

PYRAZOLO[1,5-a]PYRIMIDINE DERIVATIVES HAVING MULTIMODAL ACTIVITY AGAINST PAIN

FIELD OF THE INVENTION

5 The present invention relates to compounds having dual pharmacological activity towards both the $\alpha_2\delta$ subunit of the voltage-gated calcium channel, and the sigma-1 (σ_1) receptor. More particularly, the present invention relates to pyrazolo[1,5-a]pyrimidine- derivatives having this pharmacological activity, to processes of preparation of such compounds, to pharmaceutical compositions comprising them, and to their use in therapy, in particular for the treatment of pain.

10 BACKGROUND OF THE INVENTION

The adequate management of pain constitutes an important challenge, since currently available treatments provide in many cases only modest improvements, leaving many patients unrelieved (Turk DC, Wilson HD, Cahana A. *Lancet*; 2011, 377, 2226-2235). Pain affects a big portion of the population with an estimated prevalence of 20 % and
15 its incidence, particularly in the case of chronic pain, is increasing due to the population ageing. Additionally, pain is clearly related to comorbidities, such as depression, anxiety and insomnia, which leads to important productivity losses and socio-economical burden (Goldberg DS, McGee SJ, *BMC Public Health*, 2011, 11, 770). Existing pain therapies include non-steroidal anti-inflammatory drugs (NSAIDs), opioid
20 agonists, calcium channel blockers and antidepressants, but they are much less than optimal regarding their safety ratio. All of them show limited efficacy and a range of secondary effects that preclude their use, especially in chronic settings.

Voltage-gated calcium channels (VGCC) are required for many key functions in the body. Different subtypes of voltage-gated calcium channels have been described
25 (Zamponi et al., *Pharmacol. Rev.* 2015, 67, 821-70). The VGCC are assembled through interactions of different subunits, namely α_1 ($\text{Ca}_v\alpha_1$), β ($\text{Ca}_v\beta$) $\alpha_2\delta$ ($\text{Ca}_v\alpha_2\delta$) and γ ($\text{Ca}_v\gamma$). The α_1 subunits are the key porous forming units of the channel complex, being responsible for the Ca^{2+} conduction and generation of Ca^{2+} influx. The $\alpha_2\delta$, β , and γ subunits are auxiliary, although very important for the regulation of the channel, since
30 they increase the expression of the α_1 subunits in the plasma membrane as well as modulate their function, resulting in functional diversity in different cell types. Based on

their physiological and pharmacological properties, VGCC can be subdivided into low voltage-activated T-type ($\text{Ca}_v3.1$, $\text{Ca}_v3.2$, and $\text{Ca}_v3.3$), and high voltage-activated L- ($\text{Ca}_v1.1$ through $\text{Ca}_v1.4$), N- ($\text{Ca}_v2.2$), P/Q- ($\text{Ca}_v2.1$), and R- ($\text{Ca}_v2.3$) types, depending on the channel forming $\text{Ca}_v\alpha$ subunits. All of these five subclasses are found in the central and peripheral nervous systems. Regulation of intracellular calcium through activation of these VGCC plays obligatory roles in: 1) neurotransmitter release, 2) membrane depolarization and hyperpolarization, 3) enzyme activation and inactivation, and 4) gene regulation (Perret and Luo, *Neurotherapeutics* 2009, 6, 679-92; Zamponi et al., 2015 *supra*; Neumaier et al., *Prog. Neurobiol.* 2015, 129, 1-36). A large body of data has clearly indicated that VGCC are implicated in mediating various disease states including pain processing. Drugs interacting with the different calcium channel subtypes and subunits have been developed. Current therapeutic agents include drugs targeting L-type $\text{Ca}_v1.2$ calcium channels, particularly 1,4-dihydropyridines, which are widely used in the treatment of hypertension. T-type (Ca_v3) channels are the target of ethosuximide, widely used in absence epilepsy. Ziconotide, a peptide blocker of N-type ($\text{Ca}_v2.2$) calcium channels, has been approved as a treatment of intractable pain (Perret and Luo, 2009, *supra*; Vink and Alewood, *Br. J. Pharmacol.* 2012, 167, 970-89).

The Ca_v1 and Ca_v2 subfamilies contain an auxiliary $\alpha_2\delta$ subunit, which is the therapeutic target of the gabapentinoid drugs of value in certain epilepsies and chronic neuropathic pain. To date, there are four known $\alpha_2\delta$ subunits, each encoded by a unique gene and all possessing splice variants. Each $\alpha_2\delta$ protein is encoded by a single messenger RNA and is posttranslationally cleaved and then linked by disulfide bonds. Four genes encoding $\alpha_2\delta$ subunits have now been cloned. $\alpha_2\delta-1$ was initially cloned from skeletal muscle and shows a fairly ubiquitous distribution. The $\alpha_2\delta-2$ and $\alpha_2\delta-3$ subunits were subsequently cloned from brain. The most recently identified subunit, $\alpha_2\delta-4$, is largely nonneuronal. The human $\alpha_2\delta-4$ protein sequence shares 30, 32 and 61% identity with the human $\alpha_2\delta-1$, $\alpha_2\delta-2$ and $\alpha_2\delta-3$ subunits, respectively. The gene structure of all $\alpha_2\delta$ subunits is similar. All $\alpha_2\delta$ subunits show several splice variants (Davies et al., *Trends Pharmacol. Sci.* 2007, 28, 220-8.; Dolphin AC, *Nat Rev Neurosci.* 2012, 13, 542-55, *Biochim. Biophys. Acta* 2013, 1828, 1541-9).

The $\text{Ca}_v\alpha_2\delta-1$ subunit may play an important role in neuropathic pain development (Perret and Luo, 2009, *supra*; Vink and Alewood, 2012, *supra*). Biochemical data have indicated a significant $\text{Ca}_v\alpha_2\delta-1$, but not $\text{Ca}_v\alpha_2\delta-2$, subunit upregulation in the spinal

dorsal horn, and DRG (dorsal root ganglia) after nerve injury that correlates with neuropathic pain development. In addition, blocking axonal transport of injury-induced DRG $\text{Ca}_v\alpha_2\delta$ -1 subunit to the central presynaptic terminals diminishes tactile allodynia in nerve injured animals, suggesting that elevated DRG $\text{Ca}_v\alpha_2\delta$ -1 subunit contributes to neuropathic allodynia.

The $\text{Ca}_v\alpha_2\delta$ -1 subunit (and the $\text{Ca}_v\alpha_2\delta$ -2, but not $\text{Ca}_v\alpha_2\delta$ -3 and $\text{Ca}_v\alpha_2\delta$ -4, subunits) is the binding site for gabapentin which has anti-allodynic/ hyperalgesic properties in patients and animal models. Because injury-induced $\text{Ca}_v\alpha_2\delta$ -1 expression correlates with neuropathic pain development and maintenance, and various calcium channels are known to contribute to spinal synaptic neurotransmission and DRG neuron excitability, injury-induced $\text{Ca}_v\alpha_2\delta$ -1 subunit upregulation may contribute to the initiation and maintenance of neuropathic pain by altering the properties and/or distribution of VGCC in the subpopulation of DRG neurons and their central terminals, therefore modulating excitability and/or synaptic neuroplasticity in the dorsal horn. Intrathecal antisense oligonucleotides against the $\text{Ca}_v\alpha_2\delta$ -1 subunit can block nerve injury-induced $\text{Ca}_v\alpha_2\delta$ -1 upregulation and prevent the onset of allodynia and reverse established allodynia.

As mentioned above, the $\alpha_2\delta$ subunits of VGCC form the binding site for gabapentin and pregabalin, which are structural derivatives of the inhibitory neurotransmitter GABA although they do not bind to GABAA, GABAB, or benzodiazepine receptors, or alter GABA regulation in animal brain preparations. The binding of gabapentin and pregabalin to the $\text{Ca}_v\alpha_2\delta$ subunit results in a reduction in the calcium-dependent release of multiple neurotransmitters, leading to efficacy and tolerability for neuropathic pain management. Gabapentinoids may also reduce excitability by inhibiting synaptogenesis (Perret and Luo, 2009, *supra*; Vink and Alewood, 2012, *supra*, Zamponi et al., 2015, *supra*).

The sigma-1 (σ 1) receptor was discovered 40 years ago and initially assigned to a new subtype of the opioid family. This receptor is expressed both in the endoplasmic reticulum and in the plasma membrane and plays an important role in the regulation of intracellular calcium concentration. A signaling pathway associated with the activation of the σ 1 receptor has not been described, although it is believed that it has an amplification function of activation of intracellular cascades. In this sense, the σ 1

receptor regulates and modulates the activity of numerous voltage-dependent ion channels, including Ca²⁺-, K⁺-, Na⁺, Cl⁻, SK, and NMDA channels and the IP3 receptor.

5 It is also known that the σ 1 receptor is linked to analgesia, since σ 1 receptor agonists counteract opioid receptor mediated analgesia, while σ 1 receptor antagonists, such as haloperidol, potentiated it (Chien CC, Pasternak GW. *Neurosci. Lett.* 1995, 190, 137-9).

10 Many additional preclinical evidences have indicated a clear role of the σ 1 receptor in the treatment of pain (Zamanillo D, Romero L, Merlos M, Vela JM. *Eur. J. Pharmacol.*, 2013, 716, 78-93). The development of the σ 1 receptor knockout mice, which show no obvious phenotype and perceive normally sensory stimuli, was a key milestone in this endeavour. In physiological conditions the responses of the σ 1 receptor knockout mice to mechanical and thermal stimuli were found to be undistinguishable from WT ones but they were shown to possess a much higher resistance to develop pain behaviours
15 than WT mice when hypersensitivity entered into play. Hence, in the σ 1 receptor knockout mice, capsaicin did not induce mechanical hypersensitivity, both phases of formalin-induced pain were reduced, and cold and mechanical hypersensitivity were strongly attenuated after partial sciatic nerve ligation or after treatment with paclitaxel, which are models of neuropathic pain. Many of these actions were confirmed by the
20 use of σ 1 receptor antagonists and led to the advancement of one compound, S1RA, into clinical trials for the treatment of different pain states. Compound S1RA exerted a substantial reduction of neuropathic pain and anhedonic state following nerve injury (i.e., neuropathic pain conditions) and, as demonstrated in an operant self-administration model, the nerve-injured mice, but not sham-operated mice, acquired
25 the operant responding to obtain it (presumably to get pain relief), indicating that σ 1 receptor antagonism relieves neuropathic pain and also address some of the comorbidities (i.e., anhedonia, a core symptom in depression) related to pain states (Romero et al. *Br J Pharmacol.* 2012, 166, 2289-306).

30 Polypharmacology is a phenomenon in which a drug binds multiple rather than a single target with significant affinity. The effect of polypharmacology on therapy can be positive (effective therapy) and/or negative (side effects). Positive and/or negative effects can be caused by binding to the same or different subsets of targets; binding to some targets may have no effect. Multi-component drugs or multi-targeting drugs can

overcome toxicity and other side effects associated with high doses of single drugs by countering biological compensation, allowing reduced dosage of each compound or accessing context-specific multitarget mechanisms. Because multitarget mechanisms require their targets to be available for coordinated action, one would expect synergies to occur in a narrower range of cellular phenotypes given differential expression of the drug targets than would the activities of single agents. In fact, it has been experimentally demonstrated that synergistic drug combinations are generally more specific to particular cellular contexts than are single agent activities, such selectivity is achieved through differential expression of the drugs' targets in cell types associated with therapeutic, but not toxic, effects (Lehar et al., *Nat. Biotechnol.* 2009, 27, 659–666).

In the case of chronic pain, which is a multifactorial disease, multi-targeting drugs may produce concerted pharmacological intervention of multiple targets and signaling pathways that drive pain. Because they actually make use of biological complexity, multi-targeting (or multi-component drugs) approaches are among the most promising avenues toward treating multifactorial diseases such as pain (Gilron et al., *Lancet Neurol.* 2013, 12, 1084-95). In fact, positive synergistic interaction for several compounds, including analgesics, has been described (Schröder et al., *J. Pharmacol. Exp. Ther.* 2011, 337, 312-20. Erratum in: *J. Pharmacol. Exp. Ther.* 2012, 342, 232; Zhang et al., *Cell Death Dis.* 2014, 5:e1138; Gilron et al., 2013, *supra*).

Given the significant differences in pharmacokinetics, metabolisms and bioavailability, reformulation of drug combinations (multi-component drugs) is challenging. Further, two drugs that are generally safe when dosed individually cannot be assumed to be safe in combination. In addition to the possibility of adverse drug-drug interactions, if the theory of network pharmacology indicates that an effect on phenotype may derive from hitting multiple targets, then that combined phenotypic perturbation may be efficacious or deleterious. The major challenge to both drug combination strategies is the regulatory requirement for each individual drug to be shown to be safe as an individual agent and in combination (Hopkins et al, *Nat. Chem. Biol.* 2008, 4, 682-90).

An alternative strategy for multitarget therapy is to design a single compound with selective polypharmacology (multi-targeting drug). It has been shown that many approved drugs act on multiple targets. Dosing with a single compound may have advantages over a drug combination in terms of equitable pharmacokinetics and biodistribution. Indeed, troughs in drug exposure due to incompatible pharmacokinetics

between components of a combination therapy may create a low-dose window of opportunity where a reduced selection pressure can lead to drug resistance. In terms of drug registration, approval of a single compound acting on multiple targets faces significantly lower regulatory barriers than approval of a combination of new drugs
5 (Hopkins, 2008, *supra*).

As described above, the $\sigma 1$ receptor, as well as the $\alpha 2\delta 1$ subunit, modulate intracellular calcium concentration and the activity of voltage-dependent calcium channels. There is also robust clinical and pre-clinical evidence linking both targets with the treatment of chronic neuropathic pain. Thus, the present application, also relates to the
10 advantages of having dual activity, for the $\alpha 2\delta$ -1 subunit of voltage-gated calcium channels and the $\sigma 1$ receptor, in the same molecule to treat chronic pain.

Pain is multimodal in nature, since in nearly all pain states several mediators, signaling pathways and molecular mechanisms are implicated. Consequently, monomodal therapies can be complemented with a dual mechanism of action to provide complete
15 pain relief. Currently, combining existing therapies is a common clinical practice and many efforts are directed to assess the best combination of available drugs in clinical studies (Mao J, Gold MS, Backonja M. *J. Pain*, 2011, 12, 157-166).

Accordingly, there is still a need to find compounds that have an alternative or improved pharmacological activity in the treatment of pain, being both effective and showing the
20 desired selectivity, and having good "drugability" properties, i.e. good pharmaceutical properties related to administration, distribution, metabolism and excretion.

The authors of the present invention, have found a series of compounds that show a primary pharmacological activity towards the $\alpha 2\delta$ subunit, in particular the $\alpha 2\delta$ -1 subunit, of the voltage-gated calcium channel, or compounds that show dual
25 pharmacological activity towards both the $\alpha 2\delta$ subunit, in particular the $\alpha 2\delta$ -1 subunit, of the voltage-gated calcium channel and the $\sigma 1$ receptor resulting in an innovative, effective, complementary and alternative solution for the treatment of pain.

In view of the existing results of the currently available therapies and clinical practices, the present invention offers a solution by combining in a single compound binding to
30 two different targets relevant for the treatment of pain. This was mainly achieved by providing the compounds according to the invention that bind to both the $\sigma 1$ receptor

and the $\alpha_2\delta$ subunit, in particular the $\alpha_2\delta$ -1 subunit, of the voltage-gated calcium channel.

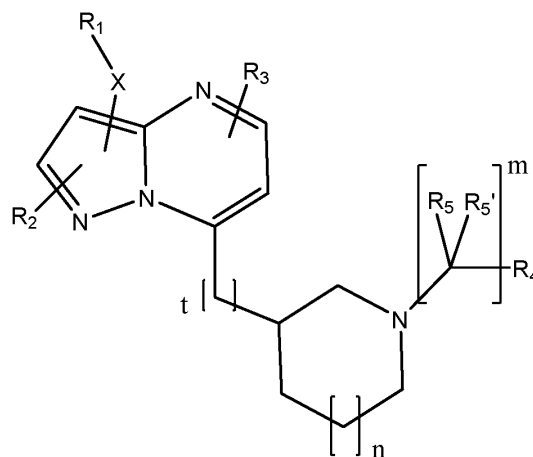
Document WO 2018154133 discloses [1,2,4]Triazolo[1,5-a]pyrimidinyl derivatives substituted with piperidine, morpholine or piperazine as O-GlcNAc hydrolase inhibitors useful for the treatment Alzheimer but is silent on dual activity for the treatment of pain.

SUMMARY OF THE INVENTION

In this invention a family of structurally distinct pyrazolo[1,5-a]pyrimidine derivatives, encompassed by formula (I), which have a pharmacological activity towards both the $\alpha_2\delta$ subunit, in particular the $\alpha_2\delta$ -1 subunit, of the voltage-gated calcium channel and the σ 1 receptor, were identified thus solving the above problem of identifying alternative or improved pain treatments by offering such compounds.

The main object of the invention is directed to a compound having a dual activity binding to the $\alpha_2\delta$ subunit, in particular the $\alpha_2\delta$ -1 subunit, of the voltage-gated calcium channel and the σ 1 receptor for use in the treatment of pain.

The invention is directed in a main aspect to a compound of general Formula (I),



(I)

wherein R₁, R₂, R₃, R₄, R₅, R₅', X, m, n and t are as defined below in the detailed description.

A further object of the invention refers to the processes for preparation of compounds of general formula (I).

A still further object of the invention refers to the use of intermediate compounds for the preparation of a compound of general formula (I).

- 5 It is also an object of the invention a pharmaceutical composition comprising a compound of formula (I).

Finally, it is an object of the invention the use of compound as a medicament and more particularly for the treatment of pain and pain related conditions.

10 DETAILED DESCRIPTION OF THE INVENTION

The invention is directed to a family of structurally distinct pyrazolo[1,5-*a*]pyrimidine derivatives, which have dual pharmacological activity towards both the $\alpha_2\delta$ subunit, in particular the $\alpha_2\delta$ -1 subunit, of the voltage-gated calcium channel and the σ_1 receptor.

- 15 The invention is directed to compounds having a dual activity binding to the $\alpha_2\delta$ subunit, in particular the $\alpha_2\delta$ -1 subunit, of the voltage-gated calcium channel and the σ_1 receptor for use in the treatment of pain and related disorders.

- As this invention is aimed at providing a compound or a chemically related series of compounds which act as dual ligands of the $\alpha_2\delta$ subunit, in particular the $\alpha_2\delta$ -1 subunit, of the voltage-gated calcium channel and the σ_1 receptor it is a preferred embodiment
20 if the compound has a binding expressed as K_i responding to the following scales:

$K_i(\sigma_1)$ is preferably < 1000 nM, more preferably < 500 nM, even more preferably < 100 nM.

$K_i(\alpha_2\delta$ -1) is preferably < 10000 nM, more preferably < 5000 nM, even more preferably < 500 nM or even more preferably < 100 nM.

- 25 Preferably, when $K_i(\sigma_1) > 1000$ nM, the following scale has been adopted for representing the binding to the σ_1 -receptor:

+ $K_i(\sigma_1) > 1000$ nM or inhibition ranges between 1% and 50 %.

Preferably, when $K_i(\alpha_2\delta-1) > 5000$ nM, the following scale has been adopted for representing the binding to the $\alpha_2\delta-1$ subunit of voltage-gated calcium channels:

+ $K_i(\alpha_2\delta-1) > 5000$ nM or inhibition ranges between 1% and 50 %

- 5 The applicant has surprisingly found that the problem of providing a new effective and alternative solution for treating pain and pain related disorders can be solved by using an analgesic approach combining two activities in a single drug (i.e., dual ligands which are bifunctional and bind to σ_1 receptor and to $\alpha_2\delta$ subunit, in particular the $\alpha_2\delta-1$ subunit, of the voltage-gated calcium channel).
- 10 As described above, the σ_1 receptor as well as the $\alpha_2\delta-1$ subunit, modulate intracellular calcium concentration and the activity of voltage-dependent calcium channels. There is also a robust clinical and pre-clinical evidence linking both targets with the treatment of chronic neuropathic pain. Thus, the present invention, also relates to the advantages of having dual activity, for the $\alpha_2\delta-1$ subunit of voltage-gated calcium channels and the
- 15 σ_1 receptor, in the same molecule to treat pain, i.e. binding to two different targets relevant for the treatment of pain.

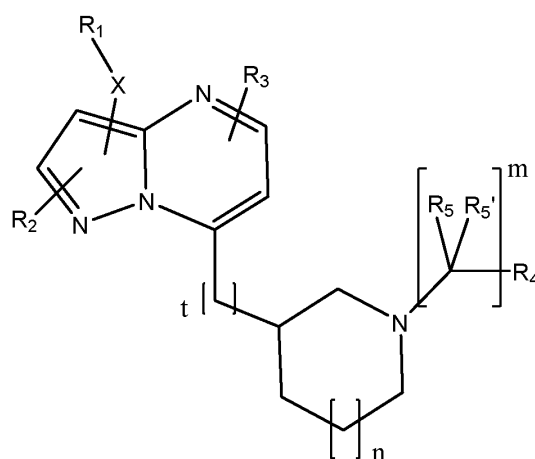
A dual compound that possess binding to both the σ_1 receptor and to the $\alpha_2\delta$ subunit of the voltage-gated calcium channel shows a highly valuable therapeutic potential by achieving an outstanding analgesia.

- 20 A further advantage of using designed multiple ligands is a lower risk of drug-drug interactions compared to cocktails or multi-component drugs, thus involving simpler pharmacokinetics and less variability among patients. Additionally, this approach may improve patient compliance and broaden the therapeutic application in relation to monomechanistic drugs, by addressing more complex aetiologies.
- 25 It has to be noted, though, that functionalities "antagonism" and "agonism" are also sub-divided in their effect into subfunctionalities like partial agonism or inverse agonism. Accordingly, the functionalities of the compounds should be considered within a relatively broad bandwidth.

- An antagonist blocks or dampens agonist-mediated responses. Known
- 30 subfunctionalities are neutral antagonists or inverse agonists.

An agonist increases the activity of the receptor above its basal level. Known subfunctionalities are full agonists, or partial agonists.

In its broader aspect, the present invention is directed to compounds of general
5 Formula (I):



(I)

wherein

m is 1, 2, 3 or 4 ;

10 n is 1 or 2;

t is 0 or 1;

X is selected from the group consisting of a bond, $-\text{[CH}_2\text{]}_p-$, $-\text{[CH}_2\text{]}_p\text{NR}_x\text{[CH}_2\text{]}_q-$, $-\text{[CH}_2\text{]}_p\text{O[CH}_2\text{]}_q-$, $-\text{[CH}_2\text{]}_p\text{NR}_xC(\text{O})\text{[CH}_2\text{]}_q-$ and $-\text{[CH}_2\text{]}_p\text{NR}_x\text{CH}(\text{CH}_3)-$;

wherein

15 p is 0, 1, 2, 3 or 4;

q is 0, 1, 2, 3 or 4;

R_x is selected from the group consisting of hydrogen, substituted or unsubstituted C₁₋₆ alkyl, substituted or unsubstituted C₂₋₆ alkenyl and substituted or unsubstituted C₂₋₆ alkynyl;

5 R₁ is selected from the group consisting of hydrogen, substituted or unsubstituted C₁₋₆ alkyl, substituted or unsubstituted C₂₋₆ alkenyl, substituted or unsubstituted C₂₋₆ alkynyl, halogen, haloalkyl, haloalkoxy, -OR₆, -NR₆R₆', -CN, cycloalkyl, aryl and heterocyclyl;

10 R₆ is selected from the group consisting of hydrogen, substituted or unsubstituted C₁₋₆ alkyl, substituted or unsubstituted C₂₋₆ alkenyl, substituted or unsubstituted C₂₋₆ alkynyl, haloalkyl, haloalkoxy; substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted alkylcycloalkyl, substituted or unsubstituted alkylaryl and substituted or unsubstituted alkylheterocyclyl;

15 R₆' is selected from the group consisting of hydrogen, substituted or unsubstituted C₁₋₆ alkyl, substituted or unsubstituted C₂₋₆ alkenyl and substituted or unsubstituted C₂₋₆ alkynyl;

alternatively R₆ and R₆' , taken together with the nitrogen atom to which they are attached, form a substituted or unsubstituted heterocyclyl;

20 R₂ is selected from the group consisting of hydrogen, substituted or unsubstituted C₁₋₆ alkyl, substituted or unsubstituted C₂₋₆ alkenyl, substituted or unsubstituted C₂₋₆ alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted alkylcycloalkyl, halogen, haloalkyl, haloalkoxy and -OR₇;

25 R₇ is selected from the group consisting of hydrogen, substituted or unsubstituted C₁₋₆ alkyl, substituted or unsubstituted C₂₋₆ alkenyl and substituted or unsubstituted C₂₋₆ alkynyl;

R₃ is selected from the group consisting of hydrogen, substituted or unsubstituted C₁₋₆ alkyl, substituted or unsubstituted C₂₋₆ alkenyl, substituted or unsubstituted C₂₋₆ alkynyl, halogen, haloalkyl, haloalkoxy and -OR₈;

R₈ is selected from the group consisting of hydrogen, substituted or unsubstituted C₁₋₆ alkyl, substituted or unsubstituted C₂₋₆ alkenyl and substituted or unsubstituted C₂₋₆ alkynyl;

5 R₄ is selected from the group consisting of substituted or unsubstituted C₁₋₆ alkyl, substituted or unsubstituted C₂₋₆ alkenyl, substituted or unsubstituted C₂₋₆ alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl and substituted or unsubstituted heterocyclyl;

10 R₅ and R₅' are independently selected from the group consisting of hydrogen, substituted or unsubstituted C₁₋₆ alkyl, substituted or unsubstituted C₂₋₆ alkenyl, substituted or unsubstituted C₂₋₆ alkynyl, haloalkyl and haloalkoxy;

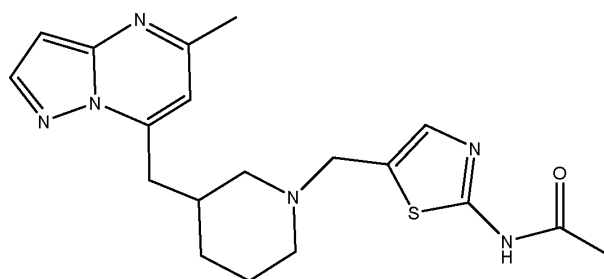
15 These compounds according to the invention are optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

20 In another embodiment, these compounds according to the invention are optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof.

Note that "or a corresponding salt thereof" does also mean "or a corresponding pharmaceutically acceptable salt thereof". This does apply to all below described embodiments and uses of "salt" being thus equivalent to "pharmaceutically acceptable salt".

25

In a particular embodiment, the following compound is excluded:



In a particular embodiment, the heterocyclcyl in R₄ is not thiazole.

In a particular embodiment, the heterocyclcyl in R₄ is a heterocyclcyl containing no sulfur atom.

- 5 In a particular embodiment, the heterocyclcyl in R₄ is a monocyclic heterocyclcyl containing no sulfur atom.

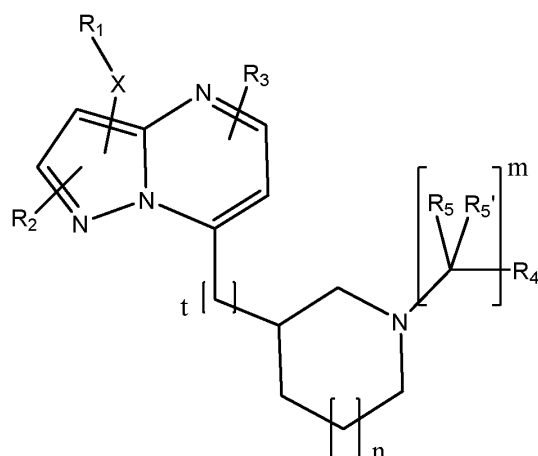
In a particular embodiment, the heterocyclcyl in R₄ is a monocyclic heterocyclcyl selected from the group consisting of oxazepan, pyrrolidine, imidazole, oxadiazole, tetrazole, azetidine, pyridine, pyrimidine, piperidine, piperazine, isothiazole, 10 tetrahydropyran, tetrahydrofuran, morpholine, thiomorpholine, furan, triazole, isoxazole, pyrazole, thiophene, pyrrole, pyrazine, oxopyrrolidine and pyrimidine.

In a particular embodiment, R₁ is selected from the group consisting of substituted or unsubstituted C₁₋₆ alkyl, substituted or unsubstituted C₂₋₆ alkenyl, substituted or unsubstituted C₂₋₆ alkynyl, halogen, haloalkyl, haloalkoxy, -OR₆, -NR₆R₆', -CN, 15 cycloalkyl, aryl and heterocyclcyl;

In a particular embodiment, R₂ is selected from the group consisting of substituted or unsubstituted C₁₋₆ alkyl, substituted or unsubstituted C₂₋₆ alkenyl, substituted or unsubstituted C₂₋₆ alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted alkylcycloalkyl, halogen, haloalkyl, haloalkoxy and -OR₇;

20

In a further embodiment the compound according to the invention is a compound of general Formula (I)



(I)

wherein

5 m is 1, 2, 3 or 4 ;

n is 1 or 2;

t is 0 or 1;

X is selected from the group consisting of a bond, $-\text{[CH}_2\text{]}_p-$, $-\text{[CH}_2\text{]}_p\text{NR}_x\text{[CH}_2\text{]}_q-$, $-\text{[CH}_2\text{]}_p\text{O[CH}_2\text{]}_q-$, $-\text{[CH}_2\text{]}_p\text{NR}_x\text{C(O)[CH}_2\text{]}_q-$ and $-\text{[CH}_2\text{]}_p\text{NR}_x\text{CH(CH}_3\text{)}-$;

10

wherein

p is 0, 1, 2, 3 or 4;

q is 0, 1, 2, 3 or 4;

R_x is selected from the group consisting of hydrogen, substituted or unsubstituted C₁₋₆ alkyl, substituted or unsubstituted C₂₋₆ alkenyl and substituted or unsubstituted C₂₋₆ alkynyl;

15

wherein the alkyl, alkenyl or alkynyl in R_x, if substituted, is substituted with one or more substituent/s selected from halogen, -CN, haloalkyl and haloalkoxy;

R₁ is selected from the group consisting of hydrogen, substituted or unsubstituted C₁₋₆ alkyl, substituted or unsubstituted C₂₋₆ alkenyl, substituted or unsubstituted C₂₋₆ alkynyl, halogen, haloalkyl, haloalkoxy, -OR₆, -NR₆R₆', -CN, cycloalkyl, aryl and heterocyclyl;

5 R₆ is selected from the group consisting of hydrogen, substituted or unsubstituted C₁₋₆ alkyl, substituted or unsubstituted C₂₋₆ alkenyl, substituted or unsubstituted C₂₋₆ alkynyl, haloalkyl, haloalkoxy; substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted alkylcycloalkyl, substituted or unsubstituted alkylaryl and substituted or unsubstituted alkylheterocyclyl;

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R₆' is selected from the group consisting of hydrogen, substituted or unsubstituted C₁₋₆ alkyl, substituted or unsubstituted C₂₋₆ alkenyl and substituted or unsubstituted C₂₋₆ alkynyl;

15 alternatively R₆ and R₆' , taken together with the nitrogen atom to which they are attached, form a substituted or unsubstituted heterocyclyl;

wherein the alkyl, alkenyl or alkynyl in R₁, if substituted, is substituted with one or more substituent/s selected from -OR₁₁, halogen, -CN, haloalkyl, haloalkoxy and -NR₁₁R₁₁';

20 wherein said cycloalkyl, aryl or heterocyclyl in R₁, if substituted, is substituted with one or more substituent/s selected from halogen, -R₁₁, -[CH₂]_rOR₁₁, =O, -NO₂, -[CH₂]_rNR₁₁R₁₁', -NR₁₁C(O)R₁₁', -NR₁₁S(O)₂R₁₁', -S(O)₂NR₁₁R₁₁', -NR₁₁C(O)NR₁₁'R₁₁'', -SR₁₁, -S(O)R₁₁, -S(O)₂R₁₁, -CN, haloalkyl, haloalkoxy, -C(O)R₁₁, -C(O)OR₁₁, -C(O)NR₁₁R₁₁', -OCH₂CH₂OR₁₁, -NR₁₁S(O)₂NR₁₁'R₁₁'' and -C(CH₃)₂OR₁₁;

25

wherein R₁₁, R₁₁' and R₁₁'' are independently selected from hydrogen, substituted or unsubstituted C₁₋₆ alkyl, substituted or unsubstituted C₂₋₆ alkenyl, substituted or unsubstituted C₂₋₆ alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted alkylcycloalkyl, substituted or unsubstituted alkylaryl and substituted or unsubstituted alkylheterocyclyl;

30

R₂ is selected from the group consisting of hydrogen, substituted or unsubstituted C₁₋₆ alkyl, substituted or unsubstituted C₂₋₆ alkenyl, substituted or unsubstituted C₂₋₆ alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted alkylcycloalkyl, halogen, haloalkyl, haloalkoxy and -OR₇;

R₇ is selected from the group consisting of hydrogen, substituted or unsubstituted C₁₋₆ alkyl, substituted or unsubstituted C₂₋₆ alkenyl and substituted or unsubstituted C₂₋₆ alkynyl;

wherein the alkyl, alkenyl or alkynyl in R₂, if substituted, is substituted with one or more substituent/s selected from -OR₂₁, halogen, -CN, haloalkyl, haloalkoxy and -NR₂₁R₂₁';

wherein said cycloalkyl in R₂, also in alkylcycloalkyl, if substituted, is substituted with one or more substituent/s selected from halogen, -R₂₁, -[CH₂]_rOR₂₁, =O, -NO₂, -[CH₂]_rNR₂₁R₂₁', -NR₂₁C(O)R₂₁', -NR₂₁S(O)₂R₂₁', -S(O)₂NR₂₁R₂₁', -NR₂₁C(O)NR₂₁'R₂₁'', -SR₂₁, -S(O)R₂₁, -S(O)₂R₂₁, -CN, haloalkyl, haloalkoxy, -C(O)R₂₁, -C(O)OR₂₁, -C(O)NR₂₁R₂₁', -OCH₂CH₂OR₂₁, -NR₂₁S(O)₂NR₂₁'R₂₁'' and -C(CH₃)₂OR₂₁;

wherein R₂₁ and R₂₁' are independently selected from hydrogen, substituted or unsubstituted C₁₋₆ alkyl, substituted or unsubstituted C₂₋₆ alkenyl and substituted or unsubstituted C₂₋₆ alkynyl;

R₃ is selected from the group consisting of hydrogen, substituted or unsubstituted C₁₋₆ alkyl, substituted or unsubstituted C₂₋₆ alkenyl, substituted or unsubstituted C₂₋₆ alkynyl, halogen, haloalkyl, haloalkoxy and -OR₈;

R₈ is selected from the group consisting of hydrogen, substituted or unsubstituted C₁₋₆ alkyl, substituted or unsubstituted C₂₋₆ alkenyl and substituted or unsubstituted C₂₋₆ alkynyl;

wherein the alkyl, alkenyl or alkynyl in R_3 , if substituted, is substituted with one or more substituent/s selected from $-OR_{31}$, halogen, $-CN$, haloalkyl, haloalkoxy and $-NR_{31}R_{31}'$;

5 wherein R_{31} and R_{31}' are independently selected from hydrogen, substituted or unsubstituted C_{1-6} alkyl, substituted or unsubstituted C_{2-6} alkenyl and substituted or unsubstituted C_{2-6} alkynyl;

10 R_4 is selected from the group consisting of substituted or unsubstituted C_{1-6} alkyl, substituted or unsubstituted C_{2-6} alkenyl, substituted or unsubstituted C_{2-6} alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl and substituted or unsubstituted heterocyclyl;

wherein the alkyl, alkenyl or alkynyl in R_4 , if substituted, is substituted with one or more substituent/s selected from $-OR_{41}$, halogen, $-CN$, haloalkyl, haloalkoxy, $-NR_{41}R_{41}'$;

15 wherein said cycloalkyl, aryl or heterocyclyl in R_4 , if substituted, is substituted with one or more substituent/s selected from halogen, $-R_{41}$, $-[CH_2]_rOR_{41}$, $=O$, $-NO_2$, $-[CH_2]_rNR_{41}R_{41}'$, $-NR_{41}C(O)R_{41}'$, $-NR_{41}S(O)_2R_{41}'$, $-S(O)_2NR_{41}R_{41}'$, $-NR_{41}C(O)NR_{41}'R_{41}''$, $-SR_{41}$, $-S(O)R_{41}$, $-S(O)_2R_{41}$, $-CN$, haloalkyl, haloalkoxy, $-C(O)R_{41}$, $-C(O)OR_{41}$, $-C(O)NR_{41}R_{41}'$, $-OCH_2CH_2OR_{41}$, $-NR_{41}S(O)_2NR_{41}'R_{41}''$ and $-C(CH_3)_2OR_{41}$;

20

wherein R_{41} , R_{41}' and R_{41}'' are independently selected from hydrogen, substituted or unsubstituted C_{1-6} alkyl, substituted or unsubstituted C_{2-6} alkenyl and substituted or unsubstituted C_{2-6} alkynyl;

25 R_5 and R_5' are independently selected from the group consisting of hydrogen, substituted or unsubstituted C_{1-6} alkyl, substituted or unsubstituted C_{2-6} alkenyl, substituted or unsubstituted C_{2-6} alkynyl, haloalkyl and haloalkoxy;

30 wherein the alkyl, alkenyl or alkynyl in R_5 and R_5' , if substituted, is substituted with one or more substituent/s selected from $-OR_{51}$, halogen, $-CN$, haloalkyl, haloalkoxy, $-NR_{51}R_{51}'$;

wherein R_{51} and R_{51}' are independently selected from hydrogen, substituted or unsubstituted C_{1-6} alkyl, substituted or unsubstituted C_{2-6} alkenyl and substituted or unsubstituted C_{2-6} alkynyl;

- 5 the alkyl, alkenyl or alkynyl, if substituted, and not defined otherwise, is substituted with one or more substituent/s selected from $-OR_{13}$, halogen, $-CN$, haloalkyl, haloalkoxy and $-NR_{13}R_{13}'$;

wherein R_{13} and R_{13}' are independently selected from hydrogen, unsubstituted C_{1-6} alkyl, unsubstituted C_{2-6} alkenyl and unsubstituted C_{2-6} alkynyl;

10

the aryl, heterocyclyl or cycloalkyl, also in alkylcycloalkyl, alkylaryl and alkylheterocyclyl, if substituted, and not defined otherwise, is substituted with one or more substituent/s selected from halogen, $-R_{14}$, $-[CH_2]_rOR_{14}$, $=O$, $-NO_2$, $-[CH_2]_rNR_{14}R_{14}'$, $-NR_{14}C(O)R_{14}'$, $-NR_{14}S(O)_2R_{14}'$, $-S(O)_2NR_{14}R_{14}'$, $-NR_{14}C(O)NR_{14}'R_{14}''$, $-SR_{14}$, $-S(O)R_{14}$, $S(O)_2R_{14}$, $-CN$, haloalkyl, haloalkoxy, $-C(O)R_{14}$, $-C(O)OR_{14}$, $-C(O)NR_{14}R_{14}'$, $-OCH_2CH_2OR_{14}$, $-NR_{14}S(O)_2NR_{14}'R_{14}''$ and $-C(CH_3)_2OR_{14}$;

15

wherein R_{14} , R_{14}' and R_{14}'' are independently selected from hydrogen, unsubstituted C_{1-6} alkyl, unsubstituted C_{2-6} alkenyl, unsubstituted C_{2-6} alkynyl, unsubstituted aryl, unsubstituted cycloalkyl and unsubstituted heterocyclyl;

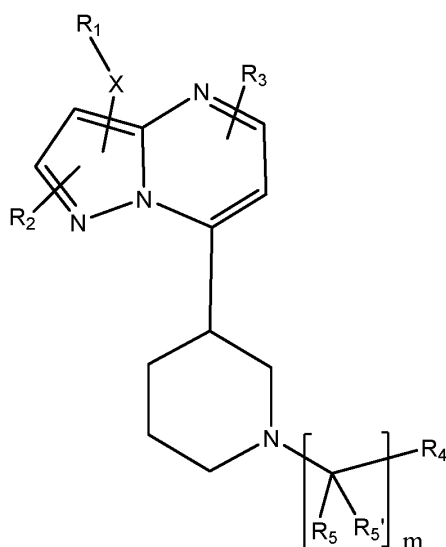
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wherein r is 0, 1, 2 or 3;

optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

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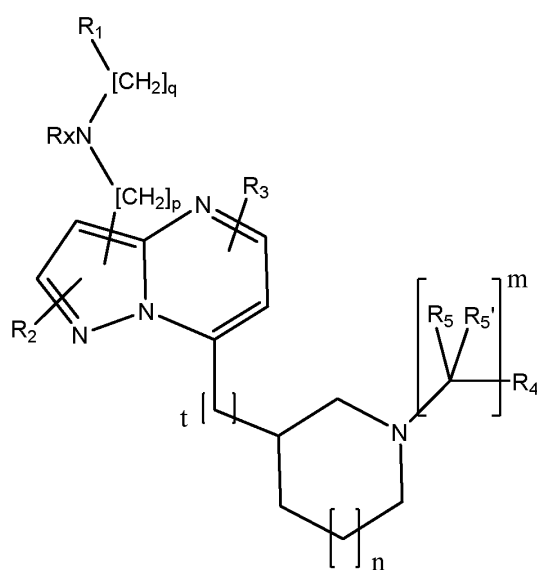
In a further embodiment the compound according to the invention of general Formula (I) is a compound of general Formula (I')



(I')

wherein R₁, R₂, R₃, R₄, R₅, R_{5'}, X and m, are as defined below in the detailed description;

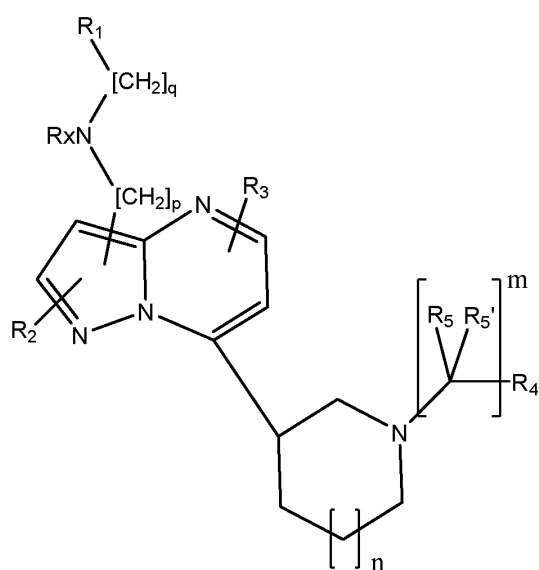
- 5 optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.
- 10 In a further embodiment the compound according to the invention of general Formula (I) is a compound of general Formula (I^{2'})

(I^{2'})

wherein R₁, R₂, R₃, R₄, R₅, R_{5'}, R_x, m, n, t, p and q are as defined below in the detailed description;

- 5 optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

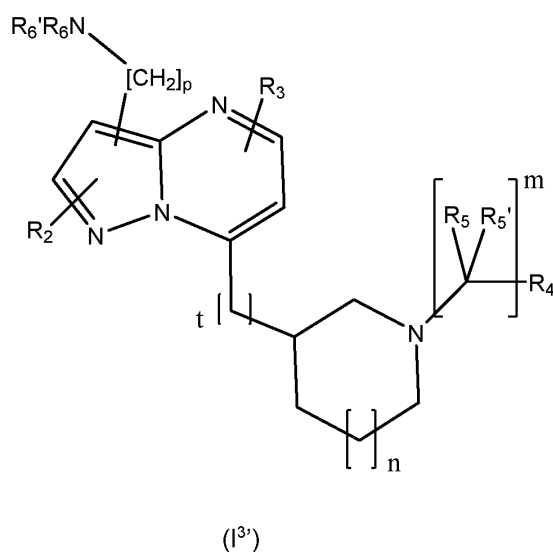
10 In a further embodiment the compound according to the invention of general Formula (I) is a compound of general Formula (I^{2'})



(I2a')

wherein R₁, R₂, R₃, R₄, R₅, R₅', R_x, m, n, p and q are as defined below in the detailed description;

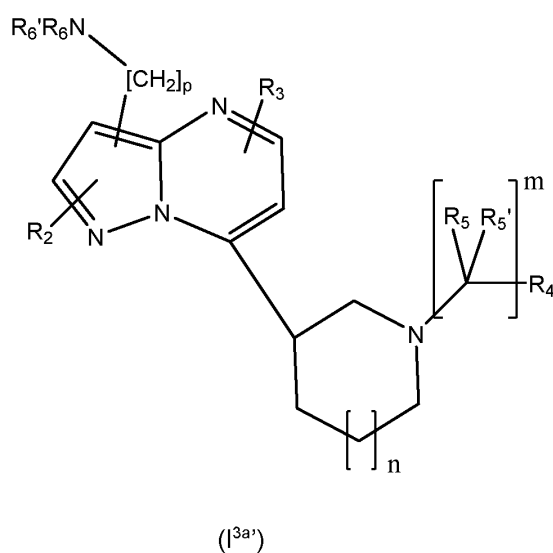
- 5 optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.
- 10 In a further embodiment the compound according to the invention of general Formula (I) is a compound of general Formula (I^{3'})



wherein R₁, R₂, R₃, R₄, R₅, R_{5'}, R₆, R_{6'}, , m, n, t and p are as defined below in the detailed description;

- 5 optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

- 10 In a further embodiment the compound according to the invention of general Formula (I) is a compound of general Formula (I^{3'})



wherein R_1 , R_2 , R_3 , R_4 , R_5 , R_5' , R_6 , R_6' , m , n , and p are as defined below in the detailed description;

optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers,
 5 preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

For clarity purposes, all groups and definitions described in the present description and referring to compounds of general Formula (I), also apply to compounds of general Markush Formulae (I'), (I''), (I^{2a'}), (I^{3'}) or (I^{3a'}) (where applicable), and to all intermediate
 10 of synthesis, when those groups are present in the mentioned general Markush formulae, since compounds of general Markush Formulae (I'), (I''), (I^{2a'}), (I^{3'}) or (I^{3a'}) are included within the scope of the larger definition of general Markush Formula (I).

For clarity purposes, the expression e.g. "the cycle in R_8 - R_8' " means the cycle resulting when R_8 and R_8' form a cycle together with the atom(s) to which they are attached. This
 15 cycle can then be substituted or not. This definition is also generally applicable and can be also applied as a definition of any other cycle (preferably cycloalkyls, heterocyclyls or aryls) formed from two different functional groups like e.g. "the cycle in R_i - R_i' " means the cycle resulting when R_i and R_i' form a cycle together with the atom(s) to which they are attached. This cycle can then be substituted or not.

In the context of this invention, alkyl is understood as meaning saturated, linear or branched hydrocarbons, which may be unsubstituted or substituted once or several times. It encompasses e.g. $-CH_3$ and $-CH_2-CH_3$. In these radicals, C_{1-2} -alkyl represents C1- or C2-alkyl, C_{1-3} -alkyl represents C1-, C2- or C3-alkyl, C_{1-4} -alkyl represents C1-, C2-, C3- or C4-alkyl, C_{1-5} -alkyl represents C1-, C2-, C3-, C4-, or C5-alkyl, C_{1-6} -alkyl
 25 represents C1-, C2-, C3-, C4-, C5- or C6-alkyl, C_{1-7} -alkyl represents C1-, C2-, C3-, C4-, C5-, C6- or C7-alkyl, C_{1-8} -alkyl represents C1-, C2-, C3-, C4-, C5-, C6-, C7- or C8-alkyl, C_{1-10} -alkyl represents C1-, C2-, C3-, C4-, C5-, C6-, C7-, C8-, C9- or C10-alkyl and C_{1-18} -alkyl represents C1-, C2-, C3-, C4-, C5-, C6-, C7-, C8-, C9-, C10-, C11-, C12-, C13-, C14-, C15-, C16-, C17- or C18-alkyl. The alkyl radicals are preferably methyl,
 30 ethyl, propyl, methylethyl, butyl, 1-methylpropyl, 2-methylpropyl, 1,1-dimethylethyl, pentyl, 1,1-dimethylpropyl, 1,2-dimethylpropyl, 2,2-dimethylpropyl, hexyl, 1-methylpentyl, if substituted also CHF_2 , CF_3 or CH_2OH etc. Preferably alkyl is understood in the context of this invention as C_{1-8} alkyl like methyl, ethyl, propyl, butyl,

pentyl, hexyl, heptyl, or octyl; preferably is C₁₋₆ alkyl like methyl, ethyl, propyl, butyl, pentyl, or hexyl; more preferably is C₁₋₄ alkyl like methyl, ethyl, propyl or butyl.

Alkenyl is understood as meaning unsaturated, linear or branched hydrocarbons, which may be unsubstituted or substituted once or several times. It encompasses groups like
 5 e.g. -CH=CH-CH₃. The alkenyl radicals are preferably vinyl (ethenyl), allyl (2-propenyl). Preferably in the context of this invention alkenyl is C₂₋₁₀-alkenyl or C₂₋₈-alkenyl like ethylene, propylene, butylene, pentylene, hexylene, heptylene or octylene; or is C₂₋₆-alkenyl like ethylene, propylene, butylene, pentylene, or hexylene; or is C₂₋₄-alkenyl, like ethylene, propylene, or butylene.

10 Alkynyl is understood as meaning unsaturated, linear or branched hydrocarbons, which may be unsubstituted or substituted once or several times. It encompasses groups like e.g. -C≡C-CH₃ (1-propynyl). Preferably alkynyl in the context of this invention is C₂₋₁₀-alkynyl or C₂₋₈-alkynyl like ethyne, propyne, butyne, pentyne, hexyne, heptyne, or octyne; or is C₂₋₆-alkynyl like ethyne, propyne, butyne, pentyne, or hexyne; or is C₂₋₄-
 15 alkynyl like ethyne, propyne, butyne, pentyne, or hexyne.

In connection with alkyl (also in alkylaryl, alkylheterocyclyl or alkylcycloalkyl), alkenyl, alkynyl and O-alkyl - unless defined otherwise - the term substituted in the context of this invention is understood as meaning replacement of at least one hydrogen radical on a carbon atom by halogen (F, Cl, Br, I), -NR_kR_{k'}, -SR_k, -S(O)R_k, -S(O)₂R_k, -OR_k, -
 20 C(O)R_k, -C(O)OR_k, -CN, -C(O)NR_kR_{k'}, haloalkyl, haloalkoxy, being R_k represented by R₁₁, R₁₃, R₂₁, R₃₁, R₄₁ or R₅₁ (being R_{k'} represented by R₁₁', R₁₃', R₂₁', R₃₁', R₄₁' or R₅₁') ; wherein R₁ to R₅₁' are as defined in the description, and wherein when different radicals R₁ to R₅₁' or when m, n, t or r are present simultaneously in Formula I they may be identical or different.

25 Most preferably in connection with alkyl (also in alkylaryl, alkylheterocyclyl or alkylcycloalkyl), alkenyl, alkynyl or O-alkyl, substituted is understood in the context of this invention that any alkyl (also in alkylaryl, alkylheterocyclyl or alkylcycloalkyl), alkenyl, alkynyl or O-alkyl which is substituted with one or more of halogen (F, Cl, Br, I), -NR_kR_{k'}, -OR_k, -CN, -SR_k, haloalkyl, haloalkoxy, being R_k represented by R₁₁, R₁₃,
 30 R₂₁, R₃₁, R₄₁ or R₅₁ (being R_{k'} represented by R₁₁', R₁₃', R₂₁', R₃₁', R₄₁' or R₅₁') ; wherein wherein R₁ to R₅₁' are as defined in the description, and wherein when different radicals R₁ to R₅₁' or when m, n, t or r are present simultaneously in Formula I they may be identical or different.

More than one replacement on the same molecule and also on the same carbon atom is possible with the same or different substituents. This includes for example 3 hydrogens being replaced on the same C atom, as in the case of CF₃, or at different places of the same molecule, as in the case of e.g. -CH(OH)-CH=CH-CHCl₂.

- 5 In the context of this invention haloalkyl is understood as meaning an alkyl being substituted once or several times by a halogen (selected from F, Cl, Br, I). It encompasses e.g. -CH₂Cl, -CH₂F, -CHCl₂, -CHF₂, -CCl₃, -CF₃ and -CH₂-CHCl₂. Preferably haloalkyl is understood in the context of this invention as halogen-substituted C₁₋₄-alkyl representing halogen substituted C1-, C2-, C3- or C4-alkyl. The
10 halogen-substituted alkyl radicals are thus preferably methyl, ethyl, propyl, and butyl. Preferred examples include -CH₂Cl, -CH₂F, -CHCl₂, -CHF₂, and -CF₃.

- In the context of this invention haloalkoxy is understood as meaning an -O-alkyl being substituted once or several times by a halogen (selected from F, Cl, Br, I). It
15 encompasses e.g. -OCH₂Cl, -OCH₂F, -OCHCl₂, -OCHF₂, -OCCl₃, -OCF₃ and -OCH₂-CHCl₂. Preferably haloalkoxy is understood in the context of this invention as halogen-substituted -OC₁₋₄-alkyl representing halogen substituted C1-, C2-, C3- or C4-alkoxy. The halogen-substituted alkyl radicals are thus preferably O-methyl, O-ethyl, O-propyl, and O-butyl. Preferred examples include -OCH₂Cl, -OCH₂F, -OCHCl₂, -
20 OCHF₂, and -OCF₃.

- In the context of this invention cycloalkyl is understood as meaning saturated and unsaturated (but not aromatic) cyclic hydrocarbons (without a heteroatom in the ring), which can be unsubstituted or once or several times substituted. Furthermore, C₃₋₄-cycloalkyl represents C3- or C4-cycloalkyl, C₃₋₅-cycloalkyl represents C3-, C4- or C5-
25 cycloalkyl, C₃₋₆-cycloalkyl represents C3-, C4-, C5- or C6-cycloalkyl, C₃₋₇-cycloalkyl represents C3-, C4-, C5-, C6- or C7-cycloalkyl, C₃₋₈-cycloalkyl represents C3-, C4-, C5-, C6-, C7- or C8-cycloalkyl, C₄₋₅-cycloalkyl represents C4- or C5-cycloalkyl, C₄₋₆-cycloalkyl represents C4-, C5- or C6-cycloalkyl, C₄₋₇-cycloalkyl represents C4-, C5-, C6- or C7-cycloalkyl, C₅₋₆-cycloalkyl represents C5- or C6-cycloalkyl and C₅₋₇-cycloalkyl
30 represents C5-, C6- or C7-cycloalkyl. Examples are cyclopropyl, 2-methylcyclopropyl, cyclopropylmethyl, cyclobutyl, cyclopentyl, cyclopentylmethyl, cyclohexyl, cycloheptyl, cyclooctyl, and also adamantyl. Preferably in the context of this invention cycloalkyl is C₃₋₈ cycloalkyl like cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, or cyclooctyl; or is C₃₋₇ cycloalkyl like cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, or

cycloheptyl; or is C₃₋₆ cycloalkyl like cyclopropyl, cyclobutyl, cyclopentyl or cyclohexyl, especially cyclopentyl or cyclohexyl.

5 Aryl is understood as meaning 5 to 18 membered mono or polycyclic ring systems with at least one aromatic ring but without heteroatoms even in only one of the rings. Examples are phenyl, naphthyl, fluoranthenyl, fluorenyl, tetralinyl or indanyl, 9H-fluorenyl or anthracenyl radicals, which can be unsubstituted or once or several times substituted. Most preferably aryl is understood in the context of this invention as phenyl, naphthyl or anthracenyl, preferably is phenyl.

10 A heterocyclyl radical or group (also called heterocyclyl hereinafter) is understood as meaning 5 to 18 membered mono or polycyclic heterocyclic ring systems, with at least one saturated or unsaturated ring which contains one or more heteroatoms selected from the group consisting of nitrogen, oxygen and/or sulfur in the ring. A heterocyclic group can also be substituted once or several times.

15 Subgroups inside the heterocyclyls as understood herein include heteroaryls and non-aromatic heterocyclyls.

20 - the heteroaryl (being equivalent to heteroaromatic radicals or aromatic heterocyclyls) is an aromatic 5 to 18 membered mono or polycyclic heterocyclic ring system of one or more rings of which at least one aromatic ring contains one or more heteroatoms selected from the group consisting of nitrogen, oxygen and/or sulfur in the ring; preferably is a 5 to 18 membered mono or polycyclic aromatic heterocyclic ring system of one or two rings of which at least one aromatic ring contains one or more heteroatoms selected from the group consisting of nitrogen, oxygen and/or sulfur in the ring, more preferably is selected from furan, benzofuran, thiophene, benzothiophene, pyrrole, pyridine, pyrimidine, pyrazine, quinoline, isoquinoline, phthalazine, benzothiazole, indole, benzotriazole, carbazole, quinazoline, thiazole, imidazole, pyrazole, oxazole, thiophene and benzimidazole;

25 - the non-aromatic heterocyclyl is a 5 to 18 membered mono or polycyclic heterocyclic ring system of one or more rings of which at least one ring – with this (or these) ring(s) then not being aromatic - contains one or more heteroatoms selected from the group consisting of nitrogen, oxygen and/or sulfur in the ring; preferably is a 5 to 18 membered mono or polycyclic heterocyclic ring system of one or two rings of which one or both rings – with

30

5 this one or two rings then not being aromatic – contain/s one or more heteroatoms selected from the group consisting of nitrogen, oxygen and/or sulfur in the ring, more preferably is selected from oxazepane, pyrrolidine, piperidine, piperazine, tetrahydropyran, morpholine, indoline, oxopyrrolidine, benzodioxane, especially is benzodioxane, morpholine, tetrahydropyran, piperidine, oxopyrrolidine and pyrrolidine.

10 Preferably in the context of this invention heterocyclyl is defined as a 5 to 18 membered mono or polycyclic heterocyclic ring system of one or more saturated or unsaturated rings of which at least one ring contains one or more heteroatoms selected from the group consisting of nitrogen, oxygen and/or sulfur in the ring. Preferably it is a 5 to 18 membered mono or polycyclic heterocyclic ring system of one or two saturated or unsaturated rings of which at least one ring contains one or more heteroatoms selected from the group consisting of nitrogen, oxygen and/or sulfur in the ring.

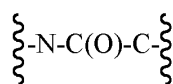
15 Preferred examples of heterocyclyls include oxazepane, pyrrolidine, imidazole, oxadiazole, tetrazole, pyridine, pyrimidine, piperidine, piperazine, benzofuran, benzimidazole, indazole, benzodiazole, thiazole, benzothiazole, tetrahydropyran, morpholine, indoline, furan, triazole, isoxazole, pyrazole, thiophene, benzothiophene, pyrrole, pyrazine, pyrrolo[2,3b]pyridine, quinoline, isoquinoline, tetrahydroisoquinoline, phthalazine, benzo-1,2,5-thiadiazole, indole, benzotriazole, benzoxazole
20 oxopyrrolidine, pyrimidine, benzodioxolane, benzodioxane, carbazole and quinazoline, especially is pyridine, pyrazine, indazole, benzodioxane, thiazole, benzothiazole, morpholine, tetrahydropyran, pyrazole, imidazole, piperidine, thiophene, indole, benzimidazole, pyrrolo[2,3b]pyridine, benzoxazole, oxopyrrolidine, pyrimidine,
25 oxazepane, azetidine and pyrrolidine.

In the context of this invention oxopyrrolidine is understood as meaning pyrrolidin-2-one.

30 An *N*-containing heterocyclyl is a heterocyclic ring system of one or more saturated or unsaturated rings of which at least one ring contains a nitrogen and optionally one or more further heteroatoms selected from the group consisting of nitrogen, oxygen and/or sulfur in the ring; preferably is a heterocyclic ring system of one or two saturated or unsaturated rings of which at least one ring contains a nitrogen and optionally one or
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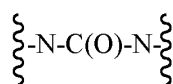
more further heteroatoms selected from the group consisting of nitrogen, oxygen and/or sulfur in the ring, more preferably is selected from oxazepane, pyrrolidine, imidazole, oxadiazole, tetrazole, azetidine, pyridine, pyrimidine, piperidine, piperazine, benzimidazole, indazole, benzothiazole, benzodiazole, morpholine, indoline, triazole, isoxazole, pyrazole, pyrrole, pyrazine, pyrrolo[2,3b]pyridine, quinoline, quinolone, isoquinoline, tetrahydrothienopyridine, phthalazine, benzo-1,2,5-thiadiazole, indole, benzotriazole, benzoxazole oxopyrrolidine, carbazole or thiazole.

10 In the context of this invention, a cyclic amide is defined as a subgroup of a heterocyclyl (as defined above) formed through the cyclization of a carbon sequence, containing at least the sequence



forming part of the cycle. Said cyclic amide may optionally be fused to a ring system. Preferably the cyclic amide is an "indoline-2-one". A cyclic amide may be substituted or unsubstituted as defined for heterocyclyl above.

20 In the context of this invention, a cyclic urea is defined as a subgroup of a heterocyclyl (as defined above) formed through the cyclization of a carbon sequence containing at least the sequence



forming part of the cycle. Said cyclic urea may optionally be fused to a ring system. Preferably the cyclic urea is "1H-benzo[d]imidazol-2(3H)-one". A cyclic urea may be substituted or unsubstituted as defined for heterocyclyl above.

25 In connection with aromatic heterocyclyls (heteroaryls), non-aromatic heterocyclyls, aryls and cycloalkyls, when a ring system falls within two or more of the above cycle definitions simultaneously, then the ring system is defined first as an aromatic heterocyclyl (heteroaryl) if at least one aromatic ring contains a heteroatom. If no aromatic ring contains a heteroatom, then the ring system is defined as a non-aromatic

heterocyclyl if at least one non-aromatic ring contains a heteroatom. If no non-aromatic ring contains a heteroatom, then the ring system is defined as an aryl if it contains at least one aryl cycle. If no aryl is present, then the ring system is defined as a cycloalkyl if at least one non-aromatic cyclic hydrocarbon is present.

5

In the context of this invention alkylaryl is understood as meaning an aryl group (see above) being connected to another atom through a C₁₋₆-alkyl (see above) which may be branched or linear and is unsubstituted or substituted once or several times. Preferably alkylaryl is understood as meaning an aryl group (see above) being connected to another atom through 1 to 4 (-CH₂-) groups. Most preferably alkylaryl is benzyl (i.e. -CH₂-phenyl). More preferably, the "alkyl" in alkylaryl is an unsubstituted alkyl.

In the context of this invention alkylheterocyclyl is understood as meaning an heterocyclyl group being connected to another atom through a C₁₋₆-alkyl (see above) which may be branched or linear and is unsubstituted or substituted once or several times. Preferably alkylheterocyclyl is understood as meaning a heterocyclyl group (see above) being connected to another atom through 1 to 4 (-CH₂-) groups. Most preferably alkylheterocyclyl is -CH₂-pyridine. More preferably, the "alkyl" in alkylheterocyclyl is an unsubstituted alkyl.

In the context of this invention alkylcycloalkyl is understood as meaning an cycloalkyl group being connected to another atom through a C₁₋₆-alkyl (see above) which may be branched or linear and is unsubstituted or substituted once or several times. Preferably alkylcycloalkyl is understood as meaning a cycloalkyl group (see above) being connected to another atom through 1 to 4 (-CH₂-) groups. Most preferably alkylcycloalkyl is -CH₂-cyclopropyl. More preferably, the "alkyl" in alkylcycloalkyl is an unsubstituted alkyl.

Preferably, the aryl is a monocyclic aryl. More preferably the aryl is a 5, 6 or 7 membered monocyclic aryl. Even more preferably the aryl is a 5 or 6 membered monocyclic aryl.

30

Preferably, the heteroaryl is a monocyclic heteroaryl. More preferably the heteroaryl is a 5, 6 or 7 membered monocyclic heteroaryl. Even more preferably the heteroaryl is a 5 or 6 membered monocyclic heteroaryl.

Preferably, the non-aromatic heterocyclyl is a monocyclic non-aromatic heterocyclyl. More preferably the non-aromatic heterocyclyl is a 4, 5, 6 or 7 membered monocyclic non-aromatic heterocyclyl. Even more preferably the non-aromatic heterocyclyl is a 5 or 6 membered monocyclic non-aromatic heterocyclyl.

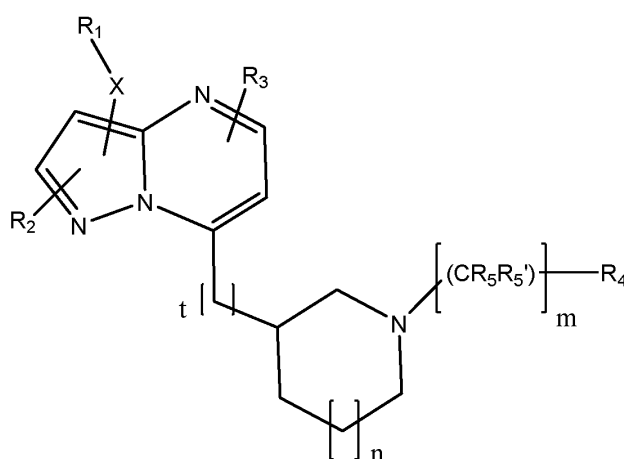
Preferably, the cycloalkyl is a monocyclic cycloalkyl. More preferably the cycloalkyl is a 3, 4, 5, 6, 7 or 8 membered monocyclic cycloalkyl. Even more preferably the cycloalkyl is a 3, 4, 5 or 6 membered monocyclic cycloalkyl.

An heterocyclyl is a ring system of one or more saturated and/or unsaturated rings of which at least one ring contains one or more heteroatoms selected from the group consisting of nitrogen, oxygen and/or sulfur in the ring; preferably is a ring system of one saturated and/or unsaturated ring containing one or more heteroatoms selected from the group consisting of nitrogen, oxygen and/or sulfur in the ring, or a ring system of two saturated and/or unsaturated rings of which at least one ring contains one or more heteroatoms selected from the group consisting of nitrogen, oxygen and/or sulfur in the ring, more preferably is selected from oxazepan, pyrrolidine, imidazole, oxadiazole, tetrazole, azetidine, pyridine, pyrimidine, piperidine, piperazine, furan, benzofuran, benzimidazole, indazole, benzothiazole, benzodiazole, thiazole, isothiazole, tetrahydropyran, tetrahydrofuran, morpholine, thiomorpholine, indoline, triazole, isoxazole, pyrazole, thiophene, benzothiophene, pyrrole, pyrazine, pyrrolo[2,3b]pyridine, quinoline, quinolone, isoquinoline, tetrahydroisoquinoline, tetrahydrothienopyridine, phthalazine, benzo-1,2,5-thiadiazole, indole, benzotriazole, benzoxazole, oxopyrrolidine, benzodioxolane, benzodioxane, carbazole, octahydro-ethanopyrrolo-pyridine, oxaspirodecane, oxadiazaspirodecane, indoline-2-one and quinazoline.

In general, such a heterocyclyl may contain between 3 and 32 atoms in the rings (preferably 4 to 20 atoms in the rings, or most preferably 5 to 18 atoms in the rings). Thus, a heterocyclyl may contain between 3 and 12 atoms in the ring (preferably 4 to 10 atoms in the ring, or 5 to 8 atoms in the ring, or 5 to 6 atoms in the ring) in case of a heterocyclyl of one ring. Such a heterocyclyl may also contain between 5 and 22 atoms in both rings together (preferably 6 to 16 atoms in both rings together, or 7 to 12 atoms in both rings together or 8 to 10 atoms in both rings together) in case of a

heterocyclyl of two rings. Such a heterocyclyl may also contain between 7 and 32 atoms in the 3 rings together (preferably 10 to 22 atoms in the three rings together, or 12 to 20 atoms in the three rings together or 10 to 18 atoms in the three rings together) in case of a heterocyclyl of three rings. Each ring of the ring system, independently of
 5 each other, can be saturated or unsaturated.

For clarity purposes, the general Markush Formula (I) is equivalent to (IZ),

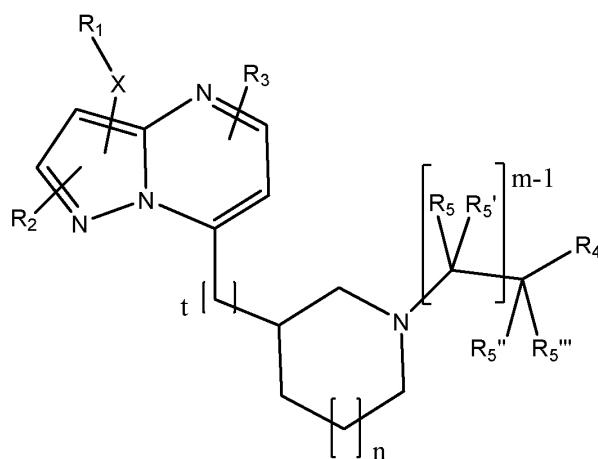


(IZ)

10 wherein only $-C(R_5R_5')-$ is included into the brackets, and m means the number of times that $-C(R_5R_5')-$ is repeated. The same would apply, when applicable, to general Markush Formulae (I), (I'), (I^{2'}), (I^{2a'}), (I^{3'}) or (I^{3a'}) and to all intermediates of synthesis.

In addition, and for clarity purposes, it should further be understood that naturally if t is 0, the pyrazolopyrimidine core and the piperidine ring are still present, when applicable,
 15 in general Markush Formulae (I), (I'), (I^{2'}), (I^{2a'}), (I^{3'}) or (I^{3a'}) and to all intermediates of synthesis.

For clarity purposes, reference is also made to the following statements below in the definitions of substitutions on alkyl etc. or aryl etc. that "when different radicals R₁ to R_{51'} or when m, n, t or r are present simultaneously in Formula I they may be identical or different". This statement is reflected in the below general Formula (I^d) being derived from and falling into general Formula (I),
 20

(I^d)

wherein R₁, R₂, R₃, R₄, R₅, R₅', X, m, n and t are as defined in the description. In addition, R₅' and R₅' are added. As said above, this statement is thus reflected in
 5 that R₅' and R₅' are or could be different from R₅ and R₅' or not.

The same would be applicable *mutatis mutandis* for general Formulas like general Formula (I) as well as the other general Formulas (I'), (I^{2'}), (I^{2a'}), (I^{3'}) or (I^{3a'}) and to all intermediates of synthesis.

In connection with aryl (including alkyl-aryl), cycloalkyl (including alkyl-cycloalkyl), or
 10 heterocyclyl (including alkyl-heterocyclyl), substituted is understood - unless defined otherwise - as meaning substitution of the ring-system of the aryl or alkyl-aryl, cycloalkyl or alkyl-cycloalkyl; heterocyclyl or alkyl-heterocyclyl with one or more of halogen (F, Cl, Br, I), -R_k, -OR_k, -[CH₂]_rOR_k, -CN, -NO₂, -NR_kR_k', -[CH₂]_rNR_kR_k', -C(O)OR_k, -C(O)R_k, -NR_kC(O)R_k', -C(O)NR_kR_k', -NR_kS(O)₂R_k', =O, -OCH₂CH₂OH, -NR_kC(O)NR_kR_k'', -S(O)₂NR_kR_k', -NR_kS(O)₂NR_kR_k'', haloalkyl, haloalkoxy, -SR_k, -S(O)R_k, -S(O)₂R_k or -C(CH₃)OR_k, or substituted or unsubstituted alkylcycloalkyl, substituted or unsubstituted
 15 alkylaryl, substituted or unsubstituted alkylheterocyclyl, with R_k, R_k' and R_k' independently being either H or a saturated or unsaturated, linear or branched, substituted or unsubstituted C₁₋₆-alkyl; a saturated or unsaturated, linear or branched, substituted or unsubstituted C₁₋₆-alkyl; a saturated or unsaturated, linear or branched, substituted or unsubstituted -O-C₁₋₆-alkyl (alkoxy); a saturated or unsaturated, linear or branched, substituted or unsubstituted -S-C₁₋₆-alkyl; a saturated or unsaturated, linear or branched, substituted or unsubstituted -C(O)-C₁₋₆-alkyl-group; a saturated or
 20

unsaturated, linear or branched, substituted or unsubstituted -C(O)-O-C₁₋₆-alkyl-group;
 a substituted or unsubstituted aryl or alkyl-aryl; a substituted or unsubstituted cycloalkyl
 or alkyl-cycloalkyl; a substituted or unsubstituted heterocyclyl or alkyl-heterocyclyl,
 being R_k one of R₁₁, R₁₄, R₂₁ or R₄₁, (being R_k' one of R₁₁', R₁₄', R₂₁' or R₄₁', being R_k'' one
 5 of R₁₁'', R₁₄'', R₂₁'' or R₄₁''); wherein R₁ to R₅₁' are as defined in the description, and
 wherein when different radicals R₁ to R₅₁' or when m, n, t or r are present simultaneously
 in Formula I they may be identical or different.

Most preferably in connection with aryl (including alkyl-aryl), cycloalkyl (including alkyl-
 cycloalkyl), or heterocyclyl (including alkyl-heterocyclyl), substituted is understood in
 10 the context of this invention that any aryl, cycloalkyl and heterocyclyl which is
 substituted is substituted (also in an alkylaryl, alkylcycloalkyl or alkylheterocyclyl) with
 one or more of halogen (F, Cl, Br, I), -R_k, -OR_k, -[CH₂]_rOR_k, -CN, -NO₂, -NR_kR_k'', -
 [CH₂]_rNR_kR_k', -C(O)R_k, NR_kC(O)R_k', -NR_kS(O)₂R_k', =O, -S(O)₂NR_kR_k', -NR_kC(O)NR_kR_k'',
 haloalkyl, haloalkoxy, -SR_k, -S(O)R_k or -S(O)₂R_k, or substituted or unsubstituted
 15 alkylcycloalkyl, substituted or unsubstituted alkylaryl, substituted or unsubstituted
 alkylheterocyclyl, being R_k one of R₁₁, R₁₄, R₂₁ or R₄₁, (being R_k' one of R₁₁', R₁₄', R₂₁' or
 R₄₁'; being R_k'' one of R₁₁'', R₁₄'', R₂₁'' or R₄₁''); wherein R₁ to R₅₁' are as defined in the
 description, and wherein when different radicals R₁ to R₅₁' or when m, n, t or r are
 present simultaneously in Formula I they may be identical or different.

20 In connection with cycloalkyl (including alkyl-cycloalkyl), or heterocyclyl (including
 alkylheterocyclyl) namely non-aromatic heterocyclyl (including non-aromatic alkyl-
 heterocyclyl), substituted is also understood - unless defined otherwise - as meaning
 substitution of the ring-system of the cycloalkyl or alkyl-cycloalkyl, non-aromatic

heterocyclyl or non aromatic alkyl-heterocyclyl with  (leading to a spiro structure)
 25 and/or with =O.

Moreover, in connection with cycloalkyl (including alkyl-cycloalkyl), or heterocyclyl
 (including alkylheterocyclyl) namely non-aromatic heterocyclyl (including non-aromatic
 alkyl-heterocyclyl), substituted is also understood - unless defined otherwise - as
 meaning substitution of the ring-system of the cycloalkyl or alkyl-cycloalkyl, non-
 30 aromatic heterocyclyl or non aromatic alkyl-heterocyclyl is spiro substituted or
 substituted with =O.

Moreover, in connection with cycloalkyl (including alkyl-cycloalkyl), or heterocyclyl (including alkylheterocyclyl) namely non-aromatic heterocyclyl (including non-aromatic alkyl-heterocyclyl), substituted is also understood - unless defined otherwise - as meaning substitution of the ring-system of the cycloalkyl or alkyl-cycloalkyl, non-
5 aromatic heterocyclyl or non aromatic alkyl-heterocyclyl with =O.

A ring system is an organic system consisting of at least one ring of connected atoms but including also systems in which two or more rings of connected atoms are joined with "joined" meaning that the respective rings are sharing one (like a spiro structure), two or more atoms being a member or members of both joined rings.
10

The term "polycyclic ring system" means that the ring system is made of two or more rings joined by sharing at least one atom.

Any compound that is a N-oxide of a compound according to the invention like a
15 compound according to general formula I defined above is understood to be also covered by the scope of the invention.

The term "leaving group" means a molecular fragment that departs with a pair of electrons in heterolytic bond cleavage. Leaving groups can be anions or neutral
20 molecules. Common anionic leaving groups are halides such as Cl⁻, Br⁻, and I⁻, and sulfonate esters, such as tosylate (TsO⁻) or mesylate.

The term "salt" is to be understood as meaning any form of the active compound used according to the invention in which it assumes an ionic form or is charged and is coupled with a counter-ion (a cation or anion) or is in solution. By this are also to be
25 understood complexes of the active compound with other molecules and ions, in particular complexes via ionic interactions.

The term "physiologically acceptable salt" means in the context of this invention any salt that is physiologically tolerated (most of the time meaning not being toxic-
30 especially not caused by the counter-ion) if used appropriately for a treatment especially if used on or applied to humans and/or mammals.

These physiologically acceptable salts can be formed with cations or bases and in the context of this invention is understood as meaning salts of at least one of the

compounds used according to the invention - usually a (deprotonated) acid - as an anion with at least one, preferably inorganic, cation which is physiologically tolerated - especially if used on humans and/or mammals. The salts of the alkali metals and alkaline earth metals are particularly preferred, and also those with NH₄, but in particular (mono)- or (di)sodium, (mono)- or (di)potassium, magnesium or calcium salts.

Physiologically acceptable salts can also be formed with anions or acids and in the context of this invention is understood as meaning salts of at least one of the compounds used according to the invention as the cation with at least one anion which are physiologically tolerated - especially if used on humans and/or mammals. By this is understood in particular, in the context of this invention, the salt formed with a physiologically tolerated acid, that is to say salts of the particular active compound with inorganic or organic acids which are physiologically tolerated - especially if used on humans and/or mammals. Examples of physiologically tolerated salts of particular acids are salts of: hydrochloric acid, hydrobromic acid, sulfuric acid, methanesulfonic acid, formic acid, acetic acid, oxalic acid, succinic acid, malic acid, tartaric acid, mandelic acid, fumaric acid, lactic acid or citric acid.

The compounds of the invention may be present in crystalline form or in the form of free compounds like a free base or acid.

Any compound that is a solvate of a compound according to the invention like a compound according to general formula I defined above is understood to be also covered by the scope of the invention. Methods of solvation are generally known within the art. Suitable solvates are pharmaceutically acceptable solvates. The term "solvate" according to this invention is to be understood as meaning any form of the active compound according to the invention in which this compound has attached to it via non-covalent binding another molecule (most likely a polar solvent). Especially preferred examples include hydrates and alcoholates, like methanolates or ethanolates.

Any compound that is a prodrug of a compound according to the invention like a compound according to general formula (I) defined above is understood to be also covered by the scope of the invention. The term "prodrug" is used in its broadest sense and encompasses those derivatives that are converted *in vivo* to the compounds of the invention. Such derivatives would readily occur to those skilled in the art, and include, depending on the functional groups present in the molecule and without limitation, the

following derivatives of the present compounds: esters, amino acid esters, phosphate esters, metal salts sulfonate esters, carbamates, and amides. Examples of well-known methods of producing a prodrug of a given acting compound are known to those skilled in the art and can be found e.g. in Krogsgaard-Larsen et al. "Textbook of Drug design and Discovery" Taylor & Francis (April 2002).

Any compound that is an *N*-oxide of a compound according to the invention like a compound according to general formula I defined above is understood to be also covered by the scope of the invention.

Unless otherwise stated, the compounds of the invention are also meant to include compounds which differ only in the presence of one or more isotopically enriched atoms. For example, compounds having the present structures except for the replacement of a hydrogen by a deuterium or tritium, or the replacement of a carbon by ¹³C- or ¹⁴C-enriched carbon or of a nitrogen by ¹⁵N-enriched nitrogen are within the scope of this invention. This would especially also apply to the provisos described above so that any mentioning of hydrogen or any "H" in a formula would also cover deuterium or tritium.

The compounds of formula (I) as well as their salts or solvates of the compounds are preferably in pharmaceutically acceptable or substantially pure form. By pharmaceutically acceptable form is meant, inter alia, having a pharmaceutically acceptable level of purity excluding normal pharmaceutical additives such as diluents and carriers, and including no material considered toxic at normal dosage levels. Purity levels for the drug substance are preferably above 50%, more preferably above 70%, most preferably above 90%. In a preferred embodiment it is above 95% of the compound of formula (I), or of its salts. This applies also to its solvates or prodrugs.

In a further embodiment the compound according to the invention of general Formula (I) is a compound wherein

m is 1, 2 or 3;

optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers,

preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

In a further embodiment the compound according to the invention of general Formula (I) is a compound wherein

5 n is 1;

optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

10 In a further embodiment the compound according to the invention of general Formula (I) is a compound wherein

p is 0, 1, 2 or 3;

optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

15 In a further embodiment the compound according to the invention of general Formula (I) is a compound wherein

20 R_x is selected from the group consisting of hydrogen and substituted or unsubstituted C₁₋₆ alkyl;

optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

25 In a further embodiment the compound according to the invention of general Formula (I) is a compound wherein

r is 0 or 1;

optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

- 5 In a further embodiment the compound according to the invention of general Formula (I) is a compound wherein

t is 0 or 1;

- optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.
- 10

In a further embodiment the compound according to the invention of general Formula (I) is a compound wherein

t is 0;

- 15 optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

- 20 In a further embodiment the compound according to the invention of general Formula (I) is a compound wherein

R₁ is selected from the group consisting of substituted or unsubstituted C₁₋₆ alkyl, substituted or unsubstituted C₂₋₆ alkenyl, substituted or unsubstituted C₂₋₆ alkynyl, halogen, haloalkyl, haloalkoxy, -OR₆, -NR₆R₆', -CN, cycloalkyl, aryl and heterocyclyl;

- 25 optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

In a further embodiment the compound according to the invention of general Formula (I) is a compound wherein

R₁ is selected from the group consisting of substituted or unsubstituted C₁₋₆ alkyl, halogen, haloalkyl, haloalkoxy, -OR₆, -NR₆R₆', -CN, cycloalkyl, aryl and heterocyclyl;

- 5 optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

10 In a further embodiment the compound according to the invention of general Formula (I) is a compound wherein

R₁ is selected from the group consisting of substituted or unsubstituted C₁₋₆ alkyl, halogen, haloalkyl, -OR₆, -NR₆R₆', -CN, cycloalkyl, aryl and heterocyclyl;

- 15 optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

In a further embodiment the compound according to the invention of general Formula (I) is a compound wherein

- 20 R₁ is selected from the group consisting of hydrogen, substituted or unsubstituted C₁₋₆ alkyl, halogen, haloalkyl, haloalkoxy, -OR₆, -NR₆R₆', -CN, cycloalkyl, aryl and heterocyclyl;

- 25 optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

In a further embodiment the compound according to the invention of general Formula (I) is a compound wherein

R₁ is selected from the group consisting of hydrogen, substituted or unsubstituted C₁₋₆ alkyl, halogen, haloalkyl, -OR₆, -NR₆R₆', -CN, cycloalkyl, aryl and heterocyclyl;

optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

- 5 In a further embodiment the compound according to the invention of general Formula (I) is a compound wherein

R₁ is selected from the group consisting of substituted or unsubstituted C₁₋₆ alkyl, substituted or unsubstituted C₂₋₆ alkenyl, substituted or unsubstituted C₂₋₆ alkynyl and haloalkyl;

- 10 optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

- 15 In a further embodiment the compound according to the invention of general Formula (I) is a compound wherein

R₁ is selected from the group consisting of halogen, haloalkoxy, -OR₆ and -CN;

- 20 optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

In a further embodiment the compound according to the invention of general Formula (I) is a compound wherein

R₁ is selected from the group consisting of cycloalkyl, aryl and heterocyclyl;

- 25 optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

In a further embodiment the compound according to the invention of general Formula (I) is a compound wherein

R₁ is -NR₆R₆';

optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

In a further embodiment the compound according to the invention of general Formula (I) is a compound wherein

R₂ is selected from the group consisting of substituted or unsubstituted C₁₋₆ alkyl, substituted or unsubstituted C₂₋₆ alkenyl, substituted or unsubstituted C₂₋₆ alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted alkylcycloalkyl, halogen, haloalkyl, haloalkoxy and -OR₇;

optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

In a further embodiment the compound according to the invention of general Formula (I) is a compound wherein

R₂ is selected from the group consisting of substituted or unsubstituted C₁₋₆ alkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted alkylcycloalkyl, halogen, haloalkyl, haloalkoxy and -OR₇;

optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

In a further embodiment the compound according to the invention of general Formula (I) is a compound wherein

R₂ is selected from the group consisting of substituted or unsubstituted C₁₋₆ alkyl, substituted or unsubstituted cycloalkyl, halogen and -OR₇;

optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

- 5 In a further embodiment the compound according to the invention of general Formula (I) is a compound wherein

R₂ is selected from the group consisting of hydrogen, substituted or unsubstituted C₁₋₆ alkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted alkylcycloalkyl, halogen, haloalkyl, haloalkoxy and -OR₇;

- 10 optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

- 15 In a further embodiment the compound according to the invention of general Formula (I) is a compound wherein

R₂ is selected from the group consisting of substituted or unsubstituted C₁₋₆ alkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted alkylcycloalkyl, halogen, haloalkyl, haloalkoxy and -OR₇;

- 20 optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof. In a further embodiment the compound according to the invention of general Formula (I) is a compound wherein

- 25 R₂ is selected from the group consisting of hydrogen, substituted or unsubstituted C₁₋₆ alkyl, substituted or unsubstituted cycloalkyl, halogen and -OR₇;

optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

In a further embodiment the compound according to the invention of general Formula (I) is a compound wherein

R₃ is selected from the group consisting of hydrogen, substituted or unsubstituted C₁₋₆ alkyl, halogen, haloalkyl, haloalkoxy and –OR₈;

- 5 optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

10 In a further embodiment the compound according to the invention of general Formula (I) is a compound wherein

R₃ is selected from the group consisting of hydrogen and substituted or unsubstituted C₁₋₆ alkyl;

- 15 optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

In a further embodiment the compound according to the invention of general Formula (I) is a compound wherein

- 20 R₄ is selected from the group consisting of substituted or unsubstituted C₁₋₆ alkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl and substituted or unsubstituted heterocyclyl;

- 25 optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

In a further embodiment the compound according to the invention of general Formula (I) is a compound wherein

R₄ is selected from the group consisting of substituted or unsubstituted C₁₋₆ alkyl, substituted or unsubstituted aryl and substituted or unsubstituted heterocyclyl;

optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

- 5 In a further embodiment the compound according to the invention of general Formula (I) is a compound wherein

R₄ is selected from the group consisting of substituted or unsubstituted C₁₋₆ alkyl, substituted or unsubstituted C₂₋₆ alkenyl and substituted or unsubstituted C₂₋₆ alkynyl;

- 10 optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

In a further embodiment the compound according to the invention of general Formula (I) is a compound wherein

- 15 R₄ is substituted or unsubstituted C₁₋₆ alkyl;

optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

20

In a further embodiment the compound according to the invention of general Formula (I) is a compound wherein

R₄ is selected from the group consisting of substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl and substituted or unsubstituted heterocyclyl;

- 25 optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

In a further embodiment the compound according to the invention of general Formula (I) is a compound wherein

R₄ is selected from the group consisting of substituted or unsubstituted aryl and substituted or unsubstituted heterocyclyl;

- 5 optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

- 10 In a further embodiment the compound according to the invention of general Formula (I) is a compound wherein

R₅ and R₅' are independently selected from the group consisting of hydrogen, substituted or unsubstituted C₁₋₆ alkyl, haloalkyl and haloalkoxy;

- 15 optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

In a further embodiment the compound according to the invention of general Formula (I) is a compound wherein

- 20 R₅ and R₅' are independently selected from the group consisting of hydrogen and substituted or unsubstituted C₁₋₆ alkyl;

- optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding
25 salt thereof, or a corresponding solvate thereof.

In a further embodiment the compound according to the invention of general Formula (I) is a compound wherein

R₆ is selected from the group consisting of hydrogen, substituted or unsubstituted C₁₋₆ alkyl, haloalkyl, haloalkoxy; substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted alkylcycloalkyl, substituted or unsubstituted alkylaryl and substituted or unsubstituted alkylheterocyclyl;

optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

10 In a further embodiment the compound according to the invention of general Formula (I) is a compound wherein

R₆ is selected from the group consisting of hydrogen, substituted or unsubstituted C₁₋₆ alkyl, haloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted alkylcycloalkyl, substituted or unsubstituted alkylaryl and substituted or unsubstituted alkylheterocyclyl;

optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

20 In a further embodiment the compound according to the invention of general Formula (I) is a compound wherein

R₆ and R₆' , taken together with the nitrogen atom to which they are attached, form a substituted or unsubstituted heterocyclyl;

optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

In a further embodiment the compound according to the invention of general Formula (I) is a compound wherein

R₆' is selected from the group consisting of hydrogen and substituted or unsubstituted C₁₋₆ alkyl;

optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

In a further embodiment the compound according to the invention of general Formula (I) is a compound wherein

R₇ is selected from the group consisting of hydrogen and substituted or unsubstituted C₁₋₆ alkyl;

optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

In a further embodiment the compound according to the invention of general Formula (I) is a compound wherein

R₈ is selected from the group consisting of hydrogen and substituted or unsubstituted C₁₋₆ alkyl;

optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

In a further embodiment the compound according to the invention of general Formula (I) is a compound wherein

R₁₁, R₁₁' and R₁₁'' are independently selected from hydrogen, substituted or unsubstituted C₁₋₆ alkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted alkylcycloalkyl, substituted or unsubstituted alkylaryl and substituted or unsubstituted alkylheterocyclyl;

optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

- 5 In a further embodiment the compound according to the invention of general Formula (I) is a compound wherein

R_{11} , R_{11}' and R_{11}'' are independently selected from hydrogen, substituted or unsubstituted C_{1-6} alkyl, substituted or unsubstituted aryl, substituted or unsubstituted heterocyclyl and substituted or unsubstituted alkylcycloalkyl;

- 10 optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

- 15 In a further embodiment the compound according to the invention of general Formula (I) is a compound wherein

R_{11} , R_{11}' and R_{11}'' are independently selected from hydrogen, substituted or unsubstituted C_{1-6} alkyl, substituted or unsubstituted heterocyclyl and substituted or unsubstituted alkylcycloalkyl;

- 20 optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

In a further embodiment the compound according to the invention of general Formula (I) is a compound wherein

- 25 R_{13} and R_{13}' are independently selected from hydrogen and unsubstituted C_{1-6} alkyl;

optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

In a further embodiment the compound according to the invention of general Formula (I) is a compound wherein

R_{14} , R_{14}' and R_{14}'' are independently selected from hydrogen, unsubstituted C_{1-6} alkyl, unsubstituted aryl, unsubstituted cycloalkyl and unsubstituted heterocyclyl;

- 5 optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

- 10 In a further embodiment the compound according to the invention of general Formula (I) is a compound wherein

R_{14} , R_{14}' and R_{14}'' are independently selected from hydrogen and unsubstituted C_{1-6} alkyl;

- 15 optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

In a further embodiment the compound according to the invention of general Formula (I) is a compound wherein

- 20 R_{21} and R_{21}' are independently selected from hydrogen and substituted or unsubstituted C_{1-6} alkyl;

optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

- 25 In a further embodiment the compound according to the invention of general Formula (I) is a compound wherein

R_{31} and R_{31}' are independently selected from hydrogen and substituted or unsubstituted C_{1-6} alkyl;

optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

- 5 In a further embodiment the compound according to the invention of general Formula (I) is a compound wherein

R_{41} , R_{41}' and R_{41}'' are independently selected from hydrogen and substituted or unsubstituted C_{1-6} alkyl;

- 10 optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

In a further embodiment the compound according to the invention of general Formula (I) is a compound wherein

- 15 R_{51} and R_{51}' are independently selected from hydrogen, substituted or unsubstituted C_{1-6} alkyl;

- 20 optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

In a further embodiment the compound according to the invention of general Formula (I) is a compound wherein

R_{51} and R_{51}' are both hydrogen;

- 25 optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

In a further embodiment the compound according to the invention of general Formula (I) is a compound wherein

the alkyl, alkenyl or alkynyl in R_1 , if substituted, is substituted with one or more substituent/s selected from $-OR_{11}$, halogen, $-CN$, haloalkyl, haloalkoxy and $-NR_{11}R_{11}'$;

- 5 optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

In a further embodiment the compound according to the invention of general Formula (I) is a compound wherein

- 10 the cycloalkyl, aryl or heterocyclyl in R_1 , if substituted, is substituted with one or more substituent/s selected from halogen, $-R_{11}$, $-[CH_2]_rOR_{11}$, $=O$, $-NO_2$, $-[CH_2]_rNR_{11}R_{11}'$, $-NR_{11}C(O)R_{11}'$, $-NR_{11}S(O)_2R_{11}'$, $-S(O)_2NR_{11}R_{11}'$, $-NR_{11}C(O)NR_{11}'R_{11}''$, $-SR_{11}$, $-S(O)R_{11}$, $-S(O)_2R_{11}$, $-CN$, haloalkyl, haloalkoxy, $-C(O)R_{11}$, $-C(O)OR_{11}$, $-C(O)NR_{11}R_{11}'$, $-OCH_2CH_2OR_{11}$, $-NR_{11}S(O)_2NR_{11}'R_{11}''$ and $-C(CH_3)_2OR_{11}$;
- 15 optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

- 20 In a further embodiment the compound according to the invention of general Formula (I) is a compound wherein

the cycloalkyl, aryl or heterocyclyl in R_1 , if substituted, is substituted with one or more substituent/s selected from halogen, $-R_{11}$, $-[CH_2]_rOR_{11}$, $=O$, $-[CH_2]_rNR_{11}R_{11}'$, $-S(O)_2R_{11}$, $-CN$, haloalkyl, $-C(O)R_{11}$ and $-C(O)NR_{11}R_{11}'$;

- 25 optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

In a further embodiment the compound according to the invention of general Formula (I) is a compound wherein

the alkyl, alkenyl or alkynyl in R_2 , if substituted, is substituted with one or more substituent/s selected from $-OR_{21}$, halogen, $-CN$, haloalkyl, haloalkoxy and $-NR_{21}R_{21}'$;

optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

In a further embodiment the compound according to the invention of general Formula (I) is a compound wherein

the cycloalkyl in R_2 , also in alkylcycloalkyl, if substituted, is substituted with one or more substituent/s selected from halogen, $-R_{21}$, $-[CH_2]_rOR_{21}$, $=O$, $-NO_2$, $-[CH_2]_rNR_{21}R_{21}'$, $-NR_{21}C(O)R_{21}'$, $-NR_{21}S(O)_2R_{21}'$, $-S(O)_2NR_{21}R_{21}'$, $-NR_{21}C(O)NR_{21}'R_{21}''$, $-SR_{21}$, $-S(O)R_{21}$, $-S(O)_2R_{21}$, $-CN$, haloalkyl, haloalkoxy, $-C(O)R_{21}$, $-C(O)OR_{21}$, $-C(O)NR_{21}R_{21}'$, $-OCH_2CH_2OR_{21}$, $-NR_{21}S(O)_2NR_{21}'R_{21}''$ and $-C(CH_3)_2OR_{21}$;

optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

In a further embodiment the compound according to the invention of general Formula (I) is a compound wherein

the alkyl, alkenyl or alkynyl in R_3 , if substituted, is substituted with one or more substituent/s selected from $-OR_{31}$, halogen, $-CN$, haloalkyl, haloalkoxy and $-NR_{31}R_{31}'$;

optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

In a further embodiment the compound according to the invention of general Formula (I) is a compound wherein

the alkyl, alkenyl or alkynyl in R_4 , if substituted, is substituted with one or more substituent/s selected from $-OR_{41}$, halogen, $-CN$, haloalkyl, haloalkoxy, $-NR_{41}R_{41}'$;

optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

- 5 In a further embodiment the compound according to the invention of general Formula (I) is a compound wherein

the cycloalkyl, aryl or heterocyclyl in R_4 , if substituted, is substituted with one or more substituent/s selected from halogen, $-R_{41}$, $-[CH_2]_rOR_{41}$, $=O$, $-NO_2$, $-[CH_2]_rNR_{41}R_{41}'$, $-NR_{41}C(O)R_{41}'$, $-NR_{41}S(O)_2R_{41}'$, $-S(O)_2NR_{41}R_{41}'$, $-NR_{41}C(O)NR_{41}'R_{41}''$, $-SR_{41}$, $-S(O)R_{41}$,
 10 $-S(O)_2R_{41}$, $-CN$, haloalkyl, haloalkoxy, $-C(O)R_{41}$, $-C(O)OR_{41}$, $-C(O)NR_{41}R_{41}'$, $-OCH_2CH_2OR_{41}$, $-NR_{41}S(O)_2NR_{41}'R_{41}''$ and $-C(CH_3)_2OR_{41}$;

optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding
 15 salt thereof, or a corresponding solvate thereof.

In a further embodiment the compound according to the invention of general Formula (I) is a compound wherein

the cycloalkyl, aryl or heterocyclyl in R_4 , if substituted, is substituted with one or more substituent/s selected from halogen, $-R_{41}$, $-[CH_2]_rOR_{41}$, $-CN$ and haloalkyl;

- 20 optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

- 25 In a further embodiment the compound according to the invention of general Formula (I) is a compound wherein

the alkyl, alkenyl or alkynyl in R_5 and R_5' , if substituted, is substituted with one or more substituent/s selected from $-OR_{51}$, halogen, $-CN$, haloalkyl, haloalkoxy, $-NR_{51}R_{51}'$;

optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers,

preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

In a further embodiment the compound according to the invention of general Formula (I) is a compound wherein

- 5 the alkyl, alkenyl or alkynyl in R_5 and R_5' , if substituted, is substituted with one or more $-OR_{51}$;

optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

In a further embodiment the compound according to the invention of general Formula (I) is a compound wherein

- 15 the alkyl, alkenyl or alkynyl, if substituted, and not defined otherwise, is substituted with one or more substituent/s selected from $-OR_{13}$, halogen, $-CN$, haloalkyl, haloalkoxy and $-NR_{13}R_{13}'$;

optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

- 20 In a further embodiment the compound according to the invention of general Formula (I) is a compound wherein

25 the aryl, heterocyclyl or cycloalkyl, also in alkylcycloalkyl, alkylaryl and alkylheterocyclyl, if substituted, and not defined otherwise, is substituted with one or more substituent/s selected from halogen, $-R_{14}$, $-[CH_2]_rOR_{14}$, $=O$, $-NO_2$, $-[CH_2]_rNR_{14}R_{14}'$, $-NR_{14}C(O)R_{14}'$, $-NR_{14}S(O)_2R_{14}'$, $-S(O)_2NR_{14}R_{14}'$, $-NR_{14}C(O)NR_{14}'R_{14}''$, $-SR_{14}$, $-S(O)R_{14}$, $S(O)_2R_{14}$, $-CN$, haloalkyl, haloalkoxy, $-C(O)R_{14}$, $-C(O)OR_{14}$, $-C(O)NR_{14}R_{14}'$, $-OCH_2CH_2OR_{14}$, $-NR_{14}S(O)_2NR_{14}'R_{14}''$ and $-C(CH_3)_2OR_{14}$;

optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers,

preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

In a further embodiment the compound according to the invention of general Formula (I) is a compound wherein

- 5 the aryl, heterocyclyl or cycloalkyl, also in alkylcycloalkyl, alkylaryl and alkylheterocyclyl, if substituted, and not defined otherwise, is substituted with one or more substituent/s selected from $-R_{14}$ and $-[CH_2]_tNR_{14}R_{14}'$;

- optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers,
 10 preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

In another preferred embodiment of the invention according to general Formula (I) the compound is a compound, wherein

m is 1, 2, 3 or 4;

- 15 and/or

n is 1 or 2;

and/or

t is 0 or 1;

and/or

- 20 r is 0, 1, 2 or 3;

and/or

X is selected from the group consisting of a bond, $-[CH_2]_p-$, $-[CH_2]_pNR_x[CH_2]_q-$, $-[CH_2]_pO[CH_2]_q-$, $-[CH_2]_pNR_xC(O)[CH_2]_q-$ and $-[CH_2]_pNR_xCH(CH_3)-$;

and/or

- 25 p is 0, 1, 2, 3 or 4;

and/or

q is 0, 1, 2, 3 or 4;

and/or

5 R_x is selected from the group consisting of hydrogen, substituted or unsubstituted C_{1-6} alkyl, substituted or unsubstituted C_{2-6} alkenyl and substituted or unsubstituted C_{2-6} alkynyl;

and/or

10 R_1 is selected from the group consisting of hydrogen, substituted or unsubstituted C_{1-6} alkyl, substituted or unsubstituted C_{2-6} alkenyl, substituted or unsubstituted C_{2-6} alkynyl, halogen, haloalkyl, haloalkoxy, $-OR_6$, $-NR_6R_6'$, $-CN$, cycloalkyl, aryl and heterocyclyl;

and/or

15 R_2 is selected from the group consisting of hydrogen, substituted or unsubstituted C_{1-6} alkyl, substituted or unsubstituted C_{2-6} alkenyl, substituted or unsubstituted C_{2-6} alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted alkylcycloalkyl, halogen, haloalkyl, haloalkoxy and $-OR_7$;

and/or

R_3 is selected from the group consisting of hydrogen, substituted or unsubstituted C_{1-6} alkyl, substituted or unsubstituted C_{2-6} alkenyl, substituted or unsubstituted C_{2-6} alkynyl, halogen, haloalkyl, haloalkoxy and $-OR_8$;

20 and/or

R_4 is selected from the group consisting of substituted or unsubstituted C_{1-6} alkyl, substituted or unsubstituted C_{2-6} alkenyl, substituted or unsubstituted C_{2-6} alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl and substituted or unsubstituted heterocyclyl;

25 and/or

R₅ and R₅' are independently selected from the group consisting of hydrogen, substituted or unsubstituted C₁₋₆ alkyl, substituted or unsubstituted C₂₋₆ alkenyl, substituted or unsubstituted C₂₋₆ alkynyl, haloalkyl and haloalkoxy;

and/or

- 5 R₆ is selected from the group consisting of hydrogen, substituted or unsubstituted C₁₋₆ alkyl, substituted or unsubstituted C₂₋₆ alkenyl, substituted or unsubstituted C₂₋₆ alkynyl, haloalkyl, haloalkoxy; substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted alkylcycloalkyl, substituted or unsubstituted alkylaryl and substituted or
10 unsubstituted alkylheterocyclyl;

and/or

R₆' is selected from the group consisting of hydrogen, substituted or unsubstituted C₁₋₆ alkyl, substituted or unsubstituted C₂₋₆ alkenyl and substituted or unsubstituted C₂₋₆ alkynyl;

- 15 and/or

R₆ and R₆' , taken together with the nitrogen atom to which they are attached, form a substituted or unsubstituted heterocyclyl;

and/or

- 20 R₇ is selected from the group consisting of hydrogen, substituted or unsubstituted C₁₋₆ alkyl, substituted or unsubstituted C₂₋₆ alkenyl and substituted or unsubstituted C₂₋₆ alkynyl;

and/or

- 25 R₈ is selected from the group consisting of hydrogen, substituted or unsubstituted C₁₋₆ alkyl, substituted or unsubstituted C₂₋₆ alkenyl and substituted or unsubstituted C₂₋₆ alkynyl;

and/or

R₁₁, R₁₁' and R₁₁'' are independently selected from hydrogen, substituted or unsubstituted C₁₋₆ alkyl, substituted or unsubstituted C₂₋₆ alkenyl, substituted or

unsubstituted C₂₋₆ alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted alkylcycloalkyl, substituted or unsubstituted alkylaryl and substituted or unsubstituted alkylheterocyclyl;

5 and/or

R₁₃ and R₁₃' are independently selected from hydrogen, unsubstituted C₁₋₆ alkyl, unsubstituted C₂₋₆ alkenyl and unsubstituted C₂₋₆ alkynyl;

and/or

10 R₁₄, R₁₄' and R₁₄'' are independently selected from hydrogen, unsubstituted C₁₋₆ alkyl, unsubstituted C₂₋₆ alkenyl, unsubstituted C₂₋₆ alkynyl, unsubstituted aryl, unsubstituted cycloalkyl and unsubstituted heterocyclyl;

and/or

15 R₂₁ and R₂₁' are independently selected from hydrogen, substituted or unsubstituted C₁₋₆ alkyl, substituted or unsubstituted C₂₋₆ alkenyl and substituted or unsubstituted C₂₋₆ alkynyl;

and/or

R₃₁ and R₃₁' are independently selected from hydrogen, substituted or unsubstituted C₁₋₆ alkyl, substituted or unsubstituted C₂₋₆ alkenyl and substituted or unsubstituted C₂₋₆ alkynyl;

20 and/or

R₄₁, R₄₁' and R₄₁'' are independently selected from hydrogen, substituted or unsubstituted C₁₋₆ alkyl, substituted or unsubstituted C₂₋₆ alkenyl and substituted or unsubstituted C₂₋₆ alkynyl;

and/or

25 R₅₁ and R₅₁' are independently selected from hydrogen, substituted or unsubstituted C₁₋₆ alkyl, substituted or unsubstituted C₂₋₆ alkenyl and substituted or unsubstituted C₂₋₆ alkynyl;

optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

- 5 In another preferred embodiment of the invention according to general Formula (I) the compound is a compound, wherein
- m is 1, 2, or 3;
- and/or
- n is 1;
- 10 and/or
- t is 0 or 1;
- and/or
- r is 0 or 1;
- and/or
- 15 X is selected from the group consisting of a bond, $-\text{[CH}_2\text{]}_p-$, $-\text{[CH}_2\text{]}_p\text{NR}_x\text{[CH}_2\text{]}_q-$, $-\text{[CH}_2\text{]}_p\text{O[CH}_2\text{]}_q-$, $-\text{[CH}_2\text{]}_p\text{NR}_x\text{C(O)[CH}_2\text{]}_q-$ and $-\text{[CH}_2\text{]}_p\text{NR}_x\text{CH(CH}_3\text{)}-$;
- and/or
- p is 0, 1, 2 or 3;
- and/or
- 20 q is 0, 1, 2, 3 or 4;
- and/or
- R_x is selected from the group consisting of hydrogen and substituted or unsubstituted C_{1-6} alkyl;
- and/or

R₁ is selected from the group consisting of hydrogen, substituted or unsubstituted C₁₋₆ alkyl, halogen, haloalkyl, -OR₆, -NR₆R₆', -CN, cycloalkyl, aryl and heterocyclyl;

and/or

5 R₂ is selected from the group consisting of hydrogen, substituted or unsubstituted C₁₋₆ alkyl, substituted or unsubstituted cycloalkyl, halogen and -OR₇;

and/or

R₃ is selected from the group consisting of hydrogen and substituted or unsubstituted C₁₋₆ alkyl;

and/or

10 R₄ is selected from the group consisting of substituted or unsubstituted C₁₋₆ alkyl, substituted or unsubstituted aryl and substituted or unsubstituted heterocyclyl;

and/or

R₅ and R₅' are independently selected from the group consisting of hydrogen and substituted or unsubstituted C₁₋₆ alkyl;

15 and/or

R₆ is selected from the group consisting of hydrogen, substituted or unsubstituted C₁₋₆ alkyl, haloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted alkylcycloalkyl, substituted or unsubstituted alkylaryl and substituted or unsubstituted alkylheterocyclyl;

20 and/or

R₆' is selected from the group consisting of hydrogen and substituted or unsubstituted C₁₋₆ alkyl;

and/or

25 R₆ and R₆' , taken together with the nitrogen atom to which they are attached, form a substituted or unsubstituted heterocyclyl;

and/or

R₇ is selected from the group consisting of hydrogen and substituted or unsubstituted C₁₋₆ alkyl;

and/or

5 R₁₁, R₁₁' and R₁₁'' are independently selected from hydrogen, substituted or unsubstituted C₁₋₆ alkyl, substituted or unsubstituted aryl, substituted or unsubstituted heterocyclyl and substituted or unsubstituted alkylcycloalkyl;

and/or

R₁₃ and R₁₃' are independently selected from hydrogen and unsubstituted C₁₋₆ alkyl;

and/or

10 R₁₄, R₁₄' and R₁₄'' are independently selected from hydrogen and unsubstituted C₁₋₆ alkyl;

and/or

R₄₁, R₄₁' and R₄₁'' are independently selected from hydrogen and substituted or unsubstituted C₁₋₆ alkyl;

15 and/or

R₅₁ and R₅₁' are both hydrogen;

optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

20

In another preferred embodiment of the invention according to general Formula (I) the compound is a compound, wherein in R₁ as defined in any of the embodiments of the present invention,

25 The alkyl in haloalkyl or haloalkoxy is C₁₋₆ alkyl like methyl, ethyl, propyl, butyl, pentyl, hexyl, isopropyl, or 2-methylpropyl; more preferably the alkyl is methyl;

and/or

- the C₁₋₆ alkyl is preferably selected from methyl, ethyl, propyl, butyl, pentyl, hexyl, isopropyl, or 2-methylpropyl; more preferably the C₁₋₆ alkyl is methyl, ethyl, isopropyl;
- 5 and/or
- the C₂₋₆ -alkenyl is preferably selected from ethylene, propylene, butylene, pentylene, hexylene, isopropylene and isobutylene;
- 10 and/or
- the C₂₋₆ -alkynyl is preferably selected from ethyne, propyne, butyne, pentyne, hexyne, isopropyne and isobutyne;
- 15 and/or
- the cycloalkyl is C₃₋₈ cycloalkyl like cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, or cyclooctyl; preferably is C₃₋₇ cycloalkyl like cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, or cycloheptyl; more preferably from C₃₋₆ cycloalkyl like cyclopropyl, cyclobutyl, cyclopentyl or cyclohexyl; more preferably the cycloalkyl is cyclopropyl;
- 20 and/or
- the aryl is selected from phenyl, naphthyl, or anthracene; preferably is naphthyl and phenyl; more preferably the aryl is phenyl;
- 25 and/or
- 30 the heterocyclyl is a heterocyclic ring system of one or more saturated or unsaturated rings of which at least one ring contains one or more heteroatoms selected from the group consisting of nitrogen, oxygen and/or sulfur in the ring; preferably is a heterocyclic ring system of one or two saturated or unsaturated rings of which at least one ring contains one or more heteroatoms selected from the group consisting of

nitrogen, oxygen and/or sulfur in the ring, more preferably is selected from oxazepan, pyrrolidine, imidazole, oxadiazole, tetrazole, azetidine, pyridine, pyrimidine, piperidine, piperazine, furan, benzofuran, benzimidazole, indazole, benzothiazole, benzodiazole, thiazole, isothiazole, tetrahydropyran, tetrahydrofuran, morpholine, thiomorpholine, indoline, triazole, isoxazole, pyrazole, thiophene, benzothiophene, pyrrole, pyrazine, pyrrolo[2,3b]pyridine, quinoline, quinolone, isoquinoline, tetrahydroisoquinoline, tetrahydrothienopyridine, phthalazine, benzo-1,2,5-thiadiazole, indole, benzotriazole, benzoxazole oxopyrrolidine, benzodioxolane, benzodioxane, carbazole, octahydro-ethanopyrrolo-pyridine, oxaspirodecane, oxadiazaspirodecane, indoline-2-one and quinazoline; preferably the heterocycl is pyridine, piperidine, pyrrolidine, piperazine, pyrazole, pyrimidine, isoxazole, isothiazole, imidazole, morpholine, thiomorpholine, tetrahydropyran, tetrahydrofuran and thiophene;

optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

In another preferred embodiment of the invention according to general Formula (I) the compound is a compound, wherein in R_2 as defined in any of the embodiments of the present invention,

The alkyl in alkylcycloalkyl, haloalkyl or haloalkoxy is C_{1-6} alkyl like methyl, ethyl, propyl, butyl, pentyl, hexyl, isopropyl, or 2-methylpropyl;

and/or

the C_{1-6} alkyl is preferably selected from methyl, ethyl, propyl, butyl, pentyl, hexyl, isopropyl, or 2-methylpropyl; more preferably the C_{1-6} alkyl is methyl or ethyl;

and/or

the C_{2-6} -alkenyl is preferably selected from ethylene, propylene, butylene, pentylene, hexylene, isopropylene and isobutylene;

and/or

the C₂₋₆ -alkynyl is preferably selected from ethyne, propyne, butyne, pentyne, hexyne, isopropyne and isobutyne;

5 and/or

the cycloalkyl is C₃₋₈ cycloalkyl like cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, or cyclooctyl; preferably is C₃₋₇ cycloalkyl like cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, or cycloheptyl; more preferably from C₃₋₆ cycloalkyl like cyclopropyl, cyclobutyl, cyclopentyl or cyclohexyl; more preferably the cycloalkyl is cyclopropyl;

optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

In another preferred embodiment of the invention according to general Formula (I) the compound is a compound, wherein in R₃ as defined in any of the embodiments of the present invention,

20 The alkyl in haloalkyl or haloalkoxy is C₁₋₆ alkyl like methyl, ethyl, propyl, butyl, pentyl, hexyl, isopropyl, or 2-methylpropyl;

and/or

25 the C₁₋₆ alkyl is preferably selected from methyl, ethyl, propyl, butyl, pentyl, hexyl, isopropyl, or 2-methylpropyl; more preferably the C₁₋₆ alkyl is methyl;

and/or

the C₂₋₆ -alkenyl is preferably selected from ethylene, propylene, butylene, pentylene, hexylene, isopropylene and isobutylene;

30

and/or

the C₂₋₆ -alkynyl is preferably selected from ethyne, propyne, butyne, pentyne, hexyne, isopropyne and isobutyne;

optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers,
5 preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

In another preferred embodiment of the invention according to general Formula (I) the compound is a compound, wherein in R₄ as defined in any of the embodiments of the
10 present invention,

the C₁₋₆ alkyl is preferably selected from methyl, ethyl, propyl, butyl, pentyl, hexyl, isopropyl, or 2-methylpropyl; more preferably the C₁₋₆ alkyl is methyl, ethyl, isopropyl or isobutyl;

and/or

15

the C₂₋₆ -alkenyl is preferably selected from ethylene, propylene, butylene, pentylene, hexylene, isopropylene and isobutylene;

and/or

20

the C₂₋₆ -alkynyl is preferably selected from ethyne, propyne, butyne, pentyne, hexyne, isopropyne and isobutyne;

and/or

25

the cycloalkyl is C₃₋₈ cycloalkyl like cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, or cyclooctyl; preferably is C₃₋₇ cycloalkyl like cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, or cycloheptyl; more preferably from C₃₋₆ cycloalkyl like cyclopropyl, cyclobutyl, cyclopentyl or cyclohexyl;

30

and/or

the aryl is selected from phenyl, naphthyl, or anthracene; preferably is naphthyl and phenyl; more preferably the aryl is phenyl;

and/or

5

the heterocyclyl is a heterocyclic ring system of one or more saturated or unsaturated rings of which at least one ring contains one or more heteroatoms selected from the group consisting of nitrogen, oxygen and/or sulfur in the ring; preferably is a heterocyclic ring system of one or two saturated or unsaturated
 10 rings of which at least one ring contains one or more heteroatoms selected from the group consisting of nitrogen, oxygen and/or sulfur in the ring, more preferably is selected from oxazepan, pyrrolidine, imidazole, oxadiazole, tetrazole, azetidine, pyridine, pyrimidine, piperidine, piperazine, furan, benzofuran, benzimidazole, indazole, benzothiazole, benzodiazole, thiazole,
 15 isothiazole, tetrahydropyran, tetrahydrofuran, morpholine, thiomorpholine, indoline, triazole, isoxazole, pyrazole, thiophene, benzothiophene, pyrrole, pyrazine, pyrrolo[2,3b]pyridine, quinoline, quinolone, isoquinoline, tetrahydroisoquinoline, tetrahydrothienopyridine, phthalazine, benzo-1,2,5-thiadiazole, indole, benzotriazole, benzoxazole oxopyrrolidine, benzodioxolane,
 20 benzodioxane, carbazole, octahydro-ethanopyrrolo-pyridine, oxaspirodecane, oxadiazaspirodecane, indoline-2-one and quinazoline; preferably the heterocyclyl is tetrahydropyran or pyridine;

optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers,
 25 preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

In another preferred embodiment of the invention according to general Formula (I) the compound is a compound, wherein in R_5 and R_5' as defined in any of the embodiments of the present invention,

30 the alkyl in haloalkyl or haloalkoxy is C_{1-6} alkyl like methyl, ethyl, propyl, butyl, pentyl, hexyl, isopropyl, or 2-methylpropyl;

and/or

the C₁₋₆ alkyl is preferably selected from methyl, ethyl, propyl, butyl, pentyl, hexyl, isopropyl, or 2-methylpropyl; more preferably the C₁₋₆ alkyl is methyl;

and/or

5

the C₂₋₆ -alkenyl is preferably selected from ethylene, propylene, butylene, pentylene, hexylene, isopropylene and isobutylene;

and/or

10

the C₂₋₆ -alkynyl is preferably selected from ethyne, propyne, butyne, pentyne, hexyne, isopropyne and isobutyne;

optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

15

In another preferred embodiment of the invention according to general Formula (I) the compound is a compound, wherein in R₆ and R₆' as defined in any of the embodiments of the present invention,

20

the alkyl in alkylaryl, alkylheterocyclyl, alkylcycloalkyl, haloalkyl or haloalkoxy is C₁₋₆ alkyl like methyl, ethyl, propyl, butyl, pentyl, hexyl, isopropyl, or 2-methylpropyl; more preferably the alkyl is methyl;

and/or

25

the C₁₋₆ alkyl is preferably selected from methyl, ethyl, propyl, butyl, pentyl, hexyl, isopropyl, or 2-methylpropyl; more preferably the C₁₋₆ alkyl is methyl, ethyl or isopropyl;

and/or

30

the C₂₋₆ -alkenyl is preferably selected from ethylene, propylene, butylene, pentylene, hexylene, isopropylene and isobutylene;

and/or

the C₂₋₆-alkynyl is preferably selected from ethyne, propyne, butyne, pentyne, hexyne, isopropyne and isobutyne;

5

and/or

the cycloalkyl is C₃₋₈ cycloalkyl like cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, or cyclooctyl; preferably is C₃₋₇ cycloalkyl like cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, or cycloheptyl; more preferably from C₃₋₆ cycloalkyl like cyclopropyl, cyclobutyl, cyclopentyl or cyclohexyl; more preferably the cycloalkyl is cyclopropyl;

10

and/or

15

the aryl is selected from phenyl, naphthyl, or anthracene; preferably is naphthyl and phenyl; more preferably the aryl is phenyl;

and/or

20

the heterocyclyl is a heterocyclic ring system of one or more saturated or unsaturated rings of which at least one ring contains one or more heteroatoms selected from the group consisting of nitrogen, oxygen and/or sulfur in the ring; preferably is a heterocyclic ring system of one or two saturated or unsaturated rings of which at least one ring contains one or more heteroatoms selected from the group consisting of nitrogen, oxygen and/or sulfur in the ring, more preferably is selected from oxazepan, pyrrolidine, imidazole, oxadiazole, tetrazole, azetidine, pyridine, pyrimidine, piperidine, piperazine, furan, benzofuran, benzimidazole, indazole, benzothiazole, benzodiazole, thiazole, isothiazole, tetrahydropyran, tetrahydrofuran, morpholine, thiomorpholine, indoline, triazole, isoxazole, pyrazole, thiophene, benzothiophene, pyrrole, pyrazine, pyrrolo[2,3b]pyridine, quinoline, quinolone, isoquinoline, tetrahydroisoquinoline, tetrahydrothienopyridine, phthalazine, benzo-1,2,5-thiadiazole, indole, benzotriazole, benzoxazole oxopyrrolidine, benzodioxolane, benzodioxane, carbazole, octahydro-ethanopyrrolo-pyridine, oxaspirodecane,

25

30

35

oxadiazaspirooundecane, indoline-2-one and quinazoline; preferably the heterocyclyl is piperidine, tetrahydropyran, morpholine, thiomorpholine, pyrrolidine or piperazine;

5 optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

10 In another preferred embodiment of the invention according to general Formula (I) the compound is a compound, wherein in R_7 as defined in any of the embodiments of the present invention,

the C_{1-6} alkyl is preferably selected from methyl, ethyl, propyl, butyl, pentyl, hexyl, isopropyl, or 2-methylpropyl; more preferably the C_{1-6} alkyl is methyl;

and/or

15 the C_{2-6} -alkenyl is preferably selected from ethylene, propylene, butylene, pentylene, hexylene, isopropylene and isobutylene;

and/or

20 the C_{2-6} -alkynyl is preferably selected from ethyne, propyne, butyne, pentyne, hexyne, isopropyne and isobutyne;

optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

25

In another preferred embodiment of the invention according to general Formula (I) the compound is a compound, wherein in R_8 as defined in any of the embodiments of the present invention,

30 the C_{1-6} alkyl is preferably selected from methyl, ethyl, propyl, butyl, pentyl, hexyl, isopropyl, or 2-methylpropyl; more preferably the C_{1-6} alkyl is methyl;

and/or

the C₂₋₆ -alkenyl is preferably selected from ethylene, propylene, butylene, pentylene, hexylene, isopropylene and isobutylene;

5 and/or

the C₂₋₆ -alkynyl is preferably selected from ethyne, propyne, butyne, pentyne, hexyne, isopropyne and isobutyne;

optionally in form of one of the stereoisomers, preferably enantiomers or
10 diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

In another preferred embodiment of the invention according to general Formula (I) the compound is a compound, wherein in R₁₁, R₁₁' and R₁₁'' as defined in any of the
15 embodiments of the present invention,

the alkyl in alkylaryl, alkylheterocyclyl, alkylcycloalkyl, haloalkyl or haloalkoxy is C₁₋₆ alkyl like methyl, ethyl, propyl, butyl, pentyl, hexyl, isopropyl, or 2-methylpropyl; more preferably the alkyl is methyl;

20 and/or

the C₁₋₆ alkyl is preferably selected from methyl, ethyl, propyl, butyl, pentyl, hexyl, isopropyl, or 2-methylpropyl; more preferably the C₁₋₆ alkyl is methyl or ethyl;

25 and/or

the C₂₋₆ -alkenyl is preferably selected from ethylene, propylene, butylene, pentylene, hexylene, isopropylene and isobutylene;

30 and/or

the C₂₋₆ -alkynyl is preferably selected from ethyne, propyne, butyne, pentyne, hexyne, isopropyne and isobutyne;

and/or

5 the cycloalkyl is C₃₋₈ cycloalkyl like cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, or cyclooctyl; preferably is C₃₋₇ cycloalkyl like cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, or cycloheptyl; more preferably from C₃₋₆ cycloalkyl like cyclopropyl, cyclobutyl, cyclopentyl or cyclohexyl; more preferably the cycloalkyl is cyclopropyl;

10 and/or

the aryl is selected from phenyl, naphthyl, or anthracene; preferably is naphthyl and phenyl; more preferably the aryl is phenyl;

15 and/or

20 the heterocyclyl is a heterocyclic ring system of one or more saturated or unsaturated rings of which at least one ring contains one or more heteroatoms selected from the group consisting of nitrogen, oxygen and/or sulfur in the ring; preferably is a heterocyclic ring system of one or two saturated or unsaturated rings of which at least one ring contains one or more heteroatoms selected from the group consisting of nitrogen, oxygen and/or sulfur in the ring, more preferably is selected from oxazepan, pyrrolidine, imidazole, oxadiazole, tetrazole, azetidine, pyridine, pyrimidine, piperidine, piperazine, furan, 25 benzofuran, benzimidazole, indazole, benzothiazole, benzodiazole, thiazole, isothiazole, tetrahydropyran, tetrahydrofuran, morpholine, thiomorpholine, indoline, triazole, isoxazole, pyrazole, thiophene, benzothiophene, pyrrole, pyrazine, pyrrolo[2,3b]pyridine, quinoline, quinolone, isoquinoline, tetrahydroisoquinoline, tetrahydrothienopyridine, phthalazine, benzo-1,2,5- 30 thiadiazole, indole, benzotriazole, benzoxazole oxopyrrolidine, benzodioxolane, benzodioxane, carbazole, octahydro-ethanopyrrolo-pyridine, oxaspirodecane, oxadiazaspiroundecane, indoline-2-one and quinazoline; preferably the heterocyclyl is triazole, oxadiazole or pyridine;

optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

- 5 In another preferred embodiment of the invention according to general Formula (I) the compound is a compound, wherein in R_{13} and R_{13}' as defined in any of the embodiments of the present invention,

the C_{1-6} alkyl is preferably selected from methyl, ethyl, propyl, butyl, pentyl, hexyl, isopropyl, or 2-methylpropyl; more preferably the C_{1-6} alkyl is methyl;

- 10 and/or

the C_{2-6} -alkenyl is preferably selected from ethylene, propylene, butylene, pentylene, hexylene, isopropylene and isobutylene;

- 15 and/or

the C_{2-6} -alkynyl is preferably selected from ethyne, propyne, butyne, pentyne, hexyne, isopropyne and isobutyne;

- 20 optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

- 25 In another preferred embodiment of the invention according to general Formula (I) the compound is a compound, wherein in R_{14} , R_{14}' and R_{14}'' as defined in any of the embodiments of the present invention,

the C_{1-6} alkyl is preferably selected from methyl, ethyl, propyl, butyl, pentyl, hexyl, isopropyl, or 2-methylpropyl; more preferably the C_{1-6} alkyl is methyl;

and/or

- 30 the C_{2-6} -alkenyl is preferably selected from ethylene, propylene, butylene, pentylene, hexylene, isopropylene and isobutylene;

and/or

5 the C₂₋₆-alkynyl is preferably selected from ethyne, propyne, butyne, pentyne, hexyne, isopropyne and isobutyne;
and/or

10 the cycloalkyl is C₃₋₈ cycloalkyl like cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, or cyclooctyl; preferably is C₃₋₇ cycloalkyl like cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, or cycloheptyl; more preferably from C₃₋₆ cycloalkyl like cyclopropyl, cyclobutyl, cyclopentyl or cyclohexyl;

and/or

15 the aryl is selected from phenyl, naphthyl, or anthracene; preferably is naphthyl and phenyl;

and/or

20 the heterocyclyl is a heterocyclic ring system of one or more saturated or unsaturated rings of which at least one ring contains one or more heteroatoms selected from the group consisting of nitrogen, oxygen and/or sulfur in the ring; preferably is a heterocyclic ring system of one or two saturated or unsaturated rings of which at least one ring contains one or more heteroatoms selected from
25 the group consisting of nitrogen, oxygen and/or sulfur in the ring, more preferably is selected from oxazepan, pyrrolidine, imidazole, oxadiazole, tetrazole, azetidine, pyridine, pyrimidine, piperidine, piperazine, furan, benzofuran, benzimidazole, indazole, benzothiazole, benzodiazole, thiazole, isothiazole, tetrahydropyran, tetrahydrofuran, morpholine, thiomorpholine,
30 indoline, triazole, isoxazole, pyrazole, thiophene, benzothiophene, pyrrole, pyrazine, pyrrolo[2,3b]pyridine, quinoline, quinolone, isoquinoline, tetrahydroisoquinoline, tetrahydrothienopyridine, phthalazine, benzo-1,2,5-thiadiazole, indole, benzotriazole, benzoxazole oxopyrrolidine, benzodioxolane, benzodioxane, carbazole, octahydro-ethanopyrrolo-pyridine, oxaspirodecane,
35 oxadiazaspiroundecane, indoline-2-one and quinazoline,

optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

5

In another preferred embodiment of the invention according to general Formula (I) the compound is a compound, wherein in R_{21} , R_{21}' and R_{21}'' as defined in any of the embodiments of the present invention,

the C_{1-6} alkyl is preferably selected from methyl, ethyl, propyl, butyl, pentyl, hexyl, isopropyl, or 2-methylpropyl;

10

and/or

the C_{2-6} -alkenyl is preferably selected from ethylene, propylene, butylene, pentylene, hexylene, isopropylene and isobutylene;

15

and/or

the C_{2-6} -alkynyl is preferably selected from ethyne, propyne, butyne, pentyne, hexyne, isopropyne and isobutyne;

20

optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

25

In another preferred embodiment of the invention according to general Formula (I) the compound is a compound, wherein in R_{31} , R_{31}' and R_{31}'' as defined in any of the embodiments of the present invention,

the C_{1-6} alkyl is preferably selected from methyl, ethyl, propyl, butyl, pentyl, hexyl, isopropyl, or 2-methylpropyl;

30

and/or

the C₂₋₆ -alkenyl is preferably selected from ethylene, propylene, butylene, pentylene, hexylene, isopropylene and isobutylene;

and/or

5

the C₂₋₆ -alkynyl is preferably selected from ethyne, propyne, butyne, pentyne, hexyne, isopropyne and isobutyne;

optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

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In another preferred embodiment of the invention according to general Formula (I) the compound is a compound, wherein in R₄₁, R₄₁' and R₄₁'' as defined in any of the embodiments of the present invention,

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the C₁₋₆ alkyl is preferably selected from methyl, ethyl, propyl, butyl, pentyl, hexyl, isopropyl, or 2-methylpropyl; more preferably the C₁₋₆ alkyl is methyl;

and/or

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the C₂₋₆ -alkenyl is preferably selected from ethylene, propylene, butylene, pentylene, hexylene, isopropylene and isobutylene;

and/or

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the C₂₋₆ -alkynyl is preferably selected from ethyne, propyne, butyne, pentyne, hexyne, isopropyne and isobutyne;

optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

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In another preferred embodiment of the invention according to general Formula (I) the compound is a compound, wherein in R₅₁ and R₅₁' as defined in any of the embodiments of the present invention,

the C₁₋₆ alkyl is preferably selected from methyl, ethyl, propyl, butyl, pentyl, hexyl, isopropyl, or 2-methylpropyl;

and/or

- 5 the C₂₋₆ -alkenyl is preferably selected from ethylene, propylene, butylene, pentylene, hexylene, isopropylene and isobutylene;

and/or

- 10 the C₂₋₆ -alkynyl is preferably selected from ethyne, propyne, butyne, pentyne, hexyne, isopropyne and isobutyne;

optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding

- 15 salt thereof, or a corresponding solvate thereof.

In another preferred embodiment of the invention according to general Formula (I) the compound is a compound, wherein

m is 1, 2, 3 or 4; preferably m is 1, 2 or 3;

- 20 optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

In another preferred embodiment of the invention according to general Formula (I) the compound is a compound, wherein

- 25 n is 1 or 2; preferably n is 1;

optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

In another preferred embodiment of the invention according to general Formula (I) the compound is a compound, wherein

t is 0 or 1;

optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

In another preferred embodiment of the invention according to general Formula (I) the compound is a compound, wherein

r is 0, 1, 2 or 3; preferably r is 0 or 1;

optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

In another preferred embodiment of the invention according to general Formula (I) the compound is a compound, wherein

X is selected from the group consisting of a bond, $-\text{[CH}_2\text{]}_p-$, $-\text{[CH}_2\text{]}_p\text{NR}_x\text{[CH}_2\text{]}_q-$, $-\text{[CH}_2\text{]}_p\text{O[CH}_2\text{]}_q-$, $-\text{[CH}_2\text{]}_p\text{NR}_x\text{C(O)[CH}_2\text{]}_q-$ and $-\text{[CH}_2\text{]}_p\text{NR}_x\text{CH(CH}_3\text{)-}$; preferably X is selected from the group consisting of a bond, $-\text{CH}_2-$, $-\text{CH}_2\text{CH}_2-$, $-\text{CH}_2\text{CH}_2\text{CH}_2-$, $-\text{CH}_2\text{O-}$, $-\text{CH}_2\text{OCH}_2-$, $-\text{NHC(O)CH}_2-$, $-\text{NHCH}_2\text{CH}_2-$, $-\text{CH}_2\text{NHCH}_2-$, $-\text{CH}_2\text{NH(CH}_2\text{)}_2-$, $-\text{CH}_2\text{NH(CH}_2\text{)}_3-$, $-\text{CH}_2\text{NH(CH}_2\text{)}_4-$, $-\text{CH}_2\text{N(methyl)CH}_2-$, $-\text{CH}_2\text{N(iPr)CH}_2-$, $-\text{CH}_2\text{N(CH}_2\text{CF}_3\text{)CH}_2-$, $-\text{CH}_2\text{NHCH(methyl)-}$, $-\text{CH}_2\text{N(methyl)CH}_2\text{CH}_2-$, $-\text{N(methyl)-}$, $-\text{N(methyl)CH}_2-$, $-\text{N(methyl)CH}_2\text{CH}_2-$ and $-\text{CH}_2\text{N(isopropyl)CH}_2-$;

optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

In another preferred embodiment of the invention according to general Formula (I) the compound is a compound, wherein

p is 0, 1, 2, 3 or 4; preferably p is 0, 1, 2 or 3;

optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

In another preferred embodiment of the invention according to general Formula (I) the compound is a compound, wherein

q is 0, 1, 2, 3 or 4;

optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

In another preferred embodiment of the invention according to general Formula (I) the compound is a compound, wherein

R_x is selected from the group consisting of hydrogen, substituted or unsubstituted C_{1-6} alkyl, substituted or unsubstituted C_{2-6} alkenyl and substituted or unsubstituted C_{2-6} alkynyl; preferably R_x is selected from the group consisting of hydrogen and substituted or unsubstituted C_{1-6} alkyl; more preferably R_x is hydrogen or a substituted or unsubstituted group selected from methyl, ethyl, isopropyl;

optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

In another preferred embodiment of the invention according to general Formula (I) the compound is a compound, wherein

R_1 is selected from the group consisting of hydrogen, substituted or unsubstituted C_{1-6} alkyl, substituted or unsubstituted C_{2-6} alkenyl, substituted or unsubstituted C_{2-6} alkynyl, halogen, haloalkyl, haloalkoxy, $-OR_6$, $-NR_6R_6'$, $-CN$, cycloalkyl, aryl and heterocyclyl; preferably, R_1 is selected from the group consisting of hydrogen, substituted or

unsubstituted C₁₋₆ alkyl, halogen, haloalkyl, -OR₆, -NR₆R₆', -CN, cycloalkyl, aryl and heterocyclyl; more preferably R₁ is hydrogen, bromine, chlorine, -CN or a substituted or unsubstituted group selected from methyl, ethyl, isopropyl, -CF₃, -OH, methoxy, -O-isopropyl, -NH₂, -NHCH₃, -N(CH₃)₂, -N(CH₃)(CH₂-cyclopropyl), -N(CH₃)(benzyl), -N(CH₃)(piperidine), -N(CH₂CF₃)(CH₂-tetrahydropyran), cyclopropyl, phenyl, pyridine, piperidine, pyrrolidine, piperazine, pyrimidine, pyrazole, isoxazole, isothiazole, imidazole, morpholine, thiomorpholine, tetrahydropyran, tetrahydrofuran and thiophene;

optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

In another preferred embodiment of the invention according to general Formula (I) the compound is a compound, wherein

R₂ is selected from the group consisting of hydrogen, substituted or unsubstituted C₁₋₆ alkyl, substituted or unsubstituted C₂₋₆ alkenyl, substituted or unsubstituted C₂₋₆ alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted alkylcycloalkyl, halogen, haloalkyl, haloalkoxy and -OR₇; preferably R₂ is selected from the group consisting of hydrogen, substituted or unsubstituted C₁₋₆ alkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted alkylcycloalkyl, halogen, haloalkyl, haloalkoxy and -OR₇; more preferably R₂ is selected from the group consisting of hydrogen, substituted or unsubstituted C₁₋₆ alkyl, substituted or unsubstituted cycloalkyl, halogen and -OR₇; even more preferably R₂ is hydrogen, bromine, chlorine or a substituted or unsubstituted group selected from methyl, ethyl, cyclopropyl, -OH and methoxy;

optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

In another preferred embodiment of the invention according to general Formula (I) the compound is a compound, wherein

R₃ is selected from the group consisting of hydrogen, substituted or unsubstituted C₁₋₆ alkyl, substituted or unsubstituted C₂₋₆ alkenyl, substituted or unsubstituted C₂₋₆ alkynyl, halogen, haloalkyl, haloalkoxy and –OR₈; preferably R₃ is selected from the group consisting of hydrogen, substituted or unsubstituted C₁₋₆ alkyl, halogen, haloalkyl, haloalkoxy and –OR₈; more preferably R₃ is selected from the group consisting of hydrogen and substituted or unsubstituted C₁₋₆ alkyl; even more preferably R₃ is hydrogen or substituted or unsubstituted methyl;

optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

In another preferred embodiment of the invention according to general Formula (I) the compound is a compound, wherein

R₄ is selected from the group consisting of substituted or unsubstituted C₁₋₆ alkyl, substituted or unsubstituted C₂₋₆ alkenyl, substituted or unsubstituted C₂₋₆ alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl and substituted or unsubstituted heterocyclyl; preferably R₄ is selected from the group consisting of substituted or unsubstituted C₁₋₆ alkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl and substituted or unsubstituted heterocyclyl; more preferably R₄ is selected from the group consisting of substituted or unsubstituted C₁₋₆ alkyl, substituted or unsubstituted aryl and substituted or unsubstituted heterocyclyl; even more preferably R₄ is a substituted or unsubstituted group selected from methyl, ethyl, isopropyl, isobutyl, phenyl, pyridine and tetrahydropyran;

optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

In another preferred embodiment of the invention according to general Formula (I) the compound is a compound, wherein

R₅ and R₅' are independently selected from the group consisting of hydrogen, substituted or unsubstituted C₁₋₆ alkyl, substituted or unsubstituted C₂₋₆ alkenyl,

substituted or unsubstituted C₂₋₆ alkynyl, haloalkyl and haloalkoxy; preferably R₅ and R₅' are independently selected from the group consisting of hydrogen, substituted or unsubstituted C₁₋₆ alkyl, haloalkyl and haloalkoxy; more preferably R₅ and R₅' are independently selected from the group consisting of hydrogen and substituted or unsubstituted C₁₋₆ alkyl; even more preferably R₅ and R₅' are independently selected from hydrogen or a substituted or unsubstituted group selected from methyl and methyl-OH;

optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

In another preferred embodiment of the invention according to general Formula (I) the compound is a compound, wherein

R₆ is selected from the group consisting of hydrogen, substituted or unsubstituted C₁₋₆ alkyl, substituted or unsubstituted C₂₋₆ alkenyl, substituted or unsubstituted C₂₋₆ alkynyl, haloalkyl, haloalkoxy; substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted alkylcycloalkyl, substituted or unsubstituted alkylaryl and substituted or unsubstituted alkylheterocyclyl; preferably R₆ is selected from the group consisting of hydrogen, substituted or unsubstituted C₁₋₆ alkylhaloalkyl, haloalkoxy; substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted alkylcycloalkyl, substituted or unsubstituted alkylaryl and substituted or unsubstituted alkylheterocyclyl; more preferably R₆ is selected from the group consisting of hydrogen, substituted or unsubstituted C₁₋₆ alkylhaloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted alkylcycloalkyl, substituted or unsubstituted alkylaryl and substituted or unsubstituted alkylheterocyclyl; even more preferably R₆ is hydrogen or a substituted or unsubstituted group selected from methyl, isopropyl, benzyl, piperidine, -CH₂-cyclopropyl and -CH₂-tetrahydropyran;

optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

In another preferred embodiment of the invention according to general Formula (I) the compound is a compound, wherein

5 R_6' is selected from the group consisting of hydrogen, substituted or unsubstituted C_{1-6} alkyl, substituted or unsubstituted C_{2-6} alkenyl and substituted or unsubstituted C_{2-6} alkynyl; preferably R_6' is selected from the group consisting of hydrogen and substituted or unsubstituted C_{1-6} alkyl; more preferably R_6' is hydrogen or a substituted or unsubstituted group selected from methyl and $-CH_2CF_3$;

10 optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

In another preferred embodiment of the invention according to general Formula (I) the compound is a compound, wherein

15 R_7 is selected from the group consisting of hydrogen, substituted or unsubstituted C_{1-6} alkyl, substituted or unsubstituted C_{2-6} alkenyl and substituted or unsubstituted C_{2-6} alkynyl; preferably R_7 is selected from the group consisting of hydrogen and substituted or unsubstituted C_{1-6} alkyl; more preferably R_7 is hydrogen or substituted or unsubstituted methyl;

20 optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

In another preferred embodiment of the invention according to general Formula (I) the compound is a compound, wherein

25 R_8 is selected from the group consisting of hydrogen, substituted or unsubstituted C_{1-6} alkyl, substituted or unsubstituted C_{2-6} alkenyl and substituted or unsubstituted C_{2-6} alkynyl; preferably R_8 is selected from the group consisting of hydrogen and substituted or unsubstituted C_{1-6} alkyl;

30 optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers,

preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

In a further embodiment the compound according to the invention of general Formula (I) is a compound wherein

- 5 R_{11} , R_{11}' and R_{11}'' are independently selected from hydrogen, substituted or unsubstituted C_{1-6} alkyl, substituted or unsubstituted C_{2-6} alkenyl, substituted or unsubstituted C_{2-6} alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted alkylcycloalkyl, substituted or unsubstituted alkylaryl and substituted or unsubstituted alkylheterocyclyl; preferably R_{11} , R_{11}' and R_{11}'' are independently selected from hydrogen, substituted or unsubstituted C_{1-6} alkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted alkylcycloalkyl, substituted or unsubstituted alkylaryl and substituted or unsubstituted alkylheterocyclyl; more preferably R_{11} , R_{11}' and R_{11}'' are independently selected from hydrogen, substituted or unsubstituted C_{1-6} alkyl, substituted or unsubstituted aryl, substituted or unsubstituted heterocyclyl and substituted or unsubstituted alkylcycloalkyl; even more preferably R_{11} , R_{11}' and R_{11}'' are hydrogen or a substituted or unsubstituted group selected from methyl, ethyl, -CH₂-cyclopropyl, phenyl, pyridine, triazole and oxadiazole;
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- 20 optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

- In a further embodiment the compound according to the invention of general Formula (I) is a compound wherein
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- R_{13} and R_{13}' are independently selected from hydrogen, unsubstituted C_{1-6} alkyl, unsubstituted C_{2-6} alkenyl and unsubstituted C_{2-6} alkynyl; preferably R_{13} and R_{13}' are independently selected from hydrogen and unsubstituted C_{1-6} alkyl; more preferably R_{13} and R_{13}' are independently selected from the group consisting of hydrogen and unsubstituted methyl;
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optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

- 5 In another preferred embodiment of the invention according to general Formula (I) the compound is a compound, wherein

10 R_{14} , R_{14}' and R_{14}'' are independently selected from hydrogen, unsubstituted C_{1-6} alkyl, unsubstituted C_{2-6} alkenyl, unsubstituted C_{2-6} alkynyl, unsubstituted aryl, unsubstituted cycloalkyl and unsubstituted heterocyclyl; preferably R_{14} , R_{14}' and R_{14}'' are independently selected from hydrogen, unsubstituted C_{1-6} alkyl, unsubstituted aryl, unsubstituted cycloalkyl and unsubstituted heterocyclyl; more preferably R_{14} , R_{14}' and R_{14}'' are independently selected from hydrogen and unsubstituted C_{1-6} alkyl; even more preferably R_{14} , R_{14}' and R_{14}'' are independently selected from hydrogen and unsubstituted methyl;

- 15 optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

- 20 In another preferred embodiment of the invention according to general Formula (I) the compound is a compound, wherein

R_{21} and R_{21}' are independently selected from hydrogen, substituted or unsubstituted C_{1-6} alkyl, substituted or unsubstituted C_{2-6} alkenyl and substituted or unsubstituted C_{2-6} alkynyl; preferably R_{21} and R_{21}' are independently selected from hydrogen and substituted or unsubstituted C_{1-6} alkyl;

- 25 optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

- 30 In another preferred embodiment of the invention according to general Formula (I) the compound is a compound, wherein

R₃₁ and R₃₁' are independently selected from hydrogen, substituted or unsubstituted C₁₋₆ alkyl, substituted or unsubstituted C₂₋₆ alkenyl and substituted or unsubstituted C₂₋₆ alkynyl; preferably R₃₁ and R₃₁' are independently selected from hydrogen, substituted or unsubstituted C₁₋₆ alkyl;

- 5 optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

10 In another preferred embodiment of the invention according to general Formula (I) the compound is a compound, wherein

- R₄₁, R₄₁' and R₄₁'' are independently selected from hydrogen, substituted or unsubstituted C₁₋₆ alkyl, substituted or unsubstituted C₂₋₆ alkenyl and substituted or unsubstituted C₂₋₆ alkynyl; preferably R₄₁, R₄₁' and R₄₁'' are independently selected from hydrogen and substituted or unsubstituted C₁₋₆ alkyl; more preferably R₄₁, R₄₁' and R₄₁''
15 are independently selected from the group consisting of hydrogen and substituted or unsubstituted methyl;

- optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding
20 salt thereof, or a corresponding solvate thereof.

In another preferred embodiment of the invention according to general Formula (I) the compound is a compound, wherein

- R₅₁ and R₅₁' are independently selected from hydrogen, substituted or unsubstituted C₁₋₆ alkyl, substituted or unsubstituted C₂₋₆ alkenyl and substituted or unsubstituted C₂₋₆
25 alkynyl; preferably R₅₁ and R₅₁' are independently selected from hydrogen and substituted or unsubstituted C₁₋₆ alkyl; more preferably R₅₁ and R₅₁' are both hydrogen;

- optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding
30 salt thereof, or a corresponding solvate thereof.

In another preferred embodiment of the invention according to general Formula (I) the compound is a compound, wherein

- the cycloalkyl, aryl or heterocyclyl in R_1 , if substituted, is substituted with one or more substituent/s selected from halogen, $-R_{11}$, $-[CH_2]_rOR_{11}$, $=O$, $-NO_2$, $-[CH_2]_rNR_{11}R_{11}'$, $-NR_{11}C(O)R_{11}'$, $-NR_{11}S(O)_2R_{11}'$, $-S(O)_2NR_{11}R_{11}'$, $-NR_{11}C(O)NR_{11}'R_{11}''$, $-SR_{11}$, $-S(O)R_{11}$, $-S(O)_2R_{11}$, $-CN$, haloalkyl, haloalkoxy, $-C(O)R_{11}$, $-C(O)OR_{11}$, $-C(O)NR_{11}R_{11}'$, $-OCH_2CH_2OR_{11}$, $-NR_{11}S(O)_2NR_{11}'R_{11}''$ and $-C(CH_3)_2OR_{11}$; preferably the cycloalkyl, aryl or heterocyclyl in R_1 , if substituted, is substituted with one or more substituent/s selected from halogen, $-R_{11}$, $-[CH_2]_rOR_{11}$, $=O$, $-[CH_2]_rNR_{11}R_{11}'$, $-S(O)_2R_{11}$, $-CN$, haloalkyl, $-C(O)R_{11}$ and $-C(O)NR_{11}R_{11}'$; more preferably the cycloalkyl, aryl or heterocyclyl in R_1 , if substituted, is substituted with one or more substituent/s selected from fluorine, chlorine, methyl, ethyl, $-CF_3$, $-CN$, $-CH_2OH$, $-CH_2OCH_3$, $-OH-OCH_3$, $-OCH_2CH_3$, $-OCH_2$ -cyclopropyl, $=O$, $-CH_2NHCH_3$, $-NH_2$, $-NHCH_3$, $-N(CH_3)_2$, $-C(O)CH_3$, $-C(O)NH_2$, $-C(O)N(CH_3)_2$, $-S(O)_2CH_3$, triazole, oxadiazole, phenyl and pyridine;
- optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

In another preferred embodiment of the invention according to general Formula (I) the compound is a compound, wherein

- the cycloalkyl, aryl or heterocyclyl in R_4 , if substituted, is substituted with one or more substituent/s selected from halogen, $-R_{41}$, $-[CH_2]_rOR_{41}$, $=O$, $-NO_2$, $-[CH_2]_rNR_{41}R_{41}'$, $-NR_{41}C(O)R_{41}'$, $-NR_{41}S(O)_2R_{41}'$, $-S(O)_2NR_{41}R_{41}'$, $-NR_{41}C(O)NR_{41}'R_{41}''$, $-SR_{41}$, $-S(O)R_{41}$, $-S(O)_2R_{41}$, $-CN$, haloalkyl, haloalkoxy, $-C(O)R_{41}$, $-C(O)OR_{41}$, $-C(O)NR_{41}R_{41}'$, $-OCH_2CH_2OR_{41}$, $-NR_{41}S(O)_2NR_{41}'R_{41}''$ and $-C(CH_3)_2OR_{41}$; preferably the cycloalkyl, aryl or heterocyclyl in R_4 , if substituted, is substituted with one or more substituent/s selected from halogen, $-R_{41}$, $-[CH_2]_rOR_{41}$, $-CN$ and haloalkyl; more preferably the cycloalkyl, aryl or heterocyclyl in R_4 , if substituted, is substituted with one or more substituent/s selected from fluorine, chlorine, $-CH_3$, $-CF_3$, $-CN$, $-OH$ and $-OCH_3$;
- optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers,

preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

In another preferred embodiment of the invention according to general Formula (I) the compound is a compound, wherein

- 5 the alkyl, alkenyl or alkynyl in R_5 and R_5' , if substituted, is substituted with one or more substituent/s selected from $-OR_{51}$, halogen, $-CN$, haloalkyl, haloalkoxy, $-NR_{51}R_{51}'$; preferably the alkyl, alkenyl or alkynyl in R_5 and R_5' , if substituted, is substituted with one or more $-OR_{51}$; more preferably the alkyl, alkenyl or alkynyl in R_5 and R_5' , if substituted, is substituted with one or more $-OH$;
- 10 optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

In another preferred embodiment of the invention according to general Formula (I) the compound is a compound, wherein

- 15 the alkyl, alkenyl or alkynyl, if substituted, and not defined otherwise, is substituted with one or more substituent/s selected from $-OR_{13}$, halogen, $-CN$, haloalkyl, haloalkoxy and $-NR_{13}R_{13}'$; preferably the alkyl, alkenyl or alkynyl, if substituted, and not defined otherwise, is substituted with one or more substituent/s selected from $-OR_{13}$ and $-NR_{13}R_{13}'$; more preferably the alkyl, alkenyl or alkynyl, if substituted, and not defined otherwise, is substituted with one or more substituent/s selected from $-OH$, $-OCH_3$ and $-NHCH_3$;
- 20 optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.
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In another preferred embodiment of the invention according to general Formula (I) the compound is a compound, wherein

- 30 the aryl, heterocyclyl or cycloalkyl, also in alkylcycloalkyl, alkylaryl and alkylheterocyclyl, if substituted, and not defined otherwise, is substituted with one or

more substituent/s selected from halogen, $-R_{14}$, $-[CH_2]_rOR_{14}$, $=O$, $-NO_2$, $-[CH_2]_rNR_{14}R_{14}'$, $-NR_{14}C(O)R_{14}'$, $-NR_{14}S(O)_2R_{14}'$, $-S(O)_2NR_{14}R_{14}'$, $-NR_{14}C(O)NR_{14}'R_{14}''$, $-SR_{14}$, $-S(O)R_{14}$, $S(O)_2R_{14}$, $-CN$, haloalkyl, haloalkoxy, $-C(O)R_{14}$, $-C(O)OR_{14}$, $-C(O)NR_{14}R_{14}'$, $-OCH_2CH_2OR_{14}$, $-NR_{14}S(O)_2NR_{14}'R_{14}''$ and $-C(CH_3)_2OR_{14}$; preferably the aryl, heterocyclyl or cycloalkyl, also in alkylcycloalkyl, alkylaryl and alkylheterocyclyl, if substituted, and not defined otherwise, is substituted with one or more substituent/s selected from $-R_{14}$ and $-[CH_2]_rNR_{14}R_{14}'$; more preferably the aryl, heterocyclyl or cycloalkyl, also in alkylcycloalkyl, alkylaryl and alkylheterocyclyl, if substituted, and not defined otherwise, is substituted with one or more substituent/s selected from methyl and $-CH_2NHCH_3$;

optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

15

In another preferred embodiment of the invention according to general Formula (I) the compound is a compound, wherein

m is 1, 2, 3 or 4; preferably m is 1, 2 or 3;

and/or

20

n is 1 or 2; preferably n is 1;

and/or

t is 0 or 1;

and/or

p is 0, 1, 2, 3 or 4; preferably p is 0, 1, 2 or 3;

25

and/or

q is 0, 1, 2, 3 or 4;

and/or

r is 0, 1, 2 or 3; preferably r is 0 or 1;

and/or

X is selected from the group consisting of a bond, $-\text{[CH}_2\text{]}_p-$, $-\text{[CH}_2\text{]}_p\text{NR}_x\text{[CH}_2\text{]}_q-$, $-\text{[CH}_2\text{]}_p\text{O[CH}_2\text{]}_q-$, $-\text{[CH}_2\text{]}_p\text{NR}_xC(\text{O})\text{[CH}_2\text{]}_q-$ and $-\text{[CH}_2\text{]}_p\text{NR}_x\text{CH(CH}_3\text{)}-$; preferably X is selected from the group consisting of a bond, $-\text{CH}_2-$, $-\text{CH}_2\text{CH}_2-$, $-\text{CH}_2\text{CH}_2\text{CH}_2-$, $-\text{CH}_2\text{O}-$, $-\text{CH}_2\text{OCH}_2-$, $-\text{NHC(O)CH}_2-$, $-\text{NHCH}_2\text{CH}_2-$, $-\text{CH}_2\text{NHCH}_2-$, $-\text{CH}_2\text{NH(CH}_2\text{)}_2-$, $-\text{CH}_2\text{NH(CH}_2\text{)}_3-$, $-\text{CH}_2\text{NH(CH}_2\text{)}_4-$, $-\text{CH}_2\text{N(methyl)CH}_2-$, $-\text{CH}_2\text{N(iPr)CH}_2-$, $-\text{CH}_2\text{N(CH}_2\text{CF}_3\text{)CH}_2-$, $-\text{CH}_2\text{NHCH(methyl)-}$, $-\text{CH}_2\text{N(methyl)CH}_2\text{CH}_2-$, $-\text{N(methyl)-}$, $-\text{N(methyl)CH}_2-$, $-\text{N(methyl)CH}_2\text{CH}_2-$ and $-\text{CH}_2\text{N(isopropyl)CH}_2-$;

10 and/or

R_x is selected from the group consisting of hydrogen, substituted or unsubstituted C_{1-6} alkyl, substituted or unsubstituted C_{2-6} alkenyl and substituted or unsubstituted C_{2-6} alkynyl; preferably R_x is selected from the group consisting of hydrogen and substituted or unsubstituted C_{1-6} alkyl; more preferably R_x is hydrogen or a substituted or unsubstituted group selected from methyl, ethyl, isopropyl;

and/or

R_1 is selected from the group consisting of hydrogen, substituted or unsubstituted C_{1-6} alkyl, substituted or unsubstituted C_{2-6} alkenyl, substituted or unsubstituted C_{2-6} alkynyl, halogen, haloalkyl, haloalkoxy, $-\text{OR}_6$, $-\text{NR}_6\text{R}_6'$, $-\text{CN}$, cycloalkyl, aryl and heterocyclyl; preferably, R_1 is selected from the group consisting of hydrogen, substituted or unsubstituted C_{1-6} alkyl, halogen, haloalkyl, $-\text{OR}_6$, $-\text{NR}_6\text{R}_6'$, $-\text{CN}$, cycloalkyl, aryl and heterocyclyl; more preferably R_1 is hydrogen, bromine, chlorine, $-\text{CN}$ or a substituted or unsubstituted group selected from methyl, ethyl, isopropyl, $-\text{CF}_3$, $-\text{OH}$, methoxy, $-\text{O-isopropyl}$, $-\text{NH}_2$, $-\text{NHCH}_3$, $-\text{N(CH}_3\text{)}_2$, $-\text{N(CH}_3\text{)(CH}_2\text{-cyclopropyl)}$, $-\text{N(CH}_3\text{)(benzyl)}$, $-\text{N(CH}_3\text{)(piperidine)}$, $-\text{N(CH}_2\text{CF}_3\text{)(CH}_2\text{-tetrahydropyran)}$, cyclopropyl, phenyl, pyridine, piperidine, pyrrolidine, piperazine, pyrimidine, pyrazole, isoxazole, isothiazole, imidazole, morpholine, thiomorpholine, tetrahydropyran, tetrahydrofuran and thiophene;

and/or

R₂ is selected from the group consisting of hydrogen, substituted or unsubstituted C₁₋₆ alkyl, substituted or unsubstituted C₂₋₆ alkenyl, substituted or unsubstituted C₂₋₆ alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted alkylcycloalkyl, halogen, haloalkyl, haloalkoxy and -OR₇; preferably R₂ is selected from the group consisting of hydrogen, substituted or unsubstituted C₁₋₆ alkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted alkylcycloalkyl, halogen, haloalkyl, haloalkoxy and -OR₇; more preferably R₂ is selected from the group consisting of hydrogen, substituted or unsubstituted C₁₋₆ alkyl, substituted or unsubstituted cycloalkyl, halogen and -OR₇; even more preferably R₂ is hydrogen, bromine, chlorine or a substituted or unsubstituted group selected from methyl, ethyl, cyclopropyl, -OH and methoxy;

and/or

R₃ is selected from the group consisting of hydrogen, substituted or unsubstituted C₁₋₆ alkyl, substituted or unsubstituted C₂₋₆ alkenyl, substituted or unsubstituted C₂₋₆ alkynyl, halogen, haloalkyl, haloalkoxy and -OR₈; preferably R₃ is selected from the group consisting of hydrogen, substituted or unsubstituted C₁₋₆ alkyl, halogen, haloalkyl, haloalkoxy and -OR₈; more preferably R₃ is selected from the group consisting of hydrogen and substituted or unsubstituted C₁₋₆ alkyl; even more preferably R₃ is hydrogen or substituted or unsubstituted methyl;

and/or

R₄ is selected from the group consisting of substituted or unsubstituted C₁₋₆ alkyl, substituted or unsubstituted C₂₋₆ alkenyl, substituted or unsubstituted C₂₋₆ alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl and substituted or unsubstituted heterocyclyl; preferably R₄ is selected from the group consisting of substituted or unsubstituted C₁₋₆ alkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl and substituted or unsubstituted heterocyclyl; more preferably R₄ is selected from the group consisting of substituted or unsubstituted C₁₋₆ alkyl, substituted or unsubstituted aryl and substituted or unsubstituted heterocyclyl; even more preferably R₄ is a substituted or unsubstituted group selected from methyl, ethyl, isopropyl, isobutyl, phenyl, pyridine, tetrahydropyran;

and/or

- R₅ and R₅' are independently selected from the group consisting of hydrogen, substituted or unsubstituted C₁₋₆ alkyl, substituted or unsubstituted C₂₋₆ alkenyl, substituted or unsubstituted C₂₋₆ alkynyl, haloalkyl and haloalkoxy; preferably R₅ and R₅' are independently selected from the group consisting of hydrogen, substituted or unsubstituted C₁₋₆ alkyl, haloalkyl and haloalkoxy; more preferably R₅ and R₅' are independently selected from the group consisting of hydrogen and substituted or unsubstituted C₁₋₆ alkyl; even more preferably R₅ and R₅' are independently selected from hydrogen or a substituted or unsubstituted group selected from methyl and methyl-OH;
- and/or
- R₆ is selected from the group consisting of hydrogen, substituted or unsubstituted C₁₋₆ alkyl, substituted or unsubstituted C₂₋₆ alkenyl, substituted or unsubstituted C₂₋₆ alkynyl, haloalkyl, haloalkoxy; substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted alkylcycloalkyl, substituted or unsubstituted alkylaryl and substituted or unsubstituted alkylheterocyclyl; preferably R₆ is selected from the group consisting of hydrogen, substituted or unsubstituted C₁₋₆ alkylhaloalkyl, haloalkoxy; substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted alkylcycloalkyl, substituted or unsubstituted alkylaryl and substituted or unsubstituted alkylheterocyclyl; more preferably R₆ is selected from the group consisting of hydrogen, substituted or unsubstituted C₁₋₆ alkylhaloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted alkylcycloalkyl, substituted or unsubstituted alkylaryl and substituted or unsubstituted alkylheterocyclyl; even more preferably R₆ is hydrogen or a substituted or unsubstituted group selected from methyl, isopropyl, benzyl, piperidine, -CH₂-cyclopropyl, -CH₂-tetrahydropyran;
- and/or
- R₆' is selected from the group consisting of hydrogen, substituted or unsubstituted C₁₋₆ alkyl, substituted or unsubstituted C₂₋₆ alkenyl and substituted or unsubstituted C₂₋₆ alkynyl; preferably R₆' is selected from the group consisting of hydrogen and substituted or unsubstituted C₁₋₆ alkyl; more preferably R₆' is hydrogen or a substituted or unsubstituted group selected from methyl and -CH₂CF₃;

and/or

R₆ and R₆' , taken together with the nitrogen atom to which they are attached, form a substituted or unsubstituted heterocyclyl selected from the group consisting of morpholine, thiomorpholine, pyrrolidine and piperazine;

5 and/or

R₇ is selected from the group consisting of hydrogen, substituted or unsubstituted C₁₋₆ alkyl, substituted or unsubstituted C₂₋₆ alkenyl and substituted or unsubstituted C₂₋₆ alkynyl; preferably R₇ is selected from the group consisting of hydrogen and substituted or unsubstituted C₁₋₆ alkyl; more preferably R₇ is hydrogen or substituted or
10 unsubstituted methyl;

and/or

R₁₁, R₁₁' and R₁₁'' are independently selected from hydrogen, substituted or unsubstituted C₁₋₆ alkyl, substituted or unsubstituted C₂₋₆ alkenyl, substituted or unsubstituted C₂₋₆ alkynyl, substituted or unsubstituted cycloalkyl, substituted or
15 unsubstituted aryl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted alkylcycloalkyl, substituted or unsubstituted alkylaryl and substituted or unsubstituted alkylheterocyclyl; preferably R₁₁, R₁₁' and R₁₁'' are independently selected from hydrogen, substituted or unsubstituted C₁₋₆ alkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heterocyclyl,
20 substituted or unsubstituted alkylcycloalkyl, substituted or unsubstituted alkylaryl and substituted or unsubstituted alkylheterocyclyl; more preferably R₁₁, R₁₁' and R₁₁'' are independently selected from hydrogen, substituted or unsubstituted C₁₋₆ alkyl, substituted or unsubstituted aryl, substituted or unsubstituted heterocyclyl and substituted or unsubstituted alkylcycloalkyl; even more preferably R₁₁, R₁₁' and R₁₁'' are
25 hydrogen or a substituted or unsubstituted group selected from methyl, ethyl, -CH₂-cyclopropyl, phenyl, pyridine, triazole and oxadiazole;

and/or

R₁₃ and R₁₃' are independently selected from hydrogen, unsubstituted C₁₋₆ alkyl, unsubstituted C₂₋₆ alkenyl and unsubstituted C₂₋₆ alkynyl; preferably R₁₃ and R₁₃' are
30 independently selected from hydrogen and unsubstituted C₁₋₆ alkyl; more preferably R₁₃ and R₁₃' are independently selected from hydrogen and unsubstituted methyl;

and/or

5 R₁₄, R₁₄' and R₁₄'' are independently selected from hydrogen, unsubstituted C₁₋₆ alkyl, unsubstituted C₂₋₆ alkenyl, unsubstituted C₂₋₆ alkynyl, unsubstituted aryl, unsubstituted cycloalkyl and unsubstituted heterocyclyl; preferably R₁₄, R₁₄' and R₁₄'' are independently selected from hydrogen, unsubstituted C₁₋₆ alkyl, unsubstituted aryl, unsubstituted cycloalkyl and unsubstituted heterocyclyl; more preferably R₁₄, R₁₄' and R₁₄'' are independently selected from hydrogen and unsubstituted C₁₋₆ alkyl; even more preferably R₁₄, R₁₄' and R₁₄'' are independently selected from hydrogen and unsubstituted methyl;

10 and/or

R₄₁, R₄₁' and R₄₁'' are independently selected from hydrogen, substituted or unsubstituted C₁₋₆ alkyl, substituted or unsubstituted C₂₋₆ alkenyl and substituted or unsubstituted C₂₋₆ alkynyl; preferably R₄₁, R₄₁' and R₄₁'' are independently selected from hydrogen and substituted or unsubstituted C₁₋₆ alkyl; more preferably R₄₁, R₄₁' and R₄₁'' are independently selected from hydrogen and substituted or unsubstituted methyl;

and/or

20 R₅₁ and R₅₁' are independently selected from hydrogen, substituted or unsubstituted C₁₋₆ alkyl, substituted or unsubstituted C₂₋₆ alkenyl and substituted or unsubstituted C₂₋₆ alkynyl; preferably R₅₁ and R₅₁' are independently selected from hydrogen and substituted or unsubstituted C₁₋₆ alkyl; more preferably R₅₁ and R₅₁' are both hydrogen;

optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

25 In a preferred embodiment

m is 1, 2 or 3.

In a preferred embodiment

n is 1.

In a preferred embodiment

t is 0 or 1.

In a preferred embodiment

t is 0.

5 In a preferred embodiment

p is 0, 1, 2 or 3.

In a preferred embodiment

q is 0, 1, 2, 3 or 4.

In a preferred embodiment

10 r is 0 or 1.

In a preferred embodiment

15 X is selected from the group consisting of a bond, $-\text{CH}_2-$, $-\text{CH}_2\text{CH}_2-$, $-\text{CH}_2\text{CH}_2\text{CH}_2-$, $-\text{CH}_2\text{O}-$, $-\text{CH}_2\text{OCH}_2-$, $-\text{NHC}(\text{O})\text{CH}_2-$, $-\text{NHCH}_2\text{CH}_2-$, $-\text{CH}_2\text{NHCH}_2-$, $-\text{CH}_2\text{NH}(\text{CH}_2)_2-$, $-\text{CH}_2\text{NH}(\text{CH}_2)_3-$, $-\text{CH}_2\text{NH}(\text{CH}_2)_4-$, $-\text{CH}_2\text{N}(\text{methyl})\text{CH}_2-$, $-\text{CH}_2\text{N}(\text{iPr})\text{CH}_2-$, $-\text{CH}_2\text{N}(\text{CH}_2\text{CF}_3)\text{CH}_2-$, $-\text{CH}_2\text{NHCH}(\text{methyl})-$, $-\text{CH}_2\text{N}(\text{methyl})\text{CH}_2\text{CH}_2-$, $-\text{N}(\text{methyl})-$, $-\text{N}(\text{methyl})\text{CH}_2-$, $-\text{N}(\text{methyl})\text{CH}_2\text{CH}_2-$ and $-\text{CH}_2\text{N}(\text{isopropyl})\text{CH}_2-$.

In a preferred embodiment

X is selected from the group consisting of $-\text{CH}_2-$, $-\text{CH}_2\text{CH}_2-$ and $-\text{CH}_2\text{CH}_2\text{CH}_2-$.

In a preferred embodiment

20 X is selected from the group consisting of $-\text{NHCH}_2\text{CH}_2-$, $-\text{CH}_2\text{NHCH}_2-$, $-\text{CH}_2\text{NH}(\text{CH}_2)_2-$, $-\text{CH}_2\text{NH}(\text{CH}_2)_3-$, $-\text{CH}_2\text{NH}(\text{CH}_2)_4-$, $-\text{CH}_2\text{N}(\text{methyl})\text{CH}_2-$, $-\text{CH}_2\text{N}(\text{iPr})\text{CH}_2-$, $-\text{CH}_2\text{N}(\text{CH}_2\text{CF}_3)\text{CH}_2-$, $-\text{CH}_2\text{NHCH}(\text{methyl})-$, $-\text{CH}_2\text{N}(\text{methyl})\text{CH}_2\text{CH}_2-$, $-\text{N}(\text{methyl})-$, $-\text{N}(\text{methyl})\text{CH}_2-$, $-\text{N}(\text{methyl})\text{CH}_2\text{CH}_2-$ and $-\text{CH}_2\text{N}(\text{isopropyl})\text{CH}_2-$.

In a preferred embodiment

R_x is hydrogen or a substituted or unsubstituted group selected from methyl, ethyl, isopropyl.

In a preferred embodiment

5 R₁ is hydrogen, bromine, chlorine, -CN or a substituted or unsubstituted group selected from methyl, ethyl, isopropyl, -CF₃, -OH, methoxy, -O-isopropyl, -NH₂, -NHCH₃, -N(CH₃)₂, -N(CH₃)(CH₂-cyclopropyl), -N(CH₃)(benzyl), -N(CH₃)(piperidine), -N(CH₂CF₃)(CH₂-tetrahydropyran), cyclopropyl, phenyl, pyridine, piperidine, pyrrolidine, piperazine, pyrimidine, pyrazole, isoxazole, isothiazole, imidazole, morpholine, thiomorpholine, tetrahydropyran, tetrahydrofuran and thiophene.

10 In a preferred embodiment

R₂ is hydrogen, bromine, chlorine or a substituted or unsubstituted group selected from methyl, ethyl, cyclopropyl, -OH and methoxy.

In a preferred embodiment

R₃ is hydrogen or substituted or unsubstituted methyl.

15 In a preferred embodiment

R₄ is a substituted or unsubstituted group selected from methyl, ethyl, isopropyl, isobutyl, phenyl, pyridine and tetrahydropyran.

In a preferred embodiment

20 R₅ and R₅' are independently selected from hydrogen or a substituted or unsubstituted group selected from methyl and methyl-OH.

In a preferred embodiment

R₅ is selected from hydrogen, methyl and methyl-OH.

In a preferred embodiment

R₅' is hydrogen.

25 In a preferred embodiment

R₅ is selected from hydrogen, methyl and methyl-OH, while R₅' is hydrogen.

In a preferred embodiment

R₆ is hydrogen or a substituted or unsubstituted group selected from methyl, isopropyl, benzyl, piperidine, -CH₂-cyclopropyl, -CH₂-tetrahydropyran.

5 In a preferred embodiment

R₆' is hydrogen or a substituted or unsubstituted group selected from methyl and -CH₂CF₃.

In a preferred embodiment

10 R₆ is hydrogen or a substituted or unsubstituted group selected from methyl, isopropyl, benzyl, piperidine, -CH₂-cyclopropyl, -CH₂-tetrahydropyran, while R₆' is hydrogen or a substituted or unsubstituted group selected from methyl and -CH₂CF₃.

In a preferred embodiment

R₆ is hydrogen.

In a preferred embodiment

15 R₆ is substituted or unsubstituted methyl.

In a preferred embodiment

R₆ is substituted or unsubstituted isopropyl.

In a preferred embodiment

20 R₆ is substituted or unsubstituted methyl, while R₆' is hydrogen or substituted or unsubstituted methyl.

In a preferred embodiment

R₆ is substituted or unsubstituted methyl, while R₆' is hydrogen.

In a preferred embodiment

R₆ and R₆' are both substituted or unsubstituted methyl.

In a preferred embodiment

R₆ and R₆' are both hydrogen.

In a preferred embodiment

- 5 R₆ is substituted or unsubstituted piperidine, while R₆' is substituted or unsubstituted methyl.

In a preferred embodiment

R₆ is substituted or unsubstituted benzyl, while R₆' is substituted or unsubstituted methyl.

In a preferred embodiment

- 10 R₆ is substituted or unsubstituted -CH₂-cyclopropyl, while R₆' is substituted or unsubstituted methyl.

In a preferred embodiment

R₆ is substituted or unsubstituted -CH₂-tetrahydropyran, while R₆' is substituted or unsubstituted -CH₂CF₃.

- 15 In a preferred embodiment

R₆ and R₆' , taken together with the nitrogen atom to which they are attached, form a substituted or unsubstituted heterocyclyl selected from the group consisting of morpholine, thiomorpholine, pyrrolidine and piperazine.

In a preferred embodiment

- 20 R₇ is hydrogen or substituted or unsubstituted methyl.

In a preferred embodiment

R₁₁, R₁₁' and R₁₁'' are hydrogen or a substituted or unsubstituted group selected from methyl, ethyl, -CH₂-cyclopropyl, phenyl, pyridine, triazole and oxadiazole.

In a preferred embodiment

R₁₁ is hydrogen or a substituted or unsubstituted group selected from methyl, ethyl, -CH₂-cyclopropyl, phenyl, pyridine, triazole and oxadiazole.

In a preferred embodiment

R₁₁' is hydrogen or substituted or unsubstituted methyl.

5 In a preferred embodiment

R₁₁ is hydrogen or a substituted or unsubstituted group selected from methyl, ethyl, -CH₂-cyclopropyl, phenyl, pyridine, triazole and oxadiazole, while R₁₁' is hydrogen or substituted or unsubstituted methyl.

In a preferred embodiment

10 R₁₁ is substituted or unsubstituted methyl, while R₁₁' is hydrogen or substituted or unsubstituted methyl.

In a preferred embodiment

R₁₁ is substituted or unsubstituted methyl, while R₁₁' is hydrogen.

In a preferred embodiment

15 R₁₁ and R₁₁' are both hydrogen.

In a preferred embodiment

R₁₁ and R₁₁' are both substituted or unsubstituted methyl.

In a preferred embodiment

R₁₃ and R₁₃' are independently selected from hydrogen and unsubstituted methyl.

20 In a preferred embodiment

R₁₃ is selected from hydrogen and unsubstituted methyl.

In a preferred embodiment

R₁₃' is hydrogen.

In a preferred embodiment

R_{13} is hydrogen or unsubstituted methyl, while R_{13}' is hydrogen.

In a preferred embodiment

R_{14} , R_{14}' and R_{14}'' are independently selected from hydrogen and unsubstituted methyl.

5 In a preferred embodiment

R_{14} is unsubstituted methyl.

In a preferred embodiment

R_{14} is unsubstituted methyl, while R_{14}' is hydrogen.

In a preferred embodiment

10 R_{41} , R_{41}' and R_{41}'' are independently selected from hydrogen and substituted or unsubstituted methyl.

In a preferred embodiment

R_{41} is selected from hydrogen and substituted or unsubstituted methyl.

In a preferred embodiment

15 R_{51} is hydrogen.

In a preferred embodiment

20 the cycloalkyl, aryl or heterocyclyl in R_1 , if substituted, is substituted with one or more substituent/s selected from fluorine, chlorine, methyl, ethyl, $-CF_3$, $-CN$, $-CH_2OH$, $-CH_2OCH_3$, $-OH-OCH_3$, $-OCH_2CH_3$, $-OCH_2$ -cyclopropyl, $=O$, $-CH_2NHCH_3$, $-NH_2$, $-NHCH_3$, $-N(CH_3)_2$, $-C(O)CH_3$, $-C(O)NH_2$, $-C(O)N(CH_3)_2$, $-S(O)_2CH_3$, triazole, oxadiazole, phenyl and pyridine.

In a preferred embodiment

the cycloalkyl, aryl or heterocyclyl in R_4 , if substituted, is substituted with one or more substituent/s selected from fluorine, chlorine, $-CH_3$, $-CF_3$, $-CN$, $-OH$ and $-OCH_3$.

In a preferred embodiment

the alkyl, alkenyl or alkynyl in R_5 and R_5' , if substituted, is substituted with one or more $-OH$.

In a preferred embodiment

- 5 the alkyl, alkenyl or alkynyl, if substituted, and not defined otherwise, is substituted with one or more substituent/s selected from $-OH$, $-OCH_3$ and $-NHCH_3$.

In a preferred embodiment

- 10 the aryl, heterocyclyl or cycloalkyl, also in alkylcycloalkyl, alkylaryl and alkylheterocyclyl, if substituted, and not defined otherwise, is substituted with one or more substituent/s selected from methyl and $-CH_2NHCH_3$.

In a preferred embodiment

the haloalkyl is $-CF_3$.

In a preferred embodiment

the haloalkoxy is $-OCF_3$.

15

In a preferred embodiment, the compounds are selected which act as dual ligands of the $\alpha 2\delta$ subunit, particularly the $\alpha 2\delta-1$ subunit, of the voltage-gated calcium channel and the σ_1 receptor:

EX	CHEMICAL NAME
1	7-(1-Benzylpiperidin-3-yl)-2-bromopyrazolo[1,5-a]pyrimidine
2	7-(1-Benzylpiperidin-3-yl)pyrazolo[1,5-a]pyrimidine
3	7-(1-Benzylpiperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidine
4	7-(1-Benzylpiperidin-3-yl)-2-ethylpyrazolo[1,5-a]pyrimidine

5	7-(1-Benzylpiperidin-3-yl)-3-bromopyrazolo[1,5-a]pyrimidine
6	7-(1-Benzylpiperidin-3-yl)-3-bromo-2,6-dimethylpyrazolo[1,5-a]pyrimidine
7	7-(1-Benzylpiperidin-3-yl)-3-bromo-6-methylpyrazolo[1,5-a]pyrimidine
8	<i>N</i> -(7-(1-Benzylpiperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)acetamide
9	<i>N</i> -(7-(1-Benzylpiperidin-3-yl)-3-methylpyrazolo[1,5-a]pyrimidin-2-yl)acetamide
10	7-(1-Benzylpiperidin-3-yl)-3-bromo-2-methylpyrazolo[1,5-a]pyrimidine
11	7-(1-Benzylpiperidin-3-yl)-3-bromo-2-ethylpyrazolo[1,5-a]pyrimidine
12	7-(1-Benzylpiperidin-3-yl)-2-phenylpyrazolo[1,5-a]pyrimidine
13	7-(1-Benzylpiperidin-3-yl)-2-(4-ethoxyphenyl)pyrazolo[1,5-a]pyrimidine
14	7-(1-Benzylpiperidin-3-yl)-2-(2-fluorophenyl)pyrazolo[1,5-a]pyrimidine
15	7-(1-Benzylpiperidin-3-yl)-2-(4-chlorophenyl)pyrazolo[1,5-a]pyrimidine
16	7-(1-Benzylpiperidin-3-yl)-2-(pyridin-4-yl)pyrazolo[1,5-a]pyrimidine
17	7-(1-Benzylpiperidin-3-yl)-2-(pyridin-3-yl)pyrazolo[1,5-a]pyrimidine
18	7-(1-Benzylpiperidin-3-yl)-2-(3,5-dichloropyridin-4-yl)pyrazolo[1,5-a]pyrimidine
19	7-(1-Benzylpiperidin-3-yl)-2-(thiophen-2-yl)pyrazolo[1,5-a]pyrimidine
20	4-(7-(1-Benzylpiperidin-3-yl)pyrazolo[1,5-a]pyrimidin-2-yl)isothiazole
21	7-(1-Benzylpiperidin-3-yl)-2-(1-methyl-1 <i>H</i> -imidazol-5-yl)pyrazolo[1,5-a]pyrimidine
22	4-(7-(1-Benzylpiperidin-3-yl)pyrazolo[1,5-a]pyrimidin-2-yl)- <i>N,N</i> -dimethylaniline
23	7-(1-Benzylpiperidin-3-yl)-2-(pyrimidin-5-yl)pyrazolo[1,5-a]pyrimidine
24	5-(7-(1-Benzylpiperidin-3-yl)pyrazolo[1,5-a]pyrimidin-2-yl)pyridin-2-amine
25	7-(1-Benzylpiperidin-3-yl)-2-(1-methyl-1 <i>H</i> -pyrazol-4-yl)pyrazolo[1,5-a]pyrimidine

26	7-(1-Benzylpiperidin-3-yl)-2-(pyridin-2-yl)pyrazolo[1,5-a]pyrimidine
27	7-(1-Benzylpiperidin-3-yl)-2-(2-methoxypyridin-3-yl)pyrazolo[1,5-a]pyrimidine
28	7-(1-Benzylpiperidin-3-yl)-2-(6-methoxypyridin-3-yl)pyrazolo[1,5-a]pyrimidine
29	7-(1-Benzylpiperidin-3-yl)-2-(2-methoxyphenyl)pyrazolo[1,5-a]pyrimidine
30	7-(1-Benzylpiperidin-3-yl)-2-(6-methoxypyridin-2-yl)pyrazolo[1,5-a]pyrimidine
31	7-(1-Benzylpiperidin-3-yl)-2-(5-methoxypyridin-3-yl)pyrazolo[1,5-a]pyrimidine
32	7-(1-Benzylpiperidin-3-yl)-2-(2-methoxypyridin-4-yl)pyrazolo[1,5-a]pyrimidine
33	7-(1-Benzylpiperidin-3-yl)-2-(3-methoxypyridin-4-yl)pyrazolo[1,5-a]pyrimidine
34	7-(1-Benzylpiperidin-3-yl)-2-(4-methoxypyridin-3-yl)pyrazolo[1,5-a]pyrimidine
35	7-(1-Benzylpiperidin-3-yl)-3-phenylpyrazolo[1,5-a]pyrimidine
36	7-(1-Benzylpiperidin-3-yl)-3-(pyridin-4-yl)pyrazolo[1,5-a]pyrimidine
37	7-(1-Benzylpiperidin-3-yl)-3-(pyridin-3-yl)pyrazolo[1,5-a]pyrimidine
38	7-(1-Benzylpiperidin-3-yl)-3-(2-methoxypyridin-4-yl)pyrazolo[1,5-a]pyrimidine
39	7-(1-Benzylpiperidin-3-yl)-3-(4-ethoxyphenyl)pyrazolo[1,5-a]pyrimidine
40	7-(1-Benzylpiperidin-3-yl)-3-(2-methoxypyridin-3-yl)pyrazolo[1,5-a]pyrimidine
41	7-(1-Benzylpiperidin-3-yl)-6-methyl-3-(pyridin-4-yl)pyrazolo[1,5-a]pyrimidine
42	7-(1-Benzylpiperidin-3-yl)-2-methyl-3-(pyridin-4-yl)pyrazolo[1,5-a]pyrimidine
43	7-(1-Benzylpiperidin-3-yl)-3-(2-methoxypyridin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidine
44	7-(1-Benzylpiperidin-3-yl)-2-methyl-3-phenylpyrazolo[1,5-a]pyrimidine
45	7-(1-Benzylpiperidin-3-yl)-3-(4-ethoxyphenyl)-2-methylpyrazolo[1,5-a]pyrimidine
46	7-(1-Benzylpiperidin-3-yl)-3-(2-methoxypyridin-4-yl)-2-methylpyrazolo[1,5-a]pyrimidine

47	4-(7-(1-Benzylpiperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-N,N-dimethylaniline
48	7-(1-Benzylpiperidin-3-yl)-3-(2-fluorophenyl)-2-methylpyrazolo[1,5-a]pyrimidine
49	7-(1-Benzylpiperidin-3-yl)-2-methyl-3-(3-methylpyridin-4-yl)pyrazolo[1,5-a]pyrimidine
50	7-(1-Benzylpiperidin-3-yl)-3-(2-fluoropyridin-4-yl)-2-methylpyrazolo[1,5-a]pyrimidine
51	7-(1-Benzylpiperidin-3-yl)-2-methyl-3-(2-methylpyridin-4-yl)pyrazolo[1,5-a]pyrimidine
52	7-(1-Benzylpiperidin-3-yl)-3-(3-fluoropyridin-4-yl)-2-methylpyrazolo[1,5-a]pyrimidine
53	7-(1-Benzylpiperidin-3-yl)-2-methyl-3-(2-(trifluoromethyl)pyridin-4-yl)pyrazolo[1,5-a]pyrimidine
54	7-(1-Benzylpiperidin-3-yl)-3-(2-ethylpyridin-4-yl)-2-methylpyrazolo[1,5-a]pyrimidine
55	3-(3-(7-(1-Benzylpiperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)phenyl)-5-methyl-1,2,4-oxadiazole
56	2-(3-(7-(1-Benzylpiperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)phenyl)-5-methyl-1,3,4-oxadiazole
57	7-(1-Benzylpiperidin-3-yl)-3-(3-methoxypyridin-4-yl)-2-methylpyrazolo[1,5-a]pyrimidine
58	7-(1-Benzylpiperidin-3-yl)-2,6-dimethyl-3-(pyridin-4-yl)pyrazolo[1,5-a]pyrimidine
59	7-(1-Benzylpiperidin-3-yl)-2,5-dimethyl-3-(pyridin-4-yl)pyrazolo[1,5-a]pyrimidine
60	7-(1-Benzylpiperidin-3-yl)-2-ethyl-3-(pyridin-4-yl)pyrazolo[1,5-a]pyrimidine
61	1-(1-(3-(7-(1-Benzylpiperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)phenyl)-1H-1,2,3-triazol-4-yl)-N-methylmethanamine
62	1-(4-(7-(1-Benzylpiperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)pyridin-2-yl)-N-methylmethanamine
63	7-(1-(2-Fluorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidine
64	7-(1-Butylpiperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidine
65	7-(1-(2,6-Difluorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidine
66	2-Methyl-7-(1-(pyridin-2-ylmethyl)piperidin-3-yl)pyrazolo[1,5-a]pyrimidine
67	2-Methyl-7-(1-phenethylpiperidin-3-yl)pyrazolo[1,5-a]pyrimidine

68	3-((3-(2-Methylpyrazolo[1,5-a]pyrimidin-7-yl)piperidin-1-yl)methyl)phenol
69	7-(1-Ethylpiperidin-3-yl)-2-methyl-3-(pyridin-4-yl)pyrazolo[1,5-a]pyrimidine
70	2-Methyl-7-(1-propylpiperidin-3-yl)-3-(pyridin-4-yl)pyrazolo[1,5-a]pyrimidine
71	7-(1-Isobutylpiperidin-3-yl)-2-methyl-3-(pyridin-4-yl)pyrazolo[1,5-a]pyrimidine
72	2-Methyl-7-(1-(pyridin-2-ylmethyl)piperidin-3-yl)-3-(pyridin-4-yl)pyrazolo[1,5-a]pyrimidine
73	6-Methyl-7-(1-phenethylpiperidin-3-yl)-3-(pyridin-4-yl)pyrazolo[1,5-a]pyrimidine
74	6-Methyl-7-(1-(pyridin-2-ylmethyl)piperidin-3-yl)-3-(pyridin-4-yl)pyrazolo[1,5-a]pyrimidine
75	2-Methyl-7-(1-(2-methylbenzyl)piperidin-3-yl)-3-(pyridin-4-yl)pyrazolo[1,5-a]pyrimidine
76	2-Methyl-7-(1-(4-methylbenzyl)piperidin-3-yl)-3-(pyridin-4-yl)pyrazolo[1,5-a]pyrimidine
77	2-Methyl-7-(1-(3-methylbenzyl)piperidin-3-yl)-3-(pyridin-4-yl)pyrazolo[1,5-a]pyrimidine
78	7-(1-Benzylpiperidin-3-yl)-2-(pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidine
79	2-((7-(1-Benzylpiperidin-3-yl)pyrazolo[1,5-a]pyrimidin-2-yl)(methyl)amino)ethanol
80	<i>N</i> ¹ -(7-(1-Benzylpiperidin-3-yl)pyrazolo[1,5-a]pyrimidin-2-yl)- <i>N</i> ¹ -methylethane-1,2-diamine
81	<i>N</i> ¹ -(7-(1-Benzylpiperidin-3-yl)pyrazolo[1,5-a]pyrimidin-2-yl)- <i>N</i> ¹ , <i>N</i> ² -dimethylethane-1,2-diamine
82	7-(1-Benzylpiperidin-3-yl)- <i>N</i> -methyl- <i>N</i> -(piperidin-4-yl)pyrazolo[1,5-a]pyrimidin-2-amine
83	<i>N</i> ¹ -(7-(1-Benzylpiperidin-3-yl)pyrazolo[1,5-a]pyrimidin-2-yl)- <i>N</i> ² -methylethane-1,2-diamine
84	(<i>R</i>)-1-(7-((<i>R</i>)-1-Benzylpiperidin-3-yl)pyrazolo[1,5-a]pyrimidin-2-yl)- <i>N</i> -methylpyrrolidin-3-amine
85	(<i>S</i>)-1-(7-((<i>S</i>)-1-Benzylpiperidin-3-yl)pyrazolo[1,5-a]pyrimidin-2-yl)- <i>N</i> -methylpyrrolidin-3-amine
86	(<i>S</i>)-1-(7-((<i>R</i>)-1-Benzylpiperidin-3-yl)pyrazolo[1,5-a]pyrimidin-2-yl)- <i>N</i> -methylpyrrolidin-3-amine
87	(<i>R</i>)-1-(7-((<i>S</i>)-1-Benzylpiperidin-3-yl)pyrazolo[1,5-a]pyrimidin-2-yl)- <i>N</i> -methylpyrrolidin-3-amine
88	7-(1-Benzylpiperidin-3-yl)-3-(pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidine

89	7-(1-Benzylpiperidin-3-yl)-2-methyl-3-(pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidine
90	7-(1-Benzylpiperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-amine
91	7-(1-Benzylpiperidin-3-yl)pyrazolo[1,5-a]pyrimidine-2-carbonitrile
92	1-(7-(1-Benzylpiperidin-3-yl)pyrazolo[1,5-a]pyrimidin-2-yl)- <i>N,N</i> -dimethylmethanamine
93	1-(7-(1-Benzylpiperidin-3-yl)pyrazolo[1,5-a]pyrimidin-2-yl)- <i>N</i> -methylmethanamine
94	<i>N</i> -Benzyl-1-(7-(1-benzylpiperidin-3-yl)pyrazolo[1,5-a]pyrimidin-2-yl)methanamine
95	(7-(1-Benzylpiperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methanol
96	1-(7-(1-Benzylpiperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)- <i>N</i> -methylmethanamine
97	<i>N</i> -((7-(1-Benzylpiperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methyl)-2-phenylethanamine
98	<i>N</i> -Benzyl-1-(7-(1-benzylpiperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methanamine
99	(7-(1-Benzylpiperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methanamine
100	7-(1-Benzylpiperidin-3-yl)-2-methyl-3-(piperazin-1-ylmethyl)pyrazolo[1,5-a]pyrimidine
101	3-((Benzyloxy)methyl)-7-(1-benzylpiperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidine
102	7-(1-Benzylpiperidin-3-yl)-2-methyl-3-(phenoxy)methylpyrazolo[1,5-a]pyrimidine
103	3-(7-(1-Benzylpiperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)propan-1-amine
104	7-(1-Benzylpiperidin-3-yl)pyrazolo[1,5-a]pyrimidin-2-ol
105	7-(1-Benzylpiperidin-3-yl)-3-bromopyrazolo[1,5-a]pyrimidin-2-ol
106	(<i>S</i>)-2-((<i>R</i>)-3-(2-Methyl-3-(pyridin-4-yl)pyrazolo[1,5-a]pyrimidin-7-yl)piperidin-1-yl)-2-phenylethanol
107	(<i>S</i>)-2-((<i>S</i>)-3-(2-methyl-3-(pyridin-4-yl)pyrazolo[1,5-a]pyrimidin-7-yl)piperidin-1-yl)-2-phenylethanol
108	(<i>R</i>)-2-((<i>S</i>)-3-(2-Methyl-3-(pyridin-4-yl)pyrazolo[1,5-a]pyrimidin-7-yl)piperidin-1-yl)-2-phenylethanol
109	(<i>R</i>)-2-((<i>R</i>)-3-(2-Methyl-3-(pyridin-4-yl)pyrazolo[1,5-a]pyrimidin-7-yl)piperidin-1-yl)-2-phenylethanol

110	2-Bromo-7-(1-(4-chlorobenzyl)piperidin-3-yl)pyrazolo[1,5-a]pyrimidine
111	2-Bromo-7-(1-(3-chlorobenzyl)piperidin-3-yl)pyrazolo[1,5-a]pyrimidine
112	2-Bromo-7-(1-(3,4-dichlorobenzyl)piperidin-3-yl)pyrazolo[1,5-a]pyrimidine
113	2-Bromo-7-(1-(3,4-difluorobenzyl)piperidin-3-yl)pyrazolo[1,5-a]pyrimidine
114	7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-(2-methoxypyridin-3-yl)pyrazolo[1,5-a]pyrimidine
115	3-(7-(1-(4-Chlorobenzyl)piperidin-3-yl)pyrazolo[1,5-a]pyrimidin-2-yl)pyridin-2-ol
116	7-(1-(3-Chlorobenzyl)piperidin-3-yl)-2-(2-methoxypyridin-3-yl)pyrazolo[1,5-a]pyrimidine
117	3-(7-(1-(3-Chlorobenzyl)piperidin-3-yl)pyrazolo[1,5-a]pyrimidin-2-yl)pyridin-2-ol
118	7-(1-(3,4-Dichlorobenzyl)piperidin-3-yl)-2-(2-methoxypyridin-3-yl)pyrazolo[1,5-a]pyrimidine
119	7-(1-(3,4-Difluorobenzyl)piperidin-3-yl)-2-(2-methoxypyridin-3-yl)pyrazolo[1,5-a]pyrimidine
120	1-(2-Bromo-7-(1-(4-chlorobenzyl)piperidin-3-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-N-((tetrahydro-2H-pyran-4-yl)methyl)methanamine
121	7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methyl-3-(pyridin-4-yl)pyrazolo[1,5-a]pyrimidine
122	7-(1-(3-Chlorobenzyl)piperidin-3-yl)-2-methyl-3-(pyridin-4-yl)pyrazolo[1,5-a]pyrimidine
123	7-(1-(3,4-Dichlorobenzyl)piperidin-3-yl)-2-methyl-3-(pyridin-4-yl)pyrazolo[1,5-a]pyrimidine
124	7-(1-(2,4-Dichlorobenzyl)piperidin-3-yl)-2-methyl-3-(pyridin-4-yl)pyrazolo[1,5-a]pyrimidine
125	7-(1-(3,4-Difluorobenzyl)piperidin-3-yl)-2-methyl-3-(pyridin-4-yl)pyrazolo[1,5-a]pyrimidine
126	2-Methyl-3-(pyridin-4-yl)-7-(1-(4-(trifluoromethyl)benzyl)piperidin-3-yl)pyrazolo[1,5-a]pyrimidine
127	7-(1-Isopentylpiperidin-3-yl)-2-methyl-3-(pyridin-4-yl)pyrazolo[1,5-a]pyrimidine
128	3-(7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-N,N-dimethylbenzamide
129	4-(7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)benzamide
130	7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methyl-3-(pyrimidin-5-yl)pyrazolo[1,5-a]pyrimidine

131	5-(7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)pyrimidin-2-amine
132	7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methyl-3-(1-methyl-1 <i>H</i> -pyrazol-4-yl)pyrazolo[1,5-a]pyrimidine
133	4-(7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-3,5-dimethylisoxazole
134	(4-(7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)pyridin-2-yl)methanol
135	(5-(7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)pyridin-2-yl)methanol
136	7-(1-(4-Chlorobenzyl)piperidin-3-yl)-3-(2-ethoxypyridin-4-yl)-2-methylpyrazolo[1,5-a]pyrimidine
137	7-(1-(4-Chlorobenzyl)piperidin-3-yl)-3-(2-(cyclopropylmethoxy)pyridin-4-yl)-2-methylpyrazolo[1,5-a]pyrimidine
138	7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methyl-3-(1-methyl-1 <i>H</i> -imidazol-5-yl)pyrazolo[1,5-a]pyrimidine
139	7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methyl-3-(pyrimidin-4-yl)pyrazolo[1,5-a]pyrimidine
140	4-(7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)pyrimidin-2-amine
141	7-(1-(4-Chlorobenzyl)piperidin-3-yl)- <i>N,N</i> ,2-trimethylpyrazolo[1,5-a]pyrimidin-3-amine
142	7-(1-Benzylpiperidin-3-yl)- <i>N,N</i> ,2-trimethylpyrazolo[1,5-a]pyrimidin-3-amine
143	<i>N</i> -Benzyl-7-(1-benzylpiperidin-3-yl)- <i>N,N</i> ,2-dimethylpyrazolo[1,5-a]pyrimidin-3-amine
144	<i>N</i> -Benzyl-1-(7-(1-(4-chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methanamine
145	<i>N</i> -Benzyl-1-(7-(1-(4-chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)- <i>N</i> -methylmethanamine
146	1-(7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)- <i>N</i> -(4-fluorobenzyl)methanamine
147	(4-(((7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methyl)amino)methyl)phenyl)methanol
148	1-(7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)- <i>N</i> -(pyridin-4-ylmethyl)methanamine
149	1-(7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)- <i>N</i> -(thiophen-2-ylmethyl)methanamine
150	1-(7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)- <i>N</i> -((5-methylthiophen-2-yl)methyl)methanamine
151	1-(7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)- <i>N</i> -((1-methyl-1 <i>H</i> -pyrazol-3-yl)methyl)methanamine

152	1-(7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-N-((5-methyl-1,3,4-oxadiazol-2-yl)methyl)methanamine
153	N-((7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methyl)-2-phenylethan-1-amine
154	N-((7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methyl)-2-(4-methoxyphenyl)ethan-1-amine
155	N-((7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methyl)ethanamine
156	N-((7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methyl)-2,2,2-trifluoroethan-1-amine
157	1-(7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-N-(cyclopropylmethyl)methanamine
158	2-(((7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methyl)amino)ethan-1-ol
159	N-((7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methyl)propan-2-amine
160	N-((7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methyl)-2-methylpropan-1-amine
161	N-((7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methyl)-3-methylbutan-1-amine
162	N-((7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methyl)-2-isopropoxyethan-1-amine
163	N-((7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methyl)-4-methoxybutan-1-amine
164	(2S,6R)-4-((7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methyl)-2,6-dimethylmorpholine
165	4-((7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methyl)morpholine
166	N-((7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methyl)-2-morpholinoethan-1-amine
167	4-((7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methyl)thiomorpholine
168	4-((7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methyl)thiomorpholine 1,1-dioxide
169	7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methyl-3-(piperidin-1-ylmethyl)pyrazolo[1,5-a]pyrimidine
170	7-(1-(4-Chlorobenzyl)piperidin-3-yl)-3-((4-(methoxymethyl)piperidin-1-yl)methyl)-2-methylpyrazolo[1,5-a]pyrimidine
171	1-((7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methyl)piperidine-4-carboxamide
172	1-((7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methyl)piperidine-4-carbonitrile

173	4-((7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methyl)piperazin-2-one
174	1-(4-((7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methyl)piperazin-1-yl)ethan-1-one
175	7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methyl-3-((4-(methylsulfonyl)piperazin-1-yl)methyl)pyrazolo[1,5-a]pyrimidine
176	1-(3-(((7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methyl)amino)propyl)pyrrolidin-2-one
177	1-(7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-N-((4-fluorotetrahydro-2H-pyran-4-yl)methyl)methanamine
178	N-((7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methyl)-(tetrahydro-2H-pyran-4-yl)ethan-1-amine
179	1-(7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-N-((1-(methylsulfonyl)piperidin-4-yl)methyl)methanamine
180	1-(4-(((7-(1-Benzylpiperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methyl)amino)methyl)piperidin-1-yl)ethan-1-one
181	1-(7-(1-(3-Fluorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-N-((tetrahydro-2H-pyran-4-yl)methyl)methanamine
182	1-(7-(1-(3,4-Difluorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-N-((tetrahydro-2H-pyran-4-yl)methyl)methanamine
183	4-((3-(2-Methyl-3-(((tetrahydro-2H-pyran-4-yl)methyl)amino)methyl)pyrazolo[1,5-a]pyrimidin-7-yl)piperidin-1-yl)methyl)benzonitrile
184	1-(2-Methyl-7-(1-((6-(trifluoromethyl)pyridin-3-yl)methyl)piperidin-3-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-N-((tetrahydro-2H-pyran-4-yl)methyl)methanamine
185	1-(2-Methyl-7-(1-((tetrahydro-2H-pyran-4-yl)methyl)piperidin-3-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-N-((tetrahydro-2H-pyran-4-yl)methyl)methanamine
186	1-(7-(1-(2,4-Dichlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-N,N-dimethylmethanamine
187	1-(7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-ethylpyrazolo[1,5-a]pyrimidin-3-yl)-N-((tetrahydro-2H-pyran-4-yl)methyl)methanamine
188	1-(7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-cyclopropylpyrazolo[1,5-a]pyrimidin-3-yl)-N-((tetrahydro-2H-pyran-4-yl)methyl)methanamine
189	1-(7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methoxypyrazolo[1,5-a]pyrimidin-3-yl)-N-((tetrahydro-2H-pyran-4-yl)methyl)methanamine
190	1-(2-Chloro-7-(1-(4-chlorobenzyl)piperidin-3-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-N-((tetrahydro-2H-pyran-4-yl)methyl)methanamine
191	1-(2-Chloro-7-(1-isopentylpiperidin-3-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-N-((tetrahydro-2H-pyran-4-yl)methyl)methanamine
192	1-(4-(((2-Chloro-7-(1-isopentylpiperidin-3-yl)pyrazolo[1,5-a]pyrimidin-3-yl)methyl)amino)methyl)piperidin-1-yl)ethan-1-one
193	(S)-1-(4-(((7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methyl)amino)methyl)piperidin-1-yl)ethan-1-one

194	(R)-1-(4-(((7-(1-(4-chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methyl)amino)methyl)piperidin-1-yl)ethan-1-one
195	(R)-N-((7-((R)-1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methyl)-1-phenylethan-1-amine
196	(R)-N-((7-((S)-1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methyl)-1-phenylethan-1-amine
197	(S)-N-((7-((R)-1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methyl)-1-phenylethan-1-amine
198	(S)-N-((7-((S)-1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methyl)-1-phenylethan-1-amine
199	(S)-1-(7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-N-((tetrahydro-2H-pyran-4-yl)methyl)methanamine
200	(R)-1-(7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-N-((tetrahydro-2H-pyran-4-yl)methyl)methanamine
201	(+/-)-1-(7-((R/S)-1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-N-(((S/R)-tetrahydrofuran-3-yl)methyl)methanamine
202	1-(7-((R)-1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-N-((R)-tetrahydrofuran-3-yl)methyl)methanamine
203	1-(7-((S)-1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-N-((S)-tetrahydrofuran-3-yl)methyl)methanamine
204	(S)-1-(7-(1-Benzylpiperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-N-((tetrahydro-2H-pyran-4-yl)methyl)methanamine
205	(R)-1-(7-(1-Benzylpiperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-N-((tetrahydro-2H-pyran-4-yl)methyl)methanamine
206	(S)-1-(7-(1-(4-Fluorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-N-((tetrahydro-2H-pyran-4-yl)methyl)methanamine
207	(R)-1-(7-(1-(4-Fluorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-N-((tetrahydro-2H-pyran-4-yl)methyl)methanamine
208	(S)-3-((3-(2-Methyl-3-(((tetrahydro-2H-pyran-4-yl)methyl)amino)methyl)pyrazolo[1,5-a]pyrimidin-7-yl)piperidin-1-yl)methyl)benzonitrile
209	(R)-3-((3-(2-Methyl-3-(((tetrahydro-2H-pyran-4-yl)methyl)amino)methyl)pyrazolo[1,5-a]pyrimidin-7-yl)piperidin-1-yl)methyl)benzonitrile
210	(S)-1-(7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-N,N-dimethylmethanamine
211	(R)-1-(7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-N,N-dimethylmethanamine
212	(R)-1-(7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-N-methylmethanamine
213	(S)-1-(7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-N-methylmethanamine
214	((S)-1-(7-(1-Benzylpiperidin-3-yl)-2-chloropyrazolo[1,5-a]pyrimidin-3-yl)-N-((tetrahydro-2H-pyran-4-yl)methyl)methanamine

215	((R)-1-(7-(1-Benzylpiperidin-3-yl)-2-chloropyrazolo[1,5-a]pyrimidin-3-yl)-N-((tetrahydro-2H-pyran-4-yl)methyl)methanamine
216	(S)-1-(4-(((7-(1-Benzylpiperidin-3-yl)-2-chloropyrazolo[1,5-a]pyrimidin-3-yl)methyl)amino)methyl)piperidin-1-yl)ethan-1-one
217	(R)-1-(4-(((7-(1-benzylpiperidin-3-yl)-2-chloropyrazolo[1,5-a]pyrimidin-3-yl)methyl)amino)methyl)piperidin-1-yl)ethan-1-one
218	4-(((7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methyl)amino)methyl)piperidine-1-carboxamide
219	(7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methanamine
220	1-(7-(1-Benzylpiperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-N-(((2R,6S)-2,6-dimethyltetrahydro-2H-pyran-4-yl)methyl)methanamine
221	(+/-)-1-(7-(((R/S)-1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-N-(((R/S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)methyl)methanamine
222	(1-(7-((R)-1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-N-((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)methyl)methanamine
223	(1-(7-((S)-1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-N-((R)-2,2-dimethyltetrahydro-2H-pyran-4-yl)methyl)methanamine
224	(+/-)-(R/S)-N-((7-((R/S)-1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methyl)-1-(tetrahydro-2H-pyran-4-yl)ethan-1-amine
225	(S)-N-((7-((R)-1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methyl)-1-(tetrahydro-2H-pyran-4-yl)ethan-1-amine
226	(R)-N-((7-((S)-1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methyl)-1-(tetrahydro-2H-pyran-4-yl)ethan-1-amine
227	(R)-1-(7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-N-(cyclopropylmethyl)-N-methylmethanamine
228	(S)-1-(7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-N-(cyclopropylmethyl)-N-methylmethanamine
229	1-(7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-N-(2,6-difluorobenzyl)-N-methylmethanamine
230	(4-(((7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methyl)(methyl)amino)methyl)phenyl)methanol
231	1-(7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-N-methyl-N-((tetrahydro-2H-pyran-4-yl)methyl)methanamine
232	N-((7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methyl)-N-((tetrahydro-2H-pyran-4-yl)methyl)propan-2-amine
233	N-((7-(1-Benzylpiperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methyl)-N-(((2R,6S)-2,6-dimethyltetrahydro-2H-pyran-4-yl)methyl)propan-2-amine
234	1-(7-(1-Benzylpiperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-N-(cyclopropylmethyl)-N-methylmethanamine
235	N-((7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methyl)-2,2,2-trifluoro-N-((tetrahydro-2H-pyran-4-yl)methyl)ethan-1-amine

236	2-(7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-N,N-dimethylethan-1-amine
237	1-(7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2,6-dimethylpyrazolo[1,5-a]pyrimidin-3-yl)-N-((tetrahydro-2H-pyran-4-yl)methyl)methanamine
238	1-(7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2,5-dimethylpyrazolo[1,5-a]pyrimidin-3-yl)-N-((tetrahydro-2H-pyran-4-yl)methyl)methanamine
239	(S)-1-(7-(1-(2-Fluorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-N-((tetrahydro-2H-pyran-4-yl)methyl)methanamine
240	(S)-1-(7-(1-(2,4-Difluorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-N-((tetrahydro-2H-pyran-4-yl)methyl)methanamine
241	(S)-1-(7-(1-(3,5-Difluorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-N-((tetrahydro-2H-pyran-4-yl)methyl)methanamine
242	1-(7-(1-(4-Methoxybenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-N-((tetrahydro-2H-pyran-4-yl)methyl)methanamine
243	(R)-4-((((7-((S)-1-Benzylpiperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methyl)amino)methyl)-1-methylpiperidin-2-one
244	(S)-4-((((7-((S)-1-Benzylpiperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methyl)amino)methyl)-1-methylpiperidin-2-one
245	(R)-5-((((7-((S)-1-Benzylpiperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methyl)amino)methyl)piperidin-2-one
246	(S)-5-((((7-((S)-1-Benzylpiperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methyl)amino)methyl)piperidin-2-one
247	(S)-1-(4-((((7-(1-(3,4-Difluorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methyl)amino)methyl)piperidin-1-yl)ethan-1-one
248	1-(7-(1-Benzylpiperidin-3-yl)-2-methoxypyrazolo[1,5-a]pyrimidin-3-yl)-N-((tetrahydro-2H-pyran-4-yl)methyl)methanamine
249	7-((1-(4-Chlorobenzyl)piperidin-3-yl)methyl)-2-methyl-3-(pyridin-4-yl)pyrazolo[1,5-a]pyrimidine
250	7-((1-(3-Chlorobenzyl)piperidin-3-yl)methyl)-2-methyl-3-(pyridin-4-yl)pyrazolo[1,5-a]pyrimidine
251	1-(7-((1-(4-Chlorobenzyl)piperidin-3-yl)methyl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-N,N-dimethylmethanamine
252	1-(7-((1-(3-Chlorobenzyl)piperidin-3-yl)methyl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-N,N-dimethylmethanamine
253	1-(7-(1-(4-Chlorobenzyl)azepan-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-N-((tetrahydro-2H-pyran-4-yl)methyl)methanamine

optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding salt thereof, or a corresponding solvate thereof.

In the following the phrase “compound of the invention” is used. This is to be understood as any compound according to the invention as described above according to general Formulae (I), (I'), (I^{2'}), (I^{2a'}), (I^{3'}) or (I^{3a'}).

5 The compounds of the invention represented by the above described Formula (I) may include enantiomers depending on the presence of chiral centres or isomers depending on the presence of multiple bonds (e.g. Z, E). The single isomers, enantiomers or diastereoisomers and mixtures thereof fall within the scope of the present invention.

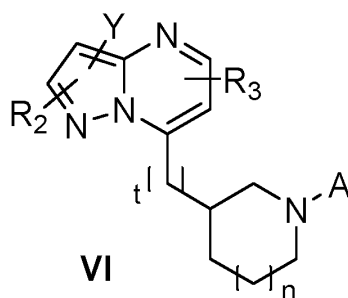
10 For the sake of clarity the expression “a compound according to Formula (I), wherein e.g. R₁, R₂, R₃, R₄, R₅, R_{5'}, X, m, n and t are as defined below in the detailed description” would (just like the expression “a compound of Formula (I) as defined in any one of claims e.g. 1 to 8” found in the claims) refer to “a compound according to Formula (I)”, wherein the definitions of the respective substituents R₁ etc. (also from the cited claims) are applied. In addition, this would also mean, though (especially in
15 regards to the claims) that also one or more disclaimers or provisos defined in the description (or used in any of the cited claims like e.g. claim 1) would be applicable to define the respective compound. Thus, a disclaimer or a proviso found in e.g. claim 1 would be also used to define the compound “of Formula (I) as defined in any one of the corresponding related claims e.g. 1 to 8”.

20 In general the processes are described below in the experimental part. The starting materials are commercially available or can be prepared by conventional methods.

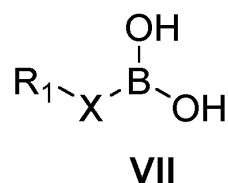
A preferred embodiment of the invention is a process for the production of a compound according to Formula (I), wherein, if not defined otherwise, R₁, R₂, R₃, R₄, R₅, R_{5'}, X, m, n and t have the meanings defined in the description.

25

In a particular embodiment there is a process for the production of a compound according to Formula (I), said process comprises treating a compound of formula (VI) in which A is $-(CR_5R_5')_m-R_4$ and Y is an halogen atom,



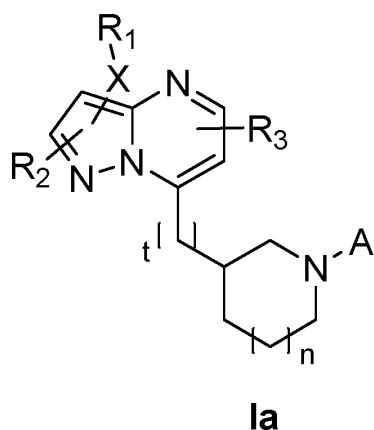
with a suitable boronic acid (or boronic ester) of formula (VII),



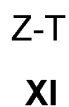
- 5 wherein R_1 , R_2 , R_3 , R_4 , R_5 , R_5' , X , m , n and t have the meanings as defined in the description.

The reaction can be carried out in the presence of a suitable Pd catalyst, such as $\text{Pd}(\text{PPh}_3)_4$, with a suitable base, such as K_2CO_3 or Na_2CO_3 , in a suitable solvent, such as mixtures of dimethoxyethane and water or mixtures of toluene, ethanol and water,
 10 at a suitable temperature, preferably heating. Alternatively, the reactions can be carried out under microwave heating.

In another particular embodiment there is a process for the production of a compound according to Formula (I), said process comprises alkylating a compound of formula (Ia)
 15 in which A is hydrogen,



with a suitable alkylating reagent of formula XI,

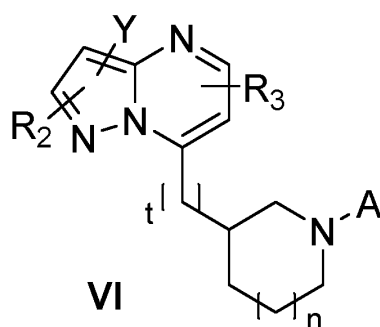


wherein T is $-(CR_5R_5')_m-R_4$ and Z is a leaving group such as iodine, bromine, chlorine;

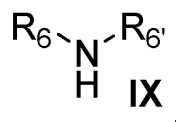
- 5 or alternatively by a reductive amination reaction with a suitable aldehyde of formula (XI), wherein Z is =O;

wherein R_1 , R_2 , R_3 , R_4 , R_5 , R_5' , X, m, n and t have the meanings as defined in the description.

- 10 In a particular embodiment there is a process for the production of a compound according to Formula (I), wherein R_1 is $-CH_2NR_6R_6'$, said process comprises reacting a compound of formula (VI) in which A is $-(CR_5R_5')_m-R_4$ and Y is an acid functionality,



with a suitable amine of formula (IX)



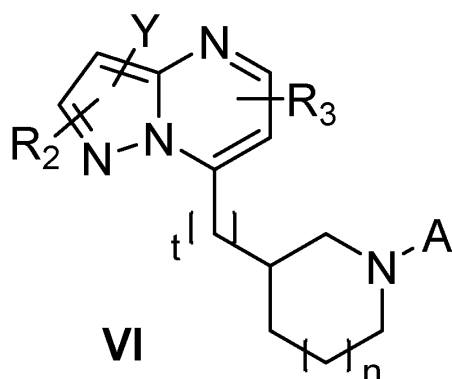
- 5 wherein and R_2 , R_3 , R_4 , R_5 , R_5' , R_6 , R_6' , m , n and t have the meanings as defined in the description.

The reaction can be carried out in the presence of a suitable coupling agent, such as *N*-(3-dimethylaminopropyl)-*N'*-ethylcarbodiimide hydrochloride, in the presence of a base, such as triethylamine, in a suitable solvent, such as dimethylformamide, at a suitable temperature, preferably room temperature; followed by reduction using a suitable reducing agent, such as AlH_3 , in a suitable solvent, such as tetrahydrofuran, at a suitable temperature, preferably between 0 °C and room temperature.

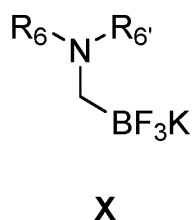
10

In a particular embodiment there is a process for the production of a compound according to Formula (I), wherein R_1 is $-CH_2NR_6R_6'$, said process comprises reacting a compound of formula (VI), in which A is $-(CR_5R_5')_m-R_4$ and Y is an halogen atom,

15



with a suitable potassium aminomethyltrifluoroborate salt of formula (X)

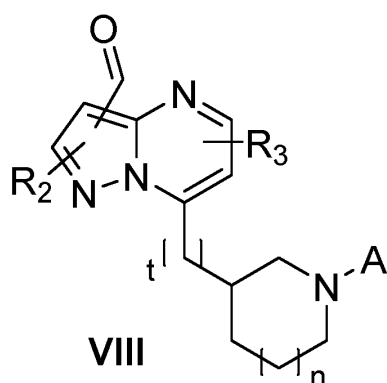


5 wherein R_2 , R_3 , R_4 , R_5 , R_5' , R_6 , R_6' , m , n and t have the meanings as defined in the description.

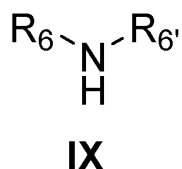
The reaction can be carried out in the presence of a suitable Pd catalyst, such as allylpalladium(II) chloride dimer, with a suitable base, such as K_3PO_4 , and a suitable phosphine ligand, such as dicyclohexyl(2',6'-dimethoxy-[1,1'-biphenyl]-2-yl)phosphine, in a suitable solvent, such as a mixture of dioxane and water, at a suitable temperature, preferably 100 °C.

10

In a particular embodiment there is a process for the production of a compound according to Formula (I), wherein R_1 is $-CH_2NR_6R_6'$, said process comprises reacting a compound of formula (VIII) in which A is $-(CR_5R_5')_m-R_4$,



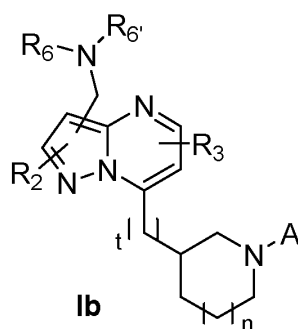
with a suitable amine of formula (IX)



wherein R_2 , R_3 , R_4 , R_5 , R_5' , R_6 , R_6' , m , n and t have the meanings as defined in the description.

The reaction can be carried out in the presence of a reducing reagent, such as sodium triacetoxyborohydride or sodium cyanoborohydride, in a suitable solvent, such as dichloromethane or methanol, optionally in the presence of an acid, preferably acetic acid, at a suitable temperature, preferably room temperature. Alternatively, the reactions can be carried out under microwave heating.

In a particular embodiment there is a process for the production of a compound according to Formula (I), wherein R_1 is $-\text{CH}_2\text{NR}_6\text{R}_6'$, said process comprises the alkylation of a derivative of Formula (Ib) in which A is hydrogen,



with a suitable alkylating reagent of formula (XI),

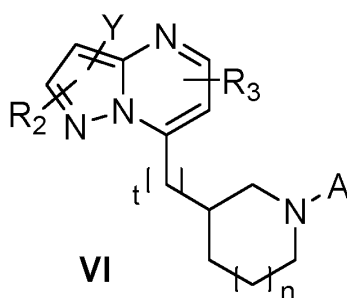


wherein T is $-(\text{CR}_5\text{R}_5')_m\text{-R}_4$ and Z is a leaving group such as iodine, bromine, chlorine;

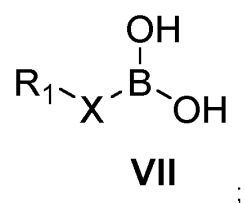
- 5 or alternatively by a reductive amination reaction with a suitable aldehyde of formula XI, where Z is =O;

wherein R_2 , R_3 , R_4 , R_5 , R_5' , R_6 , R_6' , m , n and t have the meanings as defined in the description.

- 10 In a particular embodiment there is a process for the production of a compound according to Formula (I), said process comprises treating a compound of formula (VI) in which A is $-(\text{CR}_5\text{R}_5')_m\text{-R}_4$ and Y is an halogen atom,

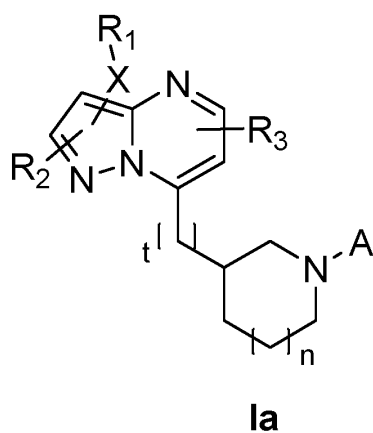


with a suitable boronic acid (or boronic ester) of formula (VII),



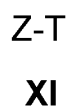
or

said process comprises alkylating a compound of formula (Ia) in which A is hydrogen,



5

with a suitable alkylating reagent of formula (XI),



wherein T is $-(\text{CR}_5\text{R}_5')_m\text{-R}_4$ and Z is a leaving group such as iodine, bromine, chlorine;

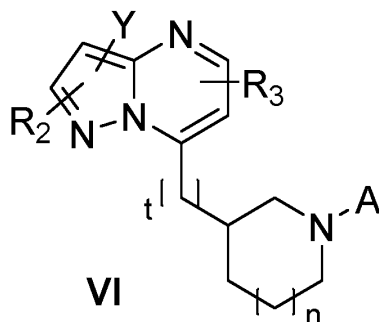
or alternatively by a reductive amination reaction with a suitable aldehyde of formula XI, wherein Z is =O;

10

and wherein R_1 , R_2 , R_3 , R_4 , R_5 , R_5' , X, m, n and t have the meanings as defined in the description.

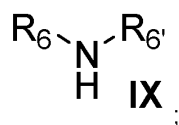
In a particular embodiment there is a process for the production of a compound according to Formula (I), wherein R_1 is $-\text{CH}_2\text{NR}_6\text{R}_6'$, said process comprises:

reacting a compound of formula (VI) in which A is $-(\text{CR}_5\text{R}_5')_m\text{-R}_4$ and Y is an acid functionality,



5

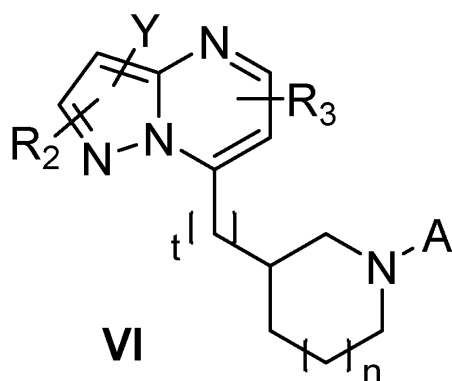
with a suitable amine of formula (IX)



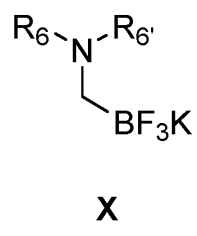
or

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reacting a compound of formula (VI), in which A is $-(\text{CR}_5\text{R}_5')_m\text{-R}_4$ and Y is an halogen atom,



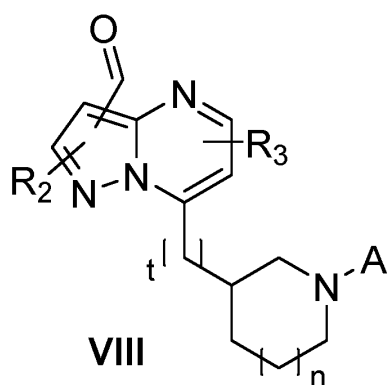
with a suitable potassium aminomethyltrifluoroborate salt of formula (X)



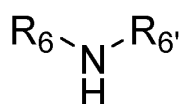
or

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reacting a compound of formula (VIII) in which A is $-(CR_5R_5')_m-R_4$,



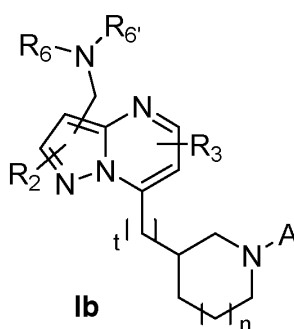
with a suitable amine of formula (IX)

**IX**

;

or

alkylating a derivative of Formula (Ib) in which A is hydrogen,



5

with a suitable alkylating reagent of formula (XI),

Z-T**XI**wherein T is $-(CR_5R_{5'})_m-R_4$ and Z is a leaving group such as iodine, bromine, chlorine;

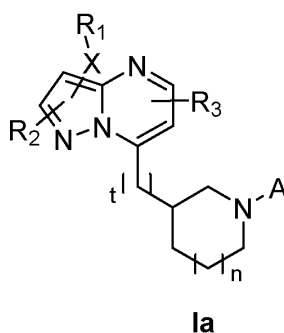
or alternatively by a reductive amination reaction with a suitable aldehyde of formula (XI), where Z is =O;

10

wherein R_2 , R_3 , R_4 , R_5 , $R_{5'}$, R_6 , $R_{6'}$, m, n and t have the meanings as defined in the description.

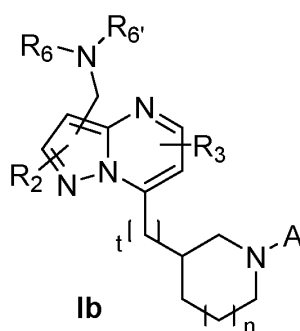
A particular embodiment of the invention refers to the use of a compound of Formula (Ia),

15



wherein R_1 , R_2 , R_3 , X , n and t have the meaning as defined in the description, and A represents either hydrogen or a protecting group of the amino function (PG, such as benzyl or *tert*-butoxycarbonyl) for the preparation of compounds of Formula (I).

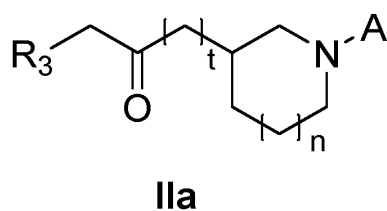
- 5 A particular embodiment of the invention refers to the use of a compound of Formula (Ib),



wherein R_2 , R_3 , R_6 , R_6' , n and t have the meaning as defined in the description, and A represents either hydrogen or a protecting group of the amino function (PG, such as benzyl or *tert*-butoxycarbonyl) for the preparation of compounds of Formula (I).

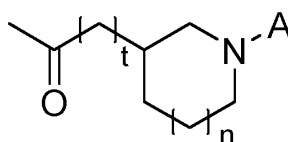
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A particular embodiment of the invention refers to the use of a compound of Formula (IIa),



wherein R_3 , n and t have the meaning as defined in the description, and A represents either hydrogen or a protecting group of the amino function (PG, such as benzyl or *tert*-butoxycarbonyl) for the preparation of compounds of Formula (I).

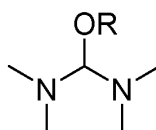
5 A particular embodiment of the invention refers to the use of a compound of Formula (IIb),



IIb

wherein n and t have the meaning as defined in the description, and A represents either hydrogen or a protecting group of the amino function (PG, such as benzyl or *tert*-butoxycarbonyl) for the preparation of compounds of Formula (I).

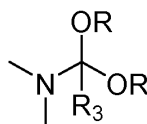
10 A particular embodiment of the invention refers to the use of a compound of Formula (IIIa),



IIIa

wherein R represents an alkyl group, for the preparation of compounds of Formula (I).

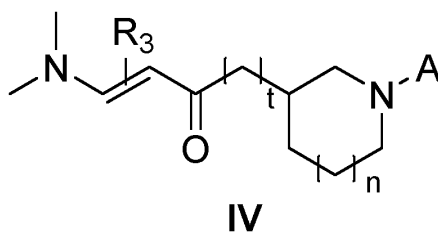
15 A particular embodiment of the invention refers to the use of a compound of Formula (IIIb),



IIIb

wherein R_3 has the meaning as defined in the description and R represents an alkyl group, for the preparation of compounds of Formula (I).

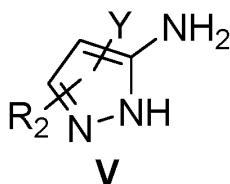
5 A particular embodiment of the invention refers to the use of a compound of Formula (IV),



wherein R_3 has the meaning as defined in the description and A represents either hydrogen or a protecting group of the amino function (PG, such as benzyl or *tert*-butoxycarbonyl) for the preparation of compounds of Formula (I).

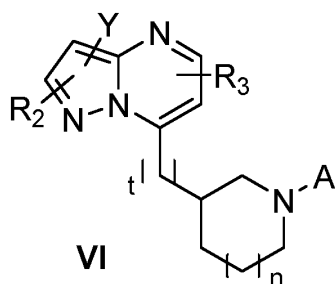
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A particular embodiment of the invention refers to the use of a compound of Formula (V),



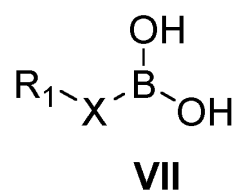
15 wherein R_2 has the meaning as defined in the description and Y represents a hydrogen, a halogen atom or an acid functionality, for the preparation of compounds of Formula (I).

A particular embodiment of the invention refers to the use of a compound of Formula (VI),



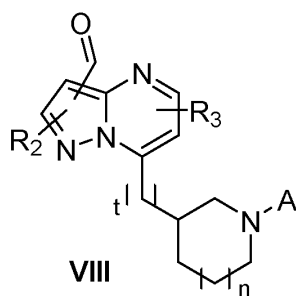
wherein R_2 , R_3 , n and t have the meaning as defined in the description, Y represents a hydrogen, a halogen atom or an acid functionality, and A represents either hydrogen or a protecting group of the amino function (PG, such as benzyl or *tert*-butoxycarbonyl) for the preparation of compounds of Formula (I).

A particular embodiment of the invention refers to the use of a compound of Formula (VII),



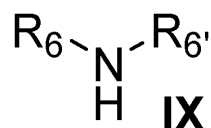
wherein R_1 has the meaning as defined in the description, for the preparation of compounds of Formula (I).

A particular embodiment of the invention refers to the use of a compound of Formula (VIII),



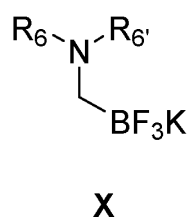
wherein R_2 , R_3 , n and t have the meaning as defined in the description, and A represents either hydrogen or a protecting group of the amino function (PG, such as benzyl or *tert*-butoxycarbonyl) for the preparation of compounds of Formula (I).

- 5 A particular embodiment of the invention refers to the use of a compound of Formula (IX),



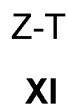
wherein R_6 and $R_{6'}$ have the meaning as defined in the description, for the preparation of compounds of Formula (I).

- 10 A particular embodiment of the invention refers to the use of a compound of Formula (X),



wherein R_6 and $R_{6'}$ have the meaning as defined in the description, for the preparation of compounds of Formula (I).

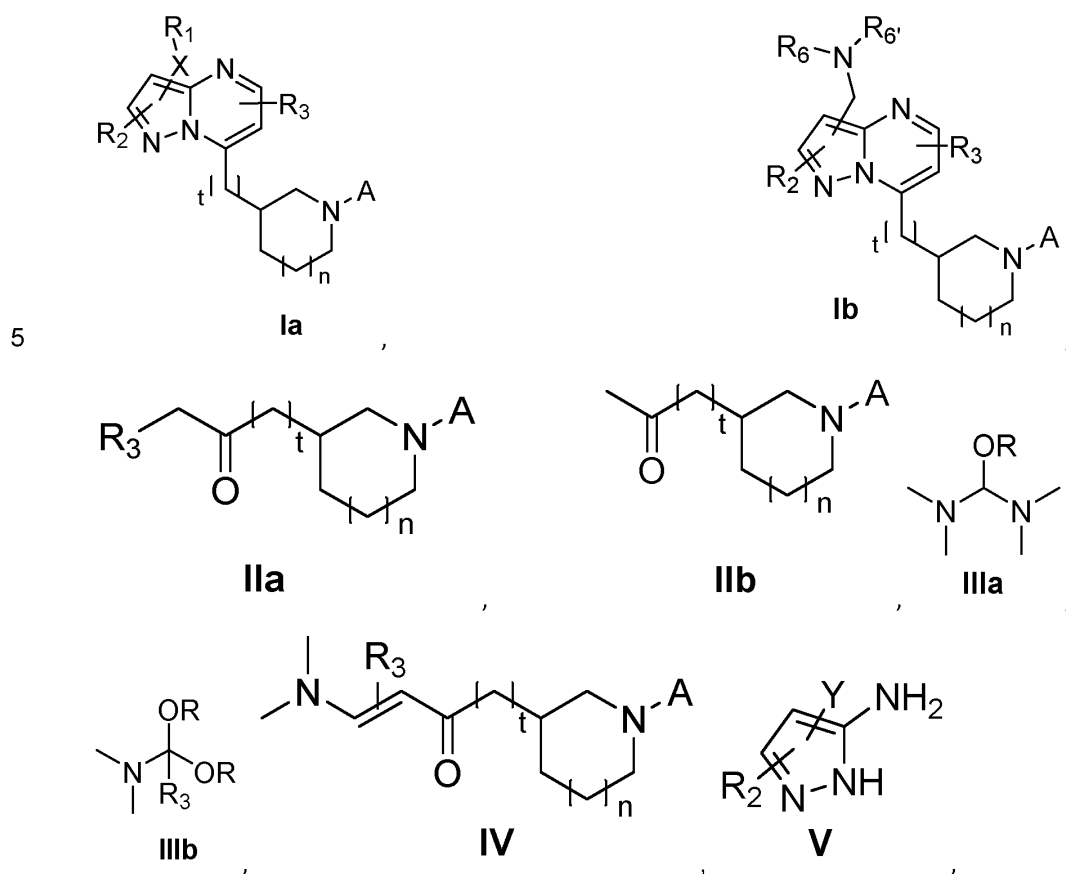
- 15 A particular embodiment of the invention refers to the use of a compound of Formula (XI),

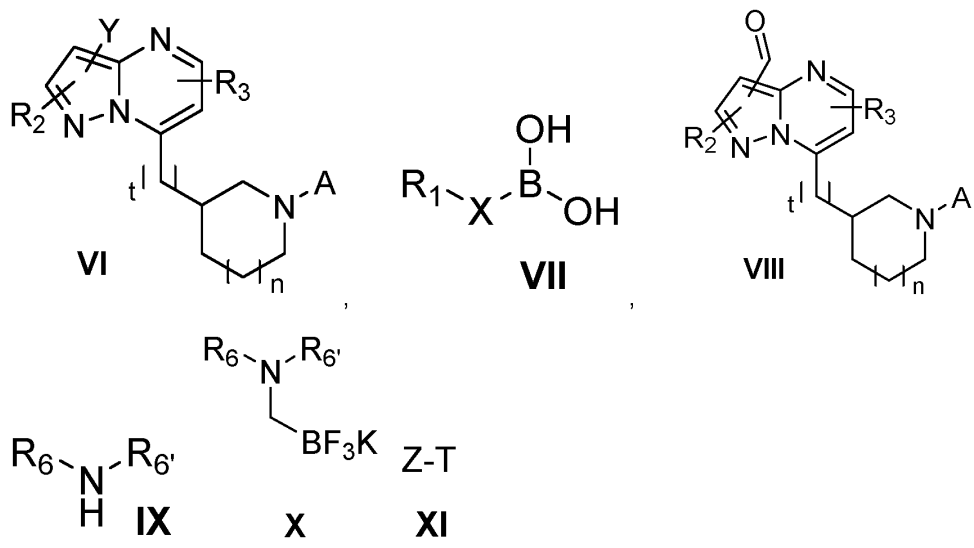


wherein T is $-\text{C}(\text{R}_5\text{R}_5)_m\text{R}_4$ and Z represents a halogen or an oxygen atom, and wherein R_4 , R_5 , $R_{5'}$ and m have the meaning as defined in the description for the preparation of compounds of Formula (I).

20

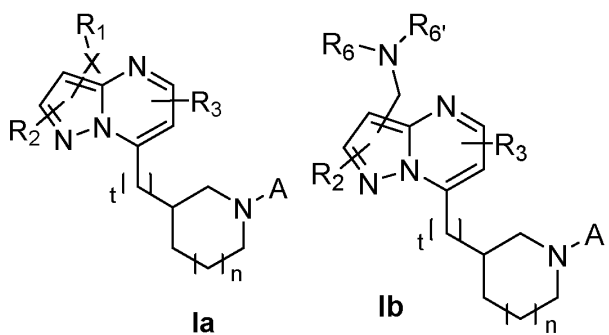
A particular embodiment of the invention refers to the use of a compound of Formula (Ia), (Ib), (IIa), (IIb), (IIIa), (IIIb), (IV), (V), (VI), (VII), (VIII), (IX), (X) or (XI),

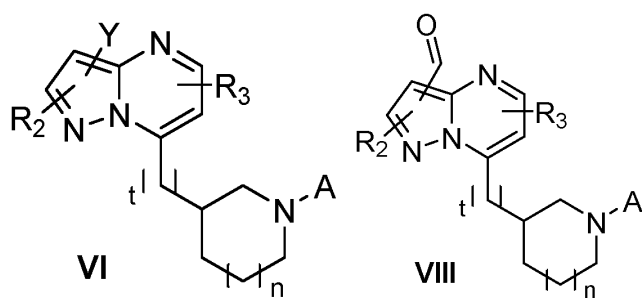




- R represents an alkyl group, Y represents a hydrogen, a halogen atom or an acid functionality, A represents either hydrogen, $-C(R_5R_5')_mR_4$ or a protecting group of the amino function (PG, such as benzyl or *tert*-butoxycarbonyl), T represents the group $-C(R_5R_5')_mR_4$, and Z represents a halogen or an oxygen atom, and wherein R_1 , R_2 , R_3 , R_4 , R_5 , R_5' , R_6 , R_6' , X, m, n and t have the meaning as defined in the description, for the preparation of compounds of Formula (I).

- 10 A particular embodiment of the invention refers to the use of a compound of Formula (Ia), (Ib), (VI) or (VIII),





Y represents a hydrogen, a halogen atom or an acid functionality, A represents either hydrogen, $-C(R_5R_5)_mR_4$ or a protecting group of the amino function (such as benzyl or *tert*-butoxycarbonyl), and wherein R_1 , R_2 , R_3 , R_4 , R_5 , R_5' , R_6 , R_6' , X, m, n and t have the meaning as defined in the description, for the preparation of compounds of Formula (I).

The obtained reaction products may, if desired, be purified by conventional methods, such as crystallisation and chromatography. Where the above described processes for the preparation of compounds of the invention give rise to mixtures of stereoisomers, these isomers may be separated by conventional techniques such as preparative chromatography. If there are chiral centers the compounds may be prepared in racemic form, or individual enantiomers may be prepared either by enantiospecific synthesis or by resolution.

One preferred pharmaceutically acceptable form of a compound of the invention is the crystalline form, including such form in pharmaceutical composition. In the case of salts and also solvates of the compounds of the invention the additional ionic and solvent moieties must also be non-toxic. The compounds of the invention may present different polymorphic forms, it is intended that the invention encompasses all such forms.

Another aspect of the invention refers to a pharmaceutical composition which comprises a compound according to the invention as described above according to general formula I or a pharmaceutically acceptable salt or stereoisomer thereof, and a pharmaceutically acceptable carrier, adjuvant or vehicle. The present invention thus provides pharmaceutical compositions comprising a compound of this invention, or a pharmaceutically acceptable salt or stereoisomers thereof together with a pharmaceutically acceptable carrier, adjuvant, or vehicle, for administration to a patient.

Examples of pharmaceutical compositions include any solid (tablets, pills, capsules, granules, etc.) or liquid (solutions, suspensions or emulsions) composition for oral, topical or parenteral administration.

5 In a preferred embodiment the pharmaceutical compositions are in oral form, either solid or liquid. Suitable dose forms for oral administration may be tablets, capsules, syrups or solutions and may contain conventional excipients known in the art such as binding agents, for example syrup, acacia, gelatin, sorbitol, tragacanth, or polyvinylpyrrolidone; fillers, for example lactose, sugar, maize starch, calcium phosphate, sorbitol or glycine; tableting lubricants, for example magnesium stearate; 10 disintegrants, for example starch, polyvinylpyrrolidone, sodium starch glycollate or microcrystalline cellulose; or pharmaceutically acceptable wetting agents such as sodium lauryl sulfate.

The solid oral compositions may be prepared by conventional methods of blending, filling or tableting. Repeated blending operations may be used to distribute the active 15 agent throughout those compositions employing large quantities of fillers. Such operations are conventional in the art. The tablets may for example be prepared by wet or dry granulation and optionally coated according to methods well known in normal pharmaceutical practice, in particular with an enteric coating.

20 The pharmaceutical compositions may also be adapted for parenteral administration, such as sterile solutions, suspensions or lyophilized products in the appropriate unit dosage form. Adequate excipients can be used, such as bulking agents, buffering agents or surfactants.

The mentioned formulations will be prepared using standard methods such as those described or referred to in the Spanish and US Pharmacopoeias and similar reference 25 texts.

Administration of the compounds or compositions of the present invention may be by any suitable method, such as intravenous infusion, oral preparations, and intraperitoneal and intravenous administration. Oral administration is preferred because of the convenience for the patient and the chronic character of the diseases 30 to be treated.

Generally an effective administered amount of a compound of the invention will depend on the relative efficacy of the compound chosen, the severity of the disorder being treated and the weight of the sufferer. However, active compounds will typically be administered once or more times a day for example 1, 2, 3 or 4 times daily, with typical
5 total daily doses in the range of from 0.1 to 1000 mg/kg/day.

The compounds and compositions of this invention may be used with other drugs to provide a combination therapy. The other drugs may form part of the same composition, or be provided as a separate composition for administration at the same time or at different time.

10 Another aspect of the invention refers to the use of a compound of the invention or a pharmaceutically acceptable salt or isomer thereof in the manufacture of a medicament.

Another aspect of the invention refers to a compound of the invention according as described above according to general formula (I), or a pharmaceutically acceptable salt
15 or isomer thereof, for use as a medicament for the treatment of pain. Preferably the pain is medium to severe pain, visceral pain, chronic pain, cancer pain, migraine, inflammatory pain, acute pain or neuropathic pain, allodynia or hyperalgesia. This may include mechanical allodynia or thermal hyperalgesia.

Another aspect of the invention refers to the use of a compound of the invention in the
20 manufacture of a medicament for the treatment or prophylaxis of pain.

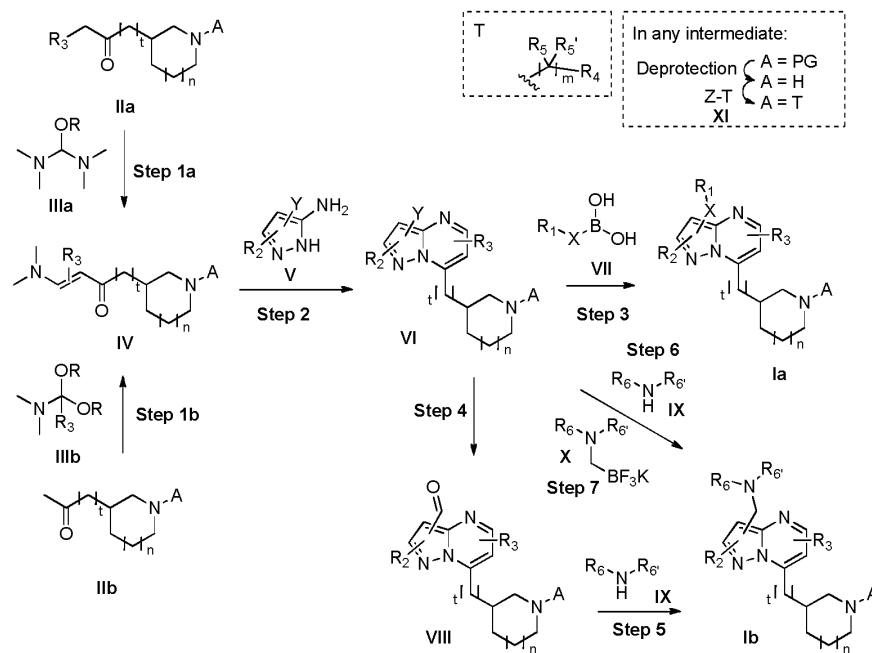
In a preferred embodiment the pain is selected from medium to severe pain, visceral pain, chronic pain, cancer pain, migraine, inflammatory pain, acute pain or neuropathic pain, allodynia or hyperalgesia, also preferably including mechanical allodynia or thermal hyperalgesia.

25 Another aspect of this invention relates to a method of treating or preventing pain which method comprises administering to a patient in need of such a treatment a therapeutically effective amount of a compound as above defined or a pharmaceutical composition thereof. Among the pain syndromes that can be treated are medium to severe pain, visceral pain, chronic pain, cancer pain, migraine, inflammatory pain,
30 acute pain or neuropathic pain, allodynia or hyperalgesia, whereas this could also include mechanical allodynia or thermal hyperalgesia.

The present invention is illustrated below with the aid of examples. These illustrations are given solely by way of example and do not limit the general scope of the present invention.

General Experimental Part**SYNTHESIS DESCRIPTION**

5 The compounds of formula I may be prepared by the process described in Scheme 1,



Scheme 1

10 wherein R_1 , R_2 , R_3 , R_4 , $R_{5-5'}$, $R_{6-6'}$, X , m , n and t have the meanings as defined in the description, R represents an alkyl group, Y represents a hydrogen, a halogen atom or an acid functionality, A represents either hydrogen, a protecting group of the amino function (PG, such as benzyl or *tert*-butoxycarbonyl) or T , wherein T represents the group $C(R_5R_{5'})_mR_4$, and Z represents a halogen or an oxygen atom.

The process can be carried out as described below:

15 **Step 1:** A compound of formula IV can be prepared by treating a carbonyl derivative of formula IIa with a suitable alkoxy-*N,N,N',N'*-tetramethylmethanediamine derivative of formula IIIa (step 1a) or by treating a carbonyl derivative of formula IIb with a suitable

1,1-dialkoxy-1-*N,N*-dimethylalkylamine derivative of formula IIIb (step 1b) at a suitable temperature, preferably between 80 °C and 100 °C.

5 Step 2: A compound of formula VI can be prepared by treating a compound of formula IV with a suitable 3-aminopyrazol derivative of formula V in a suitable solvent, such as acetic acid, at a suitable temperature, preferably between 50 °C and reflux temperature.

10 Step 3: A compound of formula Ia can be prepared by treating a compound of formula VI, in which Y is an halogen atom, with a suitable boronic acid (or boronic ester) of formula VII, in the presence of a suitable Pd catalyst, such as Pd(PPh₃)₄, with a suitable base, such as K₂CO₃ or Na₂CO₃, in a suitable solvent, such as mixtures of dimethoxyethane and water or mixtures of toluene, ethanol and water, at a suitable temperature, preferably heating. Alternatively, the reactions can be carried out under microwave heating.

15 Step 4: A compound of formula VIII can be prepared by treating a compound of formula VI, in which Y is a hydrogen atom, with POCl₃ in a suitable solvent, such as dimethylformamide, at a suitable temperature, preferably at 0 °C. Alternatively, a compound of formula VIII can be prepared by treating a compound of formula VI, in which Y is an halogen atom, with (*E*)-4,4,5,5-tetramethyl-2-styryl-1,3,2-dioxaborolane in the presence of a suitable Pd catalyst, such as Pd(dppf)Cl₂, with a suitable base, such as Na₂CO₃, in a suitable solvent, such as mixtures of toluene, ethyl acetate and water, at a suitable temperature, preferably 90 °C; followed by treatment with a suitable oxidizing agent, such as NaIO₄, in the presence of a suitable catalyst, such as OsO₄, in in a suitable solvent, such as mixtures of acetone and water, at a suitable temperature, preferably room temperature.

25 Step 5: A compound of formula Ib can be prepared by treating a compound of formula VIII with a suitable amine of formula IX in the presence of a reducing reagent, such as sodium triacetoxyborohydride or sodium cyanoborohydride, in a suitable solvent, such as dichloromethane or methanol, optionally in the presence of an acid, preferably acetic acid, at a suitable temperature, preferably room temperature. Alternatively, the reactions can be carried out under microwave heating.

30 Step 6: Alternatively, a compound of formula Ib can be prepared by reacting a compound of formula VI, in which Y is an acid functionality, with a suitable amine of formula IX in the presence of a suitable coupling agent, such as *N*-(3-

dimethylaminopropyl)-*N*'-ethylcarbodiimide hydrochloride, in the presence of a base, such as triethylamine, in a suitable solvent, such as dimethylformamide, at a suitable temperature, preferably room temperature; followed by reduction using a suitable reducing agent, such as AlH_3 , in a suitable solvent, such as tetrahydrofuran, at a
5 suitable temperature, preferably between 0 °C and room temperature.

Step 7: Alternatively, a compound of formula Ib can be prepared by reacting a compound of formula VI, in which Y is an halogen atom, with a suitable potassium aminomethyltrifluoroborate salt of formula X in the presence of a suitable Pd catalyst, such as allylpalladium(II) chloride dimer, with a suitable base, such as K_3PO_4 , and a
10 suitable phosphine ligand, such as dicyclohexyl(2',6'-dimethoxy-[1,1'-biphenyl]-2-yl)phosphine, in a suitable solvent, such as a mixture of dioxane and water, at a suitable temperature, preferably 100 °C.

Additionally, the group $\text{C}(\text{R}_5\text{R}_6)_m\text{R}_4$ (T) can be incorporated at any step of the synthesis by converting a derivative where A is a protecting group, PG, to a derivative where A
15 is H followed by a substitution reaction (see Scheme 1). The deprotection of PG may be carried out as follows:

- When the protecting group is benzyl, the deprotection can be conducted in the presence of a suitable Pd catalyst, such as 10% Pd/C, with a suitable hydrogen source, such as ammonium formate, in a suitable solvent such as ethanol, at a
20 suitable temperature such as 85 °C.
- When the protecting group is Boc (*tert*-butoxycarbonyl), the deprotection can be conducted by adding a solution of a strong acid such as HCl, in a suitable solvent such as diethyl ether, 1,4-dioxane or methanol, or with trifluoroacetic acid in dichloromethane.

25 The group T can then be introduced by means of any suitable reaction, such as:

- An alkylation reaction with a suitable alkylating reagent of formula XI as shown in Scheme 1, where Z is a leaving group such as iodine, bromine, chlorine or alternatively an epoxide opening takes place; in a suitable solvent, such as acetonitrile, dichloromethane or dimethylacetamide; in the presence of an
30 organic base, such as triethylamine or diisopropylethylamine, or an inorganic Lewis acid, such as LiClO_4 ; at a suitable temperature, comprised between room

temperature and the reflux temperature, or alternatively, the reactions can be carried out under microwave heating.

- A reductive amination reaction with a suitable aldehyde of formula XI, where Z is =O using the conditions described above in Step 5.

5 In addition, certain compounds of the present invention can also be obtained by functional group interconversion over compounds of formula Ia, Ib or any of the intermediates shown in Scheme 1. The following conversions are examples of transformations that may be carried out:

- 10 - A halogen atom may be introduced using a suitable halogenating agent, such as NBS or NIS, in the presence of benzoyl peroxide, in a suitable solvent, such as carbon tetrachloride, at a suitable temperature, preferably 70 °C.
- A halogen atom may be converted to a hydroxyl group using a suitable borylating agent, such as bis(pinacolato)diboron, in the presence of a suitable Pd catalyst, such as Pd(dppf)FeCl₂, with a suitable base, such as KOAc, in a
15 suitable solvent, such as dioxane, at a suitable temperature, preferably at 115 °C; followed by oxidation using a suitable oxidizing agent, such as hydrogen peroxide, in a suitable solvent, such as acetic acid, at a suitable temperature, preferably between 0 °C and room temperature.
- A halogen atom may be converted to an alkylamino group using a suitable
20 alkylamine in the presence of a suitable catalyst, such as Pd₂dba₃ or CuI, optionally in the presence of (S)-proline, with a suitable base, such as KO^tBu or K₂CO₃, in a suitable solvent, such as toluene or dimethylsulfoxide, at a suitable temperature, preferably 100 °C. Alternatively, the reactions can be carried out under microwave heating.
- 25 - A halogen atom may be converted to a CN group using a suitable cyanide source, such as K₄[Fe(CN)₆]·2H₂O, in the presence of a suitable Pd catalyst, such as Pd(OAc)₂, and a suitable ligand, such as 1,1'-bis(diphenylphosphino)ferrocene, with a suitable base, such as Na₂CO₃, in a
30 suitable solvent, such as N-methylpyrrolidone, at a suitable temperature, preferably 120 °C. Alternatively, the reactions can be carried out under microwave heating.
- A halogen atom may be converted to a pyrimidine ring using a suitable stannane reagent, such as tributyl (1-ethoxyvinyl)stannane, in the presence of a suitable Pd catalyst, such as PdCl₂(PPh₃)₂, in a suitable solvent, such as toluene, at a

- suitable temperature, preferably at 80 °C; followed by the conditions described in step 1a and by treatment with a suitable formimidamide source, such as formimidamide acetate, at a suitable temperature, preferably 130 °C.
- 5 - A hydroxyl or an amino group may be alkylated using a suitable alkylating agent, such as an alkyl halide or an alkyl trifluoromethanesulfonate, in the presence of a base, such as triethylamine or NaH, in a suitable solvent, such as dichloromethane or dimethylformamide, at a suitable temperature, preferably between room temperature and 85 °C.
 - 10 - A hydroxyl group may be arylated using a suitable aryl alcohol with a suitable coupling agent, such as diisopropyl azodicarboxylate, with a suitable phosphine, such as triphenylphosphine, in a suitable solvent, such as toluene, at a suitable temperature, preferably 100 °C.
 - 15 - A double bond may be reduced using a suitable hydrogen source, such as hydrogen gas atmosphere, with a suitable Pd catalyst, such as Pd(OH)₂, in a suitable solvent, such as methanol, at a suitable temperature, preferably room temperature.
 - 20 - A carbonyl group may be reduced to alcohol using a suitable reducing agent, such as sodium borohydride, in a suitable solvent, such as tetrahydrofuran, at a suitable temperature, preferably between 0 °C and room temperature.
 - 25 - A carbonyl group may be converted to a nitroethyl group using nitromethane with a suitable base, such as methylamine, in a suitable solvent, such as methanol at a suitable temperature, preferably at 60 °C; followed by reduction using a suitable reducing agent, such as sodium borohydride, in a suitable solvent, such as methanol, at a suitable temperature, preferably room temperature.
 - 30 - A nitro group may be reduced to an amino group using a suitable reducing agent, such as Zn or hydrogen-Nickel Raney, optionally in the presence of CaCl₂, in a suitable solvent, such as methanol or mixtures of ethanol and water, at a suitable temperature, preferably between 40 °C and 80 °C.
 - 35 In some of the processes described above it may be necessary to protect the reactive or labile groups present with suitable protecting groups, such as for example acetyl, allyl, Alloc (allyloxycarbonyl), Boc (*tert*-butoxycarbonyl), or benzyl for the protection of amino groups, and common silyl protecting groups for the protection of the hydroxyl group. The procedures for the introduction and removal of these protecting groups are well known in the art and can be found thoroughly described in the literature.

In addition, a compound of formula I can be obtained in enantiopure form by resolution of a racemic mixture either by chiral preparative HPLC or by crystallization of a diastereomeric salt or co-crystal. Alternatively, the resolution step can be carried out at a previous stage, using any suitable intermediate.

- 5 The compounds of formula IIa, IIb, IIIa, IIIb, V, VII, IX, X and XI used in the methods disclosed above are commercially available or can be synthesized following common procedures described in the literature and exemplified in the synthesis of some intermediates.

Examples

The following abbreviations are used in the examples:

- AcOH: acetic acid
- ACN: acetonitrile
- 5 Anh: anhydrous
- Aq: aqueous
- Boc₂O: di-*tert*-butyl dicarbonate
- Chx: cyclohexane
- Conc: concentrated
- 10 DCM: dichloromethane
- DEA: diethylamine
- DIAD: diisopropyl azodicarboxylate
- DIPEA: *N,N*-diisopropylethylamine
- DMA: *N,N*-dimethylacetamide
- 15 DME: dimethoxyethane
- DMF: dimethylformamide
- DMAP: dimethylaminopyridine
- DMSO: dimethylsulfoxide
- EDC.HCl: *N*-(3-dimethylaminopropyl)-*N'*-ethylcarbodiimide hydrochloride
- 20 Et₂O: diethyl ether
- EtOAc: ethyl acetate
- EtOH: ethanol
- h: hour/s
- HOBt: 1-hydroxybenzotriazole
- 25 HPLC: high performance liquid chromatography
- iPrOH: isopropanol
- LDA: lithium diisopropylamide

MeOH: methanol

MS: mass spectrometry

Min: minutes

MW: microwave

5 NBS: *N*-bromosuccinimide

NIS: *N*-iodosuccinimide

NMP: *N*-methyl-2-pyrrolidone

Quant: quantitative

Rt.: retention time

10 Rf: retention factor

r.t.: room temperature

Sat: saturated

Sol: solution

TEA: triethylamine

15 TFA: trifluoroacetic acid

THF: tetrahydrofuran

TLC: thin-layer chromatography

XPhos: 2-dicyclohexylphosphino-2',4',6'-triisopropylbiphenyl

Wt: weight

20

The following methods were used to determine the HPLC-MS spectra:

METHOD A

Column Acquity UPLC BEH C18 2.1x50 mm, 1.7 µm; flow rate 0.61 mL/min; A: NH₄HCO₃ 10mM; B: ACN; Gradient: 0.3 min in 98% A, 98% A to 5% A in 2.52 min, isocratic 1.02 min in 5% A.

25

METHOD B

Column Acquity UPLC BEH C18 2.1 X 50 mm, 1.7 µm, flow rate 0.60 mL/min; A: NH₄HCO₃ 10 mM, B: ACN; gradient: 0.3 min 90% A, 90% A to 5% A in 2.7 min, isocratic 0.7 min 5% A.

METHOD C

- 5 Column Acquity UPLC BEH C18 2.1 x 50 mm, 1.7 µm, flow rate 0.61 mL/min; A: NH₄HCO₃ 10 mM, B: ACN; gradient 0.3 min 98% A, 98% A to 0% A in 2.7 min; isocratic 2 min 0% A.

METHOD D

- 10 Column XBridge® Shield RP18 4.6 x 50 mm, 3.5 µm, flow rate 1.6 mL/min at 50 °C; A: 10 mM NH₄HCO₃/ 25% w/w NH₄OH (99.8:0.12) pH 9, B: ACN; gradient 0.5 min 95% A, 95% to 0% A in 3.5 min; isocratic 1.5 min 0% A.

METHOD E

- 15 Column XBridge® Shield RP18 4.6 x 50 mm, 3.5 µm, flow rate 1.5 mL/min at 30 °C; A: 10 mM NH₄HCO₃/ 25% w/w NH₄OH (99.8:0.12) pH 9, B: ACN; gradient 0.5 min 95% A, 95% to 0% A in 4.5 min; isocratic 1.5 min 0% A.

METHOD F

- 20 Column Acquity UPLC BEH C18 2.1 x 50 mm, 1.7 µm, flow rate 0.61 mL/min; A: NH₄HCO₃ 10 mM, B: ACN, C: MeOH + 0.1% formic acid; gradient 0.3 min 98% A, 98% A to 0:95:5 A:B:C in 2.7 min; 0:95:5 A:B:C to 100% B in 0.1 min; isocratic 2 min 100% B.

METHOD G

Column Acquity UPLC BEH C18 2.1 x 50 mm, 1.7 µm, flow rate 0.6 mL/min; H₂O + 0.2% v/v NH₃, B: ACN; gradient 95% A to 5% A in 4 min, 5% A to 0% A in 0.2 min, isocratic 0.48 min 0% A.

- 25 METHOD H

Column Acquity UPLC BEH C18 2.1 x 50 mm, 1.7 µm, flow rate 0.61 mL/min; A: NH₄HCO₃ 10 mM, B: ACN,; gradient 0.3 min 98% A, 98% A to 100% B in 2.65 min; isocratic 2.05 min 100% B.

METHOD I

Column XBridge® Shield RP18 4.6 x 50 mm, 3.5 µm, flow rate 1.5 mL/min at 30 °C; A: 10 mM NH₄HCO₃/ 25% w/w NH₄OH (99.8:0.12) pH 9, B: ACN; gradient 0.5 min 50% A, 50% to 5% A in 4.5 min; isocratic 1.5 min 5% A.

5 METHOD J

Column Acquity UPLC BEH C18 2.1 x 50 mm, 1.7 µm, flow rate 0.6 mL/min; H₂O + 0.1% v/v TFA, B: ACN; gradient 95% A to 5% A in 4 min, 5% A to 0% A in 0.2 min, isocratic 0.48 min 0% A.

METHOD K

- 10 CHIRALPACK® IG-3 analytical column. 4.6 x 150 mm, 3 µm, flow rate 1.0 mL/min at 25 °C; A: 20 mM NH₄HCO₃/ aq pH 9 (by DEA), B: ACN; isocratic 15 min: a) (20% A); b) (25% A); c) (30% A); d) (35% A); e) (40% A); f) (55% A); g) (60% A)

METHOD L

- 15 CHIRALPACK® IC-3 analytical column. 4.6 x 150 mm, 3 µm, flow rate 1.0 mL/min at 25 °C; A: 20 mM NH₄HCO₃/ aq pH 9 (by DEA), B: ACN; isocratic 15 min 30% A.

METHOD M

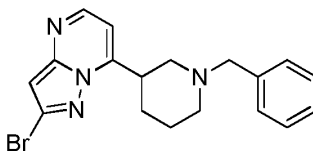
CHIRALCEL® OJ-3R analytical column. 4.6 x 150 mm, 3 µm, flow rate 1.0 mL/min at 25 °C; A: 20 mM NH₄HCO₃/ aq pH 9 (by DEA), B: ACN; isocratic 15 min 70% A.

METHOD N

- 20 Column Aquity UPLC BEH C18 2.1 x 50 mm, 1.7 µm, flow rate 0.61 mL/min; A: NH₄HCO₃ 10 mM pH 10.6, B: ACN; gradient 0.3 min 98% A, 98% A to 0% A in 2.7 min; isocratic 2 min 0% A.

Synthesis of examples

25



Example 1. 7-(1-Benzylpiperidin-3-yl)-2-bromopyrazolo[1,5-a]pyrimidine.

Step a. 1-(1-Benzylpiperidin-3-yl)-3-(dimethylamino)prop-2-en-1-one.

1-(1-Benzylpiperidin-3-yl)ethanone (1.67 g, 7.7 mmol) and 1-*tert*-butoxy-*N,N,N',N'*-tetramethylmethanediamine (1.47 g, 8.5 mmol) were stirred at 80 °C during 16 h. The reaction mixture was cooled and evaporated to dryness under vacuum to give the title compound (1.96 g, Yield: 94%).

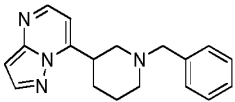
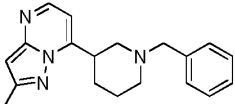
HPLC-MS (Method A): Rt: 1.44 min; ESI+-MS m/z: 273.2 (M+1).

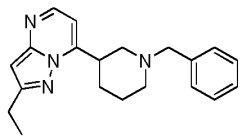
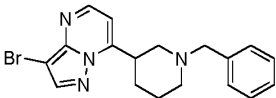
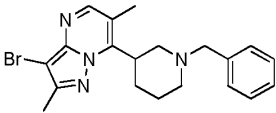
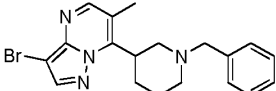
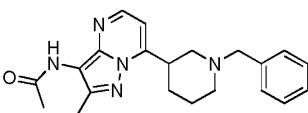
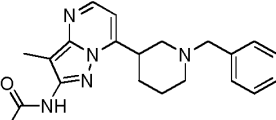
Step b. Title compound.

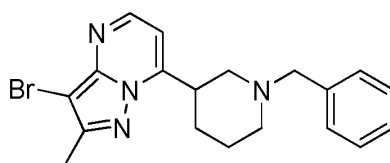
5-Bromo-1*H*-pyrazol-3-amine (535 mg, 3.3 mmol) was added to a solution of the compound obtained in step a (900 mg, 3.3 mmol) in AcOH (10 mL) and the solution was stirred at 100 °C for 16 h. The mixture was cooled down and the solvent was evaporated under vacuum. 10% Aq NaOH was added and the product was extracted with EtOAc, the combined organic layers were washed with brine, dried over anhydrous Na₂SO₄, filtered and concentrated to dryness. The crude product was purified by flash chromatography, silica gel, DCM:MeOH to give the title compound (612 mg, Yield: 50%).

HPLC-MS (Method A): Rt, 2.32 min; ESI+-MS m/z: 371 [M+H]⁺.

This method was used for the preparation of examples 2-9 using suitable starting materials:

STRUCTURE	EX	CHEMICAL NAME	Rt (min)	MS (M+H)	HPLC Method
	2	7-(1-Benzylpiperidin-3-yl)pyrazolo[1,5-a]pyrimidine	1.91	293.2	A
	3	7-(1-Benzylpiperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidine	2.03	307.3	A

	4	7-(1-Benzylpiperidin-3-yl)-2-ethylpyrazolo[1,5-a]pyrimidine	2.24	321.2	A
	5	7-(1-Benzylpiperidin-3-yl)-3-bromopyrazolo[1,5-a]pyrimidine	2.26	371	A
	6	7-(1-Benzylpiperidin-3-yl)-3-bromo-2,6-dimethylpyrazolo[1,5-a]pyrimidine	2.58	399	A
	7	7-(1-Benzylpiperidin-3-yl)-3-bromo-6-methylpyrazolo[1,5-a]pyrimidine	2.40	385	A
	8	<i>N</i> -(7-(1-Benzylpiperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)acetamide	1.92	364.2	A
	9	<i>N</i> -(7-(1-Benzylpiperidin-3-yl)-3-methylpyrazolo[1,5-a]pyrimidin-2-yl)acetamide	1.41	364.2	A



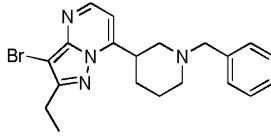
Example 10. 7-(1-Benzylpiperidin-3-yl)-3-bromo-2-methylpyrazolo[1,5-a]pyrimidine.

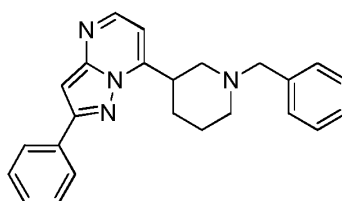
- 5 NBS (697 mg, 3.9 mmol) and benzoyl peroxide (94 mg, 0.4 mmol) were added to a solution of the compound obtained in example 3 (1.0 g, 3.3 mmol) in CCl₄ (150 mL) and the resulting mixture was heated at 70 °C for 16 h. After completion, the mixture was cooled down and the solvent was evaporated under vacuum. The residue was quickly

filtered through a plug of silica with Chx:EtOAc (95:5) and concentrated to dryness. The crude product was purified by flash chromatography, silica gel, Chx:EtOAc to give the title compound (670 mg, Yield: 53%).

HPLC-MS (Method A): Rt, 2.39 min; ESI+-MS m/z: 385.1 [M+H]⁺.

- 5 This method was used for the preparation of example 11 using suitable starting materials:

STRUCTURE	EX	CHEMICAL NAME	Rt (min)	MS (M+H)	HPLC Method
	11	7-(1-Benzylpiperidin-3-yl)-3-bromo-2-ethylpyrazolo[1,5-a]pyrimidine	2.66	399.1	C

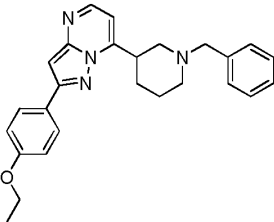
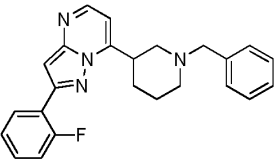
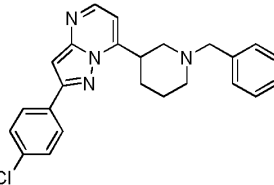
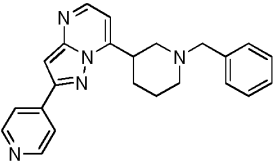
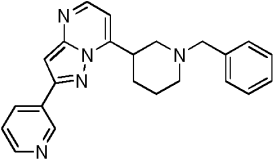
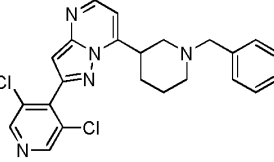


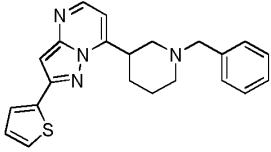
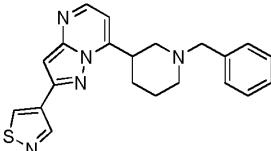
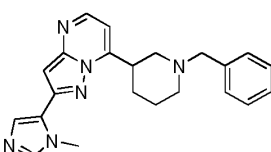
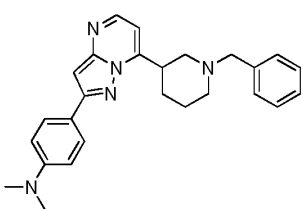
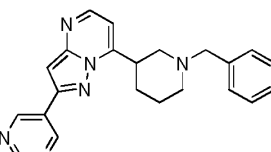
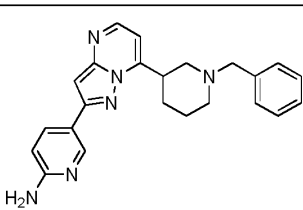
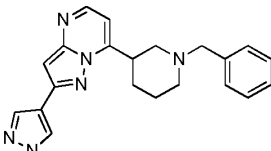
Example 12. 7-(1-Benzylpiperidin-3-yl)-2-phenylpyrazolo[1,5-a]pyrimidine.

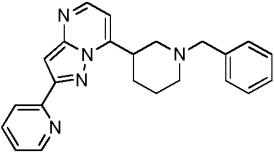
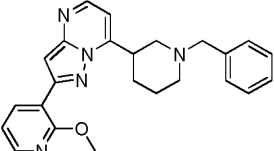
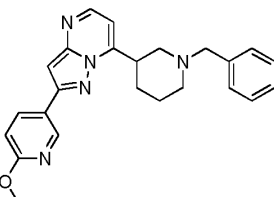
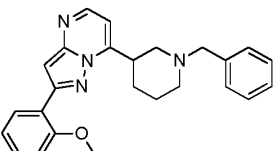
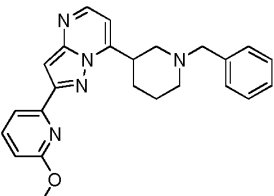
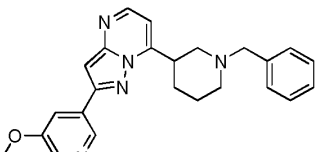
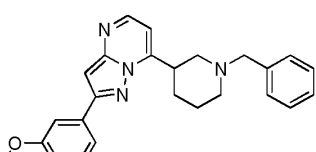
- 10 A MW tube was charged with the compound obtained in example 1 (200 mg, 0.54 mmol), phenylboronic acid (99 mg, 0.8 mmol), K₂CO₃ (223 mg, 1.6 mmol), Pd(PPh₃)₄ (12 mg, 0.01 mmol) and DME:H₂O (1:1) (6 mL) and was degassed by means of bubbling argon for 5 min. The reaction mixture was heated under MW irradiation at 130 °C for 20 min. The suspension was diluted with EtOAc and washed with aq sat NaHCO₃
- 15 sol. The organic layer was dried over anhydrous Na₂SO₄, filtered and solvent was removed under vacuum. The residue was purified by flash chromatography, silica gel, DCM:MeOH, to give the title compound (158 mg, Yield: 80%).

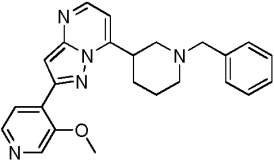
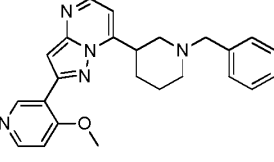
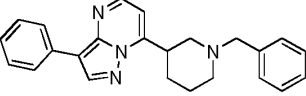
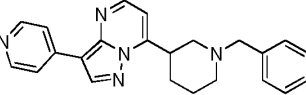
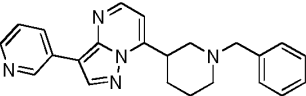
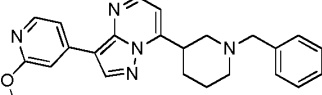
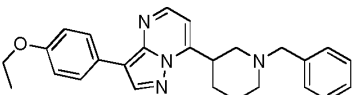
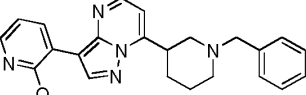
HPLC-MS (Method A): Rt, 2.56 min; ESI+-MS m/z: 369.3 [M+H]⁺.

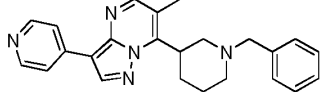
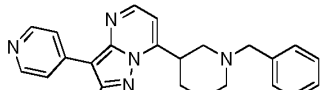
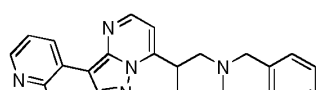
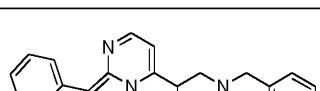
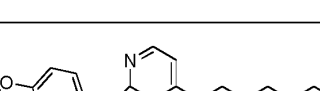
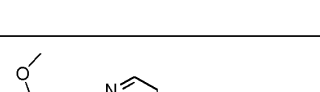
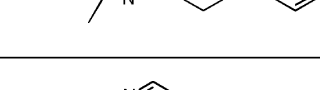
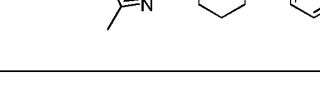
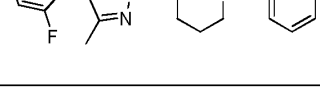
- 20 This method was used for the preparation of examples 13-60 using suitable starting materials:

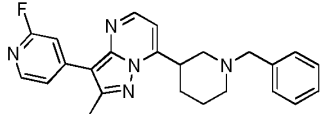
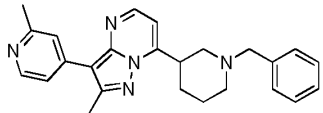
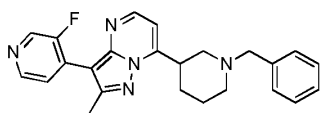
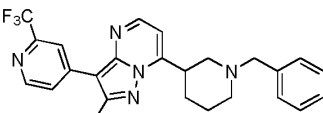
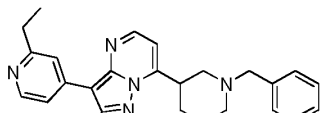
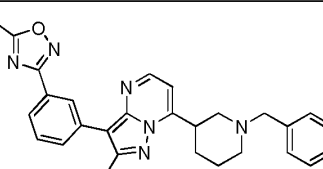
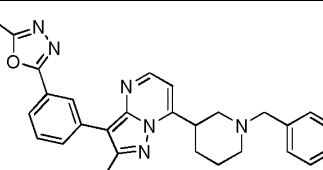
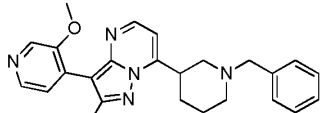
STRUCTURE	EX	CHEMICAL NAME	Rt (min)	MS (M+H)	HPLC Method
	13	7-(1-Benzylpiperidin-3-yl)-2-(4-ethoxyphenyl)pyrazolo[1,5-a]pyrimidine	2.64	413.3	A
	14	7-(1-Benzylpiperidin-3-yl)-2-(2-fluorophenyl)pyrazolo[1,5-a]pyrimidine	2.62	387.3	A
	15	7-(1-Benzylpiperidin-3-yl)-2-(4-chlorophenyl)pyrazolo[1,5-a]pyrimidine	2.77	403.3	A
	16	7-(1-Benzylpiperidin-3-yl)-2-(pyridin-4-yl)pyrazolo[1,5-a]pyrimidine	2.06	370.3	A
	17	7-(1-Benzylpiperidin-3-yl)-2-(pyridin-3-yl)pyrazolo[1,5-a]pyrimidine	2.06	370.3	A
	18	7-(1-Benzylpiperidin-3-yl)-2-(3,5-dichloropyridin-4-yl)pyrazolo[1,5-a]pyrimidine	2.48	438.3	A

	19	7-(1-Benzylpiperidin-3-yl)-2-(thiophen-2-yl)pyrazolo[1,5-a]pyrimidine	2.49	375.3	A
	20	4-(7-(1-Benzylpiperidin-3-yl)pyrazolo[1,5-a]pyrimidin-2-yl)isothiazole	2.22	376.2	A
	21	7-(1-Benzylpiperidin-3-yl)-2-(1-methyl-1H-imidazol-5-yl)pyrazolo[1,5-a]pyrimidine	1.83	373.3	A
	22	4-(7-(1-Benzylpiperidin-3-yl)pyrazolo[1,5-a]pyrimidin-2-yl)-N,N-dimethylaniline	2.59	412.3	A
	23	7-(1-Benzylpiperidin-3-yl)-2-(pyrimidin-5-yl)pyrazolo[1,5-a]pyrimidine	1.90	371.2	A
	24	5-(7-(1-Benzylpiperidin-3-yl)pyrazolo[1,5-a]pyrimidin-2-yl)pyridin-2-amine	1.85	385.3	A
	25	7-(1-Benzylpiperidin-3-yl)-2-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrimidine	1.88	373.2	A

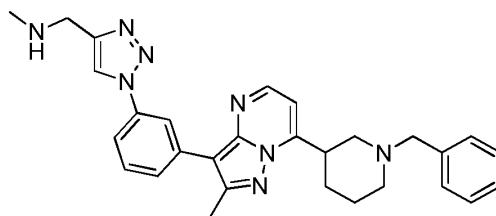
	26	7-(1-Benzylpiperidin-3-yl)-2-(pyridin-2-yl)pyrazolo[1,5-a]pyrimidine	2.11	370.2	A
	27	7-(1-Benzylpiperidin-3-yl)-2-(2-methoxypyridin-3-yl)pyrazolo[1,5-a]pyrimidine	2.45	400.1	A
	28	7-(1-Benzylpiperidin-3-yl)-2-(6-methoxypyridin-3-yl)pyrazolo[1,5-a]pyrimidine	2.40	400.1	A
	29	7-(1-Benzylpiperidin-3-yl)-2-(2-methoxyphenyl)pyrazolo[1,5-a]pyrimidine	2.54	399.2	A
	30	7-(1-Benzylpiperidin-3-yl)-2-(6-methoxypyridin-2-yl)pyrazolo[1,5-a]pyrimidine	2.53	400.1	A
	31	7-(1-Benzylpiperidin-3-yl)-2-(5-methoxypyridin-3-yl)pyrazolo[1,5-a]pyrimidine	2.41	400.2	A
	32	7-(1-Benzylpiperidin-3-yl)-2-(2-methoxypyridin-4-yl)pyrazolo[1,5-a]pyrimidine	2.12	400.2	A

	33	7-(1-Benzylpiperidin-3-yl)-2-(3-methoxypyridin-4-yl)pyrazolo[1,5-a]pyrimidine	2.12	400.2	A
	34	7-(1-Benzylpiperidin-3-yl)-2-(4-methoxypyridin-3-yl)pyrazolo[1,5-a]pyrimidine	1.98	400.2	A
	35	7-(1-Benzylpiperidin-3-yl)-3-phenylpyrazolo[1,5-a]pyrimidine	2.59	369.1	A
	36	7-(1-Benzylpiperidin-3-yl)-3-(pyridin-4-yl)pyrazolo[1,5-a]pyrimidine	2.13	370.1	A
	37	7-(1-Benzylpiperidin-3-yl)-3-(pyridin-3-yl)pyrazolo[1,5-a]pyrimidine	2.12	370.1	A
	38	7-(1-Benzylpiperidin-3-yl)-3-(2-methoxypyridin-4-yl)pyrazolo[1,5-a]pyrimidine	2.45	400.2	A
	39	7-(1-Benzylpiperidin-3-yl)-3-(4-ethoxyphenyl)pyrazolo[1,5-a]pyrimidine	2.69	413.2	A
	40	7-(1-Benzylpiperidin-3-yl)-3-(2-methoxypyridin-3-yl)pyrazolo[1,5-a]pyrimidine	2.55	400.2	A

	41	7-(1-Benzylpiperidin-3-yl)-6-methyl-3-(pyridin-4-yl)pyrazolo[1,5-a]pyrimidine	2.24	384.2	A
	42	7-(1-Benzylpiperidin-3-yl)-2-methyl-3-(pyridin-4-yl)pyrazolo[1,5-a]pyrimidine	2.18	384.2	A
	43	7-(1-Benzylpiperidin-3-yl)-3-(2-methoxypyridin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidine	2.35	414.2	A
	44	7-(1-Benzylpiperidin-3-yl)-2-methyl-3-phenylpyrazolo[1,5-a]pyrimidine	2.63	383.2	A
	45	7-(1-Benzylpiperidin-3-yl)-3-(4-ethoxyphenyl)-2-methylpyrazolo[1,5-a]pyrimidine	2.70	427.2	A
	46	7-(1-Benzylpiperidin-3-yl)-3-(2-methoxypyridin-4-yl)-2-methylpyrazolo[1,5-a]pyrimidine	2.50	414.1	A
	47	4-(7-(1-Benzylpiperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-N,N-dimethylaniline	2.67	426.2	A
	48	7-(1-Benzylpiperidin-3-yl)-3-(2-fluorophenyl)-2-methylpyrazolo[1,5-a]pyrimidine	3.09	401.2	B
	49	7-(1-Benzylpiperidin-3-yl)-2-methyl-3-(3-methylpyridin-4-yl)pyrazolo[1,5-a]pyrimidine	2.72	398.2	B

	50	7-(1-Benzylpiperidin-3-yl)-3-(2-fluoropyridin-4-yl)-2-methylpyrazolo[1,5-a]pyrimidine	2.46	402.2	A
	51	7-(1-Benzylpiperidin-3-yl)-2-methyl-3-(2-methylpyridin-4-yl)pyrazolo[1,5-a]pyrimidine	2.25	398.3	A
	52	7-(1-Benzylpiperidin-3-yl)-3-(3-fluoropyridin-4-yl)-2-methylpyrazolo[1,5-a]pyrimidine	2.22	402.2	A
	53	7-(1-Benzylpiperidin-3-yl)-2-methyl-3-(2-(trifluoromethyl)pyridin-4-yl)pyrazolo[1,5-a]pyrimidine	2.63	452.2	A
	54	7-(1-Benzylpiperidin-3-yl)-3-(2-ethylpyridin-4-yl)-2-methylpyrazolo[1,5-a]pyrimidine	2.41	412.3	A
	55	3-(3-(7-(1-Benzylpiperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)phenyl)-5-methyl-1,2,4-oxadiazole	2.62	465.2	A
	56	2-(3-(7-(1-Benzylpiperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)phenyl)-5-methyl-1,3,4-oxadiazole	2.85	465.3	B
	57	7-(1-Benzylpiperidin-3-yl)-3-(3-methoxypyridin-4-yl)-2-methylpyrazolo[1,5-a]pyrimidine	2.13	414.3	C

	58	7-(1-Benzylpiperidin-3-yl)-2,6-dimethyl-3-(pyridin-4-yl)pyrazolo[1,5-a]pyrimidine	2.35	398.2	A
	59	7-(1-Benzylpiperidin-3-yl)-2,5-dimethyl-3-(pyridin-4-yl)pyrazolo[1,5-a]pyrimidine	2.34	398.3	A
	60	7-(1-Benzylpiperidin-3-yl)-2-ethyl-3-(pyridin-4-yl)pyrazolo[1,5-a]pyrimidine	2.80	398.4	B



Example 61. 1-(1-(3-(7-(1-Benzylpiperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)phenyl)-1H-1,2,3-triazol-4-yl)-N-methylmethanamine.

- 5 Step a. *tert*-Butyl ((1-(3-bromophenyl)-1H-1,2,3-triazol-4-yl)methyl)(methyl)carbamate. TEA (0.92 mL, 6.6 mmol) and di-*tert*-butyl dicarbonate (450 mg, 2.1 mmol) were added in portions to a solution of 1-(1-(3-bromophenyl)-1H-1,2,3-triazol-4-yl)-N-methylmethanamine hydrochloride (500 mg, 1.6 mmol) in DCM (5 mL) and the reaction mixture was stirred at r.t. for 16 h. The resulting mixture was washed with aq sat
- 10 NaHCO₃ sol, water and brine. The organic layer was dried over anhydrous Na₂SO₄, filtered and concentrated to give the title compound (735 mg, Yield: Quant.).

HPLC-MS (Method A): Rt: 2.11 min; ESI+-MS m/z: 367.1 (M+1).

Step b. (3-(4-(((*tert*-Butoxycarbonyl)(methyl)amino)methyl)-1H-1,2,3-triazol-1-yl)phenyl)boronic acid.

- 15 To a solution of the compound obtained in step a (580 mg, 1.6 mmol), bis(pinacolato)diboron (802 mg, 3.2 mmol) and KOAc (465 mg, 4.7 mmol) in anhydrous DMSO (25 mL), Pd(dppf)Fe-Cl₂ (115 mg, 0.16 mmol) was added under argon atmosphere,

and the mixture was heated at 90 °C for 16 h. The mixture was dissolved with an EtOAc:Et₂O (1:1) mixture and washed with aq sat NaHCO₃ sol. The organic layer was dried over anhyd Na₂SO₄, filtered and solvent was removed under vacuum. The crude product was purified by flash chromatography, silica gel, Chx:EtOAc to give the title compound (690 mg, Yield: Quant.).

HPLC-MS (Method A): Rt: 1.52 min; ESI+-MS m/z: 333.1 (M+1).

Step c. *tert*-Butyl ((1-(3-(7-(1-benzylpiperidin-3-yl)-2-methylpyrazolo[1,5-*a*]pyrimidin-3-yl)phenyl)-1*H*-1,2,3-triazol-4-yl)methyl)(methyl)carbamate.

Starting from the compound obtained in example 10 (70 mg, 0.18 mmol) and the compound obtained in step b (90 mg, 0.27 mmol) and following the procedure described in example 12, the title compound was obtained (58 mg, Yield: 44%).

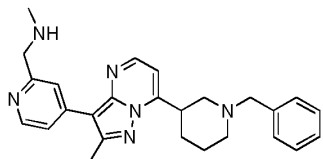
HPLC-MS (Method A): Rt: 2.71 min; ESI+-MS m/z: 593.5 (M+1).

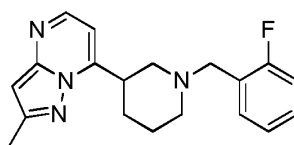
Step d. Title compound.

TFA (0.5 mL) was added to a solution of the compound obtained in step c (58 mg, 0.08 mmol) in DCM (5 mL) and the mixture was stirred at r.t. for 16 h. The reaction mixture was basified with aq sat NaHCO₃ sol and the mixture was extracted with DCM. The combined organic layers were washed with brine, dried over anhyd Na₂SO₄, filtered and concentrated to dryness. The crude product was purified by flash chromatography, silica gel, DCM:MeOH to give the title compound (22 mg, Yield: 57%).

HPLC-MS (Method A): Rt, 2.06 min; ESI+-MS m/z: 493.3 [M+H]⁺.

This method was used for the preparation of example 62 using suitable starting materials:

STRUCTURE	EX	CHEMICAL NAME	Rt (min)	MS (M+H)	HPLC Method
	62	1-(4-(7-(1-Benzylpiperidin-3-yl)-2-methylpyrazolo[1,5- <i>a</i>]pyrimidin-3-yl)pyridin-2-yl)-N-methylmethanamine	1.89	427.3	A



Example 63. 7-(1-(2-Fluorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidine.

Step a. 2-Methyl-7-(piperidin-3-yl)pyrazolo[1,5-a]pyrimidine.

A Radley tube was charged with the compound obtained in example 3 (100 mg, 0.32 mmol), ammonium formate (72 mg, 1.1 mmol), 10% Pd/C (34 mg, 0.03 mmol) and EtOH (10 mL) and the reaction mixture was stirred at 85 °C for 2 h. The suspension was filtered through Celite and the solvent was removed under vacuum to give the title compound (70 mg, Yield: 99%).

HPLC-MS (Method A): Rt: 0.92 min; ESI+-MS m/z: 217.1 (M+1).

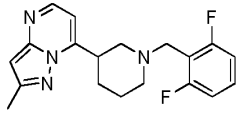
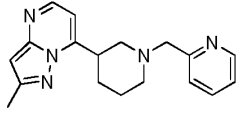
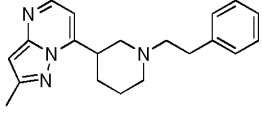
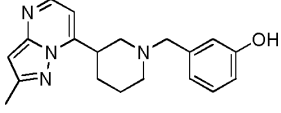
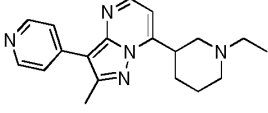
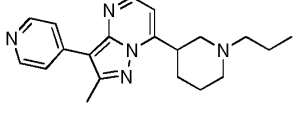
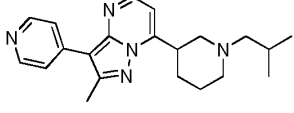
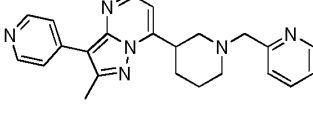
Step b. Title compound.

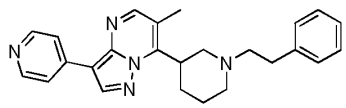
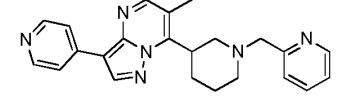
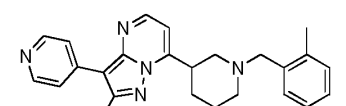
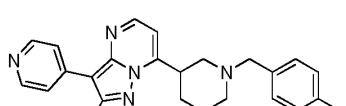
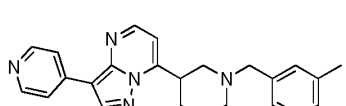
A MW tube was charged with the compound obtained in step a (75 mg, 0.35 mmol), 2-fluorobenzaldehyde (47 mg, 0.38 mmol), NaBH₃CN (65 mg, 1 mmol) and MeOH (3 mL) and the mixture was heated under MW irradiation at 120 °C for 20 min. The reaction mixture was concentrated under reduced pressure and the residue was diluted with EtOAc and washed with aq sat NaHCO₃ sol. The organic layer was dried over anhydrous Na₂SO₄, filtered and solvent was removed under vacuum. The residue was purified by flash chromatography, silica gel, DCM:MeOH, to give the title compound (41 mg, Yield: 36%).

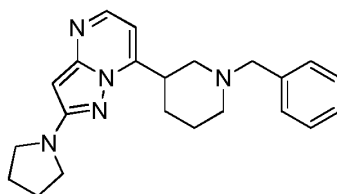
HPLC-MS (Method A): Rt, 2.06 min; ESI+-MS m/z: 325.2 [M+H]⁺.

This method was used for the preparation of examples 64-77 using suitable starting materials:

STRUCTURE	EX	CHEMICAL NAME	Rt (min)	MS (M+H)	HPLC Method
	64	7-(1-Butylpiperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidine	1.85	273.3	A

	65	7-(1-(2,6-Difluorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidine	2.05	343.2	A
	66	2-Methyl-7-(1-(pyridin-2-ylmethyl)piperidin-3-yl)pyrazolo[1,5-a]pyrimidine	1.48	308.3	A
	67	2-Methyl-7-(1-phenethylpiperidin-3-yl)pyrazolo[1,5-a]pyrimidine	2.06	321.3	A
	68	3-((3-(2-Methylpyrazolo[1,5-a]pyrimidin-7-yl)piperidin-1-yl)methyl)phenol	1.62	323.3	A
	69	7-(1-Ethylpiperidin-3-yl)-2-methyl-3-(pyridin-4-yl)pyrazolo[1,5-a]pyrimidine	1.55	322.1	A
	70	2-Methyl-7-(1-propylpiperidin-3-yl)-3-(pyridin-4-yl)pyrazolo[1,5-a]pyrimidine	1.83	336.2	A
	71	7-(1-Isobutylpiperidin-3-yl)-2-methyl-3-(pyridin-4-yl)pyrazolo[1,5-a]pyrimidine	2.31	350.2	A
	72	2-Methyl-7-(1-(pyridin-2-ylmethyl)piperidin-3-yl)-3-(pyridin-4-yl)pyrazolo[1,5-a]pyrimidine	1.66	385.2	A

	73	6-Methyl-7-(1-phenethylpiperidin-3-yl)-3-(pyridin-4-yl)pyrazolo[1,5-a]pyrimidine	2.19	398.2	A
	74	6-Methyl-7-(1-(pyridin-2-ylmethyl)piperidin-3-yl)-3-(pyridin-4-yl)pyrazolo[1,5-a]pyrimidine	1.70	385.3	A
	75	2-methyl-7-(1-(2-methylbenzyl)piperidin-3-yl)-3-(pyridin-4-yl)pyrazolo[1,5-a]pyrimidine	2.39	398.3	C
	76	2-Methyl-7-(1-(4-methylbenzyl)piperidin-3-yl)-3-(pyridin-4-yl)pyrazolo[1,5-a]pyrimidine	2.38	398.3	C
	77	2-Methyl-7-(1-(3-methylbenzyl)piperidin-3-yl)-3-(pyridin-4-yl)pyrazolo[1,5-a]pyrimidine	2.39	398.3	C



Example 78. 7-(1-Benzylpiperidin-3-yl)-2-(pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidine.

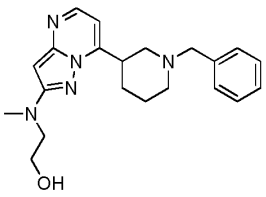
A schlenk flask was charged with the compound obtained in example 1 (125 mg, 0.33 mmol), pyrrolidine (0.05 mL, 0.67 mmol), XPhos (16 mg, 0.034 mmol), Pd₂dba₃ (15 mg, 0.0044 mmol) and KO^tBu (113 mg, 1 mmol) and was evacuated and backfilled with argon. Toluene (4 mL), degassed by means of bubbling argon for 5 min, was added and the reaction mixture was heated at 100 °C for 16 h. The reaction mixture was concentrated under reduced pressure and the residue was diluted with EtOAc and washed with aq sat NaHCO₃ sol. The organic layer was dried over anhyd Na₂SO₄, filtered

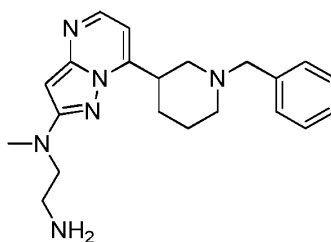
and the solvent was removed under vacuum. The residue was purified by flash chromatography, silica gel, Chx:EtOAc, to give the title compound (16 mg, Yield: 13%).

HPLC-MS (Method A): Rt, 2.42 min; ESI+-MS m/z: 362.3 [M+H]⁺.

This method was used for the preparation of example 79 using suitable starting materials:

5

STRUCTURE	EX	CHEMICAL NAME	Rt (min)	MS (M+H)	HPLC Method
	79	2-((7-(1-Benzylpiperidin-3-yl)pyrazolo[1,5-a]pyrimidin-2-yl)(methyl)amino)ethanol	1.83	366.4	A



Example 80. N¹-(7-(1-Benzylpiperidin-3-yl)pyrazolo[1,5-a]pyrimidin-2-yl)-N¹-methylethane-1,2-diamine.

10 Step a. *tert*-Butyl (2-((7-(1-benzylpiperidin-3-yl)pyrazolo[1,5-a]pyrimidin-2-yl)(methyl)amino)ethyl)carbamate.

Starting from the compound obtained in example 1 (350 mg, 0.94 mmol) and *tert*-butyl (2-(methylamino)ethyl)carbamate (197 mg, 1.13 mmol) and following the procedure described in example 78, the title compound was obtained (77 mg, Yield: 17%).

15 HPLC-MS (Method A): Rt: 2.36 min; ESI+- m/z: 465.2 (M+1).

Step b. Title compound.

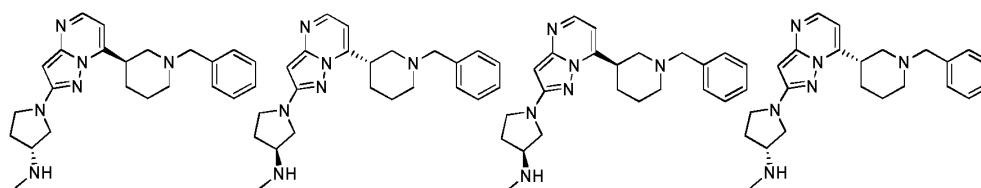
Starting from the compound obtained in step a (89 mg, 0.2 mmol) and following the procedure described in step d of example 61, the title compound was obtained (72 mg, Yield: 98%).

HPLC-MS (Method A): Rt, 1.68 min; ESI+-MS m/z: 356.3 [M+H]⁺.

This method was used for the preparation of examples 81-83 using suitable starting materials:

STRUCTURE	EX	CHEMICAL NAME	Rt (min)	MS (M+H)	HPLC Method
	81	<i>N'</i> -(7-(1-Benzylpiperidin-3-yl)pyrazolo[1,5-a]pyrimidin-2-yl)- <i>N'</i> , <i>N'</i> -dimethylethane-1,2-diamine	1.62	379.2	A
	82	7-(1-Benzylpiperidin-3-yl)- <i>N</i> -methyl- <i>N</i> -(piperidin-4-yl)pyrazolo[1,5-a]pyrimidin-2-amine	1.65	405.2	A
	83	<i>N'</i> -(7-(1-Benzylpiperidin-3-yl)pyrazolo[1,5-a]pyrimidin-2-yl)- <i>N'</i> -methylethane-1,2-diamine	1.54	365.2	A

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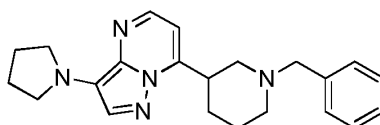


Examples 84, 85, 86 and 87. (*R*)-1-(7-((*R*)-1-Benzylpiperidin-3-yl)pyrazolo[1,5-a]pyrimidin-2-yl)-*N*-methylpyrrolidin-3-amine, (*S*)-1-(7-((*S*)-1-benzylpiperidin-3-yl)pyrazolo[1,5-a]pyrimidin-2-yl)-*N*-methylpyrrolidin-3-amine, (*S*)-1-(7-((*R*)-1-benzylpiperidin-3-yl)pyrazolo[1,5-a]pyrimidin-2-yl)-*N*-methylpyrrolidin-3-amine and (*R*)-

10

1-(7-((*S*)-1-benzylpiperidin-3-yl)pyrazolo[1,5-*a*]pyrimidin-2-yl)-*N*-methylpyrrolidin-3-amine.

Starting from 1-(7-(1-benzylpiperidin-3-yl)pyrazolo[1,5-*a*]pyrimidin-2-yl)-*N*-methylpyrrolidin-3-amine, obtained following a similar procedure to that described in example 80, a chiral preparative HPLC [Column Chiralpak IA 20 x 250 mm, 5 μ m; temperature: r.t.; eluent: n-Heptane/DCM/EtOH/Et₂NH 70/28/2/0.1 v/v/v/v; flow rate: 13 mL/min; Rt1: 11.9 min; Rt2: 13.2 min; Rt3: 13.7 min; Rt4: 13.9 min] was carried out to give the title compounds.



Example 88. 7-(1-Benzylpiperidin-3-yl)-3-(pyrrolidin-1-yl)pyrazolo[1,5-*a*]pyrimidine.

Step a. 7-(1-Benzylpiperidin-3-yl)-3-iodopyrazolo[1,5-*a*]pyrimidine.

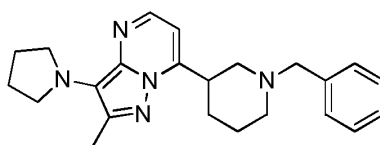
Starting from 4-iodo-1*H*-pyrazol-3-amine (153 mg, 0.73 mmol) and following the procedure described in step b of example 1, the title compound was obtained (170 mg, Yield: 55%).

HPLC-MS (Method A): Rt: 2.35 min; ESI+-MS *m/z*: 419.0 (*M*+1).

Step b. Title compound.

A MW tube was charged with the compound obtained in step a (80 mg, 0.19 mmol), pyrrolidine (0.06 mL, 0.76 mmol), CuI (14 mg, 0.077 mmol), (*S*)-proline (8 mg, 0.077 mmol), K₂CO₃ (53 mg, 0.38 mmol) and DMSO (2 mL) and the mixture was degassed by means of bubbling argon for 5 min and heated under MW irradiation at 100 °C for 3 h. The mixture was dissolved with EtOAc:Et₂O (1:1) and was washed with aq sat NaHCO₃ sol. The organic layer was dried over anhydrous Na₂SO₄, filtered and the solvent was removed under vacuum. The crude product was purified by flash chromatography, silica gel, Chx:EtOAc to give the title compound (10 mg, Yield: 14%).

HPLC-MS (Method B): Rt, 2.81 min; ESI+-MS *m/z*: 362.4 [*M*+*H*]⁺.



Example 89. 7-(1-Benzylpiperidin-3-yl)-2-methyl-3-(pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidine.

Step a. 7-(1-Benzylpiperidin-3-yl)-3-iodo-2-methylpyrazolo[1,5-a]pyrimidine.

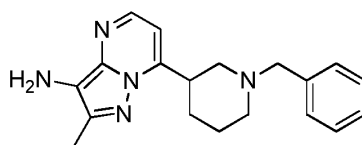
- 5 Starting from the compound obtained in example 3 (415 mg, 1.35 mmol) and NIS (426 mg, 1.9 mmol) and following the procedure described in example 10, the title compound was obtained (434 mg, Yield: 74%).

HPLC-MS (Method A): Rt: 2.46 min; ESI+-MS m/z: 433.1 (M+1).

Step b. Title compound.

- 10 Starting from the compound obtained in step a (243 mg, 0.56 mmol) and following the procedure described in step b of example 88, the title compound was obtained (10 mg, Yield: 5%).

HPLC-MS (Method A): Rt, 1.59 min; ESI+-MS m/z: 406.4 [M+H]⁺.

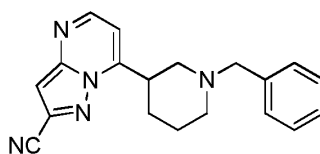


15

Example 90. 7-(1-Benzylpiperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-amine.

- A solution of the compound obtained in example 8 in conc HCl (3 mL) was stirred at 90 °C for 6 h. The reaction mixture was cooled to r.t. and basified with 10% aq sat NaHCO₃ sol and the mixture was extracted with DCM. The combined organic layers were washed with brine, dried over anhydrous Na₂SO₄, filtered and concentrated to dryness. The crude product was purified by flash chromatography, silica gel, DCM:MeOH to give the title compound (43 mg, Yield: 40%).
- 20

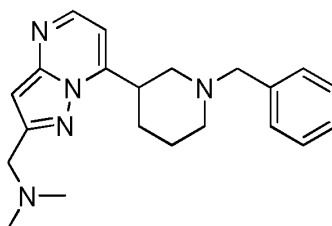
HPLC-MS (Method A): Rt, 2.94 min; ESI+-MS m/z: 320.4 [M+H]⁺.



Example 91. 7-(1-Benzylpiperidin-3-yl)pyrazolo[1,5-a]pyrimidine-2-carbonitrile

A schlenk flask was charged with the compound obtained in example 1 (90 mg, 0.24 mmol), $K_4[Fe(CN)_6] \cdot 2H_2O$ (24 mg, 0.06 mmol), 1,1'-bis(diphenylphosphino)ferrocene (28 mg, 0.05 mmol), $Pd(OAc)_2$ (2 mg, 0.006 mmol) and Na_2CO_3 (26 mg, 0.24 mmol) and was evacuated and backfilled with argon. NMP (2 mL), degassed by means of bubbling argon for 5 min, was added and the reaction mixture was heated at 120 °C for 16 h. The reaction mixture was diluted with EtOAc and washed with aq sat $NaHCO_3$ sol. The organic layer was dried over anhydrous Na_2SO_4 , filtered and solvent was removed under vacuum. The residue was purified by flash chromatography, silica gel, Chx:EtOAc, to give the title compound (8 mg, Yield: 10%).

HPLC-MS (Method A): Rt, 2.16 min; ESI+-MS m/z: 318.2 $[M+H]^+$.



Example 92. 1-(7-(1-Benzylpiperidin-3-yl)pyrazolo[1,5-a]pyrimidin-2-yl)-N,N-dimethylmethanamine.

Step a. 7-(1-Benzylpiperidin-3-yl)pyrazolo[1,5-a]pyrimidine-2-carboxylic acid.

Starting from 3-amino-1H-pyrazole-5-carboxylic acid (93 mg, 0.73 mmol) and following the procedure described in step b of example 1, the title compound was obtained (94 mg, Yield: 38%).

HPLC-MS (Method A): Rt: 1.19 min; ESI+-MS m/z: 337.2 (M+1).

Step b. 7-(1-Benzylpiperidin-3-yl)-N,N-dimethylpyrazolo[1,5-a]pyrimidine-2-carboxamide.

Dimethylamine hydrochloride (170 mg, 2.1 mmol), TEA (0.58 mL, 4.1 mmol), EDC·HCl (398 mg, 2.1 mmol), DMAP (13 mg, 0.1 mmol) and HOBt (281 mg, 2.1 mmol) were added to a solution of the compound obtained in step a (350 mg, 0.77 mmol) in DMF (15 mL) and the reaction was stirred at r.t. for 16 h. The mixture was dissolved with EtOAc:Et₂O (1:1) and was washed with aq sat NaHCO₃ sol. The organic layer was dried over anhydrous Na₂SO₄, filtered and solvent was removed under vacuum. The crude product was purified by flash chromatography, silica gel, DCM:MeOH to give the title compound (320 mg, Yield: 74%).

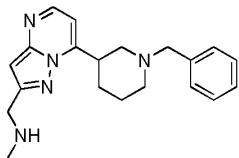
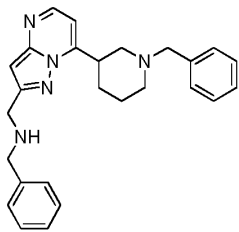
HPLC-MS (Method A): Rt: 1.78 min; ESI+-MS m/z: 364.1 (M+1).

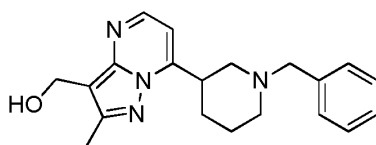
Step c. Title compound.

To a 1 M solution of AlH₃ in THF (4.4 mL, 4.4 mmol) at 0 °C, a solution of the compound obtained in step b (320 mg, 0.88 mmol) in THF (4 mL) was added and the mixture was stirred at 0 °C for 90 min. After this time, water was added dropwise and the mixture was extracted with EtOAc. The organic layer was dried over anhydrous Na₂SO₄, filtered and solvent was removed under vacuum. The crude product was purified by flash chromatography, silica gel, DCM:MeOH to give the title compound (30 mg, Yield: 10%).

HPLC-MS (Method A): Rt, 1.80 min; ESI+-MS m/z: 350.2 [M+H]⁺.

This method was used for the preparation of examples 93 and 94 using suitable starting materials:

STRUCTURE	EX	CHEMICAL NAME	Rt (min)	MS (M+H)	HPLC Method
	93	1-(7-(1-Benzylpiperidin-3-yl)pyrazolo[1,5-a]pyrimidin-2-yl)-N-methylmethanamine	1.54	336.1	A
	94	N-Benzyl-1-(7-(1-benzylpiperidin-3-yl)pyrazolo[1,5-a]pyrimidin-2-yl)methanamine	2.19	412.2	A



Example 95. (7-(1-Benzylpiperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methanol.

Step a. 7-(1-Benzylpiperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidine-3-carbaldehyde.

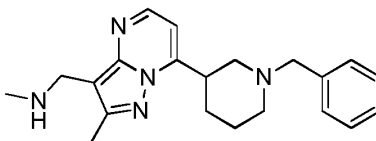
- 5 To a solution of the compound obtained in example 3 (50 mg, 0.16 mmol) in DMF (2 mL), POCl₃ (46 µL, 0.5 mmol) was added and the resulting mixture was stirred at r.t. for 16 h. The reaction mixture was cooled to 0 °C and the excess of POCl₃ was quenched by the addition of ice. The resulting solution was neutralized with 1 M aq NaOH, diluted with water and extracted with DCM. The organic layer was dried over anhydrous Na₂SO₄, filtered and solvent was removed under vacuum to give the title compound (63 mg, Yield: Quant.).
- 10

HPLC-MS (Method A): Rt: 2.00 min; ESI+-MS m/z: 335.1 (M+1).

Step b. Title compound.

- NaBH₄ (7 mg, 0.2 mmol) was added to a solution of the compound obtained in step a (63 mg, 0.19 mmol) in THF (4 mL) and the mixture was stirred at r.t. for 16 h. The reaction mixture was cooled to 0 °C and water was slowly added. The residue was extracted with DCM, the organic layer was dried over anhydrous Na₂SO₄, filtered and the solvent was removed under vacuum. The crude product was purified by flash chromatography, silica gel, Chx:EtOAc to give the title compound (12 mg, Yield: 19%).
- 15

- 20 HPLC-MS (Method A): Rt, 1.68 min; ESI+-MS m/z: 337.2 [M+H]⁺.



Example 96. 1-(7-(1-Benzylpiperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-N-methylmethanamine.

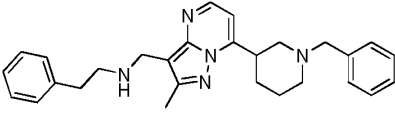
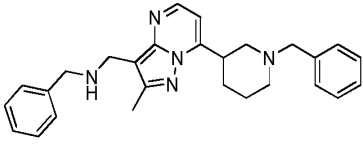
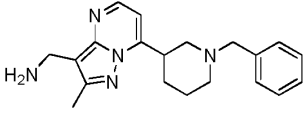
- 25 Starting from the compound obtained in step a of example 95 (80 mg, 0.24 mmol) in a 2 M solution of methylamine in THF (0.7 mL, 1.4 mmol) and following the procedure

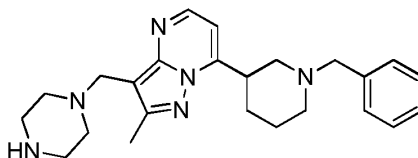
described in step b of example 63, the title compound was obtained (41 mg, Yield: 49%).

HPLC-MS (Method A): Rt, 1.46 min; ESI+-MS m/z: 350.1 [M+H]⁺.

This method was used for the preparation of examples 97-99 using suitable starting materials:

5

STRUCTURE	EX	CHEMICAL NAME	Rt (min)	MS (M+H)	HPLC Method
	97	N-((7-(1-Benzylpiperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methyl)-2-phenylethanamine	2.16	440.2	A
	98	N-Benzyl-1-((7-(1-benzylpiperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methyl)ethanamine	2.23	426.2	A
	99	(7-(1-Benzylpiperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methanamine	1.85	334.2	B



Example 100. 7-(1-Benzylpiperidin-3-yl)-2-methyl-3-(piperazin-1-ylmethyl)pyrazolo[1,5-a]pyrimidine.

10 Step a. *tert*-Butyl 4-((7-(1-benzylpiperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methyl)piperazine-1-carboxylate.

Starting from the compound obtained in step a of example 95 (100 mg, 0.3 mmol) and *tert*-butyl piperazine-1-carboxylate (278 mg, 1.5 mmol) and following the procedure described in step b of example 63, the title compound was obtained (123 mg, Yield:

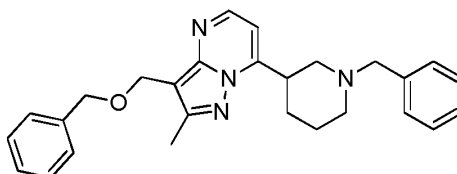
15 81%).

HPLC-MS (Method A): Rt: 2.47 min; ESI+-MS m/z: 505.3 (M+1).

Step b. Title compound.

Starting from the compound obtained in step a (123 mg, 0.24 mmol) and following the procedure described in step d of example 61, the title compound was obtained (59 mg, Yield: 60%).

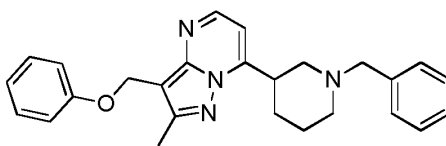
HPLC-MS (Method A): Rt, 1.55 min; ESI+-MS m/z: 405.3 [M+H]⁺.



Example 101. 3-((Benzyloxy)methyl)-7-(1-benzylpiperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidine.

NaH (60% in mineral oil) (13 mg, 0.33 mmol) was added to a solution of the compound obtained in example 95 (45 mg, 0.13 mmol) in DMF (4 mL) and the reaction was stirred at 0 °C for 30 min. Then, benzyl bromide (32 µL, 0.27 mmol) was added and the mixture was stirred 16 h at 85 °C. The mixture was dissolved with EtOAc:Et₂O (1:1) and washed with brine. The organic layer was dried over anhydrous Na₂SO₄, filtered and solvent was removed under vacuum. The crude product was purified by flash chromatography, silica gel, CH₂Cl₂:EtOAc to give the title compound (22 mg, Yield: 38%).

HPLC-MS (Method A): Rt, 2.53 min; ESI+-MS m/z: 427.2 [M+H]⁺.

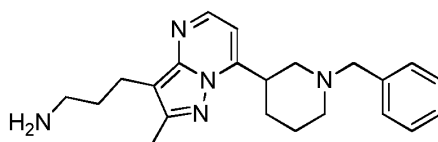


Example 102. 7-(1-Benzylpiperidin-3-yl)-2-methyl-3-(phenoxy)methylpyrazolo[1,5-a]pyrimidine.

DIAD (60 µL, 0.31 mmol) was added to a solution of the compound obtained in example 95 (80 mg, 0.24 mmol), phenol (29 mg, 0.31 mmol) and PPh₃ (81 mg, 0.31 mmol) in toluene (10 mL) and the mixture was stirred at 100 °C for 16 h. The reaction was

quenched with water, diluted with EtOAc and washed with brine. The organic layer was dried over anhydrous Na_2SO_4 , filtered and the solvent was removed under vacuum. The crude product was purified by flash chromatography, silica gel, DCM:MeOH to give the title compound (21 mg, Yield: 21%).

- 5 HPLC-MS (Method A): Rt, 2.18 min; ESI+-MS m/z: 413.3 $[\text{M}+\text{H}]^+$.



Example 103. 3-(7-(1-Benzylpiperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)propan-1-amine

- 10 Step a. *tert*-Butyl (3-(7-(1-benzylpiperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)allyl)carbamate.

A schlenk flask was charged with the compound obtained in example 10 (360 mg, 0.93 mmol), *tert*-butyl (3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)allyl)carbamate (291 mg, 1 mmol), $\text{Pd}(\text{PPh}_3)_4$ (108 mg, 0.09 mmol) and Na_2CO_3 (198 mg, 1.9 mmol) and then was evacuated and backfilled with argon. A mixture of toluene:EtOH:H₂O (3:1:1) (4 mL), degassed by means of bubbling argon for 5 min, was added and the reaction mixture was heated at 80 °C for 16 h. The suspension was diluted with EtOAc and washed with aq sat NaHCO_3 sol and brine. The organic layer was dried over anhydrous Na_2SO_4 , filtered and solvent was removed under vacuum. The residue was purified by flash chromatography, silica gel, Chx:Acetone, to give the title compound (56 mg, Yield: 13%).

15 HPLC-MS (Method A): Rt: 2.46 min; ESI+-MS m/z: 462.2 (M+1).

Step b. *tert*-Butyl (3-(7-(1-benzylpiperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)propyl)carbamate.

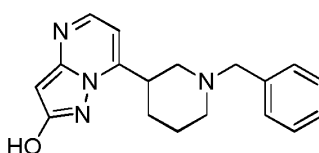
- 25 $\text{Pd}(\text{OH})_2$ (27 mg, 0.2 mmol) was added to a solution of the compound obtained in step a (90 mg, 0.2 mmol) in MeOH (4 mL) and the solution was stirred under H_2 atmosphere during 16 h. The suspension was filtered through Celite and the solvent was removed under vacuum. The residue was purified by flash chromatography, silica gel, DCM:MeOH, to give the title compound (25 mg, Yield: 28%).

HPLC-MS (Method B): Rt: 2.89 min; ESI+-MS m/z: 464.3 (M+1).

Step c. Title compound.

Starting from the compound obtained in step b (25 mg, 0.05 mmol) and following the procedure described in step d of example 61, the title compound was obtained (3 mg, Yield: 11%).

HPLC-MS (Method A): Rt, 1.56 min; ESI+-MS m/z: 364.2 [M+H]⁺.



Examples 104 and 105. 7-(1-Benzylpiperidin-3-yl)pyrazolo[1,5-a]pyrimidin-2-ol

Step a. (7-(1-Benzylpiperidin-3-yl)pyrazolo[1,5-a]pyrimidin-2-yl)boronic acid.

To a solution of the compound obtained in example 1 (50 mg, 0.13 mmol), bis(pinacolato)diboron (51 mg, 0.2 mmol) and KOAc (39 mg, 0.4 mmol) in anhydrous dioxane (5 mL) under argon atmosphere, Pd(dppf)FeCl₂ (6 mg, 0.008 mmol) was added and the mixture was heated at 115 °C for 16 h. The reaction was quenched with brine, diluted with EtOAc and washed with brine. The organic layer was dried over anhydrous Na₂SO₄, filtered and the solvent was removed under vacuum to give the title compound (70 mg, Yield: Quant).

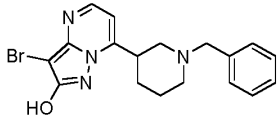
HPLC-MS (Method C): Rt: 1.56 min; ESI+-MS m/z: 337.2 (M+1).

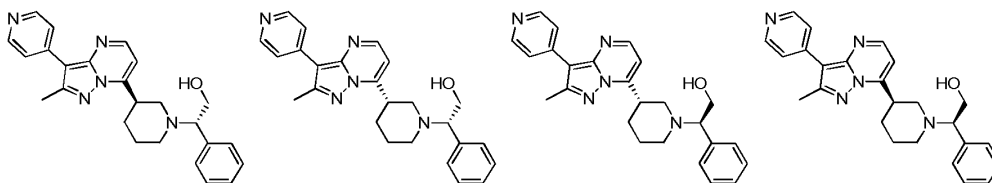
Step b. Title compound.

To a solution of the compound obtained in step a (50 mg, 0.15 mmol) in AcOH (3 mL) at 0 °C, H₂O₂ (9 µL, 0.33 mmol) was added. The solution was stirred at this temperature for 30 min and allowed to warm to r.t. during 16 h more. The reaction mixture was filtered through Celite and the solvent was removed under vacuum. The residue was purified by flash chromatography, silica gel, DCM:MeOH, to give the title compound (10 mg, Yield: 22%).

HPLC-MS (Method C): Rt, 1.43 min; ESI+-MS m/z: 309.2 [M+H]⁺.

This method was also used for the preparation of example 105.

STRUCTURE	EX	CHEMICAL NAME	Rt (min)	MS (M+H)	HPLC Method
	105	7-(1-Benzylpiperidin-3-yl)-3-bromopyrazolo[1,5-a]pyrimidin-2-ol	1.31	387.2	C



- 5 Examples 106, 107, 108 and 109. (S)-2-((R)-3-(2-Methyl-3-(pyridin-4-yl)pyrazolo[1,5-a]pyrimidin-7-yl)piperidin-1-yl)-2-phenylethanol, (S)-2-((S)-3-(2-methyl-3-(pyridin-4-yl)pyrazolo[1,5-a]pyrimidin-7-yl)piperidin-1-yl)-2-phenylethanol, (R)-2-((S)-3-(2-methyl-3-(pyridin-4-yl)pyrazolo[1,5-a]pyrimidin-7-yl)piperidin-1-yl)-2-phenylethanol and (R)-2-((R)-3-(2-methyl-3-(pyridin-4-yl)pyrazolo[1,5-a]pyrimidin-7-yl)piperidin-1-yl)-2-phenylethanol.
- 10

Step a. 2-Methyl-7-(piperidin-3-yl)-3-(pyridin-4-yl)pyrazolo[1,5-a]pyrimidine.

Starting from the compound obtained in example 42 (154 mg, 0.4 mmol) and following the procedure described in step a. of example 63, the title compound was obtained (120 mg, Yield: Quant).

- 15 HPLC-MS (Method C): Rt: 1.12 min; ESI+-MS m/z: 294.1 (M+1).

Step b. 2-(3-(2-Methyl-3-(pyridin-4-yl)pyrazolo[1,5-a]pyrimidin-7-yl)piperidin-1-yl)-2-phenylethanol.

- To a solution of 2-phenyloxirane (45 mg, 0.37 mmol) in ACN (2 mL), LiClO₄ (79 mg, 0.75 mmol) was added and the suspension was stirred until complete solution of the salts. Then, a solution of the compound obtained in step a (45 mg, 0.37 mmol) in ACN (0.5 mL) was added and the solution was stirred at 80 °C for 16 h. The suspension was diluted with EtOAc and washed with aq sat NaHCO₃ sol and brine. The organic layer was dried over anhydrous Na₂SO₄, filtered and solvent was removed under vacuum. The
- 20

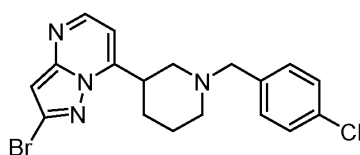
residue was purified by flash chromatography, silica gel, Chx:EtOAc, to give the title compound (34 mg, Yield: 23%).

HPLC-MS (Method C): Rt: 1.95 min; ESI+-MS m/z : 414.3 (M+1).

Step c. Title compounds.

- 5 Starting from the compound obtained in step b, a chiral preparative HPLC [Column LUX C3 21.2 x 250 mm, 5 μ m; temperature: 40 °C; eluent: MeOH/EtOH/NH₃ 70/30/0.1 v/v/v; flow rate: 50 mL/min; Rt1: 2.02 min; Rt2: 2.15 min; Rt3: 2.84; Rt4: 3.83 min] was carried out to give the title compounds.

10



Example 110. 2-Bromo-7-(1-(4-chlorobenzyl)piperidin-3-yl)pyrazolo[1,5-a]pyrimidine.

Step a. *tert*-Butyl 3-acetylpiperidine-1-carboxylate.

- 15 To a 0 °C cooled solution of 1-(*tert*-butyl) 3-ethyl piperidine-1,3-dicarboxylate (5 g, 19.43 mmol), and *N,O*-dimethylhydroxylamine hydrochloride (2.27 g, 23.32 mmol) in anhyd THF (69 mL) and under argon atmosphere, methylmagnesium chloride (3 M in THF, 35.6 mL, 107 mmol) was added dropwise. The reaction was allowed to warm up to r.t. for 16 h. Then the solution was quenched with aq sat NH₄Cl sol at 0 °C. The aq layer was extracted with EtOAc and the combined organic extracts were washed with brine, dried over MgSO₄, filtered and concentrated to give the title compound as a light brown oil (4.19 g, Yield: 95%).
- 20

HPLC-MS (Method E): Rt.: 3.33 min; ESI+ MS: m/z 254.0 [M+H]⁺.

Step b. *tert*-Butyl (*E*)-3-(3-(dimethylamino)acryloyl)piperidine-1-carboxylate.

- 25 A solution of the compound obtained in step a (4.15 g, 18.28 mmol) and 1-*tert*-butoxy-*N,N,N',N'*-tetramethylmethanedi-amine (3.82 mL, 21.93 mmol) were mixed in a sealed reactor under argon and the mixture was stirred at 100 °C for 16 h. The reaction mixture was concentrated to dryness under reduced pressure to give the title compound as a brown oil (5.50 g). This compound was used in the next step without further purification.

HPLC-MS (Method E): Rt.: 2.63 min; ESI+ MS: m/z 283.3 [M+H]⁺.

Step c. *tert*-Butyl 3-(2-bromopyrazolo[1,5-*a*]pyrimidin-7-yl)piperidine-1-carboxylate.

To a solution of the compound obtained in step b (3.2 g, 11.33 mmol) in glacial AcOH (48 mL), 5-bromo-1*H*-pyrazol-3-amine (2.01 mg, 12.47 mmol) was added. The reaction mixture was stirred at 50 °C for 9 h. The solvent was evaporated and the residue was purified by flash chromatography, silica gel, hexane/EtOAc as eluents to give the title compound as a brown foam (2.85 g, Yield: 66%).

HPLC-MS (Method D): Rt.: 2.98 min; ESI+ MS: *m/z* 381.1 [M+H]⁺.

Step d. 2-Bromo-7-(piperidin-3-yl)pyrazolo[1,5-*a*]pyrimidine hydrochloride.

The compound obtained in step c (1.04 g, 2.73 mmol) was treated with HCl (4 M in dioxane, 13.64 mL, 54.6 mmol). A yellow precipitate appeared just after the addition. The reaction mixture was stirred for 1.5 h, then the solvent was evaporated to give the title compound as a yellow solid (960 mg) which was used in the next step without further purification.

HPLC-MS (Method E): Rt.: 2.25 min; ESI+ MS: *m/z* 281.0 [M+H]⁺.

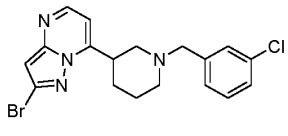
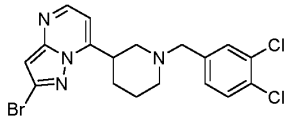
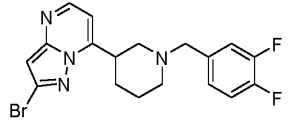
Step e. Title compound.

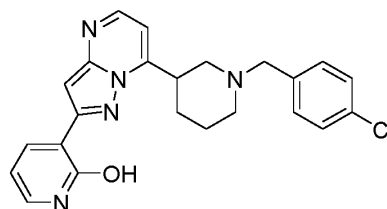
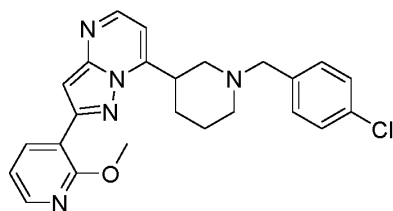
To a solution of the compound obtained in step d (80 mg, 0.25 mmol) in anhyd MeOH (2 mL) TEA (0.07 mL, 0.50 mmol) was added and the solution was stirred for 5 min. 4-Chlorobenzaldehyde (53.1 mg, 0.38 mmol) and AcOH (0.012 mL, 0.2 mmol) were added to the solution followed by sodium cyanotrihydroborate (31.7 mg, 0.50 mmol) and the reaction mixture was stirred at r.t. for 16 h. Then, solvent was evaporated and the reaction mixture was dissolved with DCM and poured into aq sat NaHCO₃ sol, the organic layer was separated and the aq layer was extracted with DCM. The combined organic extracts were washed with brine, dried over anhyd Na₂SO₄ and filtered. Solvent was evaporated and the residue was purified by flash chromatography, silica gel, DCM:MeOH as eluents to give the title compound as a yellow solid (81 mg, Yield: 78%).

HPLC-MS (Method D): Rt.: 3.43 min; ESI+ MS: *m/z* 405.0 [M+H]⁺.

This method was used for the preparation of examples 111-113 using suitable starting materials:

STRUCTURE	EX	CHEMICAL NAME	Rt (min)	MS (M+H)	HPLC Method
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	111	2-Bromo-7-(1-(3-chlorobenzyl)piperidin-3-yl)pyrazolo[1,5-a]pyrimidine	3.45	405.0	D
	112	2-Bromo-7-(1-(3,4-dichlorobenzyl)piperidin-3-yl)pyrazolo[1,5-a]pyrimidine	3.65	439.0	D
	113	2-Bromo-7-(1-(3,4-difluorobenzyl)piperidin-3-yl)pyrazolo[1,5-a]pyrimidine	3.32	407.1	D



Examples 114 and 115. 7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-(2-methoxypyridin-3-yl)pyrazolo[1,5-a]pyrimidine and 3-(7-(1-(4-chlorobenzyl)piperidin-3-yl)pyrazolo[1,5-a]pyrimidin-2-yl)pyridin-2-ol.

Step a. *tert*-Butyl 3-(2-(2-methoxypyridin-3-yl)pyrazolo[1,5-a]pyrimidin-7-yl)piperidine-1-carboxylate.

A sealed tube was charged with the compound obtained in step c of example 110 (1.67 g, 4.38 mmol), (2-methoxypyridin-3-yl)boronic acid (1.00 g, 6.57 mmol), K₂CO₃ (1.81 g, 13.14 mmol), Pd(PPh₃)₄ (500 mg, 0.44 mmol) and DME:H₂O (3:1, 26 mL). The reaction mixture was degassed by argon for 5 min and heated at 100 °C for 16 h. The suspension was diluted with EtOAc and the organic layer was separated, washed with aq sat Na₂CO₃ sol, dried over anhydrous Na₂SO₄, filtered and concentrated under vacuum. The residue was purified by flash chromatography, silica gel, DCM:MeOH, to give the title compound as a brown foam (1.28 g, Yield: 71%).

HPLC-MS (Method E): Rt.: 3.83 min; ESI+ MS: *m/z* 410.2 [M+H]⁺.

Step b. 2-(2-Methoxypyridin-3-yl)-7-(piperidin-3-yl)pyrazolo[1,5-a]pyrimidine hydrochloride and 3-(7-(piperidin-3-yl)pyrazolo[1,5-a]pyrimidin-2-yl)pyridin-2-ol hydrochloride.

5 Starting from the compound obtained in step a (790 mg, 1.92 mmol) and following the procedure described in step d of example 110, the title compounds were obtained as a 1:1 mixture (400 mg). This mixture was used in the next step without further purification.

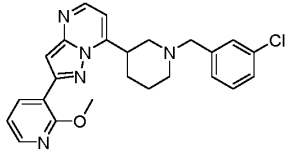
HPLC-MS (Method D): Rt.: 1.45 min; ESI+ MS: m/z 296.1 $[M+H]^+$ and Rt.: 2.03 min; ESI+ MS: m/z 310.1 $[M+H]^+$ respectively.

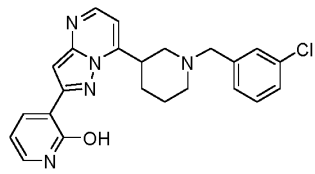
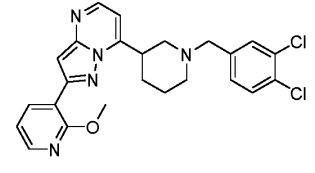
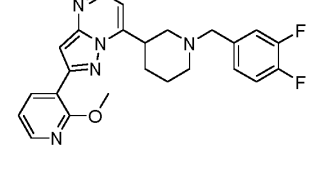
Step c. Title compounds.

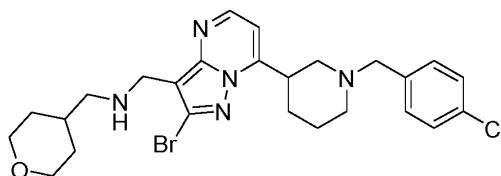
10 To a solution of the mixture of compounds obtained in step b (200 mg, 0.57 mmol) in anhyd DMA (3 mL) TEA (0.24 mL, 1.73 mmol) was added and the solution was stirred for 5 min. 1-Chloro-4-(chloromethyl)benzene (93.1 mg, 0.57 mmol) was added and the reaction mixture was stirred at 70 °C for 16 h. The reaction mixture was allowed to cool down to r.t. and was poured into aq sat NaHCO_3 sol and DCM, the organic layer was separated and the aq layer was extracted with DCM. The combined organic extracts were washed with brine, dried over anhyd Na_2SO_4 and filtered. Solvent was evaporated and the residue was purified by flash chromatography, silica gel, DCM:MeOH as eluents to give the title compounds as yellow solids (69 mg, Yield: 26% and 52 mg, Yield: 20% respectively).

20 HPLC-MS (Method D): Rt.: 3.60 min; ESI+ MS: m/z 434.1 $[M+H]^+$ and Rt.: 2.73 min; ESI+ MS: m/z 420.1 $[M+H]^+$ respectively.

This method was used for the preparation of examples 116-119 using suitable starting materials:

STRUCTURE	EX	CHEMICAL NAME	Rt (min)	MS (M+H)	HPLC Method
	116	7-(1-(3-Chlorobenzyl)piperidin-3-yl)-2-(2-methoxypyridin-3-yl)pyrazolo[1,5-a]pyrimidine	3.62	434.1	D

	117	3-(7-(1-(3-Chlorobenzyl)piperidin-3-yl)pyrazolo[1,5-a]pyrimidin-2-yl)pyridin-2-ol	2.75	420.1	D
	118	7-(1-(3,4-Dichlorobenzyl)piperidin-3-yl)-2-(2-methoxypyridin-3-yl)pyrazolo[1,5-a]pyrimidine	4.77	468.1	E
	119	7-(1-(3,4-Difluorobenzyl)piperidin-3-yl)-2-(2-methoxypyridin-3-yl)pyrazolo[1,5-a]pyrimidine	4.30	436.1	E



Example 120. 1-(2-Bromo-7-(1-(4-chlorobenzyl)piperidin-3-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-N-((tetrahydro-2H-pyran-4-yl)methyl)methanamine.

- 5 Step a. 2-Bromo-7-(1-(4-chlorobenzyl)piperidin-3-yl)pyrazolo[1,5-a]pyrimidine-3-carbaldehyde.

To a solution of the compound obtained in example 110 (175 mg, 0.43 mmol) in DMF (1.1 mL), POCl₃ (0.11 mL, 1.19 mmol) was added and the reaction mixture was stirred at r.t. for 16 h. After that time, the reaction mixture was cooled down to 0 °C and ice-water was added carefully, the mixture was basified with 2N NaOH to pH 11. The resulting suspension was extracted with EtOAc. The combined organic extracts were washed with brine, dried over anhydrous Na₂SO₄, filtered and concentrated to obtain the title compound as a brown solid (175 mg, Yield: 75%).

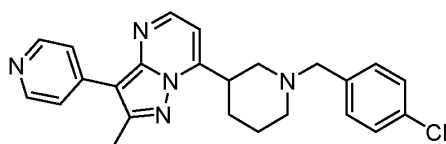
HPLC-MS (Method E): Rt.: 3.82 min; ESI+ MS: *m/z* 433.0 [M+H]⁺.

- 15 Step b. Title compound.

Starting from the compound obtained in step a (175 mg, 0.40 mmol) and (tetrahydro-2H-pyran-4-yl)methanamine (116 mg, 1.0 mmol) and following the procedure described in step e of example 110, the title compound was obtained (60 mg, Yield: 27%).

HPLC-MS (Method E): Rt.: 4.02 min; ESI+ MS: m/z 532.1 $[M+H]^+$.

5



Example 121. 7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methyl-3-(pyridin-4-yl)pyrazolo[1,5-a]pyrimidine.

Step a. *tert*-Butyl 3-(3-bromo-2-methylpyrazolo[1,5-a]pyrimidin-7-yl)piperidine-1-carboxylate.

10

Starting from the compound obtained in step b of example 110 (2 g, 7.08 mmol) and 4-bromo-5-methyl-1H-pyrazol-3-amine (1.37 g, 7.79 mmol) and following the procedure described in step c of example 110, the title compound was obtained as a brown foam (2.04 g, Yield: 73%).

15 HPLC-MS (Method E): Rt.: 3.75 min; ESI+ MS: m/z 395.1 $[M+H]^+$.

Step b. *tert*-Butyl 3-(2-methyl-3-(pyridin-4-yl)pyrazolo[1,5-a]pyrimidin-7-yl)piperidine-1-carboxylate.

20

Starting from the compound obtained in step a (1.2 g, 3.04 mmol) and 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine (0.93 g, 4.55 mmol) and following the procedure described in step a of examples 114 and 115, the title compound was obtained as a brown solid (1.78 g, Yield: 58%).

HPLC-MS (Method E): Rt.: 3.37 min; ESI+ MS: m/z 394.2 $[M+H]^+$.

Step c. 2-Methyl-7-(piperidin-3-yl)-3-(pyridin-4-yl)pyrazolo[1,5-a]pyrimidine dihydrochloride.

25

Starting from the compound obtained in step b (0.70 g, 1.78 mmol) and following the procedure described in step d of example 110, the title compound was obtained as a yellow solid (650 mg).

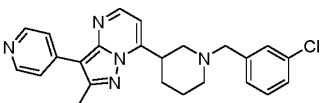
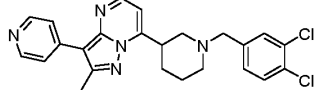
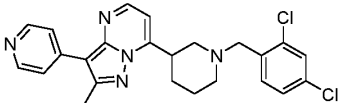
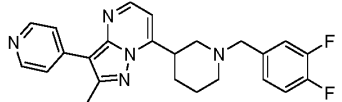
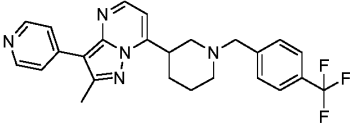
HPLC-MS (Method E): Rt.: 2.17 min; ESI+ MS: m/z 294.1 $[M+H]^+$.

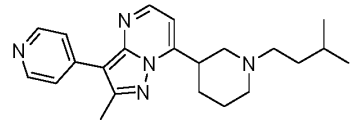
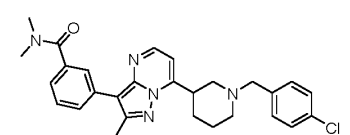
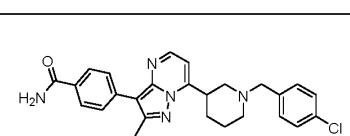
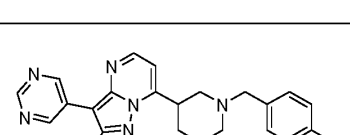
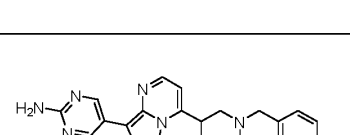
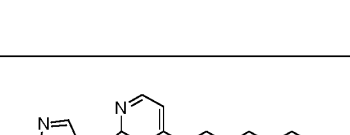
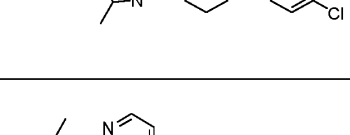
Step d. Title compound.

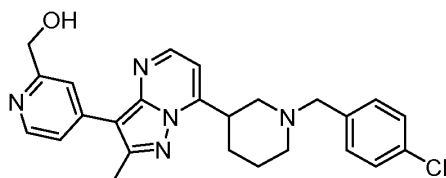
Starting from the compound obtained in step c (80 mg, 0.21 mmol) and following the procedure described in step e of example 110, the title compound was obtained (61.8 mg, Yield: 65%).

5 HPLC-MS (Method D): Rt.: 3.30 min; ESI+ MS: m/z 418.1 $[M+H]^+$.

This method was used for the preparation of examples 122-133 using suitable starting materials:

STRUCTURE	EX	CHEMICAL NAME	Rt (min)	MS (M+H)	HPLC Method
	122	7-(1-(3-Chlorobenzyl)piperidin-3-yl)-2-methyl-3-(pyridin-4-yl)pyrazolo[1,5-a]pyrimidine	4.03	418.1	E
	123	7-(1-(3,4-Dichlorobenzyl)piperidin-3-yl)-2-methyl-3-(pyridin-4-yl)pyrazolo[1,5-a]pyrimidine	4.33	452.1	E
	124	7-(1-(2,4-Dichlorobenzyl)piperidin-3-yl)-2-methyl-3-(pyridin-4-yl)pyrazolo[1,5-a]pyrimidine	4.53	452.1	E
	125	7-(1-(3,4-Difluorobenzyl)piperidin-3-yl)-2-methyl-3-(pyridin-4-yl)pyrazolo[1,5-a]pyrimidine	3.85	420.1	E
	126	2-Methyl-3-(pyridin-4-yl)-7-(1-(4-(trifluoromethyl)benzyl)piperidin-3-yl)pyrazolo[1,5-a]pyrimidine	4.07	452.2	E

	127	7-(1-(4-chlorobenzyl)piperidin-3-yl)-2-methyl-3-(pyridin-4-yl)pyrazolo[1,5-a]pyrimidine	3.70	364.2	E
	128	3-(7-(1-(4-chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-N,N-dimethylbenzamide	3.95	488.2	E
	129	4-(7-(1-(4-chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)benzamide	3.62	460.1	E
	130	7-(1-(4-chlorobenzyl)piperidin-3-yl)-2-methyl-3-(pyrimidin-5-yl)pyrazolo[1,5-a]pyrimidine	3.73	419.1	E
	131	5-(7-(1-(4-chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)pyrimidin-2-amine	3.47	434.1	E
	132	7-(1-(4-chlorobenzyl)piperidin-3-yl)-2-methyl-3-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrimidine	3.80	421.1	E
	133	4-(7-(1-(4-chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-3,5-dimethylisoxazole	4.03	436.1	E



Example 134. (4-(7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)pyridin-2-yl)methanol.

Step a. 4-Bromo-2-(((*tert*-butyldimethylsilyl)oxy)methyl)pyridine.

To a stirred solution of (4-bromopyridin-2-yl)methanol (400 mg, 2.13 mmol) in DMF (8 mL), imidazole (290 mg, 4.25 mmol) and *tert*-butyldimethylchlorosilane (321 mg, 2.13 mmol) were added. The reaction mixture was stirred at r.t. for 16 h. Then, the mixture was diluted with EtOAc and the organic layer washed with water and brine, dried over anhydrous Na_2SO_4 , filtered and concentrated under vacuum. The residue was purified by flash chromatography, silica gel, hexane:EtOAc, to give the title compound as a brown foam (514 mg, Yield: 80%).

HPLC-MS (Method E): Rt.: 3.15 min; ESI+ MS: m/z 302.0 $[\text{M}+\text{H}]^+$.

Step b. 2-(((*tert*-Butyldimethylsilyl)oxy)methyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine.

To a solution of the compound obtained in step a (514 mg, 1.7 mmol) in dioxane (10 mL), 4,4,4',4',5,5,5',5'-octamethyl-2,2'-bi(1,3,2-dioxaborolane) (518 mg, 2.04 mmol), $\text{PdCl}_2(\text{dppf})\text{-CH}_2\text{Cl}_2$ adduct (139 mg, 0.17 mmol) and potassium acetate (501 mg, 5.10 mmol) were added. The reaction mixture was degassed by argon for 5 min, and heated at 100 °C for 16 h. Then, the reaction mixture was filtered over double paper filter, the black solid on the filter was washed with EtOAc. The filtrate was concentrated under vacuum and the residue was triturated and sonicated in hexane for 30 min. The black suspension was filtered again over double paper filter and the black solid on the filter was washed with hexane. The filtrate was concentrated to give 830 mg of a brown oil which was used in the next step without further purification.

HPLC-MS (Method E): Rt.: 3.23 min; ESI+ MS: m/z 268 $[\text{M}+\text{H}]^+$.

Step c. *tert*-Butyl 3-(3-(2-(((*tert*-butyldimethylsilyl)oxy)methyl)pyridin-4-yl)-2-methylpyrazolo[1,5-a]pyrimidin-7-yl)piperidine-1-carboxylate.

Starting from the compound obtained in step b (200 mg, 0.5 mmol) and following the procedure described in step a of example 114, the title compound was obtained (125 mg, Yield: 46 %).

HPLC-MS (Method E): Rt.: 4.78 min; ESI+ MS: m/z 539.1 $[\text{M}+\text{H}]^+$.

Step d. (4-(2-Methyl-7-(piperidin-3-yl)pyrazolo[1,5-a]pyrimidin-3-yl)pyridin-2-yl)methanol dihydrochloride.

Starting from the compound obtained in step c (110 mg, 0.20 mmol) and following the procedure described in step d of example 110, the title compound was obtained (76 mg, Yield: 94 %) after evaporation of the solvent, trituration and sonication of the solid in hexane, filtration and drying under vacuum.

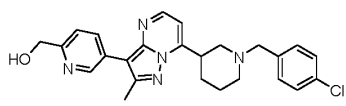
- 5 HPLC-MS (Method E): Rt.: 2.13 min; ESI+ MS: m/z 324.1 $[M+H]^+$.

Step e. Title compound.

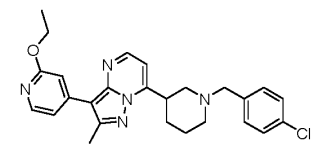
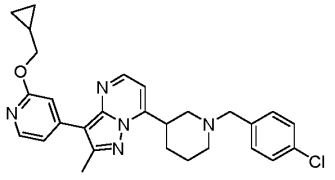
Starting from the compound obtained in step d (75 mg, 0.18 mmol) and following the procedure described in step e of example 110, the title compound was obtained (28 mg, Yield: 32%).

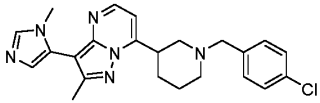
- 10 HPLC-MS (Method E): Rt.: 3.53 min; ESI+ MS: m/z 448.1 $[M+H]^+$.

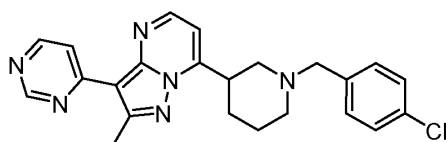
This method was used for the preparation of example 135 using suitable starting materials:

STRUCTURE	EX	CHEMICAL NAME	Rt (min)	MS (M+H)	HPLC Method
	135	(5-(7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)pyridin-2-yl)methanol	3.47	448.1	E

This method (steps b-e) was used for the preparation of examples 136-138 using suitable starting materials:

STRUCTURE	EX	CHEMICAL NAME	Rt (min)	MS (M+H)	HPLC Method
	136	7-(1-(4-Chlorobenzyl)piperidin-3-yl)-3-(2-ethoxypyridin-4-yl)-2-methylpyrazolo[1,5-a]pyrimidine	4.65	462.1	E
	137	7-(1-(4-Chlorobenzyl)piperidin-3-yl)-3-(2-(cyclopropylmethoxy)pyridin-4-yl)-2-methylpyrazolo[1,5-a]pyrimidine	4.83	488.2	E

	138	7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methyl-3-(1-methyl-1H-imidazol-5-yl)pyrazolo[1,5-a]pyrimidine	3.42	421.1	E
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Example 139. 7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methyl-3-(pyrimidin-4-yl)pyrazolo[1,5-a]pyrimidine

- 5 Step a. *tert*-Butyl 3-(3-acetyl-2-methylpyrazolo[1,5-a]pyrimidin-7-yl)piperidine-1-carboxylate.

To a solution of the compound obtained in step a of example 121 (1 g, 2.53 mmol) in toluene (3 mL), tributyl (1-ethoxyvinyl)stannane (1.70 mL, 5.06 mmol) and bis(triphenylphosphine)palladium (II) chloride (178 mg, 0.253 mmol) were added. The reaction mixture was heated at 80 °C for 24 h. After this time, solvent was evaporated and the residue was purified by flash chromatography, silica gel, hexane:EtOAc, to give the title compound as a brown foam (721 mg, Yield: 80%).

HPLC-MS (Method E): Rt.: 3.43 min; ESI+ MS: *m/z* 359.2 [M+H]⁺.

- 15 Step b. *tert*-Butyl (*E*)-3-(3-(3-(dimethylamino)acryloyl)-2-methylpyrazolo[1,5-a]pyrimidin-7-yl)piperidine-1-carboxylate.

The compound obtained in step a (721 mg, 2.01 mmol) and 1-*tert*-butoxy-*N,N,N',N'*-tetramethylmethanediamine (2 mL, 9.69 mmol) were stirred at 100 °C in a sealed reactor under argon for 3 h. The reaction mixture was concentrated to dryness under reduced pressure to give the title compound as a brown oil (832 mg, Yield: Quant).

- 20 HPLC-MS (Method E): Rt.: 3.00 min; ESI+ MS: *m/z* 414.2 [M+H]⁺.

Step c. *tert*-Butyl 3-(2-methyl-3-(pyrimidin-4-yl)pyrazolo[1,5-a]pyrimidin-7-yl)piperidine-1-carboxylate.

The compound obtained in step b (397 mg, 0.96 mmol) and formimidamide acetate (198 mg, 1.92 mmol) were stirred at 130 °C in a sealed reactor under argon for 2 h.

After this time, the reaction mixture was purified by flash chromatography, silica gel, DCM:MeOH, to give the title compound as a brown foam (100 mg, Yield: 26%).

HPLC-MS (Method E): Rt.: 3.55 min; ESI+ MS: m/z 395.2 $[M+H]^+$.

5 Step d. 2-Methyl-7-(piperidin-3-yl)-3-(pyrimidin-4-yl)pyrazolo[1,5-*a*]pyrimidine hydrochloride.

Starting from the compound obtained in step c (100 mg, 0.25 mmol) and following the procedure described in step d of example 110, the title compound was obtained (93 mg). This compound was used in the next step without further purification.

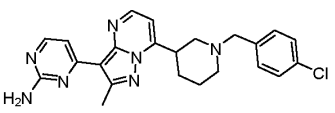
HPLC-MS (Method E): Rt.: 2.28 min; ESI+ MS: m/z 295.1 $[M+H]^+$.

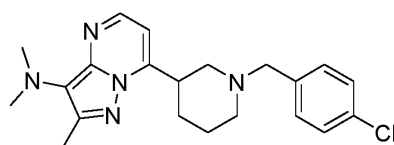
10 Step e. Title compound.

Starting from the compound obtained in step d (93 mg, 0.25 mmol) and following the procedure described in step e of example 110, the title compound was obtained (39 mg, Yield: 33%).

HPLC-MS (Method E): Rt.: 4.22 min; ESI+ MS: m/z 419.1 $[M+H]^+$.

15 This method was used for the preparation of example 140 using suitable starting materials:

STRUCTURE	EX	CHEMICAL NAME	Rt (min)	MS (M+H)	HPLC Method
	140	4-(7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5- <i>a</i>]pyrimidin-3-yl)pyrimidin-2-amine	3.83	434.1	E



20 Example 141. 7-(1-(4-Chlorobenzyl)piperidin-3-yl)-*N,N*,2-trimethylpyrazolo[1,5-*a*]pyrimidin-3-amine

Step a. *N*-(5-Methyl-1*H*-pyrazol-3-yl)acetamide.

5-Methyl-1*H*-pyrazol-3-amine (2.69 g, 27.7 mmol) was dissolved in water (24 mL), followed by the slow addition of sodium bicarbonate (6.98 g, 83.0 mmol), to which acetic anhydride (5 mL, 53.0 mmol) was added dropwise. The reaction mixture was heated at reflux for 16 h. The suspension was cooled down, filtered and the resulting solid was washed with water. The final compound was observed to be partially soluble in water, the aq phase was concentrated as well, and both solids were combined and dried under vacuum to give the title compound (1.89 g, Yield: 49%).

HPLC-MS (Method E): Rt.: 1.10 min; ESI+ MS: m/z 140.0 $[M+H]^+$.

Step b. *N*-(5-Methyl-4-nitro-1*H*-pyrazol-3-yl)acetamide.

Sulfuric acid (9.7 mL, 180 mmol) was cooled down to 0 °C and the compound obtained in step a (1.0 g, 7.19 mmol) was slowly added. Then fuming nitric acid (0.48 mL, 10.78 mmol) was added dropwise. The reaction mixture was stirred at 0 °C for 30 min. The solution was poured into ice and a solid precipitated off. The solid was filtered through a sintered funnel and dried under vacuum to give the title compound (1.89 g, Yield: 49%).

HPLC-MS (Method E): Rt.: 1.42 min; ESI+ MS: m/z 185.0 $[M+H]^+$.

Step c. 5-Methyl-4-nitro-1*H*-pyrazol-3-amine hydrochloride.

The compound obtained in step b (1.03 g, 5.59 mmol) and 6M HCl (6 mL, 36 mmol) were heated at 100 °C for 2 h. After this time, solvent was evaporated to give the title compound (793 mg). This compound was used in the next step without further purification.

HPLC-MS (Method E): Rt.: 1.38 min; ESI+ MS: m/z 143.1 $[M+H]^+$.

Step d. *tert*-Butyl 3-(2-methyl-3-nitropyrazolo[1,5-*a*]pyrimidin-7-yl)piperidine-1-carboxylate.

Starting from the compound obtained in step c (793 mg, 5.59 mmol) and following the procedure described in step c of example 110, the title compound was obtained (1.89 g, Yield: 94%).

HPLC-MS (Method E): Rt.: 3.23 min; ESI+ MS: m/z 362.1 $[M+H]^+$.

Step e. *tert*-Butyl 3-(3-amino-2-methylpyrazolo[1,5-*a*]pyrimidin-7-yl)piperidine-1-carboxylate.

To a solution of the compound obtained in step d (1.89 g, 5.23 mmol) in EtOH (31 mL), zinc (10.26 g, 157 mmol) and calcium chloride (0.29 g, 2.61 mmol) dissolved in the minimum amount of water were added. The reaction mixture was refluxed for 2 h. After this time, the suspension was filtered through a pad of Celite and the solid was washed with hot EtOH. The filtrate was concentrated and the residue was purified by flash chromatography, silica gel, EtOAc:MeOH:NH₃, to give the title compound (864 mg, Yield: 50%).

HPLC-MS (Method E): Rt.: 2.65 min; ESI+ MS: m/z 332.2 [M+H]⁺.

Step f. *tert*-Butyl 3-(3-(dimethylamino)-2-methylpyrazolo[1,5-*a*]pyrimidin-7-yl)piperidine-1-carboxylate.

Starting from the compound obtained in step e (576 mg, 1.74 mmol) and 37% aq formaldehyde (0.39 mL, 5.21 mmol) and following the procedure described in step e of example 110, the title compound was obtained (1.89 g, Yield: 94%).

HPLC-MS (Method E): Rt.: 3.35 min; ESI+ MS: m/z 360.2 [M+H]⁺.

Step g. *N,N*,2-trimethyl-7-(piperidin-3-yl)pyrazolo[1,5-*a*]pyrimidin-3-amine hydrochloride.

Starting from the compound obtained in step f (674 mg, 1.87 mmol) and following the procedure described in step d of example 110, the title compound was obtained (623 mg). This compound was used in the next step without further purification.

HPLC-MS (Method E): Rt.: 1.83 min; ESI+ MS: m/z 260.1 [M+H]⁺.

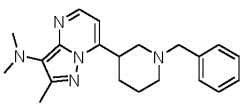
Step h. Title compound.

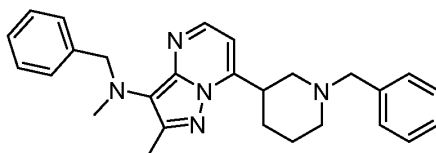
Starting from the compound obtained in step g (242 mg, 0.93 mmol) and following the procedure described in step e of example 110, the title compound was obtained (225 mg, Yield: 62%).

HPLC-MS (Method E): Rt.: 3.97 min; ESI+ MS: m/z 384.1 [M+H]⁺.

This method was used for the preparation of example 142 using suitable starting materials:

STRUCTURE	EX	CHEMICAL NAME	Rt (min)	MS (M+H)	HPLC Method
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	142	7-(1-Benzylpiperidin-3-yl)- <i>N,N</i> ,2-trimethylpyrazolo[1,5- a]pyrimidin-3-amine	3.60	350.1	E
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Example 143. *N*-Benzyl-7-(1-benzylpiperidin-3-yl)-*N*,2-dimethylpyrazolo[1,5-
a]pyrimidin-3-amine

- 5 Step a. *tert*-Butyl 3-(3-((*tert*-butoxycarbonyl)amino)-2-methylpyrazolo[1,5-a]pyrimidin-
7-yl)piperidine-1-carboxylate.

To a solution of the compound obtained in step e of example 141 (288 mg, 0.86 mmol)
in DCM (5 mL), TEA (0.18 mL, 1.30 mmol) and Boc₂O (284 mg, 1.30 mmol) were added
and the reaction mixture was stirred at r.t. for 16 h. The resulting mixture was diluted
10 with aq sat NaHCO₃ sol. The organic layer was separated and washed with brine, dried
over anhyd Na₂SO₄, filtered and concentrated to give the title compound (375 mg).

HPLC-MS (Method E): Rt.: 3.47 min; ESI+ MS: *m/z* 432.2 [M+H]⁺.

Step b. *tert*-Butyl 3-(3-((*tert*-butoxycarbonyl)(methyl)amino)-2-methylpyrazolo[1,5-
a]pyrimidin-7-yl)piperidine-1-carboxylate.

- 15 To a 0 °C cooled solution of the compound obtained in step a (390 mg, 0.90 mmol) in
DMF (3 mL), sodium hydride (60% wt in mineral oil, 54 mg, 1.35 mmol) was added
under argon and the resulting mixture was stirred for 20 min, followed by the addition
of iodomethane (0.11 mL, 1.80 mmol), the reaction mixture was stirred at r.t. for 2 h.
After this time, still starting material remained, the reactants were added again at 0 °C
20 and the reaction mixture was left stirring at r.t. for 16h. Then, the reaction mixture was
concentrated under vacuum and the residue was treated with EtOAc and aq sat
NaHCO₃ sol. The organic layer was separated and washed with brine, dried over anhyd
Na₂SO₄, filtered and concentrated to give the title compound (330 mg).

HPLC-MS (Method E): Rt.: 3.73 min; ESI+ MS: *m/z* 446.2 [M+H]⁺.

- 25 Step c. *N*,2-Dimethyl-7-(piperidin-3-yl)pyrazolo[1,5-a]pyrimidin-3-amine hydrochloride.

Starting from the compound obtained in step b (330 mg, 0.74 mmol) and following the procedure described in step d of example 110, the title compound was obtained (623 mg).

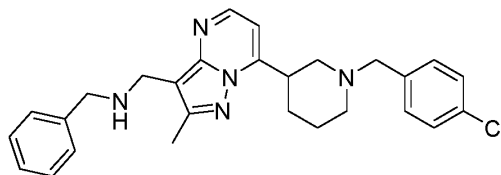
HPLC-MS (Method E): Rt.: 1.85 min; ESI+ MS: m/z 246.1 $[M+H]^+$.

5 Step d. Title compound.

Starting from the compound obtained in step c (236 mg, 0.74 mmol) and benzaldehyde (0.22 mL, 2.22 mmol) and following the procedure described in step e of example 110, the title compound was obtained (24 mg, Yield: 7%).

HPLC-MS (Method E): Rt.: 4.45 min; ESI+ MS: m/z 426.2 $[M+H]^+$.

10



Example 144. *N*-Benzyl-1-(7-(1-(4-chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methanamine

Step a. *tert*-Butyl 3-(2-methylpyrazolo[1,5-a]pyrimidin-7-yl)piperidine-1-carboxylate.

15 Starting from the compound obtained in step b of example 110 (2.0 g, 7.08 mmol) and 5-methyl-1*H*-pyrazol-3-amine (0.75 g, 7.79 mmol) and following the procedure described in step c of example 110, the title compound was obtained (2.1 g, Yield: 93%).

HPLC-MS (Method E): Rt.: 3.22 min; ESI+ MS: m/z 317.1 $[M+H]^+$.

20 Step b. 2-Methyl-7-(piperidin-3-yl)pyrazolo[1,5-a]pyrimidine hydrochloride.

Starting from the compound obtained in step a (600 mg, 1.89 mmol) and following the procedure described in step d of example 110, the title compound was obtained (403 mg). This compound was used in the next step without further purification.

HPLC-MS (Method E): Rt.: 1.98 min; ESI+ MS: m/z 217.1 $[M+H]^+$.

25 Step c. 7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidine

Starting from the compound obtained in step b (403 mg, 1.60 mmol) and following the procedure described in step e of example 110, the title compound was obtained (379 mg Yield: 68%).

HPLC-MS (Method E): Rt.: 3.78 min; ESI+ MS: m/z 341.1 $[M+H]^+$.

- 5 Step d. 7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidine-3-carbaldehyde

Starting from the compound obtained in step c (409 mg, 1.09 mmol) and following the procedure described in step a of example 120, the title compound was obtained (379 mg Yield: 98%).

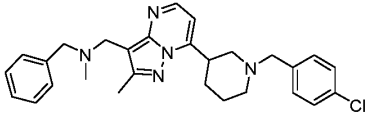
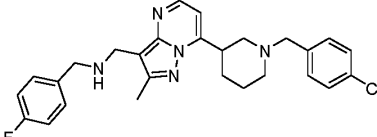
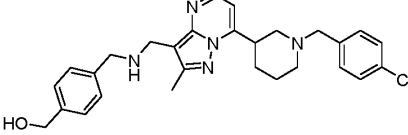
- 10 HPLC-MS (Method E): Rt.: 3.72 min; ESI+ MS: m/z 389.1 $[M+H]^+$.

Step e. Title compound.

Starting from the compound obtained in step d (200 mg, 0.54 mmol) and phenylmethanamine (0.17 mL, 1.62 mmol) and following the procedure described in step e of example 110, the title compound was obtained (63 mg, Yield: 25%).

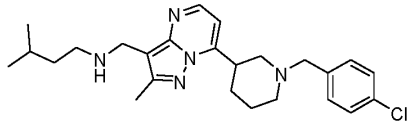
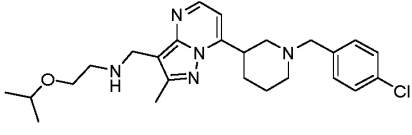
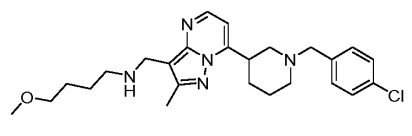
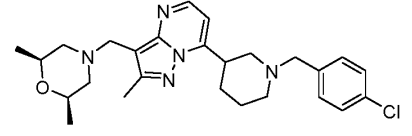
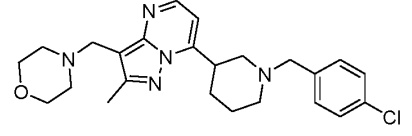
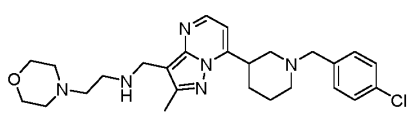
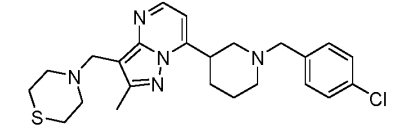
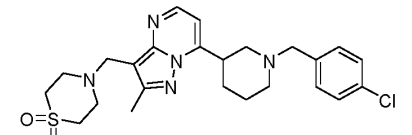
- 15 HPLC-MS (Method E): Rt.: 4.23 min; ESI+ MS: m/z 460.2 $[M+H]^+$.

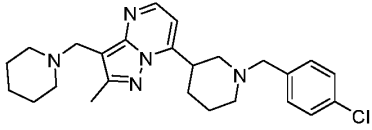
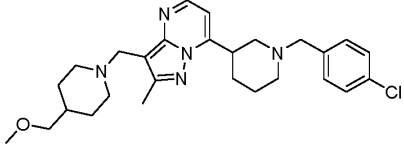
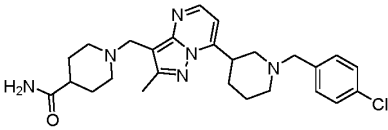
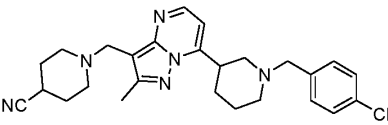
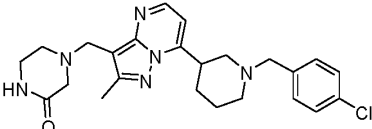
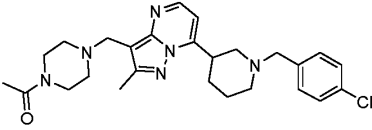
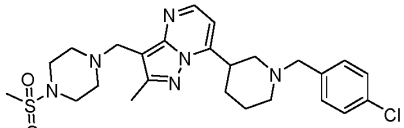
This method was used for the preparation of examples 145-192 using suitable starting materials:

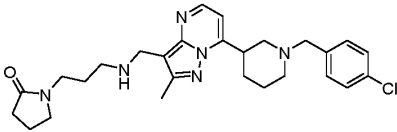
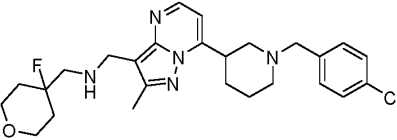
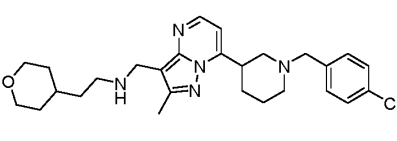
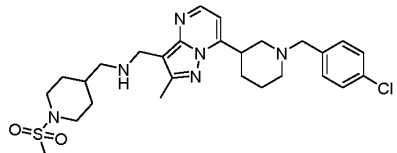
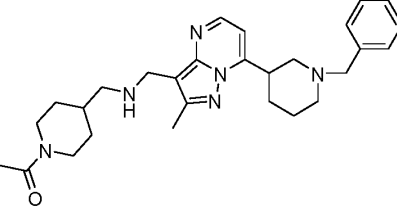
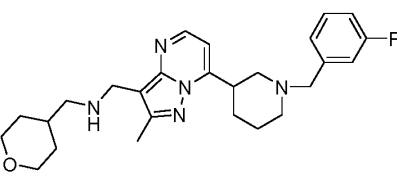
STRUCTURE	EX	CHEMICAL NAME	Rt (min)	MS (M+H)	HPLC Method
	145	<i>N</i> -Benzyl-1-(7-(1-(4-chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)- <i>N</i> -methylmethanamine	4.60	474.2	E
	146	1-(7-(1-(4-chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)- <i>N</i> -(4-fluorobenzyl)methanamine	4.23	478.2	E
	147	(4-((((7-(1-(4-chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)amino)methyl)benzyl)methanol	3.52	490.2	E

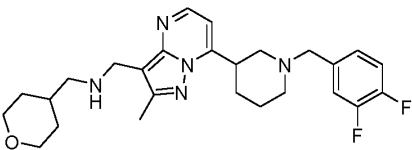
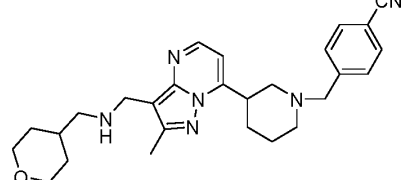
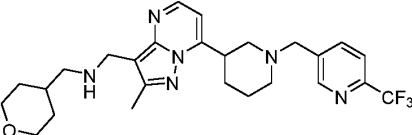
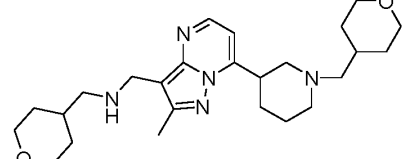
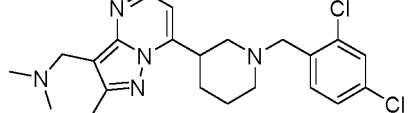
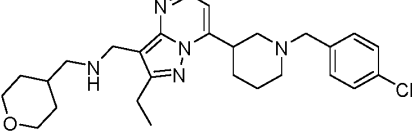
		yl)methyl)amino)methyl)phe nyl)methanol			
	148	1-(7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-N-(pyridin-4-ylmethyl)methanamine	3.35	461.2	E
	149	1-(7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-N-(thiophen-2-ylmethyl)methanamine	4.15	466.1	E
	150	1-(7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-N-((5-methylthiophen-2-yl)methyl)methanamine	4.33	480.1	E
	151	1-(7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-N-((1-methyl-1H-pyrazol-3-yl)methyl)methanamine	3.57	464.2	E
	152	1-(7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-N-((5-methyl-1,3,4-oxadiazol-2-yl)methyl)methanamine	3.05	466.2	E
	153	N-((7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methyl)-2-phenylethan-1-amine	4.23	474.1	E

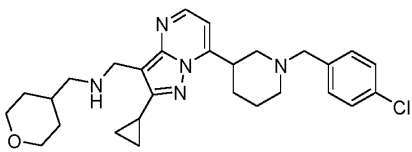
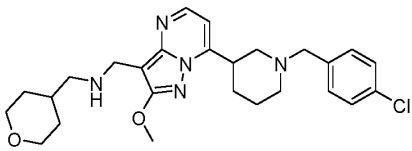
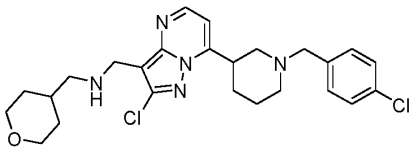
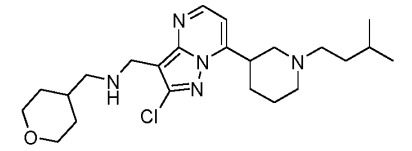
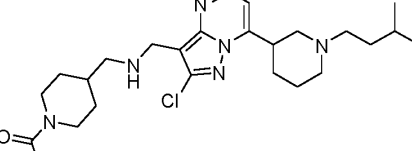
	154	<i>N</i> -((7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methyl)-2-(4-methoxyphenyl)ethan-1-amine	4.47	504.2	E
	155	<i>N</i> -((7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methyl)ethanamine	4.00	398.2	E
	156	<i>N</i> -((7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methyl)-2,2,2-trifluoroethan-1-amine	3.98	452.1	E
	157	1-(7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)- <i>N</i> -(cyclopropylmethyl)methanamine	4.50	424.2	E
	158	2-(((7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methyl)amino)ethan-1-ol	3.38	414.2	E
	159	<i>N</i> -((7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methyl)propan-2-amine	2.72	412.2	I
	160	<i>N</i> -((7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methyl)-2-methylpropan-1-amine	2.88	425.2	I

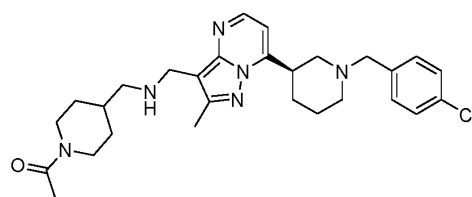
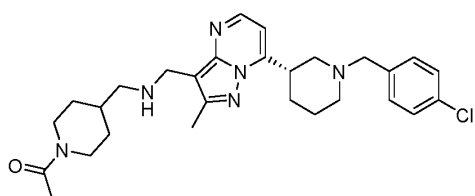
	161	<i>N</i> -((7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methyl)-3-methylbutan-1-amine	3.82	440.2	I
	162	<i>N</i> -((7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methyl)-2-isopropoxyethan-1-amine	4.32	456.2	E
	163	<i>N</i> -((7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methyl)-4-methoxybutan-1-amine	3.28	456.2	I
	164	(2 <i>S</i> ,6 <i>R</i>)-4-((7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methyl)-2,6-dimethylmorpholine	3.28	468.2	E
	165	4-((7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methyl)morpholine	3.50	440.2	E
	166	<i>N</i> -((7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methyl)-2-morpholinoethan-1-amine	4.15	483.2	E
	167	4-((7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methyl)thiomorpholine	4.05	456.1	E
	168	4-((7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methyl)thiomorpholine 1,1-dioxide	3.38	488.1	E

	169	7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methyl-3-(piperidin-1-ylmethyl)pyrazolo[1,5-a]pyrimidine	4.70	438.2	E
	170	7-(1-(4-Chlorobenzyl)piperidin-3-yl)-3-((4-(methoxymethyl)piperidin-1-yl)methyl)-2-methylpyrazolo[1,5-a]pyrimidine	4.70	482.2	E
	171	1-((7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methyl)piperidine-4-carboxamide	3.07	481.2	E
	172	1-((7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methyl)piperidine-4-carbonitrile	3.73	463.2	E
	173	4-((7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methyl)piperazin-2-one	2.95	453.2	E
	174	1-(4-((7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methyl)piperazin-1-yl)ethan-1-one	3.15	481.2	E
	175	7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methyl-3-((4-(methylsulfonyl)piperazin-1-yl)methyl)pyrazolo[1,5-a]pyrimidine	3.50	517.2	E

	176	1-(3-(((7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methyl)amino)propyl)pyrrolidin-2-one	4.20	495.2	E
	177	1-(7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-N-((4-fluorotetrahydro-2H-pyran-4-yl)methyl)methanamine	3.63	486.2	E
	178	N-((7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methyl)-2-(tetrahydro-2H-pyran-4-yl)ethan-1-amine	2.97	482.2	I
	179	1-(7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-N-((1-(methylsulfonyl)piperidin-4-yl)methyl)methanamine	3.93	546.1	E
	180	1-(4-(((7-(1-Benzylpiperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methyl)amino)methyl)piperidin-1-yl)ethan-1-one	2.50	476.1	D
	181	1-(7-(1-(3-Fluorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-N-((tetrahydro-2H-pyran-4-yl)methyl)methanamine	4.15	452.2	E

	182	1-(7-(1-(3,4-Difluorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-N-((tetrahydro-2H-pyran-4-yl)methyl)methanamine	1.87	470.2	I
	183	4-((3-(2-Methyl-3-(((tetrahydro-2H-pyran-4-yl)methyl)amino)methyl)pyrazolo[1,5-a]pyrimidin-7-yl)piperidin-1-yl)methyl)benzonitrile	1.60	459.2	I
	184	1-(2-Methyl-7-(1-((6-(trifluoromethyl)pyridin-3-yl)methyl)piperidin-3-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-N-((tetrahydro-2H-pyran-4-yl)methyl)methanamine	3.53	503.2	E
	185	1-(2-Methyl-7-(1-((tetrahydro-2H-pyran-4-yl)methyl)piperidin-3-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-N-((tetrahydro-2H-pyran-4-yl)methyl)methanamine	3.02	442.3	E
	186	1-(7-(1-(2,4-Dichlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-N,N-dimethylmethanamine	4.52	432.2	I
	187	1-(7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-ethylpyrazolo[1,5-a]pyrimidin-3-yl)-N-((tetrahydro-2H-pyran-4-yl)methyl)methanamine	4.37	482.2	E

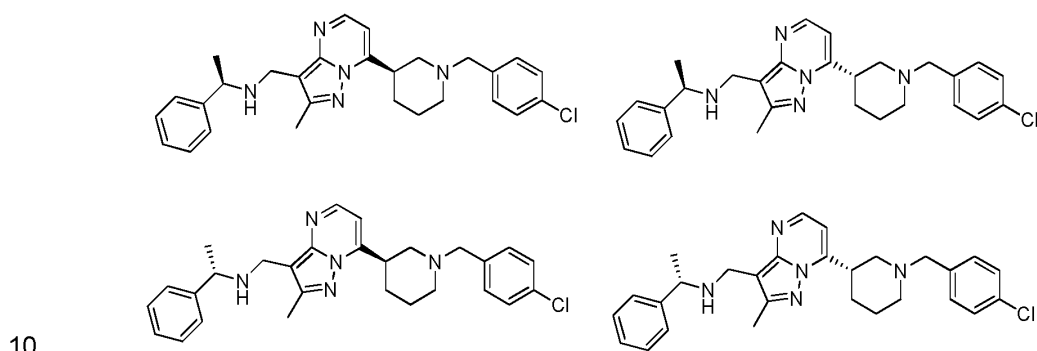
	188	1-(7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-cyclopropylpyrazolo[1,5-a]pyrimidin-3-yl)-N-((tetrahydro-2H-pyran-4-yl)methyl)methanamine	3.08	494.2	I
	189	1-(7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methoxypyrazolo[1,5-a]pyrimidin-3-yl)-N-((tetrahydro-2H-pyran-4-yl)methyl)methanamine	2.95	484.2	I
	190	1-(2-Chloro-7-(1-(4-chlorobenzyl)piperidin-3-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-N-((tetrahydro-2H-pyran-4-yl)methyl)methanamine	3.98	488.1	E
	191	1-(2-Chloro-7-(1-(4-isopentylpiperidin-3-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-N-((tetrahydro-2H-pyran-4-yl)methyl)methanamine	3.93	434.2	E
	192	1-(4-(((2-chloro-7-(1-isopentylpiperidin-3-yl)pyrazolo[1,5-a]pyrimidin-3-yl)methyl)amino)methyl)piperidin-1-yl)ethan-1-one	3.52	475.2	E



Examples 193 and 194. (S)-1-(4-(((7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methyl)amino)methyl)piperidin-1-yl)ethan-1-one

and (*R*)-1-(4-((((7-(1-(4-chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-*a*]pyrimidin-3-yl)methyl)amino)methyl)piperidin-1-yl)ethan-1-one

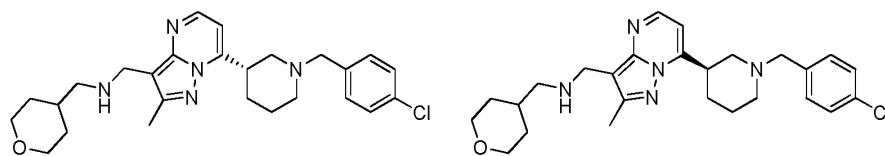
Starting from 1-(4-((((7-(1-(4-chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-*a*]pyrimidin-3-yl)methyl)amino)methyl)piperidin-1-yl)ethan-1-one, obtained following a
 5 similar procedure to that described in example 144, a chiral preparative HPLC [Column Chiralpak AD-H 20 x 250 mm, 5 μ m; temperature: r.t.; eluent: n-Heptane/EtOH/Et₂NH 70/30/0.1 v/v/v flow rate 14 mL/min; Rt1: 21.1 min; Rt2: 24.0 min] was carried out to give the title compounds.



Examples 195, 196, 197 and 198. (*R*)-*N*-((7-((*R*)-1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-*a*]pyrimidin-3-yl)methyl)-1-phenylethan-1-amine, (*R*)-*N*-((7-((*S*)-1-(4-chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-*a*]pyrimidin-3-yl)methyl)-1-phenylethan-1-amine,
 15 (*S*)-*N*-((7-((*R*)-1-(4-chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-*a*]pyrimidin-3-yl)methyl)-1-phenylethan-1-amine and (*S*)-*N*-((7-((*S*)-1-(4-chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-*a*]pyrimidin-3-yl)methyl)-1-phenylethan-1-amine

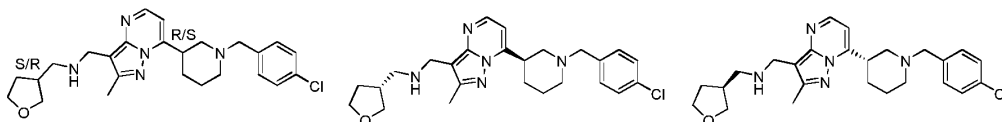
Starting from *N*-((7-(1-(4-chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-*a*]pyrimidin-3-yl)methyl)-1-phenylethanamine, obtained following a similar procedure to
 20 that described in example 144, two chiral preparative HPLC [Column Chiralpak AD-H 20 x 250 mm, 5 μ m; temperature: r.t.; eluent: n-Heptane/EtOH/Et₂NH 95/5/0.02 v/v/v; flow rate: 20 mL/min; Rt1: 6.9 min; Rt2: 8.2 min and Column Chiralpak AD-H 20 x 250 mm, 5 μ m; temperature: r.t.; eluent: n-Heptane/EtOH/Et₂NH 90/10/0.03 v/v/v; flow rate: 20 mL/min; Rt1: 7.2 min; Rt2: 9.3 min] were carried out to give the title compounds.

25



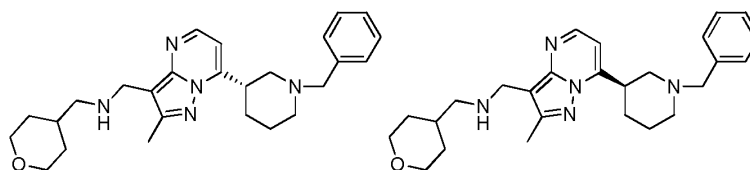
Examples 199 and 200. (S)-1-(7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-N-((tetrahydro-2H-pyran-4-yl)methyl)methanamine and (R)-1-(7-(1-(4-chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-N-((tetrahydro-2H-pyran-4-yl)methyl)methanamine

Starting from 1-(7-(1-(4-chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-N-((tetrahydro-2H-pyran-4-yl)methyl)methanamine, obtained following a similar procedure to that described in example 144, a chiral preparative HPLC [Column Reprosil AMS 20 x 250 mm, 5 μ m; temperature: 40 $^{\circ}$ C; eluent: MeOH/CO₂/NH₃ 20/80/0.2 v/v/v; flow rate: 50 mL/min; Rt1: 3.19; Rt2: 3.65] was carried out to give the title compounds.



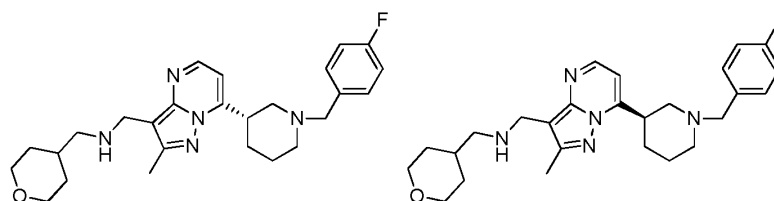
Examples 201, 202 and 203. (+/-)-1-(7-((R/S)-1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-N-(((S/R)-tetrahydrofuran-3-yl)methyl)methanamine, 1-(7-((R)-1-(4-chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-N-(((R)-tetrahydrofuran-3-yl)methyl)methanamine and 1-(7-((S)-1-(4-chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-N-(((S)-tetrahydrofuran-3-yl)methyl)methanamine.

Starting from 1-(7-(1-(4-chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-N-((tetrahydrofuran-3-yl)methyl)methanamine, obtained following a similar procedure to that described in example 144, a chiral preparative HPLC [Column LUX C3 21.1 x 250 mm, 5 μ m; temperature: r.t.; eluent: ACN/NH₃ 100/0.2 v/v; flow rate: 13 mL/min; Rt1: 3.9 min; Rt2: 4.65 min; Rt3: 5.38 min] was carried out to give the title compounds.



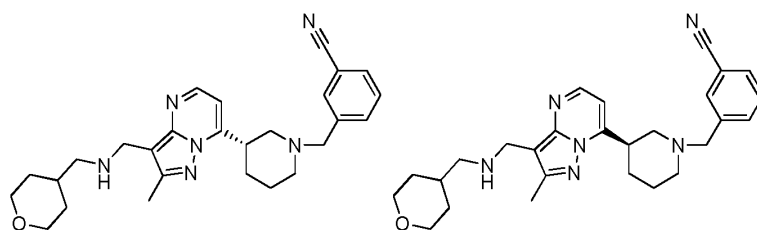
Examples 204 and 205. (S)-1-(7-(1-Benzylpiperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-N-((tetrahydro-2H-pyran-4-yl)methyl)methanamine and (R)-1-(7-(1-benzylpiperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-N-((tetrahydro-2H-pyran-4-yl)methyl)methanamine

Starting from 1-(7-(1-benzylpiperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-N-((tetrahydro-2H-pyran-4-yl)methyl)methanamine, obtained following a similar procedure to that described in example 144, a chiral preparative HPLC [Column Chiralpak AD-H 20 x 250 mm, 5 μ m; temperature: r.t.; eluent: n-Heptane/EtOH/ Et₂NH 85/15/0.05 v/v/v; flow rate: 12 mL/min; Rt1: 11.7; Rt2: 13.8 min] was carried out to give the title compounds.



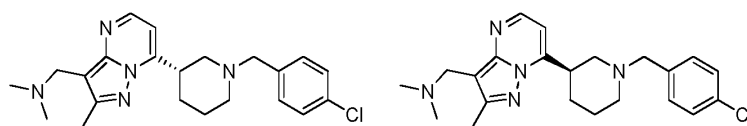
Examples 206 and 207. (S)-1-(7-(1-(4-Fluorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-N-((tetrahydro-2H-pyran-4-yl)methyl)methanamine and (R)-1-(7-(1-(4-fluorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-N-((tetrahydro-2H-pyran-4-yl)methyl)methanamine

Starting from 1-(7-(1-(4-fluorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-N-((tetrahydro-2H-pyran-4-yl)methyl)methanamine, obtained following a similar procedure to that described in example 144, a chiral preparative HPLC [Column Chiralpak AD-H 20 x 250 mm, 5 μ m; temperature: r.t.; eluent: n-Heptane/EtOH/Et₂NH 95/5/0.4 v/v/v; flow rate: 14 mL/min; Rt1: 32.5 min; Rt2: 36.1 min] was carried out to give the title compounds.



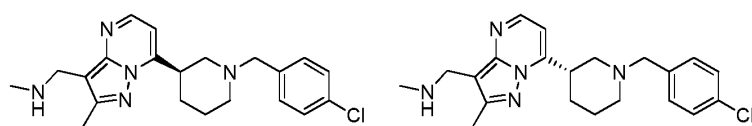
Examples 208 and 209. (S)-3-((3-(2-Methyl-3-(((tetrahydro-2H-pyran-4-yl)methyl)amino)methyl)pyrazolo[1,5-a]pyrimidin-7-yl)piperidin-1-yl)methyl)benzonitrile and (R)-3-((3-(2-methyl-3-(((tetrahydro-2H-pyran-4-yl)methyl)amino)methyl)pyrazolo[1,5-a]pyrimidin-7-yl)piperidin-1-yl)methyl)benzonitrile

Starting from 3-((3-(2-methyl-3-(((tetrahydro-2H-pyran-4-yl)methyl)amino)methyl)pyrazolo[1,5-a]pyrimidin-7-yl)piperidin-1-yl)methyl)benzonitrile, obtained following a similar procedure to that described in example 144, a chiral preparative HPLC [Column Chiralpak AD-H 20 x 250 mm, 5 μ m; temperature: r.t.; eluent: n-Heptane/EtOH/Et₂NH 70/30/0.1 v/v/v; flow rate: 12 mL/min; Rt1: 15.1 min; Rt2: 17.6 min] was carried out to give the title compounds.



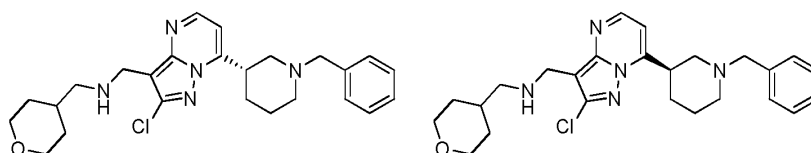
Examples 210 and 211. (S)-1-(7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-N,N-dimethylmethanamine and (R)-1-(7-(1-(4-chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-N,N-dimethylmethanamine

Starting from 1-(7-(1-(4-chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-N,N-dimethylmethanamine, obtained following a similar procedure to that described in example 144, a chiral preparative HPLC [Column Chiralcel OJ 20 x 250 mm; 5 μ m; temperature: r.t.; eluent: n-Heptane/EtOH/Et₂NH 90/10/0.03 v/v/v; flow rate: 15 mL/min; Rt1: 6.1 min; Rt2: 7.5 min] was carried out to give the title compounds.



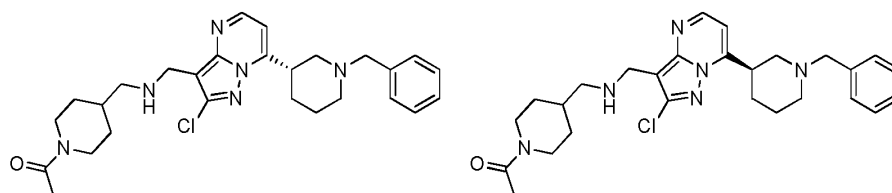
Examples 212 and 213. (*R*)-1-(7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-*N*-methylmethanamine and (*S*)-1-(7-(1-(4-chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-*N*-methylmethanamine

Starting from 1-(7-(1-(4-chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-*N*-methylmethanamine, obtained following a similar procedure to that described in example 144, a chiral preparative HPLC [Column LUX C3 21.2 X 250 , 5 μ m; temperature: r.t.; eluent MeOH/NH₃ 100/0.2 v/v; flow rate: 21 mL/min; Rt1: 2.7 min; Rt2: 2.98 min] was carried out to give the title compounds.



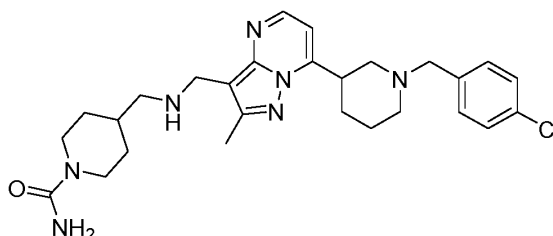
Examples 214 and 215. ((*S*)-1-(7-(1-Benzylpiperidin-3-yl)-2-chloropyrazolo[1,5-a]pyrimidin-3-yl)-*N*-((tetrahydro-2*H*-pyran-4-yl)methyl)methanamine and ((*R*)-1-(7-(1-benzylpiperidin-3-yl)-2-chloropyrazolo[1,5-a]pyrimidin-3-yl)-*N*-((tetrahydro-2*H*-pyran-4-yl)methyl)methanamine

Starting from 1-(7-(1-benzylpiperidin-3-yl)-2-chloropyrazolo[1,5-a]pyrimidin-3-yl)-*N*-((tetrahydro-2*H*-pyran-4-yl)methyl)methanamine, obtained following a similar procedure to that described in example 144, a chiral preparative HPLC [Column Chiralpak AD-H 20 x 250 mm; 5 μ m; temperature: r.t.; eluent *n*-Heptane/EtOH/Et₂NH 80/20/0.1 v/v/v; flow rate: 11 mL/min; Rt1: 13.23 min; Rt2: 16.2 min] was carried out to give the title compounds.



Examples 216 and 217. (S)-1-(4-((((7-(1-Benzylpiperidin-3-yl)-2-chloropyrazolo[1,5-a]pyrimidin-3-yl)methyl)amino)methyl)piperidin-1-yl)ethan-1-one and (R)-1-(4-((((7-(1-Benzylpiperidin-3-yl)-2-chloropyrazolo[1,5-a]pyrimidin-3-yl)methyl)amino)methyl)piperidin-1-yl)ethan-1-one

- 5 Starting from 1-(4-((((7-(1-benzylpiperidin-3-yl)-2-chloropyrazolo[1,5-a]pyrimidin-3-yl)methyl)amino)methyl)piperidin-1-yl)ethanone, obtained following a similar procedure to that described in example 144, a chiral preparative HPLC [Column Chiralpak AD-H 20 x 250 mm; 5 μ m; temperature: r.t.; eluent n-Heptane/EtOH/Et₂NH 80/20/0.1 v/v/v; flow rate: 12 mL/min; Rt1: 15.8 min; Rt2: 18.4 min] was carried out to give the title compounds.
- 10



Example 218. 4-((((7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methyl)amino)methyl)piperidine-1-carboxamide.

- 15 Step a. *tert*-Butyl ((1-(tosylcarbamoyl)piperidin-4-yl)methyl)carbamate.

To a 0 °C cooled solution of *tert*-butyl (piperidin-4-ylmethyl)carbamate (500 mg, 2.33 mmol) in anhyd DCM (16 mL) 4-methylbenzenesulfonyl isocyanate (0.5 mL, 3.29 mmol) was added dropwise under argon atmosphere. The reaction mixture was left to reach r.t. and stirred for 16h. Then, the reaction mixture was quenched with pH 5 buffer sodium acetate/AcOH sol and brine. The aq layer was extracted with DCM and the combined organic extracts were dried over MgSO₄, filtered and concentrated. The residue was purified by flash chromatography, silica gel, DCM:MeOH, to give the title compound as an oil (461 mg, Yield: 48%).

20

HPLC-MS (Method E): Rt.: 2.05 min; ESI+ MS: *m/z* 410.1 [M+H]⁺.

- 25 Step b. *tert*-Butyl ((1-carbamoylpiperidin-4-yl)methyl)carbamate.

Sodium (155 mg, 6.74 mmol) and naphthalene (860 mg, 6.71 mmol) in anhyd THF (67 mL) was stirred under argon atmosphere for 2 h until it turned to a dark green solution, then this solution was cooled down to -78°C and the compound obtained in step a (460

mg, 1.18 mmol) in anhydrous THF (22 mL) was added dropwise (30 min addition). The reaction mixture was stirred at -78 °C for 1.5 h and then allowed to reach r.t. and stirred for an additional 1.5 h at this temperature. After this time the reaction mixture was cooled down to -78°C and quenched carefully with MeOH. Then the solution was allowed to reach r.t and the solvent was evaporated. This residue was partitioned between DCM and aq sat NaHCO₃ sol and the aq layer was extracted with DCM. The combined organic extracts were dried over MgSO₄, filtered and concentrated. The residue was purified by flash chromatography, silica gel, DCM:MeOH, to give the title compound as an oil (150 mg, Yield: 52%).

HPLC-MS (Method E): Rt.: 2.10 min; ESI+ MS: m/z 258.1 [M+H]⁺.

Step c. 4-(Aminomethyl)piperidine-1-carboxamide hydrochloride.

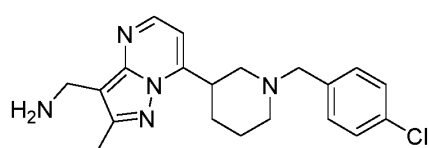
Starting from the compound obtained in step b (150 mg, 0.58 mmol) and following the procedure described in step d of example 110, the title compound was obtained (113 mg).

HPLC-MS (Method E): Rt.: 0.92 min; ESI+ MS: m/z 158.1 [M+H]⁺.

Step d. Title compound.

Starting from the compound obtained in step c (113 mg, 0.58 mmol) and the compound obtained in step d of example 144 (128 mg, 0.35 mmol) and following the procedure described in step e of example 110, the title compound was obtained (14 mg, Yield: 8%).

HPLC-MS (Method E): Rt.: 3.82 min; ESI+ MS: m/z 510.2 [M+H]⁺.



Example 219. (7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methanamine

Step a. N-((7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methyl)prop-2-en-1-amine.

Starting from the compound obtained in step d of example 144 (1.08 g, 2.93 mmol) and prop-2-en-1-amine (0.44 mL, 5.86 mmol) and following the procedure described in step e of example 110, the title compound was obtained (863 mg, Yield: 71%).

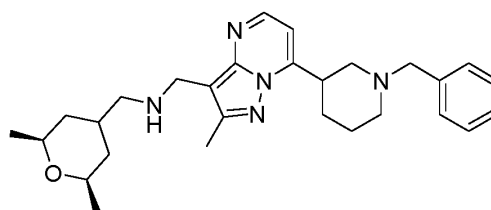
HPLC-MS (Method E): Rt.: 4.20 min; ESI+ MS: m/z 410.2 $[M+H]^+$.

5 Step b. Title compound.

To a solution of the compound obtained in step a (863 mg, 2.10 mmol) in anhyd DCM (50 mL), $\text{Pd}(\text{OAc})_2$ (47 mg, 0.20 mmol), PPh_3 (165 mg, 0.62 mmol) and 1,3-dimethylpyrimidine-2,4,6(1*H*, 3*H*, 5*H*)-trione (888 mg, 5.69 mmol) were added. The resulting mixture was stirred at r.t under argon atmosphere for 16 h. Then, the reaction mixture was quenched with aq sat NaHCO_3 sol and the aq layer was extracted with DCM. The combined organic extracts were dried over MgSO_4 , filtered and evaporated. The residue was purified by flash chromatography, silica gel, DCM:MeOH: NH_3 , to give the title compound as a solid (517 mg, Yield: 63%).

HPLC-MS (Method E): Rt.: 4.43 min; ESI+ MS: m/z 370.1 $[M+H]^+$.

15



Example 220. 1-(7-(1-Benzylpiperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-N-(((2*R*,6*S*)-2,6-dimethyltetrahydro-2*H*-pyran-4-yl)methyl)methanamine.

Step a. (2*R*,6*S*)-4-(Methoxymethylene)-2,6-dimethyltetrahydro-2*H*-pyran.

20 To a 0 °C cooled solution of LDA (2 M in THF, 4.4 mL, 8.80 mmol) a solution of (methoxymethyl)diphenylphosphine oxide (1.92 g, 7.80 mmol) in anhyd THF (30 mL) was added. The resulting red solution was cooled to -40 °C, and another solution of (2*R*,6*S*)-2,6-dimethyltetrahydro-4*H*-pyran-4-one (250 mg, 1.95 mmol) in anhyd THF (10 mL) was added. The resulting brown suspension was stirred at -40 °C for 30 min and then warmed up to 40 °C for 16 h under argon atmosphere. Then, the reaction mixture was cooled down to r.t and quenched with water. Then, brine was added to this solution and the aqueous layer was extracted with EtOAc. The combined organic extracts were dried over MgSO_4 , filtered and concentrated. The residue was purified by flash

chromatography, silica gel, hexane/EtOAc, to give the title compound as an oil (141 mg, Yield: 46%).

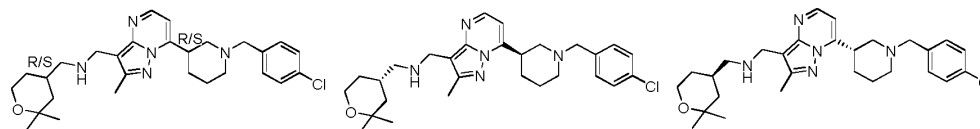
Step b. (2*R*,6*S*)-2,6-Dimethyltetrahydro-2*H*-pyran-4-carbaldehyde.

To a solution of the compound obtained in step a (140 mg, 0.89 mmol) in ACN (1 mL),
 5 2 M HCl (1.4 mL, 2.80 mmol) was added. The mixture was stirred at r.t for 5 h. The reaction mixture was diluted with 2 M HCl and the aq layer was extracted with DCM. The combined organic extracts were dried over MgSO₄, filtered and concentrated under low pressure and low temperature to avoid distillation of the product since it seemed to have a low boiling point. This gave the title compound (120 mg) that was used in the
 10 next step without further purification.

Step c. Title compound.

Starting from the compound obtained in step b (43 mg, 0.3 mmol) and (7-(1-benzylpiperidin-3-yl)-2-methylpyrazolo[1,5-*a*]pyrimidin-3-yl)methanamine (obtained following the procedure described in example 219) (150 mg, 0.44 mmol) and following
 15 the procedure described in step e of example 110, the title compound was obtained (118 mg, Yield: 85%).

HPLC-MS (Method E): Rt.: 4.50 min; ESI+ MS: *m/z* 462.3 [M+H]⁺.

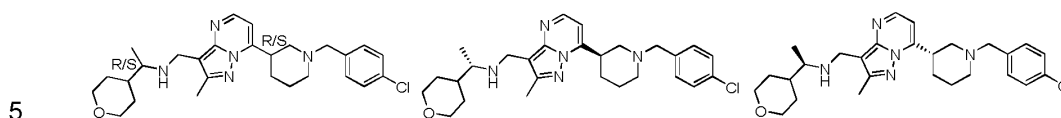


20

Examples 221, 222 and 223. (+/-)-1-(7-((*R/S*)-1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-*a*]pyrimidin-3-yl)-*N*-(((*R/S*)-2,2-dimethyltetrahydro-2*H*-pyran-4-yl)methyl)methanamine,
 (1-(7-((*R*)-1-(4-chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-*a*]pyrimidin-3-yl)-*N*-(((*S*)-2,2-dimethyltetrahydro-2*H*-pyran-4-yl)methyl)methanamine
 25 and (1-(7-((*S*)-1-(4-chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-*a*]pyrimidin-3-yl)-*N*-(((*R*)-2,2-dimethyltetrahydro-2*H*-pyran-4-yl)methyl)methanamine

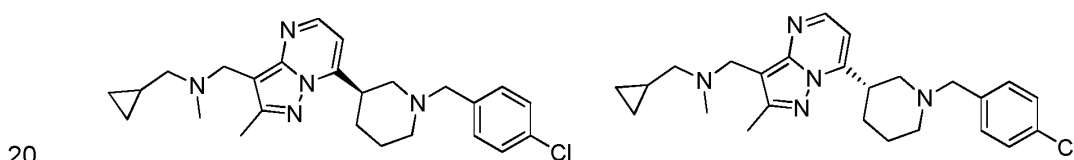
Starting from 1-(7-(1-(4-chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-*a*]pyrimidin-3-yl)-*N*-((2,2-dimethyltetrahydro-2*H*-pyran-4-yl)methyl)methanamine, obtained
 30 following a similar procedure to that described in example 220, a chiral preparative

HPLC [Column LUX A1 21.2 x 250 mm; 5 μ m; temperature: r.t.; eluent n-Heptane/iPrOH/NH₃ 80/20/0.5 v/v/v; flow rate: 21 mL/min; Rt1: 5.64 min; Rt2: 6.35; Rt3: 7.37 min] was carried out to give the title compounds.



Examples 224, 225 and 226. (+/-)-(R/S)-N-((7-((R/S)-1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methyl)-1-(tetrahydro-2H-pyran-4-yl)ethan-1-amine, (S)-N-((7-((R)-1-(4-chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methyl)-1-(tetrahydro-2H-pyran-4-yl)ethan-1-amine and (R)-N-((7-((S)-1-(4-chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methyl)-1-(tetrahydro-2H-pyran-4-yl)ethan-1-amine

Starting from N-((7-(1-(4-chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methyl)-1-(tetrahydro-2H-pyran-4-yl)ethanamine, obtained following a similar procedure to that described in example 220, a chiral preparative HPLC [Column LUX C4 21.2 x 250 mm; 5 μ m; temperature: r.t.; eluent ACN/Et₂NH 100/1 v/v; flow rate: 21 mL/min; Rt1: 7.58 min; Rt2: 8.39; Rt3: 12.03 min] was carried out to give the title compounds.



Examples 227 and 228. (R)-1-(7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-N-(cyclopropylmethyl)-N-methylmethanamine and (S)-1-(7-(1-(4-chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-N-(cyclopropylmethyl)-N-methylmethanamine

25 Step a. 1-(7-(1-(4-chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-N-(cyclopropylmethyl)-N-methylmethanamine.

Starting from the compound obtained in example 157 (685 mg, 1.6 mmol) and paraformaldehyde (976 mg, 32.5 mmol) and following the procedure described in step e of example 110, the title compound was obtained (314 mg, Yield: 43%).

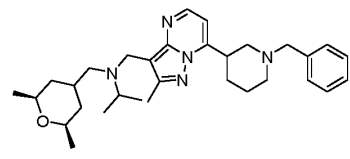
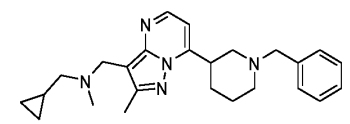
HPLC-MS (Method E): Rt.: 5.15 min; ESI+ MS: m/z 438.0 $[M+H]^+$.

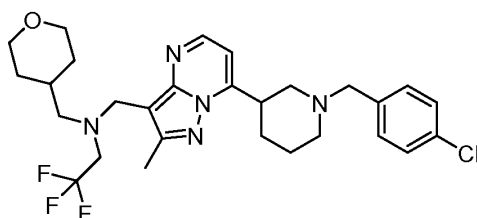
5 Step b. Title compounds.

Starting from the compound obtained in step a, a chiral preparative HPLC [Column Chiralcel OJ 20 x 250 mm; 5 μ m; temperature: r.t.; eluent n-Heptane/EtOH/Et₂NH 98/2/0.01 v/v/v; flow rate: 19 mL/min; Rt1: 7.6 min; Rt2: 11.1 min] was carried out to give the title compounds.

10 This method (step a) was used for the preparation of examples 229-234 using suitable starting materials:

STRUCTURE	EX	CHEMICAL NAME	Rt (min)	MS (M+H)	HPLC Method
	229	1-(7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-N-(2,6-difluorobenzyl)-N-methylmethanamine	4.55	510.2	E
	230	(4-(((7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methyl)(methyl)amino)methyl)phenyl)methanol	3.88	504.2	E
	231	1-(7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-N-methyl-N-((tetrahydro-2H-pyran-4-yl)methyl)methanamine	4.18	482.2	E
	232	N-((7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methyl)-N-((tetrahydro-2H-pyran-4-yl)methyl)propan-2-amine	4.85	510.2	E

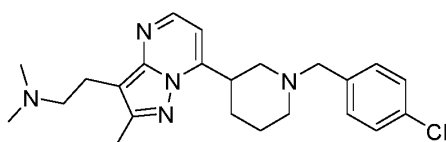
	233	<i>N</i> -((7-(1-Benzylpiperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methyl)- <i>N</i> -(((2 <i>R</i> ,6 <i>S</i>)-2,6-dimethyltetrahydro-2 <i>H</i> -pyran-4-yl)methyl)propan-2-amine	5.00	504.2	E
	234	1-(7-(1-Benzylpiperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)- <i>N</i> -(cyclopropylmethyl)- <i>N</i> -methylmethanamine	4.80	404.2	E



Example 235. *N*-((7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methyl)-2,2,2-trifluoro-*N*-((tetrahydro-2*H*-pyran-4-yl)methyl)ethan-1-amine

To a solution of 1-(7-(1-(4-chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-*N*-((tetrahydro-2*H*-pyran-4-yl)methyl)methanamine (obtained following the procedure described in example 144) (60 mg, 0.12 mmol) in DCM (4 mL), TEA (0.04 mL, 0.28 mmol) and 2,2,2-trifluoroethyl trifluoromethanesulfonate (0.14 mL, 1.0 mmol) were added and the reaction mixture was stirred under argon atmosphere at r.t. for 4 days. The reaction mixture was poured into water and the aq layer was extracted with DCM. The combined organic extracts were dried over MgSO₄, filtered and concentrated to give the title compound as an oil (58.6 mg, Yield: 74%).

HPLC-MS (Method E): Rt.: 4.52 min; ESI+ MS: *m/z* 550.2 [*M*+*H*]⁺.



Example 236. 2-(7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-N,N-dimethylethan-1-amine

Step a. (E)-7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methyl-3-(2-nitrovinyl)pyrazolo[1,5-a]pyrimidine.

- 5 To a solution of the compound obtained in step d of example 144 (500 mg, 1.35 mmol) in MeOH (10 mL), potassium acetate (532 mg, 5.42 mmol), methylamine hydrochloride (252 mg, 3.73 mmol) and nitromethane (0.08 mL, 1.49 mmol) were added. The reaction mixture was stirred under argon atmosphere at r.t for 60 h. Then, it was poured into water and a solid precipitated off. The solid was filtered, washed with water and dried
10 over vacuum to give the title compound as a yellow solid (392 mg, Yield: 70%). This solid was used in the next step without further purification.

HPLC-MS (Method E): Rt.: 4.40 min; ESI+ MS: m/z 412.2 $[M+H]^+$.

Step b. 7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methyl-3-(2-nitroethyl)pyrazolo[1,5-a]pyrimidine.

- 15 To a solution of the compound obtained in step a (343 mg, 0.83 mmol) in MeOH (10 mL), sodium borohydride (98 mg, 2.58 mmol) was slowly added portionwise to the solution at r.t. The reaction mixture was stirred under nitrogen atmosphere for 45 min. The solvent was evaporated and the residue was diluted with a mixture of EtOAc, aq sat NaHCO_3 sol and brine. The aq layer was extracted with EtOAc, the combined
20 organic extracts were dried over MgSO_4 , filtered and concentrated to give the title compound as a solid (328 mg, Yield: 95%). This solid was used in the next step without further purification.

HPLC-MS (Method E): Rt.: 3.93 min; ESI+ MS: m/z 414.2 $[M+H]^+$.

- Step c. 2-(7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)ethan-1-amine.
25

- To a solution of the compound obtained in step b (328 mg, 0.79 mmol) in MeOH (10 mL), Nickel Raney (46.5 mg, 0.79 mmol) was added and the reaction mixture was stirred under hydrogen atmosphere at 40 °C for 16 h. Then it was filtered through a pad of Celite and the solvent was evaporated to give the title compound as an oil (298 mg,
30 Yield: 98%). This compound was used in the next step without further purification.

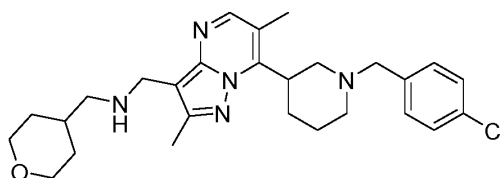
HPLC-MS (Method E): Rt.: 5.06 min; ESI+ MS: m/z 384.1 $[M+H]^+$.

Step d. Title compound.

Starting from the compound obtained in step c (135 mg, 0.35 mmol) and following the procedure described in examples 227 and 228, the title compound was obtained (72 mg, Yield: 49%).

HPLC-MS (Method E): Rt.: 4.27 min; ESI+ MS: m/z 412.2 $[M+H]^+$.

5



Example 237. 1-(7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2,6-dimethylpyrazolo[1,5-a]pyrimidin-3-yl)-N-((tetrahydro-2H-pyran-4-yl)methyl)methanamine

Step a. *tert*-Butyl 3-propionylpiperidine-1-carboxylate.

- 10 To a 0 °C stirring solution of 1-(*tert*-butyl) 3-ethyl piperidine-1,3-dicarboxylate (2.06 g, 8.0 mmol), and *N,O*-dimethylhydroxylamine hydrochloride (273 mg, 8.95 mmol) in dry THF (21 mL) and under argon atmosphere, ethylmagnesium chloride (2 M in THF, 23.0 mL, 46.0 mmol) was added dropwise. The reaction was allowed to warm up to r.t. for 3 h. Then the solution was quenched with aq sat NH_4Cl sol at 0 °C. The aq layer was
- 15 extracted with EtOAc and the combined organic extracts were washed with brine, dried over anhydrous Na_2SO_4 , filtered and concentrated to give the title compound (1.90 g, Yield: 98%) as a light brown oil.

HPLC-MS (Method E): Rt.: 3.17 min; ESI+ MS: m/z 242.0 $[M+H]^+$.

Step b. *tert*-Butyl (Z)-3-(3-(dimethylamino)-2-methylacryloyl)piperidine-1-carboxylate.

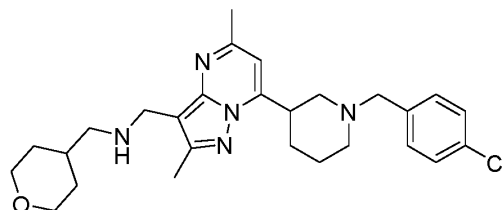
- 20 Starting from the compound obtained in step a (600 mg, 2.48 mmol) and following the procedure described in step b of example 110, the title compound was obtained (735 mg).

HPLC-MS (Method E): Rt.: 2.87 min; ESI+ MS: m/z 297.1 $[M+H]^+$.

Step c. Title compound.

- 25 Starting from the compound obtained in step b (735 mg, 2.48 mmol) and following the procedure described in example 144, the title compound was obtained (29 mg, Yield: 29% for 5 steps).

HPLC-MS (Method I): Rt.: 2.50 min; ESI+ MS: m/z 482.2 $[M+H]^+$.



Example 238. 1-(7-(1-(4-Chlorobenzyl)piperidin-3-yl)-2,5-dimethylpyrazolo[1,5-a]pyrimidin-3-yl)-N-((tetrahydro-2H-pyran-4-yl)methyl)methanamine

5 Step a. *tert*-Butyl (*E*)-3-(3-(dimethylamino)but-2-enoyl)piperidine-1-carboxylate.

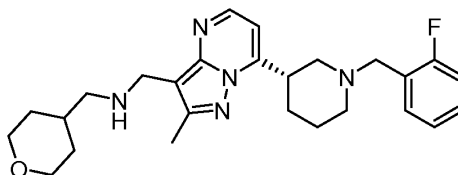
Starting from the compound obtained step a of example 110 (250 mg, 1.10 mmol) and 1,1-dimethoxy-*N,N*-dimethylethan-1-amine (176 mg, 1.32 mmol) and following the procedure described in step b of example 110, the title compound was obtained (308 mg).

10 HPLC-MS (Method E): Rt.: 2.87 min; ESI+ MS: m/z 297.1 $[M+H]^+$.

Step b. Title compound.

Starting from the compound obtained in step a (308 mg, 1.03 mmol) and following the procedure described in example 144, the title compound was obtained (80 mg, Yield: 14% for 6 steps).

15 HPLC-MS (Method I): Rt.: 2.97 min; ESI+ MS: m/z 482.2 $[M+H]^+$.



Example 239. (*S*)-1-(7-(1-(2-Fluorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-N-((tetrahydro-2H-pyran-4-yl)methyl)methanamine

20 Step a. *tert*-Butyl (*S*)-3-acetylpiperidine-1-carboxylate.

To a 0 °C stirring solution of 1-(*tert*-butyl) 3-ethyl (*S*)-piperidine-1,3-dicarboxylate (5 g, 19.43 mmol), and *N,O*-dimethylhydroxylamine hydrochloride (2.27 g, 23.32 mmol) in dry THF (40 mL), methylmagnesium chloride (3 M in THF, 35.6 mL, 107 mmol) was added dropwise under argon atmosphere. The reaction mixture was allowed to stir at

0 °C for 1 h. Then the solution was quenched with aq sat NH₄Cl sol at 0 °C. The aq layer was extracted with EtOAc and the combined organic extracts were washed with brine, dried over MgSO₄, filtered and concentrated to give the title compound (4.18 g, Yield: 95%) as a light yellow oil.

- 5 HPLC-MS (Method K (f)): Rt.: 3.83 min; ESI+ MS: *m/z* 228.0 [M+H]⁺.

Step b. *tert*-Butyl (S,E)-3-(3-(dimethylamino)acryloyl)piperidine-1-carboxylate.

- The compound obtained in step a (2.01 g, 8.84 mmol) and 1-*tert*-butoxy-*N,N,N',N'*-tetramethylmethanediamine (1.83 mL, 8.84 mmol) were mixed in a sealed reactor under argon and the mixture were stirred at 100 °C for 30 min. After this time the
10 reaction mixture was immediately cooled down to 0 °C for 15 min and then concentrated to dryness under reduced pressure to give the title compound as a yellow oil (2.49 g).

HPLC-MS (Method K (f)): Rt.: 4.98 min; ESI+ MS: *m/z* 283.3 [M+H]⁺.

Step c. *tert*-Butyl (S)-3-(2-bromopyrazolo[1,5-*a*]pyrimidin-7-yl)piperidine-1-carboxylate.

- A solution of the compound obtained in step b (2.50 g, 8.84 mmol) was dissolved in
15 glacial AcOH (15 mL) and 5-bromo-1*H*-pyrazol-3-amine (1.56 g, 8.84 mmol) was added. The reaction mixture was stirred at 50 °C for 7 h. The solvent was evaporated and the residue was purified by flash chromatography, silica gel, hexane/EtOAc as eluents to give the title compound as a yellow sticky solid (2.45 g, Yield: 70%).

HPLC-MS (Method L): Rt.: 7.68 min; ESI+ MS: *m/z* 396.1 [M+H]⁺.

- 20 Step d. *tert*-Butyl (S,E)-3-(2-methyl-3-styrylpyrazolo[1,5-*a*]pyrimidin-7-yl)piperidine-1-carboxylate.

- A solution of the compound obtained in step c (2.49 g, 6.30 mmol), (*E*)-4,4,5,5-tetramethyl-2-styryl-1,3,2-dioxaborolane (2.90 g, 12.60 mmol), Pd(dppf)Cl₂ (140 mg, 0.17 mmol) and aq sodium carbonate sol (2 M, 10.7 mL, 21.42 mmol) in toluene/EtOAc
25 (2:1, 21 mL) was degassed by means of bubbling argon and stirred at 90 °C for 16 h. The reaction mixture was diluted with EtOAc, The organic layer was washed with aq sat Na₂CO₃ sol, brine, dried over anhyd Na₂SO₄, filtered and concentrated. The residue was purified by flash chromatography, silica gel, DCM as eluent to give the title compound as a yellow oil (647 mg, Yield: 24%).

- 30 HPLC-MS (Method K (b)): Rt.: 7.07 min; ESI+ MS: *m/z* 419.1 [M+H]⁺.

Step e. (S,E)-2-Methyl-7-(piperidin-3-yl)-3-styrylpyrazolo[1,5-*a*]pyrimidine hydrochloride.

Starting from the compound obtained in step d (647 mg, 1.54 mmol) and following the procedure described in step d of example 110, the title compound was obtained (549 mg). This compound was used in the next step without further purification.

5 Step f. (S,E)-7-(1-(2-Fluorobenzyl)piperidin-3-yl)-2-methyl-3-styrylpyrazolo[1,5-a]pyrimidine.

The compound obtained in step e (175 mg, 0.49 mmol) was dissolved in dry DCM (8 mL) and TEA (0.2 mL, 1.48 mmol) was added at r.t. To this solution 2-fluorobenzaldehyde (0.1 mL, 0.99 mmol) and AcOH (0.003 mL, 0.49 mmol) were added, after 5 min of shaking, sodium triacetoxyhydroborate (218 mg, 1 mmol) was added to the solution and the reaction mixture was left at r.t. for 16 h. Then, the reaction mixture was diluted with DCM, the organic layer was washed with aq sat Na₂CO₃ sol, then dried over anhydrous Na₂SO₄ and filtered. Solvent was evaporated and the residue was purified by flash chromatography, silica gel, DCM:MeOH as eluents to give the title compound as a yellow oil (150 mg, Yield: 67 % for 2 steps).

15 HPLC-MS (Method K (a)): Rt.: 7.78 min; ESI+ MS: *m/z* 427.1 [M+H]⁺.

Step g. (S)-7-(1-(2-Fluorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidine-3-carbaldehyde.

To a solution of the compound obtained in step f (145 mg, 0.4 mmol) in acetone/water (6:1, 7 mL), NaIO₄ (218 mg, 1.02 mmol) and OsO₄ (10 mg, 0.04 mmol) were added consecutively at r.t. After the OsO₄ addition, the yellow solution became black and a light brown solid precipitated off. The resulting mixture was stirred at r.t. for 2 h, then, it was filtered through a fritted glass funnel, the grey solid washed with EtOAc. Then organic phase was washed with aq sat Na₂CO₃ sol, brine and dried over anhydrous Na₂SO₄, filtered and concentrated. The residue was purified by flash chromatography, silica gel, DCM:MeOH as eluents to give the title compound as a yellow solid (55 mg, Yield: 45%). This yellow solid was precipitated in the minimum amount of MeOH then filtered, the solid washed with the minimum amount of MeOH, then with hexane and dried under vacuum to obtain the title compound with an ee >90%.

HPLC-MS (Method K (d)): Rt.: 5.53 min; ESI+ MS: *m/z* 353.1 [M+H]⁺.

30 Step h. Title compound.

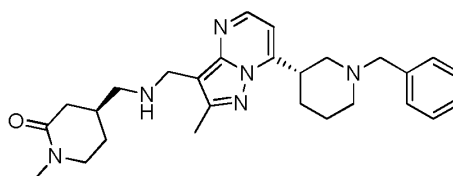
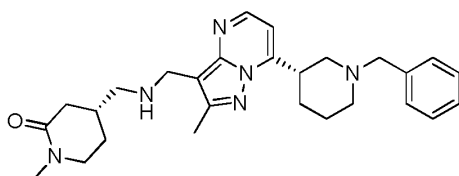
To a solution of the compound obtained in step g (50 mg, 0.14 mmol) in dry MeOH (2 mL) tetrahydro-2H-pyran-4-yl methanamine (24.0 mg, 0.21 mmol) and drops of AcOH were added. The reaction mixture was left shaking at r.t. for 15 min, sodium

cyanotrihydroborate (9.0 mg, 0.14 mmol) was added and the reaction mixture was stirred at r.t. for 3 h. Then, solvent was evaporated and the reaction mixture was dissolved with DCM and poured into aq sat NaHCO₃ sol, the organic layer was separated and the aq layer was extracted with DCM. The combined organic extracts were washed with brine, dried over anhydrous Na₂SO₄ and filtered. Solvent was evaporated and the residue was purified by flash chromatography, silica gel, DCM:MeOH as eluents to give the title compound (53 mg, Yield: 79%).

HPLC-MS (Method M): Rt.: 12.77 min; ESI+ MS: *m/z* 452.2 [M+H]⁺.

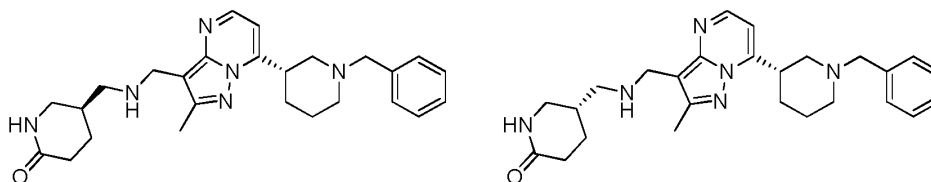
This method was used for the preparation of examples 240-242 using suitable starting materials:

STRUCTURE	EX	CHEMICAL NAME	Rt (min)	MS (M+H)	HPLC Method
	240	(S)-1-(7-(1-(2,4-Difluorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-N-((tetrahydro-2H-pyran-4-yl)methyl)methanamine	4.18	470.2	E
	241	(S)-1-(7-(1-(3,5-Difluorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-N-((tetrahydro-2H-pyran-4-yl)methyl)methanamine	4.47	470.2	E
	242	1-(7-(1-(4-Methoxybenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-N-((tetrahydro-2H-pyran-4-yl)methyl)methanamine	3.98	464.2	E



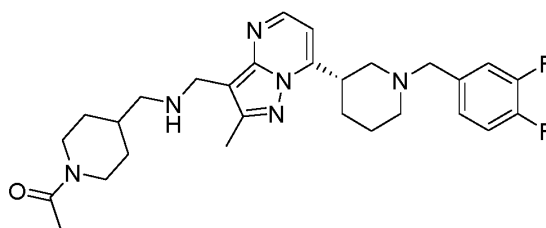
Examples 243 and 244. (*R*)-4-((((7-((*S*)-1-Benzylpiperidin-3-yl)-2-methylpyrazolo[1,5-*a*]pyrimidin-3-yl)methyl)amino)methyl)-1-methylpiperidin-2-one, (*S*)-4-((((7-((*S*)-1-Benzylpiperidin-3-yl)-2-methylpyrazolo[1,5-*a*]pyrimidin-3-yl)methyl)amino)methyl)-1-methylpiperidin-2-one.

- 5 Starting from 4-((((7-((*S*)-1-benzylpiperidin-3-yl)-2-methylpyrazolo[1,5-*a*]pyrimidin-3-yl)methyl)amino)methyl)-1-methylpiperidin-2-one, obtained following a similar procedure to that described in example 239, a chiral preparative HPLC [Column Chiralpak AD-H 20 x 250 mm; 5 μ m; temperature: r.t.; eluent n-Heptane/EtOH/Et₂NH 70/30/0.1 v/v/v; flow rate: 12 mL/min; Rt1: 13.7 min; Rt2: 17.2 min] was carried out to
10 give the title compounds.



- Examples 245 and 246. (*R*)-5-((((7-((*S*)-1-Benzylpiperidin-3-yl)-2-methylpyrazolo[1,5-*a*]pyrimidin-3-yl)methyl)amino)methyl)piperidin-2-one and (*S*)-5-((((7-((*S*)-1-Benzylpiperidin-3-yl)-2-methylpyrazolo[1,5-*a*]pyrimidin-3-yl)methyl)amino)methyl)piperidin-2-one.
15

- Starting from 5-((((7-((1-benzylpiperidin-3-yl)-2-methylpyrazolo[1,5-*a*]pyrimidin-3-yl)methyl)amino)methyl)piperidin-2-one, obtained following a similar procedure to that described in example 239, a chiral preparative HPLC [Column Chiralpak IB 20 x 250
20 mm; 5 μ m; temperature: r.t.; eluent n-Heptane/EtOH/Et₂NH 80/20/0.1 v/v/v; flow rate: 12 mL/min; Rt1: 19.8 min; Rt2: 27.3 min] was carried out to give the title compounds.



- Example 247. (*S*)-1-(4-((((7-((1-(3,4-Difluorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-*a*]pyrimidin-3-yl)methyl)amino)methyl)piperidin-1-yl)ethan-1-one.
25

Method 1:

Step a. Ethyl (S)-1-(3,4-difluorobenzyl)piperidine-3-carboxylate.

To a solution of ethyl (S)-piperidine-3-carboxylate (6.10 g, 38.80 mmol) in dry DCM (130 mL) cooled at 0 °C, DIPEA (10.13 mL, 58.2 mmol) was added dropwise under argon atmosphere, followed by 4-(bromomethyl)-1,2-difluorobenzene (4.96 mL, 38.80 mmol). The reaction mixture was allowed to warm up to r.t. and stirred for 16 h. The organic layer washed with aq sat Na₂CO₃ sol and brine. Then it was dried over anhydrous Na₂SO₄ and concentrated. The residue was purified by flash chromatography, silica gel, hexane:EtOAc as eluents to give the title compound as a yellow oil (9.65 g, Yield: 83 %).

HPLC-MS (Method K (b)): Rt.: 4.58 min; ESI+ MS: *m/z* 284.0 [M+H]⁺.

Step b. (S)-1-(1-(3,4-Difluorobenzyl)piperidin-3-yl)ethan-1-one.

Starting from the compound obtained in step a (5.20 g, 18.35 mmol) and following the procedure described in step a of example 239, the title compound was obtained as a light brown oil (4.61 g). This compound was used in the next step without further purification.

HPLC-MS (Method K (g)): Rt.: 13.03 min; ESI+ MS: *m/z* 254.0 [M+H]⁺.

Step c. (S,E)-1-(1-(3,4-Difluorobenzyl)piperidin-3-yl)-3-(dimethylamino)prop-2-en-1-one.

Starting from the compound obtained in step b (3.39 g, 13.38 mmol) and following the procedure described in step b of example 239, the title compound was obtained as a brown oil (4.10 g). This compound was used in the next step without further purification.

HPLC-MS (Method K (e)): Rt.: 5.28 min; ESI+ MS: *m/z* 309.0 [M+H]⁺.

Step d. (S)-3-Bromo-7-(1-(3,4-difluorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidine.

Starting from the compound obtained in step c (4.10 g, 13.30 mmol) and following the procedure described in step c of example 239, the title compound was obtained as a thick brown oil (3.20 g, Yield: 55% for 3 steps).

HPLC-MS (Method K (c)): Rt.: 5.57 min; ESI+ MS: *m/z* 421.0 [M+H]⁺.

Step e. (S,E)-7-(1-(3,4-Difluorobenzyl)piperidin-3-yl)-2-methyl-3-styrylpyrazolo[1,5-a]pyrimidine.

Starting from the compound obtained in step d (2.16 g, 5.13 mmol) and following the procedure described in step d of example 239, the title compound was obtained as a yellow sticky solid (1.94 g, Yield: 80%).

HPLC-MS (Method K(a)): Rt.: 7.02 min; ESI+ MS: m/z 445.1 $[M+H]^+$.

- 5 Step f. (S)-7-(1-(3,4-Difluorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidine-3-carbaldehyde.

Starting from the compound obtained in step e (1.94 g, 4.36 mmol) and following the procedure described in step g of example 239, the title compound was obtained as a white solid (500 mg, Yield: 31%).

- 10 HPLC-MS (Method K(d)): Rt.: 5.60 min; ESI+ MS: m/z 3715.1 $[M+H]^+$.

Step g. Title compound.

Starting from the compound obtained in step f (500 mg, 1.35 mmol) and 1-(4-aminomethyl)piperidin-1-yl)ethan-1-one and following the procedure described in step h of example 239, the title compound was obtained as a sticky brown solid (434 mg, Yield: 62%).

15

HPLC-MS (Method E): Rt.: 3.10 min; ESI+ MS: m/z 511.2 $[M+H]^+$.

Method 2:

Step a. Piperidin-4-ylmethanol hydrochloride.

Starting from *tert*-butyl 4-(hydroxymethyl)piperidine-1-carboxylate (1.0 g, 4.64 mmol) and following the procedure step d of example 110, the title compound was obtained (704 mg). This compound was used in the next step without further purification.

20

Step b. 1-(4-(Hydroxymethyl)piperidin-1-yl)ethan-1-one.

To a solution of the compound obtained in step a (704 mg, 4.64 mmol) in acetone (16 mL), K_2CO_3 (1.6 g, 11.6 mmol) was added followed by dropwise addition of acetic anhydride (0.52 mL, 5.57 mmol). The reaction mixture was stirred at r.t. for 3 h. Then, it was filtered through a plug of Celite, and the resulting white solid was washed with acetone several times. The combined filtrates were then concentrated under reduced pressure. The residue was purified by flash chromatography, silica gel, DCM:MeOH as eluents to give the title compound as a yellow oil (600 mg, Yield: 82%).

25

HPLC-MS (Method E): Rt.: 1.00 min; ESI+ MS: m/z 158.0 $[M+H]^+$.

30

Step c. 1-Acetylpiperidine-4-carbaldehyde.

To a 0 °C solution of the compound obtained in step b (600 mg, 3.82 mmol) in chloroform (13 mL), Dess-Martin Periodinane (1.78 g, 4.20 mmol) was added under argon atmosphere, and the reaction mixture was allowed to warm up to r.t and stirred for 2 h. Then, the resulting suspension was filtered through a plug of Celite, and the
5 resulting white solid was washed with chloroform several times. The combined filtrates were then concentrated under reduced pressure. The residue was dissolved in DCM and *MP*-carbonate resin (loading 3.5 mmol/g, 3.2 g, 11.46 mmol) was added to the solution and the reaction mixture was stirred for 3 h. Then, it was filtered through a fritted glass funnel and the resulting filtrate was concentrated under vacuum to give the
10 desired title compound as a colourless oil (238 mg, Yield: 40%). This compound must be kept in the freezer under argon atmosphere for short times as it is an unstable compound.

HPLC-MS (Method E): Rt.: 0.87 min; ESI+ MS: m/z 156.0 $[M+H]^+$.

Step d. *tert*-Butyl (S)-((7-(1-(3,4-difluorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-
15 a]pyrimidin-3-yl)methyl)carbamate.

To a solution of the compound obtained in step d (method 1) of example 247 (839 mg, 1.99 mmol) in a mixture of dioxane/water (5:1.5, 12 mL), potassium (((*tert*-butoxycarbonyl)amino)methyl)trifluoroborate (944 mg, 3.98 mmol), dicyclohexyl(2',6'-dimethoxy-[1,1'-biphenyl]-2-yl)phosphine (327 mg, 0.8 mmol), K_3PO_4 (3.38 g, 15.93
20 mmol) and allylpalladium(II) chloride dimer (61 mg, 0.17 mmol) were added, the resulting mixture was degassed by argon for 5 min and heated at 100 °C for 16 h. Then, it was cooled down to r.t and filtered through a double paper filter, the resulting solid was washed with EtOAc several times, and the combined filtrates were concentrated to dryness under vacuum. The residue was purified by flash chromatography, silica gel,
25 DCM:MeOH as eluents to give the title compound as an orange solid (556 mg, Yield: 59%).

HPLC-MS (Method E): Rt.: 3.92 min; ESI+ MS: m/z 472.1 $[M+H]^+$.

Step e. (S)-(7-(1-(3,4-Difluorobenzyl)piperidin-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)methanamine dihydrochloride.

30 Starting from the compound obtained in step d (455 mg, 0.96 mmol) and following the procedure described in step d of example 110, the title compound was obtained (358 mg). This compound was used in the next step without further purification.

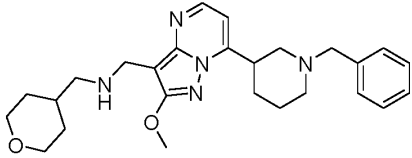
HPLC-MS (Method E): Rt.: 4.40 min; ESI+ MS: m/z 372.0 $[M+H]^+$.

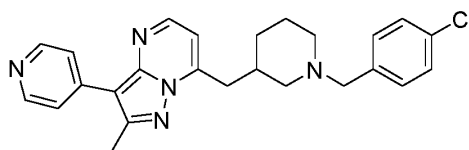
Step f. Title compound.

To a solution of the compound obtained in step e (398 mg, 1.07 mmol) in dry MeOH (14 mL), TEA (0.37 mL, 2.68 mmol) was added, followed by dropwise addition of the aldehyde obtained in step c (145 mg, 0.91 mmol) in dry MeOH (1 mL) and a few drops of AcOH. After vigorously stirring for 10 min, sodium cyanotrihydroborate (67.30 mg, 1.07 mmol) was added under argon atmosphere, the reaction mixture was stirred at r.t. for 3 h. Then, solvent was evaporated under reduced pressure, the resulting residue was partitioned between DCM (30 mL) and aq sat NaHCO₃ sol. The organic layer was separated, washed with aq sat NaHCO₃ sol, dried over MgSO₄, filtered and concentrated under vacuum. The residue was purified by preparative HPLC (XBridge C₁₈ column and 10 mM NH₄HCO₃/ 25% w/w NH₄OH (99.8:0.12):ACN as eluents) to give the title compound as a colourless oil (180 mg, Yield: 32%).

HPLC-MS (Method E): Rt.: 3.10 min; ESI+ MS: *m/z* 511.2 [M+H]⁺.

This method (2) was used for the preparation of example 248 using suitable starting materials:

STRUCTURE	EX	CHEMICAL NAME	Rt (min)	MS (M+H)	HPLC Method
	248	1-((7-(1-Benzylpiperidin-3-yl)-2-methoxypyrazolo[1,5-a]pyrimidin-3-yl)-N-((tetrahydro-2H-pyran-4-yl)methyl)methanamine	4.82	450.2	E



Example 249. 7-((1-(4-Chlorobenzyl)piperidin-3-yl)methyl)-2-methyl-3-(pyridin-4-yl)pyrazolo[1,5-a]pyrimidine.

Step a. *tert*-Butyl 3-(2-(methoxy(methyl)amino)-2-oxoethyl)piperidine-1-carboxylate.

To a solution of 2-(1-(*tert*-butoxycarbonyl)piperidin-3-yl)acetic acid (2 g, 8.22 mmol) in DCM (60 mL) cooled at 0 °C, *N,O*-dimethylhydroxylamine (653 mg, 10.69 mmol), EDC.HCl (2.36 g, 12.33 mmol), HOBt (1.89 g, 12.33 mmol) and TEA (4.6 mL, 32.9

mmol) were sequentially added and the reaction mixture was allowed to warm up to r.t and stirred for 16 h. Then, it was partitioned between DCM and 2 N HCl. The organic layer was separated, washed with 2 N HCl, 1 N NaOH, brine, dried over anhydrous Na₂SO₄, filtered and concentrated under vacuum to give the title compound as a colourless viscous oil (1.70 g, Yield: 72%). This compound was used in the next step without further purification.

HPLC-MS (Method E): Rt.: 2.83 min; ESI+ MS: *m/z* 287.1 [M+H]⁺.

Step b. *tert*-Butyl 3-(2-oxopropyl)piperidine-1-carboxylate.

To a 0 °C stirring solution of the compound obtained in step a (1.7 g, 5.94 mmol) in anhydrous THF (15 mL), methylmagnesium chloride (3 M in THF, 3.0 mL, 9 mmol) was added dropwise under argon atmosphere. The reaction was allowed to warm up to r.t and stirred for 2 h. Then, the reaction mixture was partitioned between Et₂O and 2 N HCl. The organic layer was separated, washed with brine, dried over anhydrous Na₂SO₄, filtered and concentrated under vacuum to give the title compound as a colourless oil (1.32 g, Yield: 92%). This compound was used in the next step without further purification.

HPLC-MS (Method E): Rt.: 3.00 min; ESI+ MS: *m/z* 242.1 [M+H]⁺.

Step c. *tert*-Butyl (E)-3-(4-(dimethylamino)-2-oxobut-3-en-1-yl)piperidine-1-carboxylate.

Starting from the compound obtained in step b (1.32 g, 5.47 mmol) and following the procedure described in step b of example 110, the title compound was obtained (1.62 g). This compound was used in the next step without further purification.

HPLC-MS (Method E): Rt.: 2.67 min; ESI+ MS: *m/z* 297.0 [M+H]⁺.

Step d. *tert*-Butyl 3-((3-bromo-2-methylpyrazolo[1,5-a]pyrimidin-7-yl)methyl)piperidine-1-carboxylate.

Starting from the compound obtained in step c (800 mg, 2.7 mmol) and following the procedure described in step a of example 121, the title compound was obtained (640 mg, Yield: 57%).

HPLC-MS (Method E): Rt.: 3.73 min; ESI+ MS: *m/z* 409.1 [M+H]⁺.

Step e. *tert*-Butyl 3-((2-methyl-3-(pyridin-4-yl)pyrazolo[1,5-a]pyrimidin-7-yl)methyl)piperidine-1-carboxylate.

Starting from the compound obtained in step d (220 mg, 0.53 mmol) and following the procedure described in step a of example 114, the title compound was obtained (123 mg, Yield: 55%).

HPLC-MS (Method E): Rt.: 3.42 min; ESI+ MS: m/z 408.1 $[M+H]^+$.

- 5 Step f. 2-Methyl-7-((piperidin-3-ylmethyl)-3-(pyridin-4-yl)pyrazolo[1,5-a]pyrimidine dihydrochloride.

Starting from the compound obtained in step e (123 mg, 0.30 mmol) and following the procedure described in step d of example 110, the title compound was obtained (104 mg). This compound was used in the next step without further purification.

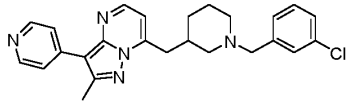
- 10 HPLC-MS (Method E): Rt.: 2.47 min; ESI+ MS: m/z 308.0 $[M+H]^+$.

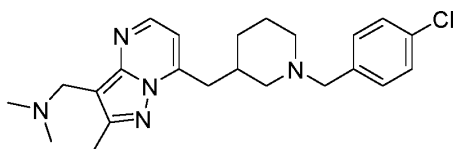
Step g. Title compound.

Starting from the compound obtained in step f (120 mg, 0.35 mmol) and following the procedure described in step e of example 110, the title compound was obtained (90 mg, Yield: 59%).

- 15 HPLC-MS (Method E): Rt.: 3.98 min; ESI+ MS: m/z 432.1 $[M+H]^+$.

This method was used for the preparation of example 250 using suitable starting materials:

STRUCTURE	EX	CHEMICAL NAME	Rt (min)	MS (M+H)	HPLC Method
	250	7-((1-(3-Chlorobenzyl)piperidin-3-yl)methyl)-2-methyl-3-(pyridin-4-yl)pyrazolo[1,5-a]pyrimidine	3.98	432.1	E



- 20 Example 251. 1-(7-((1-(4-Chlorobenzyl)piperidin-3-yl)methyl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-N,N-dimethylmethanamine

Step a. *tert*-Butyl 3-((2-methylpyrazolo[1,5-*a*]pyrimidin-7-yl)methyl)piperidine-1-carboxylate.

Starting from the compound obtained in step c of example 249, (2.15 g, 7.25 mmol) and following the procedure described in step a of example 144, the title compound was obtained (1.5 g, Yield: 60%).

HPLC-MS (Method E): Rt.: 3.20 min; ESI+ MS: *m/z* 331.0 [M+H]⁺.

Step b. 2-Methyl-7-(piperidin-3-ylmethyl)pyrazolo[1,5-*a*]pyrimidine hydrochloride.

Starting from the compound obtained in step a (1.0 g, 3.03 mmol) and following the procedure described in step d of example 110, the title compound was obtained (807 mg). This compound was used in the next step without further purification.

HPLC-MS (Method E): Rt.: 2.12 min; ESI+ MS: *m/z* 231.0 [M+H]⁺.

Step c. 7-((1-(4-Chlorobenzyl)piperidin-3-yl)methyl)-2-methylpyrazolo[1,5-*a*]pyrimidine.

Starting from the compound obtained in step b (420 mg, 1.57 mmol) and following the procedure described in step e of example 110, the title compound was obtained (245 mg, Yield: 59%).

HPLC-MS (Method E): Rt.: 3.77 min; ESI+ MS: *m/z* 355.1 [M+H]⁺.

Step d. 7-((1-(4-Chlorobenzyl)piperidin-3-yl)methyl)-2-methylpyrazolo[1,5-*a*]pyrimidine-3-carbaldehyde.

Starting from the compound obtained in step c (345 mg, 0.97 mmol) and following the procedure described in step a of example 120, the title compound was obtained (290 mg, Yield: 54%).

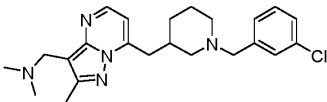
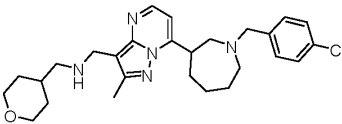
HPLC-MS (Method E): Rt.: 3.70 min; ESI+ MS: *m/z* 383.1 [M+H]⁺.

Step e. Title compound.

Starting from the compound obtained in step d (290 mg, 0.75 mmol) and dimethylamine (0.94 mL, 1.89 mmol) and following the procedure described in step e of example 110, the title compound was obtained (31 mg, Yield: 8%).

HPLC-MS (Method I): Rt.: 2.95 min; ESI+ MS: *m/z* 412.2 [M+H]⁺.

This method was used for the preparation of examples 252 and 253 using suitable starting materials:

STRUCTURE	EX	CHEMICAL NAME	Rt (min)	MS (M+H)	HPLC Method
	252	1-((7-((1-(3-Chlorobenzyl)piperidin-3-yl)methyl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-N,N-dimethylmethanamine	3.10	412.2	I
	253	1-((7-(1-(4-Chlorobenzyl)azepan-3-yl)-2-methylpyrazolo[1,5-a]pyrimidin-3-yl)-N-((tetrahydro-2H-pyran-4-yl)methyl)methanamine	3.02	482.1	I

BIOLOGICAL ACTIVITY**Pharmacological study****Human $\alpha_2\delta$ -1 subunit of $\text{Ca}_v2.2$ calcium channel assay**

5 Human $\alpha_2\delta$ -1 enriched membranes (2.5 μg) were incubated with 15 nM of radiolabeled
[^3H]-Gabapentin in assay buffer containing Hepes-KOH 10 mM, pH 7.4. NSB (non
specific binding) was measured by adding 10 μM pregabalin. The binding of the test
compound was measured at either one concentration (% inhibition at 1 or 10 μM) or
10 five different concentrations to determine affinity values (K_i). After 60 min incubation at
27 $^{\circ}\text{C}$, binding reaction was terminated by filtering through Multiscreen GF/C (Millipore)
presoaked in 0.5 % polyethyleneimine in Vacuum Manifold Station, followed by 3
washes with ice-cold filtration buffer containing 50 mM Tris-HCl, pH 7.4. Filter plates
were dried at 60 $^{\circ}\text{C}$ for 1 h and 30 μL of scintillation cocktail were added to each well
before radioactivity reading. Readings were performed in a Trilux 1450 Microbeta
15 radioactive counter (Perkin Elmer).

Human σ_1 receptor radioligand assay

Transfected HEK-293 membranes (7 μg) were incubated with 5 nM of [^3H](+)-
pentazocine in assay buffer containing Tris-HCl 50 mM at pH 8. NBS (non-specific
binding) was measured by adding 10 μM haloperidol. The binding of the test compound
20 was measured at either one concentration (% inhibition at 1 or 10 μM) or five different
concentrations to determine affinity values (K_i). Plates were incubated at 37 $^{\circ}\text{C}$ for 120
minutes. After the incubation period, the reaction mix was then transferred to
MultiScreen HTS, FC plates (Millipore), filtered and plates were washed 3 times with
ice-cold 10 mM Tris-HCL (pH7.4). Filters were dried and counted at approximately 40%
25 efficiency in a MicroBeta scintillation counter (Perkin-Elmer) using EcoScint liquid
scintillation cocktail.

Results:

As this invention is aimed at providing a compound or a chemically related series of
compounds which act as dual ligands of the $\alpha_2\delta$ subunit of voltage-gated calcium
30 channels and the σ_1 receptor it is a very preferred embodiment in which the compounds
are selected which act as dual ligands of the $\alpha_2\delta$ subunit of voltage-gated calcium

channels and the σ_1 -receptor and especially compounds which have a binding expressed as K_i responding to the following scales:

$K_i(\sigma_1)$ is preferably < 1000 nM, more preferably < 500 nM, even more preferably < 100 nM.

- 5 $K_i(\alpha_2\delta-1)$ is preferably < 10000 nM, more preferably < 5000 nM, or even more preferably < 500 nM.

The following scale has been adopted for representing the binding to σ_1 -receptor expressed as K_i :

- 10 + $K_i(\sigma_1) > 1000 \text{ nM}$
 ++ $500 \text{ nM} \leq K_i(\sigma_1) \leq 1000 \text{ nM}$
 +++ $K_i(\sigma_1) < 500 \text{ nM}$

Preferably, when $K_i(\sigma_1) > 1000 \text{ nM}$, the following scale has been adopted for

- 15 representing the binding to the σ_1 -receptor:

 + $K_i(\sigma_1) > 1000 \text{ nM}$ or inhibition ranges between 1% and 50 %.

The following scale has been adopted for representing the binding to the $\alpha_2\delta-1$ subunit of voltage-gated calcium channels expressed as K_i :

- 20 + $K_i(\alpha_2\delta-1) > 5000 \text{ nM}$
 ++ $500 \text{ nM} \leq K_i(\alpha_2\delta-1) \leq 5000 \text{ nM}$
 +++ $K_i(\alpha_2\delta-1) < 500 \text{ nM}$

Preferably, when $K_i(\alpha_2\delta-1) > 5000 \text{ nM}$, the following scale has been adopted for

- 25 representing the binding to the $\alpha_2\delta-1$ subunit of voltage-gated calcium channels:

 + $K_i(\alpha_2\delta-1) > 5000 \text{ nM}$ or inhibition ranges between 1% and 50 %

Table of Examples with binding to the σ_1 Receptor and the $\alpha_2\delta$ -1 Subunit of the voltage-gated calcium channel

All compounds prepared in the present application exhibit binding to the $\alpha_2\delta$ -1 subunit of voltage-gated calcium channels and to the σ_1 receptor, in particular the following

5 binding results are shown:

Example	$\alpha_2\delta$ binding	σ -1 binding
1	+++	++
2	+++	+
3	+++	++
4	+++	+++
5	+++	+++
6	+++	+
7	+	+
8	+	+
9	+	+
10	+++	+++
11	+++	+++
12	+	++
13	+	+
14	+++	++
15	+	+

16	++	+
17	+++	++
18	+++	++
19	++	+
20	+++	+
21	+++	+
22	++	+
23	+++	+
24	+++	+
25	+	+
26	++++	+
27	++	++
28	++	+
29	++	+
30	+	+
31	++	+
32	+	+
33	++	+
34	++	+
35	+	++

36	++	++
37	++	+
38	++	+
39	+	+
40	++	+
41	++	+
42	++	+
43	++	+
44	+	+
45	+	++
46	++	+
47	+	+
48	+	+
49	+	+
50	++	+
51	++	++
52	++	+
53	++	+
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56	++	+
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60	++	+
61	++	+
62	++	+
63	+	+
64	+	+++
65	++	+
66	+	+
67	+	+
68	+	+
69	+	+
70	+	+
71	+	+
72	++	+
73	+	+++
74	++	+
75	++	+

76	++	++
77	+	+
78	+	++
79	+	+
80	++	+
81	++	+
82	++	+
83	++	+
84	++	+
85	+	+
86	++	+
87	++	+
88	+	++
89	++	++
90	+	+
91	++	+
92	++	+
93	++	+
94	++	+
95	+	+

96	++	+
97	++	+++
98	++	+++
99	++	+
100	++	+
101	+	+++
102	+	+
103	++	+
106	+	+
107	+	+
108	+	+
109	++	+
110	+	++
111	+	+
112	+	+
113	++	+
114	+	+
115	+	+
116	+	+
117	+	+

118	+	+
119	+	+
120	+++	+++
121	++	++
122	++	+
123	++	+
124	+	++
125	++	+
126	+	+
127	+	+++
128	+	+
129	+	+
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132	++	+
133	+	+
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135	+	+
136	+	+
137	+	+

138	+	+
139	+	+
140	++	+
141	+	+++
142	+	+
143	+	++
144	++	+++
145	++	+++
146	++	+++
147	+	+++
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152	+	++
153	++	+++
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155	++	+++
156	+	++
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165	+	++
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169	++	+++
170	+++	+++
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173	+	+
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175	+	+
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247	+++	+++
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