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(71) Applicant (for all designated States except US): **ACTELION PHARMACEUTICALS LTD** [CH/CH]; Gewerbestrasse 16, CH-4123 Allschwil (CH).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **BOLLI, Martin** [CH/CH]; c/o Actelion Pharmaceuticals Ltd, Gewerbestrasse 16, CH-4123 Allschwil (CH). **BOSS, Christoph** [CH/CH]; c/o Actelion Pharmaceuticals Ltd, Gewerbestrasse 16, CH-4123 Allschwil (CH). **BROTSCHI, Christine** [CH/CH]; c/o Actelion Pharmaceuticals Ltd, Gewerbestrasse 16, CH-4123 Allschwil (CH). **HEIDMANN, Bibia** [FR/FR]; c/o Actelion Pharmaceuticals Ltd, Gewerbestrasse 16, CH-4123 Allschwil (CH). **SIFERLEN, Thierry** [FR/FR]; c/o Actelion Pharmaceuticals

Ltd, Gewerbestrasse 16, CH-4123 Allschwil (CH). **TRACHSEL, Daniel** [CH/CH]; c/o Actelion Pharmaceuticals Ltd, Gewerbestrasse 16, CH-4123 Allschwil (CH). **WILLIAMS, Jodi T.** [GB/CH]; c/o Actelion Pharmaceuticals Ltd, Gewerbestrasse 16, CH-4123 Allschwil (CH).

(74) Agent: **VELKER, Jörg**; c/o Actelion Pharmaceuticals Ltd, Gewerbestrasse 16, CH-4123 Allschwil (CH).

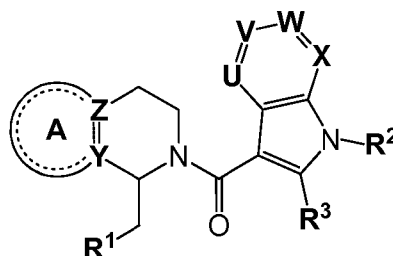
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(54) Title: NOVEL INDOLE AND PYRROLOPYRIDINE AMIDES



Formula (I)

(57) Abstract: The present invention relates to indole and pyrrolopyridine amide derivatives of formula (I) wherein R¹, R², R³, U, V, W, X, Y, Z and ring A 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.

Act 234A**Novel indole and pyrrolopyridine amides**

The present invention relates to novel indole and pyrrolopyridine amide 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 especially their use as orexin receptor antagonists.

Orexins (orexin A or OX-A and orexin B or OX-B) are novel 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 (OX₁ and OX₂ receptors). The orexin-1 receptor (OX₁) is selective for OX-A, and the orexin-2 receptor (OX₂) is capable to bind OX-A as well as OX-B. Orexins are 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, 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). Furthermore, in vitro and in vivo evidence for a critical role of orexin signaling in the ventral tegmental area in neural plasticity relevant to addiction has been published (S. L. Borgland *et al.* Neuron, **2006**, 49, 589-601). In addition, several lines of evidence demonstrate a role of the orexin system as modulator of the 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, de Lecea, L; The hypocretins: setting the arousal threshold. *Nat Rev Neurosci*, 3(5) (2002) 339-349). Orexin neurons are likely to be involved in the coordinated regulation of behavioral and physiological responses in stressful environments (Kuru, M, Ueta, Y, Serino, R, Nakazato, M, Yamamoto, Y, Shibuya, I, Yamashita, H; Centrally administered orexin/hypocretin activates HPA axis in rats. *Neuroreport*, 11(9) (2000) 1977-1980). For instance, cardiovascular responses to conditioned fear and novelty exposure could be attenuated by a dual orexin receptor antagonist in rats (Furlong, TM, Vianna, DM, Liu, L, Carrive, P; Hypocretin/orexin contributes to the expression of some but not all forms of stress and arousal. *Eur J Neurosci*, 30(8) (2009) 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, Gold, PW; The concepts of stress and stress system disorders. Overview of physical and behavioral homeostasis. *JAMA*, 267(9) (1992), 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; Corticotropin-releasing hormone physiology *European Journal of Endocrinology*, 155 (suppl_1) (2006) S71-S76).

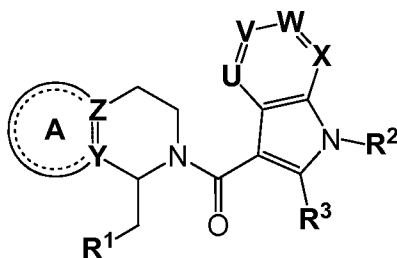
The compound (2R)-2-((1S)-6,7-dimethoxy-1-[2-(4-trifluoromethyl-phenyl)-ethyl]-3,4-dihydro-1H-isoquinolin-2-yl)-N-methyl-2-phenyl-acetamide (WO2005/118548), a dual orexin receptor antagonist, is currently in clinical development for primary insomnia. In the rat, the compound has been shown for example 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 (F. Jenck et al., *Nature Medicine* **2007**, 13, 150-155). The compound has also been shown to enhance memory function in a rat model (WO2007/105177). The compound furthermore decreased brain levels of amyloid-beta (A β) as well as A β 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 A β 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 A β to Alzheimer's disease and, thus, to the cognitive dysfunction, expressed as impairment of learning and memory. The compound is also active in an animal model of conditioned fear: the rat fear-potentiated startle paradigm (WO2009/0047723) which relates to emotional states of fear and anxiety diseases such as anxieties including phobias and post traumatic stress disorders (PTSDs). The compound has, in addition, 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]; and to attenuate the natural activation induced by orexin A in fasted hungry rats exposed to food odors [MJ Prud'homme et al., "Nutritional status modulates behavioural and olfactory bulb Fos responses to isoamyl acetate or food odour in rats: roles of orexins and leptin." *Neuroscience* **2009**, 162(4), 1287-1298].

The compound (R)-2-[(S)-1-(3,4-Dimethoxy-benzyl)-6,7-dimethoxy-3,4-dihydro-1H-isoquinolin-2-yl]-N-isopropyl-2-phenyl-acetamide has been shown to be active in the rat fear-potentiated startle paradigm; and in an animal model related to addictions [EP 2402322].

The present invention provides novel indole and pyrrolopyridine amide derivatives, which are non-peptide antagonists of human orexin receptors. These compounds are in particular of potential use in the treatment of diseases or disorders related to the orexin system, especially comprising all types of sleep disorders, of stress-related syndromes, of addictions (especially psychoactive substance use, abuse, seeking and reinstatement), of cognitive

dysfunctions in the healthy population and in psychiatric and neurologic disorders, of eating or drinking disorders.

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



Formula (I)

wherein

Z represents a carbon atom or a nitrogen atom and **Y** represents a carbon atom; and ring **A** together with the atoms **Z** and **Y** represents a 5- or 6-membered aromatic ring;

wherein, in case **Z** represents a carbon atom, said ring **A** is a benzene, a pyridine, a thiophene, a pyrazole, or a thiazole ring;

or, in case **Z** represents a nitrogen atom, said ring **A** is an imidazole or a pyrrole ring;

wherein said rings **A** independently are unsubstituted or substituted with one or two substituents independently selected from the group consisting of (C₁₋₄)alkyl, (C₁₋₄)alkoxy, (C₂₋₄)alkinyl, halogen, cyano, (C₁₋₃)fluoroalkyl, (C₁₋₃)fluoroalkoxy; (C₃₋₆)cycloalkyl, 5-membered heteroaryl, and amino;

R¹ represents aryl or heteroaryl, wherein the aryl or heteroaryl independently is:

- unsubstituted, or mono-, di-, or tri-substituted, wherein the substituents are independently selected from the group consisting of:
 - (C₁₋₄)alkyl, (C₁₋₄)alkoxy, (C₃₋₆)cycloalkyl, halogen, cyano, hydroxy, (C₁₋₃)fluoroalkyl, (C₁₋₃)fluoroalkoxy, (C₁₋₃)fluoroalkyl-sulfonyloxy, (C₁₋₄)alkyl-sulfonyl, (C₃₋₆)cycloalkyl-oxy, (C₁₋₄)alkoxy-(C₂₋₄)alkoxy, hydroxy-(C₂₋₄)alkoxy, **R**⁴**R**⁵N-(C₂₋₄)alkoxy, **R**⁶-CO-, **R**⁷-CO-(C₁₋₄)alkoxy;
 - phenyl or 5- or 6-membered heteroaryl, wherein said phenyl or 5- or 6-membered heteroaryl is independently unsubstituted, or mono-, di-, or tri-substituted, wherein the substituents are independently selected from the group consisting of (C₁₋₄)alkyl, (C₁₋₄)alkoxy, halogen, cyano, (C₁₋₃)fluoroalkyl, and (C₁₋₃)fluoroalkoxy; and
 - phenyl-(C₁₋₄)alkoxy or 5- or 6-membered heteroaryl-(C₁₋₄)alkoxy, wherein said phenyl-(C₁₋₄)alkoxy or 5- or 6-membered heteroaryl-(C₁₋₄)alkoxy is independently unsubstituted, or mono-, di-, or tri-substituted, wherein the

substituents are independently selected from the group consisting of (C₁₋₄)alkyl, (C₁₋₄)alkoxy, halogen, cyano, (C₁₋₃)fluoroalkyl, and (C₁₋₃)fluoroalkoxy;

with the proviso:

- that at maximum one substituent selected from phenyl, 5- or 6-membered heteroaryl, phenyl-(C₁₋₄)alkoxy, and 5- or 6-membered heteroaryl-(C₁₋₄)alkoxy is present; and that, if present, said substituent is attached in a position other than the ortho-position (with regard to the position at which R¹ is attached to the rest of the molecule);
- or said aryl or heteroaryl is fused to a non-aromatic 5- or 6-membered ring, wherein said ring optionally contains one or two heteroatoms independently selected from oxygen and nitrogen; wherein said ring is optionally substituted with one or two substituents independently selected from (C₁₋₃)alkyl, oxo, and halogen;

R² represents hydrogen, (C₁₋₆)alkyl, (C₃₋₆)cycloalkyl, (C₁₋₄)alkoxy-(C₂₋₄)alkyl, hydroxy-(C₂₋₄)alkyl, R⁸R⁹N-(C₂₋₄)alkyl, or (C₁₋₄)fluoroalkyl;

R³ represents hydrogen or methyl (especially hydrogen);

one of **U**, **V**, **W**, and **X** represents CR¹⁰ or N, and the remaining represent CH; wherein

- R¹⁰ represents hydrogen, fluorine, chlorine, methyl, or methoxy;

R⁴ and R⁵ independently represent hydrogen or (C₁₋₄)alkyl;

R⁶ represents hydroxy or amino;

R⁷ represents hydroxy or (C₁₋₄)alkoxy;

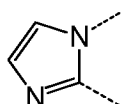
R⁸ and R⁹ independently represent hydrogen or (C₁₋₄)alkyl.

The compounds of formula (I) may contain one or more stereogenic or asymmetric centers, such as one or more asymmetric carbon atoms. The compounds of formula (I) 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), which compounds are identical to the compounds of formula (I) 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 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) are not isotopically labelled, or they are labelled only with one or more deuterium atoms. In a sub-embodiment, the compounds of formula (I) are not isotopically labelled at all. Isotopically labelled compounds of formula (I) 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, dotted lines show the point(s) of attachment of a radical drawn. For example, the radical drawn below



is an imidazol-1,2-diyl group [wherein, in case such group is used in the meaning of ring A, the atom representing the upper point of attachment (here: the nitrogen atom) is the atom Z, and the atom carrying the lower point of attachment (here: the carbon atom) is the atom Y in the meaning of the formula (I)].

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) 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, inorganic 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.

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 (C₁₋₄)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 "cycloalkyl", used alone or in combination, refers to a saturated cyclic alkyl group containing three to six carbon atoms. The term "(C_{x-y})cycloalkyl" (x and y each being an

integer), refers to a cycloalkyl group as defined before containing x to y carbon atoms. For example a (C₃₋₆)cycloalkyl group contains from three to six carbon atoms. Examples of cycloalkyl groups are cyclopropyl, cyclobutyl, cyclopentyl and cyclohexyl. Preferred is cyclopropyl.

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 (C₁₋₄)alkoxy group means a group of the formula (C₁₋₄)alkyl-O- in which the term "(C₁₋₄)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 (C₁₋₃)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 (C₁)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 (C₁₋₃)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 (C₁)fluoroalkoxy groups such as trifluoromethoxy and difluoromethoxy.

An example of **R⁸R⁹N**-(C₂₋₄)alkyl groups is dimethylaminoethyl.

An example of **R⁴R⁵N**-(C₂₋₄)alkoxy groups is dimethylaminoethoxy.

An example of **R⁶-CO-** groups is carboxy.

Examples of **R⁷-CO-(C₁₋₄)alkoxy** groups are 2-methoxy-2-oxoethoxy and carboxymethoxy.

An example of (C₁₋₃)fluoroalkyl-sulfonyloxy groups is trifluoromethyl-sulfonyloxy.

An example of (C₃₋₆)cycloalkyl-oxy groups is cyclopropyloxy.

An example of (C₁₋₄)alkoxy-(C₂₋₄)alkoxy groups is 2-methoxyethoxy.

An example of hydroxy-(C₂₋₄)alkoxy groups is 2-hydroxyethoxy.

The term "amino" refers to a H₂N- group.

The term "aryl", alone or in combination, means a phenyl or a naphthyl group. The aryl group may be unsubstituted or substituted as explicitly defined.

Particular examples of aryl groups as used for the group R¹ are phenyl, 2-naphthyl, 1-naphthyl, 3-methyl-phenyl, 4-methoxy-phenyl, 3-methoxy-phenyl, 3,5-dimethoxy-phenyl, 3,4-dimethoxy-phenyl, 2,5-dimethoxy-phenyl, 2,3-dimethoxy-phenyl, 3,4,5-trimethoxy-phenyl, 4-fluoro-phenyl, 3,4-difluoro-phenyl, 4-chloro-phenyl, 3-chloro-phenyl, 2-chloro-phenyl, 2,4-dichloro-phenyl, 3,4-dichloro-phenyl, 2,6-dichloro-phenyl, 4-cyano-phenyl, 3-cyano-phenyl, 2-cyano-phenyl, 3-carboxy-phenyl, 3-hydroxy-4-methoxy-phenyl, 4-hydroxy-3-methoxy-phenyl, 3-fluoro-4-methoxy-phenyl, 3-methoxy-4-methyl-phenyl, 4-methoxy-3-methyl-phenyl, 3-carbamoyl-phenyl, 4-trifluoromethyl-phenyl, 3-trifluoromethyl-phenyl, 3-methoxy-4-ethyl-phenyl, 4-methoxy-3-ethyl-phenyl, 4-methoxy-3-n-propoxy-phenyl, 3-methoxy-4-n-propoxy-phenyl, 4-methoxy-3-isopropoxy-phenyl, 3-methoxy-4-isopropoxy-phenyl, 4-methoxy-3-cyclopropyloxy-phenyl, 3-methoxy-4-cyclopropyloxy-phenyl, 3-cyano-4-methoxy-phenyl, 3,4-diethoxy-phenyl, 4-trifluoromethoxy-phenyl, 3-methoxy-4-trifluoromethoxy-phenyl, 3-methoxy-4-(2,2,2-trifluoroethoxy)-phenyl, 4-methoxy-3-(2,2,2-trifluoroethoxy)-phenyl, 4-methoxy-3-(2-hydroxy-ethoxy)-phenyl, 3-methoxy-4-(2-hydroxy-ethoxy)-phenyl, 3-methoxy-4-carboxymethoxy-phenyl, 3-methoxy-4-(2-methoxy-2-oxoethoxy)-phenyl, 4-methoxy-3-(2-methoxy-2-oxoethoxy)-phenyl, 3-methoxy-4-(2-dimethylamino-ethoxy)-phenyl, 4-methoxy-3-(2-dimethylamino-ethoxy)-phenyl, 3-methoxy-4-((trifluoromethoxysulfonyl)oxy)-phenyl, and 4-methoxy-3-((trifluoromethoxysulfonyl)oxy)-phenyl.

In addition to the above-listed examples of aryl groups, a particular sub-group of aryl as used for the group R¹ are "aryl fused to a non-aromatic 5- or 6-membered ring, wherein said ring optionally contains one or two heteroatoms independently selected from oxygen and nitrogen". For such groups the aryl is preferably phenyl. Examples of such groups are indanyl, tetrahydronaphthyl, 2,3-dihydrobenzofuranyl, chromanyl, chromenyl, benzo[1,3]dioxolyl, 2,3-dihydro-benzo[1,4]dioxinyl, benzo[b][1,4]dioxinyl, 1,2,3,4-tetrahydroquinoliny, and 3,4-dihydro-2H-benzo[b][1,4]oxazinyl. The above-mentioned aryl groups are optionally substituted said non-aromatic 5- or 6-membered ring with one or two substituents independently selected from (C₁₋₃)alkyl, oxo, and halogen. Particular examples of fragments forming a non-aromatic 5- or 6-membered ring fused to said aryl are selected from the group

consisting of $-(CH_2)_n-$, wherein n represents the integer 3 or 4; $-(CH_2)_p-O-$, wherein p represents the integer 1 or 2; $-CH=CH-CH_2-O-$; $-O-(CH_2)_q-O-$, wherein q represents the integer 1 or 2; $-O-(C=O)-O-$; $-O-(CF_2)-O-$; $-O-CH=CH-O-$; $-(CH_2)_3-NH-$; $-(CH_2)_3-N(CH_3)-$; $-O-(CH_2)_2-NH-$; and $-O-(CH_2)_2-N(CH_3)-$. Particular examples are benzo[1,3]dioxol-5-yl, and 2,3-dihydro-benzo[1,4]dioxin-6-yl.

In addition to the above-listed examples of aryl groups, a further particular sub-group of aryl as used for the group R^1 are aryl groups which are substituted, in a position other than the ortho-position, with phenyl or 5- or 6-membered heteroaryl, wherein said phenyl or 5- or 6-membered heteroaryl is independently unsubstituted, or mono-, di-, or tri-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. Examples of such groups are 3-pyrrazol-1-yl-phenyl, 3-[1,2,4]oxadiazol-3-yl-phenyl, 4-[1,2,3]triazol-1-yl-phenyl, 3-[1,2,3]triazol-1-yl-phenyl, 3-[1,2,4]triazol-1-yl-phenyl, 4-[1,2,3]triazol-2-yl-phenyl, 3-[1,2,3]triazol-2-yl-phenyl, 3-pyrimidin-2-yl-phenyl.

In addition to the above-listed examples of aryl groups, a further particular sub-group of aryl as used for the group R^1 are aryl groups which are substituted, in a position other than the ortho-position, with phenyl- (C_{1-4}) alkoxy or 5- or 6-membered heteroaryl- (C_{1-4}) alkoxy, wherein said phenyl- (C_{1-4}) alkoxy or 5- or 6-membered heteroaryl- (C_{1-4}) alkoxy is independently unsubstituted, or mono-, di-, or tri-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. An examples of such groups is 3-methoxy-4-benzyloxy-phenyl.

The term "heteroaryl", if not explicitly stated otherwise, means a 5- to 10-membered monocyclic or fused bicyclic aromatic ring containing 1 to a maximum of 4 heteroatoms independently selected from oxygen, nitrogen and sulfur. Examples of monocyclic heteroaryl groups are 5-membered monocyclic heteroaryl groups such as furanyl, oxazolyl, isoxazolyl, oxadiazolyl, thienyl, thiazolyl, isothiazolyl, thiadiazolyl, pyrrolyl, imidazolyl, pyrazolyl, triazolyl, and tetrazolyl; and 6-membered monocyclic heteroaryl such as pyridyl, pyrimidyl, pyridazinyl, and pyrazinyl. Examples of bicyclic heteroaryl groups comprise 8-membered bicyclic heteroaryl groups such as 4H-furo[3,2-b]pyrrolyl, pyrrolo[2,1-b]thiazolyl and imidazo[2,1-b]thiazolyl; 9-membered bicyclic heteroaryl groups such as indolyl, isoindolyl, benzofuranyl, isobenzofuranyl, benzothiophenyl, indazolyl, benzimidazolyl, benzoxazolyl, benzisoxazolyl, benzothiazolyl, benzoisothiazolyl, benzotriazolyl, benzoxadiazolyl, benzothiadiazolyl, pyrazolo[1,5-a]pyridyl, pyrazolo[1,5-a]pyrimidyl, imidazo[1,2-a]pyridyl, 1H-pyrrolo[3,2-

b]pyridyl, and 1H-pyrrolo[2,3-b]pyridyl; and 10-membered bicyclic heteroaryl groups such as quinolinyl, isoquinolinyl, naphthyridinyl, cinnolinyl, quinazolinyl, quinoxalinyl, and phthalazinyl.

Particular examples of heteroaryl groups as used for the group R¹ are 5-membered heteroaryl groups such as oxazolyl, isoxazolyl, thienyl, thiazolyl, and isothiazolyl (notably thiazolyl; especially 2-methyl-thiazol-4-yl). In addition, further particular examples of heteroaryl groups as used for the group R¹ are 6-membered monocyclic heteroaryl such as pyrimidyl, pyridazinyl, pyrazinyl and pyridyl (notably pyridyl; especially pyridin-3-yl, pyridin-2-yl, 2-chloro-pyridin-6-yl, 2-methyl-pyridin-5-yl, 2-ethyl-pyridin-5-yl, 2-methoxy-pyridin-6-yl, 2-methoxy-pyridin-5-yl, 2-cyano-pyridin-6-yl, and 2-cyano-pyridin-5-yl). In addition, further particular examples of heteroaryl groups as used for the group R¹ are 8- to 10-membered bicyclic heteroaryl groups, notably 9- or 10-membered bicyclic heteroaryl groups, such as indolyl, benzimidazolyl, benzofuranyl, benzothiophenyl, indazolyl, benzoxazolyl, benzisoxazolyl, benzothiazolyl, benzoisothiazolyl, quinolinyl, naphthyridinyl, cinnolinyl, quinazolinyl, and quinoxalinyl (notably indolyl, indazolyl, benzimidazolyl, and quinolinyl; especially indol-3-yl, 1-methyl-indol-3-yl, indazol-3-yl, benzimidazol-2-yl, quinolin-8-yl, quinolin-7-yl, and quinolin-6-yl).

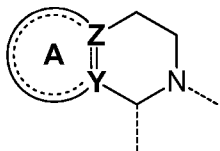
As used for the group R¹, examples of the particular sub-group of heteroaryl groups which are substituted in a position other than the ortho-position with phenyl or 5- or 6-membered heteroaryl; wherein said phenyl or 5- or 6-membered heteroaryl is independently unsubstituted, or substituted as explicitly defined; are notably oxazolyl, isoxazolyl, thienyl, thiazolyl, isothiazolyl, pyridyl, pyrimidyl and pyrazinyl.

Examples of the particular 5- or 6-membered heteroaryl groups which are substituents of the group R¹ are notably oxazolyl, isoxazolyl, oxadiazolyl, thienyl, thiazolyl, isothiazolyl, thiadiazolyl, imidazolyl, pyrazolyl, triazolyl, pyridyl, pyrimidyl, and pyrazinyl (notably oxadiazolyl, pyrazolyl, triazolyl, pyridyl, and pyrimidyl; especially pyrazol-1-yl, [1,2,4]oxadiazol-3-yl, [1,2,3]triazol-1-yl, [1,2,3]triazol-1-yl, [1,2,4]triazol-1-yl, [1,2,3]triazol-2-yl, [1,2,3]triazol-2-yl, and pyrimidin-2-yl).

Examples of the particular 5-membered heteroaryl groups which are substituents of the ring A are oxazolyl, isoxazolyl, oxadiazolyl, thienyl, thiazolyl, isothiazolyl, thiadiazolyl, imidazolyl, pyrazolyl, and triazolyl (notably pyrazolyl and triazolyl; especially triazol-2-yl).

The heteroaryl groups as defined herein may be unsubstituted or substituted as explicitly defined.

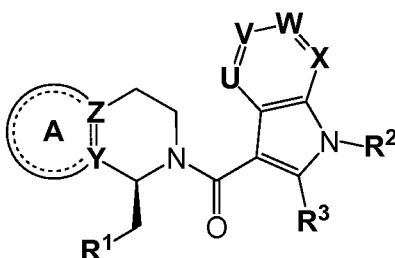
The fragment:



represents groups selected from group consisting of tetrahydroisoquinoline, tetrahydronaphthyridine, tetrahydrothienopyridine, tetrahydropyrazolopyridine, tetrahydrothiazolopyridine, tetrahydroimidazopyrazine and tetrahydropyrrolopyrazine; notably 1,2,3,4-tetrahydro-isoquinoline, 5,6,7,8-tetrahydro-[1,7]naphthyridine, 5,6,7,8-tetrahydro-[1,6]-naphthyridine, 4,5,6,7-tetrahydro-thieno[2,3-c]pyridine, 4,5,6,7-tetrahydro-thieno[3,4-c]pyridine, 4,5,6,7-tetrahydro-thieno[3,2-c]pyridine, 4,5,6,7-tetrahydro-1H-pyrazolo[3,4-c]pyridine, 4,5,6,7-tetrahydro-2H-pyrazolo[3,4-c]pyridine, 4,5,6,7-tetrahydro-1H-pyrazolo[4,3-c]pyridine, 4,5,6,7-tetrahydro-2H-pyrazolo[4,3-c]pyridine, 4,5,6,7-tetrahydro-thiazolo[5,4-c]pyridine, 5,6,7,8-tetrahydro-imidazo[1,2-a]pyrazine and 1,2,3,4-tetrahydropyrrolo[1,2-a]pyrazine. In a sub-embodiment, examples are notably 1,2,3,4-tetrahydro-isoquinoline, 5,6,7,8-tetrahydro-[1,7]naphthyridine, 4,5,6,7-tetrahydro-thieno[2,3-c]pyridine, 4,5,6,7-tetrahydro-thieno[3,4-c]pyridine, 4,5,6,7-tetrahydro-thieno[3,2-c]pyridine, 4,5,6,7-tetrahydro-1H-pyrazolo[3,4-c]pyridine, 4,5,6,7-tetrahydro-1H-pyrazolo[4,3-c]pyridine, 4,5,6,7-tetrahydro-thiazolo[5,4-c]pyridine and 5,6,7,8-tetrahydro-imidazo[1,2-a]pyrazine. These groups may be unsubstituted or substituted as explicitly defined. In particular, examples of the above-mentioned fragment are

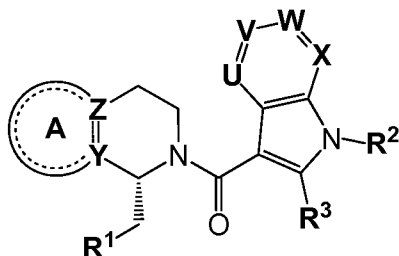
Further embodiments of the invention are presented hereinafter:

2) A second embodiment relates to compounds according to embodiment 1), which are also compounds of formula (I_{E1}):

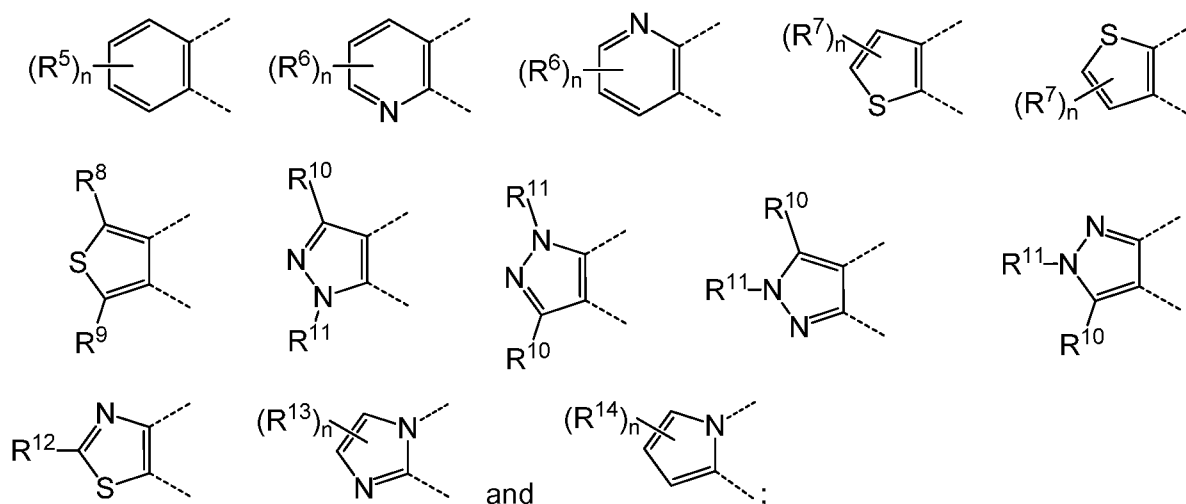


Formula (I_{E1}).

3) A third embodiment relates to compounds according to embodiment 1), which are also compounds of formula (I_{E2}):

Formula (I_{E2}).

4) Another embodiment relates to compounds according to any one of embodiments 1) to 3), wherein ring **A** together with the atoms Y and Z represents a 5- or 6-membered aromatic ring selected from the group consisting of:



wherein:

- $(R^5)_n$ represents one or two optional substituents (i.e. n is 0, 1 or 2) independently selected from the group consisting of (C_{1-4}) alkyl, (C_{1-4}) alkoxy, (C_{2-4}) alkinyl, halogen, cyano, (C_{1-3}) fluoroalkyl, (C_{1-3}) fluoroalkoxy; (C_{3-6}) cycloalkyl, 5-membered heteroaryl, and amino (notably (C_{1-4}) alkyl, (C_{1-4}) alkoxy, halogen, cyano, and (C_{1-3}) fluoroalkyl);
- $(R^6)_n$ represents one or two optional substituents (i.e. n is 0, 1 or 2) independently selected from the group consisting of (C_{1-4}) alkyl, (C_{1-4}) alkoxy, (C_{2-4}) alkinyl, halogen, cyano, (C_{1-3}) fluoroalkyl, (C_{1-3}) fluoroalkoxy; (C_{3-6}) cycloalkyl, 5-membered heteroaryl, and amino (notably (C_{1-4}) alkyl, (C_{1-4}) alkoxy, halogen, cyano, and (C_{1-3}) fluoroalkyl);
- $(R^7)_n$ represents one or two optional substituents (i.e. n is 0, 1 or 2) independently selected from the group consisting of (C_{1-4}) alkyl, (C_{1-4}) alkoxy, (C_{2-4}) alkinyl, halogen, cyano, (C_{1-3}) fluoroalkyl, (C_{1-3}) fluoroalkoxy; (C_{3-6}) cycloalkyl, 5-membered heteroaryl, and amino (notably (C_{1-4}) alkyl, (C_{1-4}) alkoxy, halogen, cyano, and (C_{1-3}) fluoroalkyl);
- R^8 , R^9 , R^{10} , R^{11} , and R^{12} independently represent hydrogen, (C_{1-4}) alkyl, (C_{1-4}) alkoxy, (C_{2-4}) alkinyl, halogen, cyano, (C_{1-3}) fluoroalkyl, (C_{1-3}) fluoroalkoxy; (C_{3-6}) cycloalkyl, 5-

membered heteroaryl, and amino (notably (C₁₋₄)alkyl, (C₁₋₄)alkoxy, halogen, cyano, and (C₁₋₃)fluoroalkyl);

- R⁸, R⁹, R¹⁰, R¹¹, and R¹² independently represent hydrogen, (C₁₋₄)alkyl, (C₁₋₄)alkoxy, (C₂₋₄)alkinyl, halogen, cyano, (C₁₋₃)fluoroalkyl, (C₁₋₃)fluoroalkoxy; (C₃₋₆)cycloalkyl, 5-membered heteroaryl, and amino (notably (C₁₋₄)alkyl, (C₁₋₄)alkoxy, halogen, cyano, and (C₁₋₃)fluoroalkyl);
- R⁸, R⁹, R¹⁰, R¹¹, and R¹² independently represent hydrogen, (C₁₋₄)alkyl, (C₁₋₄)alkoxy, (C₂₋₄)alkinyl, halogen, cyano, (C₁₋₃)fluoroalkyl, (C₁₋₃)fluoroalkoxy; (C₃₋₆)cycloalkyl, 5-membered heteroaryl, and amino (notably hydrogen, (C₁₋₄)alkyl, and amino);
- (R¹³)_n represents one or two optional substituents (i.e. n is 0, 1 or 2) independently selected from the group consisting of (C₁₋₄)alkyl, (C₁₋₄)alkoxy, (C₂₋₄)alkinyl, halogen, cyano, (C₁₋₃)fluoroalkyl, (C₁₋₃)fluoroalkoxy; (C₃₋₆)cycloalkyl, 5-membered heteroaryl, and amino (notably (C₁₋₄)alkyl, (C₁₋₄)alkoxy, halogen, cyano, and (C₁₋₃)fluoroalkyl); and
- (R¹⁴)_n represents one or two optional substituents (i.e. n is 0, 1 or 2) independently selected from the group consisting of (C₁₋₄)alkyl, (C₁₋₄)alkoxy, (C₂₋₄)alkinyl, halogen, cyano, (C₁₋₃)fluoroalkyl, (C₁₋₃)fluoroalkoxy; (C₃₋₆)cycloalkyl, 5-membered heteroaryl, and amino (notably (C₁₋₄)alkyl, (C₁₋₄)alkoxy, halogen, cyano, and (C₁₋₃)fluoroalkyl);

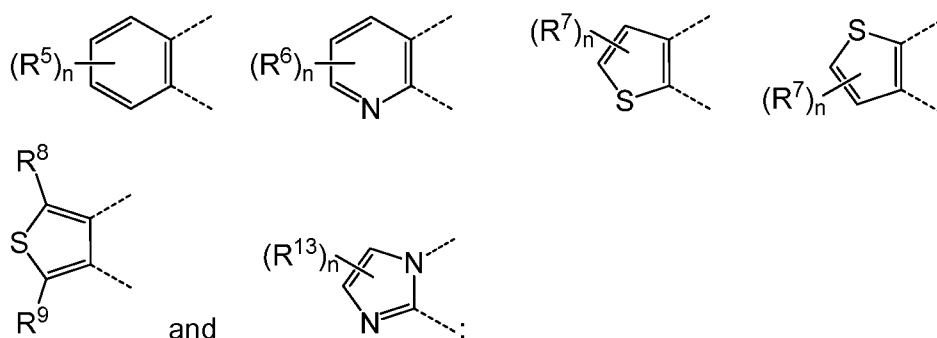
wherein it is well understood that each R⁵ to R¹⁴, and each n may be independently chosen for each respective ring A; and each of the above-listed rings A forms a particular sub-embodiment.

5) Another embodiment relates to compounds according to embodiment 4), wherein

- (R⁵)_n represents one or two optional (C₁₋₄)alkoxy substituents (i.e. n is 0, 1 or 2);
- (R⁶)_n is absent;
- (R⁷)_n represents one or two optional substituents (i.e. n is 0, 1 or 2) independently selected from the group consisting of (C₁₋₄)alkyl, (C₁₋₄)alkoxy, (C₂₋₄)alkinyl, halogen, cyano, (C₁₋₃)fluoroalkyl, and 5-membered heteroaryl (notably triazolyl); (especially (C₁₋₄)alkyl, (C₁₋₄)alkoxy, halogen, cyano, and (C₁₋₃)fluoroalkyl);
- R⁸, and R⁹ independently represent (C₁₋₄)alkyl;
- R¹⁰, and R¹¹ independently represent hydrogen, and (C₁₋₄)alkyl;
- R¹² represents hydrogen, (C₁₋₄)alkyl, or amino (especially hydrogen or amino);
- (R¹³)_n is absent; and
- (R¹⁴)_n is absent;

wherein it is well understood that each R^5 to R^{14} , and each n may be independently chosen for each respective ring **A**; and each of the above-listed rings **A** forms a particular sub-embodiment.

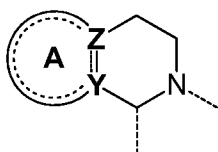
6) Another embodiment relates to compounds according to embodiments 4) or 5), wherein ring **A** together with the atoms **Y** and **Z** represents a 5- or 6-membered aromatic ring selected from the group consisting of:



wherein each of the above-listed rings **A** forms in addition a particular sub-embodiment.

7) Another embodiment relates to compounds according to any one of embodiments 1) to 6), wherein ring **A** together with the atoms **Z** and **Y** is a benzene, a pyridine, a thiophene ring, or an imidazole ring; wherein said ring **A** independently is unsubstituted or substituted as explicitly defined.

8) Another embodiment relates to compounds according to any one of embodiments 1) to 7), wherein the fragment:



is a group selected from the group consisting of 1,2,3,4-tetrahydro-isoquinoline, 5,6,7,8-tetrahydro-[1,7]naphthyridine, 4,5,6,7-tetrahydro-thieno[2,3-c]pyridine, 4,5,6,7-tetrahydro-thieno[3,4-c]pyridine, 4,5,6,7-tetrahydro-thieno[3,2-c]pyridine, 4,5,6,7-tetrahydro-1H-pyrazolo[3,4-c]pyridine, 4,5,6,7-tetrahydro-1H-pyrazolo[4,3-c]pyridine, 4,5,6,7-tetrahydro-thiazolo[5,4-c]pyridine, and 5,6,7,8-tetrahydro-imidazo[1,2-a]pyrazine (notably 1,2,3,4-tetrahydro-isoquinoline, 5,6,7,8-tetrahydro-[1,7]naphthyridine, 4,5,6,7-tetrahydro-thieno[2,3-c]pyridine, 4,5,6,7-tetrahydro-thieno[3,4-c]pyridine, 4,5,6,7-tetrahydro-thieno[3,2-c]pyridine and 5,6,7,8-tetrahydro-imidazo[1,2-a]pyrazine); wherein said groups independently are unsubstituted or substituted as explicitly defined.

9) Another embodiment relates to compounds according to any one of embodiments 1) to 8), wherein **Z** represents a carbon atom.

10) Another embodiment relates to compounds according to any one of embodiments 1) to 8), wherein **Z** represents a nitrogen atom.

11) Another embodiment relates to compounds according to any one of embodiments 1) to 10), wherein

- **R¹** represents aryl or heteroaryl, wherein the aryl or heteroaryl independently is unsubstituted, or mono-, di-, or tri-substituted; wherein
 - the substituents are independently selected from the group consisting of (C₁₋₄)alkyl, (C₁₋₄)alkoxy, (C₃₋₆)cycloalkyl, halogen, cyano, hydroxy, (C₁₋₃)fluoroalkyl, (C₁₋₃)fluoroalkoxy, (C₁₋₃)fluoroalkyl-sulfonyloxy, (C₁₋₄)alkyl-sulfonyl, (C₃₋₆)cycloalkyl-oxy, (C₁₋₄)alkoxy-(C₂₋₄)alkoxy, hydroxy-(C₂₋₄)alkoxy, **R⁴R⁵N**-(C₂₋₄)alkoxy, **R⁶-CO-**, **R⁷-CO-**(C₁₋₄)alkoxy;
- or **R¹** represents phenyl or 5- or 6-membered heteroaryl, wherein the phenyl or 5- or 6-membered heteroaryl independently is mono-, di-, or tri-substituted; wherein
 - one of said substituents is attached in a position other than the ortho-position (with regard to the position at which **R¹** is attached to the rest of the molecule); wherein said substituent is:
 - phenyl or 5- or 6-membered heteroaryl, wherein said phenyl or 5- or 6-membered heteroaryl is independently unsubstituted, or mono-, di-, or tri-substituted, wherein the substituents are independently selected from the group consisting of (C₁₋₄)alkyl, (C₁₋₄)alkoxy, halogen, cyano, (C₁₋₃)fluoroalkyl, and (C₁₋₃)fluoroalkoxy; or
 - phenyl-(C₁₋₄)alkoxy or 5- or 6-membered heteroaryl-(C₁₋₄)alkoxy, wherein said phenyl-(C₁₋₄)alkoxy or 5- or 6-membered heteroaryl-(C₁₋₄)alkoxy is independently unsubstituted, or mono-, di-, or tri-substituted, wherein the substituents are independently selected from the group consisting of (C₁₋₄)alkyl, (C₁₋₄)alkoxy, halogen, cyano, (C₁₋₃)fluoroalkyl, and (C₁₋₃)fluoroalkoxy;
 - and the other of said substituents, if present, is/are independently selected from the group consisting of (C₁₋₄)alkyl, (C₁₋₄)alkoxy, halogen, cyano, (C₁₋₃)fluoroalkyl, and (C₁₋₃)fluoroalkoxy;
- or **R¹** represents phenyl or 5- or 6-membered heteroaryl, wherein said phenyl or 5- or 6-membered heteroaryl is fused to a non-aromatic 5- or 6-membered ring, wherein

said ring optionally contains one or two heteroatoms independently selected from oxygen and nitrogen; wherein said ring is optionally substituted with one or two substituents independently selected from (C₁₋₃)alkyl, oxo, and halogen.

12) Another embodiment relates to compounds according to any one of embodiments 1) to 10), wherein

- **R¹** represents aryl or heteroaryl, wherein the aryl or heteroaryl independently is unsubstituted, or mono-, di-, or tri-substituted; wherein
 - the substituents are independently selected from the group consisting of (C₁₋₄)alkyl, (C₁₋₄)alkoxy, halogen, cyano, hydroxy, (C₁₋₃)fluoroalkyl, (C₁₋₃)fluoroalkoxy, (C₁₋₃)fluoroalkyl-sulfonyloxy, (C₃₋₆)cycloalkyl-oxy, hydroxy-(C₂₋₄)alkoxy, **R⁴R⁵N**-(C₂₋₄)alkoxy, **R⁶-CO-**, **R⁷-CO-**(C₁₋₄)alkoxy;
- or **R¹** represents phenyl (preferred) or 5- or 6-membered heteroaryl, wherein the phenyl or 5- or 6-membered heteroaryl independently is mono-, or di-substituted (preferred: mono-substituted); wherein
 - one of said substituents is attached in a position other than the ortho-position (with regard to the position at which **R¹** is attached to the rest of the molecule); wherein said substituent is:
 - phenyl or 5- or 6-membered heteroaryl (preferred), wherein said phenyl or 5- or 6-membered heteroaryl is independently unsubstituted (preferred), or mono-, di-, or tri-substituted, wherein the substituents are independently selected from the group consisting of (C₁₋₄)alkyl, (C₁₋₄)alkoxy, halogen, cyano, (C₁₋₃)fluoroalkyl, and (C₁₋₃)fluoroalkoxy; or
 - phenyl-(C₁₋₄)alkoxy or 5- or 6-membered heteroaryl-(C₁₋₄)alkoxy (notably benzyloxy), wherein said phenyl-(C₁₋₄)alkoxy or 5- or 6-membered heteroaryl-(C₁₋₄)alkoxy is independently unsubstituted (preferred), or mono-, di-, or tri-substituted, wherein the substituents are independently selected from the group consisting of (C₁₋₄)alkyl, (C₁₋₄)alkoxy, halogen, cyano, (C₁₋₃)fluoroalkyl, and (C₁₋₃)fluoroalkoxy;
 - and the other of said substituents, if present, is/are independently selected from the group consisting of (C₁₋₄)alkyl, (C₁₋₄)alkoxy, halogen, cyano, (C₁₋₃)fluoroalkyl, and (C₁₋₃)fluoroalkoxy (notably (C₁₋₄)alkyl or (C₁₋₄)alkoxy, especially (C₁₋₄)alkoxy);
- or **R¹** represents phenyl which is fused to a non-aromatic 5- or 6-membered ring, wherein said ring contains one or two oxygen atoms.

13) Another embodiment relates to compounds according to any one of embodiments 1) to 10), wherein

- **R¹** represents aryl or heteroaryl, wherein the aryl or heteroaryl independently is unsubstituted, or mono-, di-, or tri-substituted; wherein
 - the substituents are independently selected from the group consisting of (C₁₋₄)alkyl, (C₁₋₄)alkoxy, halogen, cyano, hydroxy, (C₁₋₃)fluoroalkyl, (C₁₋₃)fluoroalkoxy, (C₁₋₃)fluoroalkyl-sulfonyloxy, (C₃₋₆)cycloalkyl-oxy, hydroxy-(C₂₋₄)alkoxy, **R⁴R⁵N**-(C₂₋₄)alkoxy, **R⁶-CO-**, and **R⁷-CO-**(C₁₋₄)alkoxy; (notably selected from (C₁₋₄)alkyl, (C₁₋₄)alkoxy, halogen, cyano, (C₁₋₃)fluoroalkyl, (C₁₋₃)fluoroalkoxy, and hydroxy-(C₂₋₄)alkoxy; especially selected from (C₁₋₄)alkoxy, (C₃₋₆)cycloalkyl-oxy, and cyano);
- or **R¹** represents phenyl (preferred) or 6-membered heteroaryl, wherein the phenyl or 6-membered heteroaryl independently is mono-, or di-substituted (preferred: mono-substituted); wherein
 - one of said substituents is attached in a position other than the ortho-position (with regard to the position at which **R¹** is attached to the rest of the molecule); wherein said substituent is:
 - phenyl or 5- or 6-membered heteroaryl (preferred), wherein said phenyl or 5- or 6-membered heteroaryl is independently unsubstituted (preferred), or mono-, di-, or tri-substituted, wherein the substituents are independently selected from the group consisting of (C₁₋₄)alkyl, (C₁₋₄)alkoxy, halogen, cyano, (C₁₋₃)fluoroalkyl, and (C₁₋₃)fluoroalkoxy (especially (C₁₋₄)alkyl or halogen);
 - and the other of said substituents, if present, is independently selected from the group consisting of (C₁₋₄)alkyl, (C₁₋₄)alkoxy, halogen, cyano, (C₁₋₃)fluoroalkyl, and (C₁₋₃)fluoroalkoxy (notably (C₁₋₄)alkyl or (C₁₋₄)alkoxy; especially (C₁₋₄)alkoxy);
- or **R¹** represents a benzodioxinyl, or a benzodioxolyl group.

14) Another embodiment relates to compounds according to any one of embodiments 1) to 10), wherein

- **R¹** represents a group selected from phenyl, naphthyl, pyridinyl, quinolinyl, thiazolyl, indazolyl, indolyl, benzimidazolyl; wherein said group independently is unsubstituted or mono-, di-, or tri-substituted; wherein

- the substituents are independently selected from the group consisting of (C₁₋₄)alkyl, (C₁₋₄)alkoxy, halogen, cyano, hydroxy, (C₁₋₃)fluoroalkyl, (C₁₋₃)fluoroalkoxy, (C₁₋₃)fluoroalkyl-sulfonyloxy, (C₃₋₆)cycloalkyl-oxy, hydroxy-(C₂₋₄)alkoxy, **R**⁴**R**⁵N-(C₂₋₄)alkoxy, **R**⁶-CO-, and **R**⁷-CO-(C₁₋₄)alkoxy; (notably selected from (C₁₋₄)alkyl, (C₁₋₄)alkoxy, halogen, cyano, (C₁₋₃)fluoroalkyl, (C₁₋₃)fluoroalkoxy, and hydroxy-(C₂₋₄)alkoxy; especially selected from (C₁₋₄)alkoxy, (C₃₋₆)cycloalkyl-oxy, and cyano);
- or **R**¹ represents phenyl (preferred) or 6-membered heteroaryl, wherein the phenyl or 6-membered heteroaryl independently is mono-, or di-substituted (preferred: mono-substituted); wherein
 - one of said substituents is attached in a position other than the ortho-position (with regard to the position at which **R**¹ is attached to the rest of the molecule); wherein said substituent is:
 - phenyl or 5- or 6-membered heteroaryl (preferred), wherein said phenyl or 5- or 6-membered heteroaryl is independently unsubstituted (preferred), or mono-, di-, or tri-substituted, wherein the substituents are independently selected from the group consisting of (C₁₋₄)alkyl, (C₁₋₄)alkoxy, halogen, cyano, (C₁₋₃)fluoroalkyl, and (C₁₋₃)fluoroalkoxy (especially (C₁₋₄)alkyl or halogen);
 - and the other of said substituents, if present, is independently selected from the group consisting of (C₁₋₄)alkyl, (C₁₋₄)alkoxy, halogen, cyano, (C₁₋₃)fluoroalkyl, and (C₁₋₃)fluoroalkoxy (notably (C₁₋₄)alkyl or (C₁₋₄)alkoxy, especially (C₁₋₄)alkoxy).

15) Another embodiment relates to compounds according to any one of embodiments 1) to 10), wherein

- **R**¹ represents a phenyl, or a pyridinyl group wherein said group independently is unsubstituted or mono-, di-, or tri-substituted; wherein
 - the substituents are independently selected from the group consisting of (C₁₋₄)alkyl, (C₁₋₄)alkoxy, halogen, cyano, (C₁₋₃)fluoroalkyl, (C₁₋₃)fluoroalkoxy, and hydroxy-(C₂₋₄)alkoxy (especially selected from (C₁₋₄)alkoxy and cyano);
- or **R**¹ represents phenyl which is mono-, or di-substituted (preferred: mono-substituted); wherein
 - one of said substituents is attached in a position other than the ortho-position (with regard to the position at which **R**¹ is attached to the rest of the molecule); wherein said substituent is:

- phenyl or 5- or 6-membered heteroaryl (preferred), wherein said phenyl or 5- or 6-membered heteroaryl is independently unsubstituted (preferred), or mono-, di-, or tri-substituted, wherein the substituents are independently selected from the group consisting of (C₁₋₄)alkyl, (C₁₋₄)alkoxy, halogen, cyano, (C₁₋₃)fluoroalkyl, and (C₁₋₃)fluoroalkoxy (especially (C₁₋₄)alkyl or halogen);
- and the other of said substituents, if present, is independently selected from the group consisting of (C₁₋₄)alkyl, (C₁₋₄)alkoxy, halogen, cyano, (C₁₋₃)fluoroalkyl, and (C₁₋₃)fluoroalkoxy (notably (C₁₋₄)alkyl or (C₁₋₄)alkoxy, especially (C₁₋₄)alkoxy).

16) Another embodiment relates to compounds according to any one of embodiments 1) to 15), wherein **R**² represents hydrogen, (C₁₋₆)alkyl, (C₃₋₆)cycloalkyl, hydroxy-(C₂₋₄)alkyl, or (C₁₋₄)fluoroalkyl.

17) Another embodiment relates to compounds according to any one of embodiments 1) to 15), wherein **R**² represents (C₁₋₃)alkyl; especially methyl or ethyl.

18) Another embodiment relates to compounds according to any one of embodiments 1) to 17), wherein **R**³ represents hydrogen.

19) Another embodiment relates to compounds according to any one of embodiments 1) to 18), wherein one of **U**, **V**, **W**, and **X** represents CR¹⁰, and the remaining represent CH; wherein

- **R**¹⁰ represents hydrogen, fluorine, chlorine, methyl, or methoxy (especially hydrogen or fluorine).

20) Another embodiment relates to compounds according to any one of embodiments 1) to 18), wherein **U** or **X** represents N, and the remaining of **U**, **V**, **W**, and **X** represent CH.

21) Another embodiment relates to compounds of formula (I) according to embodiment 1) selected from the group consisting of:

- (7-Benzyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl)-(1-methyl-1H-indol-3-yl)-methanone;
- (7-Benzyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl)-(1-ethyl-1H-indol-3-yl)-methanone;
- (7-Benzyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl)-(1,2-dimethyl-1H-indol-3-yl)-methanone;
- (1-Methyl-1H-indol-3-yl)-(7-naphthalen-1-ylmethyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl)-methanone;
- (1-Ethyl-1H-indol-3-yl)-(7-naphthalen-1-ylmethyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl)-methanone;
- (1,2-Dimethyl-1H-indol-3-yl)-(7-naphthalen-1-ylmethyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl)-methanone;
- (1-Methyl-1H-indol-3-yl)-(7-naphthalen-2-ylmethyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl)-methanone;

(1-Ethyl-1H-indol-3-yl)-(7-naphthalen-2-ylmethyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl)-methanone;
(1,2-Dimethyl-1H-indol-3-yl)-(7-naphthalen-2-ylmethyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl)-methanone;
[7-(3,4-Dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-methyl-1H-indol-3-yl)-methanone;
[7-(3,4-Dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone;
[7-(3,4-Dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1,2-dimethyl-1H-indol-3-yl)-methanone;
(1-Methyl-1H-indol-3-yl)-[7-(4-trifluoromethyl-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;
[(R)-1-(3,4-Dimethoxy-benzyl)-6,7-dimethoxy-3,4-dihydro-1H-isoquinolin-2-yl]-(1-methyl-1H-indol-3-yl)-methanone;
[(S)-1-(3,4-Dimethoxy-benzyl)-6,7-dimethoxy-3,4-dihydro-1H-isoquinolin-2-yl]-(1-methyl-1H-indol-3-yl)-methanone;
(6,7-Dimethoxy-1-naphthalen-2-ylmethyl-3,4-dihydro-1H-isoquinolin-2-yl)-(1-methyl-1H-indol-3-yl)-methanone;
(1-Benzyl-6-methoxy-3,4-dihydro-1H-isoquinolin-2-yl)-(1-methyl-1H-indol-3-yl)-methanone;
[6,7-Dimethoxy-1-(3-methoxy-benzyl)-3,4-dihydro-1H-isoquinolin-2-yl]-(1-methyl-1H-indol-3-yl)-methanone;
[6,7-Dimethoxy-1-(4-methoxy-benzyl)-3,4-dihydro-1H-isoquinolin-2-yl]-(1-methyl-1H-indol-3-yl)-methanone;
[1-(2,5-Dimethoxy-benzyl)-6,7-dimethoxy-3,4-dihydro-1H-isoquinolin-2-yl]-(1-methyl-1H-indol-3-yl)-methanone;
(1-Benzo[1,3]dioxol-5-ylmethyl-6,7-dimethoxy-3,4-dihydro-1H-isoquinolin-2-yl)-(1-methyl-1H-indol-3-yl)-methanone;
[1-(4-Fluoro-benzyl)-6,7-dimethoxy-3,4-dihydro-1H-isoquinolin-2-yl]-(1-methyl-1H-indol-3-yl)-methanone;
[6,7-Dimethoxy-1-(3,4,5-trimethoxy-benzyl)-3,4-dihydro-1H-isoquinolin-2-yl]-(1-methyl-1H-indol-3-yl)-methanone;
[1-(4-Chloro-benzyl)-6,7-dimethoxy-3,4-dihydro-1H-isoquinolin-2-yl]-(1-methyl-1H-indol-3-yl)-methanone;
[(R)-1-(3,4-Dimethoxy-benzyl)-6,7-dimethoxy-3,4-dihydro-1H-isoquinolin-2-yl]-(1-ethyl-1H-indol-3-yl)-methanone;
(6,7-Dimethoxy-1-naphthalen-2-ylmethyl-3,4-dihydro-1H-isoquinolin-2-yl)-(1-ethyl-1H-indol-3-yl)-methanone;
(1-Benzyl-6-methoxy-3,4-dihydro-1H-isoquinolin-2-yl)-(1-ethyl-1H-indol-3-yl)-methanone;
[6,7-Dimethoxy-1-(3-methoxy-benzyl)-3,4-dihydro-1H-isoquinolin-2-yl]-(1-ethyl-1H-indol-3-yl)-methanone;
[6,7-Dimethoxy-1-(4-methoxy-benzyl)-3,4-dihydro-1H-isoquinolin-2-yl]-(1-ethyl-1H-indol-3-yl)-methanone;
[1-(2,5-Dimethoxy-benzyl)-6,7-dimethoxy-3,4-dihydro-1H-isoquinolin-2-yl]-(1-ethyl-1H-indol-3-yl)-methanone;
(1-Benzo[1,3]dioxol-5-ylmethyl-6,7-dimethoxy-3,4-dihydro-1H-isoquinolin-2-yl)-(1-ethyl-1H-indol-3-yl)-methanone;
(1-Ethyl-1H-indol-3-yl)-[1-(4-fluoro-benzyl)-6,7-dimethoxy-3,4-dihydro-1H-isoquinolin-2-yl]-methanone;
[6,7-Dimethoxy-1-(3,4,5-trimethoxy-benzyl)-3,4-dihydro-1H-isoquinolin-2-yl]-(1-ethyl-1H-indol-3-yl)-methanone;
[1-(4-Chloro-benzyl)-6,7-dimethoxy-3,4-dihydro-1H-isoquinolin-2-yl]-(1-ethyl-1H-indol-3-yl)-methanone;
(1H-Indol-3-yl)-(7-naphthalen-1-ylmethyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl)-methanone;
(1-Ethyl-3-methyl-4-naphthalen-2-ylmethyl-1,4,6,7-tetrahydro-pyrazolo[4,3-c]pyridin-5-yl)-(1-methyl-1H-indol-3-yl)-methanone;
(1-Ethyl-1H-indol-3-yl)-(1-ethyl-3-methyl-4-naphthalen-2-ylmethyl-1,4,6,7-tetrahydro-pyrazolo[4,3-c]pyridin-5-yl)-methanone;
(1-Methyl-1H-indol-3-yl)-(1-naphthalen-1-ylmethyl-3,4-dihydro-1H-isoquinolin-2-yl)-methanone;

(1-Ethyl-1H-indol-3-yl)-(1-naphthalen-1-ylmethyl-3,4-dihydro-1H-isoquinolin-2-yl)-methanone;
(1-Methyl-1H-indol-3-yl)-(4-naphthalen-1-ylmethyl-6,7-dihydro-4H-thieno[3,2-c]pyridin-5-yl)-methanone;
(1-Ethyl-1H-indol-3-yl)-(4-naphthalen-1-ylmethyl-6,7-dihydro-4H-thieno[3,2-c]pyridin-5-yl)-methanone;
(2-Amino-4-naphthalen-1-ylmethyl-6,7-dihydro-4H-thiazolo[5,4-c]pyridin-5-yl)-(1-methyl-1H-indol-3-yl)-methanone;
(2-Amino-4-naphthalen-1-ylmethyl-6,7-dihydro-4H-thiazolo[5,4-c]pyridin-5-yl)-(1-ethyl-1H-indol-3-yl)-methanone;
(1-Methyl-1H-indol-3-yl)-(4-naphthalen-1-ylmethyl-6,7-dihydro-4H-thiazolo[5,4-c]pyridin-5-yl)-methanone;
(1-Ethyl-1H-indol-3-yl)-(4-naphthalen-1-ylmethyl-6,7-dihydro-4H-thiazolo[5,4-c]pyridin-5-yl)-methanone;
[3-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-methyl-1H-indol-3-yl)-methanone;
[3-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone;
[2-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone;
[3-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-isopropyl-1H-indol-3-yl)-methanone;
[3-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-isobutyl-1H-indol-3-yl)-methanone;
[3-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(6-fluoro-1-methyl-1H-indol-3-yl)-methanone;
[3-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-6-fluoro-1H-indol-3-yl)-methanone;
[3-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(5-fluoro-1-methyl-1H-indol-3-yl)-methanone;
[3-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-5-fluoro-1H-indol-3-yl)-methanone;
[3-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-cyclopropyl-1H-indol-3-yl)-methanone;
[3-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-propyl-1H-indol-3-yl)-methanone;
[3-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-butyl-1H-indol-3-yl)-methanone;
[3-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-[1-(2-methoxy-ethyl)-1H-indol-3-yl]-methanone;
[3-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-[1-(2-dimethylamino-ethyl)-1H-indol-3-yl]-methanone;
[3-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(5-chloro-1-methyl-1H-indol-3-yl)-methanone;
[3-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(5-chloro-1-ethyl-1H-indol-3-yl)-methanone;

[3-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(5-methoxy-1-methyl-1H-indol-3-yl)-methanone;

[3-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-5-methoxy-1H-indol-3-yl)-methanone;

[3-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-4-methoxy-1H-indol-3-yl)-methanone;

[3-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(7-fluoro-1-methyl-1H-indol-3-yl)-methanone;

[3-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(4-fluoro-1-methyl-1H-indol-3-yl)-methanone;

[3-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-4-fluoro-1H-indol-3-yl)-methanone;

[3-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1,5-dimethyl-1H-indol-3-yl)-methanone;

[3-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(5-methoxy-1,2-dimethyl-1H-indol-3-yl)-methanone;

[3-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1H-indol-3-yl)-methanone;

[3-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1H-pyrrolo[2,3-b]pyridin-3-yl)-methanone;

[3-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1,2-dimethyl-1H-indol-3-yl)-methanone;

[7-(4-Benzyloxy-3-methoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone;

[7-(2,4-Dichloro-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-methyl-1H-indol-3-yl)-methanone;

(1-Methyl-1H-indol-3-yl)-(7-pyridin-2-ylmethyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl)-methanone;

(1-Methyl-1H-indol-3-yl)-[7-(3-trifluoromethyl-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;

[7-(1H-Indol-3-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-methyl-1H-indol-3-yl)-methanone;

(1-Methyl-1H-indol-3-yl)-[7-(1-methyl-1H-indol-3-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;

[7-(1H-Benzimidazol-2-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-methyl-1H-indol-3-yl)-methanone;

[7-(1H-Indazol-3-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-methyl-1H-indol-3-yl)-methanone;

(1-Methyl-1H-indol-3-yl)-[7-(2-methyl-thiazol-4-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;

(1-Methyl-1H-indol-3-yl)-(7-quinolin-8-ylmethyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl)-methanone;

[7-(4-Benzyloxy-3-methoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-methyl-1H-indol-3-yl)-methanone;

[7-(2,4-Dichloro-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone;

(1-Ethyl-1H-indol-3-yl)-(7-pyridin-2-ylmethyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl)-methanone;

(1-Ethyl-1H-indol-3-yl)-[7-(3-trifluoromethyl-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;

[7-(2,6-Dichloro-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone;

(1-Ethyl-1H-indol-3-yl)-[7-(1H-indol-3-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;
(1-Ethyl-1H-indol-3-yl)-[7-(1-methyl-1H-indol-3-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;
(1-Ethyl-1H-indol-3-yl)-[7-(1H-indazol-3-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;
(1-Ethyl-1H-indol-3-yl)-[7-(2-methyl-thiazol-4-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;
(1-Ethyl-1H-indol-3-yl)-[7-(quinolin-8-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;
[7-(4-Methoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-methyl-1H-indol-3-yl)-methanone;
[7-(2,3-Dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-methyl-1H-indol-3-yl)-methanone;
[7-(3-Methoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-methyl-1H-indol-3-yl)-methanone;
[7-(3,5-Dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-methyl-1H-indol-3-yl)-methanone;
[7-(3,4-Dichloro-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-methyl-1H-indol-3-yl)-methanone;
[7-(2,3-Dihydro-benzo[1,4]dioxin-6-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-methyl-1H-indol-3-yl)-methanone;
(1-Methyl-1H-indol-3-yl)-[7-(4-trifluoromethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;
[7-(2,3-Dihydro-benzo[1,4]dioxin-5-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-methyl-1H-indol-3-yl)-methanone;
(7-Benzo[1,3]dioxol-4-ylmethyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl)-(1-methyl-1H-indol-3-yl)-methanone;
(7-Benzo[1,3]dioxol-5-ylmethyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl)-(1-methyl-1H-indol-3-yl)-methanone;
[4-(3,4-Dimethoxy-benzyl)-1-ethyl-3-methyl-1,4,6,7-tetrahydro-pyrazolo[4,3-c]pyridin-5-yl]-(1-methyl-1H-indol-3-yl)-methanone;
(1-Ethyl-1H-indol-3-yl)-[7-(4-methoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;
[7-(2,3-Dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone;
(1-Ethyl-1H-indol-3-yl)-[7-(3-methoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;
[7-(3,5-Dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone;
[7-(3,4-Dichloro-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone;
[7-(2,3-Dihydro-benzo[1,4]dioxin-6-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone;
(1-Ethyl-1H-indol-3-yl)-[7-(4-trifluoromethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;
[7-(2,3-Dihydro-benzo[1,4]dioxin-5-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone;
(7-Benzo[1,3]dioxol-4-ylmethyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl)-(1-ethyl-1H-indol-3-yl)-methanone;
(7-Benzo[1,3]dioxol-5-ylmethyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl)-(1-ethyl-1H-indol-3-yl)-methanone;
[4-(3,4-Dimethoxy-benzyl)-1-ethyl-3-methyl-1,4,6,7-tetrahydro-pyrazolo[4,3-c]pyridin-5-yl]-(1-ethyl-1H-indol-3-yl)-methanone;
(1-Ethyl-1H-indol-3-yl)-[7-(4-hydroxy-3-methoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;
(1-Ethyl-1H-indol-3-yl)-[7-[4-(2-hydroxy-ethoxy)-3-methoxy-benzyl]-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;

[1-Bromo-4-(3,4-dimethoxy-benzyl)-6,7-dihydro-4H-thieno[3,4-c]pyridin-5-yl]-(1-ethyl-1H-indol-3-yl)-methanone;
[1-Methyl-1H-indol-3-yl]-(7-quinolin-6-ylmethyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl)-methanone;
[1-Ethyl-1H-indol-3-yl]-(7-quinolin-6-ylmethyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl)-methanone;
[1-Methyl-1H-indol-3-yl]-(7-quinolin-7-ylmethyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl)-methanone;
[1-Ethyl-1H-indol-3-yl]-(7-quinolin-7-ylmethyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl)-methanone;
[1-(3-Methyl-benzyl)-3,4-dihydro-1H-isoquinolin-2-yl]-(1-methyl-1H-indol-3-yl)-methanone;
[1-Ethyl-1H-indol-3-yl]-(1-(3-methyl-benzyl)-3,4-dihydro-1H-isoquinolin-2-yl)-methanone;
[1-Cyclopropyl-1H-indol-3-yl]-(1-(3,4-dimethoxy-benzyl)-3,4-dihydro-1H-isoquinolin-2-yl)-methanone;
[1-(3,4-Dimethoxy-benzyl)-3,4-dihydro-1H-isoquinolin-2-yl]-(1-ethyl-1H-indol-3-yl)-methanone;
[7-(3,4-Dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-4-fluoro-1H-indol-3-yl)-methanone;
[7-(3,4-Dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(5-fluoro-1-methyl-1H-indol-3-yl)-methanone;
(6-Chloro-1-ethyl-1H-indol-3-yl)-[7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;
(6-Chloro-1-methyl-1H-indol-3-yl)-[7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;
[7-(3,4-Dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-methyl-1H-pyrrolo[2,3-b]pyridin-3-yl)-methanone;
[7-(3,4-Dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-(2-fluoro-ethyl)-1H-indol-3-yl)-methanone;
(1-Cyclopropyl-1H-indol-3-yl)-[7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;
[7-(3,4-Dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-(2-methoxy-ethyl)-1H-indol-3-yl)-methanone;
[7-(3,4-Dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-(2-hydroxy-ethyl)-1H-indol-3-yl)-methanone;
[7-(3,4-Dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-pyrrolo[2,3-b]pyridin-3-yl)-methanone;
(1-Ethyl-1H-indol-3-yl)-[7-(3-hydroxy-4-methoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;
[4-(3,4-Dimethoxy-benzyl)-1-methyl-6,7-dihydro-4H-thieno[3,4-c]pyridin-5-yl]-(1-ethyl-1H-indol-3-yl)-methanone;
{7-[4-(2-Hydroxy-ethoxy)-3-methoxy-benzyl]-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl}-(1-methyl-1H-pyrrolo[2,3-b]pyridin-3-yl)-methanone;
{7-[4-(2-Hydroxy-ethoxy)-3-methoxy-benzyl]-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl}-(1-methyl-1H-pyrrolo[2,3-c]pyridin-3-yl)-methanone;
{7-[4-(2-Hydroxy-ethoxy)-3-methoxy-benzyl]-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl}-(1-methyl-1H-pyrrolo[3,2-c]pyridin-3-yl)-methanone;
{7-[4-(2-Hydroxy-ethoxy)-3-methoxy-benzyl]-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl}-(1-methyl-1H-pyrrolo[3,2-b]pyridin-3-yl)-methanone;
(1-Ethyl-1H-pyrrolo[2,3-b]pyridin-3-yl)-{7-[4-(2-hydroxy-ethoxy)-3-methoxy-benzyl]-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl}-methanone;

(1-Ethyl-1H-pyrrolo[2,3-c]pyridin-3-yl)-{7-[4-(2-hydroxy-ethoxy)-3-methoxy-benzyl]-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl}-methanone;

(1-Ethyl-1H-pyrrolo[3,2-c]pyridin-3-yl)-{7-[4-(2-hydroxy-ethoxy)-3-methoxy-benzyl]-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl}-methanone;

(1-Ethyl-1H-pyrrolo[3,2-b]pyridin-3-yl)-{7-[4-(2-hydroxy-ethoxy)-3-methoxy-benzyl]-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl}-methanone;

[7-(3,4-Dimethoxy-benzyl)-2,3-dimethyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-methyl-1H-indol-3-yl)-methanone;

[7-(3,4-Dimethoxy-benzyl)-2,3-dimethyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone;

[8-(3,4-Dimethoxy-benzyl)-5,8-dihydro-6H-[1,7]naphthyridin-7-yl]-(1-ethyl-1H-indol-3-yl)-methanone;

[7-(3,4-Dimethoxy-benzyl)-2-methyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-methyl-1H-pyrrolo[3,2-b]pyridin-3-yl)-methanone;

[7-(3,4-Dimethoxy-benzyl)-2-methyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(5-fluoro-1-methyl-1H-indol-3-yl)-methanone;

(1-Cyclopropyl-4-fluoro-1H-indol-3-yl)-[7-(3,4-dimethoxy-benzyl)-2-methyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;

[7-(3,4-Dimethoxy-benzyl)-2-methyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-[1-(2-hydroxy-ethyl)-1H-indol-3-yl]-methanone;

[4-(3,4-Dimethoxy-benzyl)-1,3-dimethyl-6,7-dihydro-4H-thieno[3,4-c]pyridin-5-yl]-(5-fluoro-1-methyl-1H-indol-3-yl)-methanone;

(1-Cyclopropyl-4-fluoro-1H-indol-3-yl)-[4-(3,4-dimethoxy-benzyl)-1,3-dimethyl-6,7-dihydro-4H-thieno[3,4-c]pyridin-5-yl]-methanone;

[4-(3,4-Dimethoxy-benzyl)-1,3-dimethyl-6,7-dihydro-4H-thieno[3,4-c]pyridin-5-yl]-[1-(2-hydroxy-ethyl)-1H-indol-3-yl]-methanone;

[4-(3,4-Dimethoxy-benzyl)-1-methyl-6,7-dihydro-4H-thieno[3,4-c]pyridin-5-yl]-(1-methyl-1H-pyrrolo[3,2-b]pyridin-3-yl)-methanone;

[4-(3,4-Dimethoxy-benzyl)-1-methyl-6,7-dihydro-4H-thieno[3,4-c]pyridin-5-yl]-(5-fluoro-1-methyl-1H-indol-3-yl)-methanone;

(1-Cyclopropyl-4-fluoro-1H-indol-3-yl)-[4-(3,4-dimethoxy-benzyl)-1-methyl-6,7-dihydro-4H-thieno[3,4-c]pyridin-5-yl]-methanone;

[4-(3,4-Dimethoxy-benzyl)-1-methyl-6,7-dihydro-4H-thieno[3,4-c]pyridin-5-yl]-[1-(2-hydroxy-ethyl)-1H-indol-3-yl]-methanone;

[7-(4-Cyclopropoxy-3-methoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-methyl-1H-indol-3-yl)-methanone;

[7-(4-Cyclopropoxy-3-methoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone;

[4-(3,4-Dimethoxy-benzyl)-1,3-dimethyl-6,7-dihydro-4H-thieno[3,4-c]pyridin-5-yl]-(1-methyl-1H-pyrrolo[3,2-b]pyridin-3-yl)-methanone;

(1,3-Dimethyl-4-quinolin-7-ylmethyl-1,4,6,7-tetrahydro-pyrazolo[4,3-c]pyridin-5-yl)-(1-methyl-1H-indol-3-yl)-methanone;

(1-Methyl-1H-indol-3-yl)-(1-methyl-7-quinolin-7-ylmethyl-1,4,5,7-tetrahydro-pyrazolo[3,4-c]pyridin-6-yl)-methanone;

(1-Methyl-1H-indol-3-yl)-(2-methyl-7-quinolin-7-ylmethyl-2,4,5,7-tetrahydro-pyrazolo[3,4-c]pyridin-6-yl)-methanone;

[(S)-8-(3,4-Dimethoxy-benzyl)-5,6-dihydro-8H-imidazo[1,2-a]pyrazin-7-yl]-(1-ethyl-1H-indol-3-yl)-methanone;

(1-Ethyl-1H-indol-3-yl)-[7-(4-[1,2,3]triazol-2-yl-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;

(1-Ethyl-1H-indol-3-yl)-[7-(4-[1,2,3]triazol-1-yl-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;

(1-Ethyl-1H-indol-3-yl)-[7-(3-[1,2,3]triazol-2-yl-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;

(1-Ethyl-1H-indol-3-yl)-[7-(3-[1,2,3]triazol-1-yl-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;

(1-Methyl-1H-indol-3-yl)-[7-(4-[1,2,3]triazol-2-yl-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;

(1-Methyl-1H-indol-3-yl)-[7-(4-[1,2,3]triazol-1-yl-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;

[7-(3,4-Dimethoxy-benzyl)-1-methyl-1,4,5,7-tetrahydro-pyrazolo[3,4-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone;

2-[6-(1-Ethyl-1H-indole-3-carbonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridin-7-ylmethyl]-benzonitrile;

3-[6-(1-Ethyl-1H-indole-3-carbonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridin-7-ylmethyl]-benzonitrile;

4-[6-(1-Ethyl-1H-indole-3-carbonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridin-7-ylmethyl]-benzonitrile;

(1-Ethyl-1H-indol-3-yl)-(7-pyridin-3-ylmethyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl)-methanone;

[7-(6-Chloro-pyridin-2-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone;

[7-(3,4-Difluoro-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone;

[7-(2-Chloro-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone;

[7-(3-Chloro-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone;

2-[6-(1-Methyl-1H-indole-3-carbonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridin-7-ylmethyl]-benzonitrile;

3-[6-(1-Methyl-1H-indole-3-carbonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridin-7-ylmethyl]-benzonitrile;

4-[6-(1-Methyl-1H-indole-3-carbonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridin-7-ylmethyl]-benzonitrile;

(1-Methyl-1H-indol-3-yl)-(7-pyridin-3-ylmethyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl)-methanone;

[7-(6-Chloro-pyridin-2-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-methyl-1H-indol-3-yl)-methanone;

[7-(3,4-Difluoro-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-methyl-1H-indol-3-yl)-methanone;

[7-(2-Chloro-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-methyl-1H-indol-3-yl)-methanone;

[7-(3-Chloro-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-methyl-1H-indol-3-yl)-methanone;

(1-Methyl-1H-indol-3-yl)-[7-(3-pyrimidin-2-yl-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;

(1-Ethyl-1H-indol-3-yl)-[7-(3-pyrimidin-2-yl-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;
(1-Methyl-1H-indol-3-yl)-[7-(3-pyrazol-1-yl-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;
(1-Methyl-1H-indol-3-yl)-[7-(3-[1,2,4]triazol-1-yl-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;
(1-Ethyl-1H-indol-3-yl)-[7-(3-[1,2,4]triazol-1-yl-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;
5-[6-(1-Methyl-1H-indole-3-carbonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridin-7-ylmethyl]-pyridine-2-carbonitrile;
(1-Methyl-1H-indol-3-yl)-[7-(6-methyl-pyridin-3-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;
[7-(6-Ethyl-pyridin-3-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-methyl-1H-indol-3-yl)-methanone;
5-[6-(1-Ethyl-1H-indole-3-carbonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridin-7-ylmethyl]-pyridine-2-carbonitrile;
(1-Ethyl-1H-indol-3-yl)-[7-(6-methyl-pyridin-3-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;
(1-Ethyl-1H-indol-3-yl)-[7-(6-ethyl-pyridin-3-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;
[7-(3,4-Dimethoxy-benzyl)-2-methoxy-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone;
[7-(3,4-Dimethoxy-benzyl)-3-methoxy-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone;
[7-(3,4-Dimethoxy-benzyl)-2-ethoxy-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone;
[7-(3,4-Dimethoxy-benzyl)-3-ethoxy-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone;
[7-(4-Ethoxy-3-methoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone;
(1-Ethyl-1H-indol-3-yl)-{7-[3-methoxy-4-(2,2,2-trifluoro-ethoxy)-benzyl]-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl}-methanone;
{7-[4-(2-Dimethylamino-ethoxy)-3-methoxy-benzyl]-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone;
(1-Ethyl-1H-indol-3-yl)-[7-(3-methoxy-4-propoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;
(1-Ethyl-1H-indol-3-yl)-[7-(4-isopropoxy-3-methoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;
{4-[6-(1-Ethyl-1H-indole-3-carbonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridin-7-ylmethyl]-2-methoxy-phenoxy}-acetic acid methyl ester;
(1-Ethyl-1H-indol-3-yl)-[7-(3-methoxy-4-trifluoromethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;
{4-[6-(1-Ethyl-1H-indole-3-carbonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridin-7-ylmethyl]-2-methoxy-phenoxy}-acetic acid;
[7-(3,4-Dimethoxy-benzyl)-2-ethynyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone;
[7-(3,4-Dimethoxy-benzyl)-3-ethynyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone;
[7-(3,4-Dimethoxy-benzyl)-2-ethyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone;
[3-Chloro-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone;
7-(3,4-Dimethoxy-benzyl)-6-(1-ethyl-1H-indole-3-carbonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine-3-carbonitrile;
[7-(3,4-Dimethoxy-benzyl)-3-ethyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone;
[7-(3,4-Dimethoxy-benzyl)-3-methyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone;
[2-Chloro-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone;
7-(3,4-Dimethoxy-benzyl)-6-(1-ethyl-1H-indole-3-carbonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine-2-carbonitrile;

[7-(3,4-Dimethoxy-benzyl)-2-methyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone;
Trifluoro-methanesulfonic acid 4-[6-(1-ethyl-1H-indole-3-carbonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridin-7-ylmethyl]-2-methoxy-phenyl ester;
Trifluoro-methanesulfonic acid 5-[6-(1-ethyl-1H-indole-3-carbonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridin-7-ylmethyl]-2-methoxy-phenyl ester;
[7-(3-Ethoxy-4-methoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone;
(1-Ethyl-1H-indol-3-yl)-{7-[4-methoxy-3-(2,2,2-trifluoro-ethoxy)-benzyl]-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl}-methanone;
(1-Ethyl-1H-indol-3-yl)-{7-[3-(2-hydroxy-ethoxy)-4-methoxy-benzyl]-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl}-methanone;
(1-Ethyl-1H-indol-3-yl)-[7-(4-methoxy-3-propoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;
(1-Ethyl-1H-indol-3-yl)-[7-(3-isopropoxy-4-methoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;
{5-[6-(1-Ethyl-1H-indole-3-carbonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridin-7-ylmethyl]-2-methoxy-phenoxy}-acetic acid methyl ester;
4-(3,4-Dimethoxy-benzyl)-5-(1-ethyl-1H-indole-3-carbonyl)-4,5,6,7-tetrahydro-thieno[3,4-c]pyridine-1-carbonitrile;
[1-Chloro-4-(3,4-dimethoxy-benzyl)-6,7-dihydro-4H-thieno[3,4-c]pyridin-5-yl]-(1-ethyl-1H-indol-3-yl)-methanone;
5-[6-(1-Ethyl-1H-indole-3-carbonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridin-7-ylmethyl]-2-methoxy-benzonitrile;
(1-Ethyl-1H-indol-3-yl)-[7-(4-ethyl-3-methoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;
[7-(3,4-Dimethoxy-benzyl)-3-trifluoromethyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone;
(1-Ethyl-1H-indol-3-yl)-[7-(3-methoxy-4-methyl-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;
(1-Ethyl-1H-indol-3-yl)-[7-(3-ethyl-4-methoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;
(1-Ethyl-1H-indol-3-yl)-[7-(4-methoxy-3-methyl-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;
[7-(3,4-Dimethoxy-benzyl)-3-[1,2,3]triazol-2-yl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone;
[7-(3-Cyclopropoxy-4-methoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone;
(1-Ethyl-1H-indol-3-yl)-[7-(3-[1,2,4]oxadiazol-3-yl-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;
6-[6-(1-Ethyl-1H-indole-3-carbonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridin-7-ylmethyl]-pyridine-2-carbonitrile;
6-[6-(1-Methyl-1H-indole-3-carbonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridin-7-ylmethyl]-pyridine-2-carbonitrile;
(1-Ethyl-1H-indol-3-yl)-[7-(6-methoxy-pyridin-2-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;
[7-(6-Methoxy-pyridin-2-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-methyl-1H-indol-3-yl)-methanone;
(1-Methyl-1H-indol-3-yl)-[7-(3-[1,2,4]oxadiazol-3-yl-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;
3-[6-(1-Methyl-1H-indole-3-carbonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridin-7-ylmethyl]-benzamide;
3-[6-(1-Ethyl-1H-indole-3-carbonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridin-7-ylmethyl]-benzamide;

[7-(6-Methoxy-pyridin-3-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-methyl-1H-indol-3-yl)-methanone;
and
(1-Ethyl-1H-indol-3-yl)-[7-(6-methoxy-pyridin-3-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone.

The compounds of formula (I) and their pharmaceutically acceptable salts can be used as medicaments, e.g. in the form of pharmaceutical compositions for enteral or parental administration.

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.

The present invention also relates to 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).

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

The compounds according to formula (I) are useful for the prevention or treatment of diseases or disorders related to the orexin system.

Such diseases or disorders related to the orexin system may be defined as comprising all types of sleep disorders, stress-related syndromes, addictions (especially psychoactive substance use, abuse, seeking and reinstatement), cognitive dysfunctions in the healthy population and in psychiatric and neurologic disorders, and eating or drinking disorders. Especially, such diseases or disorders related to the orexin system comprise all types of sleep disorders, stress-related syndromes, and addictions (especially psychoactive substance use, abuse, seeking and reinstatement).

In a sub-embodiment, such diseases or disorders related to the orexin system may be selected from the group consisting of sleep disorders that comprises all types of insomnias, sleep-related dystonias, restless leg syndrome, sleep apneas, jet-lag syndrome, shift-work

syndrome, delayed or advanced sleep phase syndrome or insomnias related to psychiatric disorders (notably all types of insomnias, especially primary insomnia).

In another sub-embodiment, such diseases or disorders related to the orexin system may be selected from the group consisting of cognitive dysfunctions that comprise deficits in all types of attention, learning and memory functions occurring transiently or chronically in the normal, healthy, young, adult or aging population, and also occurring transiently or chronically in psychiatric, neurologic, cardiovascular and immune disorders.

In another sub-embodiment, such diseases or disorders related to the orexin system may be selected from the group consisting of eating disorders that comprise metabolic dysfunction; dysregulated appetite control; compulsive obesities; bulimia or anorexia nervosa.

In another sub-embodiment, such diseases or disorders related to the orexin system may be selected from the group consisting of all types of addictions (especially psychoactive substance use, abuse, seeking and reinstatement) that comprise all types of psychological or physical addictions and their related tolerance and dependence components.

Eating disorders may be defined as comprising metabolic dysfunction; dysregulated appetite control; compulsive obesities; emeto-bulimia or anorexia nervosa. 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. Drinking disorders include polydipsias in psychiatric disorders and all other types of excessive fluid intake.

Sleep disorders include all types of parasomnias, insomnias, sleep-related dystonias; restless leg syndrome; sleep apneas; jet-lag syndrome; shift-work syndrome, delayed or advanced sleep phase syndrome or insomnias related to psychiatric disorders.

Insomnias are defined as comprising 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. Insomnia also include stress-related syndromes including post-traumatic stress disorders as well as other types and subtypes of anxiety disorders such as generalized anxiety, obsessive compulsive disorder, panic attacks and all types of phobic anxiety and avoidance.

Addictions may be defined as addiction to one or more rewarding stimuli, notably to one rewarding stimulus. Such rewarding stimuli may be of either natural or synthetic origin. Psychoactive substance use, abuse, seeking and reinstatement are defined as all types of

psychological or physical addictions and their related tolerance and dependence components.

Cognitive dysfunctions include deficits in all types of attention, learning and memory functions occurring transiently or chronically in the normal, healthy, young, adult or aging population, and also occurring transiently or chronically in psychiatric, neurologic, cardiovascular and immune disorders.

In another embodiment, such diseases or disorders related to the orexin system may be defined as comprising notably mental health diseases or disorders relating to orexinergic dysfunctions; especially sleep disorders, anxiety disorders, addiction disorders, cognitive dysfunctions, mood disorders, or appetite disorders; wherein sleep disorders comprise dyssomnias, parasomnias, sleep disorders associated with a general medical condition and substance-induced sleep disorders (especially sleep disorders comprise 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; and, in addition, 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); wherein anxiety disorders comprise 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; wherein addiction disorders comprise addictions to one or more rewarding stimuli 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]; wherein appetite disorders comprise eating disorders (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) and drinking disorders (comprising include polydipsias in psychiatric disorders and

all other types of excessive fluid intake); wherein cognitive dysfunctions 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]; and wherein mood disorders comprise 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; and mood disorders comprise 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 as especially major depressive episode, major depressive disorder, mood disorder due to a general medical condition; and substance-induced mood disorder.

In addition, further diseases related to the orexin system 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; treating or controlling agitation, in isolation or co-morbid with another medical condition.

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.

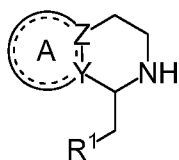
Besides, any characteristics described in this invention for the compounds of formula (I) (whether for the compounds themselves, salts thereof, compositions containing the compounds or salts thereof, uses of the compounds or salts thereof, etc.) apply *mutatis mutandis* to compounds of formula (I_{E1}) or formula (I_{E2}).

Preparation of compounds of formula (I):

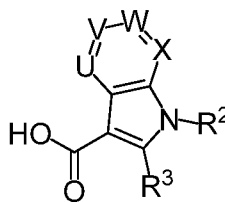
The compounds of formula (I) can be prepared by the methods given below, by the methods given in the Examples or by analogous methods. Optimum reaction conditions may vary with the particular reactants or solvents used, but such conditions can be determined by a person skilled in the art by routine optimisation procedures. The compounds obtained may also be converted into salts thereof in a manner known *per se*.

In general, all chemical transformations can be performed according to well-known standard methodologies as described in the literature or as described in the procedures or in the experimental part below.

Compounds of formula (I) of the present invention can be prepared according to the general sequence of reactions outlined below wherein A, U, V, W, X, Y, Z, R¹, R² and R³ are as defined for formula (I).



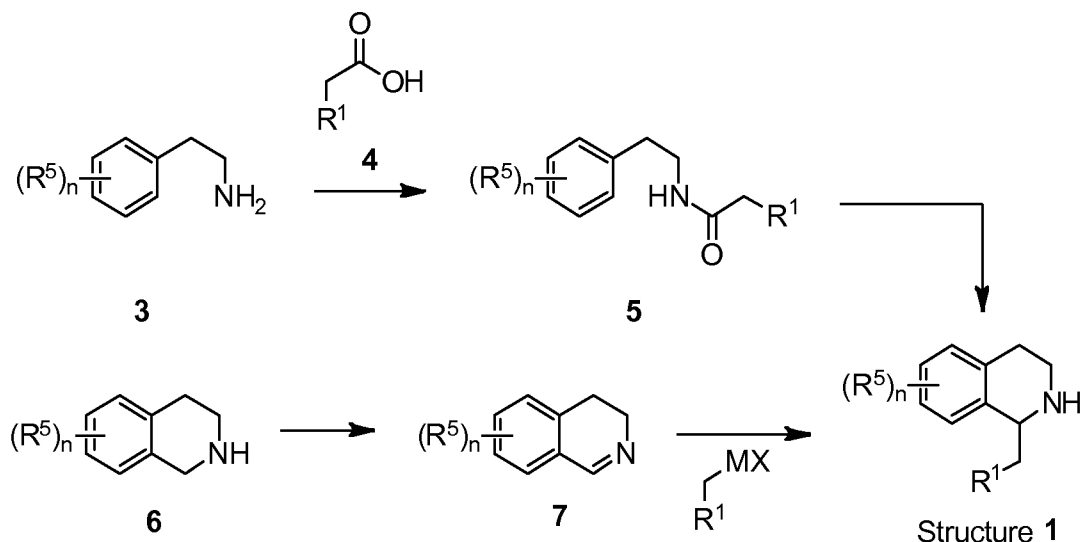
Structure 1



Structure 2

Compounds of formula (I) are prepared by reaction of an amine of Structure 1 or a salt thereof, such as a hydrochloride salt, with an acid of Structure 2 in the presence of an amide-coupling reagent such as TBTU, EDC, DCC or PyBOP and a base like DIPEA or TEA in a solvent such as MeCN or DMF.

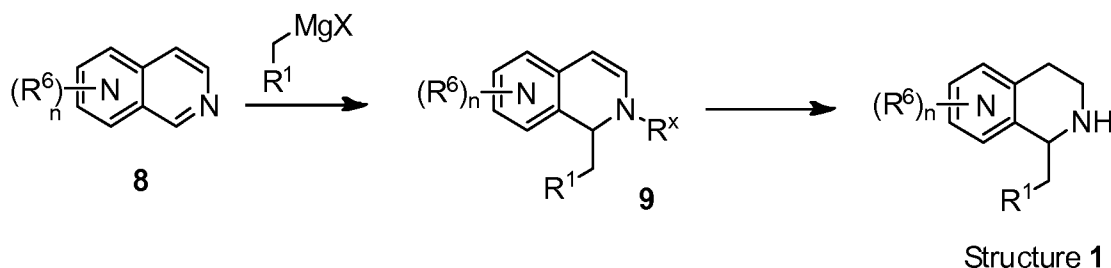
Compounds of Structure 1 may be prepared by one of the synthetic pathways described below.



Scheme 1

Compounds of Structure 1 where ring A represents phenyl may be prepared by one of the synthetic pathways described in Scheme 1. Depending on the electron-donating or electron-withdrawing nature of substituents R^5 alternative routes may be employed. For example, when substituents R^5 are electron-donating, compounds of Structure 1 are prepared as described in WO200485403 by reaction of an amine of Structure 3 or a salt thereof, such as a hydrochloride salt with an acid of Structure 4 in the presence of an amide-coupling reagent such as TBTU or PyBOP and a base like DIPEA or TEA in a solvent such as MeCN or DMF to give an amide of Structure 5. Alternatively, coupling can be accomplished by reaction with the desired acid chloride. An amide of Structure 5 is then subjected to Bischler-Napieralski conditions such as $POCl_3$ in MeCN followed by reduction of the resulting imine with sodium borohydride in a solvent like MeOH to give compounds of Structure 1. Alternatively when substituents R^5 are electron-withdrawing, compounds of Structure 1 are prepared by oxidation of a readily available 1,2,3,4-tetrahydroisoquinoline of Structure 6 in a two-step procedure involving initial bromination with NBS in a solvent such DCM followed by treatment with aq. NaOH to give a 3,4-dihydroisoquinoline of Structure 7. Alkylation of a 3,4-dihydroisoquinoline of Structure 7 with a readily available benzyl-organometallic reagent R^1-CH_2-MX such as a Grignard or Negishi reagent in a solvent like THF furnishes compounds of Structure 1.

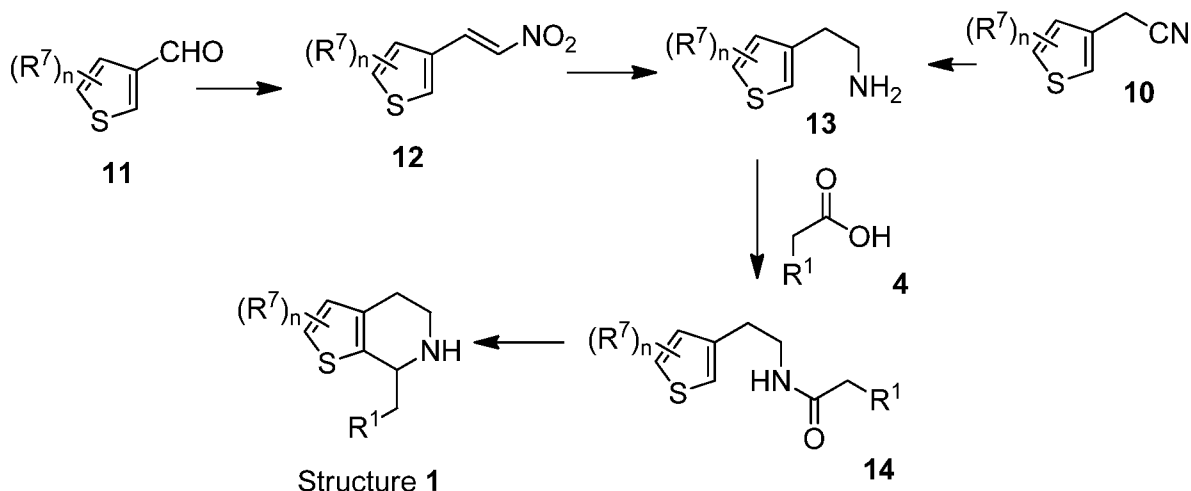
34



Scheme 2

Compounds of Structure **1** where ring A represents pyridine may be prepared in analogy to the procedure described in WO2009038812 and as illustrated in Scheme 2. Activation of a commercially available 1,6- or 1,7-naphthyridine with a haloformate such as benzyl chloroformate or a benzyl halide such as benzyl bromide in a solvent such as THF or MeCN followed by reaction with a readily available Grignard reagent $R^1\text{-CH}_2\text{-MgX}$ gives dihydronaphthyridines of Structure **9**. A compound of Structure **9** is then treated with hydrogen and palladium on charcoal in a solvent like MeOH to give a compound of Structure **1**.

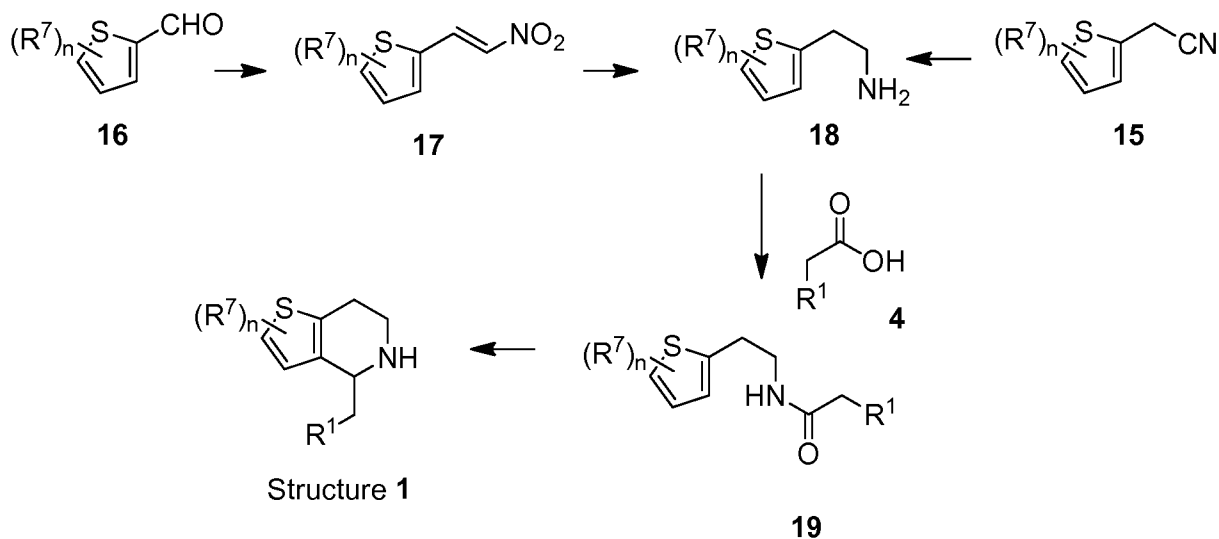
Compounds of Structure **1** where ring A represents thiophene may be prepared by following one of the sequences outlined in the schemes below:



Scheme 3

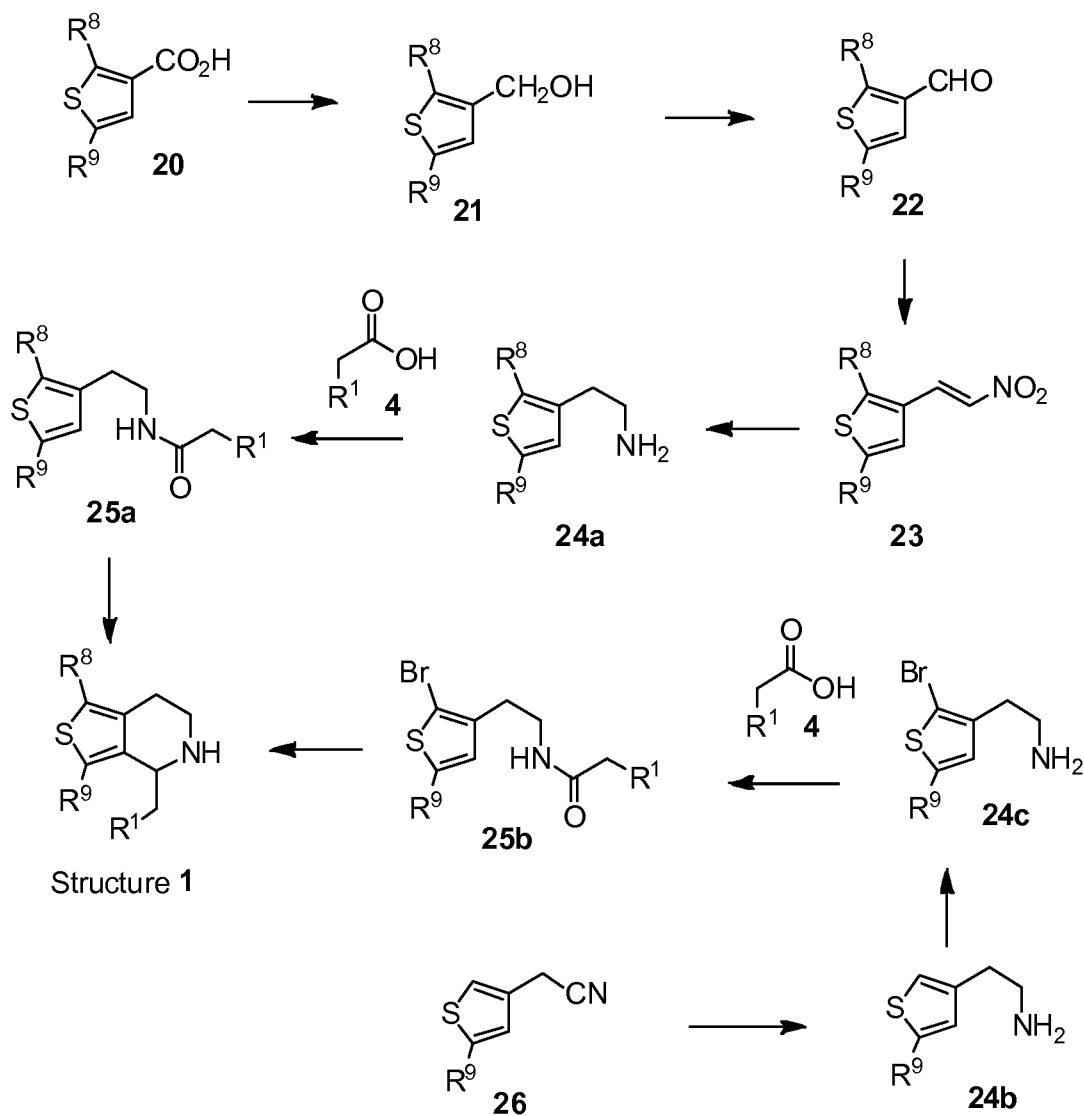
In case Structure **1** represents a 4,5,6,7-tetrahydrothieno[2,3-c]pyridine, compounds of Structure **1** may be prepared as outlined in Scheme 3. An amine of Structure **13** is either commercially available or prepared by the borane reduction of the corresponding commercially available nitrile of structure **10** in a solvent like THF. Alternatively, an amine of Structure **13** can be prepared in two steps from the corresponding commercially available aldehyde of Structure **11** via a Henry reaction with nitromethane to give a nitro olefin of

Structure **12** that can then be reduced with LAH and sulfuric acid in a solvent like THF to furnish an amine of Structure **13**. Reaction of an amine of Structure **13** or a salt thereof, such as a hydrochloride salt, with an acid of Structure **4** in the presence of an amide-coupling reagent such as TBTU or PyBOP and a base like DIPEA or TEA in a solvent such as MeCN or DMF gives an amide of Structure **14**. The amide of Structure **14** is then subjected to Bischler-Napieralski conditions such as POCl₃ in MeCN followed by reduction of the resulting imine with sodium borohydride in a solvent like MeOH to give compounds of Structure **1**.



Scheme 4

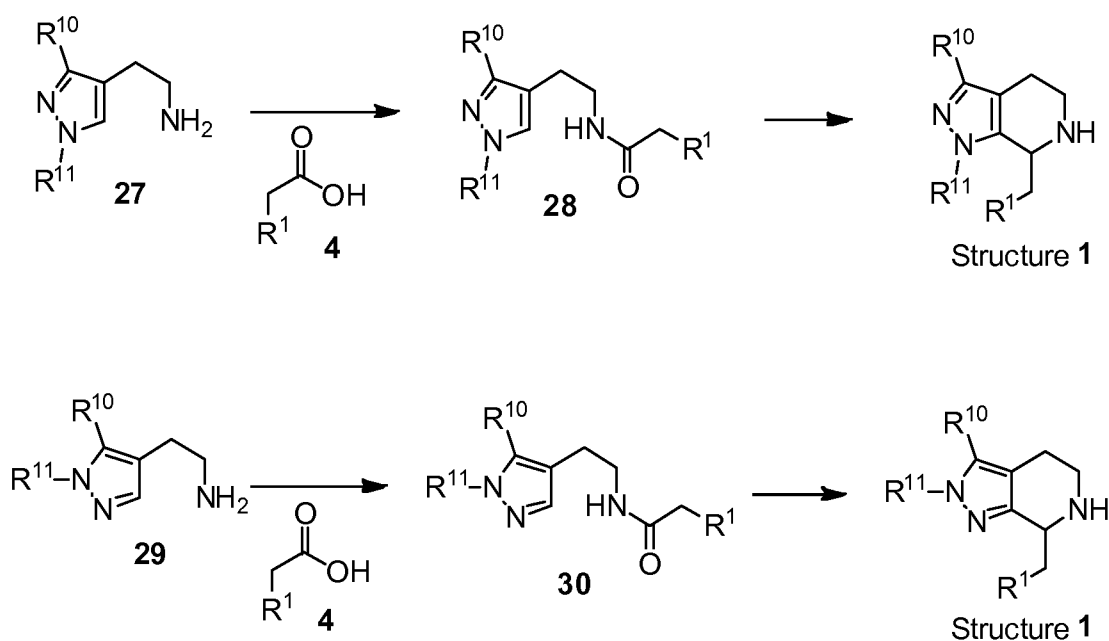
In case Structure **1** represents a 4,5,6,7-tetrahydrothieno[3,2-c]pyridine, compounds of Structure **1** may be prepared as outlined in Scheme 4. An amine of Structure **18** is either commercially available or prepared by the borane reduction of the corresponding commercially available nitrile of Structure **15** in a solvent like THF. Alternatively, an amine of Structure **18** can be prepared in two steps from the corresponding aldehyde of Structure **16** via a Henry reaction with nitromethane to give a nitro olefin of Structure **17** that can then be reduced with LAH and sulfuric acid in a solvent like THF to furnish an amine of Structure **18**. Reaction of an amine of Structure **18** or a salt thereof, such as a hydrochloride salt with an acid of Structure **4** in the presence of an amide-coupling reagent such as TBTU or PyBOP and a base like DIPEA or TEA in a solvent such as MeCN or DMF gives an amide of Structure **19**. The amide of Structure **19** is then subjected to Bischler-Napieralski conditions such as POCl₃ in MeCN followed by reduction of the resulting imine with sodium borohydride in a solvent like MeOH to give compounds of Structure **1**.



Scheme 5

In case Structure 1 represents a 4,5,6,7-tetrahydrothieno[3,4-c]pyridine, compounds of Structure 1 may be prepared by one of the synthetic pathways described in Scheme 5. In the case where substituent R^8 is already present in the starting material, a readily available acid of Structure 20 may be reduced with borane in a solvent like THF to give an alcohol of Structure 21 that can be subsequently re-oxidised with MnO_2 in a solvent like DCM to give the corresponding aldehyde of Structure 22. In a similar way as described earlier, an aldehyde of Structure 22 can be transformed via a Henry reaction with nitromethane into a nitro olefin of Structure 23 that can then be reduced with LAH and sulfuric acid in a solvent like THF to furnish an amine of Structure 24a. Reaction of an amine of Structure 24a or a salt thereof, such as a hydrochloride salt with an acid of Structure 4 in the presence of an amide-coupling reagent such as TBTU or PyBOP and a base like DIPEA or TEA in a solvent such

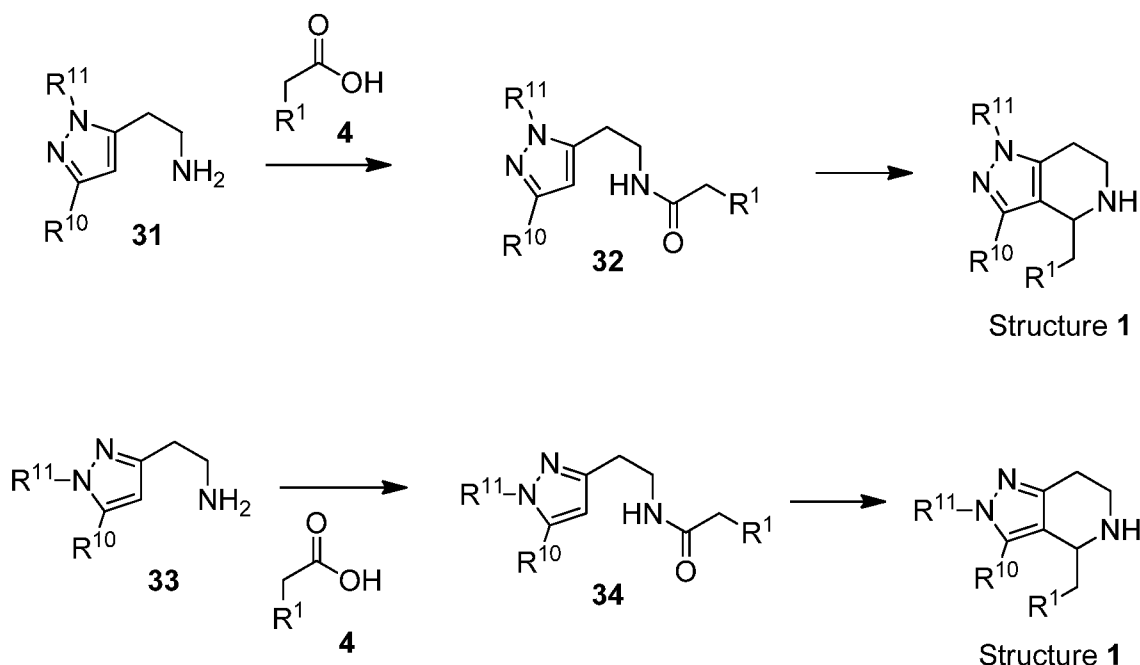
as MeCN or DMF gives an amide of Structure **25a**. The amide of Structure **25a** is then subjected to Bischler-Napieralski conditions such as POCl₃ in MeCN followed by reduction of the resulting imine with sodium borohydride in a solvent like MeOH to give compounds of Structure **1**. Alternatively, an amine of Structure **24b** is either commercially available or can be prepared by the borane reduction of the corresponding nitrile of Structure **26** in a solvent like THF. An amine of Structure **24b** can then be treated with bromine in acetic acid to give a amine of Structure **24c**, subsequent amide coupling with an acid of Structure **4** followed by a Bischler-Napieralski reaction and reduction of the resulting imine as described earlier furnishes a compound of Structure **1** where R⁸ = Br. Compounds of Structure **1** where R⁸ = Br can then be further modified in for example a Negishi coupling with a readily available organozinc reagent to give further compounds of Structure **1**. Alternatively, R⁸ can be converted to an alkoxy substituent, e.g. EtO, by following the procedure described in US2008/71084.



Scheme 6

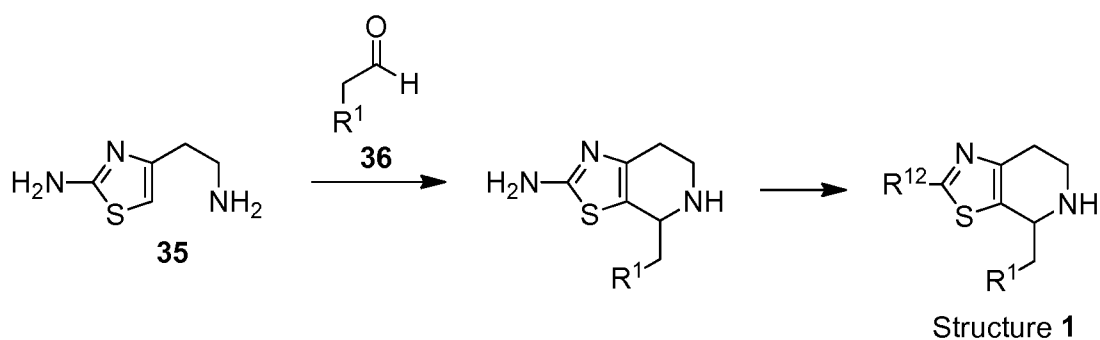
In case Structure **1** represents a 4,5,6,7-tetrahydropyrazolo[3,4-c]pyridine, compounds of Structure **1** may be prepared as outlined in Scheme 6. An amine of Structure **27**, either as a single regioisomer or a mixture of both regioisomers (**27**&**29**) or a salt thereof, may be coupled with an acid of Structure **4** in the presence of an amide-coupling reagent such as TBTU or PyBOP and a base like DIPEA or TEA in a solvent such as MeCN or DMF to give an amide of Structure **28**. The amide of Structure **28** is then subjected to Bischler-Napieralski conditions such as POCl₃ in MeCN followed by reduction of the resulting imine with sodium borohydride in a solvent like MeOH to give compounds of Structure **1**.

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Scheme 7

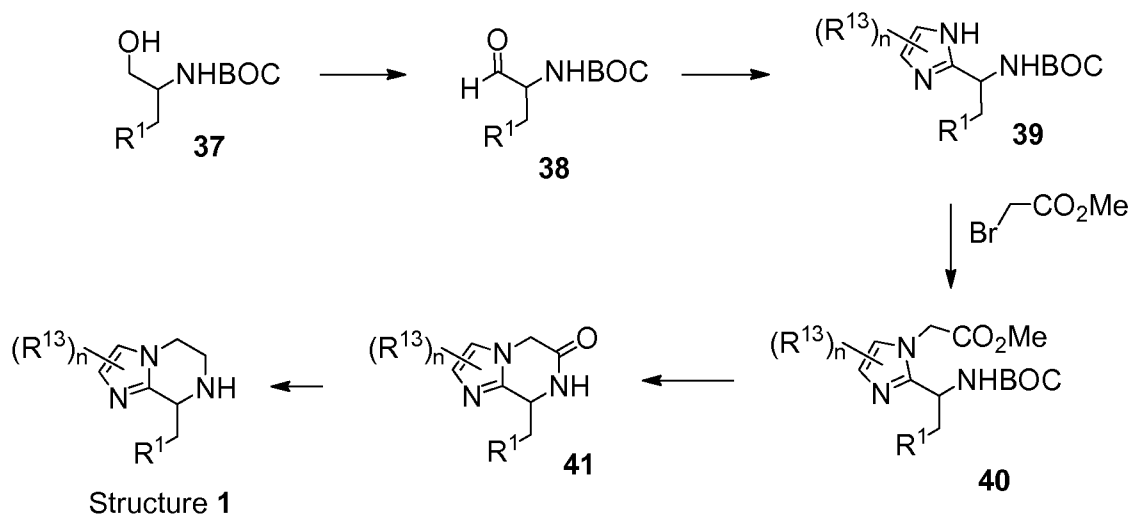
In case Structure 1 represents a 4,5,6,7-tetrahydropyrazolo[4,3-c]pyridine, compounds of Structure 1 may be prepared in analogy to the procedure described in WO2009038812 and as illustrated in Scheme 7. An amine of Structure 31, either as a single regioisomer or a mixture of both regioisomers (31, 33) or a salt thereof, may be coupled with an acid of Structure 4 in the presence of an amide-coupling reagent such as TBTU or PyBOP and a base like DIPEA or TEA in a solvent such as MeCN or DMF to give an amide of Structure 32. The amide of Structure 32 is then subjected to Bischler-Napieralski conditions such as POCl_3 in MeCN followed by reduction of the resulting imine with sodium borohydride in a solvent like MeOH to give compounds of Structure 1.



Scheme 8

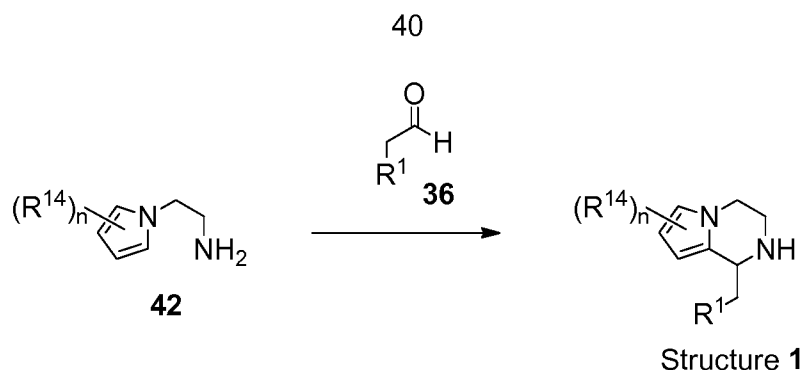
In case Structure 1 represents a 4,5,6,7-tetrahydro-thiazolo[5,4-c]pyridine, compounds of Structure 1 may be prepared either by Bischler-Napieralski conditions in analogy to the

procedure described by Zheng *et al.* in J. Med. Chem. **1999**, 42, 2287-2294. or alternatively, via a Pictet-Spengler reaction under basic conditions as depicted in Scheme 8. An amine of Structure **35**, or a salt thereof, such as a hydrobromide salt, may be reacted with an aldehyde of Structure **36**, in a solvent like MeOH in the presence of a base like aq. NaOH to furnish a compound of Structure **1** where $R^{12} = NH_2$. The nature of substituent R^{12} can be modified by methods known to someone skilled in the art, for example, protection of the 2° amine of Structure **1** with a suitable protecting group like the Boc group followed by Sandmeyer reaction of the amino-thiazole group leads to the corresponding halo-derivative. Subsequent Boc-deprotection leads to a compound of structure **1** where $R^{12} = \text{halogen}$. Alternatively prior to Boc-deprotection, the halogenated compound can be further modified to produce further compounds of Structure **1**.



Scheme 9

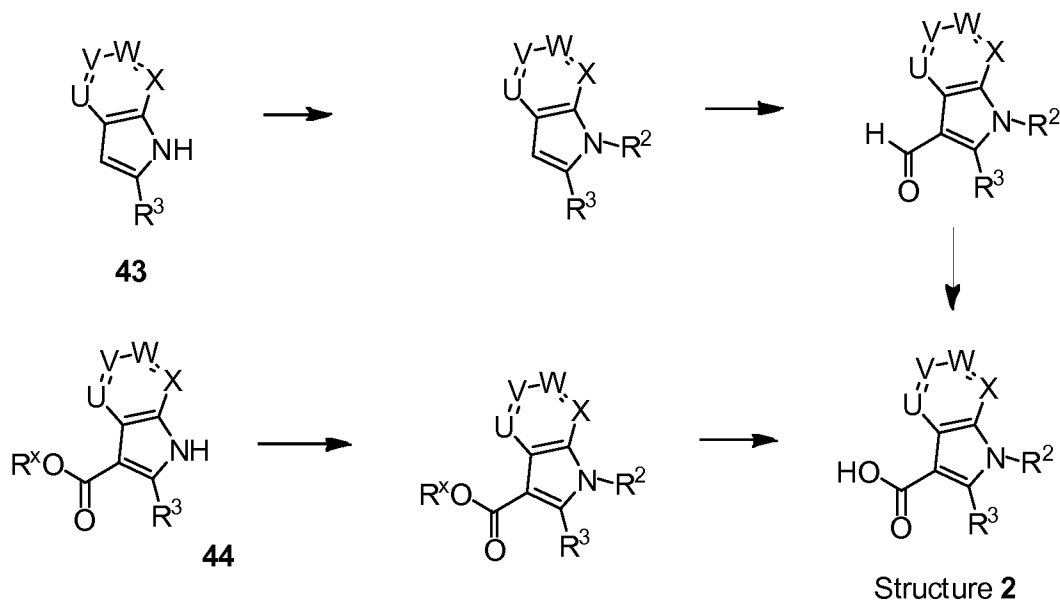
In case Structure **1** represents a 5,6,7,8-tetrahydroimidazo[1,2-a]pyrazine, compounds of Structure **1** may be prepared as outlined in Scheme 9. A Boc-protected amino alcohol of Structure **37**, either commercially available, or prepared in 2 steps from the corresponding amino acid may be oxidised using conditions like Swern to give the corresponding amino aldehyde of Structure **38**. Condensation of aldehyde **38** with a glyoxal derivative in the presence of ammonium hydroxide in a solvent like MeOH gives an imidazole of Structure **39**. Alkylation of imidazole **39** with 2-bromoacetic acid ester in the presence of a base like potassium carbonate in a solvent like DMF provides a compound of Structure **40**. Removal of the Boc group under standard acidic conditions followed by treatment with a base like triethylamine gives a cyclised compound of Structure **41**. Reduction of **41** with a reducing agent like borane in an aprotic solvent like THF furnishes a compound of Structure **1**.



Scheme 10

In case Structure 1 represents a 1,2,3,4-tetrahydropyrrolo[1,2-a]pyrazine, compounds of Structure 1 may be prepared in analogy to the procedure described in WO2009090054 and as depicted in Scheme 10. An amine of Structure 42 undergoes ring closure by reaction with an aldehyde of Structure 36 in a solvent such as MeOH in the presence of a base like aq. NaOH. Reaction times can vary between 1h and 5 days.

General process for the preparation of Acids of Structure 2

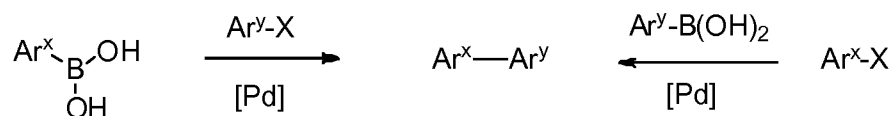


Scheme 11

Acids of Structure 2 are either commercially available or prepared as depicted in Scheme 11. A commercially available or well known indole derivative of Structure 43 may be alkylated on nitrogen by initial deprotonation with a base like sodium hydride in a solvent such as DMF or THF followed by reaction with an alkyl halide like methyl iodide. Formylation at the indole-3-position using Duff conditions (hexamethylenetetramine in TFA under reflux) followed by oxidation of the aldehyde using sodium chlorite under buffered conditions in the presence of a chlorine scavenger like 2-methyl-2-butene in a solvent mixture like THF/ⁿbutanol gives an

acid of Structure **2**. Alternatively, a commercially available ester of Structure **44** can be *N*-alkylated in the same way as described above followed by hydrolysis of the ester function with aq. NaOH in MeOH to give an acid of Structure **2**.

Generally, bi-(hetero-)aryl-like structures as present in certain groups R¹ can be synthesised using well established Suzuki chemistry in analogy to scheme 12.



Scheme 12: Synthesis of bi-(hetero-)aryl like structures; X is Br, I

Reaction of commercially available (hetero-)aryl-boronic acid derivatives (e.g. carboxylic acids or esters thereof) with commercially available (hetero-)aryl-bromides or (hetero-)aryl-iodides (or analogues thereof, such as chlorides, trifluoromethanesulfonates) in presence of a metal catalyst catalyst such as Pd(PPh₃)₄ or equivalent and a base such as Na₂CO₃ under heating in a solvent such as toluene, dioxane, THF provides the corresponding bi-(hetero-)aryl like structures which can be used directly or after generally known functional group transformations in the schemes 1 to 11 above.

Whenever the compounds of formula (I) are obtained in the form of mixtures of enantiomers, the enantiomers can be separated using methods known to the one skilled in the art: e.g. by formation and separation of diastereomeric salts or by HPLC over a chiral stationary phase such a Daicel ChiralCel OD-H (5-10 μm) column, a Daicel ChiralPak IC (5 μm) column, or a Daicel ChiralPak IA (5-10 μm) or AD-H (5 μm) column. Typical conditions of chiral HPLC are an isocratic mixture of eluent A (heptanes or CH₃CN) and eluent B (EtOH, MeOH, DCM or tBME in presence or absence of an amine such as TEA or DEA), at a flow rate of 0.8 to 150 mL/min.

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 FC or by prep. HPLC. Compounds described in the invention are characterized 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. Racemates can be separated into their

enantiomers by prep. HPLC (column: ChiralPaK AD 20x250 mm, 5 μ m, 15% EtOH in hexane).

LC-MS with acidic conditions

Method A: Agilent 1100 series with mass spectrometry detection (MS: Finnigan single quadrupole). Column: Zorbax SB-aq (3.5 μ m, 4.6 x 50 mm). Conditions: MeCN [eluent A]; water + 0.04% TFA [eluent B]. Gradient: 95% B $\rightarrow$ 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 (5 μ m, 4.6 x 50 mm). Conditions: MeCN [eluent A]; water + 0.04% TFA [eluent B]. Gradient: 95% B $\rightarrow$ 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 μ m, 4.6 x 50 mm). Conditions: MeCN [eluent A]; 13 mmol/L NH₃ in water [eluent B]. Gradient: 95% B $\rightarrow$ 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 μ m, 4.6 x 50 mm). Conditions: MeCN [eluent A]; 13 mmol/L NH₃ in water [eluent B]. Gradient: 95% B $\rightarrow$ 5% B over 1.5 min. (flow: 4.5 mL/min.). Detection: UV/Vis + MS.

Abbreviations (as used herein or in the description above):

acac	acetylacetonato
aq.	aqueous
atm	atmosphere
BSA	bovine serum albumin
Boc	Butyloxycarbonyl
d	days
DCC	dicyclohexyl carbodiimide
DCM	dichloromethane
DIBAL	diisobutylaluminium hydride
DIPEA	diisopropyl-ethylamine, Hünig's base
DMA	dimethylacetamide
DMF	dimethylformamide
DMSO	dimethylsulfoxide

dppf	1,1'-bis(diphenylphosphino)ferrocene
EDC	N-(3-dimethylaminopropyl)-N'-ethyl-carbodiimide
eq.	equivalent(s)
Et	ethyl
EtOAc	ethyl acetate
Ex.	example(s)
FC	flash chromatography on SiO ₂
h	hour(s)
HBTU	O-(benzotriazol-1-yl)-N,N,N',N'-tetramethyluronium hexafluorophosphate
HPLC	high performance liquid chromatography
HV	high vacuum conditions
ⁱ Bu	isobutyl
ⁱ Pr	isopropyl
LC-MS	liquid chromatography – mass spectrometry
Lit.	literature
Me	methyl
MeCN	acetonitrile
MeOH	methanol
MTBE	methyl- <i>tert</i> butyl ether
min	minute(s)
NaOAc	sodium acetate
ⁿ BuLi	n-butyl-lithium
NMP	N-methylpyrrolidin-2-one
ⁿ Pr	n-propyl
OAc	acetate
Ph	phenyl
PyBOP	benzotriazol-1-yl-oxy-tris-pyrrolidino-phosphonium- hexafluoro-phosphate
prep.	preparative
rac	racemic
RT	room temperature
s	second(s)
sat.	Saturated
soln.	Solution
TBTU	2-(1H-benzotriazole-1-yl)-1,2,3,3-tetramethyluronium tetrafluoroborate

TFA	trifluoroacetic acid
TFAA	trifluoroacetic anhydride
THF	tetrahydrofuran
TLC	thin layer chromatography
TMS	trimethylsilyl
t _R	retention time

The following examples illustrate the preparation of compounds of the invention but do not at all limit the scope thereof.

General method A for the synthesis of 1,2,3,4-tetrahydroisoquinolines of Structure 1

Listed in Table 1 below are 1,2,3,4-tetrahydroisoquinolines of Structure 1, prepared via Bischler-Napieralski cyclisation of the corresponding amide followed by imine reduction according to the procedure described in WO2004/085403.

Table 1

Tetrahydroisoquinoline of Structure 1	t_R [min] LC-MS / Method	MS-data m/z [M+H]⁺
rac-6,7-Dimethoxy-1-(3-methoxy-benzyl)-1,2,3,4-tetrahydro-isoquinoline.HCl	0.81 / C	314.23
rac-1-Benzo[1,3]dioxol-5-ylmethyl-6,7-dimethoxy-1,2,3,4-tetrahydro-isoquinoline.HCl	0.79 / C	328.18
rac-1-Benzyl-6-methoxy-1,2,3,4-tetrahydro-isoquinoline HCl	0.89 / C	254.19
rac-1-(4-Chloro-benzyl)-6,7-dimethoxy-1,2,3,4-tetrahydro-isoquinoline	0.87 / C	(³⁵ Cl) 318.17
rac-6,7-Dimethoxy-1-(4-methoxy-benzyl)-1,2,3,4-tetrahydro-isoquinoline.HCl	0.80 / C	314.23
rac-6,7-Dimethoxy-1-(3,4,5-trimethoxy-benzyl)-1,2,3,4-tetrahydro-isoquinoline.HCl	0.75 / C	374.22
rac-1-(4-Fluoro-benzyl)-6,7-dimethoxy-1,2,3,4-tetrahydro-isoquinoline.HCl	0.82 / C	302.17
rac-6,7-Dimethoxy-1-naphthalen-2-ylmethyl-1,2,3,4-tetrahydro-isoquinoline	0.91 / C	334.22
rac-1-(2,5-Dimethoxy-benzyl)-6,7-dimethoxy-1,2,3,4-tetrahydro-isoquinoline.HCl	0.82 / C	344.20
rac-1-(2,5-Dimethoxy-benzyl)-5,8-dimethoxy-1,2,3,4-tetrahydro-isoquinoline.HCl	0.92 / C	344.22

rac-1-(3-Fluoro-4-methoxy-benzyl)-6,7-dimethoxy-1,2,3,4-tetrahydro-isoquinoline.HCl	0.80 / C	332.18
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General method B for the synthesis of 1,2,3,4-tetrahydroisoquinolines of Structure 1

Step 1: *N*-Bromosuccinimide (9.89 g, 55.0 mmol, 1.1 eq.) was added cautiously and portionwise over 20 min at RT to a soln. of 1,2,3,4-tetrahydroisoquinoline (6.34 mL, 50.0 mmol, 1.0 eq.) in DCM (130 mL) under argon. After complete addition the reaction mixture was stirred for 2h after which 5M aq. NaOH (30 mL) was added and the mixture was stirred for 2h. The organic layer was separated and washed with water (1x) before being extracted with 2M aq. HCl (2x) and subsequently discarded. The combined acidic aq. extracts were re-basified with 5M aq. NaOH and then re-extracted with DCM (3x). The combined organic extracts were dried over Na₂SO₄, filtered and evaporated *in vacuo* to give 3,4-dihydroisoquinoline as an orange oil that was used directly in Step 2. LC-MS C: t_R = 0.72 min; $[M+H]^+$ = 132.18.

Step 2: The appropriately substituted benzylmagnesium chloride as a soln. in THF (1.14 mmol, 1.5 eq.) was added dropwise to a 5°C soln. of 3,4-dihydroisoquinoline from above (0.76 mmol) in THF (3 mL) under argon and after complete addition the reaction mixture was stirred for 1.5h. The reaction was quenched with sat. aq. NH₄Cl, diluted with H₂O and extracted with DCM (3x). The combined organic extracts were dried over Na₂SO₄, filtered and evaporated *in vacuo* to give the crude product that was purified by FC (eluent: 2.5% -> 10% MeOH in DCM).

Listed in Table 2 below are 1,2,3,4-tetrahydroisoquinolines of Structure 1, prepared according to the above procedure.

Table 2

Tetrahydroisoquinoline of Structure 1	t_R [min] LC-MS / Method	MS-data m/z $[M+H]^+$
rac-1-Naphthalen-1-ylmethyl-1,2,3,4-tetrahydro-isoquinoline	1.01 / C	274.21
rac-1-(3,4-Dimethoxy-benzyl)-1,2,3,4-tetrahydro-isoquinoline	0.83 / C	284.15
rac-1-(3-Methyl-benzyl)-1,2,3,4-tetrahydro-isoquinoline	0.97 / C	238.20

rac-8-(3,4-Dimethoxy-benzyl)-5,6,7,8-tetrahydro-[1,7]naphthyridine

The title compound was prepared starting from 1,7-naphthyridine according to the procedure described in WO2009038812. LC-MS C: t_R = 0.67 min; $[M+H]^+$ = 285.18.

2-Thiophen-3-yl-ethylamine hydrochloride.

A soln. of 3-thiopheneacetonitrile (18.44 g, 0.15 mol) in THF (245 mL) was added dropwise to a RT soln. of 1M borane.THF complex (300 mL, 0.3 mol) under argon and the resulting mixture was heated to reflux for 3h followed by stirring at RT overnight. The reaction mixture was cautiously quenched with MeOH and subsequently concentrated *in vacuo*. The residue was dissolved in MeOH (150 mL) and 4M HCl in dioxane (105 mL, 2.8 eq.) was added cautiously under vigorous stirring and the mixture was stirred for 30 min. The soln. was evaporated *in vacuo* and the residue was re-dissolved in MeOH and re-evaporated. This dissolution and evaporation procedure was repeated a further two times to give the crude product as its HCl salt that was suspended in 3:7 *i*PrOH:EtOAc and stirred for 15 min. The suspension was filtered and the residue was dried *in vacuo* to give the title compound as a white solid (20.73 g). LC-MS A: t_R = 0.33 min; $[M+H+MeCN]^+$ = 169.06.

General method C for the synthesis of substituted 2-thiophen-3-yl-ethylamines 13.

Step 1: Molecular sieves 4A (~10 wt%), butylamine (4.8 mmol, 0.12 eq.) and acetic acid (8 mmol, 0.20 eq.) were added to a soln. of the substituted thiophene-3-carbaldehyde **11** (40.00 mmol, 1 eq.) in nitromethane (23 mL) and the resulting mixture was heated to 95°C for 30 min. The reaction mixture was transferred to a new flask to remove the molecular sieves and the solvent was removed *in vacuo*. The residue was purified by FC (eluent: Hept/EtOAc) to furnish the desired nitro olefin **12**.

Step 2: H₂SO₄ (2.87 mL) was added dropwise to a stirred suspension of LiAlH₄ (4.30 g, 108 mmol, 4.46 eq.) in THF (162 mL) under ice-cooling. After stirring for 20 min a soln. of the nitro olefin **12** (24 mmol, 1.0 eq.) in THF (17 mL) was added dropwise over 20 min. After an additional 10 min the cooling bath was removed and the mixture was heated to a gentle reflux for 5 min. The reaction mixture was then cooled to 0°C and carefully quenched by the dropwise addition of *i*PrOH (18 mL), followed by 2M aq. NaOH (13 mL). The resulting suspension was filtered and the residue was rinsed with THF. The filtrate was concentrated *in vacuo* to give the desired substituted 2-thiophen-3-yl-ethylamine as its free base.

The free amine was dissolved in Et₂O (88 mL) containing *i*PrOH (3 mL) and acidified with 2M HCl in Et₂O soln. (46 mL). The resulting suspension was filtered and the white solid residue was rinsed with Et₂O and dried under high vacuum to afford the desired 2-thiophen-3-yl-ethylamine salt that was used further without purification.

Listed in Table 3 below are substituted 2-thiophen-3-yl-ethylamines **13** and substituted 2-thiophen-3-yl-ethylamine hydrochlorides, prepared according to the above mentioned method using the corresponding substituted thiophene-3-carbaldehyde **11** as starting material.

Table 3

2-thiophen-3-yl-ethylamines 13	t_R [min] LC-MS / Method	MS-data m/z [M+H+MeCN] ⁺
2-(4-Bromo-thiophen-3-yl)-ethylamine	0.28 / A	246.98
2-(5-Methyl-thiophen-3-yl)-ethylamine hydrochloride	0.56 / A	183.4
2-(4,5-Dimethyl-thiophen-3-yl)-ethylamine	0.50 / A	197.31

(2,3-Dihydro-benzo[1,4]dioxin-5-yl)-acetic acid

The title compound was prepared in 3 steps starting from (2,3-dihydro-1,4-benzodioxin-5-yl)methanol as described in US2002/0032205, Example 6. LC-MS B: t_R = 0.60 min; [M+H+MeCN]⁺ = 236.36.

Benzo[1,3]dioxol-4-yl-acetic acid

The title compound was prepared in 3 steps starting from 1,3-benzodioxol-4-ylmethanol as described above for (2,3-dihydro-benzo[1,4]dioxin-5-yl)-acetic acid. LC-MS B: t_R = 0.60 min; [M+H+MeCN]⁺ = 222.09.

General method D for the synthesis of 4,5,6,7-tetrahydro-thieno[2,3-c]pyridines of Structure 1

Step 1: TBTU (8.63 g, 26.88 mmol) was added to a RT soln. of the required arylacetic acid **4** (24.44 mmol 1.0 eq.) and DIPEA (6.3 mL, 36.67 mmol) in DMF (10 mL). After stirring for 5 min a soln. of the 2-thiophen-3-yl-ethylamine **13** or 2-thiophen-3-yl-ethylamine.HCl (24.44 mmol) and DIPEA (6.3 mL, 36.67 mmol) in DMF (10 mL) was added and the resulting mixture was stirred for 16h. The reaction mixture was diluted with MTBE and washed successively with 1M aq. NaOH (1x), 1M aq. HCl (1x) and H₂O (3x). The organic layer was dried over Na₂SO₄, filtered and evaporated *in vacuo* to give the crude product that was either triturated with Et₂O or purified by FC (eluent: Hexane/EtOAc) to give the corresponding amide **14**.

Step 2: POCl₃ (4.88 mL, 52.39 mmol) was added to a RT soln. of the amide from above (10.48 mmol 1.0 eq.) in MeCN (180 mL) and the resulting mixture was heated to 80°C and stirred for 2h. The volatiles were removed *in vacuo* and the residue was dissolved in MeOH and re-evaporated (2x). The residue was re-dissolved in MeOH and cooled to 0°C before NaBH₄ (1.27 g, 33.53 mmol) was added portionwise. After complete addition the reaction mixture was stirred for 10 min before being concentrated *in vacuo* and the residue was partitioned between H₂O and EtOAc. The phases were separated and the aq. phase was re-extracted with EtOAc (2x). The combined organic extracts were washed with brine, dried

over Na₂SO₄, filtered and evaporated *in vacuo* to give the cyclic amine product that was used further without purification.

Listed in Table 4 below are 4,5,6,7-tetrahydro-thieno[2,3-c]pyridines of Structure 1, prepared according to the above procedure.

Table 4

Tetrahydro-thieno[2,3-c]pyridine 1	t_R [min] LC-MS / Method	MS-data m/z [M+H]⁺
rac-7-Naphthalen-2-ylmethyl-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine	0.98 / C	280.16
rac-7-(3,4-Dimethoxy-benzyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine	0.81 / C	290.18
rac-7-(4-Trifluoromethyl-benzyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine	0.96 / C	297.88
rac-7-Benzyl-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine	0.90 / C	230.19
rac-7-Naphthalen-1-ylmethyl-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine	0.99 / C	280.19
rac-3-Bromo-7-(3,4-dimethoxy-benzyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine	0.99 / C	368.0
rac-7-(4-Methoxy-benzyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine	0.87 / C	260.14
rac-7-(2,3-Dimethoxy-benzyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine	0.87 / C	290.15
rac-7-(3-Methoxy-benzyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine	0.87 / C	260.08
rac-7-(3,5-Dimethoxy-benzyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine	0.87 / C	290.16
rac-7-(3,4-Dichloro-benzyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine	0.99 / C	297.81
rac-7-(2,3-Dihydro-benzo[1,4]dioxin-6-ylmethyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine	0.85 / C	288.14
rac-7-(4-Trifluoromethoxy-benzyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine	0.97 / C	314.11
rac-7-(2,3-Dihydro-benzo[1,4]dioxin-5-ylmethyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine	0.87 / C	288.13
rac-7-Benzo[1,3]dioxol-4-ylmethyl-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine	0.87 / C	274.11
rac-7-Benzo[1,3]dioxol-5-ylmethyl-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine	0.87 / C	274.11
rac-7-(2,4-Dichloro-benzyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine	1.03 / C	297.82
rac-7-Pyridin-2-ylmethyl-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine	Broad peak / C	231.19
rac-7-(3-Trifluoromethyl-benzyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine	0.95 / C	297.88
rac-7-(2,6-Dichloro-benzyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine	1.02 / C	297.81
rac-7-(1H-Indol-3-ylmethyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine	0.84 / C	269.14
rac-7-(1-Methyl-1H-indol-3-ylmethyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine	0.92 / C	283.16

rac-7-(1H-Benzoimidazol-2-ylmethyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine	0.80 / C	270.15
rac-7-(1H-Indazol-3-ylmethyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine	0.78 / C	270.14
rac-7-(2-Methyl-thiazol-4-ylmethyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine	0.77 / C	251.12
rac-8-(4,5,6,7-Tetrahydro-thieno[2,3-c]pyridin-7-ylmethyl)-quinoline	0.87 / C	281.1
rac-7-(4-Benzyloxy-3-methoxy-benzyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine	0.96 / C	366.16
rac-7-(3-Iodo-benzyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine	1.00 / C	356.03
rac-7-(4-Iodo-benzyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine	0.99 / C	356.0
rac-6-(4,5,6,7-Tetrahydro-thieno[2,3-c]pyridin-7-ylmethyl)-quinoline	0.78 / C	281.11
rac-7-(4,5,6,7-Tetrahydro-thieno[2,3-c]pyridin-7-ylmethyl)-quinoline	0.79 / C	281.13
rac-2-Methoxy-4-(4,5,6,7-tetrahydro-thieno[2,3-c]pyridin-7-ylmethyl)-phenol	0.73 / C	276.08
rac-2-Methoxy-5-(4,5,6,7-tetrahydro-thieno[2,3-c]pyridin-7-ylmethyl)-phenol	0.74 / C	276.13
rac-7-(3,4-Dimethoxy-benzyl)-2,3-dimethyl-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine	0.90 / C	318.15
rac-7-(3,4-Dimethoxy-benzyl)-2-methyl-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine	0.86 / C	304.15
rac-7-(6-Chloro-pyridin-3-ylmethyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine	0.80 / C	306.02
rac-2-(4,5,6,7-Tetrahydro-thieno[2,3-c]pyridin-7-ylmethyl)-benzonitrile	0.84 / C	255.14
rac-3-(4,5,6,7-Tetrahydro-thieno[2,3-c]pyridin-7-ylmethyl)-benzonitrile	0.84 / C	255.15
rac-4-(4,5,6,7-Tetrahydro-thieno[2,3-c]pyridin-7-ylmethyl)-benzonitrile	0.84 / C	255.12
rac-7-Pyridin-3-ylmethyl-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine	0.73 / C	231.2
rac-7-(6-Chloro-pyridin-2-ylmethyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine	0.83 / C	265.05
rac-7-(3,4-Difluoro-benzyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine	0.91 / C	265.94
rac-7-(2-Chloro-benzyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine	0.95 / C	264.12
rac-7-(3-Chloro-benzyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine	0.96 / C	264.06

rac-7-(4-[1,2,3]Triazol-2-yl-benzyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine hydrochloride and rac-7-(4-[1,2,3]triazol-1-yl-benzyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine hydrochloride

Step 1: A soln. of Boc₂O (227 mg, 1.04 mmol) in DCM (5 mL) was added dropwise to a RT soln. of rac-7-(4-iodo-benzyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine (363 mg, 1.02 mmol) and Et₃N (0.29 mL, 2.1 mmol) in DCM (15 mL) and the reaction mixture was stirred for 30 min. The reaction was quenched by the addition of 1M aq. citric acid (10 mL) and the mixture was stirred vigorously for 10 min. The layers were separated and the aq. layer was re-

extracted with DCM (2x). The combined organic layers were washed with water, dried over Na₂SO₄, filtered and evaporated *in vacuo* to give the Boc-protected product that was used directly in the next step below. LC-MS C: t_R = 1.15 min; no ionisation.

Step 2: 1*H*-1,2,3-triazole (140 mg, 2 mmol), Cs₂CO₃ (658 mg, 2 mmol), CuI (9.6 mg, 0.05 mmol) and *rac. trans-N,N*-diaminomethylcyclohexane (29 mg, 2 mmol) were added to a RT soln. of *rac*-7-(4-iodo-benzyl)-4,7-dihydro-5*H*-thieno[2,3-*c*]pyridine-6-carboxylic acid tert-butyl ester (460 mg, 1 mmol) in DMF (4 mL) under argon and the resulting mixture was heated to 120°C for 17h. The mixture was cooled to RT and partitioned between water and EtOAc. The layers were separated and the aq. phase was re-extracted with EtOAc (2x). The combined organic layers were washed with water (2x), dried over Na₂SO₄, filtered and evaporated *in vacuo* to give the crude product that was purified by FC (eluent: 100% DCM → 99:1 DCM:MeOH) to give *rac*-7-(4-[1,2,3]triazol-2-yl-benzyl)-4,7-dihydro-5*H*-thieno[2,3-*c*]pyridine-6-carboxylic acid tert-butyl ester (167 mg). LC-MS C: t_R = 1.07 min; [M+H]⁺ = 397.14. Further elution afforded *rac*-7-(4-[1,2,3]triazol-1-yl-benzyl)-4,7-dihydro-5*H*-thieno[2,3-*c*]pyridine-6-carboxylic acid tert-butyl ester (116 mg). LC-MS C: t_R = 0.94 min; [M+H]⁺ = 397.11.

Step 3a: 4M HCl in dioxane (2 mL, 19 eq.) was added to a RT soln. of *rac*-7-(4-[1,2,3]triazol-2-yl-benzyl)-4,7-dihydro-5*H*-thieno[2,3-*c*]pyridine-6-carboxylic acid tert-butyl ester (167 mg, 0.42 mmol) in dioxane (1 mL) under argon and the resulting mixture was stirred for 1h after which it appeared as a white suspension. The product was collected by filtration washing with Et₂O and dried *in vacuo* to give the title compound as a white solid (137 mg). LC-MS B: t_R = 0.50 min; [M+H]⁺ = 297.22.

Step 3b: Boc-deprotection of *rac*-7-(4-[1,2,3]triazol-1-yl-benzyl)-4,7-dihydro-5*H*-thieno[2,3-*c*]pyridine-6-carboxylic acid tert-butyl ester as described above gave the 2nd title compound as a beige solid (86 mg). LC-MS B: t_R = 0.42 min; [M+H]⁺ = 297.07.

***rac*-7-(3-[1,2,3]Triazol-2-yl-benzyl)-4,5,6,7-tetrahydro-thieno[2,3-*c*]pyridine hydrochloride and *rac*-7-(3-[1,2,3]triazol-1-yl-benzyl)-4,5,6,7-tetrahydro-thieno[2,3-*c*]pyridine hydrochloride**

The title compounds were prepared in analogy to *rac*-7-(4-[1,2,3]triazol-2-yl-benzyl)-4,5,6,7-tetrahydro-thieno[2,3-*c*]pyridine hydrochloride and *rac*-7-(4-[1,2,3]triazol-1-yl-benzyl)-4,5,6,7-tetrahydro-thieno[2,3-*c*]pyridine hydrochloride starting with *rac*-7-(3-iodo-benzyl)-4,5,6,7-tetrahydro-thieno[2,3-*c*]pyridine. LC-MS B: t_R = 0.50 min; [M+H]⁺ = 297.12 and t_R = 0.43 min; [M+H]⁺ = 297.27 respectively.

rac-7-(4-Cyclopropoxy-3-methoxy-benzyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine hydrochloride

Step 1: Boc-protection of rac-2-methoxy-4-(4,5,6,7-tetrahydro-thieno[2,3-c]pyridin-7-ylmethyl)-phenol as described above gave rac-7-(4-hydroxy-3-methoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridine-6-carboxylic acid tert-butyl ester. LC-MS C: t_R = 0.94 min; $[M+H]^+$ = 376.08.

Step 2: $Cu(OAc)_2$ (167 mg, 0.92 mmol) was stirred in DCM (6 mL) under an air atmosphere for 10 min before vinylboronic anhydride.pyridine complex (147 mg, 0.61 mmol), rac-7-(4-hydroxy-3-methoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridine-6-carboxylic acid tert-butyl ester (345 mg, 0.92 mmol) and pyridine (0.75 mL, 9.19 mmol) were added and the mixture was stirred at RT overnight. The reaction mixture was filtered through a pad of celite rinsing with additional DCM. The filtrate was evaporated *in vacuo* to give rac-7-(3-methoxy-4-vinyloxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridine-6-carboxylic acid tert-butyl ester (241 mg) as a yellow oil that was used further without purification. LC-MS C: t_R = 1.06 min; $[M+H]^+$ = 402.04.

Step 3: A soln. of TFA (0.11 mL, 1.47 mmol) in DCM (0.75 mL) was added to a 0°C soln. of Et_2Zn (1.47 mL, 2 eq.) 1M soln. in hexanes in DCM (1.5 mL) under argon and the resulting mixture was stirred for 20 min before a soln. of CH_2I_2 (0.12 mL, 1.47 mmol) in DCM (0.75 mL) was added. After a further 20 min a soln. of rac-7-(3-methoxy-4-vinyloxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridine-6-carboxylic acid tert-butyl ester (295 mg, 0.74 mmol) in DCM (1 mL) was added and the ice bath was removed. The reaction mixture was stirred for 30 min at RT before being quenched with sat. aq. $NaHCO_3$ soln. and stirred for 10 min. The solids were removed by filtration through a celite pad rinsing with DCM and the layers were separated. The organic layer was washed with water (1x), dried over Na_2SO_4 , filtered and evaporated *in vacuo* to give crude rac-7-(4-cyclopropoxy-3-methoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridine-6-carboxylic acid tert-butyl ester that was purified by prep. HPLC (column: Waters X-bridge, 30x75 mm, 10 μ m, UV/MS, basic conditions) LC-MS C: t_R = 1.05 min; $[M+H]^+$ = 416.06.

Step 4: Boc-deprotection of rac-7-(4-cyclopropoxy-3-methoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridine-6-carboxylic acid tert-butyl ester as described above gave the title compound as an orange solid (100 mg). LC-MS C: t_R = 0.87 min; No ionisation.

rac-2-[2-Methoxy-4-(4,5,6,7-tetrahydro-thieno[2,3-c]pyridin-7-ylmethyl)-phenoxy]-ethanol hydrochloride

Step 1: 2-Chloroethanol (150 μ L, 2.25 mmol) was added to a mixture of rac-7-(4-hydroxy-3-methoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridine-6-carboxylic acid tert-butyl ester (375 mg, 1.0 mmol), K_2CO_3 (221 mg, 1.60 mmol) and KI (1 mg) in DMSO (5 mL) and the reaction mixture was heated to 85°C and stirred for 3h. The reaction mixture was concentrated *in vacuo* and the residue was diluted with MTBE (30 mL) and washed with water (4x5 mL). The organic layer was dried over Na_2SO_4 , filtered and evaporated *in vacuo* to give crude tert-butyl rac-7-(4-(2-hydroxyethoxy)-3-methoxybenzyl)-4,5-dihydrothieno[2,3-c]pyridine-6(7H)-carboxylate that was purified by prep. HPLC (column: Waters X-bridge, 30x75 mm, 10 μ m, UV/MS, basic conditions) LC-MS C: t_R = 0.90 min; $[M+H]^+$ = 420.04.

Step 2: Boc-deprotection of rac-7-(4-(2-hydroxyethoxy)-3-methoxybenzyl)-4,5-dihydrothieno[2,3-c]pyridine-6(7H)-carboxylate as described above gave the title compound as a white solid (95 mg). LC-MS C: t_R = 0.71 min; $[M+H]^+$ = 320.12.

rac-2-Bromo-7-(3,4-dimethoxy-benzyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine

Step 1: Boc-protection of rac-7-(3,4-dimethoxy-benzyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine as described above gave rac-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridine-6-carboxylic acid tert-butyl ester. LC-MS C: t_R = 1.01 min; $[M+H]^+$ = 390.1.

Step 2: A soln. of NBS (653 mg, 3.67 mmol) in MeCN (10 mL) was added over a period of 5 min to a RT soln. of rac-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridine-6-carboxylic acid tert-butyl ester (1.3 g, 3.34 mmol) in MeCN (40 mL). The reaction mixture was heated to 75°C after which the volatiles were removed *in vacuo* and the residue was redissolved in MeCN and purified by prep. HPLC (column: Waters X-bridge, 30x75 mm, 10 μ m, UV/MS, basic conditions) to give a 1:1 inseparable mixture of rac-2-bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridine-6-carboxylic acid tert-butyl ester and rac-7-(2-bromo-4,5-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridine-6-carboxylic acid tert-butyl ester (0.55 g). LC-MS C: t_R = 1.07 and 1.09 min; $[M(^{79}Br)+H]^+$ = 411.83.

Step 3: TFA (0.53 mL, 6.9 mmol) was added to a RT soln. of the 1:1 mixture of regioisomers from above (0.54 g, 1.15 mmol) in DCM (5 mL). After stirring for 2h the volatiles were removed *in vacuo* and the residue was partitioned between EtOAc and sat. aq. $NaHCO_3$ soln. The phases were separated and the aq. phase was re-extracted with EtOAc (2x). The combined organic layers were washed with water, dried over Na_2SO_4 , filtered and evaporated *in vacuo* to give a 1:1 inseparable mixture of the title compound and rac-7-(2-

bromo-4,5-dimethoxy-benzyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine as a brown oil (402 mg). LC-MS C: $t_R = 0.90$ min; $[M(^{79}\text{Br})+H]^+ = 368.00$.

rac-5-(4,5,6,7-Tetrahydro-thieno[2,3-c]pyridin-7-ylmethyl)-pyridine-2-carbonitrile hydrochloride

Step 1: Boc-protection of rac-7-(6-chloro-pyridin-3-ylmethyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine as described above gave rac-7-(6-chloro-pyridin-3-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyridine-6-carboxylic acid tert-butyl ester. LC-MS D: $t_R = 0.99$ min; $[M(^{35}\text{Cl})+H]^+ = 365.15$.

Step 2: A mixture of Pd(II) trifluoroacetate (41 mg, 0.12 mmol), zinc powder (34 mg, 0.52 mmol), racemic-2-(di-*t*-butylphosphino)-1,1'-binaphtyl (96 mg, 0.24 mmol), rac-7-(6-chloro-pyridin-3-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyridine-6-carboxylic acid tert-butyl ester (1.0 g, 2.74 mmol) and $\text{Zn}(\text{CN})_2$ (180 mg, 1.54 mmol) in DMA (15 ml) was heated to 95°C for 2.5h. The reaction mixture was cooled to RT and quenched into a 1:1 mixture of brine and ice-water and the resulting mixture was 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 FC (eluent: 1:1 hexane:EtOAc) to give rac-7-(6-cyano-pyridin-3-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyridine-6-carboxylic acid tert-butyl ester as a white solid (0.69 g) LC-MS D: $t_R = 0.94$ min; $[M+H+\text{MeCN}]^+ = 397.22$.

Step 3: Boc-deprotection of rac-7-(6-cyano-pyridin-3-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyridine-6-carboxylic acid tert-butyl ester using 4M HCl in dioxane as described above gave the title compound as a white solid (0.61 g). LC-MS D: $t_R = 0.77$ min; $[M+H+\text{MeCN}]^+ = 297.06$.

rac-7-(6-Methyl-pyridin-3-ylmethyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine dihydrochloride

Step 1: Me_2Zn 1.2M soln. in toluene (4.62 ml, 5.54 mmol) was added dropwise to a RT soln. of rac-7-(6-chloro-pyridin-3-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyridine-6-carboxylic acid tert-butyl ester (1.0 g, 2.74 mmol), and [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(II) complex with CH_2Cl_2 (224 mg, 0.27 mmol) in dioxane (20 mL) and the resulting mixture was stirred overnight. The solvent was evaporated *in vacuo* and the residue was partitioned between water and EtOAc. The phases were separated and the aq. phase was re-extracted with EtOAc (2x). The combined organic extracts were dried over Na_2SO_4 , filtered and evaporated *in vacuo* to give the crude product that was purified by FC (eluent: 1:1 hexane:EtOAc) to give rac-7-(6-methyl-pyridin-3-

ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyridine-6-carboxylic acid tert-butyl ester as a white solid (0.74 g) LC-MS D: t_R = 0.92 min; $[M+H]^+$ = 345.22.

Step 2: Boc-deprotection of rac-7-(6-methyl-pyridin-3-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyridine-6-carboxylic acid tert-butyl ester using 4M HCl in dioxane as described above gave the title compound as a white solid (0.61 g). LC-MS D: t_R = 0.73 min; $[M+H]^+$ = 245.19.

rac-7-(6-Ethyl-pyridin-3-ylmethyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine dihydrochloride

The title compound was prepared in analogy to rac-7-(6-methyl-pyridin-3-ylmethyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine dihydrochloride using Et_2Zn 1M soln. in hexane. LC-MS D: t_R = 0.78 min; $[M+H]^+$ = 258.97.

rac-7-(3-Pyrimidin-2-yl-benzyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine hydrochloride

Step 1: A mixture of rac-7-(3-iodo-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridine-6-carboxylic acid tert-butyl ester (243 mg, 0.53 mmol) and Et_3N (0.22 mL, 1.60 mmol) in 2-methyltetrahydrofuran (1.5 mL) was degassed with N_2 for 1 min. 4,4,5,5-Tetramethyl-1,3,2-dioxaborolane (116 μ L, 0.80 mmol) was added dropwise and the mixture was further degassed for 30s before tri-*o*-tolylphosphine (8 mg, 0.03 mmol) followed by $Pd(OAc)_2$ (3 mg, 0.01 mmol) were added. The reaction mixture was heated to 75°C for 20h after which it was cooled in an ice-bath and quenched with sat. aq. NH_4Cl soln. (5 mL). The reaction mixture was diluted with water (5 mL) and MTBE (20 mL) and filtered through a pad of celite rinsing with additional MTBE. The layers from the filtrate were separated and the aq. layer was re-extracted with MTBE (2x). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and evaporated *in vacuo* to give rac-7-[3-(4,4,5,5-tetramethyl-1,3,2)dioxaborolan-2-yl)-benzyl]-4,7-dihydro-5H-thieno[2,3-c]pyridine-6-carboxylic acid tert-butyl ester as an orange solid (0.25 g) that was used further without purification. LC-MS D: t_R = 1.15 min; $[M+H]^+$ = 456.22.

Step 2: A mixture of rac-7-[3-(4,4,5,5-tetramethyl-1,3,2)dioxaborolan-2-yl)-benzyl]-4,7-dihydro-5H-thieno[2,3-c]pyridine-6-carboxylic acid tert-butyl ester (0.25 g, 0.55 mmol), 2-chloropyrimidine (75 mg, 0.66 mmol), 2M aq. Na_2CO_3 (3.3 mL) and 2-methyltetrahydrofuran (4.7 mL) was degassed with N_2 for 20s. $PdCl_2(dppf)$.DCM (18 mg, 0.02 mmol) was added and the reaction mixture was heated to 75°C for 22h. The reaction mixture was diluted with water (5 mL) and MTBE (20 mL) and filtered through a pad of celite rinsing with additional MTBE. The layers from the filtrate were separated and the aq. layer was re-extracted with MTBE (2x). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and evaporated *in vacuo* to give the crude product that was purified by prep. HPLC (column:

Waters X-bridge, 30x75 mm, 10 μ m, UV/MS, basic conditions) to give rac-7-(3-pyrimidin-2-yl-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridine-6-carboxylic acid tert-butyl ester as an orange solid (38 mg). LC-MS Basic: t_R = 1.04 min; $[M+H]^+$ = 408.17.

Step 3: Boc-deprotection of rac-7-(3-pyrimidin-2-yl-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridine-6-carboxylic acid tert-butyl ester using 4M HCl in dioxane as described above gave the title compound as a white solid (32 mg). LC-MS D: t_R = 0.84 min; $[M+H]^+$ = 308.17.

rac-7-(3-Pyrazol-1-yl-benzyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine hydrochloride

Step 1: A mixture of Fe(acac)₃ (70 mg, 0.2 mmol), CuO (5 mg, 0.07 mmol), 1H-pyrazole (67 mg, 1.0 mmol), Cs₂CO₃ (429 mg, 1.32 mmol) and rac-7-(3-iodo-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridine-6-carboxylic acid tert-butyl ester (300 mg, 0.66 mmol) in DMF (2 mL) was heated to 90°C for 20h. The reaction mixture was cooled to RT, filtered through a cotton wool plug and directly purified by prep. HPLC (column: Waters X-bridge, 30x75 mm, 10 μ m, UV/MS, basic conditions) to give rac-7-(3-pyrazol-1-yl-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridine-6-carboxylic acid tert-butyl ester as a white solid (10 mg). LC-MS D: t_R = 1.03 min; $[M+H]^+$ = 396.18.

Step 2: Boc-deprotection of rac-7-(3-pyrazol-1-yl-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridine-6-carboxylic acid tert-butyl ester using 4M HCl in dioxane as described above gave the title compound as a white solid (8 mg). LC-MS D: t_R = 0.85 min; $[M+H]^+$ = 296.19.

rac-7-(3-[1,2,4]Triazol-1-yl-benzyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine hydrochloride

The title compound was prepared in analogy to rac-7-(3-pyrazol-1-yl-benzyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine hydrochloride using 1,2,4-triazole. LC-MS D: t_R = 0.77 min; $[M+H]^+$ = 297.1.

General method E for the synthesis of 4,5,6,7-tetrahydro-thieno[3,2-c]pyridines of Structure 1

rac-4-Naphthalen-1-ylmethyl-4,5,6,7-tetrahydro-thieno[3,2-c]pyridine

Step 1: TBTU (2.17 g, 6.77 mmol) was added to a soln. of 2-thiopheneethylamine (0.78 g, 6.16 mmol), 1-naphthylacetic acid (1.15 g, 6.16 mmol) and DIPEA (2.64 mL, 15.39 mmol) in DMF (10 mL) and the resulting mixture was stirred for 10 min. The reaction mixture was diluted with MTBE and washed successively with 1M aq. NaOH (1x), 1M aq. HCl (1x) and H₂O (3x). The organic layer was dried over Na₂SO₄, filtered and evaporated *in vacuo* to give the crude product that was triturated with Et₂O to give 2-naphthalen-1-yl-N-(2-thiophen-2-yl-ethyl)-acetamide as a beige solid (1.55 g). LC-MS A: t_R = 0.71 min; $[M+H+MeCN]^+$ = 337.22.

Step 2: POCl₃ (2.41 mL, 25.90 mmol) was added to a RT soln. of the amide from above (1.53 g, 5.18 mmol) in MeCN (90 mL) and the resulting mixture was heated to 80°C and stirred for 2h. The volatiles were removed *in vacuo* and the residue was dissolved in MeOH and re-evaporated (2x). The residue was re-dissolved in MeOH (20 mL) and cooled to 0°C before NaBH₄ (0.63 g, 16.57 mmol) was added portionwise. After complete addition the reaction mixture was stirred for 10 min before being concentrated *in vacuo* and the residue was partitioned between water and EtOAc. The phases were separated and the aq. phase was re-extracted with EtOAc (2x). The combined organic extracts were washed with brine, dried over Na₂SO₄, filtered and evaporated *in vacuo* to give the title compound (1.48 g) that was used further without purification. LC-MS C: t_R = 0.98 min; [M+H]⁺ = 280.18.

General method F for the synthesis of 4,5,6,7-tetrahydro-thieno[3,4-c]pyridines of Structure 1

rac-4-(3,4-Dimethoxy-benzyl)-1-methyl-4,5,6,7-tetrahydro-thieno[3,4-c]pyridine

Step 1: 1M Borane.THF complex (103 mL, 0.1 mol) was added dropwise to a RT soln. of 2-methylthiophene-3-carboxylic acid (5.0 g, 35.4 mmol) in THF (60 mL) under argon and the resulting mixture was stirred for 2h. The reaction mixture was cautiously quenched with MeOH and subsequently concentrated *in vacuo*. The residue was purified by FC (eluent: 8:1->5:1 hexane:EtOAc) to give (2-methyl-thiophen-3-yl)-methanol as a colourless oil (4.17 g). ¹H NMR (CDCl₃) δ_H: 7.04 (m, 2 H), 4.63 (d, *J* = 5.2 Hz, 2 H), 2.48 (s, 3 H), 1.49 (t, *J* = 5.3 Hz, 1 H).

Step 2: MnO₂ (44.59 g, 0.51 mol) was added portionwise to a RT soln. of (2-methyl-thiophen-3-yl)-methanol (4.17 g, 32.53 mmol) in DCM (350 mL) and the resulting mixture was stirred for 18h. The reaction mixture was filtered through a pad of celite rinsing with additional DCM. The filtrate was evaporated *in vacuo* to give 2-methyl-thiophene-3-carbaldehyde as a yellow liquid (3.66 g). LC-MS C: t_R = 0.73 min; No ionisation, ¹H NMR (CDCl₃) δ_H: 10.05 (m, 1 H), 7.41 (m, 1 H), 7.10 (m, 1 H), 2.79 (m, 3 H).

Step 3: Molecular sieves 4A (~10 wt%), butylamine (0.34 mL, 3.41 mmol) and acetic acid (0.34 mL, 5.91 mmol) were added to a soln. of 2-methyl-thiophene-3-carbaldehyde (3.65 g, 28.9 mmol) in nitromethane (16 mL) and the resulting mixture was heated to 95°C for 30 min. The reaction mixture was transferred to a new flask to remove the molecular sieves and the solvent was removed *in vacuo*. The residue was purified by FC (eluent: DCM) to furnish 2-methyl-3-(*E*-2-nitrovinyl)thiophene as an orange solid (4.55 g). LC-MS B: t_R = 0.74 min; No ionisation, ¹H NMR (CDCl₃) δ_H: 8.06 (m, 1 H), 7.46 (m, 1 H), 7.14 (m, 2 H), 2.64 (m, 3 H).

Step 4: H₂SO₄ (3.2 mL) was added dropwise to a stirred suspension of LiAlH₄ (4.56 g, 120 mmol) in THF (170 mL) under ice-cooling. After stirring for 20 min a soln. of 2-methyl-3-(*E*-2-nitrovinyl)thiophene (4.55 g, 26.9 mmol) in THF (20 mL) was added dropwise over 20 min. After an additional 10 min the cooling bath was removed and the mixture was heated to a gentle reflux for 5 min. The reaction mixture was then cooled to 0°C and carefully quenched by the dropwise addition of *i*PrOH (20 mL), followed by 2M aq. NaOH (14 mL). The resulting suspension was filtered and the residue was rinsed with THF. The filtrate was concentrated *in vacuo* and then re-dissolved in Et₂O (100 mL) containing 1% *i*PrOH. An excess of 2M HCl in Et₂O was added and the mixture was stirred for 30 min before being filtered to give 2-(2-methyl-thiophen-3-yl)-ethylamine hydrochloride as a white solid (2.82 g). LC-MS B: *t*_R = 0.37 min; [M+H]⁺ = 142.24.

Step 5: TBTU (735 mg, 2.29 mmol) was added to a RT soln. of 3,4-dimethoxyphenylacetic acid (409 mg, 2.08 mmol) and DIPEA (0.45 mL, 2.6 mmol) in DMF (3 mL). After stirring for 5 min a soln. of 2-(2-methyl-thiophen-3-yl)-ethylamine hydrochloride (370 mg, 2.08 mmol) and DIPEA (0.45 mL, 2.6 mmol) in DMF (1.5 mL) was added and the resulting mixture was stirred for 30 min. The reaction mixture was diluted with MTBE and washed successively with 1M aq. NaOH (1x), 1M aq. HCl (1x) and H₂O (3x). The organic layer was dried over Na₂SO₄, filtered and evaporated *in vacuo* to give the crude product that was filtered through a silica plug eluting with TBME to give 2-(3,4-dimethoxyphenyl)-*N*-[2-(2-methyl-thiophen-3-yl)-ethyl]acetamide as a yellow oil (569 mg). LC-MS C: *t*_R = 0.77 min; [M+H]⁺ = 320.17.

Step 6: POCl₃ (0.75 mL, 8.1 mmol) was added to a RT soln. of 2-(3,4-dimethoxy-phenyl)-*N*-[2-(2-methyl-thiophen-3-yl)-ethyl]-acetamide (517 mg, 1.62 mmol) in MeCN (25 mL) and the resulting mixture was heated to 80°C and stirred for 2h. The volatiles were removed *in vacuo* and the residue was dissolved in MeOH and re-evaporated (2x). The residue was re-dissolved in MeOH (5 mL) and cooled to 0°C before NaBH₄ (196 mg, 5.18 mmol) was added portionwise. After complete addition the reaction mixture was stirred for 10 min before being concentrated *in vacuo* and the residue was partitioned between water and EtOAc. The phases were separated and the aq. phase was re-extracted with EtOAc (2x). The combined organic extracts were washed with brine, dried over Na₂SO₄, filtered and evaporated *in vacuo* to give the title compound as an orange solid (212 mg) that was used further without purification. LC-MS C: *t*_R = 0.86 min; [M+H]⁺ = 304.16.

rac-4-(3,4-Dimethoxy-benzyl)-1,3-dimethyl-4,5,6,7-tetrahydro-thieno[3,4-c]pyridine

The title compound was prepared in analogy to rac-4-(3,4-dimethoxy-benzyl)-1-methyl-4,5,6,7-tetrahydro-thieno[3,4-c]pyridine in 4 steps starting from 2,5-dimethylthiophene-3-carboxaldehyde. LC-MS C: *t*_R = 0.92 min; [M+H]⁺ = 318.19.

rac-1-Bromo-4-(3,4-dimethoxy-benzyl)-4,5,6,7-tetrahydro-thieno[3,4-c]pyridine

Step 1: A soln. of Br₂ (0.93 mL, 18 mmol) in AcOH (5 mL) was added over 10 min to a 0°C soln. of 2-thiophen-3-yl-ethylamine hydrochloride (2.95 g, 18 mmol) in AcOH (10 mL). The resulting suspension was warmed to RT and stirred for 5 min. The reaction mixture was basified with 5M aq. NaOH soln. under ice-cooling and then extracted with MTBE (3x). The combined organic extracts were washed with water (2x) and then extracted with 1M aq. HCl (2x). The combined acidic aq. extracts were back extracted once with MTBE and then re-basified with 2M aq. NaOH soln. and finally re-extracted with MTBE (3x). The combined MTBE extracts were dried over Na₂SO₄, filtered and evaporated *in vacuo* to give 2-(2-bromo-thiophen-3-yl)ethylamine as an orange oil (2.89 g). ¹H NMR (CDCl₃) δ_H: 7.24 (m, 1 H), 6.85 (m, 1 H), 2.96 (m, 2 H), 2.75 (t, *J* = 6.8 Hz, 2 H), 1.27 (d, *J* = 0.8 Hz, 2 H).

Step 2: TBTU (4.9 g, 15.26 mmol) was added to a RT soln. of 3,4-dimethoxyphenylacetic acid (2.72 g, 13.88 mmol) and DIPEA (3.56 mL, 15.26 mmol) in DMF (20 mL). After stirring for 5 min a soln. of 2-(2-bromo-thiophen-3-yl)-ethylamine (2.86 g, 2.08 mmol) and DIPEA (0.45 mL, 2.6 mmol) in DMF (1.5 mL) was added and the resulting mixture was stirred for 6 h. The reaction mixture was diluted with MTBE and washed successively with 1M aq. NaOH (1x), 1M aq. HCl (1x) and H₂O (3x). The organic layer was dried over Na₂SO₄, filtered and evaporated *in vacuo* to give the crude product that was filtered through a silica plug eluting with TBME to give *N*-[2-(2-bromo-thiophen-3-yl)-ethyl]-2-(3,4-dimethoxyphenyl)acetamide as a beige solid (3.47 g). LC-MS C: t_R = 0.79 min; [M(⁷⁹Br)+H]⁺ = 383.93.

Step 3: A soln. of Tf₂O (4.84 mL, 28.75 mmol) in DCM (25 mL) was added dropwise over 60 min to a 0°C soln. of *N*-[2-(2-bromo-thiophen-3-yl)-ethyl]-2-(3,4-dimethoxyphenyl)acetamide (2.21 g, 5.75 mmol) and DMAP (2.11 g, 17.25 mmol) in DCM (150 mL). The reaction mixture was stirred for 2h before the cooling bath was removed and stirring was continued overnight. The reaction mixture was cooled to 0°C and carefully quenched with sat. aq. Na₂CO₃ soln. The layers were separated and the organic layer was washed with water (2x) and 0.5M aq. HCl. The organic layer was dried over Na₂SO₄, filtered and evaporated *in vacuo* and the residue was dissolved in MeCN and purified by prep. HPLC (column: Waters X-bridge, 30x75 mm, 10 μm, UV/MS, basic conditions) to give the imine intermediate (300 mg). This intermediate was dissolved in MeOH (5 mL) and cooled to 0°C before NaBH₄ (696 mg, 18.4 mmol) was added portionwise. After complete addition the reaction mixture was stirred for 20 min before being concentrated *in vacuo* and the residue was partitioned between water and EtOAc. The phases were separated and the aq. phase was re-extracted with EtOAc (2x). The combined organic extracts were washed with brine, dried over Na₂SO₄, filtered and

evaporated *in vacuo* to give the title compound as an orange solid (281 mg) that was used further without purification. LC-MS C: $t_R = 0.91$ min; $[M(^{79}\text{Br})+H]^+ = 367.95$.

General method G for the synthesis of 4,5,6,7-tetrahydropyrazolo[3,4-c]pyridines of Structure 1

rac-7-(1-Methyl-4,5,6,7-tetrahydro-1H-pyrazolo[3,4-c]pyridin-7-ylmethyl)quinoline and rac-7-(2-Methyl-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-c]pyridin-7-ylmethyl)quinoline

Step 1: A soln. of 2-(1-methyl-1H-pyrazol-4-yl)ethan-1-amine (500 mg, 3.99 mmol) and DIPEA (1.03 mL, 5.99 mmol) in DMF (2 mL) was added to a RT soln. of 7-quinolineacetic acid (748 mg, 3.99 mmol), DIPEA (1.03 mL, 5.99 mmol) and TBTU (1.35 g, 4.194 mmol) in DMF (2 mL) and the resulting mixture was stirred for 48h. Water was added (5 mL) and the mixture was basified with sat. aq. NaHCO_3 soln. and 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 prep. HPLC (column: Waters X-bridge, 30x75 mm, 10 μm , UV/MS, basic conditions) to give N-[2-(1-methyl-1H-pyrazol-4-yl)-ethyl]-2-quinolin-7-yl-acetamide as a light yellow oil (235 mg). LC-MS D: $t_R = 0.61$ min; $[M+H]^+ = 295.19$.

Step 2: POCl_3 (372 μL , 3.99 mmol) was added to a soln. of N-[2-(1-methyl-1H-pyrazol-4-yl)-ethyl]-2-quinolin-7-yl-acetamide (235 mg, 0.80 mmol) in MeCN (10 mL) and the resulting mixture was heated to 80°C and stirred overnight. The volatiles were removed *in vacuo* and the residue was dissolved in MeOH and re-evaporated (2x). The residue was re-dissolved in MeOH (10 mL) and cooled to 0°C before NaBH_4 (97 mg, 2.56 mmol) was added portionwise. After complete addition the reaction mixture was stirred for 10 min before being concentrated *in vacuo* and the residue was partitioned between water and EtOAc. The phases were separated and the aq. phase was re-extracted with EtOAc (2x). The combined organic extracts were washed with brine, dried over Na_2SO_4 , filtered and evaporated *in vacuo* to give approximately a 1:5 inseparable mixture of the title compounds respectively as a brown oil (164 mg) that was used further without purification. LC-MS D: $t_R = 0.65$ min; $[M+H]^+ = 279.18$.

rac-7-(3,4-Dimethoxy-benzyl)-1-methyl-4,5,6,7-tetrahydro-1H-pyrazolo[3,4-c]pyridine and rac-7-(3,4-Dimethoxy-benzyl)-2-methyl-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-c]pyridine

The title compounds were prepared in analogy to rac-7-(1-methyl-4,5,6,7-tetrahydro-1H-pyrazolo[3,4-c]pyridin-7-ylmethyl)quinoline and rac-7-(2-methyl-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-c]pyridin-7-ylmethyl)quinoline starting from 3,4-dimethoxyphenylacetic acid. LC-MS D: $t_R = 0.65$ min; $[M+H]^+ = 288.19$.

General method H for the synthesis of 4,5,6,7-tetrahydropyrazolo[4,3-c]pyridines of Structure 1

2-(1-Ethyl-3-methyl-1H-pyrazol-5-yl)ethanamine and 2-(1,3-Dimethyl-1H-pyrazol-5-yl)ethanamine

The title compounds were prepared as described in WO2007/122591. LC-MS A: t_R = 0.22 min; $[M+H]^+$ = 154.34 and LC-MS D: t_R = 0.54 min; $[M+H]^+$ = 140.19 respectively.

4,5,6,7-Tetrahydropyrazolo[4,3-c]pyridines of Structure 1 were prepared in analogy to 4,5,6,7-tetrahydropyrazolo[3,4-c]pyridines of Structure 1 via initial amide coupling of the appropriate aryl acetic acid and the required substituted pyrazoleethanamine followed by Bischler-Napieralski cyclisation and reduction.

Listed in Table 5 below are 4,5,6,7-tetrahydropyrazolo[4,3-c]pyridines of Structure 1, prepared according to the above procedure.

Table 5

Tetrahydropyrazolo[4,3-c]pyridine 1	t_R [min] LC-MS / Method	MS-data m/z [M+H]⁺
rac-4-(3,4-Dimethoxy-benzyl)-1-ethyl-3-methyl-4,5,6,7-tetrahydro-1H-pyrazolo[4,3-c]pyridine	0.72 / D	316.47
1-Ethyl-3-methyl-4-naphthalen-2-ylmethyl-4,5,6,7-tetrahydro-1H-pyrazolo[4,3-c]pyridine	0.83 / D	306.22
rac-1-Ethyl-3-methyl-4-(4-trifluoromethyl-benzyl)-4,5,6,7-tetrahydro-1H-pyrazolo[4,3-c]pyridine	0.83 / D	324.19
rac-7-(1,3-Dimethyl-4,5,6,7-tetrahydro-1H-pyrazolo[4,3-c]pyridin-4-ylmethyl)-quinoline	0.66 / D	293.2

General method I for the synthesis of 4,5,6,7-tetrahydro-thiazolo[5,4-c]pyridines of Structure 1

rac-4-Naphthalen-1-ylmethyl-4,5,6,7-tetrahydro-thiazolo[5,4-c]pyridin-2-ylamine

Step 1: DIBAL 1.7M in toluene (18 mL, 26.9 mmol) was added dropwise to a -78°C soln. of 1-naphthylacetic acid ethyl ester (3.0 g, 14.0 mmol) in toluene (60 mL) and the resulting mixture was stirred for 1h. The reaction was quenched by the addition of MeOH and the mixture was warmed to 10°C before a soln. of potassium sodium tartrate (18 g in 30 mL H₂O) was added slowly. The biphasic mixture was stirred for 2h before the layers were separated. The toluene layer was dried over Na₂SO₄, filtered and evaporated *in vacuo* to give 1-naphthaleneacetaldehyde as a yellow oil (2.12 g) that was used directly in the next step. LC-MS C: t_R = 0.87 min; No ionisation.

Step 2: A soln. of 1-naphthaleneacetaldehyde (2.12 g, 8.72 mmol) in MeOH (20 mL) was added in one portion to a soln. of 4-(2-aminoethyl)thiazol-2-amine in 2M aq. NaOH (20 mL) and MeOH (30 mL) and the resulting mixture was heated to 80°C for 2h. The reaction mixture was concentrated *in vacuo* and the remaining aq. phase was acidified with 2M aq. HCl and extracted with DCM (3x). These organic extracts were discarded and the aq. layer was re-basified with 5M aq. NaOH and re-extracted with ⁿBuOH (3x). The combined organic extracts were dried over Na₂SO₄, filtered and evaporated *in vacuo* to give the title compound as an orange solid (1.0 g). LC-MS C: t_R = 0.74 min; [M+H]⁺ = 296.1.

rac-4-Naphthalen-1-ylmethyl-4,5,6,7-tetrahydro-thiazolo[5,4-c]pyridine

Step 1: A soln. of Boc₂O (712 mg, 3.26 mmol) in DCM (10 mL) was added to a RT suspension of rac-4-naphthalen-1-ylmethyl-4,5,6,7-tetrahydro-thiazolo[5,4-c]pyridin-2-ylamine (900 mg, 3.2 mmol) and Et₃N (0.47 mL, 3.36 mmol) in DCM (10 mL) and the resulting mixture was stirred for 6h. The DCM was evaporated *in vacuo* and the residue was partitioned between EtOAc and H₂O. The layers were separated and the organic layer was washed once with H₂O, dried over Na₂SO₄, filtered and evaporated *in vacuo* to give rac-2-amino-4-naphthalen-1-ylmethyl-6,7-dihydro-4H-thiazolo[5,4-c]pyridine-5-carboxylic acid tert-butyl ester as an orange solid (1.15 g). LC-MS C: t_R = 0.93 min; [M+H]⁺ = 396.1.

Step 2: A soln. of rac-2-amino-4-naphthalen-1-ylmethyl-6,7-dihydro-4H-thiazolo[5,4-c]pyridine-5-carboxylic acid tert-butyl ester (1.14 g, 2.88 mmol) in DMF (9 mL) was added over 5 min to a rapidly stirred 65°C soln. of ^tbutyl nitrite (0.51 mL, 4.32 mmol) in DMF (6 mL) and the resulting mixture was stirred for 40 min. The reaction mixture was cooled to RT and acidified with 2M aq. HCl (4.5 mL) and stirred for a further 5 min. The mixture was basified with 2M aq. NaOH (4.6 mL), diluted with H₂O (50 mL) and extracted with EtOAc (3x30 mL). The combined organic extracts were washed with H₂O (3x20 mL), dried over Na₂SO₄, filtered and evaporated *in vacuo* to give the Boc-protected intermediate that was subsequently dissolved in 4M HCl in dioxane (8 mL) and stirred for 40 min. The reaction mixture was evaporated *in vacuo* and the residue was partitioned between H₂O and EtOAc and filtered through a pad of celite. The layers were separated and the aq. phase was basified with 2M aq. NaOH and extracted with EtOAc (3x). The combined organic extracts were dried over Na₂SO₄, filtered and evaporated *in vacuo* to give the title compound as a brown solid (0.44 g) that was used further without purification. LC-MS C: t_R = 0.82 min; No ionisation.

General method J for the synthesis of 5,6,7,8-tetrahydro-imidazo[1,2-a]pyrazines of Structure 1

rac-8-(3,4-Dimethoxy-benzyl)-5,6,7,8-tetrahydro-imidazo[1,2-a]pyrazine hydrochloride

Step 1: Borane.THF complex 1M soln. in THF (55 mL, 55 mmol) was added dropwise to a 0°C suspension of *L*-3,4-dimethoxyphenyl alanine (5.0 g, 22.2 mmol) in THF (15 mL) and the resulting mixture was heated to 60°C and stirred overnight. The reaction mixture was cooled to 0°C and quenched with MeOH and stirred for 30 min. The volatiles were removed *in vacuo* and the residue was partitioned between DCM and 2M aq. HCl and stirred for a further 5h. The layers were separated and the aq. layer was basified with 2M NaOH and extracted with DCM (3x). The combined organic layers were washed with brine, dried over Na₂SO₄, filtered and evaporated *in vacuo* to give (S)-2-amino-3-(3,4-dimethoxyphenyl)propan-1-ol as a colourless oil (2.54 g) that was used further without purification. LC-MS D: t_R = 0.57 min; [M+H+MeCN]⁺ = 253.17.

Step 2: A soln. of Boc₂O (2.88 g, 13 mmol) in DCM (20 mL) was added dropwise to a 0°C suspension of (S)-2-amino-3-(3,4-dimethoxyphenyl)propan-1-ol (2.54 g, 12 mmol) and Et₃N (2.01 mL, 14 mmol) in DCM (30 mL) under argon and after complete addition the resulting cream suspension was warmed to RT and stirred overnight. The reaction mixture was washed successively with 1M aq. citric acid (20 mL), brine and the organic layer was dried over Na₂SO₄, filtered and evaporated *in vacuo* to give [(S)-2-(3,4-dimethoxy-phenyl)-1-hydroxymethyl-ethyl]carbamic acid tert-butyl ester as a light yellow solid (3.88 g) that was used further without purification. LC-MS D: t_R = 0.74 min; [M+H-Me]⁺ = 297.1.

Step 3: DMSO (1.08 mL, 15.15 mmol) was added dropwise to a -60°C soln. of oxalyl chloride (0.69 mL, 8.26 mmol) in DCM (16 mL) and the resulting mixture was stirred for 15 min before a soln. of [(S)-2-(3,4-dimethoxy-phenyl)-1-hydroxymethyl-ethyl]carbamic acid tert-butyl ester (2.14 g, 6.89 mmol) in DCM (8 mL) was added. After stirring for 3h DIPEA (5.9 mL, 34.43 mmol) was added and the reaction mixture was warmed to RT. The reaction mixture was poured into H₂O and extracted with DCM (2x). The combined organic layers were washed with 1M aq. citric acid, brine, dried over and Na₂SO₄, filtered and evaporated *in vacuo* to give the crude aldehyde as a light yellow oil that was purified by FC (eluent: 95:5 DCM:MeOH) to furnish [(S)-2-(3,4-dimethoxy-phenyl)-1-formyl-ethyl]-carbamic acid tert-butyl ester as a colourless oil (0.89 g). LC-MS D: t_R = 0.70-0.82 min; [M+H]⁺ = 310.2.

Step 4: A mixture of [(S)-2-(3,4-dimethoxy-phenyl)-1-formyl-ethyl]-carbamic acid tert-butyl ester (994 mg, 3.21 mmol), 40% aq. glyoxal soln. (0.73 mL, 6.43 mmol) and 25% aq. NH₄OH soln. (1.21 mL, 16.07 mmol) were dissolved in MeOH (20 mL) at RT and stirred overnight. The MeOH was evaporated *in vacuo* and the remaining residue further dried under high

vacuum to give [rac-2-(3,4-dimethoxy-phenyl)-1-(1H-imidazol-2-yl)-ethyl]-carbamic acid tert-butyl ester as a light yellow oil (1.23 g) that was used further without purification. LC-MS D: t_R = 0.74 min; $[M+H]^+$ = 348.17.

Step 5: [rac-2-(3,4-Dimethoxy-phenyl)-1-(1H-imidazol-2-yl)-ethyl]-carbamic acid tert-butyl ester (1.03 g, 2.95 mmol) and K_2CO_3 (531 mg, 3.84 mmol) were added to a RT soln. of bromoacetic acid methylester (0.54 mL, 5.91 mmol) in DMF (10 mL) and the resulting suspension was stirred overnight. The reaction mixture was poured into H_2O and extracted with EtOAc (4x). The combined organic extracts were dried over Na_2SO_4 , filtered and evaporated *in vacuo* to give the crude product as a brown oil which was purified by chromatography (SiO_2 , eluent: 95:5 DCM:MeOH) to give {2-[rac-1-tert-butoxycarbonylamino-2-(3,4-dimethoxy-phenyl)-ethyl]-imidazol-1-yl}-acetic acid methyl ester as a light yellow solid (202 mg). LC-MS D: t_R = 0.77 min; $[M+H]^+$ = 420.15.

Step 6: 4M HCl in dioxane (2.41 mL, 9.63 mmol) was added dropwise to a 0°C soln. of {2-[rac-1-tert-butoxycarbonylamino-2-(3,4-dimethoxy-phenyl)-ethyl]-imidazol-1-yl}-acetic acid methyl ester (202 mg, 0.48 mmol) in DCM (10 mL) and the resulting mixture was warmed to RT and stirred overnight. The reaction mixture was concentrated *in vacuo* and the residue was re-dissolved in DCM (10 mL) before Et_3N (270 μ L, 1.93 mmol) was added. The mixture was heated to 40°C for 4h and subsequently stirred at RT overnight. The reaction mixture was poured into H_2O and extracted with DCM (3x). The combined organic extracts were dried over Na_2SO_4 , filtered and evaporated *in vacuo* to give rac-8-(3,4-dimethoxy-benzyl)-7,8-dihydro-imidazo[1,2-a]pyrazin-6-one as a light cream solid (150 mg) that was used further without purification. LC-MS D: t_R = 0.56 min; $[M+H]^+$ = 288.15.

Step 7: Borane.THF complex 1M soln. in THF (1.31 mL, 1.31 mmol) was added dropwise to a 0°C soln. of rac-8-(3,4-dimethoxy-benzyl)-7,8-dihydro-imidazo[1,2-a]pyrazin-6-one (94 mg, 0.33 mmol) in THF (3 mL) and the resulting mixture was warmed to RT and stirred overnight. The reaction mixture was cooled to 0°C and quenched with MeOH (3 mL) before being concentrated *in vacuo*. The residue was re-dissolved in MeOH (3 mL) before 4M HCl in dioxane (0.33 mL, 1.31 mmol) was added slowly. The mixture was stirred for 30 min after which it was evaporated, re-dissolved in MeOH and again evaporated *in vacuo* to give the title compound as a white solid (98 mg). LC-MS B: t_R = 0.45 min; $[M+H]^+$ = 274.04.

General method K for the synthesis of Indole-3-Carboxylic Acids 2

Step 1: NaH (0.54 g, 14 mmol) was added portionwise to a 0°C soln. of methyl indole-3-carboxylate (2.0 g, 11 mmol) in DMF (20 mL) under argon and the resulting mixture was warmed to RT and stirred for 15 min before being cooled back to 0°C. The alkyl halide (12.6

mmol, 1.15 eq.) was added dropwise and the reaction mixture was stirred for 5 min before being warmed to RT and stirred overnight. The reaction mixture was quenched into ice water and extracted with DCM (3x). The combined organic extracts were washed with brine, dried over Na₂SO₄, filtered and evaporated *in vacuo* to give the crude product that was used directly in Step 2.

Step 2: 2M aq. NaOH soln. (15 mL) was added to a RT soln. of the crude ester from above (11 mmol) in MeOH (30 mL) and the resulting mixture was heated to reflux for 2h. The MeOH was evaporated *in vacuo* and the remaining aq. layer was extracted once with DCM. This organic extract was discarded and the aq. phase was acidified with 2M aq. HCl to precipitate the acid product. The product was collected by filtration washing with H₂O and dried in a vacuum oven at 40°C overnight.

Listed in Table 6 below are carboxylic acids of Structure 2, prepared according to the above-mentioned method K, using methyl indole-3-carboxylate as starting material.

Table 6

Carboxylic Acid 2	<i>t_R</i> [min] LC-MS / Method	MS-data m/z [M+H] ⁺
1-Isopropyl-1H-indole-3-carboxylic acid	0.86 / A	203.99
1-Propyl-1H-indole-3-carboxylic acid	0.87 / A	204.01
1-Butyl-1H-indole-3-carboxylic acid	0.91 / A	218.04
1-Isobutyl-1H-indole-3-carboxylic acid	0.91 / A	217.99
1-(2-Hydroxy-ethyl)-1H-indole-3-carboxylic acid	0.77 / B	247.13 (MeCN adduct)
1-(2-Methoxy-ethyl)-1H-indole-3-carboxylic acid	0.78 / A	220.01
1-(2-Fluoro-ethyl)-1H-indole-3-carboxylic acid	0.96 / B	242.37 (MeCN adduct)
1-(2-Dimethylamino-ethyl)-1H-indole-3-carboxylic acid	0.58 / A	233.03

Listed in Table 7 below are carboxylic acids of Structure 2, prepared according to the above-mentioned method K, using the corresponding substituted methyl or ethyl indole-3-carboxylate or 1H-pyrrolopyridine-3-carboxylic acid methyl ester as starting material.

Table 7

Carboxylic Acid 2	<i>t_R</i> [min] LC-MS / Method	MS-data m/z [M+H] ⁺
6-Fluoro-1,2-dimethyl-1H-indole-3-carboxylic acid	0.84 / A	207.91

1-Ethyl-6-fluoro-2-methyl-1H-indole-3-carboxylic acid	0.88 / A	221.95
1-Methyl-1H-pyrrolo[2,3-b]pyridine-3-carboxylic acid	0.65 / A	177.02
1-Ethyl-1H-pyrrolo[2,3-b]pyridine-3-carboxylic acid	0.69 / A	191.01

General method L for the synthesis of Indole-3-Carboxylic Acids 2

Step 1: NaH (0.74 mmol) was added in one portion to a 0°C soln. of the appropriately substituted 1H-indole-3-carbaldehyde (0.61 mmol) in DMF (5 mL) under argon and the resulting mixture was warmed to RT and stirred for 15 min before being cooled back to 0°C. The alkyl halide (0.67 mmol, 1.1 eq.) was added dropwise and the reaction mixture was stirred for 5 min before being warmed to RT and stirred for 30 min. The reaction mixture was quenched into ice water and extracted with DCM (3X). The combined organic extracts were washed with brine, dried over Na₂SO₄, filtered and evaporated *in vacuo* to give the crude product that was used directly in Step 2.

Step 2: 2-Methyl-2-butene 2M soln. in THF (7.0 mmol) was added in one portion to a RT soln. of the crude aldehyde from above (0.61 mmol) in THF (10 mL) and *t*-butanol (2.8 mL) followed by a soln. of sodium chlorite (1.83 mmol) and sodium dihydrogen phosphate dihydrate (2.75 mmol) in H₂O (2.5 mL). The resulting colourless soln. was stirred at RT for 14h. Additional sodium chlorite (1.53 mmol) and sodium dihydrogen phosphate dihydrate (1.83 mmol) in H₂O (4 mL) were added and stirring was continued for 24h after which the reaction mixture was extracted with DCM (2x). The combined organic extracts were washed with 2M aq. NaOH soln. (5 mL) and after separation the aq. layer was acidified with 2M aq. HCl to precipitate the acid product that was collected by filtration and dried in a vacuum oven at 40°C overnight.

Listed in Table 8 below are carboxylic acids of Structure 2, prepared according to the above-mentioned method L, using the corresponding substituted 1H-indole-3-carbaldehyde as starting material.

Table 8

Carboxylic Acid 2	<i>t_R</i> [min] LC-MS / Method	MS-data m/z [M+H] ⁺
4-Fluoro-1-methyl-1H-indole-3-carboxylic acid	0.75 / A	193.98
1-Ethyl-4-fluoro-1H-indole-3-carboxylic acid	0.80 / A	208.00
5-Fluoro-1-methyl-1H-indole-3-carboxylic acid	0.80 / A	193.93
1-Ethyl-5-fluoro-1H-indole-3-carboxylic acid	0.84 / A	207.94

6-Fluoro-1-methyl-1H-indole-3-carboxylic acid	0.81 / A	234.94 (MeCN adduct)
1-Ethyl-6-fluoro-1H-indole-3-carboxylic acid	0.85 / A	207.94
7-Fluoro-1-methyl-1H-indole-3-carboxylic acid	0.81 / A	235.03 (MeCN adduct)
1-Ethyl-7-fluoro-1H-indole-3-carboxylic acid	0.86 / A	249.03 (MeCN adduct)
1,4-Dimethyl-1H-indole-3-carboxylic acid	0.82 / A	190.00
1,5-Dimethyl-1H-indole-3-carboxylic acid	0.82 / A	No ionisation
1-Ethyl-5-methyl-1H-indole-3-carboxylic acid	0.86 / A	204.02
1,6-Dimethyl-1H-indole-3-carboxylic acid	0.82 / A	No ionisation
1-Ethyl-4-methoxy-1H-indole-3-carboxylic acid	0.85 / A	220.01
5-Methoxy-1-methyl-1H-indole-3-carboxylic acid	0.77 / A	205.98
1-Ethyl-5-methoxy-1H-indole-3-carboxylic acid	0.81 / A	220.02
5-Chloro-1-methyl-1H-indole-3-carboxylic acid	0.84 / A	250.97 (³⁵ Cl+MeCN)
5-Chloro-1-ethyl-1H-indole-3-carboxylic acid	0.88 / A	265.03 (³⁵ Cl+MeCN)
6-Chloro-1-methyl-1H-indole-3-carboxylic acid	0.85 / A	250.99 (³⁵ Cl+MeCN)
6-Chloro-1-ethyl-1H-indole-3-carboxylic acid	0.99 / A	264.99 (³⁵ Cl+MeCN)

1-Cyclopropyl-1H-indole-3-carboxylic acid

The title compound was prepared from methyl indole-3-carboxylate following the conditions described by Tsuritani *et al.* in Org. Lett. 2008, 10, 1653-1655., followed by hydrolysis of the ester with 2M aq. NaOH soln. as described above. LC-MS A: t_R = 0.85 min; $[M+H]^+$ = 201.99.

1-Cyclopropyl-4-fluoro-1H-indole-3-carboxylic acid

The title compound was prepared from 4-fluoro-1H-indole-3-carbaldehyde following the conditions described by Tsuritani *et al.* in Org. Lett. 2008, 10, 1653-1655., followed by oxidation of the aldehyde with sodium chlorite as described above. LC-MS B: t_R = 0.63 min; $[M+H]^+$ = 220.3.

Listed in Table 9 below are carboxylic acids of Structure 2, prepared from the corresponding 1H-pyrrolopyridine according to the procedure described by Giordanetto *et al.* in Bioorg. Med. Chem. Lett. 2007, 17, 4232-4241., followed by oxidation of the aldehyde with sodium chlorite as described above.

Table 9

Carboxylic Acid 2	t_R [min]	MS-data m/z
	LC-MS / Method	$[M+H]^+$
1-Methyl-1H-pyrrolo[3,2-b]pyridine-3-carboxylic acid	0.56 / A	177.01

1-Ethyl-1H-pyrrolo[3,2-b]pyridine-3-carboxylic acid	0.46 / A	191.18
1-Methyl-1H-pyrrolo[3,2-c]pyridine-3-carboxylic acid	0.29 / B	177.43
1-Ethyl-1H-pyrrolo[3,2-c]pyridine-3-carboxylic acid	0.38 / B	191.20
1-Methyl-1H-pyrrolo[2,3-c]pyridine-3-carboxylic acid	0.28 / B	177.24
1-Ethyl-1H-pyrrolo[2,3-c]pyridine-3-carboxylic acid	0.36 / B	191.29

General method M for the synthesis of example compounds of Formula (I)

TBTU (34 mg, 0.11 mmol) was added to a RT soln. of the required acid **2** (0.1 mmol) and DIPEA (25 μ L, 0.15 mmol) in DMF (0.5 mL) and after stirring for 5 min a soln. of the required amine **1** as its free base or HCl salt (0.1 mmol) and DIPEA (25 μ L, 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 (column: Waters X-bridge, 30x75 mm, 10 μ m, UV/MS, basic conditions) to furnish the desired product.

Listed in Table 10 below are example compounds, prepared according to the above-mentioned method **M**, from the corresponding amine **1**, either readily available or prepared as described above and the corresponding indole carboxylic acid **2**, either readily available or prepared as described above.

Table 10

Example No.	Compound of Formula (I)	t_R [min] LC-MS / Method	MS-data m/z [M+H] ⁺
1	rac-(7-Benzyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl)-(1-methyl-1H-indol-3-yl)-methanone	1.0 D	387.15
2	rac-(7-Benzyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl)-(1-ethyl-1H-indol-3-yl)-methanone	1.02 D	401.13
3	rac-(7-Benzyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl)-(1,2-dimethyl-1H-indol-3-yl)-methanone	1.02 D	401.15
4	rac-(1-Methyl-1H-indol-3-yl)-(7-naphthalen-1-ylmethyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl)-methanone	1.04 D	437.16
5	rac-(1-Ethyl-1H-indol-3-yl)-(7-naphthalen-1-ylmethyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl)-methanone	1.07 D	451.15
6	rac-(1,2-Dimethyl-1H-indol-3-yl)-(7-naphthalen-1-ylmethyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl)-methanone	1.05 D	451.15

7	rac-(1-Methyl-1H-indol-3-yl)-(7-naphthalen-2-ylmethyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl)-methanone	1.04 C	437.09
8	rac-(1-Ethyl-1H-indol-3-yl)-(7-naphthalen-2-ylmethyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl)-methanone	1.06 C	451.14
9	rac-(1,2-Dimethyl-1H-indol-3-yl)-(7-naphthalen-2-ylmethyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl)-methanone	1.06 C	451.12
10	rac-[7-(3,4-Dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-methyl-1H-indol-3-yl)-methanone	0.92 C	447.12
11	rac-[7-(3,4-Dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone	0.96 D	461.12
12	rac-[7-(3,4-Dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1,2-dimethyl-1H-indol-3-yl)-methanone	0.93 C	461.14
13	rac-(1-Methyl-1H-indol-3-yl)-[7-(4-trifluoromethyl-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone	1.02 C	455.08
14	rac-(1-Ethyl-1H-indol-3-yl)-[7-(4-trifluoromethyl-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone	1.04 C	469.15
15	rac-(1,2-Dimethyl-1H-indol-3-yl)-[7-(4-trifluoromethyl-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone	1.04 C	469.06
16	rac-[1-(3,4-Dimethoxy-benzyl)-6,7-dimethoxy-3,4-dihydro-1H-isoquinolin-2-yl]-(1-methyl-1H-indol-3-yl)-methanone	0.88 D	501.21
16a	[(R)-1-(3,4-Dimethoxy-benzyl)-6,7-dimethoxy-3,4-dihydro-1H-isoquinolin-2-yl]-(1-methyl-1H-indol-3-yl)-methanone	0.88 D	501.19
16b	[(S)-1-(3,4-Dimethoxy-benzyl)-6,7-dimethoxy-3,4-dihydro-1H-isoquinolin-2-yl]-(1-methyl-1H-indol-3-yl)-methanone	0.88 D	501.18
17	rac-(6,7-Dimethoxy-1-naphthalen-2-ylmethyl-3,4-dihydro-1H-isoquinolin-2-yl)-(1-methyl-1H-indol-3-yl)-methanone	0.99 D	491.18
18	rac-(1-Benzyl-6-methoxy-3,4-dihydro-1H-isoquinolin-2-yl)-(1-methyl-1H-indol-3-yl)-methanone	0.99 D	411.18
19	rac-[6,7-Dimethoxy-1-(3-methoxy-benzyl)-3,4-dihydro-1H-isoquinolin-2-yl]-(1-methyl-1H-indol-3-yl)-methanone	0.93 D	471.19
20	rac-[6,7-Dimethoxy-1-(4-methoxy-benzyl)-3,4-dihydro-1H-isoquinolin-2-yl]-(1-methyl-1H-indol-3-yl)-methanone	0.92 D	471.2
21	rac-[1-(2,5-Dimethoxy-benzyl)-6,7-dimethoxy-3,4-dihydro-1H-isoquinolin-2-yl]-(1-methyl-1H-indol-3-yl)-methanone	0.92 D	501.25

22	rac-(1-Benzo[1,3]dioxol-5-ylmethyl-6,7-dimethoxy-3,4-dihydro-1H-isoquinolin-2-yl)-(1-methyl-1H-indol-3-yl)-methanone	0.92 D	485.16
23	rac-[1-(4-Fluoro-benzyl)-6,7-dimethoxy-3,4-dihydro-1H-isoquinolin-2-yl]-(1-methyl-1H-indol-3-yl)-methanone	0.94 D	459.08
24	rac-[6,7-Dimethoxy-1-(3,4,5-trimethoxy-benzyl)-3,4-dihydro-1H-isoquinolin-2-yl]-(1-methyl-1H-indol-3-yl)-methanone	0.88 D	531.16
25	rac-[1-(3-Fluoro-4-methoxy-benzyl)-6,7-dimethoxy-3,4-dihydro-1H-isoquinolin-2-yl]-(1-methyl-1H-indol-3-yl)-methanone	0.92 D	489.08
26	rac-[1-(4-Chloro-benzyl)-6,7-dimethoxy-3,4-dihydro-1H-isoquinolin-2-yl]-(1-methyl-1H-indol-3-yl)-methanone	0.98 D	(³⁵ Cl) 475.17
27	rac-[1-(2,5-Dimethoxy-benzyl)-5,8-dimethoxy-3,4-dihydro-1H-isoquinolin-2-yl]-(1-methyl-1H-indol-3-yl)-methanone	1.0 D	501.19
28	rac-[1-(3,4-Dimethoxy-benzyl)-6,7-dimethoxy-3,4-dihydro-1H-isoquinolin-2-yl]-(1-ethyl-1H-indol-3-yl)-methanone	0.91 D	515.2
28a	[(R)-1-(3,4-Dimethoxy-benzyl)-6,7-dimethoxy-3,4-dihydro-1H-isoquinolin-2-yl]-(1-ethyl-1H-indol-3-yl)-methanone	0.91 D	515.15
28b	[(S)-1-(3,4-Dimethoxy-benzyl)-6,7-dimethoxy-3,4-dihydro-1H-isoquinolin-2-yl]-(1-ethyl-1H-indol-3-yl)-methanone	0.91 D	515.19
29	rac-(6,7-Dimethoxy-1-naphthalen-2-ylmethyl-3,4-dihydro-1H-isoquinolin-2-yl)-(1-ethyl-1H-indol-3-yl)-methanone	1.02 D	505.19
30	rac-(1-Benzyl-6-methoxy-3,4-dihydro-1H-isoquinolin-2-yl)-(1-ethyl-1H-indol-3-yl)-methanone	1.01 D	425.04
31	rac-[6,7-Dimethoxy-1-(3-methoxy-benzyl)-3,4-dihydro-1H-isoquinolin-2-yl]-(1-ethyl-1H-indol-3-yl)-methanone	0.96 D	485.2
32	rac-[6,7-Dimethoxy-1-(4-methoxy-benzyl)-3,4-dihydro-1H-isoquinolin-2-yl]-(1-ethyl-1H-indol-3-yl)-methanone	0.95 D	485.21
33	rac-[1-(2,5-Dimethoxy-benzyl)-6,7-dimethoxy-3,4-dihydro-1H-isoquinolin-2-yl]-(1-ethyl-1H-indol-3-yl)-methanone	0.95 D	515.2
34	rac-(1-Benzo[1,3]dioxol-5-ylmethyl-6,7-dimethoxy-3,4-dihydro-1H-isoquinolin-2-yl)-(1-ethyl-1H-indol-3-yl)-methanone	0.94 D	499.19
35	rac-(1-Ethyl-1H-indol-3-yl)-[1-(4-fluoro-benzyl)-6,7-dimethoxy-3,4-dihydro-1H-isoquinolin-2-yl]-methanone	0.96 D	473.17
36	rac-[6,7-Dimethoxy-1-(3,4,5-trimethoxy-benzyl)-3,4-dihydro-1H-isoquinolin-2-yl]-(1-ethyl-1H-indol-3-yl)-methanone	0.91 D	545.19

37	rac-(1-Ethyl-1H-indol-3-yl)-[1-(3-fluoro-4-methoxy-benzyl)-6,7-dimethoxy-3,4-dihydro-1H-isoquinolin-2-yl]-methanone	0.95 D	503.19
38	rac-[1-(4-Chloro-benzyl)-6,7-dimethoxy-3,4-dihydro-1H-isoquinolin-2-yl]-(1-ethyl-1H-indol-3-yl)-methanone	1.0 D	(³⁵ Cl) 488.99
39	rac-[1-(2,5-Dimethoxy-benzyl)-5,8-dimethoxy-3,4-dihydro-1H-isoquinolin-2-yl]-(1-ethyl-1H-indol-3-yl)-methanone	1.03 D	515.2
40	rac-(1H-Indol-3-yl)-(7-naphthalen-1-ylmethyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl)-methanone	0.99 D	423.05
41	rac-(1-Ethyl-3-methyl-4-naphthalen-2-ylmethyl-1,4,6,7-tetrahydro-pyrazolo[4,3-c]pyridin-5-yl)-(1-methyl-1H-indol-3-yl)-methanone	0.93 D	463.08
42	rac-[1-Ethyl-3-methyl-4-(4-trifluoromethyl-benzyl)-1,4,6,7-tetrahydro-pyrazolo[4,3-c]pyridin-5-yl]-(1-methyl-1H-indol-3-yl)-methanone	0.93 D	481.15
43	rac-(1-Ethyl-1H-indol-3-yl)-(1-ethyl-3-methyl-4-naphthalen-2-ylmethyl-1,4,6,7-tetrahydro-pyrazolo[4,3-c]pyridin-5-yl)-methanone	0.95 D	477.16
44	rac-(1-Ethyl-1H-indol-3-yl)-[1-ethyl-3-methyl-4-(4-trifluoromethyl-benzyl)-1,4,6,7-tetrahydro-pyrazolo[4,3-c]pyridin-5-yl]-methanone	0.95 D	494.96
45	rac-(1-Methyl-1H-indol-3-yl)-(1-naphthalen-1-ylmethyl-3,4-dihydro-1H-isoquinolin-2-yl)-methanone	1.03 C	431.13
46	rac-(1-Ethyl-1H-indol-3-yl)-(1-naphthalen-1-ylmethyl-3,4-dihydro-1H-isoquinolin-2-yl)-methanone	1.06 C	445.14
47	rac-(1-Methyl-1H-indol-3-yl)-(4-naphthalen-1-ylmethyl-6,7-dihydro-4H-thieno[3,2-c]pyridin-5-yl)-methanone	1.03 C	437.07
48	rac-(1-Ethyl-1H-indol-3-yl)-(4-naphthalen-1-ylmethyl-6,7-dihydro-4H-thieno[3,2-c]pyridin-5-yl)-methanone	1.06 C	451.10
49	rac-(2-Amino-4-naphthalen-1-ylmethyl-6,7-dihydro-4H-thiazolo[5,4-c]pyridin-5-yl)-(1-methyl-1H-indol-3-yl)-methanone	0.83 C	453.08
50	rac-(2-Amino-4-naphthalen-1-ylmethyl-6,7-dihydro-4H-thiazolo[5,4-c]pyridin-5-yl)-(1-ethyl-1H-indol-3-yl)-methanone	0.87 C	467.09
51	rac-(1-Methyl-1H-indol-3-yl)-(4-naphthalen-1-ylmethyl-6,7-dihydro-4H-thiazolo[5,4-c]pyridin-5-yl)-methanone	0.92 C	438.05

52	rac-(1-Ethyl-1H-indol-3-yl)-(4-naphthalen-1-ylmethyl-6,7-dihydro-4H-thiazolo[5,4-c]pyridin-5-yl)-methanone	0.96 C	452.08
53	rac-[3-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-methyl-1H-indol-3-yl)-methanone	0.99 C	(⁷⁹ Br) 524.99
54	rac-[3-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone	1.03 D	(⁸¹ Br) 540.96
55[#]	rac-[2-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone	1.02 C	(⁷⁹ Br) 538.98
56	rac-[3-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-isopropyl-1H-indol-3-yl)-methanone	1.05 D	(⁷⁹ Br) 552.79
57	rac-[3-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-isobutyl-1H-indol-3-yl)-methanone	1.08 D	(⁸¹ Br) 568.96
58	rac-[3-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(6-fluoro-1-methyl-1H-indol-3-yl)-methanone	1.01 D	(⁸¹ Br) 544.99
59	rac-[3-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-6-fluoro-1H-indol-3-yl)-methanone	1.04 D	(⁸¹ Br) 558.87
60	rac-[3-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(5-fluoro-1-methyl-1H-indol-3-yl)-methanone	1.0 D	(⁸¹ Br) 544.86
61	rac-[3-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-5-fluoro-1H-indol-3-yl)-methanone	1.03 D	(⁷⁹ Br) 556.91
62	rac-[3-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(6-fluoro-1,2-dimethyl-1H-indol-3-yl)-methanone	1.02 D	(⁸¹ Br) 558.67
63	rac-[3-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-6-fluoro-2-methyl-1H-indol-3-yl)-methanone	1.04 D	(⁸¹ Br) 572.9
64	rac-[3-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-cyclopropyl-1H-indol-3-yl)-methanone	1.05 D	(⁷⁹ Br) 550.93
65	rac-[3-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-propyl-1H-indol-3-yl)-methanone	1.06 D	(⁸¹ Br) 554.76

66	rac-[3-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-butyl-1H-indol-3-yl)-methanone	1.09 D	(⁷⁹ Br) 566.89
67	rac-[3-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-[1-(2-methoxy-ethyl)-1H-indol-3-yl]-methanone	1.01 D	(⁷⁹ Br) 570.91
68	rac-[3-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-[1-(2-dimethylamino-ethyl)-1H-indol-3-yl]-methanone	0.99 D	(⁷⁹ Br) 581.99
69	rac-[3-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(5-chloro-1-methyl-1H-indol-3-yl)-methanone	1.04 D	(⁷⁹ Br, ³⁵ Cl) 558.84
70	rac-[3-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(5-chloro-1-ethyl-1H-indol-3-yl)-methanone	1.07 D	(⁷⁹ Br, ³⁵ Cl) 572.82
71	rac-[3-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(5-methoxy-1-methyl-1H-indol-3-yl)-methanone	0.98 D	(⁷⁹ Br) 554.81
72	rac-[3-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-5-methoxy-1H-indol-3-yl)-methanone	1.01 D	(⁸¹ Br) 570.86
73	rac-[3-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-4-methoxy-1H-indol-3-yl)-methanone	1.01 D	(⁸¹ Br) 570.94
74	rac-[3-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(7-fluoro-1-methyl-1H-indol-3-yl)-methanone	1.03 D	(⁸¹ Br) 544.86
75	rac-[3-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-7-fluoro-1H-indol-3-yl)-methanone	1.06 D	(⁸¹ Br) 558.96
76	rac-[3-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(4-fluoro-1-methyl-1H-indol-3-yl)-methanone	0.99 D	(⁸¹ Br) 544.93
77	rac-[3-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-4-fluoro-1H-indol-3-yl)-methanone	1.02 D	(⁷⁹ Br) 556.93

78	rac-[3-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1,6-dimethyl-1H-indol-3-yl)-methanone	1.04 D	(⁷⁹ Br) 538.93
79	rac-[3-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1,5-dimethyl-1H-indol-3-yl)-methanone	1.03 D	(⁸¹ Br) 540.97
80	rac-[3-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-5-methyl-1H-indol-3-yl)-methanone	1.05 D	(⁸¹ Br) 554.77
81	rac-[3-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1,4-dimethyl-1H-indol-3-yl)-methanone	1.02 D	(⁸¹ Br) 540.92
82	rac-[3-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(5-methoxy-1,2-dimethyl-1H-indol-3-yl)-methanone	0.99 D	(⁸¹ Br) 570.9
83	rac-[3-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1H-indol-3-yl)-methanone	0.96 D	(⁷⁹ Br) 510.92
84	rac-[3-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1H-pyrrolo[2,3-b]pyridin-3-yl)-methanone	0.88 D	(⁷⁹ Br) 511.88
85	rac-[3-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1,2-dimethyl-1H-indol-3-yl)-methanone	1.02 D	(⁷⁹ Br) 538.95
86	rac-[7-(4-Benzoyloxy-3-methoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone	1.04 C	537.05
87	rac-[7-(2,4-Dichloro-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-methyl-1H-indol-3-yl)-methanone	1.06 C	(³⁵ Cl) 454.93
88	rac-(1-Methyl-1H-indol-3-yl)-(7-pyridin-2-ylmethyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl)-methanone	0.84 C	388.08
89	rac-(1-Methyl-1H-indol-3-yl)-[7-(3-trifluoromethyl-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone	1.01 C	455.02
90	rac-[7-(2,6-Dichloro-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-methyl-1H-indol-3-yl)-methanone	1.05 C	(³⁵ Cl) 454.93
91	rac-[7-(1H-Indol-3-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-methyl-1H-indol-3-yl)-methanone	0.93 C	425.89

92	rac-(1-Methyl-1H-indol-3-yl)-[7-(1-methyl-1H-indol-3-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone	0.99 C	440.03
93	rac-[7-(1H-Benzoimidazol-2-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-methyl-1H-indol-3-yl)-methanone	0.81 C	426.76
94	rac-[7-(1H-Indazol-3-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-methyl-1H-indol-3-yl)-methanone	0.87 C	426.84
95	rac-(1-Methyl-1H-indol-3-yl)-[7-(2-methyl-thiazol-4-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone	0.88 C	408.04
96	rac-(1-Methyl-1H-indol-3-yl)-(7-quinolin-8-ylmethyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl)-methanone	0.96 C	438.05
97	rac-[7-(4-Benzyloxy-3-methoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-methyl-1H-indol-3-yl)-methanone	1.02 C	522.95
98	rac-[7-(2,4-Dichloro-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone	1.08 C	468.98
99	rac-(1-Ethyl-1H-indol-3-yl)-(7-pyridin-2-ylmethyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl)-methanone	0.88 C	402.08
100	rac-(1-Ethyl-1H-indol-3-yl)-[7-(3-trifluoromethyl-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone	1.04 C	469.02
101	rac-[7-(2,6-Dichloro-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone	1.08 C	No ionisation
102	rac-(1-Ethyl-1H-indol-3-yl)-[7-(1H-indol-3-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone	0.96 C	440.08
103	rac-(1-Ethyl-1H-indol-3-yl)-[7-(1-methyl-1H-indol-3-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone	1.02 C	454.07
104	rac-(1-Ethyl-1H-indol-3-yl)-[7-(1H-indazol-3-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone	0.90 C	441.06
105	rac-(1-Ethyl-1H-indol-3-yl)-[7-(2-methyl-thiazol-4-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone	0.92 C	422.01
106	rac-(1-Ethyl-1H-indol-3-yl)-(7-quinolin-8-ylmethyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl)-methanone	0.99 C	452.05
107	rac-[7-(4-Methoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-methyl-1H-indol-3-yl)-methanone	0.97 D	417.05
108	rac-[7-(2,3-Dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-methyl-1H-indol-3-yl)-methanone	0.97 D	447.05

109	rac-[7-(3-Methoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-methyl-1H-indol-3-yl)-methanone	0.97 D	417.04
110	rac-[7-(3,5-Dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-methyl-1H-indol-3-yl)-methanone	0.96 D	447.06
111	rac-[7-(3,4-Dichloro-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-methyl-1H-indol-3-yl)-methanone	1.04 D	(³⁵ Cl) 454.96
112	rac-[7-(2,3-Dihydro-benzo[1,4]dioxin-6-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-methyl-1H-indol-3-yl)-methanone	0.95 D	445.03
113	rac-(1-Methyl-1H-indol-3-yl)-[7-(4-trifluoromethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone	1.03 D	471.01
114	rac-[7-(2,3-Dihydro-benzo[1,4]dioxin-5-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-methyl-1H-indol-3-yl)-methanone	0.95 D	445.03
115	rac-(7-Benzo[1,3]dioxol-4-ylmethyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl)-(1-methyl-1H-indol-3-yl)-methanone	0.96 D	431.02
116	rac-(7-Benzo[1,3]dioxol-5-ylmethyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl)-(1-methyl-1H-indol-3-yl)-methanone	0.95 D	431.02
117	rac-[4-(3,4-Dimethoxy-benzyl)-1-ethyl-3-methyl-1,4,6,7-tetrahydro-pyrazolo[4,3-c]pyridin-5-yl]-(1-methyl-1H-indol-3-yl)-methanone	0.79 D	473.14
118	rac-(1-Ethyl-1H-indol-3-yl)-[7-(4-methoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone	0.99 D	431.06
119	rac-[7-(2,3-Dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone	0.99 D	461.06
120	rac-(1-Ethyl-1H-indol-3-yl)-[7-(3-methoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone	1.0 D	431.07
121	rac-[7-(3,5-Dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone	0.99 D	461.07
122	rac-[7-(3,4-Dichloro-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone	1.06 D	(³⁵ Cl) 468.99
123	rac-[7-(2,3-Dihydro-benzo[1,4]dioxin-6-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone	0.98 D	458.92
124	rac-(1-Ethyl-1H-indol-3-yl)-[7-(4-trifluoromethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone	1.05 D	485.04

125	rac-[7-(2,3-Dihydro-benzo[1,4]dioxin-5-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone	0.98 D	458.93
126	rac-(7-Benzo[1,3]dioxol-4-ylmethyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl)-(1-ethyl-1H-indol-3-yl)-methanone	0.99 D	445.03
127	rac-(7-Benzo[1,3]dioxol-5-ylmethyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl)-(1-ethyl-1H-indol-3-yl)-methanone	0.98 D	445.04
128	rac-[4-(3,4-Dimethoxy-benzyl)-1-ethyl-3-methyl-1,4,6,7-tetrahydro-pyrazolo[4,3-c]pyridin-5-yl]-(1-ethyl-1H-indol-3-yl)-methanone	0.82 D	487.16
129	rac-(1-Ethyl-1H-indol-3-yl)-[7-(4-hydroxy-3-methoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone	0.89 D	447.04
130	rac-(1-Ethyl-1H-indol-3-yl)-{7-[4-(2-hydroxy-ethoxy)-3-methoxy-benzyl]-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone	0.85 C	490.91
131	rac-[1-Bromo-4-(3,4-dimethoxy-benzyl)-6,7-dihydro-4H-thieno[3,4-c]pyridin-5-yl]-(1-ethyl-1H-indol-3-yl)-methanone	1.02 C	(⁷⁹ Br) 538.94
132	rac-(1-Methyl-1H-indol-3-yl)-(7-quinolin-6-ylmethyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl)-methanone	0.89 D	438.02
133	rac-(1-Ethyl-1H-indol-3-yl)-(7-quinolin-6-ylmethyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl)-methanone	0.92 D	452.02
134	rac-(1-Methyl-1H-indol-3-yl)-(7-quinolin-7-ylmethyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl)-methanone	0.89 D	438.02
135	rac-(1-Ethyl-1H-indol-3-yl)-(7-quinolin-7-ylmethyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl)-methanone	0.92 D	452.0
136	rac-[1-(3-Methyl-benzyl)-3,4-dihydro-1H-isoquinolin-2-yl]-(1-methyl-1H-indol-3-yl)-methanone	1.01 D	394.98
137	rac-(1-Ethyl-1H-indol-3-yl)-[1-(3-methyl-benzyl)-3,4-dihydro-1H-isoquinolin-2-yl]-methanone	1.04 D	409.19
138	rac-(1-Cyclopropyl-1H-indol-3-yl)-[1-(3,4-dimethoxy-benzyl)-3,4-dihydro-1H-isoquinolin-2-yl]-methanone	0.97 D	467.06
139	rac-[1-(3,4-Dimethoxy-benzyl)-3,4-dihydro-1H-isoquinolin-2-yl]-(1-ethyl-1H-indol-3-yl)-methanone	0.96 D	455.04
140	rac-[7-(3,4-Dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-4-fluoro-1H-indol-3-yl)-methanone	0.94 D	479.1
141	rac-[7-(3,4-Dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(5-fluoro-1-methyl-1H-indol-3-yl)-methanone	0.93 D	465.03

142	rac-(6-Chloro-1-ethyl-1H-indol-3-yl)-[7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone	1.0 D	(³⁵ Cl) 494.99
143	rac-(6-Chloro-1-methyl-1H-indol-3-yl)-[7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone	0.97 D	(³⁵ Cl) 481.01
144	rac-[7-(3,4-Dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-methyl-1H-pyrrolo[2,3-b]pyridin-3-yl)-methanone	0.84 D	448.05
145	rac-[7-(3,4-Dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-[1-(2-fluoro-ethyl)-1H-indol-3-yl]-methanone	0.92 D	479.03
146	rac-(1-Cyclopropyl-1H-indol-3-yl)-[7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone	0.97 D	473.04
147	rac-[7-(3,4-Dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-[1-(2-methoxy-ethyl)-1H-indol-3-yl]-methanone	0.93 D	490.93
148	rac-[7-(3,4-Dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-[1-(2-hydroxy-ethyl)-1H-indol-3-yl]-methanone	0.86 D	477.0
149	rac-[7-(3,4-Dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-pyrrolo[2,3-b]pyridin-3-yl)-methanone	0.87 D	462.03
150	rac-(1-Ethyl-1H-indol-3-yl)-[7-(3-hydroxy-4-methoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone	0.91 C	447.04
151	rac-[4-(3,4-Dimethoxy-benzyl)-1-methyl-6,7-dihydro-4H-thieno[3,4-c]pyridin-5-yl]-(1-ethyl-1H-indol-3-yl)-methanone	0.98 D	475.08
152	rac-{7-[4-(2-Hydroxy-ethoxy)-3-methoxy-benzyl]-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl}-(1-methyl-1H-pyrrolo[2,3-b]pyridin-3-yl)-methanone	0.77 D	478.07
153	rac-{7-[4-(2-Hydroxy-ethoxy)-3-methoxy-benzyl]-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl}-(1-methyl-1H-pyrrolo[2,3-c]pyridin-3-yl)-methanone	0.74 D	478.05
154	rac-{7-[4-(2-Hydroxy-ethoxy)-3-methoxy-benzyl]-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl}-(1-methyl-1H-pyrrolo[3,2-c]pyridin-3-yl)-methanone	0.74 D	478.06
155	rac-{7-[4-(2-Hydroxy-ethoxy)-3-methoxy-benzyl]-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl}-(1-methyl-1H-pyrrolo[3,2-b]pyridin-3-yl)-methanone	0.77 D	478.06

156	rac-(1-Ethyl-1H-pyrrolo[2,3-b]pyridin-3-yl)-{7-[4-(2-hydroxy-ethoxy)-3-methoxy-benzyl]-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl}-methanone	0.80 D	492.07
157	rac-(1-Ethyl-1H-pyrrolo[2,3-c]pyridin-3-yl)-{7-[4-(2-hydroxy-ethoxy)-3-methoxy-benzyl]-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl}-methanone	0.76 D	492.06
158	rac-(1-Ethyl-1H-pyrrolo[3,2-c]pyridin-3-yl)-{7-[4-(2-hydroxy-ethoxy)-3-methoxy-benzyl]-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl}-methanone	0.76 D	492.05
159	rac-(1-Ethyl-1H-pyrrolo[3,2-b]pyridin-3-yl)-{7-[4-(2-hydroxy-ethoxy)-3-methoxy-benzyl]-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl}-methanone	0.79 D	492.08
160	rac-[7-(3,4-Dimethoxy-benzyl)-2,3-dimethyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-methyl-1H-indol-3-yl)-methanone	0.99 D	475.07
161	rac-[7-(3,4-Dimethoxy-benzyl)-2,3-dimethyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone	1.02 D	488.9
162	rac-[8-(3,4-Dimethoxy-benzyl)-5,8-dihydro-6H-[1,7]naphthyridin-7-yl]-(1-ethyl-1H-indol-3-yl)-methanone	0.83 C	456.17
163	rac-[7-(3,4-Dimethoxy-benzyl)-2-methyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-methyl-1H-pyrrolo[3,2-b]pyridin-3-yl)-methanone	0.87 D	462.07
164	rac-[7-(3,4-Dimethoxy-benzyl)-2-methyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(5-fluoro-1-methyl-1H-indol-3-yl)-methanone	0.96 D	479.11
165	rac-(1-Cyclopropyl-4-fluoro-1H-indol-3-yl)-[7-(3,4-dimethoxy-benzyl)-2-methyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone	0.99 D	505.08
166	rac-[7-(3,4-Dimethoxy-benzyl)-2-methyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-[1-(2-hydroxy-ethyl)-1H-indol-3-yl]-methanone	0.89 D	491.02
167	rac-[4-(3,4-Dimethoxy-benzyl)-1,3-dimethyl-6,7-dihydro-4H-thieno[3,4-c]pyridin-5-yl]-(5-fluoro-1-methyl-1H-indol-3-yl)-methanone	0.99 D	493.12

168	rac-(1-Cyclopropyl-4-fluoro-1H-indol-3-yl)-[4-(3,4-dimethoxy-benzyl)-1,3-dimethyl-6,7-dihydro-4H-thieno[3,4-c]pyridin-5-yl]-methanone	1.01 D	519.08
169	rac-[4-(3,4-Dimethoxy-benzyl)-1,3-dimethyl-6,7-dihydro-4H-thieno[3,4-c]pyridin-5-yl]-[1-(2-hydroxy-ethyl)-1H-indol-3-yl]-methanone	0.92 D	505.11
170	rac-[4-(3,4-Dimethoxy-benzyl)-1-methyl-6,7-dihydro-4H-thieno[3,4-c]pyridin-5-yl]-(1-methyl-1H-pyrrolo[3,2-b]pyridin-3-yl)-methanone	0.87 D	462.1
171	rac-[4-(3,4-Dimethoxy-benzyl)-1-methyl-6,7-dihydro-4H-thieno[3,4-c]pyridin-5-yl]-(5-fluoro-1-methyl-1H-indol-3-yl)-methanone	0.96 D	479.11
172	rac-(1-Cyclopropyl-4-fluoro-1H-indol-3-yl)-[4-(3,4-dimethoxy-benzyl)-1-methyl-6,7-dihydro-4H-thieno[3,4-c]pyridin-5-yl]-methanone	0.98 D	505.1
173	rac-[4-(3,4-Dimethoxy-benzyl)-1-methyl-6,7-dihydro-4H-thieno[3,4-c]pyridin-5-yl]-[1-(2-hydroxy-ethyl)-1H-indol-3-yl]-methanone	0.89 D	491.04
174	rac-[7-(4-Cyclopropoxy-3-methoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-methyl-1H-indol-3-yl)-methanone	0.97 D	473.1
175	rac-[7-(4-Cyclopropoxy-3-methoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone	0.99 D	487.13
176	rac-[4-(3,4-Dimethoxy-benzyl)-1,3-dimethyl-6,7-dihydro-4H-thieno[3,4-c]pyridin-5-yl]-(1-methyl-1H-pyrrolo[3,2-b]pyridin-3-yl)-methanone	0.90 D	476.13
177	rac-(1,3-Dimethyl-4-quinolin-7-ylmethyl-1,4,6,7-tetrahydro-pyrazolo[4,3-c]pyridin-5-yl)-(1-methyl-1H-indol-3-yl)-methanone	0.75 D	450.11
178[#]	rac-(1-Methyl-1H-indol-3-yl)-(1-methyl-7-quinolin-7-ylmethyl-1,4,5,7-tetrahydro-pyrazolo[3,4-c]pyridin-6-yl)-methanone	0.76 D	436.11
179[#]	rac-(1-Methyl-1H-indol-3-yl)-(2-methyl-7-quinolin-7-ylmethyl-2,4,5,7-tetrahydro-pyrazolo[3,4-c]pyridin-6-yl)-methanone	0.76 D	436.13
180	rac-8-(3,4-Dimethoxy-benzyl)-5,6-dihydro-8H-imidazo[1,2-a]pyrazin-7-yl]-(1-ethyl-1H-indol-3-yl)-methanone	0.77 D	445.14
181	rac-(1-Ethyl-1H-indol-3-yl)-[7-(4-[1,2,3]triazol-2-yl-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone	1.0 C	468.1

182	rac-(1-Ethyl-1H-indol-3-yl)-[7-(4-[1,2,3]triazol-1-yl-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone	0.90 C	468.09
183	rac-(1-Ethyl-1H-indol-3-yl)-[7-(3-[1,2,3]triazol-2-yl-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone	1.0 C	468.08
184	rac-(1-Ethyl-1H-indol-3-yl)-[7-(3-[1,2,3]triazol-1-yl-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone	0.9 C	468.10
185	rac-(1-Methyl-1H-indol-3-yl)-[7-(4-[1,2,3]triazol-2-yl-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone	0.98 C	454.05
186	rac-(1-Methyl-1H-indol-3-yl)-[7-(4-[1,2,3]triazol-1-yl-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone	0.87 C	454.09
187	rac-[7-(3,4-Dimethoxy-benzyl)-1-methyl-1,4,5,7-tetrahydro-pyrazolo[3,4-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone	0.82 D	459.07
188	rac-2-[6-(1-Ethyl-1H-indole-3-carbonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridin-7-ylmethyl]-benzonitrile	0.94 C	425.91
189	rac-3-[6-(1-Ethyl-1H-indole-3-carbonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridin-7-ylmethyl]-benzonitrile	0.95 C	425.92
190	rac-4-[6-(1-Ethyl-1H-indole-3-carbonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridin-7-ylmethyl]-benzonitrile	0.95 C	425.9
191	rac-(1-Ethyl-1H-indol-3-yl)-(7-pyridin-3-ylmethyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl)-methanone	0.84 C	402.19
192	rac-[7-(6-Chloro-pyridin-2-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone	0.96 C	(³⁵ Cl) 436.1
193	rac-[7-(3,4-Difluoro-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone	1.0 C	437.18
194	rac-[7-(2-Chloro-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone	1.02 C	(³⁵ Cl) 435.1
195	rac-[7-(3-Chloro-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone	1.03 C	(³⁵ Cl) 435.11
196	rac-2-[6-(1-Methyl-1H-indole-3-carbonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridin-7-ylmethyl]-benzonitrile	0.91 C	412.15
197	rac-3-[6-(1-Methyl-1H-indole-3-carbonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridin-7-ylmethyl]-benzonitrile	0.92 C	412.14
198	rac-4-[6-(1-Methyl-1H-indole-3-carbonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridin-7-ylmethyl]-benzonitrile	0.92 C	412.13

199	rac-(1-Methyl-1H-indol-3-yl)-(7-pyridin-3-ylmethyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl)-methanone	0.81 C	388.17
200	rac-[7-(6-Chloro-pyridin-2-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-methyl-1H-indol-3-yl)-methanone	0.92 C	(³⁵ Cl) 422.09
201	rac-[7-(3,4-Difluoro-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-methyl-1H-indol-3-yl)-methanone	0.97 C	423.11
202	rac-[7-(2-Chloro-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-methyl-1H-indol-3-yl)-methanone	0.99 C	(³⁵ Cl) 421.11
203	rac-[7-(3-Chloro-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-methyl-1H-indol-3-yl)-methanone	1.01 C	(³⁵ Cl) 421.1
204	rac-(1-Methyl-1H-indol-3-yl)-[7-(3-pyrimidin-2-yl-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone	0.95 C	465.19
205	rac-(1-Ethyl-1H-indol-3-yl)-[7-(3-pyrimidin-2-yl-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone	0.98 C	479.17
206	rac-(1-Methyl-1H-indol-3-yl)-[7-(3-pyrazol-1-yl-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone	0.95 C	453.3
207	rac-(1-Methyl-1H-indol-3-yl)-[7-(3-[1,2,4]triazol-1-yl-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone	0.87 C	454.15
208	rac-(1-Ethyl-1H-indol-3-yl)-[7-(3-[1,2,4]triazol-1-yl-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone	0.90 C	468.18
209	rac-5-[6-(1-Methyl-1H-indole-3-carbonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridin-7-ylmethyl]-pyridine-2-carbonitrile	0.88 D	413.18
210	rac-(1-Methyl-1H-indol-3-yl)-[7-(6-methyl-pyridin-3-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone	0.86 D	402.23
211	rac-[7-(6-Ethyl-pyridin-3-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-methyl-1H-indol-3-yl)-methanone	0.89 D	416.21
212	rac-5-[6-(1-Ethyl-1H-indole-3-carbonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridin-7-ylmethyl]-pyridine-2-carbonitrile	0.91 D	427.11
213	rac-(1-Ethyl-1H-indol-3-yl)-[7-(6-methyl-pyridin-3-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone	0.89 D	416.24
214	rac-(1-Ethyl-1H-indol-3-yl)-[7-(6-ethyl-pyridin-3-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone	0.93 D	430.21

#Regioisomer separated by prep. HPLC

Example 215**rac-[7-(3,4-Dimethoxy-benzyl)-2-methoxy-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone**

NaOMe ~5.4M in MeOH (14 μ L, 0.08 mmol) was added to a mixture of Example 55 (27 mg, 0.05 mmol) and CuBr (1 mg) in NMP (0.5 mL) and the reaction mixture was heated to 110°C for 1h. The reaction was quenched with H₂O, filtered and purified directly by prep. HPLC (column: Waters X-bridge, 19x30 mm, 10 μ m, UV/MS, basic conditions) to give the title compound as a white solid (5 mg). LC-MS C: t_R = 0.94 min; [M-OMe]⁺ = 458.94.

Example 216**rac-[7-(3,4-Dimethoxy-benzyl)-3-methoxy-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone**

The title compound was prepared from Example 54 following the procedure as described for Example 215. LC-MS C: t_R = 0.95 min; [M+H]⁺ = 490.88.

Example 217**rac-[7-(3,4-Dimethoxy-benzyl)-2-ethoxy-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone**

The title compound was prepared from Example 55 and NaOEt following the procedure as described for Example 215. LC-MS C: t_R = 0.98 min; [M-OEt]⁺ = 458.96.

Example 218**rac-[7-(3,4-Dimethoxy-benzyl)-3-ethoxy-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone**

The title compound was prepared from Example 54 and NaOEt following the procedure as described for Example 215. LC-MS C: t_R = 0.99 min; [M+H]⁺ = 505.08.

Example 219**rac-[7-(4-Ethoxy-3-methoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone**

EtI (4 μ L, 0.05 mmol) was added to a mixture of Example 129 (10 mg, 0.02 mmol) and K₂CO₃ (5 mg, 0.03 mmol) in acetone (0.5 mL) and the resulting mixture was heated to 50°C for 20h. The reaction was quenched with H₂O, filtered and purified directly by prep. HPLC (column: Waters X-bridge, 19x30 mm, 10 μ m, UV/MS, basic conditions) to give the title compound as a white solid (5 mg). LC-MS C: t_R = 0.98 min; [M+H]⁺ = 475.04.

Example 220

rac-(1-Ethyl-1H-indol-3-yl)-{7-[3-methoxy-4-(2,2,2-trifluoro-ethoxy)-benzyl]-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl}-methanone

The title compound was prepared from Example 129 and 2,2,2-trifluoroethyl trifluoromethanesulphonate following the procedure as described for Example 219. LC-MS C: $t_R = 1.01$ min; $[M+H]^+ = 529.08$.

Example 221

rac-{7-[4-(2-Dimethylamino-ethoxy)-3-methoxy-benzyl]-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl}-(1-ethyl-1H-indol-3-yl)-methanone

The title compound was prepared from Example 129 and 2-chloro-*N,N*-dimethylethylamine.HCl following the procedure as described for Example 219. LC-MS C: $t_R = 0.94$ min; $[M+H]^+ = 518.07$.

Example 222

rac-(1-Ethyl-1H-indol-3-yl)-[7-(3-methoxy-4-propoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone

The title compound was prepared from Example 129 and ⁿPrI following the procedure as described for Example 219. LC-MS C: $t_R = 1.03$ min; $[M+H]^+ = 488.92$.

Example 223

rac-(1-Ethyl-1H-indol-3-yl)-[7-(4-isopropoxy-3-methoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone

The title compound was prepared from Example 129 and ⁱPrI following the procedure as described for Example 219. LC-MS C: $t_R = 1.02$ min; $[M+H]^+ = 488.9$.

Example 224

rac-{4-[6-(1-Ethyl-1H-indole-3-carbonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridin-7-ylmethyl]-2-methoxy-phenoxy}-acetic acid methyl ester

The title compound was prepared from Example 129 and methyl bromoacetate following the procedure as described for Example 219. LC-MS C: $t_R = 0.93$ min; $[M+H]^+ = 519.0$.

Example 225

rac-(1-Ethyl-1H-indol-3-yl)-[7-(3-methoxy-4-trifluoromethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone

A mixture of Example 129 (14 mg, 0.03 mmol) and K₂CO₃ (5 mg, 0.03 mmol) in DMF (0.5 mL) was heated to 50°C for 5 min before 5-(trifluoromethyl)dibenzothiophenium trifluoromethanesulfonate (14 mg, 0.03 mmol) was added and the reaction mixture was stirred for 18h. The reaction mixture was diluted with DMF (0.5 mL), filtered and purified

directly by prep. HPLC (column: Waters X-bridge, 19x30 mm, 10 μ m, UV/MS, basic conditions) to give the title compound as a beige solid (1.3 mg). LC-MS C: t_R = 1.05 min; $[M+H]^+$ = 514.88.

Example 226

rac-[4-[6-(1-Ethyl-1H-indole-3-carbonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridin-7-ylmethyl]-2-methoxy-phenoxy}-acetic acid

2M aq. NaOH (0.5 mL) was added to a RT soln. of Example 224 (5 mg, 0.01 mmol) in EtOH (0.5 mL) and the resulting mixture was stirred for 1h. The reaction mixture was diluted with DMF (0.5 mL), filtered and purified directly by prep. HPLC (column: Waters X-bridge, 19x30 mm, 10 μ m, UV/MS, basic conditions) to give the title compound as a white solid (4 mg). LC-MS C: t_R = 0.58 min; $[M+H]^+$ = 505.04.

Example 227

rac-[7-(3,4-Dimethoxy-benzyl)-2-ethynyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone

A mixture of Example 55 (32 mg, 0.06 mmol), CuI (0.5 mg) and Et₃N (0.62 mL) in THF (1 mL) was degassed with N₂ for 30s before Pd(PPh₃)₂Cl₂ (1 mg) was added. The reaction mixture was stirred for 1 min before TMS-ethyne (16 μ L, 0.12 mmol) was added and the mixture was heated to 80°C for 30 min. The reaction mixture was filtered through a cotton wool plug and concentrated *in vacuo*. The residue was re-dissolved in MeOH (2 mL) and 2M aq. K₂CO₃ (0.5 mL) was added and the mixture was stirred at RT for 20 min. The MeOH was evaporated *in vacuo* and the residue was dissolved in DMF (0.5 mL), filtered and purified directly by prep. HPLC (column: Waters X-bridge, 19x30 mm, 10 μ m, UV/MS, basic conditions) to give the title compound as a white solid (14 mg). LC-MS C: t_R = 0.96 min; $[M+H]^+$ = 484.99.

Example 228

rac-[7-(3,4-Dimethoxy-benzyl)-3-ethynyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone

The title compound was prepared from Example 54 following the procedure as described for Example 227. LC-MS C: t_R = 0.96 min; $[M+H]^+$ = 485.02.

Example 229

rac-[7-(3,4-Dimethoxy-benzyl)-2-ethyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone

A RT soln. of Example 227 (13 mg, 0.03 mmol) in EtOH (0.5 mL) was degassed with N₂ for 30s before 10% dry Pd/C (5 mg) was added. The N₂ atmosphere was replaced with H₂ and the reaction mixture was stirred for 18h. The mixture was diluted with EtOH (3 mL) and

filtered before being concentrated *in vacuo*. The residue was re-dissolved in DMF (0.5 mL) and purified directly by prep. HPLC (column: Waters X-bridge, 19x30 mm, 10 μ m, UV/MS, basic conditions) to give the title compound as a white solid (7 mg). LC-MS C: t_R = 1.03 min; $[M+H]^+$ = 488.89.

Example 230

rac-[3-Chloro-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone

A mixture of Example 54 (18 mg, 0.03 mmol) and CuCl (5 mg, 0.05 mmol) in DMF (0.5 mL) was heated to 120°C for 18h. The reaction mixture was diluted with DMF (0.5 mL), filtered and purified directly by prep. HPLC (column: Waters X-bridge, 19x30 mm, 10 μ m, UV/MS, basic conditions) to give the title compound as a white solid (10 mg). LC-MS C: t_R = 1.0 min; $[M(^{35}\text{Cl})+H]^+$ = 494.97.

Example 231

rac-7-(3,4-Dimethoxy-benzyl)-6-(1-ethyl-1H-indole-3-carbonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine-3-carbonitrile

A mixture of Example 54 (18 mg, 0.03 mmol) and CuCN (4.5 mg, 0.05 mmol) in DMF (0.5 mL) was heated to 120°C for 22h. The reaction mixture was diluted with DMF (0.5 mL), filtered and purified directly by prep. HPLC (column: Waters X-bridge, 19x30 mm, 10 μ m, UV/MS, basic conditions) to give the title compound as a white solid (5 mg). LC-MS C: t_R = 0.91 min; $[M(^{35}\text{Cl})+H]^+$ = 486.04.

Example 232

rac-[7-(3,4-Dimethoxy-benzyl)-3-ethyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone

A RT mixture of Example 54 (21 mg, 0.04 mmol), ethylboronic acid (5.8 mg, 0.08 mmol), Pd(dppf)Cl₂.DCM (3.2 mg, 0.004 mmol) and Cs₂CO₃ (26 mg, 0.08 mmol) in THF (0.5 mL) was degassed with N₂ for 30s before being heated to 75°C for 17h. The reaction mixture was diluted with DMF (0.5 mL), filtered and purified directly by prep. HPLC (column: Waters X-bridge, 19x30 mm, 10 μ m, UV/MS, basic conditions) to give the title compound as a white solid (9 mg). LC-MS C: t_R = 1.02 min; $[M(^{35}\text{Cl})+H]^+$ = 488.9.

Example 233

rac-[7-(3,4-Dimethoxy-benzyl)-3-methyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone

The title compound was prepared from Example 54 and potassium methyltrifluoroborate following the procedure as described for Example 232. LC-MS C: t_R = 0.98 min; $[M+H]^+$ = 475.07.

Example 234

rac-[2-Chloro-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone

The title compound was prepared from Example 55 following the procedure as described for Example 230. LC-MS C: t_R = 1.02 min; $[M(^{35}\text{Cl})+H]^+$ = 494.99.

Example 235

rac-7-(3,4-Dimethoxy-benzyl)-6-(1-ethyl-1H-indole-3-carbonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine-2-carbonitrile

The title compound was prepared from Example 55 following the procedure as described for Example 231. LC-MS C: t_R = 0.92 min; $[M+H]^+$ = 486.04.

Example 236

rac-[7-(3,4-Dimethoxy-benzyl)-2-methyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone

The title compound was prepared from Example 55 following the procedure as described for Example 233. LC-MS C: t_R = 0.99 min; $[M+H]^+$ = 475.07.

Example 237

rac-Trifluoro-methanesulfonic acid 4-[6-(1-ethyl-1H-indole-3-carbonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridin-7-ylmethyl]-2-methoxy-phenyl ester

4-Nitrophenyl trifluoromethanesulfonate (200 mg, 0.74 mmol) and K_2CO_3 (204 mg, 1.47 mmol) were added to a RT soln. of Example 129 (329 mg, 0.74 mmol) in DMF (5 mL) and the resulting mixture was stirred for 20h. The reaction was quenched with water (20 mL) and extracted with EtOAc (3x). The combined organic layers were washed with 0.5M aq. NaOH, H_2O , dried over Na_2SO_4 , filtered and evaporated *in vacuo* to give the title compound as a yellow oil (292 mg). LC-MS C: t_R = 1.05 min; $[M+H]^+$ = 578.88.

Example 238

rac-Trifluoro-methanesulfonic acid 5-[6-(1-ethyl-1H-indole-3-carbonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridin-7-ylmethyl]-2-methoxy-phenyl ester

The title compound was prepared from Example 150 following the procedure as described for Example 237. LC-MS C: t_R = 1.04 min; $[M+H]^+$ = 578.94.

Example 239

rac-[7-(3-Ethoxy-4-methoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone

The title compound was prepared from Example 150 following the procedure as described for Example 219. LC-MS C: t_R = 0.98 min; $[M+H]^+$ = 475.06.

Example 240

rac-(1-Ethyl-1H-indol-3-yl)-{7-[4-methoxy-3-(2,2,2-trifluoro-ethoxy)-benzyl]-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl}-methanone

The title compound was prepared from Example 150 following the procedure as described for Example 220. LC-MS C: t_R = 1.01 min; $[M+H]^+$ = 529.02.

Example 241

rac-(1-Ethyl-1H-indol-3-yl)-{7-[3-(2-hydroxy-ethoxy)-4-methoxy-benzyl]-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl}-methanone

The title compound was prepared from Example 150 and 2-chloroethanol following the procedure as described for Example 221. LC-MS C: t_R = 0.86 min; $[M+H]^+$ = 490.89.

Example 242

rac-{7-[3-(2-Dimethylamino-ethoxy)-4-methoxy-benzyl]-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl}-(1-ethyl-1H-indol-3-yl)-methanone

The title compound was prepared from Example 150 following the procedure as described for Example 221. LC-MS C: t_R = 0.94 min; $[M+H]^+$ = 518.1.

Example 243

rac-(1-Ethyl-1H-indol-3-yl)-[7-(4-methoxy-3-propoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone

The title compound was prepared from Example 150 following the procedure as described for Example 222. LC-MS C: t_R = 1.02 min; $[M+H]^+$ = 488.91.

Example 244

rac-(1-Ethyl-1H-indol-3-yl)-[7-(3-isopropoxy-4-methoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone

The title compound was prepared from Example 150 following the procedure as described for Example 223. LC-MS C: t_R = 1.01 min; $[M+H]^+$ = 488.97.

Example 245

rac-{5-[6-(1-Ethyl-1H-indole-3-carbonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridin-7-ylmethyl]-2-methoxy-phenoxy}-acetic acid methyl ester

The title compound was prepared from Example 150 following the procedure as described for Example 224. LC-MS C: t_R = 0.93 min; $[M+H]^+$ = 519.04.

Example 246

rac-4-(3,4-Dimethoxy-benzyl)-5-(1-ethyl-1H-indole-3-carbonyl)-4,5,6,7-tetrahydro-thieno[3,4-c]pyridine-1-carbonitrile

The title compound was prepared from Example 131 following the procedure as described for Example 231. LC-MS C: t_R = 0.92 min; $[M+H]^+$ = 486.02.

Example 247

rac-[1-Chloro-4-(3,4-dimethoxy-benzyl)-6,7-dihydro-4H-thieno[3,4-c]pyridin-5-yl]-(1-ethyl-1H-indol-3-yl)-methanone

The title compound was prepared from Example 131 following the procedure as described for Example 230. LC-MS C: t_R = 1.02 min; $[M(^{35}\text{Cl})+H]^+$ = 495.06.

Example 248

rac-5-[6-(1-Ethyl-1H-indole-3-carbonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridin-7-ylmethyl]-2-methoxy-benzonitrile

ZnCN₂ (5 mg, 0.045 mmol) and Pd(PPh₃)₄ (2 mg) were added to a RT soln. of Example 238 (24 mg, 0.04 mmol) in DMF (0.5 mL) and the resulting mixture was heated to 110°C for 18h. The reaction mixture was diluted with DMF (0.5 mL), filtered and purified directly by prep. HPLC (column: Waters X-bridge, 19x30 mm, 10 μ m, UV/MS, basic conditions) to give the title compound as a white solid (2 mg). LC-MS C: t_R = 0.95 min; $[M+H]^+$ = 456.04.

Example 249

rac-(1-Ethyl-1H-indol-3-yl)-[7-(4-ethyl-3-methoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone

Et₂Zn (80 μ L, 0.08 mmol) was added to a RT mixture of Example 237 (23 mg, 0.04 mmol) and Pd(dppf)Cl₂.DCM (3.2 mg, 0.004 mmol) in dioxane (1 mL) and the reaction mixture was heated to 110°C for 4h. The reaction mixture was diluted with DMF (0.5 mL), filtered and

purified directly by prep. HPLC (column: Waters X-bridge, 19x30 mm, 10 μ m, UV/MS, basic conditions) to give the title compound as a white solid (10 mg). LC-MS C: t_R = 1.08 min; $[M+H]^+$ = 458.95.

Example 250

rac-[7-(3,4-Dimethoxy-benzyl)-3-trifluoromethyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone

Step 1: *rac-trans-N,N'*-dimethyl-1,2-cyclohexanediamine (1 mg) was added to a mixture of Example 54 (27 mg, 0.05 mmol), CuI (0.5 mg) and NaI (15 mg, 0.1 mmol) in dioxane (0.5 mL) and the resulting mixture was heated to 110°C for 36h. The reaction mixture was diluted with DMF (0.5 mL), filtered and purified directly by prep. HPLC (column: Waters X-bridge, 19x30 mm, 10 μ m, UV/MS, basic conditions) to give *rac*-[7-(3,4-dimethoxy-benzyl)-3-iodo-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)methanone as a white solid (19 mg). LC-MS C: t_R = 1.03 min; $[M+H]^+$ = 586.76.

Step 2: A soln. of methyl chlorodifluoroacetate (9 mg, 0.06 mmol) in DMF (250 μ L) was added dropwise to a 120°C mixture of *rac*-[7-(3,4-dimethoxy-benzyl)-3-iodo-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)methanone (18 mg, 0.03 mmol), CuI (9 mg, 0.05 mmol) and KF (3 mg, 0.05 mmol) in DMF (350 μ L) and the resulting mixture was heated for 20h. The reaction mixture was diluted with DMF (0.5 mL), filtered and purified directly by prep. HPLC (column: Waters X-bridge, 19x30 mm, 10 μ m, UV/MS, basic conditions) to give the title compound as a beige solid (3 mg). LC-MS C: t_R = 1.0 min; $[M+H]^+$ = 529.05.

Example 251

rac-(1-Ethyl-1H-indol-3-yl)-[7-(3-methoxy-4-methyl-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone

The title compound was prepared from Example 237 and Me₂Zn following the procedure as described for Example 249. LC-MS C: t_R = 1.04 min; $[M+H]^+$ = 445.07.

Example 252

rac-(1-Ethyl-1H-indol-3-yl)-[7-(3-ethyl-4-methoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone

The title compound was prepared from Example 238 following the procedure as described for Example 249. LC-MS C: t_R = 1.07 min; $[M+H]^+$ = 458.96.

Example 253

rac-(1-Ethyl-1H-indol-3-yl)-[7-(4-methoxy-3-methyl-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone

The title compound was prepared from Example 238 and Me₂Zn following the procedure as described for Example 249. LC-MS C: t_R = 1.04 min; [M+H]⁺ = 445.07.

Example 254

rac-[7-(3,4-Dimethoxy-benzyl)-3-[1,2,3]triazol-2-yl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone

A mixture of Example 54 (14 mg, 0.026 mmol), 1*H*-1,2,3-triazole (3 µL, 0.05 mmol), Cs₂CO₃ (17 mg, 0.05 mmol), CuI (1 mg) and *rac-trans-N,N'*-dimethyl-1,2-cyclohexanediamine (1 mg) in DMF (1 mL) was heated to 120°C for 18h. The reaction mixture was diluted with DMF (0.5 mL), filtered and purified directly by prep. HPLC (column: Waters X-bridge, 19x30 mm, 10 µm, UV/MS, basic conditions) to give the title compound as a beige solid (1 mg). LC-MS C: t_R = 0.85 min; [M+H]⁺ = 528.0. Note: Although the asymmetric triazole regioisomer was also formed it was not isolated.

Example 255

rac-[7-(3-Cyclopropoxy-4-methoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone

Step 1: Cu(OAc)₂ (20 mg, 0.11 mmol) was stirred in DCM (2 mL) under an air atmosphere for 10 min before vinylboronic anhydride.pyridine complex (18 mg, 0.075 mmol), Example 150 (50 mg, 0.11 mmol) and pyridine (93 µL, 0.09 mmol) were added and the mixture was stirred at RT overnight. The reaction mixture was filtered through a pad of celite rinsing with additional DCM. The filtrate was evaporated *in vacuo* and the residue was re-dissolved in DMF (0.5 mL) and purified directly by prep. HPLC (column: Waters X-bridge, 30x75 mm, 10 µm, UV/MS, basic conditions) to give *rac*-(1-ethyl-1H-indol-3-yl)-[7-(4-methoxy-3-vinyloxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone as a yellow oil (26 mg). LC-MS C: t_R = 0.99 min; [M+H]⁺ = 473.11.

Step 2: A soln. of TFA (8 µL, 0.11 mmol) in DCM (200 µL) was added to a 0°C soln. of Et₂Zn (110 µL, 2 eq.) 1M soln. in hexanes in DCM (150 µL) under argon and the resulting mixture was stirred for 20 min before a soln. of CH₂I₂ (9 µL, 0.11 mmol) in DCM (150 µL) was added. After a further 20 min a soln. of *rac*-(1-ethyl-1H-indol-3-yl)-[7-(4-methoxy-3-vinyloxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone (26 mg, 0.055 mmol) in DCM (250 µL) was added and the ice bath was removed. The reaction mixture was stirred for 30 min at RT before being quenched with sat. aq. NaHCO₃ soln. and stirred for 10 min. The solids were

removed by filtration through a celite pad rinsing with DCM and the two layers were separated. The organic layer was washed with water (1x), dried over Na₂SO₄, filtered and evaporated *in vacuo*. The residue was re-dissolved in DMF (0.5 mL) and purified directly by prep. HPLC (column: Waters X-bridge, 19x30 mm, 10 µm, UV/MS, basic conditions) to give the title compound as a yellow solid (6 mg). LC-MS C: t_R = 0.99 min; $[M+H]^+$ = 487.14.

Example 256**rac-(1-Ethyl-1H-indol-3-yl)-[7-(3-[1,2,4]oxadiazol-3-yl-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone**

NH₂OH (33 µL, ~50% in H₂O) was added to a soln. of Example 189 (11 mg, 0.025 mmol) in EtOH (0.5 mL) and the resulting mixture was stirred at RT for 18h. The volatiles were removed *in vacuo* and the residue was re-dissolved in trimethyl orthoformate (0.5 mL) before BF₃.Et₂O (3 µL) was added and the mixture was heated to 60°C for 1h in an Emrys Optimiser microwave reactor. The volatiles were removed *in vacuo* and the residue was dissolved in MeCN (1 mL) and purified directly by prep. HPLC (column: Waters X-bridge, 19x30 mm, 10 µm, UV/MS, basic conditions) to give the title compound as a yellow solid (1 mg). LC-MS D: t_R = 0.96 min; $[M+H]^+$ = 469.16.

Example 257**rac-6-[6-(1-Ethyl-1H-indole-3-carbonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridin-7-ylmethyl]-pyridine-2-carbonitrile**

A mixture of Example 192 (22 mg, 0.05 mmol), Pd(TFA)₂ (1 mg), Zn powder (1 mg), racemic-2-(di-*t*-butylphosphino)-1,1'-binaphthyl (2 mg) and Zn(CN)₂ (3.5 mg, 0.03 mmol) in DMA (0.5 mL) was heated to 95°C for 75 min. The reaction mixture was cooled to RT, diluted with DMF (0.5 mL), filtered and purified directly by prep. HPLC (column: Waters X-bridge, 19x30 mm, 10 µm, UV/MS, basic conditions) to give the title compound as a white solid (16 mg). LC-MS D: t_R = 0.92 min; $[M+H]^+$ = 427.13.

Example 258**rac-6-[6-(1-Methyl-1H-indole-3-carbonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridin-7-ylmethyl]-pyridine-2-carbonitrile**

The title compound was prepared from Example 200 following the procedure as described for Example 257. LC-MS D: t_R = 0.89 min; $[M+H]^+$ = 413.17.

Example 259**rac-(1-Ethyl-1H-indol-3-yl)-[7-(6-methoxy-pyridin-2-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone**

NaOMe ~5.4M in MeOH (50 μ L) was added to a soln. of Example 192 (22 mg, 0.05 mmol) in 1:1 MeOH:dioxane (0.5 mL) and the resulting mixture was heated to 70°C for 48h. The reaction mixture was cooled to RT, diluted with DMF (0.5 mL), filtered and purified directly by prep. HPLC (column: Waters X-bridge, 19x30 mm, 10 μ m, UV/MS, basic conditions) to give the title compound as a white solid (16 mg). LC-MS D: t_R = 0.98 min; $[M+H]^+$ = 432.18.

Example 260**rac-[7-(6-Methoxy-pyridin-2-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-methyl-1H-indol-3-yl)-methanone**

The title compound was prepared from Example 200 following the procedure as described for Example 259. LC-MS D: t_R = 0.95 min; $[M+H]^+$ = 418.2.

Example 261**rac-(1-Methyl-1H-indol-3-yl)-[7-(3-[1,2,4]oxadiazol-3-yl-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone**

The title compound was prepared from Example 197 following the procedure as described for Example 257. LC-MS D: t_R = 0.89 min; $[M+H]^+$ = 413.17.

Example 262: rac-3-[6-(1-Methyl-1H-indole-3-carbonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridin-7-ylmethyl]-benzamide and**Example 263: rac-3-[6-(1-Methyl-1H-indole-3-carbonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridin-7-ylmethyl]-benzoic acid**

2M aq. NaOH (0.24 mL, 0.48 mmol) was added to a RT soln. of Example 197 (50 mg, 0.12 mmol) in dioxane (1 mL) and the resulting mixture was heated to 95°C for 24h. The reaction was monitored by LCMS and stopped after complete consumption of nitrile starting material. The reaction mixture was neutralized with 4M HCl in dioxane and evaporated *in vacuo*. The residue was dissolved in DMF (1 mL), filtered and purified directly by prep. HPLC (column: Waters X-bridge, 30x75 mm, 10 μ m, UV/MS, basic conditions) to give both title compounds as white solids (24 mg and 16 mg). LC-MS D: t_R = 0.82 min; $[M+H]^+$ = 430.15 and t_R = 0.6 min; $[M+H]^+$ = 417.14 respectively.

Example 264: rac-3-[6-(1-Ethyl-1H-indole-3-carbonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridin-7-ylmethyl]-benzamide and

Example 265: rac-3-[6-(1-Ethyl-1H-indole-3-carbonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridin-7-ylmethyl]-benzoic acid

The title compounds were prepared from Example 189 following the procedure as described for Examples 262 and 263. LC-MS D: $t_R = 0.85$ min; $[M+H]^+ = 444.19$ and $t_R = 0.63$ min; $[M+H]^+ = 445.14$ respectively.

Example 266

rac-[7-(6-Methoxy-pyridin-3-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-methyl-1H-indol-3-yl)-methanone

The title compound was prepared from (7-((6-chloropyridin-3-yl)methyl)-4,5-dihydrothieno[2,3-c]pyridin-6(7H)-yl)(1-methyl-1H-indol-3-yl)methanone following the procedure as described for Example 259. LC-MS D: $t_R = 0.91$ min; $[M+H]^+ = 418.19$.

Example 267

rac-(1-Ethyl-1H-indol-3-yl)-[7-(6-methoxy-pyridin-3-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone

The title compound was prepared from (7-((6-chloropyridin-3-yl)methyl)-4,5-dihydrothieno[2,3-c]pyridin-6(7H)-yl)(1-ethyl-1H-indol-3-yl)methanone following the procedure as described for Example 259. LC-MS D: $t_R = 0.95$ min; $[M+H]^+ = 432.21$.

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 μ g/ml G418, 100 U/ml penicillin, 100 μ g/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% CO₂.

Human orexin-A as an agonist is prepared as 1 mM stock soln. in MeOH: water (1:1), diluted in HBSS containing 0.1 % bovine serum albumin (BSA), NaHCO₃: 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 soln. 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), NaHCO₃: 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, NaHCO₃: 0.375g/l, 5 mM probenecid (Sigma) and 3 µM of the fluorescent calcium indicator fluo-4 AM (1 mM stock soln. 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% CO₂ 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 10 min or (where explicitly indicated) 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 IC₅₀ value (the concentration of compound needed to inhibit 50 % of the agonistic response) is determined and may be normalized using the obtained IC₅₀ value of a on-plate reference compound. Optimized conditions were achieved by adjustment of pipetting speed and cell splitting regime. The calculated IC₅₀ 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 IC₅₀ values have been determined several times for the same compound, the geometric mean has been given. Antagonistic activities of example compounds are displayed in Table 11.

Table 11.

Example	IC₅₀ OX1 [nM]	IC₅₀ OX2 [nM]	Example	IC₅₀ OX1 [nM]	IC₅₀ OX2 [nM]	Example	IC₅₀ OX1 [nM]	IC₅₀ OX2 [nM]
1	2744	30	89	1750	87	179	1287	75
2	2340	52	90	2890	275	180	298	38
3	4637	53	91	346	14	181	160	37
4	98	47	92	43	11	182	165	22
5	118	75	93	144	8	183	25	30
6	98	144	94	319	22	184	22	24
7	103	64	95	1980	62	185	236	28
8	184	95	96	36	5	186	154	15
9	90	119	97	1530	43	187	99	62

Example	IC₅₀ OX1 [nM]	IC₅₀ OX2 [nM]	Example	IC₅₀ OX1 [nM]	IC₅₀ OX2 [nM]	Example	IC₅₀ OX1 [nM]	IC₅₀ OX2 [nM]
10	81	20	98	3630	37	188	264	20
11	30	14	99	1340	41	189	68	6
12	171	81	100	2680	94	190	146	26
13	1323	168	101	>6090	217	191	165	11
14	1522	787	102	310	34	192	39	3
15	4056	437	103	106	27	193	290	55
16a	666	31	104	278	35	194	188	24
16b	1180	184	105	1130	45	195	657	33
17	533	85	106	50	8	196	275	12
18	1064	24	107	345	13	197	46	2
19	845	19	108	571	15	198	132	15
20	829	59	109	228	6	199	270	8
21	1852	122	110	60	8	200	47	3
22	354	23	111	2140	30	201	324	14
23	1806	198	112	143	12	202	198	18
24	1529	92	113	2430	80	203	302	21
25	952	917	114	81	17	204	5	8
26	2782	130	115	79	7	205	8	10
27	355	378	116	215	20	206	6	7
28a	480	26	117	621	250	207	35	6
28b	1105	265	118	112	32	208	50	7
29	868	74	119	124	18	209	>566*	16*
30	1624	27	120	264	10	210	459*	9*
31	889	21	121	54	13	211	212*	17*
32	763	47	122	1770	65	212	406*	31*
33	1626	164	123	84	20	213	293*	23*
34	632	51	124	4420	208	214	106*	19*
35	3318	72	125	143	29	215	64	10
36	900	71	126	67	10	216	35	14
37	1693	613	127	87	35	217	90	10
38	5389	46	128	1120	219	218	69	13

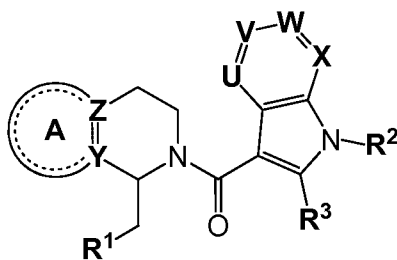
Example	IC₅₀ OX1 [nM]	IC₅₀ OX2 [nM]	Example	IC₅₀ OX1 [nM]	IC₅₀ OX2 [nM]	Example	IC₅₀ OX1 [nM]	IC₅₀ OX2 [nM]
39	3621	812	129	109	9	219	15	11
40	130	48	130	9	8	220	66	22
41	46	100	131	73	27	221	1730	139
42	500	400	132	25	12	222	48	18
43	238	68	133	29	10	223	28	18
44	1278	855	134	19	7	224	41	14
45	261	20	135	30	19	225	556	178
46	203	48	136	721	98	226	684	120
47	398	65	137	1010	120	227	31	25
48	607	83	138	27	16	228	64	22
49	394	33	139	21	17	229	54	46
50	314	39	140	13	16	230	32	21
51	494	76	141	22	18	231	29	16
52	469	102	142	1180	121	232	33	29
53	34	23	143	822	116	233	21	17
54	31	23	144	71	13	234	66	55
55	82	106	145	12	12	235	114	23
56	48	158	146	15	23	236	33	27
57	518	196	147	27	11	237	179	108
58	356	118	148	15	10	238	58	161
59	243	157	149	96	14	239	7	13
60	69	47	150	74	15	240	16	22
61	80	119	151	16	9	241	23	14
62	679	309	152	93	19	242	1270	797
63	1949	592	153	1930	67	243	13	19
64	42	77	154	1700	95	244	23	16
65	86	91	155	62	17	245	94	14
66	164	188	156	92	20	246	75	21
67	61	36	157	1420	61	247	70	31
68	245	217	158	607	21	248	38	11
69	343	195	159	82	20	249	79	116

Example	IC₅₀ OX1 [nM]	IC₅₀ OX2 [nM]	Example	IC₅₀ OX1 [nM]	IC₅₀ OX2 [nM]	Example	IC₅₀ OX1 [nM]	IC₅₀ OX2 [nM]
70	302	234	160	70	251	250	98	147
71	146	256	161	75	247	251	43	65
72	47	483	162	7	13	252	72	128
73	181	516	163	184	16	253	58	93
74	100	202	164	66	67	254	14	21
75	273	430	165	268	33	255	14	20
76	123	47	166	35	45	256	30	7
77	77	60	167	188	47	257	106	3
78	12090	418	168	162	23	258	67	2
79	176	196	169	58	94	259	33	2
80	267	311	170	173	18	260	33	2
81	597	2768	171	48	30	261	11	4
82	190	250	172	65	21	262	127*	5*
83	45	60	173	18	14	263	3348*	565*
84	38	22	174	28	15	264	190*	7*
85	127	175	175	27	17	265	2832*	413*
86	5820	59	176	44	57	266	148*	8*
87	3750	44	177	1374	111	267	120*	11*
88	910	52	178	1608	101			

* IC₅₀ values measured using a compound incubation time of 120 min.

Claims

1. A compound of formula (I)



Formula (I)

wherein

Z represents a carbon atom or a nitrogen atom and **Y** represents a carbon atom; and ring **A** together with the atoms **Z** and **Y** represents a 5- or 6-membered aromatic ring;

wherein, in case **Z** represents a carbon atom, said ring **A** is a benzene, a pyridine, a thiophene, a pyrazole, or a thiazole ring;

or, in case **Z** represents a nitrogen atom, said ring **A** is an imidazole or a pyrrole ring;

wherein said rings **A** independently are unsubstituted or substituted with one or two substituents independently selected from the group consisting of (C₁₋₄)alkyl, (C₁₋₄)alkoxy, (C₂₋₄)alkinyl, halogen, cyano, (C₁₋₃)fluoroalkyl, (C₁₋₃)fluoroalkoxy; (C₃₋₆)cycloalkyl, 5-membered heteroaryl, and amino;

R¹ represents aryl or heteroaryl, wherein the aryl or heteroaryl independently is:

- unsubstituted, or mono-, di-, or tri-substituted, wherein the substituents are independently selected from the group consisting of:
 - (C₁₋₄)alkyl, (C₁₋₄)alkoxy, (C₃₋₆)cycloalkyl, halogen, cyano, hydroxy, (C₁₋₃)fluoroalkyl, (C₁₋₃)fluoroalkoxy, (C₁₋₃)fluoroalkyl-sulfonyloxy, (C₁₋₄)alkyl-sulfonyl, (C₃₋₆)cycloalkyl-oxy, (C₁₋₄)alkoxy-(C₂₋₄)alkoxy, hydroxy-(C₂₋₄)alkoxy, **R**⁴**R**⁵N-(C₂₋₄)alkoxy, **R**⁶-CO-, **R**⁷-CO-(C₁₋₄)alkoxy;
 - phenyl or 5- or 6-membered heteroaryl, wherein said phenyl or 5- or 6-membered heteroaryl is independently unsubstituted, or mono-, di-, or tri-substituted, wherein the substituents are independently selected from the group consisting of (C₁₋₄)alkyl, (C₁₋₄)alkoxy, halogen, cyano, (C₁₋₃)fluoroalkyl, and (C₁₋₃)fluoroalkoxy; and
 - phenyl-(C₁₋₄)alkoxy or 5- or 6-membered heteroaryl-(C₁₋₄)alkoxy, wherein said phenyl-(C₁₋₄)alkoxy or 5- or 6-membered heteroaryl-(C₁₋₄)alkoxy is independently unsubstituted, or mono-, di-, or tri-substituted, wherein the substituents are independently selected from the group consisting of

(C₁₋₄)alkyl, (C₁₋₄)alkoxy, halogen, cyano, (C₁₋₃)fluoroalkyl, and (C₁₋₃)fluoroalkoxy;

with the proviso:

- that at maximum one substituent selected from phenyl, 5- or 6-membered heteroaryl, phenyl-(C₁₋₄)alkoxy, and 5- or 6-membered heteroaryl-(C₁₋₄)alkoxy is present; and that, if present, said substituent is attached in a position other than the ortho-position;
- or said aryl or heteroaryl is fused to a non-aromatic 5- or 6-membered ring, wherein said ring optionally contains one or two heteroatoms independently selected from oxygen and nitrogen; wherein said ring is optionally substituted with one or two substituents independently selected from (C₁₋₃)alkyl, oxo, and halogen;

R² represents hydrogen, (C₁₋₆)alkyl, (C₃₋₆)cycloalkyl, (C₁₋₄)alkoxy-(C₂₋₄)alkyl, hydroxy-(C₂₋₄)alkyl, **R**⁸**R**⁹N-(C₂₋₄)alkyl, or (C₁₋₄)fluoroalkyl;

R³ represents hydrogen or methyl;

one of **U**, **V**, **W**, and **X** represents **CR**¹⁰ or N, and the remaining represent CH; wherein

- **R**¹⁰ represents hydrogen, fluorine, chlorine, methyl, or methoxy;

R⁴ and **R**⁵ independently represent hydrogen or (C₁₋₄)alkyl;

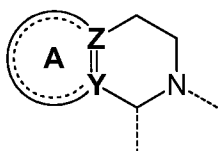
R⁶ represents hydroxy or amino;

R⁷ represents hydroxy or (C₁₋₄)alkoxy;

R⁸ and **R**⁹ independently represent hydrogen or (C₁₋₄)alkyl;

or a salt thereof.

2. A compound according to claim 1; wherein the fragment:



is a group selected from the group consisting of 1,2,3,4-tetrahydro-isoquinoline, 5,6,7,8-tetrahydro-[1,7]naphthyridine, 4,5,6,7-tetrahydro-thieno[2,3-c]pyridine, 4,5,6,7-tetrahydro-thieno[3,4-c]pyridine, 4,5,6,7-tetrahydro-thieno[3,2-c]pyridine, 4,5,6,7-tetrahydro-1H-pyrazolo[3,4-c]pyridine, 4,5,6,7-tetrahydro-1H-pyrazolo[4,3-c]pyridine, 4,5,6,7-tetrahydro-thiazolo[5,4-c]pyridine, and 5,6,7,8-tetrahydro-imidazo[1,2-a]pyrazine; wherein said groups independently are unsubstituted or substituted in ring **A** with one or two substituents independently selected from the group consisting of (C₁₋₄)alkyl, (C₁₋₄)alkoxy, (C₂₋₄)alkinyl,

halogen, cyano, (C₁₋₃)fluoroalkyl, (C₁₋₃)fluoroalkoxy; (C₃₋₆)cycloalkyl, 5-membered heteroaryl, and amino;

or a salt thereof.

3. A compound according to claim 1 or 2; wherein

- **R¹** represents aryl or heteroaryl, wherein the aryl or heteroaryl independently is unsubstituted, or mono-, di-, or tri-substituted; wherein
 - the substituents are independently selected from the group consisting of (C₁₋₄)alkyl, (C₁₋₄)alkoxy, (C₃₋₆)cycloalkyl, halogen, cyano, hydroxy, (C₁₋₃)fluoroalkyl, (C₁₋₃)fluoroalkoxy, (C₁₋₃)fluoroalkyl-sulfonyloxy, (C₁₋₄)alkyl-sulfonyl, (C₃₋₆)cycloalkyl-oxy, (C₁₋₄)alkoxy-(C₂₋₄)alkoxy, hydroxy-(C₂₋₄)alkoxy, **R⁴R⁵N**-(C₂₋₄)alkoxy, **R⁶-CO-**, **R⁷-CO-**(C₁₋₄)alkoxy;
- or **R¹** represents phenyl or 5- or 6-membered heteroaryl, wherein the phenyl or 5- or 6-membered heteroaryl independently is mono-, di-, or tri-substituted; wherein
 - one of said substituents is attached in a position other than the ortho-position; wherein said substituent is:
 - phenyl or 5- or 6-membered heteroaryl, wherein said phenyl or 5- or 6-membered heteroaryl is independently unsubstituted, or mono-, di-, or tri-substituted, wherein the substituents are independently selected from the group consisting of (C₁₋₄)alkyl, (C₁₋₄)alkoxy, halogen, cyano, (C₁₋₃)fluoroalkyl, and (C₁₋₃)fluoroalkoxy; or
 - phenyl-(C₁₋₄)alkoxy or 5- or 6-membered heteroaryl-(C₁₋₄)alkoxy, wherein said phenyl-(C₁₋₄)alkoxy or 5- or 6-membered heteroaryl-(C₁₋₄)alkoxy is independently unsubstituted, or mono-, di-, or tri-substituted, wherein the substituents are independently selected from the group consisting of (C₁₋₄)alkyl, (C₁₋₄)alkoxy, halogen, cyano, (C₁₋₃)fluoroalkyl, and (C₁₋₃)fluoroalkoxy;
 - and the other of said substituents, if present, is/are independently selected from the group consisting of (C₁₋₄)alkyl, (C₁₋₄)alkoxy, halogen, cyano, (C₁₋₃)fluoroalkyl, and (C₁₋₃)fluoroalkoxy;
- or **R¹** represents phenyl or 5- or 6-membered heteroaryl, wherein said phenyl or 5- or 6-membered heteroaryl is fused to a non-aromatic 5- or 6-membered ring, wherein said ring optionally contains one or two heteroatoms independently selected from oxygen and nitrogen; wherein said ring is optionally substituted with one or two substituents independently selected from (C₁₋₃)alkyl, oxo, and halogen;

or a salt thereof.

4. A compound according to any one of claims 1 to 3; wherein

- **R¹** represents aryl or heteroaryl, wherein the aryl or heteroaryl independently is unsubstituted, or mono-, di-, or tri-substituted; wherein
 - the substituents are independently selected from the group consisting of (C₁₋₄)alkyl, (C₁₋₄)alkoxy, halogen, cyano, hydroxy, (C₁₋₃)fluoroalkyl, (C₁₋₃)fluoroalkoxy, (C₁₋₃)fluoroalkyl-sulfonyloxy, (C₃₋₆)cycloalkyl-oxy, hydroxy-(C₂₋₄)alkoxy, **R⁴R⁵N**-(C₂₋₄)alkoxy, **R⁶-CO-**, and **R⁷-CO-**(C₁₋₄)alkoxy;
- or **R¹** represents phenyl or 6-membered heteroaryl, wherein the phenyl or 6-membered heteroaryl independently is mono-, or di-substituted; wherein
 - one of said substituents is attached in a position other than the ortho-position; wherein said substituent is:
 - phenyl or 5- or 6-membered heteroaryl, wherein said phenyl or 5- or 6-membered heteroaryl is independently unsubstituted, or mono-, di-, or tri-substituted, wherein the substituents are independently selected from the group consisting of (C₁₋₄)alkyl, (C₁₋₄)alkoxy, halogen, cyano, (C₁₋₃)fluoroalkyl, and (C₁₋₃)fluoroalkoxy;
 - and the other of said substituents, if present, is independently selected from the group consisting of (C₁₋₄)alkyl, (C₁₋₄)alkoxy, halogen, cyano, (C₁₋₃)fluoroalkyl, and (C₁₋₃)fluoroalkoxy;
- or **R¹** represents a benzodioxinyl, or a benzodioxolyl group;

or a salt thereof.

5. A compound according to any one of claims 1 to 4; wherein

- **R¹** represents a phenyl, or a pyridinyl group wherein said group independently is unsubstituted or mono-, di-, or tri-substituted; wherein
 - the substituents are independently selected from the group consisting of (C₁₋₄)alkyl, (C₁₋₄)alkoxy, halogen, cyano, (C₁₋₃)fluoroalkyl, (C₁₋₃)fluoroalkoxy, and hydroxy-(C₂₋₄)alkoxy;
- or **R¹** represents phenyl which is mono-, or di-substituted; wherein
 - one of said substituents is attached in a position other than the ortho-position; wherein said substituent is:
 - phenyl or 5- or 6-membered heteroaryl, wherein said phenyl or 5- or 6-membered heteroaryl is independently unsubstituted, or mono-, di-, or tri-substituted, wherein the substituents are independently selected

from the group consisting of (C₁₋₄)alkyl, (C₁₋₄)alkoxy, halogen, cyano, (C₁₋₃)fluoroalkyl, and (C₁₋₃)fluoroalkoxy;

- and the other of said substituents, if present, is independently selected from the group consisting of (C₁₋₄)alkyl, (C₁₋₄)alkoxy, halogen, cyano, (C₁₋₃)fluoroalkyl, and (C₁₋₃)fluoroalkoxy;

or a salt thereof.

6. A compound according to any one of claims 1 to 5; wherein **R**² represents hydrogen, (C₁₋₆)alkyl, (C₃₋₆)cycloalkyl, hydroxy-(C₂₋₄)alkyl, or (C₁₋₄)fluoroalkyl or a salt thereof.

7. A compound according to any one of claims 1 to 6; wherein **R**³ represents hydrogen or a salt thereof.

8. A compound according to any one of claims 1 to 7; wherein one of **U**, **V**, **W**, and **X** represents **CR**¹⁰, and the remaining represent CH; wherein **R**¹⁰ represents hydrogen, fluorine, chlorine, methyl, or methoxy; or a salt thereof.

9. A compound according to any one of claims 1 to 8; wherein **U** or **X** represents N, and the remaining of **U**, **V**, **W**, and **X** represent CH; or a salt thereof.

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

- (7-Benzyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl)-(1-methyl-1H-indol-3-yl)-methanone;
- (7-Benzyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl)-(1-ethyl-1H-indol-3-yl)-methanone;
- (7-Benzyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl)-(1,2-dimethyl-1H-indol-3-yl)-methanone;
- (1-Methyl-1H-indol-3-yl)-(7-naphthalen-1-ylmethyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl)-methanone;
- (1-Ethyl-1H-indol-3-yl)-(7-naphthalen-1-ylmethyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl)-methanone;
- (1,2-Dimethyl-1H-indol-3-yl)-(7-naphthalen-1-ylmethyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl)-methanone;
- (1-Methyl-1H-indol-3-yl)-(7-naphthalen-2-ylmethyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl)-methanone;
- (1-Ethyl-1H-indol-3-yl)-(7-naphthalen-2-ylmethyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl)-methanone;
- (1,2-Dimethyl-1H-indol-3-yl)-(7-naphthalen-2-ylmethyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl)-methanone;
- [7-(3,4-Dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-methyl-1H-indol-3-yl)-methanone;
- [7-(3,4-Dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone;
- [7-(3,4-Dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1,2-dimethyl-1H-indol-3-yl)-methanone;
- (1-Methyl-1H-indol-3-yl)-[7-(4-trifluoromethyl-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;

[(R)-1-(3,4-Dimethoxy-benzyl)-6,7-dimethoxy-3,4-dihydro-1H-isoquinolin-2-yl]-(1-methyl-1H-indol-3-yl)-methanone;

[(S)-1-(3,4-Dimethoxy-benzyl)-6,7-dimethoxy-3,4-dihydro-1H-isoquinolin-2-yl]-(1-methyl-1H-indol-3-yl)-methanone;

(6,7-Dimethoxy-1-naphthalen-2-ylmethyl-3,4-dihydro-1H-isoquinolin-2-yl)-(1-methyl-1H-indol-3-yl)-methanone;

(1-Benzyl-6-methoxy-3,4-dihydro-1H-isoquinolin-2-yl)-(1-methyl-1H-indol-3-yl)-methanone;

[6,7-Dimethoxy-1-(3-methoxy-benzyl)-3,4-dihydro-1H-isoquinolin-2-yl]-(1-methyl-1H-indol-3-yl)-methanone;

[6,7-Dimethoxy-1-(4-methoxy-benzyl)-3,4-dihydro-1H-isoquinolin-2-yl]-(1-methyl-1H-indol-3-yl)-methanone;

[1-(2,5-Dimethoxy-benzyl)-6,7-dimethoxy-3,4-dihydro-1H-isoquinolin-2-yl]-(1-methyl-1H-indol-3-yl)-methanone;

(1-Benzo[1,3]dioxol-5-ylmethyl-6,7-dimethoxy-3,4-dihydro-1H-isoquinolin-2-yl)-(1-methyl-1H-indol-3-yl)-methanone;

[1-(4-Fluoro-benzyl)-6,7-dimethoxy-3,4-dihydro-1H-isoquinolin-2-yl]-(1-methyl-1H-indol-3-yl)-methanone;

[6,7-Dimethoxy-1-(3,4,5-trimethoxy-benzyl)-3,4-dihydro-1H-isoquinolin-2-yl]-(1-methyl-1H-indol-3-yl)-methanone;

[1-(4-Chloro-benzyl)-6,7-dimethoxy-3,4-dihydro-1H-isoquinolin-2-yl]-(1-methyl-1H-indol-3-yl)-methanone;

[(R)-1-(3,4-Dimethoxy-benzyl)-6,7-dimethoxy-3,4-dihydro-1H-isoquinolin-2-yl]-(1-ethyl-1H-indol-3-yl)-methanone;

(6,7-Dimethoxy-1-naphthalen-2-ylmethyl-3,4-dihydro-1H-isoquinolin-2-yl)-(1-ethyl-1H-indol-3-yl)-methanone;

(1-Benzyl-6-methoxy-3,4-dihydro-1H-isoquinolin-2-yl)-(1-ethyl-1H-indol-3-yl)-methanone;

[6,7-Dimethoxy-1-(3-methoxy-benzyl)-3,4-dihydro-1H-isoquinolin-2-yl]-(1-ethyl-1H-indol-3-yl)-methanone;

[6,7-Dimethoxy-1-(4-methoxy-benzyl)-3,4-dihydro-1H-isoquinolin-2-yl]-(1-ethyl-1H-indol-3-yl)-methanone;

[1-(2,5-Dimethoxy-benzyl)-6,7-dimethoxy-3,4-dihydro-1H-isoquinolin-2-yl]-(1-ethyl-1H-indol-3-yl)-methanone;

(1-Benzo[1,3]dioxol-5-ylmethyl-6,7-dimethoxy-3,4-dihydro-1H-isoquinolin-2-yl)-(1-ethyl-1H-indol-3-yl)-methanone;

(1-Ethyl-1H-indol-3-yl)-[1-(4-fluoro-benzyl)-6,7-dimethoxy-3,4-dihydro-1H-isoquinolin-2-yl]-methanone;

[6,7-Dimethoxy-1-(3,4,5-trimethoxy-benzyl)-3,4-dihydro-1H-isoquinolin-2-yl]-(1-ethyl-1H-indol-3-yl)-methanone;

[1-(4-Chloro-benzyl)-6,7-dimethoxy-3,4-dihydro-1H-isoquinolin-2-yl]-(1-ethyl-1H-indol-3-yl)-methanone;

(1H-Indol-3-yl)-(7-naphthalen-1-ylmethyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl)-methanone;

(1-Ethyl-3-methyl-4-naphthalen-2-ylmethyl-1,4,6,7-tetrahydro-pyrazolo[4,3-c]pyridin-5-yl)-(1-methyl-1H-indol-3-yl)-methanone;

(1-Ethyl-1H-indol-3-yl)-(1-ethyl-3-methyl-4-naphthalen-2-ylmethyl-1,4,6,7-tetrahydro-pyrazolo[4,3-c]pyridin-5-yl)-methanone;

(1-Methyl-1H-indol-3-yl)-(1-naphthalen-1-ylmethyl-3,4-dihydro-1H-isoquinolin-2-yl)-methanone;

(1-Ethyl-1H-indol-3-yl)-(1-naphthalen-1-ylmethyl-3,4-dihydro-1H-isoquinolin-2-yl)-methanone;

(1-Methyl-1H-indol-3-yl)-(4-naphthalen-1-ylmethyl-6,7-dihydro-4H-thieno[3,2-c]pyridin-5-yl)-methanone;

(1-Ethyl-1H-indol-3-yl)-(4-naphthalen-1-ylmethyl-6,7-dihydro-4H-thieno[3,2-c]pyridin-5-yl)-methanone;

(2-Amino-4-naphthalen-1-ylmethyl-6,7-dihydro-4H-thiazolo[5,4-c]pyridin-5-yl)-(1-methyl-1H-indol-3-yl)-methanone;

(2-Amino-4-naphthalen-1-ylmethyl-6,7-dihydro-4H-thiazolo[5,4-c]pyridin-5-yl)-(1-ethyl-1H-indol-3-yl)-methanone;

(1-Methyl-1H-indol-3-yl)-(4-naphthalen-1-ylmethyl-6,7-dihydro-4H-thiazolo[5,4-c]pyridin-5-yl)-methanone;
(1-Ethyl-1H-indol-3-yl)-(4-naphthalen-1-ylmethyl-6,7-dihydro-4H-thiazolo[5,4-c]pyridin-5-yl)-methanone;
[3-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-methyl-1H-indol-3-yl)-methanone;
[3-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone;
[2-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone;
[3-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-isopropyl-1H-indol-3-yl)-methanone;
[3-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-isobutyl-1H-indol-3-yl)-methanone;
[3-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(6-fluoro-1-methyl-1H-indol-3-yl)-methanone;
[3-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-6-fluoro-1H-indol-3-yl)-methanone;
[3-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(5-fluoro-1-methyl-1H-indol-3-yl)-methanone;
[3-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-5-fluoro-1H-indol-3-yl)-methanone;
[3-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-cyclopropyl-1H-indol-3-yl)-methanone;
[3-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-propyl-1H-indol-3-yl)-methanone;
[3-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-butyl-1H-indol-3-yl)-methanone;
[3-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-[1-(2-methoxy-ethyl)-1H-indol-3-yl]-methanone;
[3-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-[1-(2-dimethylamino-ethyl)-1H-indol-3-yl]-methanone;
[3-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(5-chloro-1-methyl-1H-indol-3-yl)-methanone;
[3-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(5-chloro-1-ethyl-1H-indol-3-yl)-methanone;
[3-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(5-methoxy-1-methyl-1H-indol-3-yl)-methanone;
[3-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-5-methoxy-1H-indol-3-yl)-methanone;
[3-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-4-methoxy-1H-indol-3-yl)-methanone;

[3-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(7-fluoro-1-methyl-1H-indol-3-yl)-methanone;

[3-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(4-fluoro-1-methyl-1H-indol-3-yl)-methanone;

[3-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-4-fluoro-1H-indol-3-yl)-methanone;

[3-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1,5-dimethyl-1H-indol-3-yl)-methanone;

[3-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(5-methoxy-1,2-dimethyl-1H-indol-3-yl)-methanone;

[3-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1H-indol-3-yl)-methanone;

[3-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1H-pyrrolo[2,3-b]pyridin-3-yl)-methanone;

[3-Bromo-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1,2-dimethyl-1H-indol-3-yl)-methanone;

[7-(4-Benzyloxy-3-methoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone;

[7-(2,4-Dichloro-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-methyl-1H-indol-3-yl)-methanone;

(1-Methyl-1H-indol-3-yl)-(7-pyridin-2-ylmethyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl)-methanone;

(1-Methyl-1H-indol-3-yl)-[7-(3-trifluoromethyl-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;

[7-(1H-Indol-3-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-methyl-1H-indol-3-yl)-methanone;

(1-Methyl-1H-indol-3-yl)-[7-(1-methyl-1H-indol-3-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;

[7-(1H-Benzimidazol-2-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-methyl-1H-indol-3-yl)-methanone;

[7-(1H-Indazol-3-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-methyl-1H-indol-3-yl)-methanone;

(1-Methyl-1H-indol-3-yl)-[7-(2-methyl-thiazol-4-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;

(1-Methyl-1H-indol-3-yl)-(7-quinolin-8-ylmethyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl)-methanone;

[7-(4-Benzyloxy-3-methoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-methyl-1H-indol-3-yl)-methanone;

[7-(2,4-Dichloro-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone;

(1-Ethyl-1H-indol-3-yl)-(7-pyridin-2-ylmethyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl)-methanone;

(1-Ethyl-1H-indol-3-yl)-[7-(3-trifluoromethyl-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;

[7-(2,6-Dichloro-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone;

(1-Ethyl-1H-indol-3-yl)-[7-(1H-indol-3-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;

(1-Ethyl-1H-indol-3-yl)-[7-(1-methyl-1H-indol-3-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;

(1-Ethyl-1H-indol-3-yl)-[7-(1H-indazol-3-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;

(1-Ethyl-1H-indol-3-yl)-[7-(2-methyl-thiazol-4-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;

(1-Ethyl-1H-indol-3-yl)-(7-quinolin-8-ylmethyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl)-methanone;

[7-(4-Methoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-methyl-1H-indol-3-yl)-methanone;

[7-(2,3-Dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-methyl-1H-indol-3-yl)-methanone;
[7-(3-Methoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-methyl-1H-indol-3-yl)-methanone;
[7-(3,5-Dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-methyl-1H-indol-3-yl)-methanone;
[7-(3,4-Dichloro-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-methyl-1H-indol-3-yl)-methanone;
[7-(2,3-Dihydro-benzo[1,4]dioxin-6-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-methyl-1H-indol-3-yl)-methanone;
(1-Methyl-1H-indol-3-yl)-[7-(4-trifluoromethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;
[7-(2,3-Dihydro-benzo[1,4]dioxin-5-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-methyl-1H-indol-3-yl)-methanone;
(7-Benzo[1,3]dioxol-4-ylmethyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl)-(1-methyl-1H-indol-3-yl)-methanone;
(7-Benzo[1,3]dioxol-5-ylmethyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl)-(1-methyl-1H-indol-3-yl)-methanone;
[4-(3,4-Dimethoxy-benzyl)-1-ethyl-3-methyl-1,4,6,7-tetrahydro-pyrazolo[4,3-c]pyridin-5-yl]-(1-methyl-1H-indol-3-yl)-methanone;
(1-Ethyl-1H-indol-3-yl)-[7-(4-methoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;
[7-(2,3-Dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone;
(1-Ethyl-1H-indol-3-yl)-[7-(3-methoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;
[7-(3,5-Dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone;
[7-(3,4-Dichloro-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone;
[7-(2,3-Dihydro-benzo[1,4]dioxin-6-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone;
(1-Ethyl-1H-indol-3-yl)-[7-(4-trifluoromethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;
[7-(2,3-Dihydro-benzo[1,4]dioxin-5-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone;
(7-Benzo[1,3]dioxol-4-ylmethyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl)-(1-ethyl-1H-indol-3-yl)-methanone;
(7-Benzo[1,3]dioxol-5-ylmethyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl)-(1-ethyl-1H-indol-3-yl)-methanone;
[4-(3,4-Dimethoxy-benzyl)-1-ethyl-3-methyl-1,4,6,7-tetrahydro-pyrazolo[4,3-c]pyridin-5-yl]-(1-ethyl-1H-indol-3-yl)-methanone;
(1-Ethyl-1H-indol-3-yl)-[7-(4-hydroxy-3-methoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;
(1-Ethyl-1H-indol-3-yl)-[7-[4-(2-hydroxy-ethoxy)-3-methoxy-benzyl]-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;
[1-Bromo-4-(3,4-dimethoxy-benzyl)-6,7-dihydro-4H-thieno[3,4-c]pyridin-5-yl]-(1-ethyl-1H-indol-3-yl)-methanone;
(1-Methyl-1H-indol-3-yl)-(7-quinolin-6-ylmethyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl)-methanone;
(1-Ethyl-1H-indol-3-yl)-(7-quinolin-6-ylmethyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl)-methanone;
(1-Methyl-1H-indol-3-yl)-(7-quinolin-7-ylmethyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl)-methanone;
(1-Ethyl-1H-indol-3-yl)-(7-quinolin-7-ylmethyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl)-methanone;
[1-(3-Methyl-benzyl)-3,4-dihydro-1H-isoquinolin-2-yl]-(1-methyl-1H-indol-3-yl)-methanone;

(1-Ethyl-1H-indol-3-yl)-[1-(3-methyl-benzyl)-3,4-dihydro-1H-isoquinolin-2-yl]-methanone;
(1-Cyclopropyl-1H-indol-3-yl)-[1-(3,4-dimethoxy-benzyl)-3,4-dihydro-1H-isoquinolin-2-yl]-methanone;
[1-(3,4-Dimethoxy-benzyl)-3,4-dihydro-1H-isoquinolin-2-yl]-(1-ethyl-1H-indol-3-yl)-methanone;
[7-(3,4-Dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-4-fluoro-1H-indol-3-yl)-methanone;
[7-(3,4-Dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(5-fluoro-1-methyl-1H-indol-3-yl)-methanone;
(6-Chloro-1-ethyl-1H-indol-3-yl)-[7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;
(6-Chloro-1-methyl-1H-indol-3-yl)-[7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;
[7-(3,4-Dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-methyl-1H-pyrrolo[2,3-b]pyridin-3-yl)-methanone;
[7-(3,4-Dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-(2-fluoro-ethyl)-1H-indol-3-yl)-methanone;
(1-Cyclopropyl-1H-indol-3-yl)-[7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;
[7-(3,4-Dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-(2-methoxy-ethyl)-1H-indol-3-yl)-methanone;
[7-(3,4-Dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-(2-hydroxy-ethyl)-1H-indol-3-yl)-methanone;
[7-(3,4-Dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-pyrrolo[2,3-b]pyridin-3-yl)-methanone;
(1-Ethyl-1H-indol-3-yl)-[7-(3-hydroxy-4-methoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;
[4-(3,4-Dimethoxy-benzyl)-1-methyl-6,7-dihydro-4H-thieno[3,4-c]pyridin-5-yl]-(1-ethyl-1H-indol-3-yl)-methanone;
{7-[4-(2-Hydroxy-ethoxy)-3-methoxy-benzyl]-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl}-(1-methyl-1H-pyrrolo[2,3-b]pyridin-3-yl)-methanone;
{7-[4-(2-Hydroxy-ethoxy)-3-methoxy-benzyl]-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl}-(1-methyl-1H-pyrrolo[2,3-c]pyridin-3-yl)-methanone;
{7-[4-(2-Hydroxy-ethoxy)-3-methoxy-benzyl]-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl}-(1-methyl-1H-pyrrolo[3,2-c]pyridin-3-yl)-methanone;
{7-[4-(2-Hydroxy-ethoxy)-3-methoxy-benzyl]-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl}-(1-methyl-1H-pyrrolo[3,2-b]pyridin-3-yl)-methanone;
(1-Ethyl-1H-pyrrolo[2,3-b]pyridin-3-yl)-{7-[4-(2-hydroxy-ethoxy)-3-methoxy-benzyl]-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl}-methanone;
(1-Ethyl-1H-pyrrolo[2,3-c]pyridin-3-yl)-{7-[4-(2-hydroxy-ethoxy)-3-methoxy-benzyl]-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl}-methanone;
(1-Ethyl-1H-pyrrolo[3,2-c]pyridin-3-yl)-{7-[4-(2-hydroxy-ethoxy)-3-methoxy-benzyl]-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl}-methanone;
(1-Ethyl-1H-pyrrolo[3,2-b]pyridin-3-yl)-{7-[4-(2-hydroxy-ethoxy)-3-methoxy-benzyl]-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl}-methanone;

[7-(3,4-Dimethoxy-benzyl)-2,3-dimethyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-methyl-1H-indol-3-yl)-methanone;

[7-(3,4-Dimethoxy-benzyl)-2,3-dimethyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone;

[8-(3,4-Dimethoxy-benzyl)-5,8-dihydro-6H-[1,7]naphthyridin-7-yl]-(1-ethyl-1H-indol-3-yl)-methanone;

[7-(3,4-Dimethoxy-benzyl)-2-methyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-methyl-1H-pyrrolo[3,2-b]pyridin-3-yl)-methanone;

[7-(3,4-Dimethoxy-benzyl)-2-methyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(5-fluoro-1-methyl-1H-indol-3-yl)-methanone;

(1-Cyclopropyl-4-fluoro-1H-indol-3-yl)-[7-(3,4-dimethoxy-benzyl)-2-methyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;

[7-(3,4-Dimethoxy-benzyl)-2-methyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-[1-(2-hydroxy-ethyl)-1H-indol-3-yl]-methanone;

[4-(3,4-Dimethoxy-benzyl)-1,3-dimethyl-6,7-dihydro-4H-thieno[3,4-c]pyridin-5-yl]-(5-fluoro-1-methyl-1H-indol-3-yl)-methanone;

(1-Cyclopropyl-4-fluoro-1H-indol-3-yl)-[4-(3,4-dimethoxy-benzyl)-1,3-dimethyl-6,7-dihydro-4H-thieno[3,4-c]pyridin-5-yl]-methanone;

[4-(3,4-Dimethoxy-benzyl)-1,3-dimethyl-6,7-dihydro-4H-thieno[3,4-c]pyridin-5-yl]-[1-(2-hydroxy-ethyl)-1H-indol-3-yl]-methanone;

[4-(3,4-Dimethoxy-benzyl)-1-methyl-6,7-dihydro-4H-thieno[3,4-c]pyridin-5-yl]-(1-methyl-1H-pyrrolo[3,2-b]pyridin-3-yl)-methanone;

[4-(3,4-Dimethoxy-benzyl)-1-methyl-6,7-dihydro-4H-thieno[3,4-c]pyridin-5-yl]-(5-fluoro-1-methyl-1H-indol-3-yl)-methanone;

(1-Cyclopropyl-4-fluoro-1H-indol-3-yl)-[4-(3,4-dimethoxy-benzyl)-1-methyl-6,7-dihydro-4H-thieno[3,4-c]pyridin-5-yl]-methanone;

[4-(3,4-Dimethoxy-benzyl)-1-methyl-6,7-dihydro-4H-thieno[3,4-c]pyridin-5-yl]-[1-(2-hydroxy-ethyl)-1H-indol-3-yl]-methanone;

[7-(4-Cyclopropoxy-3-methoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-methyl-1H-indol-3-yl)-methanone;

[7-(4-Cyclopropoxy-3-methoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone;

[4-(3,4-Dimethoxy-benzyl)-1,3-dimethyl-6,7-dihydro-4H-thieno[3,4-c]pyridin-5-yl]-(1-methyl-1H-pyrrolo[3,2-b]pyridin-3-yl)-methanone;

(1,3-Dimethyl-4-quinolin-7-ylmethyl-1,4,6,7-tetrahydro-pyrazolo[4,3-c]pyridin-5-yl)-(1-methyl-1H-indol-3-yl)-methanone;

(1-Methyl-1H-indol-3-yl)-(1-methyl-7-quinolin-7-ylmethyl-1,4,5,7-tetrahydro-pyrazolo[3,4-c]pyridin-6-yl)-methanone;

(1-Methyl-1H-indol-3-yl)-(2-methyl-7-quinolin-7-ylmethyl-2,4,5,7-tetrahydro-pyrazolo[3,4-c]pyridin-6-yl)-methanone;

[(S)-8-(3,4-Dimethoxy-benzyl)-5,6-dihydro-8H-imidazo[1,2-a]pyrazin-7-yl]-(1-ethyl-1H-indol-3-yl)-methanone;

(1-Ethyl-1H-indol-3-yl)-[7-(4-[1,2,3]triazol-2-yl-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;

(1-Ethyl-1H-indol-3-yl)-[7-(4-[1,2,3]triazol-1-yl-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;

(1-Ethyl-1H-indol-3-yl)-[7-(3-[1,2,3]triazol-2-yl-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;

(1-Ethyl-1H-indol-3-yl)-[7-(3-[1,2,3]triazol-1-yl-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;

(1-Methyl-1H-indol-3-yl)-[7-(4-[1,2,3]triazol-2-yl-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;

(1-Methyl-1H-indol-3-yl)-[7-(4-[1,2,3]triazol-1-yl-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;

[7-(3,4-Dimethoxy-benzyl)-1-methyl-1,4,5,7-tetrahydro-pyrazolo[3,4-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone;

2-[6-(1-Ethyl-1H-indole-3-carbonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridin-7-ylmethyl]-benzonitrile;

3-[6-(1-Ethyl-1H-indole-3-carbonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridin-7-ylmethyl]-benzonitrile;

4-[6-(1-Ethyl-1H-indole-3-carbonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridin-7-ylmethyl]-benzonitrile;

(1-Ethyl-1H-indol-3-yl)-(7-pyridin-3-ylmethyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl)-methanone;

[7-(6-Chloro-pyridin-2-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone;

[7-(3,4-Difluoro-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone;

[7-(2-Chloro-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone;

[7-(3-Chloro-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone;

2-[6-(1-Methyl-1H-indole-3-carbonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridin-7-ylmethyl]-benzonitrile;

3-[6-(1-Methyl-1H-indole-3-carbonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridin-7-ylmethyl]-benzonitrile;

4-[6-(1-Methyl-1H-indole-3-carbonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridin-7-ylmethyl]-benzonitrile;

(1-Methyl-1H-indol-3-yl)-(7-pyridin-3-ylmethyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl)-methanone;

[7-(6-Chloro-pyridin-2-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-methyl-1H-indol-3-yl)-methanone;

[7-(3,4-Difluoro-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-methyl-1H-indol-3-yl)-methanone;

[7-(2-Chloro-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-methyl-1H-indol-3-yl)-methanone;

[7-(3-Chloro-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-methyl-1H-indol-3-yl)-methanone;

(1-Methyl-1H-indol-3-yl)-[7-(3-pyrimidin-2-yl-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;

(1-Ethyl-1H-indol-3-yl)-[7-(3-pyrimidin-2-yl-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;

(1-Methyl-1H-indol-3-yl)-[7-(3-pyrazol-1-yl-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;

(1-Methyl-1H-indol-3-yl)-[7-(3-[1,2,4]triazol-1-yl-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;

(1-Ethyl-1H-indol-3-yl)-[7-(3-[1,2,4]triazol-1-yl-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;

5-[6-(1-Methyl-1H-indole-3-carbonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridin-7-ylmethyl]-pyridine-2-carbonitrile;

(1-Methyl-1H-indol-3-yl)-[7-(6-methyl-pyridin-3-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;

[7-(6-Ethyl-pyridin-3-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-methyl-1H-indol-3-yl)-methanone;
5-[6-(1-Ethyl-1H-indole-3-carbonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridin-7-ylmethyl]-pyridine-2-carbonitrile;
(1-Ethyl-1H-indol-3-yl)-[7-(6-methyl-pyridin-3-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;
(1-Ethyl-1H-indol-3-yl)-[7-(6-ethyl-pyridin-3-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;
[7-(3,4-Dimethoxy-benzyl)-2-methoxy-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone;
[7-(3,4-Dimethoxy-benzyl)-3-methoxy-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone;
[7-(3,4-Dimethoxy-benzyl)-2-ethoxy-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone;
[7-(3,4-Dimethoxy-benzyl)-3-ethoxy-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone;
[7-(4-Ethoxy-3-methoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone;
(1-Ethyl-1H-indol-3-yl)-{7-[3-methoxy-4-(2,2,2-trifluoro-ethoxy)-benzyl]-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl}-methanone;
{7-[4-(2-Dimethylamino-ethoxy)-3-methoxy-benzyl]-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone;
(1-Ethyl-1H-indol-3-yl)-[7-(3-methoxy-4-propoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;
(1-Ethyl-1H-indol-3-yl)-[7-(4-isopropoxy-3-methoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;
{4-[6-(1-Ethyl-1H-indole-3-carbonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridin-7-ylmethyl]-2-methoxy-phenoxy}-acetic acid methyl ester;
(1-Ethyl-1H-indol-3-yl)-[7-(3-methoxy-4-trifluoromethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;
{4-[6-(1-Ethyl-1H-indole-3-carbonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridin-7-ylmethyl]-2-methoxy-phenoxy}-acetic acid;
[7-(3,4-Dimethoxy-benzyl)-2-ethynyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone;
[7-(3,4-Dimethoxy-benzyl)-3-ethynyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone;
[7-(3,4-Dimethoxy-benzyl)-2-ethyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone;
[3-Chloro-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone;
7-(3,4-Dimethoxy-benzyl)-6-(1-ethyl-1H-indole-3-carbonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine-3-carbonitrile;
[7-(3,4-Dimethoxy-benzyl)-3-ethyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone;
[7-(3,4-Dimethoxy-benzyl)-3-methyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone;
[2-Chloro-7-(3,4-dimethoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone;
7-(3,4-Dimethoxy-benzyl)-6-(1-ethyl-1H-indole-3-carbonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine-2-carbonitrile;
[7-(3,4-Dimethoxy-benzyl)-2-methyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone;
Trifluoro-methanesulfonic acid 4-[6-(1-ethyl-1H-indole-3-carbonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridin-7-ylmethyl]-2-methoxy-phenyl ester;
Trifluoro-methanesulfonic acid 5-[6-(1-ethyl-1H-indole-3-carbonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridin-7-ylmethyl]-2-methoxy-phenyl ester;
[7-(3-Ethoxy-4-methoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone;

(1-Ethyl-1H-indol-3-yl)-{7-[4-methoxy-3-(2,2,2-trifluoro-ethoxy)-benzyl]-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl}-methanone;

(1-Ethyl-1H-indol-3-yl)-{7-[3-(2-hydroxy-ethoxy)-4-methoxy-benzyl]-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl}-methanone;

(1-Ethyl-1H-indol-3-yl)-[7-(4-methoxy-3-propoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;

(1-Ethyl-1H-indol-3-yl)-[7-(3-isopropoxy-4-methoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;

{5-[6-(1-Ethyl-1H-indole-3-carbonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridin-7-ylmethyl]-2-methoxy-phenoxy}-acetic acid methyl ester;

4-(3,4-Dimethoxy-benzyl)-5-(1-ethyl-1H-indole-3-carbonyl)-4,5,6,7-tetrahydro-thieno[3,4-c]pyridine-1-carbonitrile;

[1-Chloro-4-(3,4-dimethoxy-benzyl)-6,7-dihydro-4H-thieno[3,4-c]pyridin-5-yl]-(1-ethyl-1H-indol-3-yl)-methanone;

5-[6-(1-Ethyl-1H-indole-3-carbonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridin-7-ylmethyl]-2-methoxy-benzonitrile;

(1-Ethyl-1H-indol-3-yl)-[7-(4-ethyl-3-methoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;

[7-(3,4-Dimethoxy-benzyl)-3-trifluoromethyl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone;

(1-Ethyl-1H-indol-3-yl)-[7-(3-methoxy-4-methyl-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;

(1-Ethyl-1H-indol-3-yl)-[7-(3-ethyl-4-methoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;

(1-Ethyl-1H-indol-3-yl)-[7-(4-methoxy-3-methyl-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;

[7-(3,4-Dimethoxy-benzyl)-3-[1,2,3]triazol-2-yl-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone;

[7-(3-Cyclopropoxy-4-methoxy-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-ethyl-1H-indol-3-yl)-methanone;

(1-Ethyl-1H-indol-3-yl)-[7-(3-[1,2,4]oxadiazol-3-yl-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;

6-[6-(1-Ethyl-1H-indole-3-carbonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridin-7-ylmethyl]-pyridine-2-carbonitrile;

6-[6-(1-Methyl-1H-indole-3-carbonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridin-7-ylmethyl]-pyridine-2-carbonitrile;

(1-Ethyl-1H-indol-3-yl)-[7-(6-methoxy-pyridin-2-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;

[7-(6-Methoxy-pyridin-2-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-methyl-1H-indol-3-yl)-methanone;

(1-Methyl-1H-indol-3-yl)-[7-(3-[1,2,4]oxadiazol-3-yl-benzyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;

3-[6-(1-Methyl-1H-indole-3-carbonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridin-7-ylmethyl]-benzamide;

3-[6-(1-Ethyl-1H-indole-3-carbonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridin-7-ylmethyl]-benzamide;

[7-(6-Methoxy-pyridin-3-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-(1-methyl-1H-indol-3-yl)-methanone;

and

(1-Ethyl-1H-indol-3-yl)-[7-(6-methoxy-pyridin-3-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyridin-6-yl]-methanone;

or a salt thereof.

11. A pharmaceutical composition containing, as active principle, one or more compounds according to any one of claims 1 to 10, or a pharmaceutically acceptable salt thereof, and at least one pharmaceutically acceptable carrier.
12. A compound according to any one of claims 1 to 10, or a pharmaceutically acceptable salt thereof, for use as a medicament.
13. A compound according to any one of claims 1 to 10, or a pharmaceutically acceptable salt thereof, for the prevention or treatment of diseases selected from the group consisting of all types of sleep disorders, of stress-related syndromes, of addictions, of cognitive dysfunctions in the healthy population and in psychiatric and neurologic disorders, of eating or drinking disorders.
14. A compound according to any one of claims 1 to 10, or a pharmaceutically acceptable salt thereof, for use in the preparation of a medicament for the prevention or treatment of diseases selected from the group consisting of all types of sleep disorders, of stress-related syndromes, of addictions, of cognitive dysfunctions in the healthy population and in psychiatric and neurologic disorders, of eating or drinking disorders.

INTERNATIONAL SEARCH REPORT

International application No
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A. CLASSIFICATION OF SUBJECT MATTER INV. C07D401/04 C07D471/04 C07D487/04 C07D495/04 C07D513/04 C07D519/00 A61K31/404 A61K31/437 A61P25/30 A61P25/22 ADD. According to International Patent Classification (IPC) or to both national classification and IPC		
B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) C07D A61K Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) EPO-Internal, CHEM ABS Data, WPI Data		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 2005/118548 A1 (ACTELION PHARMACEUTICALS LTD [CH]; WELLER THOMAS [CH]; KOBERSTEIN RALF) 15 December 2005 (2005-12-15) cited in the application page 1, line 3 - line 7; claim 1 -----	1-14
A	WO 2007/122591 A2 (ACTELION PHARMACEUTICALS LTD [CH]; AISSAOUI HAMED [FR]; BOSS CHRISTOPH) 1 November 2007 (2007-11-01) cited in the application page 1, line 3 - line 7; claim 1 -----	1-14
A	WO 2008/147518 A1 (MERCK & CO INC [US]; BRESLIN MICHAEL J [US]; COLEMAN PAUL J [US]; COX) 4 December 2008 (2008-12-04) page 1, line 5 - line 19; claim 1 -----	1-14
☐ Further documents are listed in the continuation of Box C. ☒ See patent family annex.		
* Special categories of cited documents : "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier application or patent but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art "&" document member of the same patent family		
Date of the actual completion of the international search		Date of mailing of the international search report
18 May 2012		25/05/2012
Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016		Authorized officer Seelmann, Ingo

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