 mmol), TBTU (111 mg, 0.35 mmol) and DIPEA (57 µL, 0.33 mmol) in DMF (1.5 ml) under argon and the resulting mixture was stirred for 22h. The reaction mixture was quenched with sat. aq. $NaHCO_3$ and stirred for 10 min before being diluted with water and extracted with DCM (3x). The combined organic extracts were washed with 2M aq. NaOH (1x), 2M aq. HCl (1x) and brine (1x), dried over Na_2SO_4, filtered and evaporated *in* *vacuo*. The crude product was purified by prep. HPLC (method F) to give the title compound as a white solid. LC-MS D: t_R = 0.93 min; $[M+H]^+$ = 474.91.

3-[(*R*)-4-(2-[1,2,3]Triazol-2-yl-benzoyl)-morpholin-3-ylmethyl]-benzonitrile (B-29)

$Pd_2(dba)_3$ (11 mg, 0.01 mmol), dppf (7 mg, 0.01 mmol), H_2O (45 µL, 2.49 mmol) and zinc cyanide (73 mg, 0.62 mmol) were added to a RT solution of [(*R*)-3-(3-iodo-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone **B-28** (118 mg, 0.25 mmol) in DMF (2.49 mL, ~0.1M soln.) and argon was bubbled through the reaction mixture for 5 min before it was heated to 90°C for 17h. The reaction mixture was cooled to RT and quenched with sat. aq. NH_4Cl before being extracted with EtOAc (3x). The combined organic extracts were dried over Na_2SO_4, filtered and evaporated *in vacuo* to give the crude product that was purified by flash chromatography (eluting with a gradient of 25% to 75% EtOAc in hexane) to give the title compound as a yellow solid. LC-MS D: t_R = 0.81 min; $[M+H]^+$ = 374.05.

[(*R*)-3-(3-Iodo-benzyl)-morpholin-4-yl]-(5-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone (B-30)

The title compound was prepared from **B-5** and **E-3** in analogy to the procedure described for **B-28**. LC-MS D: t_R = 0.94 min; $[M+H]^+$ = 488.85.

3-[(*R*)-4-(5-Methyl-2-[1,2,3]triazol-2-yl-benzoyl)-morpholin-3-ylmethyl]-benzonitrile (B-31)

The title compound was prepared from **B-30** in analogy to the procedure described for **B-29**. LC-MS D: t_R = 0.85 min; $[M+H]^+$ = 388.04.

(*R*)-3-(3-Iodo-4-methoxy-benzyl)-morpholine (B-32)

The title compound was prepared from **C-7** in analogy to the procedure described for **A-12**. LC-MS B: t_R = 0.48 min; $[M+H]^+$ = 334.06.

(*R*)-3-(3-Iodo-4-methoxy-benzyl)-morpholine-4-carboxylic acid tert-butyl ester (B-33)

The title compound was prepared from **B-32** in analogy to the procedure described for **B-6**. LC-MS B: t_R = 0.91 min; $[M-Me]^+$ = 418.86.

(*R*)-3-(3-Cyano-4-methoxy-benzyl)-morpholine-4-carboxylic acid tert-butyl ester (B-34)

The title compound was prepared from **B-33** in analogy to the procedure described for **B-29**. LC-MS B: t_R = 0.76 min; $[M-Me]^+$ = 318.13.

(*R*)-3-(4-Methoxy-3-[1,2,4]oxadiazol-3-yl-benzyl)-morpholine-4-carboxylic acid tert-butyl ester (B-35)

The title compound was prepared from **B-34** in analogy to the procedure described for **Example 1**. LC-MS B: t_R = 0.72 min; $[M+H-{}^tBu]^+$ = 320.04.

(*R*)-3-(4-Methoxy-3-[1,2,4]oxadiazol-3-yl-benzyl)-morpholine hydrochloride (B-36)

The title compound was prepared from **B-35** in analogy to the procedure described for **A-7**. LC-MS B: t_R = 0.37 min; $[M+H]^+$ = 276.11.

(*R*)-3-(3-Cyano-benzyl)-morpholine-4-carboxylic acid tert-butyl ester (B-37)

The title compound was prepared from **B-6** in analogy to the procedure described for **B-29**. LC-MS B: t_R = 0.77 min; $[M-Me]^+$ = 288.18.

(*R*)-3-(3-[1,2,4]Oxadiazol-3-yl-benzyl)-morpholine-4-carboxylic acid tert-butyl ester (B-38)

The title compound was prepared from **B-37** in analogy to the procedure described for **Example 1**. LC-MS A: t_R = 0.88 min; $[M+H-{}^tBu]^+$ = 290.01.

(*R*)-3-(3-[1,2,4]Oxadiazol-3-yl-benzyl)-morpholine hydrochloride (B-39)

The title compound was prepared from **B-38** in analogy to the procedure described for **A-7**. LC-MS B: t_R = 0.37 min; $[M+H]^+$ = 276.11.

(*R*)-3-(2-Fluoro-5-[1,2,4]oxadiazol-3-yl-benzyl)-morpholine hydrochloride (B-40)

The title compound was prepared from (*R*)-2-amino-3-(5-bromo-2-fluorophenyl)propan-1-ol (Chiral Quest), in analogy to the sequence of reactions described for the preparation of **B-39**. LC-MS A: t_R = 0.51 min; $[M+H]^+$ = 264.13.

***rac*-3-(4-Methyl-3-[1,2,4]oxadiazol-3-yl-benzyl)-morpholine hydrochloride (B-41)**

The title compound was prepared from **G-36** in analogy to the sequence of reactions described for the preparation of **B-39**. LC-MS A: t_R = 0.54 min; $[M+H]^+$ = 260.21.

***rac*-3-(4-Chloro-3-[1,2,4]oxadiazol-3-yl-benzyl)-morpholine hydrochloride (B-42)**

The title compound was prepared from **G-37** in analogy to the sequence of reactions described for the preparation of **B-39**. LC-MS A: t_R = 0.53 min; $[M({}^{35}Cl)+H]^+$ = 321.13.

(*R*)-3-(2-Fluoro-5-pyrimidin-2-yl-benzyl)-morpholine hydrochloride (B-43)

The title compound was prepared from (*R*)-2-amino-3-(5-bromo-2-fluorophenyl)propan-1-ol (Chiral Quest) or **G-30**, in analogy to the sequence of reactions described for the preparation of **B-18**. LC-MS A: t_R = 0.52 min; $[M+H]^+$ = 273.85.

(*R*)-3-(2-Fluoro-5-(pyridazin-3-yl)benzyl)morpholine hydrochloride (B-44)

The title compound was prepared from (*R*)-2-amino-3-(5-bromo-2-fluorophenyl)propan-1-ol (Chiral Quest) or **G-30**, in analogy to the sequence of reactions described for the preparation of **B-18**, substituting 2-bromopyrimidine for 3-bromopyridazine hydrobromide. LC-MS A: t_R = 0.48 min; $[M+H+MeCN]^+$ = 315.22.

Example compounds 1 and 2

Example 1: [(*R*)-3-(3-[1,2,4]Oxadiazol-3-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone

Step 1: Hydroxylamine ~50% in H_2O (72 µL, 1.17 mmol) was added to a RT suspension of 3-[(*R*)-4-(2-[1,2,3]triazol-2-yl-benzoyl)-morpholin-3-ylmethyl]-benzonitrile **B-29** (30 mg, 0.08 mmol) in EtOH (1 mL) and the resulting suspension was heated to 70°C for 45 min. The volatiles were removed *in vacuo* and the crude hydroxyamidine intermediate was used directly in step 2.

Step 2: p-Toluenesulfonic acid monohydrate (1 mg, 5 mol%) was added to a solution of crude hydroxyamidine from step 1 in trimethyl orthoformate (1 mL) and the resulting mixture was heated to 100°C for 15 min. The reaction mixture was cooled to RT and filtered through a silica plug (eluting with EtOAc) to give the crude product that was subsequently purified by prep. HPLC (method F) to give the title compound as a white solid. LC-MS D: t_R = 0.82 min; $[M+H]^+$ = 417.03.

Example 2: (5-Methyl-2-[1,2,3]triazol-2-yl-phenyl)-[(*R*)-3-(3-[1,2,4]oxadiazol-3-yl-benzyl)-morpholin-4-yl]-methanone

The title compound was prepared from **B-31** in analogy to the procedure described for **Example 1**. LC-MS D: t_R = 0.82 min; $[M+H]^+$ = 431.02.

General method C for the synthesis of 3-benzyl morpholines of Structure 1

(*R*)-2-Amino-3-(4-methoxy-phenyl)-propan-1-ol (C-4)

The title compound was prepared from *p*-methoxy-D-phenyl alanine in analogy to the procedure described for **A-8**. LC-MS A: t_R = 0.43 min; $[M+H]^+$ = 182.29.

2-Chloro-*N*-[(*R*)-1-hydroxymethyl-2-(4-methoxy-phenyl)-ethyl]-acetamide (C-5)

The title compound was prepared from **C-4** in analogy to the procedure described for **A-9**. LC-MS A: t_R = 0.61 min; $[M(^{35}Cl)+H]^+$ = 257.88.

(*R*)-5-(4-Methoxy-benzyl)-morpholin-3-one (C-6)

The title compound was prepared from **C-5** in analogy to the procedure described for **A-10**. LC-MS A: t_R = 0.62 min; $[M+H+MeCN]^+$ = 263.17.

(*R*)-5-(3-Iodo-4-methoxy-benzyl)-morpholin-3-one (C-7)

A solution of NIS (559 mg, 2.49 mmol) in DCM (3 mL) was added dropwise to a RT solution of (*R*)-5-(4-methoxy-benzyl)-morpholin-3-one **C-6** (500 mg, 2.26 mmol) and trifluoromethanesulfonic acid (220 µL, 2.49 mmol) in DCM (3 mL) under argon and the resulting mixture was stirred for 40 min. The reaction was quenched with sat. aq. $NaHCO_3$

and the layers were separated. The organic layer was washed with water (2x), dried over Na_2SO_4, filtered and evaporated *in vacuo* to give the crude product that was purified by flash chromatography (eluting with a gradient of 50% to 100% EtOAc in hexane) to give the title compound as a pale yellow solid. LC-MS B: t_R = 0.62 min; $[M+H+MeCN]^+$ = 388.95.

(*R*)-5-(4-Methoxy-3-pyrazol-1-yl-benzyl)-morpholin-3-one (C-8)

A mixture of (*R*)-5-(3-iodo-4-methoxy-benzyl)-morpholin-3-one **C-7** (60 mg, 0.17 mmol), pyrazole (18 mg, 0.30 mmol), K_2CO_3 (48 mg, 0.35 mmol), copper(I) chloride (1.7 mg, 0.02 mmol) and L-proline (4 mg, 0.04 mmol) in DMF (1 mL) was heated under argon to 110°C for 168h. The reaction mixture was cooled to RT and partitioned between water and DCM before being filtered through a celite plug. The layers were separated and the aqueous phase was re-extracted with DCM (2x). The combined organic phases were washed with brine, dried over Na_2SO_4, filtered and evaporated *in vacuo* to give the crude product that was purified by flash chromatography (Biotage SP1, 10g SNAP-cartridge eluting with 95:5 DCM:MeOH) to give the title compound as a brown oil. LC-MS B: t_R = 0.53 min; $[M+H]^+$ = 288.16.

(*R*)-3-(4-Methoxy-3-pyrazol-1-yl-benzyl)-morpholine (C-9)

The title compound was prepared from **C-8** in analogy to the procedure described for **A-12**. LC-MS B: t_R = 0.44 min; $[M+H]^+$ = 273.91.

General method D for the synthesis of example compounds of formula (I)

(*R*)-3-(4-Methoxy-benzyl)-morpholine (D-5)

The title compound was prepared from **C-6** in analogy to the procedure described for **A-12**. LC-MS B: t_R = 0.38 min; $[M+H]^+$ = 208.27.

[(*R*)-3-(4-Methoxy-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone (D-6)

The title compound was prepared from **D-5** and **E-2** in analogy to the procedure described for **B-28**. LC-MS B: t_R = 0.72 min; $[M+H]^+$ = 378.99.

[(*R*)-3-(3-Iodo-4-methoxy-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone (D-7)

The title compound was prepared from **D-6** in analogy to the procedure described for **C-7**. LC-MS B: t_R = 0.80 min; $[M+H]^+$ = 504.81.

{(*R*)-3-[4-Methoxy-3-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-morpholin-4-yl}-(2-[1,2,3]triazol-2-yl-phenyl)-methanone (D-8)

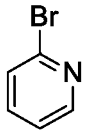
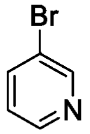
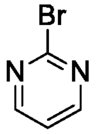
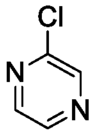
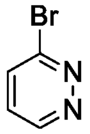
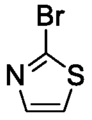
The title compound was prepared from **D-7** in analogy to the procedure described for **B-7**. LC-MS B: t_R = 0.81 min; $[M+H]^+$ = 505.02.

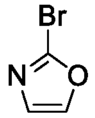
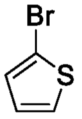
Example compounds 3 to 10

The aryl halide (0.20 mmol) followed by K_2CO_3 (82 mg, 0.60 mmol) were added successively in one portion to a RT solution of {(*R*)-3-[4-methoxy-3-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-morpholin-4-yl}-(2-[1,2,3]triazol-2-yl-phenyl)-methanone **D-8** (100 mg, 0.20 mmol) in dioxane (1.8 mL) and H_2O (0.9 mL) under argon. The resulting mixture was degassed with argon for 1 min before $Pd(PPh_3)_4$ (12 mg, 0.01 mmol) was added and the reaction mixture was heated to 90°C for 1h. The reaction mixture was cooled to RT and quenched with water. The resulting suspension was passed through a phase separator filter extracting with DCM (2x). The combined organic extracts were filtered through a celite plug and evaporated *in vacuo*. The crude product was purified by prep. HPLC (method E) to furnish the desired product.

Listed in Table 5 below are example compounds, prepared from **D-8** according to the above Suzuki procedure.

Table 5

Example No.	Aryl halide	Compound of Formula (I)	t_R [min] LC-MS Method	MS-data m/z $[M+H]^+$
3		[(*R*)-3-(4-Methoxy-3-pyridin-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone	0.54 B	455.94
4		[(*R*)-3-(4-Methoxy-3-pyridin-3-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone	0.56 B	455.95
5		[(*R*)-3-(4-Methoxy-3-pyrimidin-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone	0.59 B	456.93
6		[(*R*)-3-(4-Methoxy-3-pyrazin-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone	0.66 B	456.93
7		[(*R*)-3-(4-Methoxy-3-pyridazin-3-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone	0.61 B	456.94
8		[(*R*)-3-(4-Methoxy-3-thiazol-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone	0.74 B	461.90

9		[(*R*)-3-(4-Methoxy-3-oxazol-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone	0.63 B	445.92
10		[(*R*)-3-(4-Methoxy-3-thiophen-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone	0.85 B	460.91

General method E for the synthesis of *o*-triazolocarboxylic acids of Structure 2

2-Fluoro-3-methyl-6-(2*H*-1,2,3-triazol-2-yl)benzoic acid (E-1)

The title compound was prepared in analogy to the procedure described in WO2008/069997.

Cs_2CO_3 (6.98 g, 21.4 mmol) was added portionwise to a RT solution of 2-fluoro-6-iodo-3-methyl-benzoic acid (3.0 g, 10.7 mmol) in DMF (15 mL) under argon followed by 1*H*-1,2,3-triazole (1.24 mL, 21.4 mmol) and Cu(I)I (103 mg, 0.536 mmol) and the resulting blue suspension was stirred at 80°C overnight. The reaction mixture was quenched with 2M aq. HCl and filtered through a celite plug before being extracted with DCM (3x). The combined organic layers were dried over Na_2SO_4, filtered and evaporated *in vacuo* to give the crude product that was purified by prep. HPLC (method E) to give the title compound as a pale yellow solid. LC-MS B: t_R = 0.55 min; $[M+H]^+$ = 222.01.

Listed in Table 6 below are *o*-triazolocarboxylic acids of Structure **2**, unless otherwise stated, prepared from the corresponding commercially available iodo-carboxylic acid according to the above procedures.

Table 6

No.	**Carboxylic Acid 2**	**t_R [min] LC-MS Method**	**MS-data m/z $[M+H]^+$**
E-2	2-(2*H*-1,2,3-Triazol-2-yl)benzoic acid	0.55 A	190.08
E-3	5-Methyl-2-(2*H*-1,2,3-triazol-2-yl)benzoic acid	0.53 B	204.13
E-4	4-Methyl-2-(2*H*-1,2,3-triazol-2-yl)benzoic acid	0.53 B	204.23
E-5	5-Chloro-2-(2*H*-1,2,3-triazol-2-yl)benzoic acid	0.66 A	(^{35}Cl) 224.3
E-6	4,5-Dimethyl-2-(2*H*-1,2,3-triazol-2-yl)benzoic acid	0.59 B	218.09

E-7	5-Fluoro-2-(2*H*-1,2,3-triazol-2-yl)benzoic acid	0.49 B	208.32
E-8$^{\#}$	4-Fluoro-2-(2*H*-1,2,3-triazol-2-yl)benzoic acid	0.51 B	208.16
E-9	2-Fluoro-3-methoxy-6-(2*H*-1,2,3-triazol-2-yl)benzoic acid	0.48 B	238.01
E-10	5-Methoxy-2-(2*H*-1,2,3-triazol-2-yl)benzoic acid	0.49 B	220.19
E-11$^{\#\dagger}$	5-Methoxy-4-methyl-2-(2*H*-1,2,3-triazol-2-yl)benzoic acid	0.68 A	234.05
E-12	4,5-Dimethoxy-2-(2*H*-1,2,3-triazol-2-yl)benzoic acid	0.46 B	250.03
E-13	5-Cyano-2-(2*H*-1,2,3-triazol-2-yl)benzoic acid	0.46 B	No ionisation
E-14	6-Methyl-3-(2*H*-1,2,3-triazol-2-yl)picolinic acid	0.30 B	205.35
E-15$^{\#}$	3-Fluoro-2-(2*H*-1,2,3-triazol-2-yl)benzoic acid	0.56 A	208.08
E-16$^{\#\dagger}$	3,5-Dimethyl-2-(2*H*-1,2,3-triazol-2-yl)benzoic acid	0.66 A	218.10
E-17	4-Chloro-2-(2*H*-1,2,3-triazol-2-yl)benzoic acid	0.66 A	(^{35}Cl) 224.10
E-18$^{\#}$	4-Methoxy-2-(2*H*-1,2,3-triazol-2-yl)benzoic acid	0.60 A	220.05
E-19$^{\#\dagger}$	4-Fluoro-5-methoxy-2-(2*H*-1,2,3-triazol-2-yl)benzoic acid	0.64 A	238.1
E-20	3,4-Dimethyl-2-(2*H*-1,2,3-triazol-2-yl)benzoic acid	0.65 A	218.30
E-21$^{\#}$	2-(2*H*-1,2,3-triazol-2-yl)-4-(trifluoromethyl)benzoic acid	0.72 A	No ionisation
E-22$^{\#\dagger}$	4-Chloro-5-methoxy-2-(2*H*-1,2,3-triazol-2-yl)benzoic acid	0.70 A	(^{35}Cl) 254.01
E-23$^{\#}$	3-Chloro-2-(2*H*-1,2,3-triazol-2-yl)benzoic acid	0.61 A	(^{35}Cl) 224.09
E-24$^{\#}$	4,5-Difluoro-2-(2*H*-1,2,3-triazol-2-yl)benzoic acid	0.56 B	No ionisation

E-25	2-Methyl-6-(2*H*-1,2,3-triazol-2-yl)benzoic acid	0.51 B	204.41
E-26	2-Fluoro-6-(2*H*-1,2,3-triazol-2-yl)benzoic acid	0.46 B	208.21

[#] Prepared from the corresponding *o*-bromo-carboxylic acid

[ǂ] Corresponding *o*-bromo-carboxylic acid was prepared according to the procedure described below

Synthesis of 2-bromo-substituted benzoic acids was performed in analogy to described methods (Tetrahedron Letters, **2009**, *50*, 1267-1269, J. Org. Chem, **2007**, *72*, 9786-9789).

2-Bromo-5-methoxy-4-methyl-benzoic acid

Br_2 (0.74 mL, 14.4 mmol) was added to a RT suspension of 3-methoxy-4-methylbenzoic acid (2.0 g, 12 mmol) in acetic acid (15 mL) and water (15 mL) and the resulting mixture was heated to 60°C for 2h. The reaction mixture was cooled to RT and filtered rinsing with cold water (40 mL) to yield 2-bromo-5-methoxy-4-methylbenzoic acid as a white solid that was used further without purification. LC-MS A: t_R = 0.76 min, $[M+H]^+$ = No ionisation. ^1H NMR (DMSO) δ_H: 7.49 (s, 1 H), 7.29 (s, 1 H), 3.82 (s, 3 H), 2.17 (s, 3 H).

2-Bromo-4-fluoro-5-methoxy-benzoic acid

The title compound was prepared from 4-fluoro-3-methoxybenzoic acid in analogy to the above described method. LC-MS A: t_R = 0.72 min, $[M+H]^+$ = No ionisation. ^1H NMR (DMSO) δ_H: 13.52 (bs, 1 H), 7.77 (dd, 1 H), 7.44 (dd, 1 H), 4.01 (s, 3 H).

2-Bromo-3,5-dimethyl-benzoic acid

The title compound was prepared from 3,5-dimethyl-benzoic acid in analogy to the above described method. LC-MS A: t_R = 0.75 min, $[M+H]^+$ = No ionisation. ^1H NMR (DMSO) δ_H: 7.56 (s, 1 H), 7.28 (m, 2 H), 2.36 (s, 3 H), 2.27 (s, 3 H).

2-Bromo-4-chloro-5-methoxybenzoic acid

The title compound was prepared from 4-chloro-3-methoxybenzoic acid in analogy to the above described method. LC-MS A: t_R = 0.77 min, $[M+H]^+$ = No ionisation. ^1H NMR (DMSO) δ_H: 13.60 (bs, 1 H), 7.82 (s, 1 H), 7.47 (s, 1 H), 3.91 (s, 3 H).

3-Methyl-2-(2*H*-1,2,3-triazol-2-yl)benzoic acid (E-27)

Step 1: K_2CO_3 (8.18 g, 59.2 mmol) was added to a RT solution of 2-fluoro-3-methylbenzonitrile (4.0 g, 29.6 mmol) and 1*H*-1,2,3-triazole (1.72 mL, 29.6 mmol) in DMF (80 mL) and the resulting suspension was heated to 120°C for 4h. The reaction mixture was cooled to RT and quenched with water before being extracted with EtOAc (3x). The combined organic extracts were washed with brine, dried over Na_2SO_4, filtered and evaporated *in vacuo* to give the crude product that was purified by flash chromatography (eluting with a gradient of 33% to 50% EtOAc in hexane) to give 3-methyl-2-(2*H*-1,2,3-triazol-2-yl)benzonitrile as a white solid. LC-MS B: t_R = 0.62 min; $[M+H]^+$ = 185.16.

Step 2: 4M aq. NaOH (10 mL, 40.2 mmol) was added to a RT solution of 3-methyl-2-(2*H*-1,2,3-triazol-2-yl)benzonitrile (1.48 g, 8.04 mmol) in MeOH (15 mL) and the resulting mixture was heated to 90°C for 50h. The reaction mixture was cooled to RT and diluted with water before the organic solvent was removed *in vacuo*. The remaining aqueous phase was acidified with 1M aq. HCl and extracted with EtOAc (3x). The combined organic phases were washed with brine, dried over Na_2SO_4, filtered and evaporated *in vacuo* to give the title compound that was used further without purification. LC-MS B: t_R = 0.50 min; $[M+H]^+$ = 186.17.

5-Chloro-4-methyl-2-(2*H*-1,2,3-triazol-2-yl)benzoic acid (E-28)

Cs_2CO_3 (742 mg, 2.28 mmol) was added portionwise to a RT solution of 2-bromo-5-chloro-4-methyl-benzoic acid methyl ester (300 mg, 1.14 mmol) in DMF (3 mL) followed by 1*H*-1,2,3-triazole (0.1 mL, 1.71 mmol), Cu(I)I (13 mg, 0.068 mmol) and DMCDA (40 μL, 0.23 mmol). The resulting suspension was heated to 120°C for 4h. The reaction mixture was cooled to RT, quenched with 2M aq. HCl and extracted with EtOAc (3x). The combined organic layers were dried over Na_2SO_4, filtered and evaporated *in vacuo* to give the crude product that was purified by prep. HPLC (method E) to give the title compound as a pale yellow solid. LC-MS A: t_R = 0.72 min; $[M(^{35}Cl)+H]^+$ = 238.01.

2-(2*H*-1,2,3-Triazol-2-yl)-3-(trifluoromethyl)benzoic acid (E-29)

The title compound was prepared from 2-iodo-3-(trifluoromethyl)benzonitrile in analogy to the procedure described for **E-27**. LC-MS A: t_R = 0.68 min; $[M+H]^+$ = No ionisation; ^1H NMR (DMSO) δ_H: 12.01 (m, 1 H), 8.20 (m, 2 H), 8.10 (s, 2 H), 7.95 (m, 1 H).

General method G for the synthesis of 3-benzyl morpholines of Structure 1

(2-Fluoro-5-iodo-phenyl)-methanol (G-6)

Borane.THF complex 1M soln. (94 mL, 94 mmol) was added dropwise to a 0°C suspension of 2-fluoro-5-iodobenzoic acid (10 g, 37.6 mmol) in THF (60 mL) under argon and after complete addition the reaction mixture was heated to 70°C for 2h. The reaction mixture was cooled to 0°C and quenched with MeOH and after stirring for 5 min the reaction mixture was evaporated *in vacuo*. The residue was partitioned between 2M aq. HCl and MeOH and stirred for 30 min at 50°C before being concentrated *in vacuo*. The remaining aqueous phase was diluted with additional water and extracted with DCM (3x). The combined organic extracts were dried (Na_2SO_4), filtered and evaporated *in vacuo* to give the title compound as a yellow solid that was used further without purification. LC-MS B: t_R = 0.66 min; $[M+H+Na]^+$

= 275.99; ^{1}H NMR (DMSO) δ_H: 7.77 (dd, J_1 = 7.0 Hz, J_2 = 2.3 Hz, 1 H), 7.64 (m, 1 H), 7.01 (dd, J_1 = 10.1 Hz, J_2 = 8.6 Hz, 1 H), 5.38 (t, J = 5.8 Hz, 1 H), 4.52 (d, J = 5.8 Hz, 2 H).

Listed in Table 7 below are intermediates of type **G-2**, prepared from the corresponding commercially available carboxylic acid according to the above procedure.

Table 7

No.	Intermediate	t_R [min] LC-MS Method	MS-data m/z [M+H+Na]$^+$
G-7	(2-Chloro-5-iodo-phenyl)-methanol	0.79 A	No ionisation
G-8	(5-Iodo-2-methyl-phenyl)-methanol	0.77 A	272.09
G-9	(3-Chloro-5-iodo-phenyl)-methanol	0.75 B	No ionisation
G-10	(3-Bromo-5-fluoro-phenyl)-methanol	0.72 A	No ionisation
G-11	(2-Fluoro-3-iodo-phenyl)-methanol	0.64 B	276.04
G-12	(3-Iodo-4-methyl-phenyl)-methanol	0.70 B	272.14
G-13	(4-Chloro-3-iodo-phenyl)-methanol	0.70 B	(^{35}Cl) 291.83

2-Bromomethyl-1-fluoro-4-iodo-benzene (G-14)

Phosphorus tribromide 1.0 M soln. in DCM (18.9 mL, 18.9 mmol) was added dropwise to a 0°C solution of (2-fluoro-5-iodo-phenyl)-methanol **G-6** (9.52 g, 37.8 mmol) in DCM (215 mL) and the resulting mixture was stirred for 1h before being quenched with water. The layers were separated and the aqueous phase was re-extracted with DCM (2x). The combined organic extracts were washed with brine, dried over Na_2SO_4, filtered and evaporated *in vacuo* to give the crude product that was purified by flash chromatography (eluting with 5% EtOAc in hexane) to give the title compound as a white solid. LC-MS B: t_R = 0.92 min; No ionisation; ^{1}H NMR (DMSO) δ_H: 7.93 (dd, J_1 = 7.1 Hz, J_2 = 2.3 Hz, 1 H), 7.74 (ddd, J_1 = 8.6 Hz, J_2 = 4.9 Hz, J_3 = 2.3 Hz, 1 H), 7.10 (dd, J_1 = 10.0 Hz, J_2 = 8.7 Hz, 1 H), 4.66 (s, 2 H).

Listed in Table 8 below are intermediates of type **G-3**, prepared from the corresponding benzyl alcohol **G-2**, according to the above procedure.

Table 8

No.	Intermediate	t_R [min] LC-MS Method	MS-data m/z $[M+H]^+$
G-15	2-Bromomethyl-1-chloro-4-iodo-benzene	0.96 A	No ionisation
G-16	2-Bromomethyl-4-iodo-1-methyl-benzene	0.96 A	No ionisation
G-17	1-Bromomethyl-3-chloro-5-iodo-benzene	1.01 B	No ionisation
G-18	1-Bromo-3-bromomethyl-5-fluoro-benzene	0.92 A	No ionisation
G-19	1-Bromomethyl-2-fluoro-3-iodo-benzene	0.90 B	No ionisation
G-20	4-Bromomethyl-2-iodo-1-methyl-benzene	0.97 B	No ionisation
G-21	4-Bromomethyl-1-chloro-2-iodo-benzene	0.94 A	No ionisation

2-tert-Butoxycarbonylamino-2-(2-fluoro-5-iodo-benzyl)-malonic acid diethyl ester (G-22)

A solution of diethyl(Boc-amino)malonate (6.96 g, 25.3 mmol, either commercially available or prepared by conventional Boc-protection of diethylaminomalonate hydrochloride) in DMF (7 mL) was added dropwise to a 0°C suspension of sodium hydride (0.926 g, 23.2 mmol) in DMF (45 mL) under N_2 and then a solution of 2-bromomethyl-1-fluoro-4-iodo-benzene **G-14** (6.62 g, 21.1 mmol) in DMF (30 mL) was added to the suspension. The resulting solution was warmed to RT and stirred for 1h. The reaction was quenched by the addition of water and the mixture was extracted with DCM (3x). The combined organic extracts were washed with brine, dried over Na_2SO_4, filtered and evaporated *in vacuo* to give the crude product as a white solid that was used further without purification. LC-MS B: t_R = 1.05 min; $[M+H]^+$ = 510.02.

Listed in Table 9 below are intermediates of type **G-4**, prepared from the corresponding benzyl bromide **G-3**, according to the above procedure.

Table 9

No.	Intermediate	t_R [min] LC-MS Method	MS-data m/z $[M+H]^+$
G-23	2-tert-Butoxycarbonylamino-2-(2-chloro-5-iodo-benzyl)-malonic acid diethyl ester	1.07 A	(^{35}Cl) 526.02
G-24	2-tert-Butoxycarbonylamino-2-(5-iodo-2-methyl-benzyl)-malonic acid diethyl ester	1.07 A	506.00
G-25	2-tert-Butoxycarbonylamino-2-(3-chloro-5-iodo-benzyl)-malonic acid diethyl ester	1.12 B	(^{35}Cl) 526.14
G-26	2-(3-Bromo-5-fluoro-benzyl)-2-tert-butoxycarbonylamino-malonic acid diethyl ester	1.05 A	No ionisation
G-27	2-tert-Butoxycarbonylamino-2-(2-fluoro-3-iodo-benzyl)-malonic acid diethyl ester	1.03 B	509.92
G-28	2-tert-Butoxycarbonylamino-2-(3-iodo-4-methyl-benzyl)-malonic acid diethyl ester	1.08 B	506.04
G-29	2-tert-Butoxycarbonylamino-2-(4-chloro-3-iodo-benzyl)-malonic acid diethyl ester	1.06 A	(^{35}Cl) 469.88

***rac*-2-tert-Butoxycarbonylamino-3-(2-fluoro-5-iodo-phenyl)-propionic acid (G-30)**

A suspension of 2-tert-butoxycarbonylamino-2-(2-fluoro-5-iodo-benzyl)-malonic acid diethyl ester **G-22** in EtOH (113 mL) was heated to 40°C and water (50 mL) was then added giving an easily stirrable emulsion. 1M aq. NaOH (93 mL) was carefully added and reaction mixture was heated to 100°C for 16h. The reaction mixture was cooled to RT and the volatiles were removed *in vacuo*. The remaining aqueous phase was extracted once with TBME and this extract was discarded. The aqueous layer was acidified with 25% aq. HCl and extracted with TBME (2x). The combined organic layers were washed with water, dried over Na_2SO_4, filtered and evaporated *in vacuo* to give the crude product that was purified by flash chromatography (eluting with a gradient of 25% to 50% EtOAc in hexane) to give the title compound as a white solid. LC-MS B: t_R = 0.80 min; $[M-Me]^+$ = 394.95.

Listed in Table 10 below are intermediates of type **G-5**, prepared from the corresponding malonic acid derivative **G-4**, according to the above procedure.

Table 10

No.	Intermediate	t_R [min] LC-MS Method	MS-data m/z $[M\text{-}Me]^+$
G-31	*rac*-2-tert-Butoxycarbonylamino-3-(2-chloro-5-iodo-phenyl)-propionic acid	0.88 A	(^{35}Cl) 410.85
G-32	*rac*-2-tert-Butoxycarbonylamino-3-(5-iodo-2-methyl-phenyl)-propionic acid	0.88 A	390.91
G-33	*rac*-2-tert-Butoxycarbonylamino-3-(3-chloro-5-iodo-phenyl)-propionic acid	0.87 B	(^{35}Cl) 410.80
G-34	*rac*-3-(3-Bromo-5-fluoro-phenyl)-2-tert-butoxycarbonylamino-propionic acid	0.85 A	(^{79}Br) 347.01
G-35	*rac*-2-tert-Butoxycarbonylamino-3-(2-fluoro-3-iodo-phenyl)-propionic acid	0.79 B	394.92
G-36	*rac*-2-tert-Butoxycarbonylamino-3-(3-iodo-4-methyl-phenyl)-propionic acid	0.84 B	391.00
G-37	*rac*-2-tert-Butoxycarbonylamino-3-(4-chloro-3-iodo-phenyl)-propionic acid	0.84 B	(^{35}Cl) 410.87

General method H for the synthesis of 3-benzyl morpholines of Structure 1

rac-2-Amino-3-(3-iodo-phenyl)-2-methyl-propionic acid ethyl ester (H-5)

Step 1: A suspension of DL-alanine ethyl ester hydrochloride (10 g, 65.1 mmol) in DCM (150 mL) was washed with 2M aq. NaOH and the layers were separated. The organic phase was dried over Na_2SO_4, filtered and the filtrate was cooled to 0°C before $MgSO_4$ hydrate (11.3 g) followed by pivalaldeyde (7.72 g, 89.6 mmol) were added and the resulting mixture was warmed to RT and stirred for 16h. The reaction mixture was filtered and evaporated *in vacuo* to give *rac*-ethyl 2-((2,2-dimethylpropylidene)amino)propanoate that was used further without purification.

Step 2: 3-Iodobenzyl bromide (14.4 g, 48.6 mmol) was added to a RT solution of *rac*-ethyl 2-((2,2-dimethylpropylidene)amino)propanoate (10 g, 48.6 mmol) from above in toluene (100 mL) under argon and the resulting mixture was cooled to -10°C before KO^{t}Bu (10.9 g, 97.2 mmol) was added portionwise. The reaction mixture was stirred at 0°C for 4h before being quenched with water. The toluene was evaporated *in vacuo* and the remaining aqueous phase was extracted with EtOAC (3x). The combined organic extracts were dried over Na_2SO_4, filtered and evaporated *in vacuo*. The residue was stirred in 1M aq. HCl overnight after which LCMS showed the desired product. EtOAc was added and the mixture was stirred for 30 min before the layers were separated. The organic phase was discarded and the aqueous phase was basified with 2M aq. NaOH and re-extracted with EtOAc (3x). The combined organic extracts were dried over Na_2SO_4, filtered and evaporated *in vacuo* to give the title compound that was used further without purification. LC-MS D: t_R = 0.88 min; $[M+H+MeCN]^+$ = 375.06.

***rac*-2-Amino-3-(3-iodo-phenyl)-2-methyl-propan-1-ol (H-6)**

BH_3.THF Complex 1 M soln. in THF (9 mL, 9 mmol) was added dropwise to a 0°C solution of *rac*-2-amino-3-(3-iodo-phenyl)-2-methyl-propionic acid ethyl ester **H-5** (1.2 g, 3.6 mol) in THF (10 mL) under argon and the resulting mixture was stirred for 5 min at 0°C before being warmed to RT and stirred overnight. The reaction mixture was cooled to 0°C and quenched with MeOH before being evaporated *in vacuo*. The residue was partioned between 2M aq. HCl and TBME and stirred for 30 min. The phases were separated and the aqueous phase was re-extracted with TBME (2x) and the combined organic extracts were discarded. The aqueous layer was basified with 2M aq. NaOH and re-extracted with DCM (3x). The combined DCM extracts were washed with brine, dried over Na_2SO_4, filtered and evaporated *in vacuo* to give the title compound as a white solid. LC-MS D: t_R = 0.74 min; $[M+H+MeCN]^+$ = 333.02.

***rac*-2-Chloro-*N*-[1-hydroxymethyl-2-(3-iodo-phenyl)-1-methyl-ethyl]-acetamide (H-7)**

NaOH 1M aq. soln. (10 mL) followed by NaOH 32% (270 μL) were added to a 0°C solution of *rac*-2-amino-3-(3-iodo-phenyl)-2-methyl-propan-1-ol **H-6** (850 mg, 2.92 mmol) in DCM (10 mL). After 10 min a solution of chloroacetyl chloride (261 mL, 3.21 mmol) in DCM (10 mL) was added dropwise to the reaction mixture maintaining the temperature below 5°C. The resulting suspension was heated to 35°C for 30 min after which complete formation of product was observed by LCMS. The layers were separated and the aqueous layer extracted with DCM (2x). The combined organic extracts were washed with brine, dried over Na_2SO_4, filtered and evaporated *in vacuo* to give the title compound that was used further without purification. LC-MS A: t_R = 0.79 min; $[M(^{35}Cl)+H]^+$ = 367.91.

***rac*-5-(3-Iodo-benzyl)-5-methyl-morpholin-3-one (H-8)**

A solution of *rac*-2-chloro-*N*-[1-hydroxymethyl-2-(3-iodo-phenyl)-1-methyl-ethyl]-acetamide **H-7** (1.0 g, 2.7 mmol) in THF (13 mL) was added dropwise to a RT solution of KO^{t}Bu (6.8 mL, 6.8 mmol, 1M soln. in THF) under argon and the reaction mixture was stirred for 20 min. The reaction was quenched with 1M aq. HCl, diluted with water and concentrated *in vacuo*. The remaining aqueous phase was extracted with DCM (3x) and the combined organic extracts were dried over Na_2SO_4, filtered and evaporated *in vacuo* to give the title compound that was used further without purification. LC-MS A: t_R = 0.75 min; $[M+H+MeCN]^+$ = 373.02.

***rac*-5-Methyl-5-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-3-one (H-9)**

DMCDA (85 μL, 0.538 mmol) followed by 1*H*-1,2,3-triazole (0.31 mL, 5.38 mmol) were added to a mixture of *rac*-5-(3-iodo-benzyl)-5-methyl-morpholin-3-one **H-8** (890 mg, 2.69 mmol), Cs_2CO_3 (1.75 g, 5.38 mmol) and CuI (77 mg, 0.40 mmol) in DMF (5 mL) under argon and the resulting blue suspension was heated to 120°C for 18h. The reaction mixture was cooled to RT before being quenched with water and filtered over celite rinsing with water and DCM. The layers were separated and the aqueous phase was re-extracted with DCM (2x). The combined organic extracts were washed with brine, dried over Na_2SO_4, filtered and evaporated *in vacuo*. The crude product was purified by flash chromatography (eluting with a gradient of 75% to 100% EtOAc in hexane) to give the title compound as a pale brown solid. LC-MS A: t_R = 0.69 min; $[M+H]^+$ = 273.21.

***rac*-3-Methyl-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholine (H-10)**

The title compound was prepared from **H-9** in analogy to the procedure described for **A-12**. LC-MS A: t_R = 0.55 min; $[M+H]^+$ = 259.07.

General method I for the synthesis of 3-benzyl morpholines of Structure 1

(*R*)-3-Oxo-5-(3-[1,2,3]triazol-2-yl-benzyl)-morpholine-4-carboxylic acid tert-butyl ester (I-5)

Boc_2O (1.79 g, 8.19 mmol) was added in one portion to a RT solution of (*R*)-5-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-3-one **A-13** (1.06 g, 4.09 mmol) and DMAP (51 mg, 0.41 mmol) in Et_3N:MeCN 3:1 (16 mL) under Argon and the resulting mixture was stirred for 1.5h. The reaction mixture was diluted with EtOAc, transferred to a separating funnel and washed successively with 3% aq. HCl, sat. aq. $NaHCO_3$ and brine. The organic phase was dried over Na_2SO_4, filtered and evaporated *in vacuo* to give the title compound that was used further without purification. LC-MS B: t_R = 0.81 min; $[M+H-Boc]^+$ = 259.17.

[(*R*)-2-(2-Oxo-propoxy)-1-(3-[1,2,3]triazol-2-yl-benzyl)-ethyl]-carbamic acid tert-butyl ester (I-6)

MeLi 1.6 M in Et_2O (3.6 mL, 5.82 mmol) was added dropwise to a -78°C solution of (*R*)-3-oxo-5-(3-[1,2,3]triazol-2-yl-benzyl)-morpholine-4-carboxylic acid tert-butyl ester **I-5** (1.49 g, 4.16 mmol) in THF (15 mL) and the resulting mixture was stirred at -78°C for 3h. The reaction mixture was quenched with sat. aq. NH_4Cl, warmed to RT and the solvent was removed *in vacuo*. The remaining aqueous layer was extracted with EtOAc (3x) and the combined organic extracts were washed with brine, dried over Na_2SO_4, filtered and evaporated *in vacuo*. The crude product was purified by flash chromatography (eluting with

20% to 50% EtOAc in hexane) to give the title compound as a yellow solid. LC-MS B: t_R = 0.81 min; $[M+H-Boc]^+$ = 259.17.

(3*R*,5*R*)-3-Methyl-5-(3-[1,2,3]triazol-2-yl-benzyl)-morpholine (I-7) and (3*S*,5*R*)-3-Methyl-5-(3-[1,2,3]triazol-2-yl-benzyl)-morpholine (I-8)

Step 1: [(*R*)-2-(2-Oxo-propoxy)-1-(3-[1,2,3]triazol-2-yl-benzyl)-ethyl]-carbamic acid tert-butyl ester **(I-6)** (500 mg, 1.34 mmol) was dissolved in TFA (5 mL) at 0°C and stirred for 1h. The reaction mixture was evaporated *in vacuo* and used directly in Step 2.

Step 2: The Boc-cleaved intermediate from above was dissolved in MeOH (10 mL) and cooled to 0°C. Sodium borohydride (52 mg, 1.37 mmol) was then added and the resulting mixture was stirred for 1h. The reaction mixture was quenched with water and the solvent was evaporated *in vacuo*. The remaining aqueous phase was extracted once with DCM and this extract was discarded. The aqueous layer was basified with 5M aq. NaOH and re-extracted with DCM (3x). The combined basic organic extracts were washed with brine, dried over Na_2SO_4, filtered and evaporated *in vacuo* to give the crude product that was purified by flash chromatography (eluting with 95:5 DCM:MeOH) to give the first title compound as a colourless oil. LC-MS A: t_R = 0.55 min; $[M+H]^+$ = 259.20. Continued elution afforded the second title compound (major product) as a colourless oil. LC-MS A: t_R = 0.54 min; $[M+H]^+$ = 259.21.

General method J for the synthesis of 3-benzyl morpholines of Structure 1

(*R*)-*N*-[(*R*)-1-(3-Iodo-benzyl)-2-hydroxy-ethyl]-2-chloro-propionamide and (*S*)-*N*-[(*R*)-1-(3-Iodo-benzyl)-2-hydroxy-ethyl]-2-chloro-propionamide (J-5)

The title compounds were prepared as a mixture of diastereomers from **A-8** and *rac*-2-chloropropanoyl chloride in analogy to the procedure described for **H-7**. LC-MS A: t_R = 0.76 min; $[M(^{35}Cl)+H]^+$ = 367.98.

(2*R*,5*R*)-5-(3-Iodo-benzyl)-2-methyl-morpholin-3-one (J-6)

The title compound was prepared as a single *cis*-stereoisomer from **J-5** in analogy to the procedure described for **H-8**. LC-MS A: t_R = 0.76 min; $[M+H+MeCN]^+$ = 373.04.

(2*R*,5*R*)-2-Methyl-5-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-3-one (J-7) and (2*S*,5*R*)-2-Methyl-5-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-3-one (J-8)

The title compounds were prepared from **J-6** in analogy to the procedure described for **H-9**. **J-7** LC-MS A: t_R = 0.69 min; $[M+H]^+$ = 273.11. **J-8** (minor product) LC-MS A: t_R = 0.70 min; $[M+H]^+$ = 273.14.

(2*R*,5*R*)-2-Methyl-5-(3-[1,2,3]triazol-2-yl-benzyl)-morpholine (J-9)

The title compound was prepared from **J-7** in analogy to the procedure described for **A-12**. LC-MS A: t_R = 0.57 min; $[M+H]^+$ = 259.07.

(2*S*,5*R*)-2-Methyl-5-(3-[1,2,3]triazol-2-yl-benzyl)-morpholine (J-10)

The title compound was prepared from **J-8** in analogy to the procedure described for **A-12**. LC-MS A: t_R = 0.55 min; $[M+H]^+$ = 259.07.

(2*R*,5*R*)-2-Ethyl-5-(3-[1,2,3]triazol-2-yl-benzyl)-morpholine (J-11)

The title compound was prepared from **A-8** and *rac*-2-chlorobutanoyl chloride in analogy to the sequence of reactions described for **J-9**. LC-MS A: t_R = 0.59 min; $[M+H]^+$ = 273.17.

(2*R*,5*R*)-5-(2-Fluoro-5-[1,2,3]triazol-2-yl-benzyl)-2-methyl-morpholine (J-12)

The title compound was prepared from (*R*)-2-amino-3-(5-bromo-2-fluorophenyl)propan-1-ol (Chiral Quest) or **G-30**, in analogy to the sequence of reactions described for the preparation of **J-9**. LC-MS A: t_R = 0.57 min; $[M+H]^+$ = 277.11.

(2*R*,5*R*)-5-(2-Fluoro-5-[1,2,3]triazol-1-yl-benzyl)-2-methyl-morpholine (J-13)

The title compound was prepared from (*R*)-2-amino-3-(5-bromo-2-fluorophenyl)propan-1-ol (Chiral Quest), in analogy to the sequence of reactions described for the preparation of **J-9** and **A-16**. LC-MS A: t_R = 0.50 min; $[M+H+MeCN]^+$ = 318.14.

(2*R*,5*R*)-2-Methyl-5-(3-pyrimidin-2-yl-benzyl)-morpholine hydrochloride (J-14)

The title compound was prepared from **A-8** and *rac*-2-chloropropanoyl chloride, in analogy to the sequence of reactions described for the preparation of **B-18**. LC-MS A: t_R = 0.53 min; $[M+H]^+$ = 270.14.

(2*R*,5*R*)-5-(2-Fluoro-5-pyrimidin-2-yl-benzyl)-2-methyl-morpholine hydrochloride (J-15)

The title compound was prepared from (*R*)-2-amino-3-(5-bromo-2-fluorophenyl)propan-1-ol (Chiral Quest) and *rac*-2-chloropropanoyl chloride, in analogy to the sequence of reactions described for the preparation of **B-18**. LC-MS A: t_R = 0.56 min; $[M+H]^+$ = 288.24.

(2*R*,5*R*)-5-(2-Fluoro-5-pyridazin-3-yl-benzyl)-2-methyl-morpholine hydrochloride (J-16)

The title compound was prepared from (*R*)-2-amino-3-(5-bromo-2-fluorophenyl)propan-1-ol (Chiral Quest) and *rac*-2-chloropropanoyl chloride, in analogy to the sequence of reactions described for the preparation of **B-18** substituting 2-bromopyrimidine for 3-bromopyridazine hydrobromide. LC-MS A: t_R = 0.52 min; $[M+H]^+$ = 288.25.

General method K for the synthesis of 3-benzyl morpholines of Structure 1

[(*R*)-1-Hydroxymethyl-2-(3-iodo-phenyl)-ethyl]-carbamic acid tert-butyl ester (K-9)

A solution of Boc-3-iodo-D-phenylalanine (6.32 g,16.2 mmol) and 4-methyl-morpholine (1.87 ml, 17 mol) in THF (13 mL) was added dropwise to a -15°C solution of isobutyl chloroformate (2.22 mL, 17 mmol) in THF (13 mL) and the resulting suspension was stirred for 1h. The cold reaction mixture was filtered and the filter cake was rinsed with THF. The filtrate was added dropwise to a 0°C solution of $NaBH_4$ (0.92 g, 24.2 mmol) in dimethylacetamide (7 mL) and the resulting suspension was warmed to RT and stirred for 1h. The reaction mixture was cooled back to 0°C and quenched with 1M aq. citric acid. Additional water was added and the mixture was concentrated *in vacuo*. The remaining aqueous phase was acidified with 1M aq. HCl before being filtered. The filter cake was rinsed with water and dried under HV to give the title compound as an orange solid that was used further without purification. LC-MS A: t_R = 0.84 min; $[M-Me]^+$ = 362.93.

[(*R*)-1-Formyl-2-(3-iodo-phenyl)-ethyl]-carbamic acid tert-butyl ester (K-10)

A solution of [(*R*)-1-hydroxymethyl-2-(3-iodo-phenyl)-ethyl]-carbamic acid tert-butyl ester **K-9** (5.32 g, 14.1 mmol) in DCM (100 mL) was added dropwise to a RT suspension of DMP (6.78 g, 15.5 mmol) in DCM (40 mL) and the resulting mixture was stirred for 1.5h. The reaction was quenched with 20% aq. $NaHCO_3$ and 10% aq. $Na_2S_2O_3$ and stirred for 1h. The layers were separated and the aqueous layer was extracted with DCM (2x). The combined organic extracts were washed with 1M aq. HCl, brine, dried over Na_2SO_4, filtered and evaporated *in vacuo*. The crude product was subsequently triturated with a little DCM to give the title compound as an orange solid. LC-MS A: t_R = 0.87 min; $[M+H]^+$ = No ionisation.

[(1*R*,2*S*)-2-Hydroxy-1-(3-iodo-benzyl)-propyl]-carbamic acid tert-butyl ester and [(1*R*,2*R*)-2-Hydroxy-1-(3-iodo-benzyl)-propyl]-carbamic acid tert-butyl ester (K-11)

Methylmagnesium bromide 3.0 M soln. in Et_2O (8.4 mL, 25.2 mmol) was added dropwise to a -78°C solution of [(*R*)-1-formyl-2-(3-iodo-phenyl)-ethyl]-carbamic acid tert-butyl ester **K-10** (4.72 g, 12.6 mmol) in THF (100 mL) and the resulting mixture was warmed to 0°C and stirred for 15 min. The reaction was quenched with sat. aq. NH_4Cl and the volatiles were removed *in vacuo*. The remaining aqueous phase was extracted with DCM (3x) and the combined organic extracts were washed with brine, dried over Na_2SO_4, filtered and evaporated *in vacuo*. The crude product purified by flash chromatography (eluting with 25% to 50% EtOAc in hexane) to give the title compounds as an ~1:1 mixture of diastereomers. LC-MS A: t_R = 0.88 min; $[M+H]^+$ = 376.97.

(2*S*,3*R*)-3-Amino-4-(3-iodo-phenyl)-butan-2-ol hydrochloride and (2*R*,3*R*)-3-Amino-4-(3-iodo-phenyl)-butan-2-ol hydrochloride (K-12)

The title compounds were prepared from **K-11** in analogy to the procedure described for **A-7**. LC-MS A: t_R = 0.55 min; $[M+H+MeCN]^+$ = 333.10.

2-Chloro-*N*-[(1*R*,2*S*)-2-hydroxy-1-(3-iodo-benzyl)-propyl]-acetamide and 2-Chloro-*N*-[(1*R*,2*R*)-2-hydroxy-1-(3-iodo-benzyl)-propyl]-acetamide (K-13)

The title compounds were prepared from **K-12** and chloroacetyl chloride in analogy to the procedure described for **H-7**. LC-MS A: t_R = 0.75 min; $[M(^{35}Cl)+H]^+$ = 367.91.

(5*R*,6*S*)-5-(3-Iodo-benzyl)-6-methyl-morpholin-3-one and (5*R*,6*R*)-5-(3-Iodo-benzyl)-6-methyl-morpholin-3-one (K-14)

The title compounds were prepared from **K-13** in analogy to the procedure described for **H-8**. LC-MS A: t_R = 0.76 min; $[M+H+MeCN]^+$ = 372.92.

(5*R*,6*R*)-6-Methyl-5-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-3-one and (5*R*,6*S*)-6-Methyl-5-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-3-one (K-15 & K-16)

The title compounds were prepared from **K-14** in analogy to the procedure described for **H-9** and the two diastereomers were subsequently separated by flash chromatography (eluting with a gradient of 50% to 70% EtOAc in hexane). **K-15** or **K16** LC-MS A: t_R = 0.70 min; $[M+H]^+$ = 273.18. **K-16** or **K-15** LC-MS A: t_R = 0.69 min; $[M+H]^+$ = 273.27.

(2*R*,3*R*)-2-Methyl-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholine (K-17)

The title compound was prepared from **K-15** or **K-16** in analogy to the procedure described for **A-12**. LC-MS A: t_R = 0.55 min; $[M+H]^+$ = 259.21 or t_R = 0.56 min; $[M+H]^+$ = 259.30.

(2*S*,3*R*)-2-Methyl-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholine (K-18)

The title compound was prepared from **K-16** or **K-15** in analogy to the procedure described for **A-12**. LC-MS A: t_R = 0.56 min; $[M+H]^+$ = 259.30 or t_R = 0.55 min; $[M+H]^+$ = 259.21.

General method L for the synthesis of example compounds of formula (I)

***rac*-{3-[4-Methyl-3-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-morpholin-4-yl}-(2-[1,2,3]triazol-2-yl-phenyl)-methanone (L-3)**

The title compound was prepared from *rac*-2-tert-butoxycarbonylamino-3-(3-iodo-4-methyl-phenyl)-propionic acid **G-36**, in analogy to the sequence of reactions described for the preparation of **D-8**. LC-MS B: t_R = 0.96 min; $[M+H]^+$ = 489.12.

***rac*-{3-[4-Chloro-3-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-morpholin-4-yl}-(2-[1,2,3]triazol-2-yl-phenyl)-methanone (L-4)**

The title compound was prepared from *rac*-2-tert-Butoxycarbonylamino-3-(4-chloro-3-iodo-phenyl)-propionic acid **G-37**, in analogy to the sequence of reactions described for the preparation of **D-8**. LC-MS A: t_R = 0.93 min; $[M(^{35}Cl)+H]^+$ = 508.96.

Example compounds 11 to 54

General method F-1 for the synthesis of example compounds of formula (I)

TBTU (34 mg, 0.11 mmol) was added to a RT solution of the required acid **2** (0.1 mmol) and DIPEA (25 μL, 0.15 mmol) in DMF (0.5 mL) and after stirring for 5 min a solution of the required amine **1** as its free base or HCl salt (0.1 mmol) and DIPEA (25 μL, 0.15 mmol) in DMF (0.5 mL) was added. The resulting mixture was stirred for up to 4d before being purified directly by prep. HPLC (method F) to furnish the desired product.

General method F-2 for the synthesis of example compounds of formula (I)

A freshly prepared solution of the corresponding acid chloride of carboxylic acid **2** (0.11 mmol) in MeCN (0.5 mL) was added to a solution of the required amine **1** as its free base or HCl salt (0.1 mmol) and Et_3N (0.2 mmol) in MeCN (0.5 mL) and the resulting mixture was stirred at RT for up to 4d. The reaction mixture was subsequently purified directly by prep. HPLC (method F) to furnish the desired product. Example compounds prepared according to General Method F-2 include Examples 68 to 74.

Listed in Tables 11 and 12 below are example compounds, prepared according to the above-mentioned methods **F-1** and **F-2**, from the corresponding amine **1**, prepared as described above and the corresponding carboxylic acid **2**, prepared as described above.

Table 11

Example No.	**Amine 1**	**Acid 2**	**Compound of Formula (I)**
11	A-15	E-3	(5-Methyl-2-[1,2,3]triazol-2-yl-phenyl)-[(*R*)-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone; LC-MS D: t_R = 0.85 min; $[M+H]^+$ = 430.05
12	A-15	E-2	[(*R*)-3-(3-[1,2,3]Triazol-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS B: t_R = 0.73 min; $[M+H]^+$ = 416.0
13	A-26	E-2	[(*S*)-3-(3-[1,2,3]Triazol-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS D: t_R = 0.85 min; $[M+H]^+$ = 416.05
14	C-9	E-2	[(*R*)-3-(4-Methoxy-3-pyrazol-1-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS D: t_R = 0.82 min; $[M+H]^+$ = 444.99
15	A-16	E-3	(5-Methyl-2-[1,2,3]triazol-2-yl-phenyl)-[(*R*)-3-(3-[1,2,3]triazol-1-yl-benzyl)-morpholin-4-yl]-methanone; LC-MS D: t_R = 0.79 min; $[M+H]^+$ = 430.00
16	A-12	E-2	[(*R*)-3-(3-Pyrazol-1-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS D: t_R = 0.83 min; $[M+H]^+$ = 415.07
17	B-18	E-3	(5-Methyl-2-[1,2,3]triazol-2-yl-phenyl)-[(*R*)-3-(3-pyrimidin-2-yl-benzyl)-morpholin-4-yl]-methanone; LC-MS D: t_R = 0.82 min; $[M+H]^+$ = 441.06

18	B-18	E-2	[(*R*)-3-(3-Pyrimidin-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS D: t_R = 0.82 min; $[M+H]^+$ = 426.96
19	A-12	E-3	(5-Methyl-2-[1,2,3]triazol-2-yl-phenyl)-[(*R*)-3-(3-pyrazol-1-yl-benzyl)-morpholin-4-yl]-methanone; LC-MS D: t_R = 0.83 min; $[M+H]^+$ = 429.04
20	A-12	E-7	(5-Fluoro-2-[1,2,3]triazol-2-yl-phenyl)-[(*R*)-3-(3-pyrazol-1-yl-benzyl)-morpholin-4-yl]-methanone; LC-MS D: t_R = 0.85 min; $[M+H]^+$ = 433.02
21	A-12	E-1	(2-Fluoro-3-methyl-6-[1,2,3]triazol-2-yl-phenyl)-[(*R*)-3-(3-pyrazol-1-yl-benzyl)-morpholin-4-yl]-methanone; LC-MS D: t_R = 0.90 min; $[M+H]^+$ = 447.02
22	A-12	E-4	(4-Methyl-2-[1,2,3]triazol-2-yl-phenyl)-[(*R*)-3-(3-pyrazol-1-yl-benzyl)-morpholin-4-yl]-methanone; LC-MS D: t_R = 0.83 min; $[M+H]^+$ = 429.02
23	A-18	E-3	(5-Methyl-2-[1,2,3]triazol-2-yl-phenyl)-[(*R*)-3-(3-[1,2,4]triazol-1-yl-benzyl)-morpholin-4-yl]-methanone; LC-MS D: t_R = 0.78 min; $[M+H]^+$ = 430.03
24	B-19	E-3	(5-Methyl-2-[1,2,3]triazol-2-yl-phenyl)-[(*R*)-3-(3-pyridin-2-yl-benzyl)-morpholin-4-yl]-methanone; LC-MS D: t_R = 0.84 min; $[M+H]^+$ = 440.04
25	B-20	E-3	(5-Methyl-2-[1,2,3]triazol-2-yl-phenyl)-[(*R*)-3-(3-pyridin-3-yl-benzyl)-morpholin-4-yl]-methanone; LC-MS D: t_R = 0.80 min; $[M+H]^+$ = 440.07
26	A-15	E-7	(5-Fluoro-2-[1,2,3]triazol-2-yl-phenyl)-[(*R*)-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone; LC-MS D: t_R = 0.87 min; $[M+H]^+$ = 434.02
27	A-15	E-4	(4-Methyl-2-[1,2,3]triazol-2-yl-phenyl)-[(*R*)-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone; LC-MS D: t_R = 0.87 min; $[M+H]^+$ = 430.05
28	B-21	E-3	(5-Methyl-2-[1,2,3]triazol-2-yl-phenyl)-[(*R*)-3-(3-pyridin-4-yl-benzyl)-morpholin-4-yl]-methanone; LC-MS D: t_R = 0.79 min; $[M+H]^+$ = 440.06

29	A-15	E-1	(2-Fluoro-3-methyl-6-[1,2,3]triazol-2-yl-phenyl)-[(*R*)-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone; LC-MS D: t_R = 0.93 min; $[M+H]^+$ = 448.05
30	A-15	E-5	(5-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[(*R*)-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone; LC-MS D: t_R = 0.87 min; $[M(^{35}Cl)+H]^+$ = 449.99
31	A-15	E-13	4-[1,2,3]Triazol-2-yl-3-[(*R*)-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholine-4-carbonyl]-benzonitrile; LC-MS D: t_R = 0.80 min; $[M+H]^+$ = 441.04
32	A-15	E-10	(5-Methoxy-2-[1,2,3]triazol-2-yl-phenyl)-[(*R*)-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone; LC-MS D: t_R = 0.86 min; $[M+H]^+$ = 446.05
33	A-15	E-9	(2-Fluoro-3-methoxy-6-[1,2,3]triazol-2-yl-phenyl)-[(*R*)-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone; LC-MS D: t_R = 0.86 min; $[M+H]^+$ = 464.07
34	A-15	E-12	(4,5-Dimethoxy-2-[1,2,3]triazol-2-yl-phenyl)-[(*R*)-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone; LC-MS D: t_R = 0.81 min; $[M+H]^+$ = 476.09
35	A-15	E-6	(4,5-Dimethyl-2-[1,2,3]triazol-2-yl-phenyl)-[(*R*)-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone; LC-MS D: t_R = 0.88 min; $[M+H]^+$ = 444.09
36	A-15	E-8	(4-Fluoro-2-[1,2,3]triazol-2-yl-phenyl)-[(*R*)-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone; LC-MS D: t_R = 0.85 min; $[M+H]^+$ = 434.06
37	A-15	E-11	(5-Methoxy-4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-[(*R*)-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone; LC-MS D: t_R = 0.90 min; $[M+H]^+$ = 460.06
38	A-20	E-3	(5-Methyl-2-[1,2,3]triazol-2-yl-phenyl)-[(*R*)-3-(3-pyrrol-1-yl-benzyl)-morpholin-4-yl]-methanone; LC-MS B: t_R = 0.84 min; $[M+H]^+$ = 427.94
39	B-22	E-3	{(*R*)-3-[3-(4-Methyl-pyrimidin-2-yl)-benzyl]-morpholin-4-yl}-(5-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS D: t_R = 0.86 min; $[M+H]^+$ = 455.07

40	B-22	E-2	{(*R*)-3-[3-(4-Methyl-pyrimidin-2-yl)-benzyl]-morpholin-4-yl}-(2-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS D: t_R = 0.85 min; $[M+H]^+$ = 441.04
41	B-23	E-3	(5-Methyl-2-[1,2,3]triazol-2-yl-phenyl)-[(*R*)-3-(3-pyrazin-2-yl-benzyl)-morpholin-4-yl]-methanone; LC-MS D: t_R = 0.79 min; $[M+H]^+$ = 441.05
42	B-24	E-2	[(*R*)-3-(3-Oxazol-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS D: t_R = 0.81 min; $[M+H]^+$ = 416.04
43	B-25	E-3	(5-Methyl-2-[1,2,3]triazol-2-yl-phenyl)-[(*R*)-3-(3-thiazol-2-yl-benzyl)-morpholin-4-yl]-methanone; LC-MS D: t_R = 0.87 min; $[M+H]^+$ = 445.99
44	B-25	E-2	[(*R*)-3-(3-Thiazol-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS D: t_R = 0.85 min; $[M+H]^+$ = 432.00
45	B-26	E-3	(5-Methyl-2-[1,2,3]triazol-2-yl-phenyl)-[(*R*)-3-(3-thiophen-2-yl-benzyl)-morpholin-4-yl]-methanone; LC-MS D: t_R = 0.97 min; $[M+H]^+$ = 445.01
46	B-26	E-2	[(*R*)-3-(3-Thiophen-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS D: t_R = 0.94 min; $[M+H]^+$ = 431.00
47	B-27	E-3	(5-Methyl-2-[1,2,3]triazol-2-yl-phenyl)-[(*R*)-3-(3-pyridazin-3-yl-benzyl)-morpholin-4-yl]-methanone; LC-MS D: t_R = 0.78 min; $[M+H]^+$ = 441.05
48	B-27	E-2	[(*R*)-3-(3-Pyridazin-3-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS D: t_R = 0.75 min; $[M+H]^+$ = 426.92
49	B-18	E-1	(2-Fluoro-3-methyl-6-[1,2,3]triazol-2-yl-phenyl)-[(*R*)-3-(3-pyrimidin-2-yl-benzyl)-morpholin-4-yl]-methanone; LC-MS D: t_R = 0.85 min; $[M+H]^+$ = 458.93
50	B-18	E-10	(5-Methoxy-2-[1,2,3]triazol-2-yl-phenyl)-[(*R*)-3-(3-pyrimidin-2-yl-benzyl)-morpholin-4-yl]-methanone; LC-MS D: t_R = 0.83 min; $[M+H]^+$ = 456.96

51	B-18	E-5	(5-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[(*R*)-3-(3-pyrimidin-2-yl-benzyl)-morpholin-4-yl]-methanone; LC-MS D: t_R = 0.84 min; $[M(^{35}Cl)+H]^+$ = 460.99
52	A-15	E-14	(6-Methyl-3-[1,2,3]triazol-2-yl-pyridin-2-yl)-[(*R*)-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone; LC-MS D: t_R = 0.82 min; $[M+H]^+$ = 431.06
53	A-12	E-14	(6-Methyl-3-[1,2,3]triazol-2-yl-pyridin-2-yl)-[(*R*)-3-(3-pyrazol-1-yl-benzyl)-morpholin-4-yl]-methanone; LC-MS D: t_R = 0.80 min; $[M+H]^+$ = 430.03
54	A-15	E-15	(3-Fluoro-2-[1,2,3]triazol-2-yl-phenyl)-[(*R*)-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone; LC-MS D: t_R = 0.84 min; $[M+H]^+$ = 434.04

Example compound 55:

[(*R*)-3-(4-Hydroxy-3-pyrimidin-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone

Boron tribromide 1M soln. in DCM (0.8 mL, 0.8 mmol) was added to a -78°C solution of [(*R*)-3-(4-methoxy-3-pyrimidin-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone **Example 5** (72 mg, 0.16 mmol) in DCM (5 mL) and after complete addition the the reaction mixture was warmed to RT and stirred for 6h. The reaction was quenched with sat. aq. $NaHCO_3$ and the layers were separated. The aqueous layer was extracted with DCM (2x) and the combined organic extracts were dried over Na_2SO_4, filtered and evaporated *in vacuo*. The crude product was purified by prep. HPLC (method F) to give the title compound as a white solid. LC-MS D: t_R = 0.80 min; $[M+H]^+$ = 443.03.

Example compounds 56 to 191

Table 12

Example No.	Amine 1	Acid 2	Compound of Formula (I)
56	A-34	E-3	[(*R*)-3-(2-Fluoro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(5-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS D: t_R = 0.87 min; $[M+H]^+$ = 448.07
57	A-34	E-2	[(*R*)-3-(2-Fluoro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS D: t_R = 0.86 min; $[M+H]^+$ = 434.06

58	B-36	E-3	[(*R*)-3-(4-Methoxy-3-[1,2,4]oxadiazol-3-yl-benzyl)-morpholin-4-yl]-(5-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS D: t_R = 0.85 min; $[M+H]^+$ = 416.05
59	B-36	E-2	[(*R*)-3-(4-Methoxy-3-[1,2,4]oxadiazol-3-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS D: t_R = 0.78 min; $[M+H]^+$ = 447.04
60	B-36	E-4	[(*R*)-3-(4-Methoxy-3-[1,2,4]oxadiazol-3-yl-benzyl)-morpholin-4-yl]-(4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS D: t_R = 0.82 min; $[M+H]^+$ = 461.06
61	B-36	E-8	(4-Fluoro-2-[1,2,3]triazol-2-yl-phenyl)-[(*R*)-3-(4-methoxy-3-[1,2,4]oxadiazol-3-yl-benzyl)-morpholin-4-yl]-methanone; LC-MS D: t_R = 0.81 min; $[M+H]^+$ = 465.04
62	A-34	E-4	[(*R*)-3-(2-Fluoro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS D: t_R = 0.90 min; $[M+H]^+$ = 448.09
63	B-36	E-25	[(*R*)-3-(4-Methoxy-3-[1,2,4]oxadiazol-3-yl-benzyl)-morpholin-4-yl]-(2-methyl-6-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS D: t_R = 0.75 min; $[M+H]^+$ = 461.07
64	A-15	E-27	(3-Methyl-2-[1,2,3]triazol-2-yl-phenyl)-[(*R*)-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone; LC-MS D: t_R = 0.86 min; $[M+H]^+$ = 430.09
65	A-40	E-3	[(*R*)-3-(4-Methyl-3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(5-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS D: t_R = 0.87 min; $[M+H]^+$ = 444.06
66	A-40	E-2	[(*R*)-3-(4-Methyl-3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS D: t_R = 0.86 min; $[M+H]^+$ = 430.04
67	A-40	E-4	[(*R*)-3-(4-Methyl-3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS D: t_R = 0.88 min; $[M+H]^+$ = 444.10
68	I-7	E-2	[(3*R*,5*R*)-3-Methyl-5-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS D: t_R = 0.88 min; $[M+H]^+$ = 430.09

69	I-7	E-4	[(3*R*,5*R*)-3-Methyl-5-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS D: t_R = 0.92 min; $[M+H]^+$ = 444.13
70	I-7	E-27	[(3*R*,5*R*)-3-Methyl-5-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(3-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS D: t_R = 0.90 min; $[M+H]^+$ = 444.14
71	I-8	E-4	[(3*S*,5*R*)-3-Methyl-5-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS D: t_R = 0.92 min; $[M+H]^+$ = 444.08
72	I-8	E-27	[(3*S*,5*R*)-3-Methyl-5-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(3-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS D: t_R = 0.91 min; $[M+H]^+$ = 444.12
73	I-8	E-3	[(3*S*,5*R*)-3-Methyl-5-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(5-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS D: t_R = 0.92 min; $[M+H]^+$ = 444.15
74	I-8	E-6	(4,5-Dimethyl-2-[1,2,3]triazol-2-yl-phenyl)-[(3*S*,5*R*)-3-methyl-5-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone; LC-MS D: t_R = 0.95 min; $[M+H]^+$ = 457.82
75	A-15	E-16	(3,5-Dimethyl-2-[1,2,3]triazol-2-yl-phenyl)-[(*R*)-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone; LC-MS D: t_R = 0.90 min; $[M+H]^+$ = 444.14
76	A-15	E-21	[(*R*)-3-(3-[1,2,3]Triazol-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-4-trifluoromethyl-phenyl)-methanone; LC-MS D: t_R = 0.92 min; $[M+H]^+$ = 484.13
77	A-15	E-17	(4-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[(*R*)-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone; LC-MS D: t_R = 0.89 min; $[M(^{35}Cl)+H]^+$ = 450.07
78	A-15	E-19	(4-Fluoro-5-methoxy-2-[1,2,3]triazol-2-yl-phenyl)-[(*R*)-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone; LC-MS D: t_R = 0.88 min; $[M+H]^+$ = 464.11
79*	B-41	E-6	(4,5-Dimethyl-2-[1,2,3]triazol-2-yl-phenyl)-[(*R*)-3-(4-methyl-3-[1,2,4]oxadiazol-3-yl-benzyl)-morpholin-4-yl]-methanone; LC-MS A: t_R = 0.90 min; $[M+H]^+$ = 459.11

80	B-39	E-24	(4,5-Difluoro-2-[1,2,3]triazol-2-yl-phenyl)-[(*R*)-3-(3-[1,2,4]oxadiazol-3-yl-benzyl)-morpholin-4-yl]-methanone; LC-MS A: t_R = 0.85 min; $[M+H]^+$ = 453.07
81	B-39	E-4	(4-Methyl-2-[1,2,3]triazol-2-yl-phenyl)-[(*R*)-3-(3-[1,2,4]oxadiazol-3-yl-benzyl)-morpholin-4-yl]-methanone; LC-MS A: t_R = 0.85 min; $[M+H]^+$ = 431.10
82	B-39	E-15	(3-Fluoro-2-[1,2,3]triazol-2-yl-phenyl)-[(*R*)-3-(3-[1,2,4]oxadiazol-3-yl-benzyl)-morpholin-4-yl]-methanone; LC-MS A: t_R = 0.90 min; $[M+H]^+$ = 460.06
83	B-39	E-27	(3-Methyl-2-[1,2,3]triazol-2-yl-phenyl)-[(*R*)-3-(3-[1,2,4]oxadiazol-3-yl-benzyl)-morpholin-4-yl]-methanone; LC-MS A: t_R = 0.83 min; $[M+H]^+$ = 431.09
84	B-39	E-5	(5-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[(*R*)-3-(3-[1,2,4]oxadiazol-3-yl-benzyl)-morpholin-4-yl]-methanone; LC-MS A: t_R = 0.87 min; $[M(^{35}Cl)+H]^+$ = 451.04
85	B-39	E-6	(4,5-Dimethyl-2-[1,2,3]triazol-2-yl-phenyl)-[(*R*)-3-(3-[1,2,4]oxadiazol-3-yl-benzyl)-morpholin-4-yl]-methanone; LC-MS A: t_R = 0.87 min; $[M+H]^+$ = 445.13
86	B-39	E-17	(4-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[(*R*)-3-(3-[1,2,4]oxadiazol-3-yl-benzyl)-morpholin-4-yl]-methanone; LC-MS A: t_R = 0.87 min; $[M(^{35}Cl)+H]^+$ = 451.09
87	B-39	E-21	[(*R*)-3-(3-[1,2,4]Oxadiazol-3-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-4-trifluoromethyl-phenyl)-methanone; LC-MS A: t_R = 0.89 min; $[M+H]^+$ = 485.09
88	B-39	E-7	(5-Fluoro-2-[1,2,3]triazol-2-yl-phenyl)-[(*R*)-3-(3-[1,2,4]oxadiazol-3-yl-benzyl)-morpholin-4-yl]-methanone; LC-MS A: t_R = 0.82 min; $[M+H]^+$ = 435.02
89	B-39	E-16	(3,5-Dimethyl-2-[1,2,3]triazol-2-yl-phenyl)-[(*R*)-3-(3-[1,2,4]oxadiazol-3-yl-benzyl)-morpholin-4-yl]-methanone; LC-MS A: t_R = 0.86 min; $[M+H]^+$ = 445.09
90*	B-42	E-2	[(R)-3-(4-Chloro-3-[1,2,4]oxadiazol-3-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS A: t_R = 0.84 min; $[M(^{35}Cl)+H]^+$ = 451.04

91	A-15	E-24	(4,5-Difluoro-2-[1,2,3]triazol-2-yl-phenyl)-[(*R*)-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone; LC-MS D: t_R = 0.87 min; $[M+H]^+$ = 452.11
92	A-15	E-20	(3,4-Dimethyl-2-[1,2,3]triazol-2-yl-phenyl)-[(*R*)-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone; LC-MS D: t_R = 0.89 min; $[M+H]^+$ = 444.16
93	A-15	E-18	(4-Methoxy-2-[1,2,3]triazol-2-yl-phenyl)-[(*R*)-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone; LC-MS D: t_R = 0.85 min; $[M+H]^+$ = 446.13
94	A-34	E-20	(3,4-Dimethyl-2-[1,2,3]triazol-2-yl-phenyl)-[(*R*)-3-(2-fluoro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone; LC-MS D: t_R = 0.90 min; $[M+H]^+$ = 462.17
95	A-34	E-18	[(*R*)-3-(2-Fluoro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(4-methoxy-2-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS D: t_R = 0.86 min; $[M+H]^+$ = 464.11
96	J-10	E-4	[(2*S*,5*R*)-2-Methyl-5-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS D: t_R = 0.90 min; $[M+H]^+$ = 444.18
97	J-9	E-27	[(2*R*,5*R*)-2-Methyl-5-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(3-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS D: t_R = 0.91 min; $[M+H]^+$ = 444.13
98	J-9	E-6	(4,5-Dimethyl-2-[1,2,3]triazol-2-yl-phenyl)-[(2*R*,5*R*)-2-methyl-5-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone; LC-MS D: t_R = 0.91 min; $[M+H]^+$ = 458.00
99	J-9	E-20	(3,4-Dimethyl-2-[1,2,3]triazol-2-yl-phenyl)-[(2*R*,5*R*)-2-methyl-5-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone; LC-MS D: t_R = 0.94 min; $[M+H]^+$ = 457.91
100	J-9	E-2	[(2*R*,5*R*)-2-Methyl-5-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS D: t_R = 0.86 min; $[M+H]^+$ = 430.17
101	J-9	E-4	[(2*R*,5*R*)-2-Methyl-5-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS D: t_R = 0.89 min; $[M+H]^+$ = 444.19

102*	H-10	E-3	[(*R*)-3-Methyl-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(5-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS A: t_R = 0.94 min; $[M+H]^+$ = 444.11
103	A-15	E-28	(5-Chloro-4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-[(*R*)-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone; LC-MS D: t_R = 0.90 min; $[M(^{35}Cl)+H]^+$ = 464.18
104	A-15	E-22	(4-Chloro-5-methoxy-2-[1,2,3]triazol-2-yl-phenyl)-[(*R*)-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone; LC-MS D: t_R = 0.92 min; $[M(^{35}Cl)+H]^+$ = 480.16
105	A-37	E-4	[(*R*)-3-(3-Chloro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS D: t_R = 0.95 min; $[M(^{35}Cl)+H]^+$ = 464.16
106	A-37	E-27	[(*R*)-3-(3-Chloro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(3-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS D: t_R = 0.94 min; $[M(^{35}Cl)+H]^+$ = 464.17
107	A-15	E-23	(3-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[(*R*)-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone; LC-MS D: t_R = 0.87 min; $[M(^{35}Cl)+H]^+$ = 449.73
108	J-14	E-2	[(2*R*,5*R*)-2-Methyl-5-(3-pyrimidin-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS D: t_R = 0.82 min; $[M+H]^+$ = 441.16
109	J-14	E-3	[(2*R*,5*R*)-2-Methyl-5-(3-pyrimidin-2-yl-benzyl)-morpholin-4-yl]-(5-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS D: t_R = 0.86 min; $[M+H]^+$ = 455.15
110	J-14	E-4	[(2*R*,5*R*)-2-Methyl-5-(3-pyrimidin-2-yl-benzyl)-morpholin-4-yl]-(4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS D: t_R = 0.85 min; $[M+H]^+$ = 455.16
111	J-14	E-27	[(2*R*,5*R*)-2-Methyl-5-(3-pyrimidin-2-yl-benzyl)-morpholin-4-yl]-(3-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS D: t_R = 0.88 min; $[M+H]^+$ = 455.14
112	J-14	E-20	(3,4-Dimethyl-2-[1,2,3]triazol-2-yl-phenyl)-[(2*R*,5*R*)-2-methyl-5-(3-pyrimidin-2-yl-benzyl)-morpholin-4-yl]-methanone; LC-MS D: t_R = 0.91 min; $[M+H]^+$ = 469.19

113	J-14	E-5	(5-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[(2*R*,5*R*)-2-methyl-5-(3-pyrimidin-2-yl-benzyl)-morpholin-4-yl]-methanone; LC-MS D: t_R = 0.87 min; $[M(^{35}Cl)+H]^+$ = 475.13
114	J-14	E-17	(4-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[(2*R*,5*R*)-2-methyl-5-(3-pyrimidin-2-yl-benzyl)-morpholin-4-yl]-methanone; LC-MS D: t_R = 0.89 min; $[M(^{35}Cl)+H]^+$ = 475.13
115	J-12	E-3	[(2*R*,5*R*)-5-(2-Fluoro-5-[1,2,3]triazol-2-yl-benzyl)-2-methyl-morpholin-4-yl]-(5-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS D: t_R = 0.90 min; $[M+H]^+$ = 462.15
116	J-12	E-2	[(2*R*,5*R*)-5-(2-Fluoro-5-[1,2,3]triazol-2-yl-benzyl)-2-methyl-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS D: t_R = 0.90 min; $[M+H]^+$ = 448.15
117	J-12	E-4	[(2*R*,5*R*)-5-(2-Fluoro-5-[1,2,3]triazol-2-yl-benzyl)-2-methyl-morpholin-4-yl]-(4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS D: t_R = 0.90 min; $[M+H]^+$ = 462.18
118	J-12	E-27	[(2*R*,5*R*)-5-(2-Fluoro-5-[1,2,3]triazol-2-yl-benzyl)-2-methyl-morpholin-4-yl]-(3-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS D: t_R = 0.92 min; $[M+H]^+$ = 462.15
119	A-36	E-3	[(*R*)-3-(2-Methyl-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(5-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS D: t_R = 0.90 min; $[M+H]^+$ = 4444.18
120	A-35	E-4	[(*R*)-3-(2-Chloro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS D: t_R = 0.92 min; $[M(^{35}Cl)+H]^+$ = 464.07
121	A-36	E-2	[(*R*)-3-(2-Methyl-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS D: t_R = 0.87 min; $[M+H]^+$ = 430.20
122	A-35	E-27	[(*R*)-3-(2-Chloro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(3-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS D: t_R = 0.92 min; $[M(^{35}Cl)+H]^+$ = 464.11

123	A-36	E-4	[(*R*)-3-(2-Methyl-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS D: t_R = 0.92 min; $[M+H]^+$ = 444.36
124	A-36	E-27	[(*R*)-3-(2-Methyl-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(3-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS D: t_R = 0.90 min; $[M+H]^+$ = 444.22
125	A-35	E-3	[(*R*)-3-(2-Chloro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(5-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS D: t_R = 0.91 min; $[M(^{35}Cl)+H]^+$ = 464.12
126	A-35	E-2	[(*R*)-3-(2-Chloro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS D: t_R = 0.89 min; $[M(^{35}Cl)+H]^+$ = 450.09
127	A-34	E-27	[(*R*)-3-(2-Fluoro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(3-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS D: t_R = 0.88 min; $[M+H]^+$ = 448.14
128	A-34	E-6	(4,5-Dimethyl-2-[1,2,3]triazol-2-yl-phenyl)-[(*R*)-3-(2-fluoro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone; LC-MS D: t_R = 0.90 min; $[M+H]^+$ = 462.14
129	A-34	E-5	(5-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[(*R*)-3-(2-fluoro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone; LC-MS D: t_R = 0.89 min; $[M(^{35}Cl)+H]^+$ = 468.10
130	A-34	E-17	(4-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[(*R*)-3-(2-fluoro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone; LC-MS D: t_R = 0.90 min; $[M(^{35}Cl)+H]^+$ = 468.09
131	A-34	E-10	[(*R*)-3-(2-Fluoro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(5-methoxy-2-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS D: t_R = 0.89 min; $[M+H]^+$ = 464.16
132	A-34	E-1	(2-Fluoro-3-methyl-6-[1,2,3]triazol-2-yl-phenyl)-[(*R*)-3-(2-fluoro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone; LC-MS D: t_R = 0.89 min; $[M+H]^+$ = 466.15
133	A-34	E-9	(2-Fluoro-3-methoxy-6-[1,2,3]triazol-2-yl-phenyl)-[(*R*)-3-(2-fluoro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone; LC-MS D: t_R = 0.87 min; $[M+H]^+$ = 482.16

134	A-34	E-11	[(*R*)-3-(2-Fluoro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(5-methoxy-4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS D: t_R = 0.92 min; $[M+H]^+$ = 478.17
135	A-34	E-23	(3-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[(*R*)-3-(2-fluoro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone; LC-MS D: t_R = 0.88 min; $[M(^{35}Cl)+H]^+$ = 468.10
136	A-34	E-26	[(*R*)-3-(2-Fluoro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(2-fluoro-6-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS D: t_R = 0.87 min; $[M+H]^+$ = 452.08
137	A-34	E-24	(4,5-Difluoro-2-[1,2,3]triazol-2-yl-phenyl)-[(*R*)-3-(2-fluoro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone; LC-MS D: t_R = 0.89 min; $[M+H]^+$ = 470.14
138	A-34	E-21	[(*R*)-3-(2-Fluoro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-4-trifluoromethyl-phenyl)-methanone; LC-MS D: t_R = 0.93 min; $[M+H]^+$ = 502.11
139	A-34	E-22	(4-Chloro-5-methoxy-2-[1,2,3]triazol-2-yl-phenyl)-[(*R*)-3-(2-fluoro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone; LC-MS D: t_R = 0.93 min; $[M(^{35}Cl)+H]^+$ = 498.13
140	J-13	E-3	[(2*R*,5*R*)-5-(2-Fluoro-5-[1,2,3]triazol-1-yl-benzyl)-2-methyl-morpholin-4-yl]-(5-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS D: t_R = 0.80 min; $[M+H_2O]^+$ = 479.20
141	J-13	E-4	[(2*R*,5*R*)-5-(2-Fluoro-5-[1,2,3]triazol-1-yl-benzyl)-2-methyl-morpholin-4-yl]-(4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS D: t_R = 0.81 min; $[M+H_2O]^+$ = 479.21
142	J-11	E-3	[(2*R*,5*R*)-2-Ethyl-5-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(5-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS D: t_R = 0.94 min; $[M+H]^+$ = 457.93
143	J-11	E-2	[(2*R*,5*R*)-2-Ethyl-5-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS D: t_R = 0.91 min; $[M+H]^+$ = 444.14
144	J-11	E-4	[(2*R*,5*R*)-2-Ethyl-5-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS D: t_R = 0.44 min; $[M+H]^+$ = 457.95

145*	A-38	E-2	[(*R*)-3-(3-Fluoro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS D: t_R = 0.88 min; $[M+H]^+$ = 434.24
146*	A-38	E-4	[(*R*)-3-(3-Fluoro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS D: t_R = 0.90 min; $[M+H]^+$ = 448.27
147	J-15	E-3	[(2*R*,5*R*)-5-(2-Fluoro-5-pyrimidin-2-yl-benzyl)-2-methyl-morpholin-4-yl]-(5-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS D: t_R = 0.88 min; $[M+H]^+$ = 473.18
148	J-15	E-2	[(2*R*,5*R*)-5-(2-Fluoro-5-pyrimidin-2-yl-benzyl)-2-methyl-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS D: t_R = 0.88 min; $[M+H]^+$ = 459.06
149	J-15	E-4	[(2*R*,5*R*)-5-(2-Fluoro-5-pyrimidin-2-yl-benzyl)-2-methyl-morpholin-4-yl]-(4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS D: t_R = 0.88 min; $[M+H]^+$ = 473.14
150	J-15	E-27	[(2*R*,5*R*)-5-(2-Fluoro-5-pyrimidin-2-yl-benzyl)-2-methyl-morpholin-4-yl]-(3-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS D: t_R = 0.90 min; $[M+H]^+$ = 473.13
151	J-15	E-20	(3,4-Dimethyl-2-[1,2,3]triazol-2-yl-phenyl)-[(2*R*,5*R*)-5-(2-fluoro-5-pyrimidin-2-yl-benzyl)-2-methyl-morpholin-4-yl]-methanone; LC-MS D: t_R = 0.92 min; $[M+H]^+$ = 487.17
152	J-15	E-5	(5-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[(2*R*,5*R*)-5-(2-fluoro-5-pyrimidin-2-yl-benzyl)-2-methyl-morpholin-4-yl]-methanone; LC-MS D: t_R = 0.90 min; $[M(^{35}Cl)+H]^+$ = 493.10
153	J-15	E-17	(4-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[(2*R*,5*R*)-5-(2-fluoro-5-pyrimidin-2-yl-benzyl)-2-methyl-morpholin-4-yl]-methanone; LC-MS D: t_R = 0.91 min; $[M(^{35}Cl)+H]^+$ = 493.08
154	J-15	E-23	(3-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[(2*R*,5*R*)-5-(2-fluoro-5-pyrimidin-2-yl-benzyl)-2-methyl-morpholin-4-yl]-methanone; LC-MS D: t_R = 0.89 min; $[M(^{35}Cl)+H]^+$ = 493.07

155	B-43	E-3	[(*R*)-3-(2-Fluoro-5-pyrimidin-2-yl-benzyl)-morpholin-4-yl]-(5-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS D: t_R = 0.85 min; $[M+H]^+$ = 458.89
156	B-43	E-4	[(*R*)-3-(2-Fluoro-5-pyrimidin-2-yl-benzyl)-morpholin-4-yl]-(4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS D: t_R = 0.87 min; $[M+H]^+$ = 459.07
157	B-43	E-27	[(*R*)-3-(2-Fluoro-5-pyrimidin-2-yl-benzyl)-morpholin-4-yl]-(3-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS D: t_R = 0.85 min; $[M+H]^+$ = 458.81
158	B-43	E-20	(3,4-Dimethyl-2-[1,2,3]triazol-2-yl-phenyl)-[(*R*)-3-(2-fluoro-5-pyrimidin-2-yl-benzyl)-morpholin-4-yl]-methanone; LC-MS D: t_R = 0.88 min; $[M+H]^+$ = 473.17
159	B-43	E-5	(5-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[(*R*)-3-(2-fluoro-5-pyrimidin-2-yl-benzyl)-morpholin-4-yl]-methanone; LC-MS D: t_R = 0.87 min; $[M(^{35}Cl)+H]^+$ = 479.06
160	B-43	E-17	(4-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[(*R*)-3-(2-fluoro-5-pyrimidin-2-yl-benzyl)-morpholin-4-yl]-methanone; LC-MS D: t_R = 0.88 min; $[M(^{35}Cl)+H]^+$ = 479.08
161	B-43	E-23	(3-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[(*R*)-3-(2-fluoro-5-pyrimidin-2-yl-benzyl)-morpholin-4-yl]-methanone; LC-MS D: t_R = 0.86 min; $[M(^{35}Cl)+H]^+$ = 479.11
162	K-18	E-3	[(2*S*,3*R*)-2-Methyl-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(5-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone **or** [(2*R*,3*R*)-2-Methyl-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(5-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS D: t_R = 0.90 min; $[M+H]^+$ = 444.15
163	K-18	E-4	[(2*S*,3*R*)-2-Methyl-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone **or** [(2*R*,3*R*)-2-Methyl-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS D: t_R = 0.91 min; $[M+H]^+$ = 444.13

164	K-18	E-27	[(2*S*,3*R*)-2-Methyl-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(3-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone **or** [(2*R*,3*R*)-2-Methyl-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(3-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS D: t_R = 0.89 min; $[M+H]^+$ = 444.14
165	J-16	E-4	[(2*R*,5*R*)-5-(2-Fluoro-5-pyridazin-3-yl-benzyl)-2-methyl-morpholin-4-yl]-(4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS D: t_R = 0.79 min; $[M+H]^+$ = 473.16
166	B-44	E-4	[(*R*)-3-(2-Fluoro-5-pyridazin-3-yl-benzyl)-morpholin-4-yl]-(4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS D: t_R = 0.76 min; $[M+H]^+$ = 459.03
167	K-17	E-3	[(2*R*,3*R*)-2-Methyl-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(5-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone **or** [(2*S*,3*R*)-2-Methyl-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(5-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS D: t_R = 0.90 min; $[M+H]^+$ = 444.09
168	K-17	E-4	[(2*R*,3*R*)-2-Methyl-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone **or** [(2*S*,3*R*)-2-Methyl-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS D: t_R = 0.91 min; $[M+H]^+$ = 444.16
169	A-35	E-20	[(*R*)-3-(2-Chloro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(3,4-dimethyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS D: t_R = 0.94 min; $[M(^{35}Cl)+H]^+$ = 478.11
170	A-35	E-17	[(*R*)-3-(2-Chloro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(4-chloro-2-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS D: t_R = 0.95 min; $[M(^{35}Cl)+H]^+$ = 484.06
171	A-35	E-23	[(*R*)-3-(2-Chloro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(3-chloro-2-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS D: t_R = 0.91 min; $[M(^{35}Cl)+H]^+$ = 484.03
172	J-9	E-23	(3-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[(2*R*,5*R*)-2-methyl-5-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone; LC-MS D: t_R = 0.91 min; $[M(^{35}Cl)+H]^+$ = 464.07

173	J-12	E-23	(3-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[(2*R*,5*R*)-5-(2-fluoro-5-[1,2,3]triazol-2-yl-benzyl)-2-methyl-morpholin-4-yl]-methanone; LC-MS D: t_R = 0.92 min; $[M(^{35}Cl)+H]^+$ = 482.10
174	B-40	E-3	[(*R*)-3-(2-Fluoro-5-[1,2,4]oxadiazol-3-yl-benzyl)-morpholin-4-yl]-(5-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS A: t_R = 0.85 min; $[M+H]^+$ = 449.11
175	B-40	E-4	[(*R*)-3-(2-Fluoro-5-[1,2,4]oxadiazol-3-yl-benzyl)-morpholin-4-yl]-(4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS A: t_R = 0.86 min; $[M+H]^+$ = 449.11
176	B-40	E-5	(5-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[(*R*)-3-(2-fluoro-5-[1,2,4]oxadiazol-3-yl-benzyl)-morpholin-4-yl]-methanone; LC-MS A: t_R = 0.86 min; $[M(^{35}Cl)+H]^+$ = 469.07
177	B-40	E-27	[(*R*)-3-(2-Fluoro-5-[1,2,4]oxadiazol-3-yl-benzyl)-morpholin-4-yl]-(3-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS A: t_R = 0.85 min; $[M+H]^+$ = 449.10
178	B-40	E17	(4-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[(*R*)-3-(2-fluoro-5-[1,2,4]oxadiazol-3-yl-benzyl)-morpholin-4-yl]-methanone; LC-MS A: t_R = 0.88 min; $[M(^{35}Cl)+H]^+$ = 469.04
179	B-40	E-6	(4,5-Dimethyl-2-[1,2,3]triazol-2-yl-phenyl)-[(*R*)-3-(2-fluoro-5-[1,2,4]oxadiazol-3-yl-benzyl)-morpholin-4-yl]-methanone; LC-MS A: t_R = 0.88 min; $[M+H]^+$ = 463.11
180	B-40	E-23	(3-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[(*R*)-3-(2-fluoro-5-[1,2,4]oxadiazol-3-yl-benzyl)-morpholin-4-yl]-methanone; LC-MS A: t_R = 0.86 min; $[M(^{35}Cl)+H]^+$ = 469.04
181	B-40	E-20	(3,4-Dimethyl-2-[1,2,3]triazol-2-yl-phenyl)-[(*R*)-3-(2-fluoro-5-[1,2,4]oxadiazol-3-yl-benzyl)-morpholin-4-yl]-methanone; LC-MS A: t_R = 0.88 min; $[M+H]^+$ = 463.12
182	A-15	E-29	[(*R*)-3-(3-[1,2,3]Triazol-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-3-trifluoromethyl-phenyl)-methanone; LC-MS D: t_R = 0.89 min; $[M+H]^+$ = 484.18
183*	A-39	E-4	[(*R*)-3-(2-Fluoro-3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS D: t_R = 0.82 min; $[M+H]^+$ = 448.14

184	J-9	E-5	(5-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[(2*R*,5*R*)-2-methyl-5-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone; LC-MS D: t_R = 0.90 min; $[M(^{35}Cl)+H]^+$ = 464.13
185	J-9	E-17	(4-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[(2*R*,5*R*)-2-methyl-5-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone; LC-MS D: t_R = 0.92 min; $[M(^{35}Cl)+H]^+$ = 464.14
186	J-12	E-5	(5-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[(2*R*,5*R*)-5-(2-fluoro-5-[1,2,3]triazol-2-yl-benzyl)-2-methyl-morpholin-4-yl]-methanone; LC-MS D: t_R = 0.92 min; $[M(^{35}Cl)+H]^+$ = 482.13
187	J-12	E-17	(4-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[(2*R*,5*R*)-5-(2-fluoro-5-[1,2,3]triazol-2-yl-benzyl)-2-methyl-morpholin-4-yl]-methanone; LC-MS D: t_R = 0.93 min; $[M(^{35}Cl)+H]^+$ = 482.10
188	A-42	E-3	[(*R*)-3-(2-Methyl-5-pyrazol-1-yl-benzyl)-morpholin-4-yl]-(5-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS D: t_R = 0.85 min; $[M+H]^+$ = 443.16
189	A-42	E-4	[(*R*)-3-(2-Methyl-5-pyrazol-1-yl-benzyl)-morpholin-4-yl]-(4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS D: t_R = 0.87 min; $[M+H]^+$ = 443.14
190	A-42	E-27	[(*R*)-3-(2-Methyl-5-pyrazol-1-yl-benzyl)-morpholin-4-yl]-(3-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone; LC-MS D: t_R = 0.86 min; $[M+H]^+$ = 443.18
191	A-36	E-17	(4-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(2-methyl-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone; LC-MS A: t_R = 0.94 min; $[M(^{35}Cl)+H]^+$ = 464.11

*Initially prepared as a racemate and isolated following prep. chiral HPLC

Example compounds 192 to 194

Example 192: [(*R*)-3-(4-Methyl-3-pyrimidin-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone

The title compound was prepared from L-3 in analogy to the procedure described for Example 5 and isolated following prep. chiral HPLC. LC-MS A: t_R = 0.79 min; $[M+H]^+$ = 441.09.

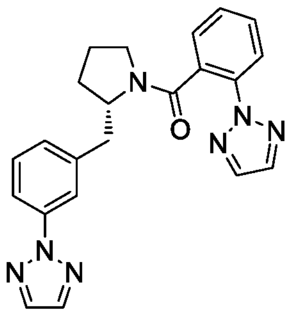
Example 193: [(R)-3-(4-Methyl-3-thiazol-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone

The title compound was prepared from **L-3** in analogy to the procedure described for Example 8 and isolated following prep. chiral HPLC. LC-MS A: t_R = 0.86 min; $[M+H]^+$ = 446.10.

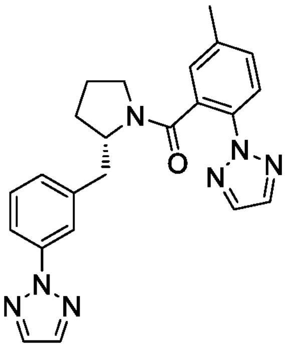
Example 194: [(R)-3-(4-Chloro-3-pyrimidin-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone

The title compound was prepared from **L-4** in analogy to the procedure described for Example 5 and isolated following prep. chiral HPLC. LC-MS D: t_R = 0.81 min; $[M+H]^+$ = 461.07.

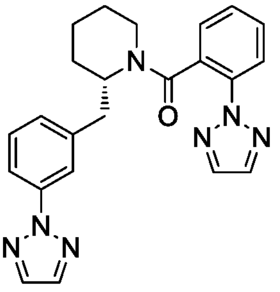
Reference compounds



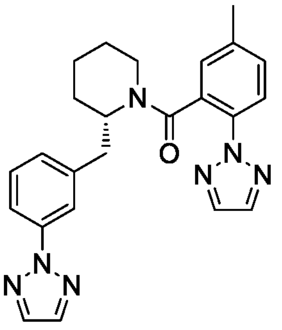
Ref. compound 1



Ref. compound 2



Ref. compound 3



Ref. compound 4

Reference compound 1: [(*S*)-2-(3-[1,2,3]Triazol-2-yl-benzyl)-pyrrolidin-1-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone

Step 1: (*S*)-Tetrahydro-pyrrolo[1,2-c][1,2,3]oxathiazole 1,1-dioxide was prepared from commercially available L-prolinol following the procedure described for Example 2 in US5,130,432. ^1H NMR ($CDCl_3$) δ_H: 4.58 (dd, J_1 = 8.6 Hz, J_2 = 6.9 Hz, 1 H), 4.30 (m, 1 H), 4.07 (dd, J_1 = 8.7 Hz, J_2 = 6.0 Hz, 1 H), 3.72 (m, 1 H), 3.30 (dt, J_1 = 11.2 Hz, J_2 = 7.1 Hz, 1 H), 2.21 (m, 1 H), 1.99 (m, 2 H), 1.85 (m, 1 H).

Step 2: (*S*)-2-(3-Iodo-benzyl)-pyrrolidine was prepared from 1,3-diiodobenzene and (*S*)-tetrahydro-pyrrolo[1,2-c][1,2,3]oxathiazole 1,1-dioxide in analogy to the procedure described for Example 4 in US5,130,432. LC-MS A: t_R = 0.57 min; $[M+H]^+$ = 287.99.

Step 3: (*S*)-2-(3-Iodo-benzyl)-pyrrolidine-1-carboxylic acid tert-butyl ester was prepared from (*S*)-2-(3-iodo-benzyl)-pyrrolidine in analogy to the procedure described for **B-6**. LC-MS A: t_R = 1.02 min; $[M+H]^+$ = 387.91.

Step 4: (*S*)-2-(3-[1,2,3]Triazol-2-yl-benzyl)-pyrrolidine-1-carboxylic acid tert-butyl ester was prepared from (*S*)-2-(3-iodo-benzyl)-pyrrolidine-1-carboxylic acid tert-butyl ester and 1*H*-

1,2,3-triazole in analogy to the procedure described for **A-13**. LC-MS A: t_R = 0.97 min; $[M+H-{}^tBu]^+$ = 273.16.

Step 5: 2-(3-(*S*)-1-Pyrrolidin-2-ylmethyl-phenyl)-2*H*-[1,2,3]triazole hydrochloride was prepared from (*S*)-2-(3-[1,2,3]triazol-2-yl-benzyl)-pyrrolidine-1-carboxylic acid tert-butyl ester in analogy to the procedure described for **A-7**. LC-MS A: t_R = 0.55 min; $[M+H]^+$ = 229.19.

Step 6: The title compound was prepared from 2-(3-(*S*)-1-pyrrolidin-2-ylmethyl-phenyl)-2H-[1,2,3]triazole hydrochloride and 2-(2*H*-1,2,3-triazol-2-yl)benzoic acid **E-2** following the procedure described for **B-28**. LC-MS D: t_R = 0.92 min; $[M+H]^+$ = 400.19.

Reference compound 2: (5-Methyl-2-[1,2,3]triazol-2-yl-phenyl)-[(*S*)-2-(3-[1,2,3]triazol-2-yl-benzyl)-pyrrolidin-1-yl]-methanone

The title compound was prepared from 2-(3-(*S*)-1-pyrrolidin-2-ylmethyl-phenyl)-2*H*-[1,2,3]triazole hydrochloride and 5-methyl-2-(2*H*-1,2,3-triazol-2-yl)benzoic acid **E-3** following the procedure described for **B-28**. LC-MS D: t_R = 0.96 min; $[M+H]^+$ = 414.21.

Reference compound 3: [(*S*)-2-(3-[1,2,3]Triazol-2-yl-benzyl)-piperidin-1-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone

Step 1: (*S*)-2-Hydroxymethyl-piperidine-1-carboxylic acid benzyl ester was prepared from commercially available (*S*)-1-((benzyloxy)carbonyl)piperidine-2-carboxylic acid following the procedure described for **A-8**. LC-MS B: t_R = 0.67 min; $[M+H]^+$ = 250.24.

Step 2: (*S*)-1-Piperidin-2-yl-methanol; A solution of (*S*)-2-hydroxymethyl-piperidine-1-carboxylic acid benzyl ester (4.33 g, 17 mmol) in MeOH (50 mL) was degased with argon for 5 min before 10% palladium on activated charcoal (185 mg, 1 mol%) was added and the argon atmosphere was then replaced with hydrogen (hydrogen was bubbled through the reaction mixture for 5 min). The reaction mixture was stirred at RT for 4h after which the mixture was filtered over a pad of celite washing with additional MeOH and the filtrate was evaporated *in vacuo*. The crude product appeared as a pale yellow oil and was not further purified. LC-MS B: t_R = 0.12 min; $[M+H]^+$ = 116.22.

Step 3: (*S*)-Hexahydro-[1,2,3]oxathiazolo[3,4-a]pyridine 1,1-dioxide was prepared from (*S*)-1-piperidin-2-yl-methanol in analogy to the procedure described for Example 2 in US5,130,432. ^{1}H NMR ($CDCl_3$) δ_H: 4.60 (m, 1 H), 4.21 (m, 1 H), 3.62 (m, 1 H), 3.47 (m, 1 H), 2.81 (m, 1 H), 1.90 (m, 3 H), 1.67 (m, 1 H), 1.39 (m, 2 H).

Step 4: (*S*)-2-(3-Iodo-benzyl)-piperidine was prepared from 1,3-diiodobenzene and (*S*)-hexahydro-[1,2,3]oxathiazolo[3,4-a]pyridine 1,1-dioxide in analogy to the procedure described for Example 4 in US5,130,432. LC-MS B: t_R = 0.54 min; $[M+H]^+$ = 302.07.

Step 5: (*S*)-2-(3-Iodo-benzyl)-piperidine-1-carboxylic acid tert-butyl ester was prepared from (*S*)-2-(3-iodo-benzyl)-piperidine in analogy to the procedure described for **B-6**. LC-MS B: t_R = 1.08 min; $[M\text{-}Me]^+$ = 386.86.

Step 6: (*S*)-2-(3-[1,2,3]Triazol-2-yl-benzyl)-piperidine-1-carboxylic acid tert-butyl ester was prepared from (*S*)-2-(3-iodo-benzyl)-piperidine-1-carboxylic acid tert-butyl ester and 1*H*-1,2,3-triazole in analogy to the procedure described for **A-13**. LC-MS C: t_R = 1.05 min; $[M+H\text{-}{}^tBu]^+$ = 287.08.

Step 7: (*S*)-2-(3-[1,2,3]Triazol-2-yl-benzyl)-piperidine hydrochloride was prepared from (*S*)-2-(3-[1,2,3]triazol-2-yl-benzyl)-piperidine-1-carboxylic acid tert-butyl ester in analogy to the procedure described for **A-7**. LC-MS C: t_R = 0.90 min; $[M+H]^+$ = 243.17.

Step 8: The title compound was prepared from (*S*)-2-(3-[1,2,3]triazol-2-yl-benzyl)-piperidine hydrochloride and 2-(2*H*-1,2,3-triazol-2-yl)benzoic acid **E-2** following the procedure described for **B-28**. LC-MS D: t_R = 0.91 min; $[M+H]^+$ = 414.05.

Reference compound 4: (5-Methyl-2-[1,2,3]triazol-2-yl-phenyl)-[(*S*)-2-(3-[1,2,3]triazol-2-yl-benzyl)-piperidin-1-yl]-methanone

The title compound was prepared from (*S*)-2-(3-[1,2,3]triazol-2-yl-benzyl)-piperidine hydrochloride and 5-methyl-2-(2*H*-1,2,3-triazol-2-yl)benzoic acid **E-3** following the procedure described for **B-28**. LC-MS D: t_R = 0.94 min; $[M+H]^+$ = 427.92.

II. Biological Assays

Antagonistic activities on both orexin receptors have been measured for each example compound using the following procedure:

***In vitro* assay: Intracellular calcium measurements:**

Chinese hamster ovary (CHO) cells expressing the human orexin-1 receptor and the human orexin-2 receptor, respectively, are grown in culture medium (Ham F-12 with *L*-Glutamine) containing 300 µg/mL G418, 100 U/mL penicillin, 100 µg/mL streptomycin and 10 % heat inactivated fetal calf serum (FCS). The cells are seeded at 20’000 cells / well into 384-well black clear bottom sterile plates (Greiner). The seeded plates are incubated overnight at 37°C in 5% CO_2.

Human orexin-A as an agonist is prepared as 1 mM stock solution in MeOH: water (1:1), diluted in HBSS containing 0.1 % bovine serum albumin (BSA), $NaHCO_3$: 0.375g/L and 20 mM HEPES for use in the assay at a final concentration of 3 nM.

Antagonists are prepared as 10 mM stock solution in DMSO, then diluted in 384-well plates using DMSO followed by a transfer of the dilutions into in HBSS containing 0.1 % bovine serum albumin (BSA), NaHCO$_3$: 0.375g/L and 20 mM HEPES. On the day of the assay, 50 μL of staining buffer (HBSS containing 1% FCS, 20 mM HEPES, NaHCO$_3$: 0.375g/L, 5 mM probenecid (Sigma) and 3 μM of the fluorescent calcium indicator fluo-4 AM (1 mM stock solution in DMSO, containing 10% pluronic) is added to each well. The 384-well cell-plates are incubated for 50 min at 37° C in 5% CO$_2$ followed by equilibration at RT for 30 min before measurement.

Within the Fluorescent Imaging Plate Reader (FLIPR Tetra, Molecular Devices), antagonists are added to the plate in a volume of 10 μL/well, incubated for 120 min and finally 10 μL/well of agonist is added. Fluorescence is measured for each well at 1 second intervals, and the height of each fluorescence peak is compared to the height of the fluorescence peak induced by 3 nM orexin-A with vehicle in place of antagonist. The IC$_{50}$ value (the concentration of compound needed to inhibit 50 % of the agonistic response) is determined and may be normalized using the obtained IC$_{50}$ value of an on-plate reference compound. Optimized conditions were achieved by adjustment of pipetting speed and cell splitting regime. The calculated IC$_{50}$ values may fluctuate depending on the daily cellular assay performance. Fluctuations of this kind are known to those skilled in the art. In the case where IC$_{50}$ values have been determined several times for the same compound, the geometric mean has been given. Antagonistic activities of example compounds are shown in Tables 13 and 14.

Table 13

Example	**IC$_{50}$ OX1 [nM]**	**IC$_{50}$ OX2 [nM]**	**Example**	**IC$_{50}$ OX1 [nM]**	**IC$_{50}$ OX2 [nM]**	**Example**	**IC$_{50}$ OX1 [nM]**	**IC$_{50}$ OX2 [nM]**
1	40	803	**21**	2	1649	**41**	8	1043
2	7	406	**22**	3	318	**42**	34	2009
3	4	3340	**23**	34	4780	**43**	0.3	273
4	6	1880	**24**	3	1030	**44**	2	457
5	4	2950	**25**	11	1400	**45**	0.1	119
6	12	1940	**26**	21	822	**46**	0.5	163
7	26	6090	**27**	2	274	**47**	13	2380
8	1	335	**28**	43	2107	**48**	39	4440
9	2	468	**29**	4	333	**49**	3	582
10	0.5	31	**30**	4	199	**50**	2	942

11	2	196	**31**	33	360	**51**	3	229
12	17	1235	**32**	7	489	**52**	43	1630
13	966	4439	**33**	14	1200	**53**	27	3404
14	3	905	**34**	5	1230	**54**	46	1824
15	24	3160	**35**	1	25			
16	30	1822	**36**	41	889			
17	2	396	**37**	4	209	**Ref. 1**	4	40
18	22	1892	**38**	1	131	**Ref. 2**	0.5	8
19	2	369	**39**	5	231	**Ref. 3**	1	12
20	25	1527	**40**	34	762	**Ref. 4**	0.3	2

Table 14

Example	**IC_{50} OX1 [nM]**	**IC_{50} OX2 [nM]**	**Example**	**IC_{50} OX1 [nM]**	**IC_{50} OX2 [nM]**	**Example**	**IC_{50} OX1 [nM]**	**IC_{50} OX2 [nM]**
55	27	2010	**102**	25	1508	**149**	4	263
56	4	837	**103**	0.7	47	**150**	9	506
57	48	2736	**104**	3	117	**151**	8	818
58	0.7	42	**105**	2	101	**152**	4	129
59	1	80	**106**	3	335	**153**	3	85
60	0.7	34	**107**	5	435	**154**	13	447
61	1	60	**108**	10	855	**155**	3	371
62	3	404	**109**	1	105	**156**	3	571
63	9	49	**110**	2	176	**157**	39	2590
64	6	784	**111**	7	983	**158**	3	2260
65	2	261	**112**	3	839	**159**	6	490
66	16	992	**113**	2	110	**160**	3	268
67	2	274	**114**	1	83	**161**	16	655
68	16	1297	**115**	2	146	**162**	24	2530
69	0.9	314	**116**	21	899	**163**	22	1864
70	5	2610	**117**	5	107	**164**	29	4040
71	35	2190	**118**	10	728	**165**	14	1296

72	8	2460	**119**	6	593	**166**	13	1395
73	10	1850	**120**	3	531	**167**	19	2382
74	11	355	**121**	26	1640	**168**	40	3505
75	3	547	**122**	6	1610	**169**	5	2440
76	2	133	**123**	5	939	**170**	7	451
77	1	96	**124**	9	997	**171**	10	675
78	17	528	**125**	7	626	**172**	3	93
79	0.4	13	**126**	40	1480	**173**	16	455
80	28	645	**127**	26	1500	**174**	8	642
81	2	212	**128**	0.7	30	**175**	3	359
82	41	1140	**129**	12	188	**176**	11	240
83	7	403	**130**	3	191	**177**	25	893
84	5	246	**131**	4	1131	**178**	2	165
85	1	21	**132**	8	1170	**179**	2	34
86	42	2652	**133**	22	2600	**180**	19	830
87	3	227	**134**	11	336	**181**	11	1567
88	30	893	**135**	16	1880	**182**	7	371
89	7	420	**136**	37	574	**183**	15	2130
90	12	475	**137**	30	202	**184**	2	96
91	10	612	**138**	4	159	**185**	2	39
92	3	2633	**139**	10	191	**186**	11	181
93	5	2086	**140**	27	1110	**187**	6	58
94	6	3578	**141**	16	429	**188**	21	2130
95	11	1199	**142**	5	287	**189**	12	1090
96	10	390	**143**	19	485	**190**	25	3770
97	3	237	**144**	5	104	**191**	12	1040
98	1	24	**145**	34	1514	**192**	16	2606
99	5	1223	**146**	3	282	**193**	1	238
100	6	289	**147**	3	171	**194**	33	2257
101	2	155	**148**	39	1935			

CYP3A4 Inhibition assay

The CYP3A4 inhibition assay was performed using human liver microsomes and testosterone 6β-hydroxylation as a P450 isoform-specific marker. In a total volume of 150 µL, ^{14}C-testosterone at a final concentration of 40 µM in a 100 mM phosphate buffer (pH 7.4) was incubated in a 96-well plate with 0.3 mg/mL of human liver microsomes in an Eppendorf thermomixer at 37 °C and 400 rpm. A 1.0 µL-aliquot of the 150-fold concentrated compound stock solution, prepared in DMSO, was added to yield final inhibitor concentrations of 0, 0.1, 0.5, 1.0, 5.0, 10, 25, and 50 µM. The reaction was initiated by addition of 15 µL of the NADPH-regenerating system containing the glucose-6-phosphate dehydrogenase and terminated after 7 min with a 75 µL-aliquot of methanol. After centrifugation at 465 g and 4 °C for 20 min, a 50 µL-aliquot of the supernatant was submitted to HPLC according to the method described below. The total concentration of DMSO in the assay including controls without inhibitor was 1 %.

Nicardipine was run in parallel as a reference inhibitor of CYP3A4 activity at final concentrations of 0, 0.1, 0.5, 1.0, 5.0, 10, 25, and 50 µM. Stock solutions thereof were prepared in DMSO.

The chromatographic separation of testosterone and 6β-hydroxytestosterone was achieved on a Phenomenex Luna C18(2) column (5 µm, 2.0 x 10 mm) at RT with a flow rate of 0.6 mL/min. Mobile phases consisted of 1 % aqueous formic acid (phase A) and methanol (phase B) using a gradient method with 0.9 min total run time. Using these chromatographic conditions, the 6β-hydroxy metabolite exhibited a retention time of 0.6 min.

The quantification of 6β-hydroxytestosterone was carried out using a quadrupole mass spectrometer equipped with an ionspray interface operating in positive ion mode. The parameters of the mass detector were set as follows: capillary voltage 5 kV, auxiliary gas 40 psi, collision gas 3 mTorr, and transfer capillary temperature 420°C. The mass transition used for 6β-hydroxytestosterone was 305.1 to 269.3 with a scan time of 30 ms.

Compounds of the present invention were tested in the above CYP3A4 assay and inhibition values for reference compounds and particular example compounds are given in Table 15.

Table 15

Example	CYP3A4 IC_{50} [µM]	Example	CYP3A4 IC_{50} [µM]	Example	CYP3A4 IC_{50} [µM]]	Example	CYP3A4 IC_{50} [µM]
1	>50	**51**	20	**106**	14	**154**	24
2	43	**52**	>50	**107**	22	**155**	30

3	21	**53**	>50	**108**	46	**156**	>50
4	1.2	**54**	>50	**109**	43	**158**	40
5	>50	**56**	33	**110**	>50	**159**	17
6	26	**57**	20	**111**	40	**160**	17
7	>50	**58**	42	**112**	>50	**161**	33
8	3.2	**59**	32	**113**	26	**163**	14
9	8.4	**60**	41	**114**	35	**165**	20
11	43	**61**	42	**115**	24	**166**	19
12	30	**62**	29	**116**	21	**168**	8.5
14	>50	**64**	33	**117**	23	**169**	29
15	14	**65**	22	**118**	23	**170**	9.8
16	43	**66**	36	**119**	19	**171**	13
17	33	**67**	25	**120**	19	**172**	23
18	39	**68**	24	**121**	18	**173**	21
19	32	**71**	14	**122**	18	**174**	50
20	25	**73**	6.8	**123**	27	**175**	35
21	20	**75**	15	**124**	22	**176**	22
22	41	**76**	7.5	**125**	22	**178**	24
23	6	**77**	16	**126**	17	**179**	29
24	>50	**78**	22	**127**	30	**180**	36
26	24	**81**	33	**129**	26	**181**	36
27	31	**83**	25	**130**	20	**182**	14
28	0.3	**84**	21	**131**	35	**183**	>50
29	39	**85**	25	**132**	19	**184**	19
30	17	**87**	15	**133**	37	**185**	20
31	>50	**90**	21	**134**	19	**186**	19
32	>50	**91**	17	**135**	30	**187**	14
33	>50	**92**	44	**138**	7.4	**188**	14
34	>50	**93**	>50	**139**	13	**189**	17
35	20	**94**	30	**141**	19	**190**	26
36	36	**95**	49	**142**	9.2	**191**	14
37	17	**96**	28	**143**	9.1	**192**	>50

39	18	**97**	11	**144**	9.6	**193**	0.6
42	5.1	**98**	9.7	**145**	22		
43	1.2	**99**	9.6	**146**	40		
44	2	**100**	13	**147**	28		
47	6	**101**	9.7	**149**	31	**Ref. 1**	5.5
48	9.6	**102**	17	**150**	32	**Ref. 2**	3.3
49	21	**104**	13	**152**	15	**Ref. 3**	6.1
50	>50	**105**	21	**153**	18	**Ref. 4**	7.7

Measurement of brain and systemic concentration after oral administration:

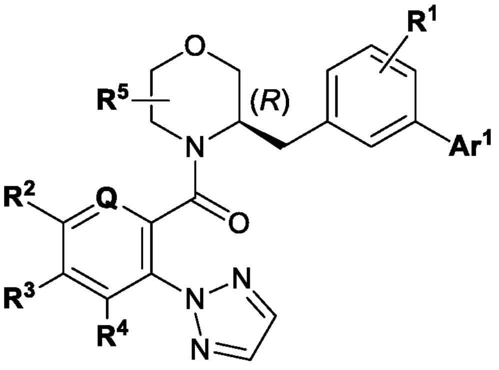
In order to assess brain penetration, the concentration of the compound is measured in plasma ([P]), and brain ([B]), sampled 1h or 3h (or at different time points) following oral administration (100 mg/kg) to male wistar rats (n=3). The compounds are formulated either in 100% PEG 400 or 10% PEG400 / 90% MC0.5%. Samples are collected in the same animal at the same time point (+/- 5 min). Blood is sampled from the vena cava caudalis into containers with EDTA as anticoagulant and centrifuged to yield plasma. Brain is sampled after cardiac perfusion of 10 mL NaCl 0.9% and homogenized into one volume of cold phosphate buffer (pH 7.4). All samples are extracted with MeOH and analyzed by LC-MS/MS. Concentrations are determined with the help of calibration curves. Inter-individual variations between the three rats were limited. Particular compounds of the present invention tested as described above gave brain concentrations ([B]) as shown in Table 16 below; wherein the compounds of Examples 11-37 and 94 were formulated in 100% PEG400 and sampled at 3h. All other examples below were formulated in 10% PEG400 / 90% MC0.5% and sampled at 1h.

Table 16

Example	[B] [ng/g]	Example	[B] [ng/g]	Example	[B] [ng/g]	Example	[B] [ng/g]
11	46	**30**	1869	**77**	1609	**120**	5133
12	11888	**35**	59	**87**	1875	**130**	5833
16	160	**37**	881	**92**	1971	**156**	613
21	36	**62**	4423	**94**	654		
27	5500	**64**	2371	**100**	529		
29	423	**76**	1376	**116**	5933		

Claims

1. A compound of formula (I)



Formula (I)

wherein

Ar¹ represents a 5- or 6-membered heteroaryl selected from the group consisting of pyrrolyl, pyrazolyl, triazolyl, oxazolyl, thiazolyl, oxadiazolyl, thiophenyl, pyridinyl, pyrimidinyl, pyrazinyl, and pyridazinyl; wherein said heteroaryl is unsubstituted, mono-, or di-substituted, wherein the substituents are independently selected from the group consisting of (C_{1-4})alkyl, (C_{1-4})alkoxy, halogen, cyano, (C_{1-3})fluoroalkyl, and (C_{1-3})fluoroalkoxy;

R^1 represents one optional substituent selected from (C_{1-4})alkyl, (C_{1-4})alkoxy, hydroxy, and halogen;

R^2 represents hydrogen, (C_{1-4})alkyl, (C_{1-4})alkoxy, halogen, or cyano;

R^3 represents hydrogen, (C_{1-4})alkyl, (C_{1-4})alkoxy, (C_{1-3})fluoroalkyl, or halogen;

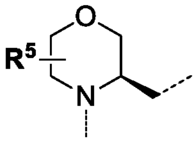
R^4 represents hydrogen, (C_{1-4})alkyl, (C_{1-3})fluoroalkyl, or halogen;

R^5 represents one optional substituent on any ring carbon atom of the morpholine ring, wherein said substituent independently is methyl or ethyl; and

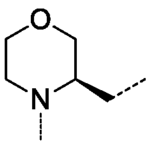
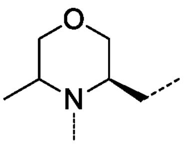
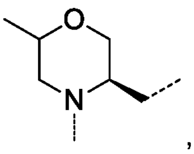
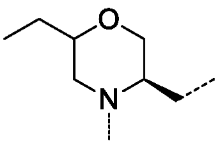
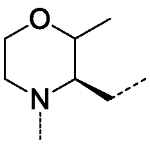
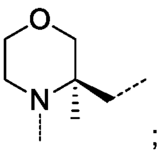
Q represents CR^6; or, in case **R^2** is (C_{1-4})alkyl or (C_{1-4})alkoxy, **Q** represents CR^6 or N; wherein **R^6** represents hydrogen, fluoro or methyl;

or a pharmaceutically acceptable salt thereof.

2. A compound according to claim 1; wherein
the morpholine ring of the compounds of formula (I):



is a ring selected from the group consisting of:

, , , , , and ;

Ar^1 represents a 5- or 6-membered heteroaryl selected from the group consisting of pyrrolyl, pyrazolyl, triazolyl, oxazolyl, thiazolyl, oxadiazolyl, thiophenyl, pyridinyl, pyrimidinyl, pyrazinyl, and pyridazinyl; wherein said heteroaryl is unsubstituted or mono-substituted with (C_{1-4})alkyl;

R^1 represents one optional substituent selected from methyl, methoxy, hydroxy, and halogen;

R^2 represents hydrogen, methyl, methoxy, halogen, or cyano;

R^3 represents hydrogen, methyl, methoxy, trifluoroalkyl, or halogen;

R^4 represents hydrogen, methyl, trifluoroalkyl, or halogen;

Q represents **CR**^{6}; or, in case **R**^{2} is methyl, **Q** represents **CR**^{6} or N; wherein

R^6 represents hydrogen, fluoro or methyl;

or a pharmaceutically acceptable salt thereof.

3. A compound according to claims 1 or 2; wherein **Ar**^{1} represents pyrazol-1-yl, [1,2,3]triazol-2-yl, [1,2,4]oxadiazol-3-yl, or pyrimidin-2-yl, which groups are unsubstituted, or in case of pyrimidin-2-yl, optionally mono-substituted with methyl;

or a pharmaceutically acceptable salt thereof.

4. A compound according to any one of claims 1 to 3; wherein **R**^{2} represents hydrogen, methyl, methoxy, cyano, fluoro, or chloro; **R**^{3} represents hydrogen, methyl, trifluoromethyl, fluoro, or chloro; **R**^{4} represent hydrogen, methyl, trifluoromethyl, or fluoro; and **Q** represents **CR**^{6}; or, in case **R**^{2} is methyl, **Q** represents **CR**^{6} or N; wherein **R**^{6} represents hydrogen, fluoro or methyl;

or a pharmaceutically acceptable salt thereof.

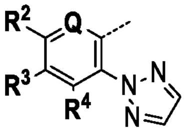
5. A compound according to any one of claims 1 to 4; wherein **Q** represents CH;

or a pharmaceutically acceptable salt thereof.

6. A compound according to any one of claims 1 to 3; wherein **R**^{2} represents hydrogen or chloro; **R**^{3} represents hydrogen, chloro, methyl or trifluoromethyl, **R**^{4} represent hydrogen or methyl; and **Q** represents CH;

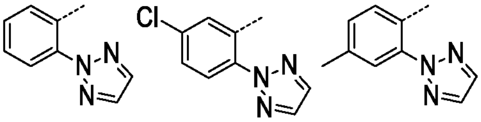
or a pharmaceutically acceptable salt thereof.

7. A compound according to any one of claims 1 to 3; wherein the group



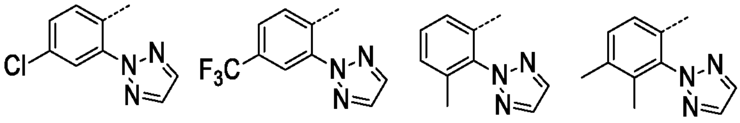
is a group independently selected from the following groups A) to F):

A)



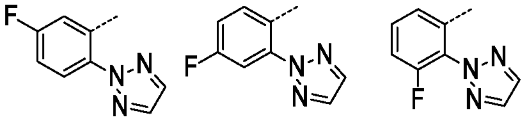
;

B)



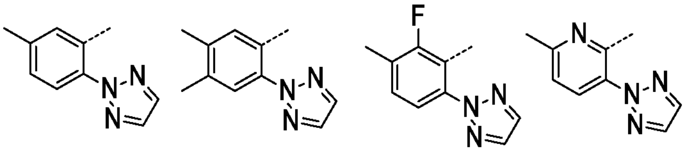
;

C)



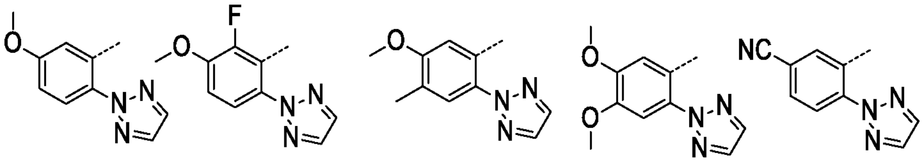
;

D)



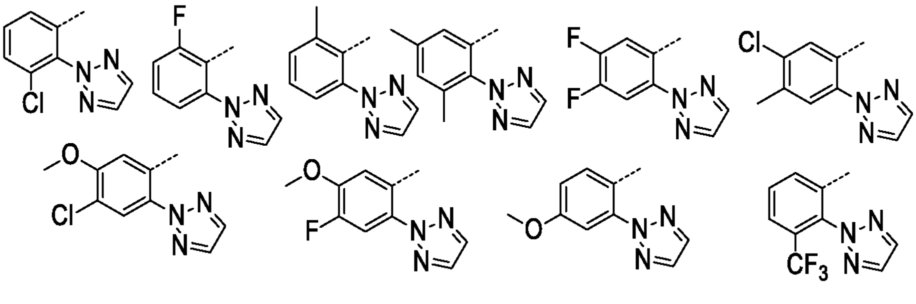
;

E)



;

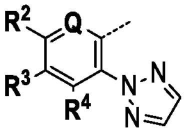
F)



;

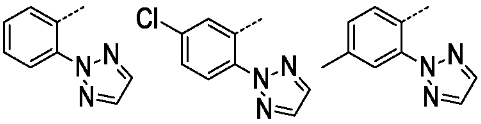
or a pharmaceutically acceptable salt thereof.

8. A compound according to any one of claims 1 to 3; wherein the group



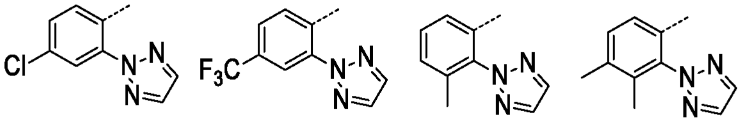
is a group selected from the group consisting of the following groups A) and B):

A)



;

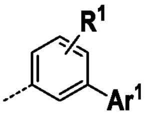
B)



;

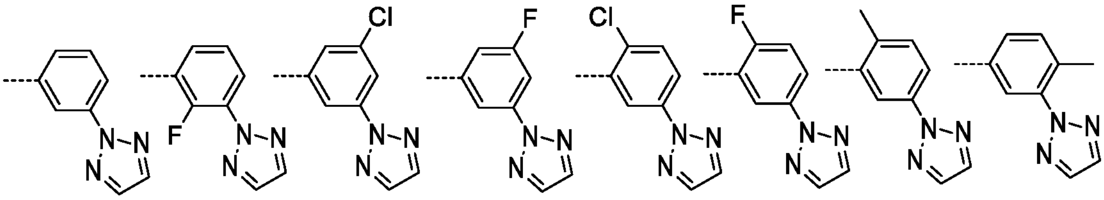
or a pharmaceutically acceptable salt thereof.

9. A compound according to any one of claims 1, 2, or 4 to 8; wherein the group



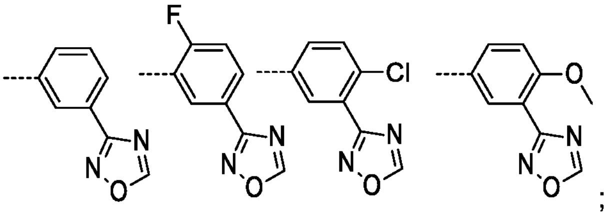
is a group independently selected from the following groups A) to H):

A)



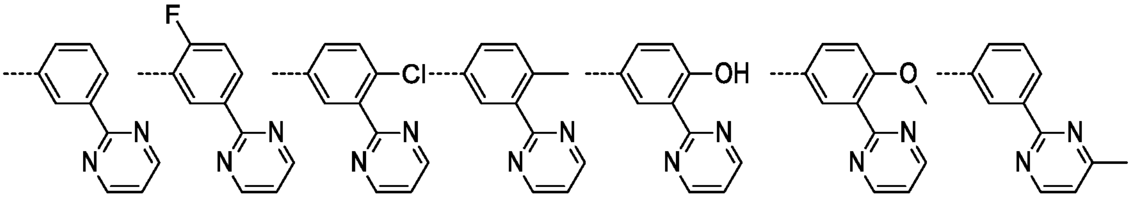
;

B)



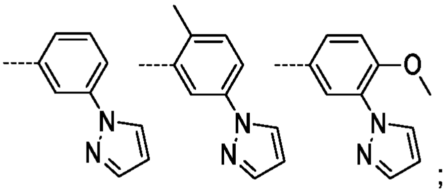
;

C)

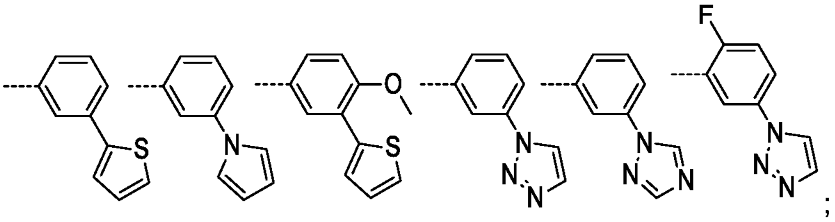


;

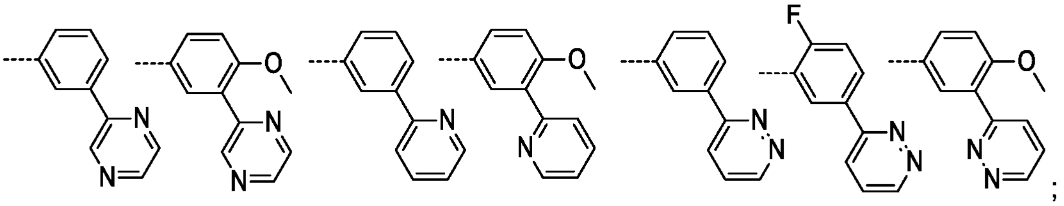
D)



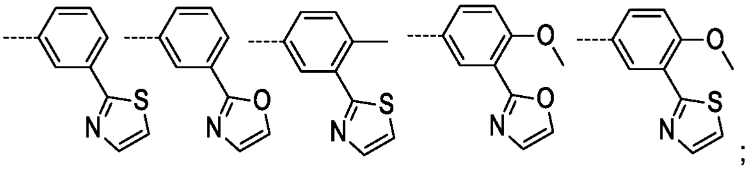
E)



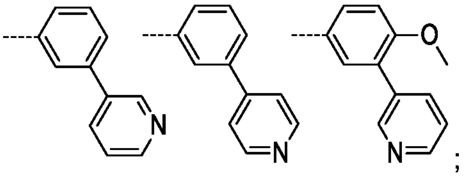
F)



G)

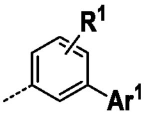


H)



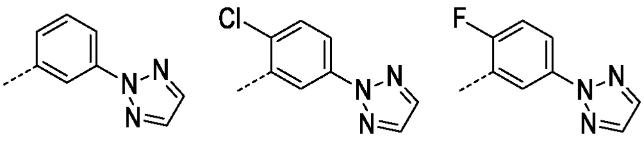
or a pharmaceutically acceptable salt thereof.

10. A compound according to any one of claims 1, 2, or 4 to 8; wherein the group



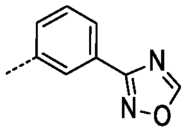
is a group selected from the group consisting of the following groups A) and B):

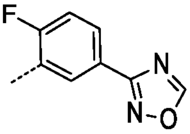
A)



; and

B)





;

or a pharmaceutically acceptable salt thereof.

11. A compound according to claim 1 selected from the group consisting of:

[(R)-3-(3-[1,2,4]Oxadiazol-3-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone;

(5-Methyl-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-[1,2,4]oxadiazol-3-yl-benzyl)-morpholin-4-yl]-methanone;

[(R)-3-(4-Methoxy-3-pyridin-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(R)-3-(4-Methoxy-3-pyridin-3-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(R)-3-(4-Methoxy-3-pyrimidin-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(R)-3-(4-Methoxy-3-pyrazin-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(R)-3-(4-Methoxy-3-pyridazin-3-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(R)-3-(4-Methoxy-3-thiazol-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(R)-3-(4-Methoxy-3-oxazol-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(R)-3-(4-Methoxy-3-thiophen-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone;

(5-Methyl-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone;

[(R)-3-(3-[1,2,3]Triazol-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(S)-3-(3-[1,2,3]Triazol-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(R)-3-(4-Methoxy-3-pyrazol-1-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone;

(5-Methyl-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-[1,2,3]triazol-1-yl-benzyl)-morpholin-4-yl]-methanone;

[(R)-3-(3-Pyrazol-1-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone;

(5-Methyl-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-pyrimidin-2-yl-benzyl)-morpholin-4-yl]-methanone;

[(R)-3-(3-Pyrimidin-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone;

(5-Methyl-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-pyrazol-1-yl-benzyl)-morpholin-4-yl]-methanone;

(5-Fluoro-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-pyrazol-1-yl-benzyl)-morpholin-4-yl]-methanone;

(2-Fluoro-3-methyl-6-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-pyrazol-1-yl-benzyl)-morpholin-4-yl]-methanone;

(4-Methyl-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-pyrazol-1-yl-benzyl)-morpholin-4-yl]-methanone;

(5-Methyl-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-[1,2,4]triazol-1-yl-benzyl)-morpholin-4-yl]-methanone;

(5-Methyl-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-pyridin-2-yl-benzyl)-morpholin-4-yl]-methanone;

(5-Methyl-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-pyridin-3-yl-benzyl)-morpholin-4-yl]-methanone;

(5-Fluoro-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone;

(4-Methyl-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone;

(5-Methyl-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-pyridin-4-yl-benzyl)-morpholin-4-yl]-methanone;

(2-Fluoro-3-methyl-6-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone;

(5-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone;

4-[1,2,3]Triazol-2-yl-3-[(R)-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholine-4-carbonyl]-benzonitrile;

(5-Methoxy-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone;

(2-Fluoro-3-methoxy-6-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone;

(4,5-Dimethoxy-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone;

(4,5-Dimethyl-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone;

(4-Fluoro-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone;
(5-Methoxy-4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone;
(5-Methyl-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-pyrrol-1-yl-benzyl)-morpholin-4-yl]-methanone;
{(R)-3-[3-(4-Methyl-pyrimidin-2-yl)-benzyl]-morpholin-4-yl}-(5-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;
{(R)-3-[3-(4-Methyl-pyrimidin-2-yl)-benzyl]-morpholin-4-yl}-(2-[1,2,3]triazol-2-yl-phenyl)-methanone;
(5-Methyl-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-pyrazin-2-yl-benzyl)-morpholin-4-yl]-methanone;
[(R)-3-(3-Oxazol-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone;
(5-Methyl-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-thiazol-2-yl-benzyl)-morpholin-4-yl]-methanone;
[(R)-3-(3-Thiazol-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone;
(5-Methyl-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-thiophen-2-yl-benzyl)-morpholin-4-yl]-methanone;
[(R)-3-(3-Thiophen-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone;
(5-Methyl-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-pyridazin-3-yl-benzyl)-morpholin-4-yl]-methanone;
[(R)-3-(3-Pyridazin-3-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone;
(2-Fluoro-3-methyl-6-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-pyrimidin-2-yl-benzyl)-morpholin-4-yl]-methanone;
(5-Methoxy-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-pyrimidin-2-yl-benzyl)-morpholin-4-yl]-methanone;
(5-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-pyrimidin-2-yl-benzyl)-morpholin-4-yl]-methanone;
(6-Methyl-3-[1,2,3]triazol-2-yl-pyridin-2-yl)-[(R)-3-(3-pyrazol-1-yl-benzyl)-morpholin-4-yl]-methanone;
(6-Methyl-3-[1,2,3]triazol-2-yl-pyridin-2-yl)-[(R)-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone; and
(3-Fluoro-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone;

or a pharmaceutically acceptable salt thereof.

12. A compound according to claim 1 selected from the group consisting of:

[(R)-3-(4-Hydroxy-3-pyrimidin-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(R)-3-(2-Fluoro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(5-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(R)-3-(2-Fluoro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(R)-3-(4-Methoxy-3-[1,2,4]oxadiazol-3-yl-benzyl)-morpholin-4-yl]-(5-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(R)-3-(4-Methoxy-3-[1,2,4]oxadiazol-3-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(R)-3-(4-Methoxy-3-[1,2,4]oxadiazol-3-yl-benzyl)-morpholin-4-yl]-(4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

(4-Fluoro-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(4-methoxy-3-[1,2,4]oxadiazol-3-yl-benzyl)-morpholin-4-yl]-methanone;

[(R)-3-(2-Fluoro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(R)-3-(4-Methoxy-3-[1,2,4]oxadiazol-3-yl-benzyl)-morpholin-4-yl]-(2-methyl-6-[1,2,3]triazol-2-yl-phenyl)-methanone;

(3-Methyl-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone;

[(R)-3-(4-Methyl-3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(5-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(R)-3-(4-Methyl-3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(R)-3-(4-Methyl-3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(3R,5R)-3-Methyl-5-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(3R,5R)-3-Methyl-5-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(3R,5R)-3-Methyl-5-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(3-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(3S,5R)-3-Methyl-5-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(3S,5R)-3-Methyl-5-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(3-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(3S,5R)-3-Methyl-5-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(5-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

(4,5-Dimethyl-2-[1,2,3]triazol-2-yl-phenyl)-[(3S,5R)-3-methyl-5-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone;

(3,5-Dimethyl-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone;

[(R)-3-(3-[1,2,3]Triazol-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-4-trifluoromethyl-phenyl)-methanone;

(4-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone;

(4-Fluoro-5-methoxy-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone;

(4,5-Dimethyl-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(4-methyl-3-[1,2,4]oxadiazol-3-yl-benzyl)-morpholin-4-yl]-methanone;
(4,5-Difluoro-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-[1,2,4]oxadiazol-3-yl-benzyl)-morpholin-4-yl]-methanone;
(4-Methyl-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-[1,2,4]oxadiazol-3-yl-benzyl)-morpholin-4-yl]-methanone;
(3-Fluoro-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-[1,2,4]oxadiazol-3-yl-benzyl)-morpholin-4-yl]-methanone;
(3-Methyl-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-[1,2,4]oxadiazol-3-yl-benzyl)-morpholin-4-yl]-methanone;
(5-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-[1,2,4]oxadiazol-3-yl-benzyl)-morpholin-4-yl]-methanone;
(4,5-Dimethyl-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-[1,2,4]oxadiazol-3-yl-benzyl)-morpholin-4-yl]-methanone;
(4-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-[1,2,4]oxadiazol-3-yl-benzyl)-morpholin-4-yl]-methanone;
[(R)-3-(3-[1,2,4]Oxadiazol-3-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-4-trifluoromethyl-phenyl)-methanone;
(5-Fluoro-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-[1,2,4]oxadiazol-3-yl-benzyl)-morpholin-4-yl]-methanone;
(3,5-Dimethyl-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-[1,2,4]oxadiazol-3-yl-benzyl)-morpholin-4-yl]-methanone;
[(R)-3-(4-Chloro-3-[1,2,4]oxadiazol-3-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone;
(4,5-Difluoro-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone;
(3,4-Dimethyl-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone;
(4-Methoxy-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone;
(3,4-Dimethyl-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(2-fluoro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone;
[(R)-3-(2-Fluoro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(4-methoxy-2-[1,2,3]triazol-2-yl-phenyl)-methanone;
[(2S,5R)-2-Methyl-5-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;
[(2R,5R)-2-Methyl-5-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(3-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;
(4,5-Dimethyl-2-[1,2,3]triazol-2-yl-phenyl)-[(2R,5R)-2-methyl-5-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone;
(3,4-Dimethyl-2-[1,2,3]triazol-2-yl-phenyl)-[(2R,5R)-2-methyl-5-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone;
[(2R,5R)-2-Methyl-5-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone;
[(2R,5R)-2-Methyl-5-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;
[(R)-3-Methyl-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(5-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;
(5-Chloro-4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone;
(4-Chloro-5-methoxy-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone;
[(R)-3-(3-Chloro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;
[(R)-3-(3-Chloro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(3-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;
(3-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone;
[(2R,5R)-2-Methyl-5-(3-pyrimidin-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(2R,5R)-2-Methyl-5-(3-pyrimidin-2-yl-benzyl)-morpholin-4-yl]-(5-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(2R,5R)-2-Methyl-5-(3-pyrimidin-2-yl-benzyl)-morpholin-4-yl]-(4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(2R,5R)-2-Methyl-5-(3-pyrimidin-2-yl-benzyl)-morpholin-4-yl]-(3-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

(3,4-Dimethyl-2-[1,2,3]triazol-2-yl-phenyl)-[(2R,5R)-2-methyl-5-(3-pyrimidin-2-yl-benzyl)-morpholin-4-yl]-methanone;

(5-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[(2R,5R)-2-methyl-5-(3-pyrimidin-2-yl-benzyl)-morpholin-4-yl]-methanone;

(4-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[(2R,5R)-2-methyl-5-(3-pyrimidin-2-yl-benzyl)-morpholin-4-yl]-methanone;

[(2R,5R)-5-(2-Fluoro-5-[1,2,3]triazol-2-yl-benzyl)-2-methyl-morpholin-4-yl]-(5-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(2R,5R)-5-(2-Fluoro-5-[1,2,3]triazol-2-yl-benzyl)-2-methyl-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(2R,5R)-5-(2-Fluoro-5-[1,2,3]triazol-2-yl-benzyl)-2-methyl-morpholin-4-yl]-(4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(2R,5R)-5-(2-Fluoro-5-[1,2,3]triazol-2-yl-benzyl)-2-methyl-morpholin-4-yl]-(3-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(R)-3-(2-Methyl-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(5-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(R)-3-(2-Chloro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(R)-3-(2-Methyl-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(R)-3-(2-Chloro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(3-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(R)-3-(2-Methyl-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(R)-3-(2-Methyl-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(3-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(R)-3-(2-Chloro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(5-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(R)-3-(2-Chloro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(R)-3-(2-Fluoro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(3-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

(4,5-Dimethyl-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(2-fluoro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone;

(5-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(2-fluoro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone;

(4-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(2-fluoro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone;

[(R)-3-(2-Fluoro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(5-methoxy-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

(2-Fluoro-3-methyl-6-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(2-fluoro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone;

(2-Fluoro-3-methoxy-6-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(2-fluoro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone;

[(R)-3-(2-Fluoro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(5-methoxy-4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

(3-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(2-fluoro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone;

[(R)-3-(2-Fluoro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(2-fluoro-6-[1,2,3]triazol-2-yl-phenyl)-methanone;

(4,5-Difluoro-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(2-fluoro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone;

[(R)-3-(2-Fluoro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-4-trifluoromethyl-phenyl)-methanone;

(4-Chloro-5-methoxy-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(2-fluoro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone;

[(2R,5R)-5-(2-Fluoro-5-[1,2,3]triazol-1-yl-benzyl)-2-methyl-morpholin-4-yl]-(5-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(2R,5R)-5-(2-Fluoro-5-[1,2,3]triazol-1-yl-benzyl)-2-methyl-morpholin-4-yl]-(4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(2R,5R)-2-Ethyl-5-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(5-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(2R,5R)-2-Ethyl-5-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(2R,5R)-2-Ethyl-5-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(R)-3-(3-Fluoro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(R)-3-(3-Fluoro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(2R,5R)-5-(2-Fluoro-5-pyrimidin-2-yl-benzyl)-2-methyl-morpholin-4-yl]-(5-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(2R,5R)-5-(2-Fluoro-5-pyrimidin-2-yl-benzyl)-2-methyl-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(2R,5R)-5-(2-Fluoro-5-pyrimidin-2-yl-benzyl)-2-methyl-morpholin-4-yl]-(4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(2R,5R)-5-(2-Fluoro-5-pyrimidin-2-yl-benzyl)-2-methyl-morpholin-4-yl]-(3-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

(3,4-Dimethyl-2-[1,2,3]triazol-2-yl-phenyl)-[(2R,5R)-5-(2-fluoro-5-pyrimidin-2-yl-benzyl)-2-methyl-morpholin-4-yl]-methanone;

(5-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[(2R,5R)-5-(2-fluoro-5-pyrimidin-2-yl-benzyl)-2-methyl-morpholin-4-yl]-methanone;

(4-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[(2R,5R)-5-(2-fluoro-5-pyrimidin-2-yl-benzyl)-2-methyl-morpholin-4-yl]-methanone;

(3-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[(2R,5R)-5-(2-fluoro-5-pyrimidin-2-yl-benzyl)-2-methyl-morpholin-4-yl]-methanone;

[(R)-3-(2-Fluoro-5-pyrimidin-2-yl-benzyl)-morpholin-4-yl]-(5-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(R)-3-(2-Fluoro-5-pyrimidin-2-yl-benzyl)-morpholin-4-yl]-(4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(R)-3-(2-Fluoro-5-pyrimidin-2-yl-benzyl)-morpholin-4-yl]-(3-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

(3,4-Dimethyl-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(2-fluoro-5-pyrimidin-2-yl-benzyl)-morpholin-4-yl]-methanone;

(5-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(2-fluoro-5-pyrimidin-2-yl-benzyl)-morpholin-4-yl]-methanone;

(4-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(2-fluoro-5-pyrimidin-2-yl-benzyl)-morpholin-4-yl]-methanone;

(3-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(2-fluoro-5-pyrimidin-2-yl-benzyl)-morpholin-4-yl]-methanone;

[(2S,3R)-2-Methyl-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(5-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(2S,3R)-2-Methyl-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(2S,3R)-2-Methyl-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(3-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(2R,5R)-5-(2-Fluoro-5-pyridazin-3-yl-benzyl)-2-methyl-morpholin-4-yl]-(4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(R)-3-(2-Fluoro-5-pyridazin-3-yl-benzyl)-morpholin-4-yl]-(4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(2R,3R)-2-Methyl-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(5-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(2R,3R)-2-Methyl-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(R)-3-(2-Chloro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(3,4-dimethyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(R)-3-(2-Chloro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(4-chloro-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(R)-3-(2-Chloro-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(3-chloro-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

(3-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[(2R,5R)-2-methyl-5-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone;

(3-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[(2R,5R)-5-(2-fluoro-5-[1,2,3]triazol-2-yl-benzyl)-2-methyl-morpholin-4-yl]-methanone;

[(R)-3-(2-Fluoro-5-[1,2,4]oxadiazol-3-yl-benzyl)-morpholin-4-yl]-(5-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

[(R)-3-(2-Fluoro-5-[1,2,4]oxadiazol-3-yl-benzyl)-morpholin-4-yl]-(4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

(5-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(2-fluoro-5-[1,2,4]oxadiazol-3-yl-benzyl)-morpholin-4-yl]-methanone;

[(R)-3-(2-Fluoro-5-[1,2,4]oxadiazol-3-yl-benzyl)-morpholin-4-yl]-(3-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

(4-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(2-fluoro-5-[1,2,4]oxadiazol-3-yl-benzyl)-morpholin-4-yl]-methanone;

(4,5-Dimethyl-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(2-fluoro-5-[1,2,4]oxadiazol-3-yl-benzyl)-morpholin-4-yl]-methanone;

(3-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(2-fluoro-5-[1,2,4]oxadiazol-3-yl-benzyl)-morpholin-4-yl]-methanone;

(3,4-Dimethyl-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(2-fluoro-5-[1,2,4]oxadiazol-3-yl-benzyl)-morpholin-4-yl]-methanone;

[(R)-3-(3-[1,2,3]Triazol-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-3-trifluoromethyl-phenyl)-methanone;

[(R)-3-(2-Fluoro-3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-(4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;

(5-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[(2R,5R)-2-methyl-5-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone;

(4-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[(2R,5R)-2-methyl-5-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone;

(5-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[(2R,5R)-5-(2-fluoro-5-[1,2,3]triazol-2-yl-benzyl)-2-methyl-morpholin-4-yl]-methanone;
(4-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[(2R,5R)-5-(2-fluoro-5-[1,2,3]triazol-2-yl-benzyl)-2-methyl-morpholin-4-yl]-methanone;
[(R)-3-(2-Methyl-5-pyrazol-1-yl-benzyl)-morpholin-4-yl]-(5-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;
[(R)-3-(2-Methyl-5-pyrazol-1-yl-benzyl)-morpholin-4-yl]-(4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;
[(R)-3-(2-Methyl-5-pyrazol-1-yl-benzyl)-morpholin-4-yl]-(3-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone;
(4-Chloro-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(2-methyl-5-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone;
[(R)-3-(4-Methyl-3-pyrimidin-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone;
[(R)-3-(4-Methyl-3-thiazol-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone; and
[(R)-3-(4-Chloro-3-pyrimidin-2-yl-benzyl)-morpholin-4-yl]-(2-[1,2,3]triazol-2-yl-phenyl)-methanone;

or a pharmaceutically acceptable salt thereof.

13. The compound according to claim 1 which is (4-methyl-2-[1,2,3]triazol-2-yl-phenyl)-[(R)-3-(3-[1,2,3]triazol-2-yl-benzyl)-morpholin-4-yl]-methanone;

or a pharmaceutically acceptable salt thereof.

14. A pharmaceutical composition comprising, as active principle, one or more compounds according to any one of claims 1 to 13, or a pharmaceutically acceptable salt thereof, and at least one therapeutically inert excipient.

15. A compound according to any one of claims 1 to 13, or a pharmaceutically acceptable salt thereof, for use as a medicament.

16. A compound according to any one of claims 1 to 13, or a pharmaceutically acceptable salt thereof, when used in the prevention or treatment of a disease selected from the group consisting of anxiety disorders, addiction disorders, mood disorders, and appetite disorders.

17. Use of a compound according to any one of claims 1 to 13, or of a pharmaceutically acceptable salt thereof, in the preparation of a medicament for the prevention or treatment of a disease selected from the group consisting of anxiety disorders, addiction disorders, mood disorders, and appetite disorders.

18. A method of treatment of a disease selected from the group consisting anxiety disorders, addiction disorders, mood disorders, and appetite disorders; comprising administering to a patient an effective amount of a compound of formula (I) as defined in any one of claims 1 to 13, in free or pharmaceutically acceptable salt form.