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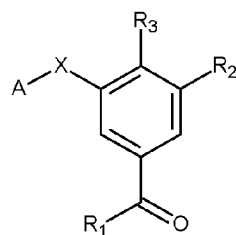
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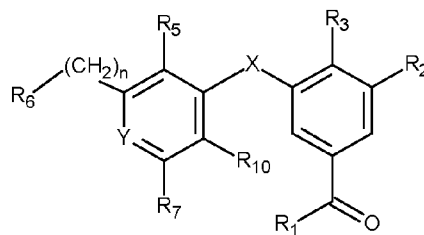
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(54) Title: COMPOUNDS, IN PARTICULAR FOR USE IN THE TREATMENT OF A DISEASE OR CONDITION FOR WHICH A BROMODOMAIN INHIBITOR IS INDICATED



(1)



(3)

(57) Abstract: The invention relates to a compound for use in the treatment of a disease or condition for which a bromodomain inhibitor is indicated characterized by a general formula (1) and a compound according to formula (3).

Compounds, in particular for use in the treatment of a disease or condition for which a bromodomain inhibitor is indicated

DESCRIPTION

Field of the Invention

- 5 The present invention relates to novel compounds, to pharmaceutical compositions containing such compounds and to their use in therapy.

Background of the Invention

Within eukaryotes, long strands of DNA are packed within the nucleus in a dynamic form allowing intermittent and regulated access to genes for transcription. This form is achieved
10 by the winding of sections of DNA around octameric groups of histone proteins to form nucleosomes. Repeating nucleosomes units along the DNA strand aggregate and fold to form tightly packed chromatin. The degree of chromatin packing varies throughout the cell cycle; regulated chromatin loosening allows transcription machinery to access and transcribe selected genes.

15 Chromatin packing is influenced by a series of post-translational modifications of histone proteins and in particular of histones H3 and H4. Indeed, the post-translational acetylation of lysine residues within histone proteins has been recognized to play a critical role in the packing of chromatin and regulation of gene transcription.

Such acetylated lysines are generally recognized by a small protein domain referred to as a
20 bromodomain. Bromodomain binding (commonly referred to as “reading”) of acetylated lysines initiates the recruitment of regulatory complexes, thereby influencing chromatin structure.

Small-molecule inhibitors of selected bromodomain/histone interactions (hereafter “bromodomain inhibitors”) have been identified and show promise as future therapeutics,
25 notably relative to cancer and inflammatory diseases. Acetylated lysines of p53, a tumor suppressor, have further been reported to associate with bromodomains.

Some 50 human proteins have thus far been identified as containing a single or tandem bromodomain that cluster into eight major families using structure-based analysis.

Whereas extensive research efforts have recently been undertaken to find small-molecule
30 inhibitors of the so-called BET family of bromodomains (consisting of BRD2, BRD2, BRD4 and BRD-t), resulting in I-BET and JQ-1 inhibitors, among others, lesser advancements have been achieved relative to other bromodomain-containing proteins.

One latter such protein of high therapeutic interest is CBP (CREB-binding protein or CREBBP), initially identified as a protein capable of binding to the cAMP response element binding protein (CREB) and acting as CREB transcriptional co-activator. More recently, CBP has been shown to function as a transcriptional coactivator for numerous oncogenes and tumor suppressors. Moreover, specific inhibition of CBP has been proposed as a treatment of obesity-linked diabetes and atherosclerosis (Tsuchida A. et al, "Nuclear receptors as targets for drug development: molecular mechanisms for regulation of obesity and insulin resistance by peroxisome proliferator-activated receptor gamma, CREB-binding protein, and adiponectin" *J.Pharmacol.Sci.*, 97:164-170, 2005). I-BET and JQ-1 inhibitors only weakly inhibit the interaction of CBP with peptide binding partners (half maximal inhibition concentration (IC_{50}) $\geq 50 \mu M$). Indeed, few highly potent inhibitors of CBP have been reported to date.

In Borah et al. "A Small Molecule Binding to the Coactivator CREB-Binding Protein Blocks Apoptosis in Cardiomyocytes" (*Chemistry&Biology*, 18: 531–541, 2011), ischemin inhibitors are reported to provide up 100% inhibition of CBP at 50 μM , with CBP-inhibitor complex dissociation constant (K_D) values down to 19 μM at best.

In "Target Structure-Based Discovery of Small Molecules that Block Human p53 and CREB Binding Protein Association" (*Chemistry&Biology*, 13: 81-90, 2006), Sachchidanand et al. describe a series of small-molecule inhibitors containing an unsaturated ring connected to a $-NHCOCH_3$ group, which bind to the acetylated lysine binding site of CBP. N-acetylated aniline derivatives such as paracetamol are likewise discussed as binders of the bromodomain fold of CBP in Chung et al. "Fragment-Based Discovery of Bromodomain Inhibitors Part 1: Inhibitor Binding Modes and Implications for Lead Discovery" (*J.Med.Chem.*, 55: 576-586, 2011). N-alkylated compounds comprising aromatic rings as well as phenol derivatives acting as inhibitors of p53/CBP association are further reported in WO 2007/084625 A2.

Compound 27, a tetrahydro- γ -carboline derivative reported in "Targeting low-druggability bromodomains: Fragment based screening and inhibitor design against the BAZ2B bromodomain" by Ferguson et al. (*J.Med.Chem.* 56 (24): 10183–10187, 2013) provides a thermal shift which the authors indicate would be expected to correspond to a low micromolar lead for CBP.

A 2012 presentation by P. Brennan entitled "Isoxazole Inhibitors of Bromodomains" and a related publication by Hay et al. entitled "The design and synthesis of 5- and 6-isoxazolylbenzimidazoles as selective inhibitors of the BET bromodomains" (*MedChemComm*, 4: 140-144, 2013), report on isoxazole inhibitors of CBP with IC_{50} values down to 170 nM on Alpha Screen (BDOIA298) and 1.26 μM at best, respectively.

Hewings et al. reported compounds with IC₅₀ values on CBP of 3.4 μM at best in "3,5-Dimethylisoxazoles Act As Acetyl-lysine-mimetic Bromodomain Ligands" (*J. Med. Chem.*, 54: 6761-6770, 2011). Later, in Hewings et al. "Optimization of 3,5-Dimethylisoxazole Derivatives as Potent Bromodomain Ligands" (*J. Med. Chem.*, 56, 3217-3227, 2013), small-molecule compounds with IC₅₀ values on CBP of 771 nM are reported at best.

In "4-Acyl Pyrroles: Mimicking Acetylated Lysines in Histone Code Reading" by Lukas et al. (*Angew. Chem. Int. Ed.*, 52:14055-14059, 2013), a phenyl sulfonamide substituted 4-acyl pyrrole identified as XD14 is reported to have a K_D of 237 nM and 1.6 μM on BRD4 and CBP, respectively.

In "A Series of Potent CREBBP Bromodomain Ligands Reveals an Induced-Fit Pocket Stabilized by a Cation-π Interaction" by Rooney et al. (*Angew. Chem.*, 126:6240-6244, 2014), substituted dihydroquinoxalinones reached IC₅₀ values down to 323 nM.

In "[1,2,4]Triazolo[4,3-a]phthalazines: inhibitors of diverse bromodomains" of Federov et al. (*J. Med. Chem.*, 57 (2):462–476, 2014), table 1 includes compounds with IC₅₀ values on CBP of 200 nM at best.

The Structural Genomics Consortium has published compounds I-CBP112 (a tetrahydro benzoxazepine derivative), with an IC₅₀ of 170 nM on CBP, and SGC-CBP30 (an isoxazole derivative), with an IC₅₀ of 69 nM on CBP, at <http://www.thesgc.org/chemical-probes/epigenetics> (see also Hay et al. "Discovery and Optimization of Small-Molecule Ligands for the CBP/p300 Bromodomains" *J. Am. Chem. Soc.*, 136 (26): 9308–9319, 2014).

As such, there remains a need for novel, chemically-diverse and potent inhibitors of CBP.

Moreover, there remains a need for CPB inhibitors that are selective for CBP relative to other bromodomains, meaning that they bind to CBP with more potency than (have a lower K_D or IC₅₀ than on) other bromodomains. Finally, it is advantageous that such inhibitors are synthetically accessible, i.e. can be synthesized according to few, standard synthetic steps.

It is of note that EP 1 666 473 A1 discloses broad class of carboxylic acid compounds as selective antagonists of prostoglandin D2 and indicated as useful for the treatment of diseases such as allergic diseases, systemic mastocytosis, disorders accompanied by systemic mast cell activation, anaphylactic shock, bronchoconstriction, urticarial, eczema, acne, allergic bronchial pulmonary aspergillosis, sinusitis, migraine, nasal polypus, anaphylactic vasculitis, eosinophilic syndrome, contact dermatitis, diseases accompanied by itch, inflammation, chronic obstructive pulmonary diseases, ischemic reperfusion injury, cerebrovascular accident, autoimmune disease, traumatic brain disorder, hepatopathy, graft rejection, chronic rheumatoid arthritis, pleurisy, osteoarthritis, Crohn's disease, ulcerative

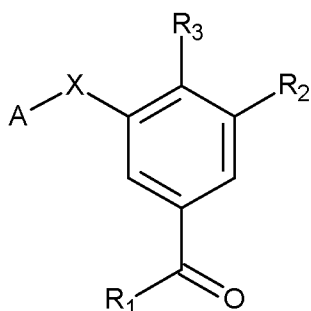
colitis, irritable bowel syndrome, interstitial cystitis, muscular dystrophy, polymyositis, multiple sclerosis, sleep and platelet aggregation.

WO 2012/116170 A1 discloses a wide range of compounds, though specific embodiments define a narrow chemical space, which are indicated as inhibitors of bromodomains. Among other important differences to the compounds of the present invention, WO 2012/116170 A1 does not disclose a compound comprising a substituted phenyl ring as is mandatory in the compounds of the present invention and further comprises linker moieties not corresponding to those of the present invention.

It is therefore an object of the present invention to provide a novel class of compounds useful as inhibitors of the CBP/acetylated lysine interaction (hereafter "CBP inhibitors"). Pharmaceutical compositions containing such compounds are further objects of the present invention. A method of treating a disease or condition for which a bromodomain inhibitor is indicated is also subject of the present invention.

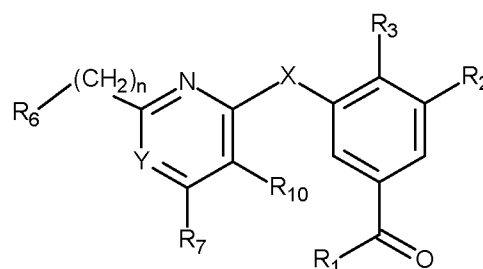
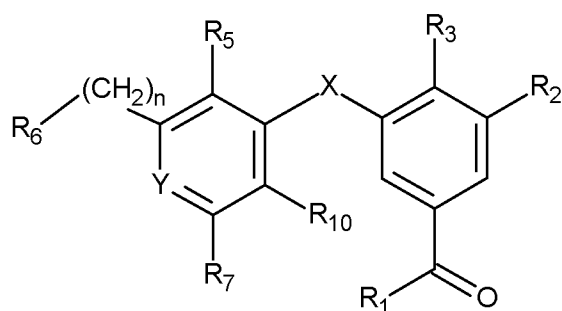
Summary of the Invention

A first aspect of the present invention relates to a compound for use in the treatment of a disease or condition for which a bromodomain inhibitor is indicated characterized by a general formula (1),



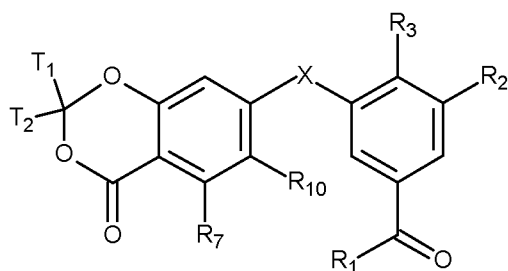
(1), as discussed below.

A second aspect of the present invention relates to a compound, or prodrug or salt thereof, of formula (3),



(3), or

(4), or



(5), particularly of formula (3), as discussed below.

A third aspect of the present invention relates to a method of treating a disease or condition for which a bromodomain inhibitor is indicated in a subject in need thereof which comprises administering a therapeutically effective amount of a compound, or salt or prodrug thereof, where said compound is characterized by the general formula (1), (2), (3), (4) or (5), particularly by the general formula (1), (2) or (3).

A fourth aspect of the present invention relates to a pharmaceutical composition comprising a therapeutically effective amount of a compound of general formula (3), (4) or (5), particularly of general formula (3), and one or more pharmaceutically acceptable carriers, diluents or excipients.

As used herein, unless otherwise specified, the term “**bromodomain inhibitor**” refers to a compound that inhibits the binding of a bromodomain with its cognate acetylated lysine or lysines of one or more proteins. In particular, said cognate acetylated lysines are among the residues of one or more histones. More particularly, said histones are H3 or H4.

In particular, said bromodomain is CBP and/or EP300. A CBP or EP300 bromodomain inhibitor is a compound that has a IC_{50} that is less than 100 μM as measured according to the IC_{50} measurement method provided in the examples section hereafter, **and/or** a thermal shift of greater than or equal to 1 $^{\circ}C$ as measured according to the thermal shift measurement method provided in the examples section hereafter, **and/or** a K_D of less than 50 μM as measured according to the K_D measurement method provided in the examples section hereafter.

As used herein, unless otherwise specified, the term “**effective amount**” refers to the amount of compound needed to elicit a biological or medical response within a human or within a human tissue, by a researcher or a clinician.

As used herein, unless otherwise specified, the term “**therapeutically effective amount**” refers to any amount of compound that will result in improved treatment, healing, prevention or amelioration of a disease or condition in a subject, or decreased advancement of a disease or condition in a subject, relative to a corresponding subject who has not received such an amount.

As used herein, unless otherwise specified, the term “**parent compound**” refers to all of the atoms of the general formulas (1), (2) and (3) provided herein having a single possible chemical identity.

Compounds of the present invention may be in the form of a “**salt**”, meaning in the form of an ionic compound resulting from a neutralization reaction of an organic or inorganic acid with an organic or inorganic base. In particular, such salts are pharmaceutically acceptable salts. For a review on suitable salts see Berge et al., J. Pharm. Sci., 66:1 -19, (1977). The resultant salt may precipitate from solution and be collected by filtration or may be recovered by evaporation of the solvent.

Compounds of the present invention may be in the form of a “**prodrug**”, which is an inactive or less than fully active precursor form of the compound that is converted into the compound by normal metabolic processes, e.g., hydrolysis by, for example, an esterase of an ester form of the compound, and in particular of a methyl ester form of the compound, to generate a carboxylic acid. Suitable prodrugs are recognizable to those skilled in the art, without undue experimentation. Nevertheless, reference is made to the teaching of Burger's Medicinal Chemistry and Drug Discovery, 5th Edition, Vol 1: Principles and Practice.

As used herein, unless otherwise specified, the term “**substituent group**” refers to a chemical group in which one hydrogen atom has been replaced by a bond to a non-hydrogen atom on the parent compound.

As used herein, unless otherwise specified, the term “**alkyl**” refers to a saturated hydrocarbon substituent group containing 1 to 6, particularly 1 to 3 carbon atoms, that is linear or branched. Examples of alkyl groups include, without limitation, methyl, ethyl, propyl, n-butyl, isobutyl, pentyl, isopentyl, neopentyl, hexyl, 2-methylpentyl, 3-methylpentyl, 2,2-methylpentyl, 2,3-methylpentyl and the like.

As used herein, unless otherwise specified, the term “**heteroalkyl**” refers to a saturated hydrocarbon substituent group containing 1 to 5, particularly 1 to 3 carbon atoms, that is linear or branched, wherein at least one carbon is replaced with an oxygen or a nitrogen atom.

As used herein, unless otherwise specified, the term “**alkanol**” refers to an alkyl substituent group in which one or more hydrogen atom is replaced by a hydroxyl group. Examples of alkanol substituent groups include, without limitation, methanol, ethanol, propanol, n-butanol, isobutanol and the like. Alkanol groups as used herein may optionally include further substituent groups.

As used herein, unless otherwise specified, the term “**haloalkyl**” refers to an alkyl substituent group in which one or more hydrogen atom is replaced by a halogen atom. In particular, this

halogen atom is a Cl or F. Examples of haloalkyl substituent groups include, without limitation, CF₃, CHF₂, CH₂F, CH₂CF₃, CH₂CHF₂, CH₂CH₂F, CHFCH₂F, CF₂CF₃, CF₂CHF₂, CF₂CH₂F and the like. Haloalkyl groups as used herein may optionally include further substituent groups.

5 As used herein, unless otherwise specified, the term "**alkoxy**" refers to an oxygen-alkyl substituent group, wherein the oxygen atom is used to attach the alkoxy group to the parent compound. Examples of alkoxy substituent groups include, without limitation, methoxy, ethoxy, propoxy, isopropoxy, n-butoxy, sec-butoxy, tert-butoxy, n-pentoxy, neopentoxy, n-hexoxy and the like. Alkoxy groups as used herein may optionally include further substituent
10 groups.

As used herein, unless otherwise specified, the term "**ether**" refers to an oxygen-alkyl or oxygen-aryl or oxygen-alkyl-aryl substituent group, wherein the oxygen atom is connected to two alkyl or two aryl groups, or to one alkyl and one aryl group, wherein these alkyl and/or aryl groups do not belong to the parent compound. Ether groups as used herein may
15 optionally include further substituent groups.

As used herein, unless otherwise specified, the term "**heterocycle**" refers to a saturated heterocycle or a heteroaryl substituent group. The term "**saturated heterocycle**" refers to a saturated cyclic group wherein at least one carbon is replaced with an oxygen, a nitrogen or a sulphur atom. Examples of saturated heterocycle substituent groups include, without
20 limitation, morpholine, piperazine, pyrrolidine, thiolane, tetrahydrofuran, imidazolidine, pyrazolidine, oxazolidine, thiazolidine, piperidine, oxane groups and the like. Saturated heterocycle groups as used herein may optionally include further substituent groups.

As used herein, unless otherwise specified, the term "**aryl**" refers to a hydrocarbon with alternating double and single bonds between the carbon atoms forming a ring structure. The
25 term "**heteroaryl**" refers to aryl compounds in which at least one carbon atom is replaced with an oxygen, a nitrogen or a sulphur atom. Examples of aryl or hetero aryl substituent groups include, without limitation, benzene, pyridine, pyrrole, quinolone, imidazole, triazine, pyrazine, pyrimidine, pyradazine, thiazine, dioxin, tetrazole, triazole, thiadiazole, pyrazole, oxazole, thiazole, furan and the like. Aryl or heteroaryl groups as used herein may optionally
30 include further substituent groups.

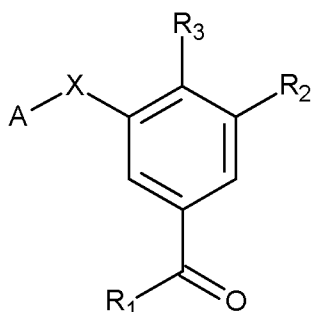
As used herein, unless otherwise specified, the term "**-COOH or salt thereof**" refers to a carboxyl group or a salt derivative of the carboxyl group preferably selected from the group of alkali metals. .

In view of the close relationship between the compounds of general formula (1), (2), (3), (4)
35 or (5) and the tautomers thereof, any reference to the compounds of the general formula (1),

(2), (3), (4) or (5) is to be understood as referring also to the corresponding tautomers. The same applies to a hydrate or a solvate.

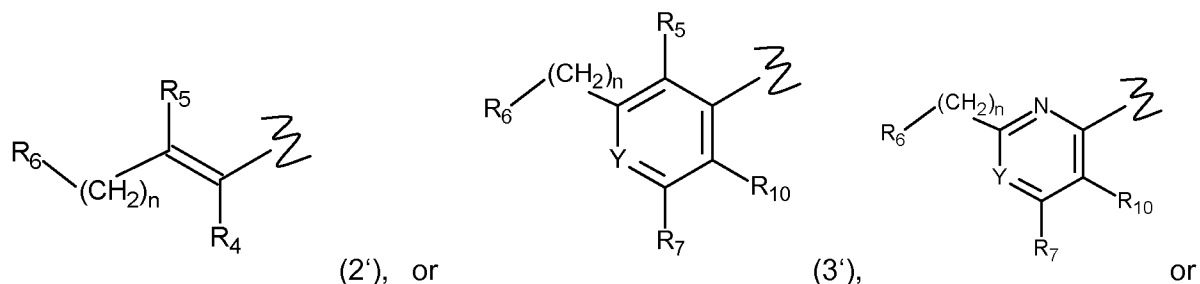
Detailed description of the Invention

According to the first aspect the present invention relates to a compound for use in the treatment of a disease or condition for which a bromodomain inhibitor is indicated characterized by a general formula (1),



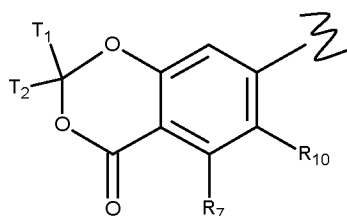
(1), wherein

- R₁ is a C₁-C₃ alkyl, cyclopropane, a C₁-C₃ haloalkyl, halocyclopropane or -NHR₈, wherein R₈ is a C₁-C₃ alkyl, cyclopropane, a C₁-C₃ haloalkyl or halocyclopropane;
- R₂ is H, F, a C₁-C₄ alkyl or a C₁-C₄ alkanol;
- R₃ is H, F, Cl, a C₁-C₆ alkyl, a C₁-C₃ haloalkyl, a C₁-C₄ alkoxy, a C₁-C₄ alkanol, a C₂-C₄ ether, a 3- to 6-membered saturated heterocycle, a 3- to 6-membered heteroaryl, a benzyloxy or a substituted amine of the form -NHR₈, wherein R₈ is a C₁-C₃ alkyl, cyclopropane, a C₁-C₃ haloalkyl or halocyclopropane;
- X is -C(=O)NH-, -NHC(=O)-, -C(=O)NR₁₂-, -NR₁₂C(=O)-, -NHC(=O)NH-, -N(R₉)C(=O)NH-, -NHC(=O)NR₉-, -C(=S)NH-, -NHC(=S)-, -NHC(=S)NH-, -N(R₉)C(=S)NH-, -NHC(=S)N(R₉)-, -N-S(=O)₂-, -S(=O)₂-N-, particularly X is -C(=O)NH-, -NHC(=O)-, -C(=O)NR₁₂-, -NR₁₂C(=O)-, -NHC(=O)NH-, -N(R₉)C(=O)NH-, -NHC(=O)NR₉-, -C(=S)NH-, -NHC(=S)-, -NHC(=S)NH-, -N(R₉)C(=S)NH-, -NHC(=S)N(R₉)-, wherein
 - R₉ is C₁-C₃ alkyl, C₁-C₃ alkoxy, C₁-C₃ haloalkyl, C₁-C₃ alkanol, C₂-C₄ ether, 3- to 6-membered heterocycle, or substituted or unsubstituted aryl, and wherein
 - R₁₂ is -(CH₂)_r-phenyl with r being 0, 1 or 2 and said phenyl may be substituted with one or more electron donating groups, in particular one or more electron donating groups selected from -OR₁₃, with R₁₃ being H, a methyl group or an ethyl group;
- A is selected from



- R_4 is H or a methyl group;
- R_5 is H, -COOH or salt thereof, a C_1 - C_3 alkoxyl, a C_1 - C_3 alkyl, a C_1 - C_3 alkyl ester, a heteroaryl, a substituted or unsubstituted C_1 - C_6 alkoxyl or a sulfonic acid, a sulfonamide, particularly an S-linked sulfonamide, that may be singly substituted with a C_1 - C_3 alkyl group or with a C_3 - C_6 cyclic alkyl; and
- R_6 is H, -COOH or salt thereof, a C_1 - C_3 alkoxyl, a C_1 - C_3 alkyl, a C_1 - C_3 alkyl ester, a substituted or unsubstituted heteroaryl, a substituted or unsubstituted C_1 - C_6 alkoxyl or a sulfonic acid, a sulfonamide, particularly an S-linked sulfonamide, that may be singly substituted with a C_1 - C_3 alkyl group or with a C_3 - C_6 cyclic alkyl; and wherein
- R_7 and R_{10} being independently from each other selected from
 - H, Br, Cl, F, NO_2 or
 - substituted or unsubstituted C_1 - C_3 alkanol, C_1 - C_3 alkyl, C_1 - C_3 haloalkyl, substituted or unsubstituted C_1 - C_3 alkoxy, C_3 - C_6 cycloalkyl, C_2 - C_4 alkyl ether, 3- to 6-membered saturated heterocycle, a 3- to 6-membered heteroaryl moiety, wherein said moieties may be substituted or unsubstituted, wherein the substituents of said substituted moieties with respect to R_4 and R_7 are selected from 3- to 6-membered heteroaryls and aryls, or 3- to 6-membered saturated heterocycles, which may also be substituted with one or more hydroxyl, amine or C_1 - C_3 alkoxy groups;
- n is 0, 1 or 2;
- Y is N, CH or C- R_{11} , with
 - R_{11} being a hydroxyl, a C_1 - C_5 heteroalkyl, particularly a $-(CH_2)_p-OT_3$ or a $-(CH_2)_p-N(T_3)(T_4)$, with T_3 and T_4 being independently from each other H or C_1 - C_3 alkyl, and p is 0, 1, 2, 3, 4 or 5, a substituted or unsubstituted C_1 - C_6 alkoxyl, a heteroaryl, a saturated heterocycle, $-O-(CH_2)_q$ -phenyl or $-O-(CH_2)_q$ -heterocycle, with q being 0, 1 or 2, wherein the saturated heterocycle or the $-O-(CH_2)_q$ -heterocycle are preferably C_3 - C_6 heterocycles, more preferably C_5 - C_6 heterocycles,

or wherein R^6 and Y are connected forming a cyclic moiety of the formula 5'

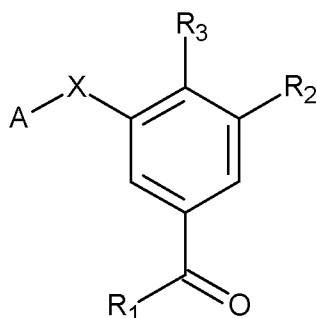


(5'), with T_1 and T_2 being independently from each other H, CH_3

or CH_2CH_3 , particularly H, and R_7 and R_{10} having the same meaning as above.

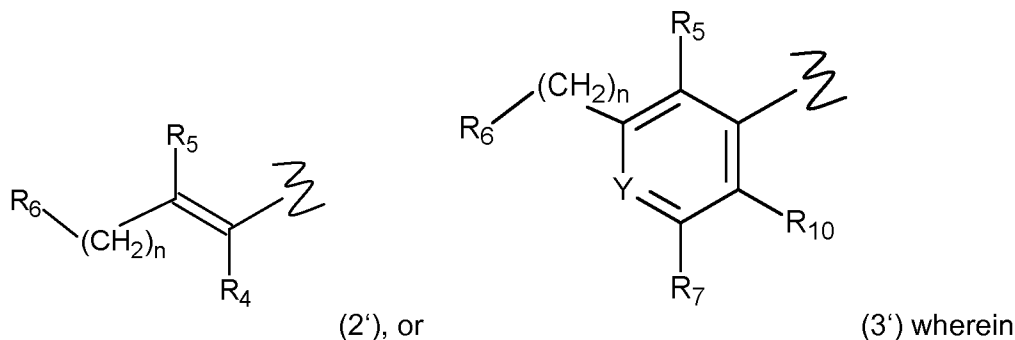
According to one embodiment of the first aspect the present invention relates to a compound for use in the treatment of a disease or condition for which a bromodomain inhibitor is

5 indicated characterized by a general formula (1),



(1)

- R_1 is a $\text{C}_1\text{-C}_3$ alkyl, cyclopropane, a $\text{C}_1\text{-C}_3$ haloalkyl, halocyclopropane or $-\text{NHR}_8$, wherein R_8 is a $\text{C}_1\text{-C}_3$ alkyl, cyclopropane, a $\text{C}_1\text{-C}_3$ haloalkyl or halocyclopropane;
- R_2 is H, F, a $\text{C}_1\text{-C}_4$ alkyl or a $\text{C}_1\text{-C}_4$ alkanol;
- 10 - R_3 is H, F, Cl, a $\text{C}_1\text{-C}_6$ alkyl, a $\text{C}_1\text{-C}_3$ haloalkyl, a $\text{C}_1\text{-C}_4$ alkoxy, a $\text{C}_1\text{-C}_4$ alkanol, a $\text{C}_2\text{-C}_4$ ether, a 3- to 6-membered saturated heterocycle, a 3- to 6-membered heteroaryl, a benzyloxy or a substituted amine of the form $-\text{NHR}_8$, wherein R_8 is a $\text{C}_1\text{-C}_3$ alkyl, cyclopropane, a $\text{C}_1\text{-C}_3$ haloalkyl or halocyclopropane;
- X is $-\text{C}(=\text{O})\text{NH}-$, $-\text{NHC}(=\text{O})-$, $-\text{C}(=\text{O})\text{NR}_{12}-$, $-\text{NR}_{12}\text{C}(=\text{O})-$, $-\text{NHC}(=\text{O})\text{NH}-$,
15 $-\text{N}(\text{R}_9)\text{C}(=\text{O})\text{NH}-$, $-\text{NHC}(=\text{O})\text{NR}_9-$, $-\text{C}(=\text{S})\text{NH}-$, $-\text{NHC}(=\text{S})-$, $-\text{NHC}(=\text{S})\text{NH}-$,
 $-\text{N}(\text{R}_9)\text{C}(=\text{S})\text{NH}-$, $-\text{NHC}(=\text{S})\text{N}(\text{R}_9)-$, wherein
 - R_9 is $\text{C}_1\text{-C}_3$ alkyl, $\text{C}_1\text{-C}_3$ alkoxy, $\text{C}_1\text{-C}_3$ haloalkyl, $\text{C}_1\text{-C}_3$ alkanol, $\text{C}_2\text{-C}_4$ ether, 3- to 6-membered heterocycle, or substituted or unsubstituted aryl, and wherein
 - R_{12} is $-(\text{CH}_2)_r\text{-phenyl}$ with r being 0, 1 or 2 and said phenyl may be substituted
20 with one or more electron donating groups, in particular one or more electron donating groups selected from $-\text{OR}_{13}$, with R_{13} being H, a methyl group or an ethyl group;
- A is selected from



- R₄ is H or a methyl group;
- R₅ is H, -COOH or salt thereof, a C₁-C₃ alkoxy, a C₁-C₃ alkyl, a C₁-C₃ alkyl ester, a heteroaryl, a substituted or unsubstituted C₁-C₆ alkoxy or a sulfonic acid, a sulfonamide that may be singly substituted with a C₁-C₃ alkyl group or with a C₃-C₆ cyclic alkyl; and
- R₆ is H, -COOH or salt thereof, a C₁-C₃ alkoxy, a C₁-C₃ alkyl, a C₁-C₃ alkyl ester, a heteroaryl, a substituted or unsubstituted C₁-C₆ alkoxy or a sulfonic acid, a sulfonamide that may be singly substituted with a C₁-C₃ alkyl group or with a C₃-C₆ cyclic alkyl; and wherein
- R₇ and R₁₀ being independently from each other selected from
 - H, Cl, F or
 - C₁-C₃ alkanol, C₁-C₃ alkyl, C₁-C₃ haloalkyl, C₁-C₃ alkoxy, C₃-C₆ cycloalkyl, C₂-C₄ alkyl ether, 3- to 6-membered saturated heterocycle, a 3- to 6-membered heteroaryl moiety, wherein said moieties may be substituted or unsubstituted, wherein the substituents of said substituted moieties with respect to R₄ and R₇ are selected from 3- to 6-membered heteroaryls and aryls, or 3- to 6-membered saturated heterocycles, which may also be substituted with one or more hydroxyl, amine or C₁-C₃ alkoxy groups;
- n is 0, 1 or 2;
- Y is N, CH or C-R₁₁, with
- R₁₁ being a substituted or unsubstituted C₁-C₆ alkoxy, a heteroaryl, -O-(CH₂)_q-phenyl or -O-(CH₂)_q-heterocycle, with q being 0, 1 or 2.

In some embodiments, R₁ is a C₁-C₃ alkyl, cyclopropane, a C₁-C₃ haloalkyl, halocyclopropane or -NHR₈, wherein R₈ is a C₁-C₃ alkyl, cyclopropane, a C₁-C₃ haloalkyl or halocyclopropane.

In some embodiments, R₂ is H, F, a C₁-C₄ alkyl or a C₁-C₄ alkanol.

In some embodiments, R₃ is H, F, Cl, a C₁-C₆ alkyl, a C₁-C₃ haloalkyl, a C₁-C₄ alkoxy, a C₁-C₄ alkanol, a C₂-C₄ ether, a 3- to 6-membered saturated heterocycle, a 3- to 6-membered

heteroaryl, a benzyloxy or a substituted amine of the form -NHR_8 , wherein R_8 is a $\text{C}_1\text{-C}_3$ alkyl, cyclopropane, a $\text{C}_1\text{-C}_3$ haloalkyl or halocyclopropane.

In some embodiments, X is -C(=O)NH- , -NHC(=O)- , $\text{-C(=O)NR}_{12}\text{-}$, $\text{-NR}_{12}\text{C(=O)-}$, -NHC(=O)NH- , $\text{-N(R}_9\text{)C(=O)NH-}$, $\text{-NHC(=O)NR}_9\text{-}$, -C(=S)NH- , -NHC(=S)- , -NHC(=S)NH- , $\text{-N(R}_9\text{)C(=S)NH-}$, $\text{-NHC(=S)N(R}_9\text{)-}$, wherein R_9 is $\text{C}_1\text{-C}_3$ alkyl, $\text{C}_1\text{-C}_3$ alkoxy, $\text{C}_1\text{-C}_3$ haloalkyl, $\text{C}_1\text{-C}_3$ alkanol, $\text{C}_2\text{-C}_4$ ether, 3- to 6-membered heterocycle, or substituted or unsubstituted aryl, and wherein R_{12} is $\text{-(CH}_2\text{)}_r\text{-phenyl}$ with r being 0, 1 or 2 and said phenyl may be substituted with one or more electron donating groups, in particular one or more electron donating groups selected from -OR_{13} , with R_{13} being H, a methyl group or an ethyl group.

10 In some embodiments, X is -C(=O)NH- , -NHC(=O)- , $\text{-C(=O)NR}_{12}\text{-}$, $\text{-NR}_{12}\text{C(=O)-}$, $\text{-NR}_{12}\text{C(=O)-}$, -NHC(=O)NH- , $\text{-N(R}_9\text{)C(=O)NH-}$, $\text{-NHC(=O)NR}_9\text{-}$, -C(=S)NH- , -NHC(=S)- , -NHC(=S)NH- , $\text{-N(R}_9\text{)C(=S)NH-}$, $\text{-NHC(=S)N(R}_9\text{)-}$, $\text{-N-S(=O)}_2\text{-}$, $\text{-S(=O)}_2\text{-N-}$, in particular -C(=O)NH- , -NHC(=O)- , -NHC(=O)NH- , $\text{-N(R}_9\text{)C(=O)NH-}$, $\text{-NHC(=O)NR}_9\text{-}$, $\text{-N-S(=O)}_2\text{-}$, $\text{-S(=O)}_2\text{-N-}$, more particularly -C(=O)NH- or -NHC(=O)- , wherein R_9 is a $\text{C}_1\text{-C}_3$ alkyl, $\text{C}_1\text{-C}_3$ alkoxy, $\text{C}_1\text{-C}_3$ haloalkyl, $\text{C}_1\text{-C}_3$ alkanol, $\text{C}_2\text{-C}_4$ ether, 3- to 6-membered heterocycle, or substituted or unsubstituted aryl, and wherein R_{12} is $\text{-(CH}_2\text{)}_r\text{-phenyl}$ with r being 0, 1 or 2 and said phenyl is substituted with one or more electron donating groups, in particular one or more electron donating groups selected from -OR_{12} , with R_{12} being H, a methyl group or an ethyl group,

In some embodiments, R_4 is H or a methyl group.

20 In some embodiments, R_5 is H, -COOH or salt thereof, a $\text{C}_1\text{-C}_3$ alkoxyl, a $\text{C}_1\text{-C}_3$ alkyl, a $\text{C}_1\text{-C}_3$ alkyl ester, a heteroaryl, a substituted or unsubstituted $\text{C}_1\text{-C}_6$ alkoxyl or a sulfonic acid, an S-linked sulfonamide that may be singly substituted with a $\text{C}_1\text{-C}_3$ alkyl group or with a $\text{C}_3\text{-C}_6$ cyclic alkyl, and preferably R_5 is H-COOH or salt thereof, $\text{C}_1\text{-C}_3$ alkyl ester, in particular methylester, a tetrazole, which is preferably linked by its carbon moiety.

25 In some embodiments, R_5 is H, -COOH or salt thereof, a $\text{C}_1\text{-C}_3$ alkoxyl, a $\text{C}_1\text{-C}_3$ alkyl, a $\text{C}_1\text{-C}_3$ alkyl ester, a heteroaryl, a substituted or unsubstituted $\text{C}_1\text{-C}_6$ alkoxyl or a sulfonic acid, a sulfonamide that may be singly substituted with a $\text{C}_1\text{-C}_3$ alkyl group or with a $\text{C}_3\text{-C}_6$ cyclic alkyl.

In some embodiments, R_6 is H, -COOH or salt thereof, a $\text{C}_1\text{-C}_3$ alkoxyl, a $\text{C}_1\text{-C}_3$ alkyl, a $\text{C}_1\text{-C}_3$ alkyl ester, a substituted or unsubstituted heteroaryl, a substituted or unsubstituted $\text{C}_1\text{-C}_6$ alkoxyl or a sulfonic acid, an S-linked sulfonamide that may be singly substituted with a $\text{C}_1\text{-C}_3$ alkyl group or with a $\text{C}_3\text{-C}_6$ cyclic alkyl, and preferably R_5 is H-COOH or salt thereof, $\text{C}_1\text{-C}_3$ alkyl ester, in particular methylester, a tetrazole.

30 In some embodiments, R_6 is H, -COOH or salt thereof, a $\text{C}_1\text{-C}_3$ alkoxyl, a $\text{C}_1\text{-C}_3$ alkyl, a $\text{C}_1\text{-C}_3$ alkyl ester, a heteroaryl, a substituted or unsubstituted $\text{C}_1\text{-C}_6$ alkoxyl or a sulfonic acid, a

sulfonamide that may be singly substituted with a C₁-C₃ alkyl group or with a C₃-C₆ cyclic alkyl.

In some embodiments, R₇ and R₁₀ being independently from each other selected from

H, Br, Cl, F, NO₂ or substituted or unsubstituted C₁-C₃ alkanol, C₁-C₃ alkyl, C₁-C₃ haloalkyl, substituted or unsubstituted C₁-C₃ alkoxy, C₃-C₆ cycloalkyl, C₂-C₄ alkyl ether, 3- to 6-membered saturated heterocycle, a 3- to 6-membered heteroaryl moiety, wherein said moieties may be substituted or unsubstituted, wherein the substituents of said substituted moieties with respect to R₄ and R₇ are selected from 3- to 6-membered heteroaryls and aryls, or 3- to 6-membered saturated heterocycles, which may also be substituted with one or more hydroxyl, amine or C₁-C₃ alkoxy groups, wherein in particular R₇ is pyridine, furan, CH₂OH, CH₂OCH₃ or CH₂-O-tetrahydropyran, more particularly furan, and R₁₀ is H or methyl, more particularly H.

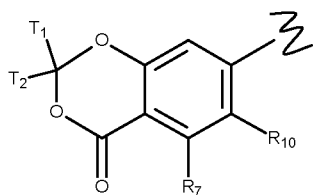
In some embodiments, R₇ and R₁₀ are independently from each other selected from H, Cl, F or C₁-C₃ alkanol, C₁-C₃ alkyl, C₁-C₃ haloalkyl, C₁-C₃ alkoxy, C₃-C₆ cycloalkyl, C₂-C₄ alkyl ether, 3- to 6-membered saturated heterocycle, a 3- to 6-membered heteroaryl moiety, wherein said moieties may be substituted or unsubstituted, wherein the substituents of said substituted moieties with respect to R₄ and R₇ are selected from 3- to 6-membered heteroaryls and aryls, or 3- to 6-membered saturated heterocycles, which may also be substituted with one or more hydroxyl, amine or C₁-C₃ alkoxy groups.

In some embodiments, n is 0, 1 or 2.

In some embodiments, Y is N, CH or C-R₁₁, with R₁₁ being a hydroxyl, a C₁-C₅ heteroalkyl, particularly a -(CH₂)_p-OT₃ or a -(CH₂)_p-N(T₃)(T₄), with T₃ and T₄ being independently from each other H or C₁-C₃ alkyl, and p is 0, 1, 2, 3, 4 or 5, a substituted or unsubstituted C₁-C₆ alkoxy, a heteroaryl, a saturated heterocycle, -O-(CH₂)_q-phenyl or -O-(CH₂)_q-heterocycle, with q being 0, 1 or 2, wherein the saturated heterocycle or the -O-(CH₂)_q-heterocycle are preferably C₃-C₆ heterocycles, more preferably C₅-C₆ heterocycles,

In some embodiments, Y is N, CH or C-R₁₁, with R₁₁ being a substituted or unsubstituted C₁-C₆ alkoxy, a heteroaryl, -O-(CH₂)_q-phenyl or -O-(CH₂)_q-heterocycle, with q being 0, 1 or 2.

In some embodiments, R⁶ and Y are connected forming a cyclic moiety of the formula 5'



(5'), with T₁ and T₂ being independently from each other H, CH₃ or CH₂CH₃, particularly H, and R₇ and R₁₀ having the same meaning as above.

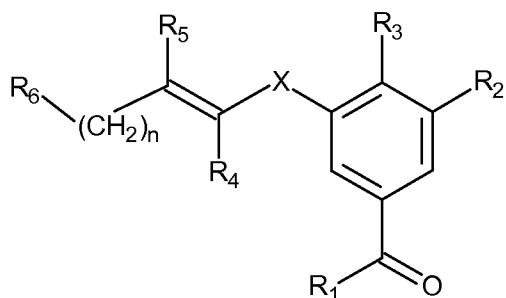
In some embodiments, the compound according to first aspect of the invention is characterized by a general formula (1), wherein R_1 is a methyl or $-NHR_8$ where R_8 is a methyl, in particular R_1 is a methyl; and/or R_2 is a hydrogen; and/or R_3 is H, F, a C_1 - C_6 alkyl or a C_1 - C_4 alkoxy, a benzyloxy or a morpholino, in particular R_3 is an ethoxy, a propoxy, a butoxy, cyclopropane, cyclopropylethoxy, benzyloxy or a morpholino, more particularly ethoxy; and/or R_4 is H or a methyl group; and/or R_5 is H, -COOH or salt thereof, a C_1 - C_3 alkoxyl, a C_1 - C_3 alkyl, a C_1 - C_3 alkyl ester, a heteroaryl, a substituted or unsubstituted C_1 - C_6 alkoxyl or a sulfonic acid, an S-linked sulfonamide that may be singly substituted with a C_1 - C_3 alkyl group or with a C_3 - C_6 cyclic alkyl, and preferably R_5 is H-COOH or salt thereof, C_1 - C_3 alkyl ester, in particular methylester a tetrazole, which is preferably linked by its carbon moiety, and/or R_6 is H, -COOH or salt thereof, a C_1 - C_3 alkoxyl, a C_1 - C_3 alkyl, a C_1 - C_3 alkyl ester, a substituted or unsubstituted heteroaryl, a substituted or unsubstituted C_1 - C_6 alkoxyl or a sulfonic acid, an S-linked sulfonamide that may be singly substituted with a C_1 - C_3 alkyl group or with a C_3 - C_6 cyclic alkyl, and preferably R_5 is H-COOH or salt thereof, C_1 - C_3 alkyl ester, in particular methylester, a tetrazole; and/or n is 0 or 1, in particular n is 0; and/or Y is N, CH or $C-R_{11}$ with R_{11} being a hydroxyl, a substituted or unsubstituted C_1 - C_6 alkoxyl, a saturated heterocycle,, $-O-(CH_2)_q$ -phenyl or $-O-(CH_2)_q$ -heterocycle, and q is 0, 1 or 2, wherein the saturated heterocycle or the $-O-(CH_2)_q$ -heterocycle are preferably C_3 - C_6 heterocycles, more preferably C_5 - C_6 heterocycles, wherein said phenyl and said heterocycle of R_{11} may optionally be substituted with one or more methoxy or hydroxy groups, wherein preferably Y is CH, $-O-(CH_2)_q$ -heterocycle or hydroxyl, and/or X is $-C(=O)NH-$, $-NHC(=O)-$, $-C(=O)NR_{12}-$, $-NR_{12}C(=O)-$, $-NR_{12}C(=O)-$, $-NHC(=O)NH-$, $-N(R_9)C(=O)NH-$, $-NHC(=O)NR_9-$, $-C(=S)NH-$, $-NHC(=S)-$, $-NHC(=S)NH-$, $-N(R_9)C(=S)NH-$, $-NHC(=S)N(R_9)-$, $-N-S(=O)_2-$, $-S(=O)_2-N-$, in particular $-C(=O)NH-$, $-NHC(=O)-$, $-NHC(=O)NH-$, $-N(R_9)C(=O)NH-$, $-NHC(=O)NR_9-$, more particularly $-C(=O)NH-$ or $-NHC(=O)-$, wherein R_9 is a C_1 - C_3 alkyl, C_1 - C_3 alkoxy, C_1 - C_3 haloalkyl, C_1 - C_3 alkanol, C_2 - C_4 ether, 3- to 6-membered heterocycle, or substituted or unsubstituted aryl, and wherein R_{12} is $-(CH_2)_r$ -phenyl with r being 0, 1 or 2 and said phenyl is substituted with one or more electron donating groups, in particular one or more electron donating groups selected from $-OR_{12}$, with R_{12} being H, a methyl group or an ethyl group, and/or R_7 and R_{10} being independently from each other selected from H, Br, Cl, F, NO_2 or substituted or unsubstituted C_1 - C_3 alkanol, C_1 - C_3 alkyl, C_1 - C_3 haloalkyl, substituted or unsubstituted C_1 - C_3 alkoxy, C_3 - C_6 cycloalkyl, C_2 - C_4 alkyl ether, 3- to 6-membered saturated heterocycle, a 3- to 6-membered heteroaryl moiety, wherein said moieties may be substituted or unsubstituted, wherein the substituents of said substituted moieties with respect to R_4 and R_7 are selected from 3- to 6-membered heteroaryls and aryls, or 3- to 6-membered saturated heterocycles, which may also be substituted with one or more hydroxyl, amine or C_1 - C_3 alkoxy groups, wherein in particular R_7 is pyridine, furan, CH_2OH , CH_2OCH_3

or CH₂-O-tetrahydropyran, more particularly furan, and R₁₀ is H or methyl, more particularly H, and wherein A has the same meaning as defined previously.

In some embodiments, the compound according to first aspect of the invention is characterized by a general formula (1), wherein R₁ is a methyl or -NHR₈ where R₈ is a methyl, in particular R₁ is a methyl; and/or R₂ is a hydrogen; and/or R₃ is H, F, a C₁-C₆ alkyl or a C₁-C₄ alkoxy, a benzyloxy or a morpholino, in particular R₃ is an ethoxy, a propoxy, a butoxy, cyclopropane, cyclopropylethoxy, benzyloxy or a morpholino, more particularly ethoxy; and/or R₄ is H or a methyl group; and/or R₅ is H, -COOH or salt thereof, a C₁-C₃ alkoxyl, a C₁-C₃ alkyl, a C₁-C₃ alkyl ester, a heteroaryl, a substituted or unsubstituted C₁-C₆ alkoxyl or a sulfonic acid, a sulfonamide that may be singly substituted with a C₁-C₃ alkyl group or with a C₃-C₆ cyclic alkyl, and preferably R₅ is H-COOH or salt thereof, C₁-C₃ alkyl ester, tetrazole, in particular methylester, and/or R₆ is H, -COOH or salt thereof, a C₁-C₃ alkoxyl, a C₁-C₃ alkyl, a C₁-C₃ alkyl ester, a heteroaryl, a substituted or unsubstituted C₁-C₆ alkoxyl or a sulfonic acid, a sulfonamide that may be singly substituted with a C₁-C₃ alkyl group or with a C₃-C₆ cyclic alkyl, and preferably R₅ is H-COOH or salt thereof, C₁-C₃ alkyl ester, tetrazole, in particular methylester; and/or n is 0 or 1, in particular n is 0; and/or Y is N, CH or C-R₁₁ with R₁₁ being a substituted or unsubstituted C₁-C₆ alkoxyl, a heteroaryl, in particular morpholino or piperazine bonded via a N atom, -O-(CH₂)_q-phenyl or -O-(CH₂)_q-heterocycle, morpholino, piperazine or pyridine and q is 0, 1 or 2, wherein said phenyl and said heterocycle of R₁₁ may optionally be substituted with one or more methoxy or hydroxy groups, wherein preferably Y is CH, and/or X is -C(=O)NH-, -NHC(=O)-, -C(=O)NR₁₂-, -NR₁₂C(=O)-, -NR₁₂C(=O)-, -NHC(=O)NH-, -N(R₉)C(=O)NH-, -NHC(=O)NR₉-, -C(=S)NH-, -NHC(=S)-, -NHC(=S)NH-, -N(R₉)C(=S)NH-, -NHC(=S)N(R₉)-, in particular -C(=O)NH-, -NHC(=O)-, -NHC(=O)NH-, -N(R₉)C(=O)NH-, -NHC(=O)NR₉-, more particularly -C(=O)NH- or -NHC(=O)-, wherein R₉ is a C₁-C₃ alkyl, C₁-C₃ alkoxy, C₁-C₃ haloalkyl, C₁-C₃ alkanol, C₂-C₄ ether, 3- to 6-membered heterocycle, or substituted or unsubstituted aryl, and wherein R₁₂ is -(CH₂)_r-phenyl with r being 0, 1 or 2 and said phenyl is substituted with one or more electron donating groups, in particular one or more electron donating groups selected from -OR₁₂, with R₁₂ being H, a methyl group or an ethyl group, and/or R₇ and R₁₀ being independently from each other selected from H, Cl, F or C₁-C₃ alkanol, C₁-C₃ alkyl, C₁-C₃ haloalkyl, C₁-C₃ alkoxy, C₃-C₆ cycloalkyl, C₂-C₄ alkyl ether, 3- to 6-membered saturated heterocycle, a 3- to 6-membered heteroaryl moiety, wherein said moieties may be substituted or unsubstituted, wherein the substituents of said substituted moieties with respect to R₄ and R₇ are selected from 3- to 6-membered heteroaryls and aryls, or 3- to 6-membered saturated heterocycles, which may also be substituted with one or more hydroxyl, amine or C₁-C₃ alkoxy groups, wherein in particular R₇ is pyridine, furan, CH₂OH, CH₂OCH₃ or CH₂-O-tetrahydropyran, more

particularly furan, and R_{10} is H or methyl, more particularly H, and wherein A has the same meaning as defined previously.

In some embodiments, the compound according to first aspect of the invention is characterized by a general formula (2),



(2), wherein

R_1 is a C_1 - C_3 alkyl, cyclopropane, a C_1 - C_3 haloalkyl, halocyclopropane or $-NHR_8$, wherein R_8 is a C_1 - C_3 alkyl, cyclopropane, a C_1 - C_3 haloalkyl or halocyclopropane;

R_2 is H, F, a C_1 - C_4 alkyl or a C_1 - C_4 alkanol;

R_3 is H, F, Cl, a C_1 - C_6 alkyl, a C_1 - C_3 haloalkyl, a C_1 - C_4 alkoxy, a C_1 - C_4 alkanol, a C_2 - C_4 ether, a 3- to 6-membered saturated heterocycle, a 3- to 6-membered heteroaryl, a benzyloxy or a substituted amine of the form $-NHR_8$, wherein R_8 is a C_1 - C_3 alkyl, cyclopropane, a C_1 - C_3 haloalkyl or halocyclopropane;

X is $-C(=O)NH-$, $-NHC(=O)-$, $-C(=O)NR_{12}-$, $-NR_{12}C(=O)-$, $-NR_{12}C(=O)-$, $-NHC(=O)NH-$, $-N(R_9)C(=O)NH-$, $-NHC(=O)NR_9-$, $-C(=S)NH-$, $-NHC(=S)-$, $-NHC(=S)NH-$, $-N(R_9)C(=S)NH-$, $-NHC(=S)N(R_9)-$, $-N-S(=O)_2-$, $-S(=O)_2-N-$, particularly X is $-C(=O)NH-$, $-NHC(=O)-$, $-C(=O)NR_{12}-$, $-NR_{12}C(=O)-$, $-NHC(=O)NH-$, $-N(R_9)C(=O)NH-$, $-NHC(=O)NR_9-$, $-C(=S)NH-$, $-NHC(=S)-$, $-NHC(=S)NH-$, $-N(R_9)C(=S)NH-$, $-NHC(=S)N(R_9)-$, wherein

R_9 is C_1 - C_3 alkyl, C_1 - C_3 alkoxy, C_1 - C_3 haloalkyl, C_1 - C_3 alkanol, C_2 - C_4 ether, 3- to 6-membered heterocycle, or substituted or unsubstituted aryl, and wherein

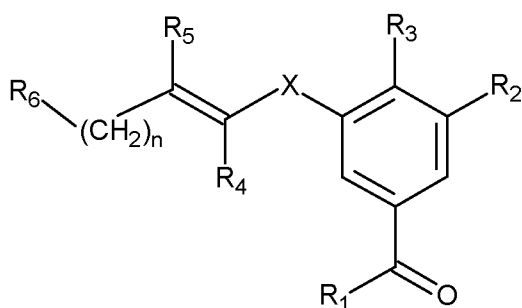
R_{12} is $-(CH_2)_r$ -phenyl with r being 0, 1 or 2 and said phenyl may be substituted with one or more electron donating groups, in particular one or more electron donating groups selected from $-OR_{13}$, with R_{13} being H, a methyl group or an ethyl group;

R_4 is H or a methyl group;

R_5 being H, $-COOH$ or salt thereof, a C_1 - C_3 alkoxy, a C_1 - C_3 alkyl, a C_1 - C_3 alkyl ester, a heteroaryl, a substituted or unsubstituted C_1 - C_6 alkoxy or a sulfonic acid, a sulfonamide, particularly an S-linked sulfonamide, that may be singly substituted with a C_1 - C_3 alkyl group or with a C_3 - C_6 cyclic alkyl; and

R_6 being H, -COOH or salt thereof, a C_1 - C_3 alkoxy, a C_1 - C_3 alkyl, a C_1 - C_3 alkyl ester, substituted or unsubstituted a heteroaryl, a substituted or unsubstituted C_1 - C_6 alkoxy or a sulfonic acid, a sulfonamide, particularly an S-linked sulfonamide, that may be singly substituted with a C_1 - C_3 alkyl group or with a C_3 - C_6 cyclic alkyl; and wherein n is 0, 1 or 2.

- 5 In some embodiments, the compound according to first aspect of the invention is characterized by a general formula (2),



(2), wherein

R_1 is a C_1 - C_3 alkyl, cyclopropane, a C_1 - C_3 haloalkyl, halocyclopropane or $-NHR_8$, wherein R_8 is a C_1 - C_3 alkyl, cyclopropane, a C_1 - C_3 haloalkyl or halocyclopropane;

- 10 R_2 is H, F, a C_1 - C_4 alkyl or a C_1 - C_4 alkanol;

R_3 is H, F, Cl, a C_1 - C_6 alkyl, a C_1 - C_3 haloalkyl, a C_1 - C_4 alkoxy, a C_1 - C_4 alkanol, a C_2 - C_4 ether, a 3- to 6-membered saturated heterocycle, a 3- to 6-membered heteroaryl, a benzyloxy or a substituted amine of the form $-NHR_8$, wherein R_8 is a C_1 - C_3 alkyl, cyclopropane, a C_1 - C_3 haloalkyl or halocyclopropane

- 15 X is $-C(=O)NH-$, $-NHC(=O)-$, $-C(=O)NR_{12}-$, $-NR_{12}C(=O)-$, $-NR_{12}C(=O)-$, $-NHC(=O)NH-$, $-N(R_9)C(=O)NH-$, $-NHC(=O)NR_9-$, $-C(=S)NH-$, $-NHC(=S)-$, $-NHC(=S)NH-$, $-N(R_9)C(=S)NH-$, $-NHC(=S)N(R_9)-$, wherein

R_9 is C_1 - C_3 alkyl, C_1 - C_3 alkoxy, C_1 - C_3 haloalkyl, C_1 - C_3 alkanol, C_2 - C_4 ether, 3- to 6-membered heterocycle, or substituted or unsubstituted aryl, and wherein

- 20 R_{12} is $-(CH_2)_r$ -phenyl with r being 0, 1 or 2 and said phenyl may be substituted with one or more electron donating groups, in particular one or more electron donating groups selected from $-OR_{13}$, with R_{13} being H, a methyl group or an ethyl group,

R_4 is H or a methyl group,

- 25 R_5 is H, -COOH or salt thereof, a C_1 - C_3 alkoxy, a C_1 - C_3 alkyl, a C_1 - C_3 alkyl ester, a heteroaryl, a substituted or unsubstituted C_1 - C_6 alkoxy or a sulfonic acid, a sulfonamide that may be singly substituted with a C_1 - C_3 alkyl group or with a C_3 - C_6 cyclic alkyl; and

R_6 is H, -COOH or salt thereof, a C_1 - C_3 alkoxy, a C_1 - C_3 alkyl, a C_1 - C_3 alkyl ester, a heteroaryl, a substituted or unsubstituted C_1 - C_6 alkoxy or a sulfonic acid, a sulfonamide that

may be singly substituted with a C₁-C₃ alkyl group or with a C₃-C₆ cyclic alkyl; and wherein n is 0, 1 or 2.

In some embodiments, R₁ is a C₁-C₃ alkyl, cyclopropane, a C₁-C₃ haloalkyl, halocyclopropane or -NHR₈, wherein R₈ is a C₁-C₃ alkyl, cyclopropane, a C₁-C₃ haloalkyl or halocyclopropane. In some embodiments, R₁ is a methyl or -NHR₈ where R₈ is a C₁-C₃ alkyl. In some embodiments, R₁ is a methyl or -NHR₈ where R₈ is a methyl, in particular R₁ is a methyl.

In some embodiments, R₂ is H, F, a C₁-C₄ alkyl or a C₁-C₄ alkanol. In some embodiments, R₂ is a hydrogen, a methyl or a C₁-C₄ alkanol. In some embodiments, R₂ is a hydrogen.

In some embodiments, R₃ is H, F, Cl, a C₁-C₆ alkyl, a C₁-C₃ haloalkyl, a C₁-C₄ alkoxy, a C₁-C₄ alkanol, a C₂-C₄ ether, a 3- to 6-membered saturated heterocycle, a 3- to 6-membered heteroaryl, a benzyloxy or a substituted amine of the form -NHR₈, wherein R₈ is a C₁-C₃ alkyl, cyclopropane, a C₁-C₃ haloalkyl or halocyclopropane. In some embodiments, R₃ is H, F, a C₁-C₆ alkyl or a C₁-C₄ alkoxy, a benzyloxy or a morpholino, in particular R₃ is an ethoxy, a propoxy, a butoxy, cyclopropane, cyclopropylethoxy, benzyloxy or a morpholino, more particularly ethoxy. In some embodiments, R₃ is H, F, a C₁-C₆ alkyl or a C₁-C₄ alkoxy, in particular R₃ is an ethoxy.

In some embodiments, X is -C(=O)NH-, -NHC(=O)-, -C(=O)NR₁₂-, -NR₁₂C(=O)-, -NR₁₂C(=O)-, -NHC(=O)NH-, -N(R₉)C(=O)NH-, -NHC(=O)NR₉-, -C(=S)NH-, -NHC(=S)-, -NHC(=S)NH-, -N(R₉)C(=S)NH-, -NHC(=S)N(R₉)-, wherein R₉ is C₁-C₃ alkyl, C₁-C₃ alkoxy, C₁-C₃ haloalkyl, C₁-C₃ alkanol, C₂-C₄ ether, 3- to 6-membered heterocycle, or substituted or unsubstituted aryl, and wherein R₁₂ is -(CH₂)_r-phenyl with r being 0, 1 or 2 and said phenyl may be substituted with one or more electron donating groups, in particular one or more electron donating groups selected from -OR₁₃, with R₁₃ being H, a methyl group or an ethyl group.

In some embodiments, X is -C(=O)NH-, -NHC(=O)-, -NHC(=O)NH-, -N(R₉)C(=O)NH-, -NHC(=O)NR₉-, -C(=S)NH-, -NHC(=S)-, -NHC(=S)NH-, -N(R₉)C(=S)NH-, -NHC(=S)N(R₉)-, in particular -C(=O)NH-, -NHC(=O)-, -NHC(=O)NH-, -N(R₉)C(=O)NH-, -NHC(=O)NR₉-, more particularly -C(=O)NH- or -NHC(=O)-, wherein R₉ is a C₁-C₃ alkyl, C₁-C₃ alkoxy, C₁-C₃ haloalkyl, C₁-C₃ alkanol, C₂-C₄ ether, 3- to 6-membered heterocycle, or substituted or unsubstituted aryl.

In some embodiments, X is -C(=O)NH-, -NHC(=O)-, -NHC(=O)NH-, -N(R₉)C(=O)NH-, -NHC(=O)NR₉, in particular X is -C(=O)NH- or -NHC(=O)-wherein R₉ is a C₁-C₃ alkyl, C₁-C₃ alkoxy, C₁-C₃ haloalkyl, C₁-C₃ alkanol, C₂-C₄ ether, 3- to 6-membered heterocycle, or substituted or unsubstituted aryl, wherein in particular R₉ is a C₁-C₃ alkoxy, C₁-C₃ haloalkyl,

C₁-C₃ alkanol, C₂-C₄ ether, 3- to 6-membered heterocycle, or substituted or unsubstituted aryl.

In some embodiments, R₄ is H or a methyl group.

5 In some embodiments, R₅ is H, -COOH or salt thereof, a C₁-C₃ alkoxy, a C₁-C₃ alkyl, a C₁-C₃ alkyl ester, a heteroaryl, a substituted or unsubstituted C₁-C₆ alkoxy or a sulfonic acid, a sulfonamide, particularly an S-linked sulfonamide, that may be singly substituted with a C₁-C₃ alkyl group or with a C₃-C₆ cyclic alkyl.

10 In some embodiments, R₅ is H, -COOH or salt thereof, C₁-C₃ alkyl ester, in particular methylester, tetrazole, which is preferably linked by its carbon moiety, more particularly R₅ is H.

In some embodiments, R₅ is H, -COOH or salt thereof, a C₁-C₃ alkoxy, a C₁-C₃ alkyl, a C₁-C₃ alkyl ester, a heteroaryl, a substituted or unsubstituted C₁-C₆ alkoxy or a sulfonic acid, a sulfonamide that may be singly substituted with a C₁-C₃ alkyl group or with a C₃-C₆ cyclic alkyl. In some embodiments, R₅ is H-COOH or salt thereof, tetrazole, particularly a tetrazole
15 bonded to the parent compound at the N1 position, C₁-C₃ alkyl ester, in particular methylester.

In some embodiments, R₆ is H, -COOH or salt thereof, a C₁-C₃ alkoxy, a C₁-C₃ alkyl, a C₁-C₃ alkyl ester, substituted or unsubstituted a heteroaryl, a substituted or unsubstituted C₁-C₆ alkoxy or a sulfonic acid, a sulfonamide, particularly an S-linked sulfonamide, that may be
20 singly substituted with a C₁-C₃ alkyl group or with a C₃-C₆ cyclic alkyl.

In some embodiments, R₆ is H, -COOH or salt thereof, C₁-C₃ alkyl ester, in particular methylester, a substituted or unsubstituted heteroaryl, a tetrazole, which is preferably linked by its carbon moiety.

25 In some embodiments, R₆ is H, -COOH or salt thereof, a C₁-C₃ alkoxy, a C₁-C₃ alkyl, a C₁-C₃ alkyl ester, a heteroaryl, a substituted or unsubstituted C₁-C₆ alkoxy or a sulfonic acid, a sulfonamide that may be singly substituted with a C₁-C₃ alkyl group or with a C₃-C₆ cyclic alkyl. In some embodiments, R₆ is H-COOH or salt thereof, tetrazole, particularly a tetrazole bonded to the parent compound at the N1 position, C₁-C₃ alkyl ester, in particular methylester.

30 In some embodiments, n is 0, 1 or 2. In some embodiments, n is 0.

In some embodiments, the compound according to first aspect of the invention is characterized by a general formula (2), wherein R₁ is a methyl or -NHR₈ where R₈ is a C₁-C₃ alkyl; and/or R₂ is a hydrogen, a methyl or a C₁-C₄ alkanol; and/or R₃ is H, F, a C₁-C₆ alkyl or a C₁-C₄ alkoxy, a benzyloxy or a morpholino, in particular R₃ is an ethoxy, a propoxy, a

butoxy, cyclopropane, cyclopropylethoxy, benzyloxy or a morpholino, more particularly ethoxy; and/or R_4 is H or a methyl group; and/or R_5 is H, $-\text{COOH}$ or salt thereof, $\text{C}_1\text{-C}_3$ alkyl ester, in particular methylester; or tetrazole, which is preferably linked by its carbon moiety, more particularly R_5 is H and/or R_6 is H, $-\text{COOH}$ or salt thereof, $\text{C}_1\text{-C}_3$ alkyl ester, in particular methylester; a substituted or unsubstituted heteroaryl, tetrazole, which is preferably linked by its carbon moiety, and/or n is 0, 1 or 2; and/or X is $-\text{C}(=\text{O})\text{NH}-$, $-\text{NHC}(=\text{O})-$, $-\text{NHC}(=\text{O})\text{NH}-$, $-\text{N}(\text{R}_9)\text{C}(=\text{O})\text{NH}-$, $-\text{NHC}(=\text{O})\text{NR}_9-$, $-\text{C}(=\text{S})\text{NH}-$, $-\text{NHC}(=\text{S})-$, $-\text{NHC}(=\text{S})\text{NH}-$, $-\text{N}(\text{R}_9)\text{C}(=\text{S})\text{NH}-$, $-\text{NHC}(=\text{S})\text{N}(\text{R}_9)-$, in particular $-\text{C}(=\text{O})\text{NH}-$, $-\text{NHC}(=\text{O})-$, $-\text{NHC}(=\text{O})\text{NH}-$, $-\text{N}(\text{R}_9)\text{C}(=\text{O})\text{NH}-$, $-\text{NHC}(=\text{O})\text{NR}_9-$, more particularly $-\text{C}(=\text{O})\text{NH}-$ or $-\text{NHC}(=\text{O})-$, wherein R_9 is a $\text{C}_1\text{-C}_3$ alkyl, $\text{C}_1\text{-C}_3$ alkoxy, $\text{C}_1\text{-C}_3$ haloalkyl, $\text{C}_1\text{-C}_3$ alkanol, $\text{C}_2\text{-C}_4$ ether, 3- to 6-membered heterocycle, or substituted or unsubstituted aryl.

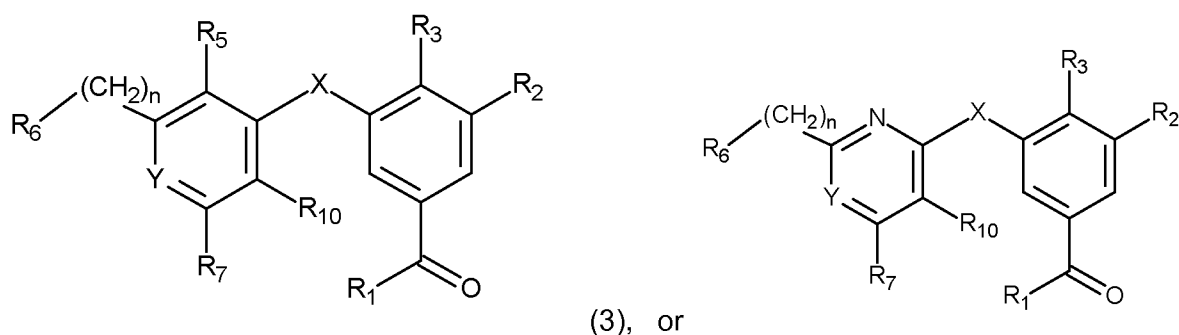
In some embodiments, the compound according to first aspect of the invention is characterized by a general formula (2), wherein R_1 is a methyl or $-\text{NHR}_8$ where R_8 is a $\text{C}_1\text{-C}_3$ alkyl; R_2 is a hydrogen, a methyl or a $\text{C}_1\text{-C}_4$ alkanol; R_3 is H, F, a $\text{C}_1\text{-C}_6$ alkyl or a $\text{C}_1\text{-C}_4$ alkoxy, a benzyloxy or a morpholino, in particular R_3 is an ethoxy, a propoxy, a butoxy, cyclopropane, cyclopropylethoxy, benzyloxy or a morpholino, more particularly ethoxy; R_4 is H or a methyl group; R_5 is H- COOH or salt thereof, tetrazole, particularly a tetrazole bonded to the parent compound at the N1 position, $\text{C}_1\text{-C}_3$ alkyl ester, in particular methylester; R_6 is H- COOH or salt thereof, tetrazole, particularly a tetrazole bonded to the parent compound at the N1 position, $\text{C}_1\text{-C}_3$ alkyl ester, in particular methylester; n is 0, 1 or 2; X is $-\text{C}(=\text{O})\text{NH}-$, $-\text{NHC}(=\text{O})-$, $-\text{NHC}(=\text{O})\text{NH}-$, $-\text{N}(\text{R}_9)\text{C}(=\text{O})\text{NH}-$, $-\text{NHC}(=\text{O})\text{NR}_9-$, $-\text{C}(=\text{S})\text{NH}-$, $-\text{NHC}(=\text{S})-$, $-\text{NHC}(=\text{S})\text{NH}-$, $-\text{N}(\text{R}_9)\text{C}(=\text{S})\text{NH}-$, $-\text{NHC}(=\text{S})\text{N}(\text{R}_9)-$, in particular $-\text{C}(=\text{O})\text{NH}-$, $-\text{NHC}(=\text{O})-$, $-\text{NHC}(=\text{O})\text{NH}-$, $-\text{N}(\text{R}_9)\text{C}(=\text{O})\text{NH}-$, $-\text{NHC}(=\text{O})\text{NR}_9-$, more particularly $-\text{C}(=\text{O})\text{NH}-$ or $-\text{NHC}(=\text{O})-$, wherein R_9 is a $\text{C}_1\text{-C}_3$ alkyl, $\text{C}_1\text{-C}_3$ alkoxy, $\text{C}_1\text{-C}_3$ haloalkyl, $\text{C}_1\text{-C}_3$ alkanol, $\text{C}_2\text{-C}_4$ ether, 3- to 6-membered heterocycle, or substituted or unsubstituted aryl.

In some embodiments, the compound according to first aspect of the invention is characterized by a general formula (2), wherein R_1 is a methyl or $-\text{NHR}_8$ where R_8 is a methyl, in particular R_1 is a methyl; and/or R_2 is a hydrogen; and/or R_3 is H, F, a $\text{C}_1\text{-C}_6$ alkyl or a $\text{C}_1\text{-C}_4$ alkoxy, in particular R_3 is an ethoxy; and/or R_4 is H or a methyl group; and/or R_5 is H, $-\text{COOH}$ or salt thereof, $\text{C}_1\text{-C}_3$ alkyl ester, in particular methylester, a tetrazole, which is preferably linked by its carbon moiety, more particularly R_5 is H; and/or R_6 is H, $-\text{COOH}$ or salt thereof, $\text{C}_1\text{-C}_3$ alkyl ester, in particular methylester, a substituted or unsubstituted heteroaryl, tetrazole, which is preferably linked by its carbon moiety; and/or n is 0; and/or X is $-\text{C}(=\text{O})\text{NH}-$, $-\text{NHC}(=\text{O})-$, $-\text{NHC}(=\text{O})\text{NH}-$, $-\text{N}(\text{R}_9)\text{C}(=\text{O})\text{NH}-$, $-\text{NHC}(=\text{O})\text{NR}_9-$, in particular X is $-\text{C}(=\text{O})\text{NH}-$ or $-\text{NHC}(=\text{O})-$ —wherein R_9 is a $\text{C}_1\text{-C}_3$ alkyl, $\text{C}_1\text{-C}_3$ alkoxy, $\text{C}_1\text{-C}_3$ haloalkyl, $\text{C}_1\text{-C}_3$ alkanol, $\text{C}_2\text{-C}_4$ ether, 3- to 6-membered heterocycle, or substituted or unsubstituted aryl,

wherein in particular R_9 is a C_1 - C_3 alkoxy, C_1 - C_3 haloalkyl, C_1 - C_3 alkanol, C_2 - C_4 ether, 3- to 6-membered heterocycle, or substituted or unsubstituted aryl.

In some embodiments, the compound according to first aspect of the invention is characterized by a general formula (2), wherein R_1 is a methyl or $-NHR_8$ where R_8 is a methyl, in particular R_1 is a methyl; R_2 is a hydrogen; and/or R_3 is H, F, a C_1 - C_6 alkyl or a C_1 - C_4 alkoxy, in particular R_3 is an ethoxy; R_4 is H or a methyl group; R_5 is H, $-\text{COOH}$ or salt thereof, C_1 - C_3 alkyl ester, tetrazole, in particular methylester; R_6 is H, $-\text{COOH}$ or salt thereof, C_1 - C_3 alkyl ester, tetrazole, in particular methylester; n is 0; X is $-\text{C}(=\text{O})\text{NH}-$, $-\text{NHC}(=\text{O})-$, $-\text{NHC}(=\text{O})\text{NH}-$, $-\text{N}(\text{R}_9)\text{C}(=\text{O})\text{NH}-$, $-\text{NHC}(=\text{O})\text{NR}_9$, in particular X is $-\text{C}(=\text{O})\text{NH}-$ or $-\text{NHC}(=\text{O})-$, wherein R_9 is a C_1 - C_3 alkyl, C_1 - C_3 alkoxy, C_1 - C_3 haloalkyl, C_1 - C_3 alkanol, C_2 - C_4 ether, 3- to 6-membered heterocycle, or substituted or unsubstituted aryl, wherein in particular R_9 is a C_1 - C_3 alkoxy, C_1 - C_3 haloalkyl, C_1 - C_3 alkanol, C_2 - C_4 ether, 3- to 6-membered heterocycle, or substituted or unsubstituted aryl.

In some embodiments, the compound according to first aspect of the invention is characterized general formula (3) or (4),



(4), particularly of formula (3) wherein

R_1 is a C_1 - C_3 alkyl, cyclopropane, a C_1 - C_3 haloalkyl, halocyclopropane or $-NHR_8$, wherein R_8 is a C_1 - C_3 alkyl, cyclopropane, a C_1 - C_3 haloalkyl or halocyclopropane;

R_2 is H, F, a C_1 - C_4 alkyl or a C_1 - C_4 alkanol;

R_3 is H, F, Cl, a C_1 - C_6 alkyl, a C_1 - C_3 haloalkyl, a C_1 - C_4 alkoxy, a C_1 - C_4 alkanol, a C_2 - C_4 ether, a 3- to 6-membered saturated heterocycle, a 3- to 6-membered heteroaryl, a benzyloxy or a substituted amine of the form $-NHR_8$, wherein R_8 is a C_1 - C_3 alkyl, cyclopropane, a C_1 - C_3 haloalkyl or halocyclopropane;

X is $-\text{C}(=\text{O})\text{NH}-$, $-\text{NHC}(=\text{O})-$, $-\text{C}(=\text{O})\text{NR}_{12}-$, $-\text{NR}_{12}\text{C}(=\text{O})-$, $-\text{NR}_{12}\text{C}(=\text{O})-$, $-\text{NHC}(=\text{O})\text{NH}-$, $-\text{N}(\text{R}_9)\text{C}(=\text{O})\text{NH}-$, $-\text{NHC}(=\text{O})\text{NR}_9-$, $-\text{C}(=\text{S})\text{NH}-$, $-\text{NHC}(=\text{S})-$, $-\text{NHC}(=\text{S})\text{NH}-$, $-\text{N}(\text{R}_9)\text{C}(=\text{S})\text{NH}-$, $-\text{NHC}(=\text{S})\text{N}(\text{R}_9)-$, $-\text{N}-\text{S}(=\text{O})_2-$, $-\text{S}(=\text{O})_2-\text{N}-$, wherein R_9 is C_1 - C_3 alkyl, C_1 - C_3 alkoxy, C_1 - C_3 haloalkyl, C_1 - C_3 alkanol, C_2 - C_4 ether, 3- to 6-membered heterocycle, or substituted or unsubstituted aryl, and wherein R_{12} is $-(\text{CH}_2)_r$ -phenyl with r being 0, 1 or 2 and said phenyl

may be substituted with one or more electron donating groups, in particular one or more electron donating groups selected from $-OR_{13}$, with R_{13} being H, a methyl group or an ethyl group;

R_5 being H, $-COOH$ or salt thereof, a C_1-C_3 alkoxy, a C_1-C_3 alkyl, a C_1-C_3 alkyl ester, a heteroaryl, a substituted or unsubstituted C_1-C_6 alkoxy or a sulfonic acid, a sulfonamide, particularly an S-linked sulfonamide, that may be singly substituted with a C_1-C_3 alkyl group or with a C_3-C_6 cyclic alkyl; and

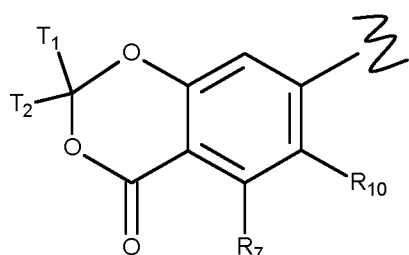
R_6 being H, $-COOH$ or salt thereof, a C_1-C_3 alkoxy, a C_1-C_3 alkyl, a C_1-C_3 alkyl ester, a substituted or unsubstituted heteroaryl, a substituted or unsubstituted C_1-C_6 alkoxy or a sulfonic acid, a sulfonamide, particularly an S-linked sulfonamide, that may be singly substituted with a C_1-C_3 alkyl group or with a C_3-C_6 cyclic alkyl; and wherein

R_7 and R_{10} being independently from each other selected from H, Br, Cl, F, NO_2 or substituted or unsubstituted C_1-C_3 alkanol, C_1-C_3 alkyl, C_1-C_3 haloalkyl, substituted or unsubstituted C_1-C_3 alkoxy, C_3-C_6 cycloalkyl, C_2-C_4 alkyl ether, 3- to 6-membered saturated heterocycle, a 3- to 6-membered heteroaryl moiety, wherein said moieties may be substituted or unsubstituted, wherein the substituents of said substituted moieties with respect to R_4 and R_7 are selected from 3- to 6-membered heteroaryls and aryls, or 3- to 6-membered saturated heterocycles, which may also be substituted with one or more hydroxyl, amine or C_1-C_3 alkoxy groups;

n is 0, 1 or 2;

Y is N, CH or $C-R_{11}$, with R_{11} being a hydroxyl, a C_1-C_5 heteroalkyl, particularly a $-(CH_2)_p-OT_3$ or a $-(CH_2)_p-N(T_3)(T_4)$, with T_3 and T_4 being independently from each other H or C_1-C_3 alkyl, and p is 0, 1, 2, 3, 4 or 5, a substituted or unsubstituted C_1-C_6 alkoxy, a heteroaryl, a saturated heterocycle, $-O-(CH_2)_q$ -phenyl or $-O-(CH_2)_q$ -heterocycle, with q being 0, 1 or 2, wherein the saturated heterocycle or the $-O-(CH_2)_q$ -heterocycle are preferably C_3-C_6 heterocycles, more preferably C_5-C_6 heterocycles, or

wherein R^6 and Y are connected forming a cyclic moiety of the formula 5'



(5'), with T_1 and T_2 being independently from each other H,

CH_3 or CH_2CH_3 , particularly H, and R_7 and R_{10} having the same meaning as above.

- In some embodiments, the compound according to first aspect of the invention is characterized by a general formula (3), wherein R_1 is a C_1 - C_3 alkyl, cyclopropane, a C_1 - C_3 haloalkyl, halocyclopropane or $-NHR_8$, wherein R_8 is a C_1 - C_3 alkyl, cyclopropane, a C_1 - C_3 haloalkyl or halocyclopropane; R_2 is H, F, a C_1 - C_4 alkyl or a C_1 - C_4 alkanol; R_3 is H, F, Cl, a C_1 - C_6 alkyl, a C_1 - C_3 haloalkyl, a C_1 - C_4 alkoxy, a C_1 - C_4 alkanol, a C_2 - C_4 ether, a 3- to 6-membered saturated heterocycle, a 3- to 6-membered heteroaryl, a benzyloxy or a substituted amine of the form $-NHR_8$, wherein R_8 is a C_1 - C_3 alkyl, cyclopropane, a C_1 - C_3 haloalkyl or halocyclopropane X is $-C(=O)NH-$, $-NHC(=O)-$, $-C(=O)NR_{12}-$, $-NR_{12}C(=O)-$, $-NR_{12}C(=O)-$, $-NHC(=O)NH-$, $-N(R_9)C(=O)NH-$, $-NHC(=O)NR_9-$, $-C(=S)NH-$, $-NHC(=S)-$, $-NHC(=S)NH-$, $-N(R_9)C(=S)NH-$, $-NHC(=S)N(R_9)-$, wherein R_9 is C_1 - C_3 alkyl, C_1 - C_3 alkoxy, C_1 - C_3 haloalkyl, C_1 - C_3 alkanol, C_2 - C_4 ether, 3- to 6-membered heterocycle, or substituted or unsubstituted aryl, and wherein R_{12} is $-(CH_2)_r$ -phenyl with r being 0, 1 or 2 and said phenyl may be substituted with one or more electron donating groups, in particular one or more electron donating groups selected from $-OR_{13}$, with R_{13} being H, a methyl group or an ethyl group; R_5 being H, $-COOH$ or salt thereof, a C_1 - C_3 alkoxy, a C_1 - C_3 alkyl, a C_1 - C_3 alkyl ester, a heteroaryl, a substituted or unsubstituted C_1 - C_6 alkoxy or a sulfonic acid, a sulfonamide that may be singly substituted with a C_1 - C_3 alkyl group or with a C_3 - C_6 cyclic alkyl; and R_6 being H, $-COOH$ or salt thereof, a C_1 - C_3 alkoxy, a C_1 - C_3 alkyl, a C_1 - C_3 alkyl ester, a heteroaryl, a substituted or unsubstituted C_1 - C_6 alkoxy or a sulfonic acid, a sulfonamide that may be singly substituted with a C_1 - C_3 alkyl group or with a C_3 - C_6 cyclic alkyl; and wherein R_7 and R_{10} being independently from each other selected from H, Cl, F or C_1 - C_3 alkanol, C_1 - C_3 alkyl, C_1 - C_3 haloalkyl, C_1 - C_3 alkoxy, C_3 - C_6 cycloalkyl, C_2 - C_4 alkyl ether, 3- to 6-membered saturated heterocycle, a 3- to 6-membered heteroaryl moiety, wherein said moieties may be substituted or unsubstituted, wherein the substituents of said substituted moieties with respect to R_4 and R_7 are selected from 3- to 6-membered heteroaryls and aryls, or 3- to 6-membered saturated heterocycles, which may also be substituted with one or more hydroxyl, amine or C_1 - C_3 alkoxy groups; n is 0, 1 or 2; Y being N, CH or $C-R_{11}$, with R_{11} being a substituted or unsubstituted C_1 - C_6 alkoxy, a heteroaryl, $-O-(CH_2)_q$ -phenyl or $-O-(CH_2)_q$ -heterocycle, with q being 0, 1 or 2.
- In some embodiments, R_1 is a C_1 - C_3 alkyl, cyclopropane, a C_1 - C_3 haloalkyl, halocyclopropane or $-NHR_8$, wherein R_8 is a C_1 - C_3 alkyl, cyclopropane, a C_1 - C_3 haloalkyl or halocyclopropane. In some embodiments, R_1 is a methyl or $-NHR_8$ where R_8 is a C_1 - C_3 . In some embodiments, R_1 is a methyl or $-NHR_8$ where R_8 is a methyl, in particular R_1 is a methyl.
- In some embodiments, R_2 is H, F, a C_1 - C_4 alkyl or a C_1 - C_4 alkanol. In some embodiments, R_2 is a hydrogen, a methyl or a C_1 - C_4 alkanol. In some embodiments, R_2 is a hydrogen.

In some embodiments, R_3 is H, F, Cl, a C_1 - C_6 alkyl, a C_1 - C_3 haloalkyl, a C_1 - C_4 alkoxy, a C_1 - C_4 alkanol, a C_2 - C_4 ether, a 3- to 6-membered saturated heterocycle, a 3- to 6-membered heteroaryl, a benzyloxy or a substituted amine of the form $-NHR_8$, wherein R_8 is a C_1 - C_3 alkyl, cyclopropane, a C_1 - C_3 haloalkyl or halocyclopropane. In some embodiments, R_3 is H, F, a C_1 - C_6 alkyl or a C_1 - C_4 alkoxy, a benzyloxy or a morpholino, in particular R_3 is an ethoxy, a propoxy, a butoxy, cyclopropane, cyclopropylethoxy, benzyloxy or a morpholino, more particularly ethoxy. In some embodiments, R_3 is ethoxy, a propoxy, a butoxy, cyclopropane, cyclopropylethoxy, benzyloxy or a morpholino, more particularly ethoxy.

In some embodiments, X is $-C(=O)NH-$, $-NHC(=O)-$, $-NHC(=O)NH-$, $-N(R_9)C(=O)NH-$, $-NHC(=O)NR_9-$, $-C(=S)NH-$, $-NHC(=S)-$, $-NHC(=S)NH-$, $-N(R_9)C(=S)NH-$, $-NHC(=S)N(R_9)-$, $-N-S(=O)_2-$, $-S(=O)_2-N-$, in particular $-C(=O)NH-$, $-NHC(=O)-$, $-NHC(=O)NH-$, $-N(R_9)C(=O)NH-$, $-NHC(=O)NR_9-$, more particularly $-C(=O)NH-$ or $-NHC(=O)-$, wherein R_9 is a C_1 - C_3 alkyl, C_1 - C_3 alkoxy, C_1 - C_3 haloalkyl, C_1 - C_3 alkanol, C_2 - C_4 ether, 3- to 6-membered heterocycle, or substituted or unsubstituted aryl.

In some embodiments, X is $-C(=O)NH-$, $-NHC(=O)-$, $-C(=O)NR_{12}-$, $-NR_{12}C(=O)-$, $-NR_{12}C(=O)-$, $-NHC(=O)NH-$, $-N(R_9)C(=O)NH-$, $-NHC(=O)NR_9-$, $-C(=S)NH-$, $-NHC(=S)-$, $-NHC(=S)NH-$, $-N(R_9)C(=S)NH-$, $-NHC(=S)N(R_9)-$, wherein R_9 is C_1 - C_3 alkyl, C_1 - C_3 alkoxy, C_1 - C_3 haloalkyl, C_1 - C_3 alkanol, C_2 - C_4 ether, 3- to 6-membered heterocycle, or substituted or unsubstituted aryl, and wherein R_{12} is $-(CH_2)_r$ -phenyl with r being 0, 1 or 2 and said phenyl may be substituted with one or more electron donating groups, in particular one or more electron donating groups selected from $-OR_{13}$, with R_{13} being H, a methyl group or an ethyl group.

In some embodiments, X is $-C(=O)NH-$, $-NHC(=O)-$, $-NHC(=O)NH-$, $-N(R_9)C(=O)NH-$, $-NHC(=O)NR_9-$, $-C(=S)NH-$, $-NHC(=S)-$, $-NHC(=S)NH-$, $-N(R_9)C(=S)NH-$, $-NHC(=S)N(R_9)-$, in particular $-C(=O)NH-$, $-NHC(=O)-$, $-NHC(=O)NH-$, $-N(R_9)C(=O)NH-$, $-NHC(=O)NR_9-$, more particularly $-C(=O)NH-$ or $-NHC(=O)-$, wherein R_9 is a C_1 - C_3 alkyl, C_1 - C_3 alkoxy, C_1 - C_3 haloalkyl, C_1 - C_3 alkanol, C_2 - C_4 ether, 3- to 6-membered heterocycle, or substituted or unsubstituted aryl.

In some embodiments, X is $C(=O)NH-$, $-NHC(=O)-$, $-NHC(=O)NH-$, $-N(R_9)C(=O)NH-$, $-NHC(=O)NR_9$, in particular X is $-C(=O)NH-$ or $-NHC(=O)-$, wherein R_9 is a C_1 - C_3 alkyl, C_1 - C_3 alkoxy, C_1 - C_3 haloalkyl, C_1 - C_3 alkanol, C_2 - C_4 ether, 3- to 6-membered heterocycle, or substituted or unsubstituted aryl, wherein in particular R_9 is a C_1 - C_3 alkoxy, C_1 - C_3 haloalkyl, C_1 - C_3 alkanol, C_2 - C_4 ether, 3- to 6-membered heterocycle, or substituted or unsubstituted aryl.

In some embodiments, R_5 is H, $-COOH$ or salt thereof, a C_1 - C_3 alkoxyl, a C_1 - C_3 alkyl, a C_1 - C_3 alkyl ester, a heteroaryl, a substituted or unsubstituted C_1 - C_6 alkoxyl or a sulfonic acid, an S-

linked sulfonamide that may be singly substituted with a C₁-C₃ alkyl group or with a C₃-C₆ cyclic alkyl.

In some embodiments, R₅ is H, -COOH or salt thereof, a C₁-C₃ alkoxy, a C₁-C₃ alkyl, a C₁-C₃ alkyl ester, a heteroaryl, a substituted or unsubstituted C₁-C₆ alkoxy or a sulfonic acid, a sulfonamide that may be singly substituted with a C₁-C₃ alkyl group or with a C₃-C₆ cyclic alkyl. In some embodiments, R₅ is H-COOH or salt thereof, tetrazole, particularly a tetrazole bonded to the parent compound at the N1 position, C₁-C₃ alkyl ester, in particular methylester.

In some embodiments, R₆ is H, -COOH or salt thereof, a C₁-C₃ alkoxy, a C₁-C₃ alkyl, a C₁-C₃ alkyl ester, a substituted or unsubstituted heteroaryl, a substituted or unsubstituted C₁-C₆ alkoxy or a sulfonic acid, an S-linked sulfonamide that may be singly substituted with a C₁-C₃ alkyl group or with a C₃-C₆ cyclic alkyl.

In some embodiments, R₆ is H, -COOH or salt thereof, a C₁-C₃ alkoxy, a C₁-C₃ alkyl, a C₁-C₃ alkyl ester, a heteroaryl, a substituted or unsubstituted C₁-C₆ alkoxy or a sulfonic acid, a sulfonamide that may be singly substituted with a C₁-C₃ alkyl group or with a C₃-C₆ cyclic alkyl. In some embodiments, R₆ is H-COOH or salt thereof, tetrazole, particularly a tetrazole bonded to the parent compound at the N1 position, C₁-C₃ alkyl ester, in particular methylester.

In some embodiments, n is 0, 1 or 2. In some embodiments, n is 0.

In some embodiments, R₇ and R₁₀ being independently from each other selected from H, Cl, F or C₁-C₃ alkanol, C₁-C₃ alkyl, C₁-C₃ haloalkyl, C₁-C₃ alkoxy, C₃-C₆ cycloalkyl, C₂-C₄ alkyl ether, 3- to 6-membered saturated heterocycle, a 3- to 6-membered heteroaryl moiety, wherein said moieties may be substituted or unsubstituted, wherein the substituents of said substituted moieties with respect to R₄ and R₇ are selected from 3- to 6-membered heteroaryls and aryls, or 3- to 6-membered saturated heterocycles, which may also be substituted with one or more hydroxyl, amine or C₁-C₃ alkoxy groups.

In some embodiments, R₇ is pyridine, furan, CH₂OH, CH₂OCH₃ or CH₂-O-tetrahydropyran, in particular pyridine and furan, more particularly furan.

In some embodiments, R₇ is pyridine, furan, CH₂OH, CH₂OCH₃ or CH₂-O-tetrahydropyran, more particularly furan.

In some embodiments, R₁₀ is H or methyl, in particular H.

In some embodiments, Y is N, CH or C-R₁₁ with R₁₁ being a hydroxyl, a C₁-C₅ heteroalkyl, particularly a -(CH₂)_p-OT₃ or a -(CH₂)_p-N(T₃)(T₄), with T₃ and T₄ being independently from each other H or C₁-C₃ alkyl, and p is 0, 1, 2, 3, 4 or 5, a substituted or unsubstituted C₁-C₆

alkoxyl, a saturated heterocycle, $-\text{O}-(\text{CH}_2)_q\text{-phenyl}$ or $-\text{O}-(\text{CH}_2)_q\text{-heterocycle}$, wherein the saturated heterocycle or the $-\text{O}-(\text{CH}_2)_q\text{-heterocycle}$ are preferably $\text{C}_3\text{-C}_6$ heterocycles, more preferably $\text{C}_5\text{-C}_6$ heterocycles, and q is 0, 1 or 2, wherein said phenyl and said heterocycle of R_{11} may optionally be substituted with one or more methoxy or hydroxy groups, wherein preferably Y is CH , $-\text{O}-(\text{CH}_2)_q\text{-heterocycle}$ or hydroxyl.

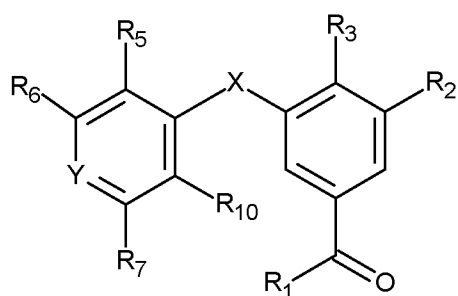
In some embodiments, Y is N , CH or C-R_{11} with R_{11} being a hydroxyl, a substituted or unsubstituted $\text{C}_1\text{-C}_6$ alkoxyl, a saturated heterocycle, $-\text{O}-(\text{CH}_2)_q\text{-phenyl}$ or $-\text{O}-(\text{CH}_2)_q\text{-heterocycle}$, and q is 0, 1 or 2, wherein the saturated heterocycle or the $-\text{O}-(\text{CH}_2)_q\text{-heterocycle}$ are preferably $\text{C}_3\text{-C}_6$ heterocycles, more preferably $\text{C}_5\text{-C}_6$ heterocycles, wherein said phenyl and said heterocycle of R_{11} is substituted with one or more methoxy or hydroxy groups, wherein preferably Y is CH , $-\text{O}-(\text{CH}_2)_q\text{-heterocycle}$ or hydroxyl.

In some embodiments, Y is N , CH or C-R_{11} , with R_{11} being a substituted or unsubstituted $\text{C}_1\text{-C}_6$ alkoxyl, a heteroaryl, $-\text{O}-(\text{CH}_2)_q\text{-phenyl}$ or $-\text{O}-(\text{CH}_2)_q\text{-heterocycle}$, with q being 0, 1 or 2.

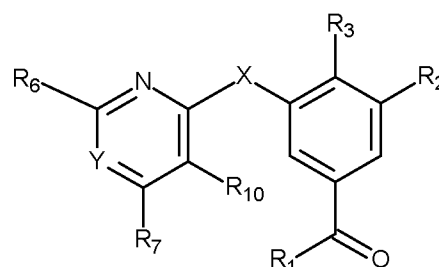
In some embodiments, Y is N , CH or C-R_{11} with R_{11} being a substituted or unsubstituted $\text{C}_1\text{-C}_6$ alkoxyl, a heteroaryl, in particular morpholino or piperazine bonded via a N atom, $-\text{O}-(\text{CH}_2)_q\text{-phenyl}$ or $-\text{O}-(\text{CH}_2)_q\text{-heterocycle}$, morpholino, piperazine or pyridine and q is 0, 1 or 2, wherein said phenyl and said heterocycle of R_{11} may optionally be substituted with one or more methoxy or hydroxy groups, wherein preferably Y is CH .

In some embodiments, Y is N , CH or C-R_{11} with R_{11} being a substituted or unsubstituted $\text{C}_1\text{-C}_6$ alkoxyl, a heteroaryl, in particular morpholino or piperazine bonded via a N atom, $-\text{O}-(\text{CH}_2)_q\text{-phenyl}$ or $-\text{O}-(\text{CH}_2)_q\text{-heterocycle}$, morpholino, piperazine or pyridine and q is 0, 1 or 2, wherein said phenyl and said heterocycle of R_{11} is substituted with one or more methoxy or hydroxy groups, wherein preferably Y is CH .

In some embodiments, the compound according to first aspect of the invention is characterized by a general formula (3a) or (4a)



(3a), or



(4a),

particularly of formula (3a), wherein

R_1 is a methyl or $-\text{NHR}_8$ where R_8 is a $\text{C}_1\text{-C}_3$; and/or R_2 is a hydrogen, a methyl or a $\text{C}_1\text{-C}_4$ alkanol; and/or R_3 is H , F , a $\text{C}_1\text{-C}_6$ alkyl or a $\text{C}_1\text{-C}_4$ alkoxy, a benzyloxy or a morpholino, in

particular R_3 is an ethoxy, a propoxy, a butoxy, cyclopropane, cyclopropylethoxy, benzyloxy or a morpholino, more particularly ethoxy; and/or R_5 is H, -COOH or salt thereof, a C_1 - C_3 alkoxy, a C_1 - C_3 alkyl, a C_1 - C_3 alkyl ester, a heteroaryl, a substituted or unsubstituted C_1 - C_6 alkoxy or a sulfonic acid, an S-linked sulfonamide that may be singly substituted with a C_1 - C_3 alkyl group or with a C_3 - C_6 cyclic alkyl, and/or R_6 is H, -COOH or salt thereof, a C_1 - C_3 alkoxy, a C_1 - C_3 alkyl, a C_1 - C_3 alkyl ester, a substituted or unsubstituted heteroaryl, a substituted or unsubstituted C_1 - C_6 alkoxy or a sulfonic acid, an S-linked sulfonamide that may be singly substituted with a C_1 - C_3 alkyl group or with a C_3 - C_6 cyclic alkyl; and/or R_{10} is H or methyl, in particular H; and/or R_7 is pyridine, furan, CH_2OH , CH_2OCH_3 or CH_2 -O-tetrahydropyran, more particularly furan; and/or Y is N, CH or C- R_{11} with R_{11} being a hydroxyl, a C_1 - C_5 heteroalkyl, particularly a $-(CH_2)_p-OT_3$ or a $-(CH_2)_p-N(T_3)(T_4)$, with T_3 and T_4 being independently from each other H or C_1 - C_3 alkyl, and p is 0, 1, 2, 3, 4 or 5, a substituted or unsubstituted C_1 - C_6 alkoxy, a saturated heterocycle, $-O-(CH_2)_q$ -phenyl or $-O-(CH_2)_q$ -heterocycle, wherein the saturated heterocycle or the $-O-(CH_2)_q$ -heterocycle are preferably C_3 - C_6 heterocycles, more preferably C_5 - C_6 heterocycles, and q is 0, 1 or 2, wherein said phenyl and said heterocycle of R_{11} may optionally be substituted with one or more methoxy or hydroxy groups, wherein preferably Y is CH, $-O-(CH_2)_q$ -heterocycle or hydroxyl; and/or X is $-C(=O)NH-$, $-NHC(=O)-$, $-NHC(=O)NH-$, $-N(R_9)C(=O)NH-$, $-NHC(=O)NR_9-$, $-C(=S)NH-$, $-NHC(=S)-$, $-NHC(=S)NH-$, $-N(R_9)C(=S)NH-$, $-NHC(=S)N(R_9)-$, $-N-S(=O)_2-$, $-S(=O)_2-N-$, in particular $-C(=O)NH-$, $-NHC(=O)-$, $-NHC(=O)NH-$, $-N(R_9)C(=O)NH-$, $-NHC(=O)NR_9-$, more particularly $-C(=O)NH-$ or $-NHC(=O)-$, wherein R_9 is a C_1 - C_3 alkyl, C_1 - C_3 alkoxy, C_1 - C_3 haloalkyl, C_1 - C_3 alkanol, C_2 - C_4 ether, 3- to 6-membered heterocycle, or substituted or unsubstituted aryl.

In some embodiments, the compound according to first aspect of the invention is characterized by a general formula (3a), wherein R_1 is a methyl or $-NHR_8$ where R_8 is a C_1 - C_3 ; R_2 is a hydrogen, a methyl or a C_1 - C_4 alkanol; R_3 is H, F, a C_1 - C_6 alkyl or a C_1 - C_4 alkoxy, a benzyloxy or a morpholino, in particular R_3 is an ethoxy, a propoxy, a butoxy, cyclopropane, cyclopropylethoxy, benzyloxy or a morpholino, more particularly ethoxy; R_5 is H, -COOH or salt thereof, a C_1 - C_3 alkoxy, a C_1 - C_3 alkyl, a C_1 - C_3 alkyl ester, a heteroaryl, a substituted or unsubstituted C_1 - C_6 alkoxy or a sulfonic acid, a sulfonamide that may be singly substituted with a C_1 - C_3 alkyl group or with a C_3 - C_6 cyclic alkyl; R_6 is H, -COOH or salt thereof, a C_1 - C_3 alkoxy, a C_1 - C_3 alkyl, a C_1 - C_3 alkyl ester, a heteroaryl, a substituted or unsubstituted C_1 - C_6 alkoxy or a sulfonic acid, a sulfonamide that may be singly substituted with a C_1 - C_3 alkyl group or with a C_3 - C_6 cyclic alkyl; R_{10} is H or methyl, in particular H; R_7 is pyridine, furan, CH_2OH , CH_2OCH_3 or CH_2 -O-tetrahydropyran, more particularly furan; Y is N, CH or C- R_{11} with R_{11} being a substituted or unsubstituted C_1 - C_6 alkoxy, a heteroaryl, in particular morpholino or piperazine bonded via a N atom, $-O-(CH_2)_q$ -phenyl or $-O-(CH_2)_q$ -heterocycle, morpholino, piperazine or pyridine and q is 0, 1 or 2, wherein said phenyl and

said heterocycle of R_{11} may optionally be substituted with one or more methoxy or hydroxy groups, wherein preferably Y is CH; X is $-C(=O)NH-$, $-NHC(=O)-$, $-NHC(=O)NH-$, $-N(R_9)C(=O)NH-$, $-NHC(=O)NR_9-$, $-C(=S)NH-$, $-NHC(=S)-$, $-NHC(=S)NH-$, $-N(R_9)C(=S)NH-$, $-NHC(=S)N(R_9)-$, in particular $-C(=O)NH-$, $-NHC(=O)-$, $-NHC(=O)NH-$, $-N(R_9)C(=O)NH-$, $-NHC(=O)NR_9-$, more particularly $-C(=O)NH-$ or $-NHC(=O)-$, wherein R_9 is a C_1 - C_3 alkyl, C_1 - C_3 alkoxy, C_1 - C_3 haloalkyl, C_1 - C_3 alkanol, C_2 - C_4 ether, 3- to 6-membered heterocycle, or substituted or unsubstituted aryl.

In some embodiments, the compound according to first aspect of the invention is characterized by a general formula (3a) or (4a), particularly of formula (3a), R_1 is a methyl or $-NHR_8$ where R_8 is a methyl, in particular R_1 is a methyl; and/or R_2 is a hydrogen; and/or R_3 is ethoxy, a propoxy, a butoxy, cyclopropane, cyclopropylethoxy, benzyloxy or a morpholino, more particularly ethoxy; and/or R_5 is H, $-COOH$ or salt thereof, a C_1 - C_3 alkoxy, a C_1 - C_3 alkyl, a C_1 - C_3 alkyl ester, a heteroaryl, a substituted or unsubstituted C_1 - C_6 alkoxy or a sulfonic acid, an S-linked sulfonamide that may be singly substituted with a C_1 - C_3 alkyl group or with a C_3 - C_6 cyclic alkyl; and/or R_6 is H, $-COOH$ or salt thereof, a C_1 - C_3 alkoxy, a C_1 - C_3 alkyl, a C_1 - C_3 alkyl ester, a substituted or unsubstituted heteroaryl, a substituted or unsubstituted C_1 - C_6 alkoxy or a sulfonic acid, an S-linked sulfonamide that may be singly substituted with a C_1 - C_3 alkyl group or with a C_3 - C_6 cyclic alkyl; and/or R_{10} is H or methyl, in particular H; and/or R_7 is pyridine, furan, CH_2OH , CH_2OCH_3 or CH_2 -O-tetrahydropyran, in particular furan; and/or Y is N, CH or C- R_{11} with R_{11} being a hydroxyl, a substituted or unsubstituted C_1 - C_6 alkoxy, a saturated heterocycle, $-O-(CH_2)_q$ -phenyl or $-O-(CH_2)_q$ -heterocycle, and q is 0, 1 or 2, wherein the saturated heterocycle or the $-O-(CH_2)_q$ -heterocycle are preferably C_3 - C_6 heterocycles, more preferably C_5 - C_6 heterocycles, wherein said phenyl and said heterocycle of R_{11} is substituted with one or more methoxy or hydroxy groups, wherein preferably Y is CH, $-O-(CH_2)_q$ -heterocycle or hydroxyl; and/or X is $C(=O)NH-$, $-NHC(=O)-$, $-NHC(=O)NH-$, $-N(R_9)C(=O)NH-$, $-NHC(=O)NR_9-$, in particular X is $-C(=O)NH-$ or $-NHC(=O)-$, wherein R_9 is a C_1 - C_3 alkyl, C_1 - C_3 alkoxy, C_1 - C_3 haloalkyl, C_1 - C_3 alkanol, C_2 - C_4 ether, 3- to 6-membered heterocycle, or substituted or unsubstituted aryl, wherein in particular R_9 is a C_1 - C_3 alkoxy, C_1 - C_3 haloalkyl, C_1 - C_3 alkanol, C_2 - C_4 ether, 3- to 6-membered heterocycle, or substituted or unsubstituted aryl.

In some embodiments, the compound according to first aspect of the invention is characterized by a general formula (3a), wherein R_1 is a methyl or $-NHR_8$ where R_8 is a methyl, in particular R_1 is a methyl; R_2 is a hydrogen; R_3 is ethoxy, a propoxy, a butoxy, cyclopropane, cyclopropylethoxy, benzyloxy or a morpholino, more particularly ethoxy; R_5 is $-COOH$ or salt thereof, a C_1 - C_3 alkyl ester, a sulfonic acid, a sulfonamide that may be singly substituted with a C_1 - C_3 alkyl group or with a C_3 - C_6 cyclic alkyl, or a 5-membered heteroaryl, in particular H, $-COOH$ or salt thereof, tetrazole, particularly a tetrazole bonded to the parent

compound at the N1 position, C₁-C₃ alkyl ester, in particular methylester; R₆ is H, -COOH or salt thereof, a C₁-C₃ alkoxy, a C₁-C₃ alkyl, a C₁-C₃ alkyl ester, a heteroaryl, a substituted or unsubstituted C₁-C₆ alkoxy or a sulfonic acid, a sulfonamide that may be singly substituted with a C₁-C₃ alkyl group or with a C₃-C₆ cyclic alkyl, in particular H, -COOH or salt thereof, 5 tetrazole, particularly a tetrazole bonded to the parent compound at the N1 position, C₁-C₃ alkyl ester, in particular methylester; R₁₀ is H or methyl, in particular H; and/or R₇ is pyridine, furan, CH₂OH, CH₂OCH₃ or CH₂-O-tetrahydropyran, in particular furan; and/or Y is N, CH or C-R₁₁ with R₁₁ being a substituted or unsubstituted C₁-C₆ alkoxy, a heteroaryl, in particular morpholino or piperazine bonded via a N atom, -O-(CH₂)_q-phenyl or -O-(CH₂)_q-heterocycle, 10 morpholino, piperazine or pyridine and q is 0, 1 or 2, wherein said phenyl and said heterocycle of R₁₁ is substituted with one or more methoxy or hydroxy groups, wherein preferably Y is CH; and/or X is C(=O)NH-, -NHC(=O)-, -NHC(=O)NH-, -N(R₉)C(=O)NH-, -NHC(=O)NR₉, in particular X is -C(=O)NH- or -NHC(=O)-, wherein R₉ is a C₁-C₃ alkyl, C₁-C₃ alkoxy, C₁-C₃ haloalkyl, C₁-C₃ alkanol, C₂-C₄ ether, 3- to 6-membered heterocycle, or 15 substituted or unsubstituted aryl, wherein in particular R₉ is a C₁-C₃ alkoxy, C₁-C₃ haloalkyl, C₁-C₃ alkanol, C₂-C₄ ether, 3- to 6-membered heterocycle, or substituted or unsubstituted aryl.

The selection of R₅ and R₆, in the previously discussed embodiments, may be dependent on the selection of X.

20 In some embodiments, X is -N(R₉)C(=O)NH-, -NHC(=O)NR₉-, -NHC(=O)NH-, -N(R₉)C(=S)NH- or -NHC(=S)N(R₉)-, -NHC(=S)NH- or -NHC(=S)N(R₉)-, then R₅ is -COOH or salt thereof, a C₁-C₃ alkyl ester, a sulfonic acid, an S-linked sulfonamide that may be singly substituted with a C₁-C₃ alkyl group or with a C₃-C₆ cyclic alkyl, or a 5-membered heteroaryl, in particular H, -COOH or salt thereof, C₁-C₃ alkyl ester, in particular methylester, a 25 substituted or unsubstituted heteroaryl, in particular tetrazole, and R₆ is H, a C₁-C₃ alkoxy or a C₁-C₃ alkyl, in particular H; wherein n, R₁, R₂, R₃, A, R₄, R₇, R₈, R₉, R₁₀, Y, R₁₁ have the same meaning as defined previously.

In some embodiments, X is -C(=O)NH-, -NHC(=O)-, -C(=O)NR₁₂-, -NR₁₂C(=O)-, -C(=S)NH-, -NHC(=S)-, then R₅ is H, a C₁-C₃ alkoxy or a C₁-C₃ alkyl; in particular H, and R₆ is -COOH or salt thereof, a C₁-C₃ alkyl ester, a sulfonic acid, a substituted or unsubstituted heteroaryl, an S-linked sulfonamide that may be singly substituted with a C₁-C₃ alkyl group or with a C₃-C₆ cyclic alkyl, or a 5-membered heteroaryl, in particular H, -COOH or salt thereof, C₁-C₃ alkyl ester, in particular methylester, a substituted or unsubstituted heteroaryl, a tetrazole, wherein 30 n, R₁, R₂, R₃, A, R₄, R₇, R₈, R₉, R₁₀, Y, R₁₁ have the same meaning as defined previously.

35 In some embodiments, X is -N(R₉)C(=O)NH-, -NHC(=O)NR₉-, -NHC(=O)NH-, -N(R₉)C(=S)NH- or -NHC(=S)N(R₉)-, -NHC(=S)NH- or -NHC(=S)N(R₉)-, then R₅ is H, -COOH

or salt thereof, a C₁-C₃ alkoxy, a C₁-C₃ alkyl, a C₁-C₃ alkyl ester, a heteroaryl, a substituted or unsubstituted C₁-C₆ alkoxy or a sulfonic acid, a sulfonamide that may be singly substituted with a C₁-C₃ alkyl group or with a C₃-C₆ cyclic alky, and R₆ is H, a C₁-C₃ alkoxy or a C₁-C₃ alkyl, in particular H, wherein n, R₁, R₂, R₃, A, R₄, R₇, R₈, R₉, R₁₀, Y, R₁₁ have the same meaning as defined previously.

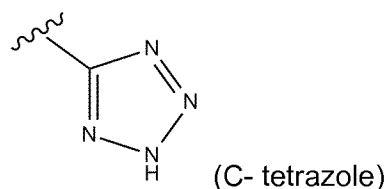
In some embodiments, X is -N(R₉)C(=O)NH-, -NHC(=O)NR₉-, -NHC(=O)NH-, -N(R₉)C(=S)NH- or -NHC(=S)N(R₉)-, -NHC(=S)NH- or -NHC(=S)N(R₉)-, then R₅ is H, -COOH or salt thereof, tetrazole, particularly a tetrazole bonded to the parent compound at the N1 position, C₁-C₃ alkyl ester, in particular methylester and R₆ is H, wherein n, R₁, R₂, R₃, A, R₄, R₇, R₈, R₉, R₁₀, Y, R₁₁ have the same meaning as defined previously.

In some embodiments, X is -C(=O)NH-, -NHC(=O)-, -C(=O)NR₁₂-, -NR₁₂C(=O)-, -C(=S)NH-, -NHC(=S)-, then R₅ is H, a C₁-C₃ alkoxy or a C₁-C₃ alkyl, in particular H, R₆ is H, -COOH or salt thereof, a C₁-C₃ alkoxy, a C₁-C₃ alkyl, a C₁-C₃ alkyl ester, a heteroaryl, a substituted or unsubstituted C₁-C₆ alkoxy or a sulfonic acid, a sulfonamide that may be singly substituted with a C₁-C₃ alkyl group or with a C₃-C₆ cyclic alky, wherein n, R₁, R₂, R₃, A, R₄, R₇, R₈, R₉, R₁₀, Y, R₁₁ have the same meaning as defined previously.

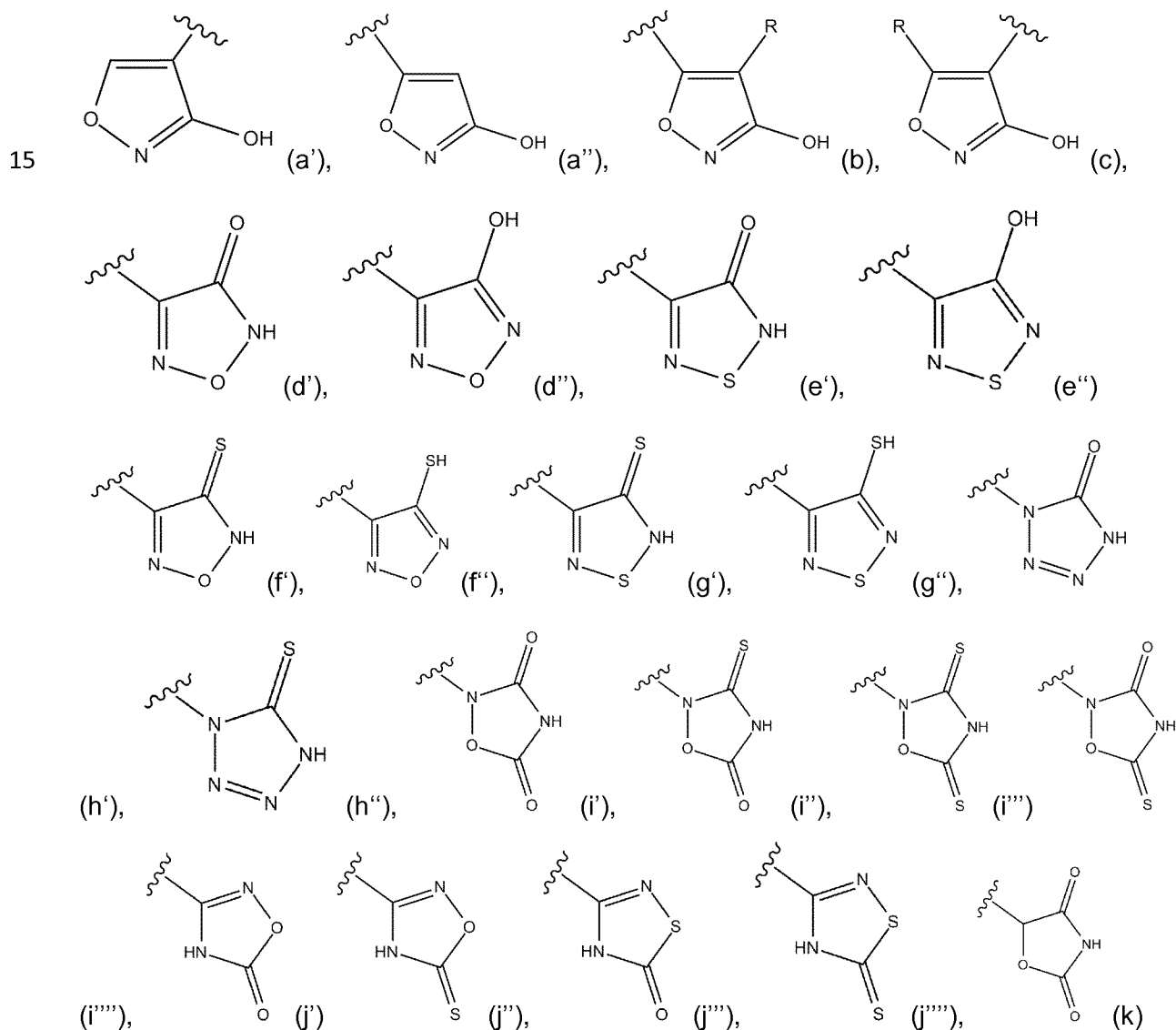
In some embodiments, X is -C(=O)NH-, -NHC(=O)-, -C(=O)NR₁₂-, -NR₁₂C(=O)-, -C(=S)NH-, -NHC(=S)-, then R₅ is H and R₆ is H, -COOH or salt thereof, tetrazole, particularly a tetrazole bonded to the parent compound at the N1 position, C₁-C₃ alkyl ester, in particular methylester, wherein n, R₁, R₂, R₃, A, R₄, R₇, R₈, R₉, R₁₀, Y, R₁₁ have the same meaning as defined previously.

A preferred embodiment for R₁ is a methyl. A preferred embodiment for R₂ is a H. Preferred embodiments for R₃ are an ethoxy, a propoxy, a butoxy, cyclopropane, cyclopropylethoxy, benzyloxy or a morpholino, more particularly ethoxy. Preferred embodiments for R₄ are H or a methyl group. A preferred embodiment for R₅ is H

Preferred embodiments for R₆ are -COOH or salt thereof, a C₁-C₃ alkyl ester, an S-linked sulfonamide that may be singly substituted with a C₁-C₃ alkyl group or with a C₃-C₆ cyclic alkyl or a substituted or unsubstituted heteroaryl, more preferred a C₁-C₃ alkyl ester, particularly -COOH or salt thereof, a methylester, a tetrazole, particularly linked by its carbon moiety (C- tetrazole).



Preferred embodiments for the substituted or unsubstituted heteroaryl of R₆ are 3-hydroxy-isoxazole bound via C4 (a') or C5 (a''), 4-alkyl-3-hydroxy-isoxazole bound via C5, where said alkyl (depicted with R) is a C₁-C₃ alkyl, 5-alkyl-3-hydroxy-isoxazole bound via C4, where said alkyl (depicted with R) is a C₁-C₃ alkyl, 1,2,5-oxadiazol-3(2H)-one bound via C4 (d') or 1,2,5-oxadiazol-3-ol bound via C4 (d''), 1,2,5-thiadiazol-3(2H)-one bound via C4 (e') or 1,2,5-thiadiazol-3-ol bound via C4 (e''), 1,2,5-oxadiazole-3(2H)-thione bound via C4 (f') or 1,2,5-oxadiazole-3-thiol bound via C4 (f''), 1,2,5-thiadiazole-3(2H)-thione bound via C4 (g') or 1,2,5-thiadiazole-3-thiol bound via C4 (g''), 1H-tetrazol-5-one bound via N4 (h') or 1H-tetrazol-5-thione bound via N4 (h''), 1,2,4-oxadiazolidine-3,5-dione bound via N2 (i') or 1,2,4-oxadiazolidine-3,5-dithione bound via N2 (i''), 1,2,4-oxadiazolidine-3,5-dione bound via N2 (i''') or 5-thioxo 1,2,4-oxadiazolidine-3-dione bound via N2 (i'''), 1,2,4-oxadiazol-5(4H)-one bound via C3 (j') or 1,2,4-oxadiazole-5(4H)-thione bound via C3 (j''), 1,2,4-thiadiazol-5(4H)-one bound via C3 (j''') or 1,2,4-thiadiazole-5(4H)-thione bound via C3 (j'''), 2,4-oxazolidinedione bound via C5 (k) more preferred are a'', b, c, h', h'', j', j'' and j'''.



Preferred embodiments for R_7 are H, NO_2 , $\text{C}_2\text{-C}_4$ alkyl ether, heteroaryl, particularly pyridine and furan, more particularly furan, a 3- to 6-membered saturated heterocycle, particularly tetrazole, a substituted or unsubstituted $\text{C}_1\text{-C}_3$ alkoxy, particularly a the $-\text{O}-(\text{CH}_2)_q-$ heterocycle with q being 0, 1 or 2.

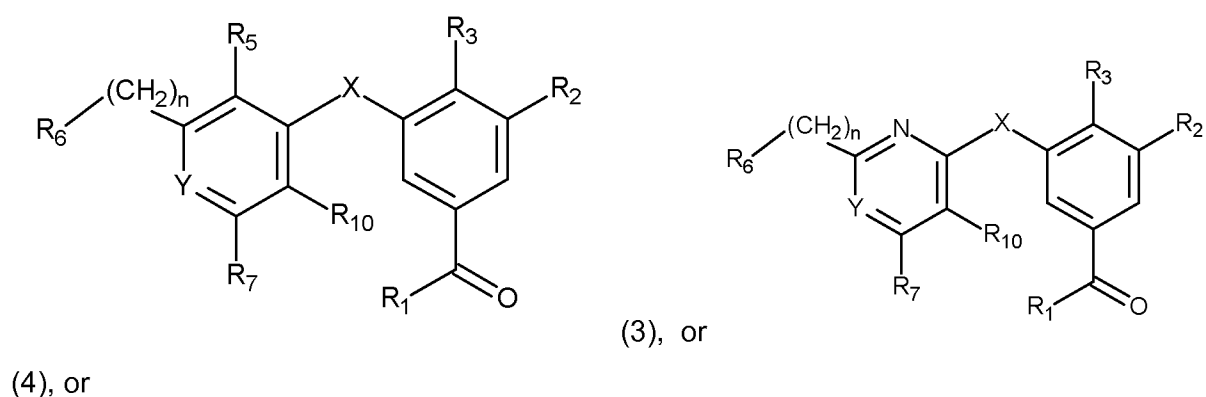
5 Preferred embodiments for R_7 are H, Br, furan, in particular H.

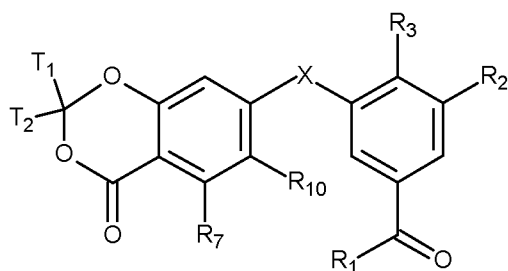
Preferred embodiments for Y are CH or C-R_{11} , with R_{11} being a hydroxyl, a saturated heterocycle, a substituted or unsubstituted $\text{C}_1\text{-C}_6$ alkoxy, $-\text{O}-(\text{CH}_2)_q\text{-heterocycle}$, with q being 0, 1 or 2, more preferred is Y being CH or C-R_{11} , with R_{11} being H, a hydroxyl or $-\text{O}-(\text{CH}_2)_q\text{-heterocycle}$, with q being 0, 1 or 2.

10 Further preferred embodiments for R_6 and R_7 or Y are

- each of R_6 and R_7 is a tetrazole, particularly one of R_6 or R_7 is a tetrazole connected by its carbon moiety,
- R_6 is a tetrazole connected by its carbon moiety and R_7 is a tetrazole connected by its nitrogen moiety;
- 15 - each of R_6 and R_7 is a tetrazole, which are both connected by their carbon moiety,
- R_6 is a tetrazole, particularly a tetrazole connected by its carbon moiety, and R_7 is furan,
- R_6 is $-\text{COOH}$ or salt thereof, a $\text{C}_1\text{-C}_3$ alkyl ester and R_7 is a tetrazole, particularly a tetrazole connected by its carbon moiety,
- 20 - R_6 is a tetrazole, particularly a tetrazole connected by its carbon moiety, and R_7 is $-\text{O}-(\text{CH}_2)_q\text{-heterocycle}$, with q being 0, 1 or 2,
- R_6 is a tetrazole, particularly a tetrazole connected by its carbon moiety, and Y is C-R_{11} , with R_{11} being H, a hydroxyl or $-\text{O}-(\text{CH}_2)_q\text{-heterocycle}$, with q being 0, 1 or 2.

A second aspect of the present invention relates to a compound, or prodrug or salt thereof, of
25 formula (3) (4) or (5),





(5), particularly of formula (3), wherein

- R_1 is a C_1 - C_3 alkyl, cyclopropane, a C_1 - C_3 haloalkyl, halocyclopropane or $-NHR_8$, wherein R_8 is a C_1 - C_3 alkyl, cyclopropane, a C_1 - C_3 haloalkyl or halocyclopropane;
- R_2 is H, F, a C_1 - C_4 alkyl or a C_1 - C_4 alkanol;
- 5 - R_3 is H, F, Cl, a C_1 - C_6 alkyl, a C_1 - C_3 haloalkyl, a C_1 - C_4 alkoxy, a C_1 - C_4 alkanol, a C_2 - C_4 ether, a 3- to 6-membered saturated heterocycle, a 3- to 6-membered heteroaryl, a benzyloxy or a substituted amine of the form $-NHR_8$, wherein R_8 is a C_1 - C_3 alkyl, cyclopropane, a C_1 - C_3 haloalkyl or halocyclopropane;
- X is $-C(=O)NH-$, $-NHC(=O)-$, $-C(=O)NR_{12}-$, $-NR_{12}C(=O)-$, $-NR_{12}C(=O)-$, $-NHC(=O)NH-$,
 10 $-N(R_9)C(=O)NH-$, $-NHC(=O)NR_9-$, $-C(=S)NH-$, $-NHC(=S)-$, $-NHC(=S)NH-$,
 $-N(R_9)C(=S)NH-$, $-NHC(=S)N(R_9)-$, $-N-S(=O)_2-$, $-S(=O)_2-N-$, particularly X is $-C(=O)NH-$,
 $-NHC(=O)-$, $-C(=O)NR_{12}-$, $-NR_{12}C(=O)-$, $-NHC(=O)NH-$,
 $-N(R_9)C(=O)NH-$, $-NHC(=O)NR_9-$, $-C(=S)NH-$, $-NHC(=S)-$, $-NHC(=S)NH-$,
 $-N(R_9)C(=S)NH-$, $-NHC(=S)N(R_9)-$, wherein
 15 - R_9 is C_1 - C_3 alkyl, C_1 - C_3 alkoxy, C_1 - C_3 haloalkyl, C_1 - C_3 alkanol, C_2 - C_4 ether, 3- to 6-membered heterocycle, or substituted or unsubstituted aryl, and wherein
 - R_{12} is $-(CH_2)_r$ -phenyl with r being 0, 1 or 2 and said phenyl may be substituted with one or more electron donating groups, in particular one or more electron donating groups selected from $-OR_{13}$, with R_{13} being H, a methyl group or an
 20 ethyl group;
- R_5 being H, $-COOH$ or salt thereof, a C_1 - C_3 alkoxy, a C_1 - C_3 alkyl, a C_1 - C_3 alkyl ester, a heteroaryl, a substituted or unsubstituted C_1 - C_6 alkoxy or a sulfonic acid, a sulfonamide, particularly an S-linked sulfonamide, that may be singly substituted with a C_1 - C_3 alkyl group or with a C_3 - C_6 cyclic alkyl; and
- 25 - R_6 being H, $-COOH$ or salt thereof, a C_1 - C_3 alkoxy, a C_1 - C_3 alkyl, a C_1 - C_3 alkyl ester, a substituted or unsubstituted heteroaryl, a substituted or unsubstituted C_1 - C_6 alkoxy or a sulfonic acid, a sulfonamide, particularly an S-linked sulfonamide, that may be singly substituted with a C_1 - C_3 alkyl group or with a C_3 - C_6 cyclic alkyl; and wherein
- R_7 and R_{10} being independently from each other selected from
 30 - H, Br, Cl, F, NO_2 or

- substituted or unsubstituted C₁-C₃ alkanol, C₁-C₃ alkyl, C₁-C₃ haloalkyl, substituted or unsubstituted C₁-C₃ alkoxy, C₃-C₆ cycloalkyl, C₂-C₄ alkyl ether, 3- to 6-membered saturated heterocycle, a 3- to 6-membered heteroaryl moiety, wherein said moieties may be substituted or unsubstituted, wherein the substituents of said substituted moieties with respect to R₄ and R₇ are selected from 3- to 6-membered heteroaryls and aryls, or 3- to 6-membered saturated heterocycles, which may also be substituted with one or more hydroxyl, amine or C₁-C₃ alkoxy groups;
- n is 0, 1 or 2;
- Y being N, CH or C-R₁₁, with R₁₁ being a hydroxyl, a C₁-C₅ heteroalkyl, particularly a -(CH₂)_p-OT₃ or a -(CH₂)_p-N(T₃)(T₄), with T₃ and T₄ being independently from each other H or C₁-C₃ alkyl, and p is 0, 1, 2, 3, 4 or 5, a substituted or unsubstituted C₁-C₆ alkoxy, a heteroaryl, a saturated heterocycle, -O-(CH₂)_q-phenyl or -O-(CH₂)_q-heterocycle, with q being 0, 1 or 2, wherein the saturated heterocycle or the -O-(CH₂)_q-heterocycle are preferably C₃-C₆ heterocycles, more preferably C₅-C₆ heterocycles, and
- in case of formula (5) T₁ and T₂ being independently from each other H, CH₃ or CH₂CH₃, particularly H.

One embodiment of the second aspect of the present invention relates to a compound, or prodrug or salt thereof, of formula (3), wherein R₁ is a C₁-C₃ alkyl, cyclopropane, a C₁-C₃ haloalkyl, halocyclopropane or -NHR₈, wherein R₈ is a C₁-C₃ alkyl, cyclopropane, a C₁-C₃ haloalkyl or halocyclopropane; R₂ is H, F, a C₁-C₄ alkyl or a C₁-C₄ alkanol; R₃ is H, F, Cl, a C₁-C₆ alkyl, a C₁-C₃ haloalkyl, a C₁-C₄ alkoxy, a C₁-C₄ alkanol, a C₂-C₄ ether, a 3- to 6-membered saturated heterocycle, a 3- to 6-membered heteroaryl, a benzyloxy or a substituted amine of the form -NHR₈, wherein R₈ is a C₁-C₃ alkyl, cyclopropane, a C₁-C₃ haloalkyl or halocyclopropane X is -C(=O)NH-, -NHC(=O)-, -C(=O)NR₁₂-, -NR₁₂C(=O)-, -NR₁₂C(=O)-, -NHC(=O)NH-, -N(R₉)C(=O)NH-, -NHC(=O)NR₉-, -C(=S)NH-, -NHC(=S)-, -NHC(=S)NH-, -N(R₉)C(=S)NH-, -NHC(=S)N(R₉)-, wherein R₉ is C₁-C₃ alkyl, C₁-C₃ alkoxy, C₁-C₃ haloalkyl, C₁-C₃ alkanol, C₂-C₄ ether, 3- to 6-membered heterocycle, or substituted or unsubstituted aryl, and wherein R₁₂ is -(CH₂)_r-phenyl with r being 0, 1 or 2 and said phenyl may be substituted with one or more electron donating groups, in particular one or more electron donating groups selected from -OR₁₃, with R₁₃ being H, a methyl group or an ethyl group; R₅ being H, -COOH or salt thereof, a C₁-C₃ alkoxy, a C₁-C₃ alkyl, a C₁-C₃ alkyl ester, a heteroaryl, a substituted or unsubstituted C₁-C₆ alkoxy or a sulfonic acid, a sulfonamide that may be singly substituted with a C₁-C₃ alkyl group or with a C₃-C₆ cyclic alkyl; and R₆ being H, -COOH or salt thereof, a C₁-C₃ alkoxy, a C₁-C₃ alkyl, a C₁-C₃ alkyl ester, a heteroaryl, a substituted or unsubstituted C₁-C₆ alkoxy or a sulfonic acid, a sulfonamide that

may be singly substituted with a C₁-C₃ alkyl group or with a C₃-C₆ cyclic alkyl; and wherein R₇ and R₁₀ being independently from each other selected from H, Cl, F or C₁-C₃ alkanol, C₁-C₃ alkyl, C₁-C₃ haloalkyl, C₁-C₃ alkoxy, C₃-C₆ cycloalkyl, C₂-C₄ alkyl ether, 3- to 6-membered saturated heterocycle, a 3- to 6-membered heteroaryl moiety, wherein said moieties may be substituted or unsubstituted, wherein the substituents of said substituted moieties with respect to R₄ and R₇ are selected from 3- to 6-membered heteroaryls and aryls, or 3- to 6-membered saturated heterocycles, which may also be substituted with one or more hydroxyl, amine or C₁-C₃ alkoxy groups; n is 0, 1 or 2; Y being N, CH or C-R₁₁, with R₁₁ being a substituted or unsubstituted C₁-C₆ alkoxy, a heteroaryl, -O-(CH₂)_q-phenyl or -O-(CH₂)_q-heterocycle, with q being 0, 1 or 2.

In some embodiments, R₁ is a C₁-C₃ alkyl, cyclopropane, a C₁-C₃ haloalkyl, halocyclopropane or -NHR₈, wherein R₈ is a C₁-C₃ alkyl, cyclopropane, a C₁-C₃ haloalkyl or halocyclopropane. In some embodiments, R₁ is a methyl or -NHR₈ where R₈ is a C₁-C₃. In some embodiments, R₁ is a methyl or -NHR₈ where R₈ is a methyl, in particular R₁ is a methyl.

In some embodiments, R₂ is H, F, a C₁-C₄ alkyl or a C₁-C₄ alkanol. In some embodiments, R₂ is a hydrogen, a methyl or a C₁-C₄ alkanol. In some embodiments, R₂ is a hydrogen.

In some embodiments, R₃ is H, F, Cl, a C₁-C₆ alkyl, a C₁-C₃ haloalkyl, a C₁-C₄ alkoxy, a C₁-C₄ alkanol, a C₂-C₄ ether, a 3- to 6-membered saturated heterocycle, a 3- to 6-membered heteroaryl, a benzyloxy or a substituted amine of the form -NHR₈, wherein R₈ is a C₁-C₃ alkyl, cyclopropane, a C₁-C₃ haloalkyl or halocyclopropane. In some embodiments, R₃ is H, F, a C₁-C₆ alkyl or a C₁-C₄ alkoxy, a benzyloxy or a morpholino, in particular R₃ is an ethoxy, a propoxy, a butoxy, cyclopropane, cyclopropylethoxy, benzyloxy or a morpholino, more particularly ethoxy. In some embodiments, R₃ is ethoxy, a propoxy, a butoxy, cyclopropane, cyclopropylethoxy, benzyloxy or a morpholino, more particularly ethoxy.

In some embodiments, X is -C(=O)NH-, -NHC(=O)-, -C(=O)NR₁₂-, -NR₁₂C(=O)-, -NR₁₂C(=O)-, -NHC(=O)NH-, -N(R₉)C(=O)NH-, -NHC(=O)NR₉-, -C(=S)NH-, -NHC(=S)-, -NHC(=S)NH-, -N(R₉)C(=S)NH-, -NHC(=S)N(R₉)-, -N-S(=O)₂-, -S(=O)₂-N-, particularly X is -C(=O)NH-, -NHC(=O)-, -C(=O)NR₁₂-, -NR₁₂C(=O)-, -NHC(=O)NH-, -N(R₉)C(=O)NH-, -NHC(=O)NR₉-, -C(=S)NH-, -NHC(=S)-, -NHC(=S)NH-, -N(R₉)C(=S)NH-, -NHC(=S)N(R₉)-, wherein R₉ is C₁-C₃ alkyl, C₁-C₃ alkoxy, C₁-C₃ haloalkyl, C₁-C₃ alkanol, C₂-C₄ ether, 3- to 6-membered heterocycle, or substituted or unsubstituted aryl, and wherein R₁₂ is -(CH₂)_r-phenyl with r being 0, 1 or 2 and said phenyl may be substituted with one or more electron donating groups, in particular one or more electron donating groups selected from -OR₁₃, with R₁₃ being H, a methyl group or an ethyl group.

In some embodiments, X is $-C(=O)NH-$, $-NHC(=O)-$, $-C(=O)NR_{12}-$, $-NR_{12}C(=O)-$, $-NR_{12}C(=O)-$, $-NHC(=O)NH-$, $-N(R_9)C(=O)NH-$, $-NHC(=O)NR_9-$, $-C(=S)NH-$, $-NHC(=S)-$, $-NHC(=S)NH-$, $-N(R_9)C(=S)NH-$, $-NHC(=S)N(R_9)-$, wherein R_9 is C_1-C_3 alkyl, C_1-C_3 alkoxy, C_1-C_3 haloalkyl, C_1-C_3 alkanol, C_2-C_4 ether, 3- to 6-membered heterocycle, or substituted or unsubstituted aryl, and wherein R_{12} is $-(CH_2)_r$ -phenyl with r being 0, 1 or 2 and said phenyl may be substituted with one or more electron donating groups, in particular one or more electron donating groups selected from $-OR_{13}$, with R_{13} being H, a methyl group or an ethyl group.

In some embodiments, X is $-C(=O)NH-$, $-NHC(=O)-$, $-NHC(=O)NH-$, $-N(R_9)C(=O)NH-$, $-NHC(=O)NR_9-$, $-C(=S)NH-$, $-NHC(=S)-$, $-NHC(=S)NH-$, $-N(R_9)C(=S)NH-$, $-NHC(=S)N(R_9)-$, in particular $-C(=O)NH-$, $-NHC(=O)-$, $-NHC(=O)NH-$, $-N(R_9)C(=O)NH-$, $-NHC(=O)NR_9-$, more particularly $-C(=O)NH-$ or $-NHC(=O)-$, wherein R_9 is a C_1-C_3 alkyl, C_1-C_3 alkoxy, C_1-C_3 haloalkyl, C_1-C_3 alkanol, C_2-C_4 ether, 3- to 6-membered heterocycle, or substituted or unsubstituted aryl.

In some embodiments, X is $C(=O)NH-$, $-NHC(=O)-$, $-NHC(=O)NH-$, $-N(R_9)C(=O)NH-$, $-NHC(=O)NR_9$, in particular X is $-C(=O)NH-$ or $-NHC(=O)-$, wherein R_9 is a C_1-C_3 alkyl, C_1-C_3 alkoxy, C_1-C_3 haloalkyl, C_1-C_3 alkanol, C_2-C_4 ether, 3- to 6-membered heterocycle, or substituted or unsubstituted aryl, wherein in particular R_9 is a C_1-C_3 alkoxy, C_1-C_3 haloalkyl, C_1-C_3 alkanol, C_2-C_4 ether, 3- to 6-membered heterocycle, or substituted or unsubstituted aryl.

In some embodiments, R_5 is H, $-COOH$ or salt thereof, a C_1-C_3 alkoxyl, a C_1-C_3 alkyl, a C_1-C_3 alkyl ester, a heteroaryl, a substituted or unsubstituted C_1-C_6 alkoxyl or a sulfonic acid, a sulfonamide, particularly an S-linked sulfonamide, that may be singly substituted with a C_1-C_3 alkyl group or with a C_3-C_6 cyclic alkyl

In some embodiments, R_5 is H, $-COOH$ or salt thereof, a C_1-C_3 alkoxyl, a C_1-C_3 alkyl, a C_1-C_3 alkyl ester, a heteroaryl, a substituted or unsubstituted C_1-C_6 alkoxyl or a sulfonic acid, a sulfonamide that may be singly substituted with a C_1-C_3 alkyl group or with a C_3-C_6 cyclic alkyl. In some embodiments, R_5 is H- $COOH$ or salt thereof, tetrazole, particularly a tetrazole bonded to the parent compound at the N1 position, C_1-C_3 alkyl ester, in particular methylester.

In some embodiments, R_6 is H, $-COOH$ or salt thereof, a C_1-C_3 alkoxyl, a C_1-C_3 alkyl, a C_1-C_3 alkyl ester, a substituted or unsubstituted heteroaryl, a substituted or unsubstituted C_1-C_6 alkoxyl or a sulfonic acid, a sulfonamide, particularly an S-linked sulfonamide, that may be singly substituted with a C_1-C_3 alkyl group or with a C_3-C_6 cyclic alkyl.

In some embodiments, R_6 is H, $-COOH$ or salt thereof, a C_1-C_3 alkoxyl, a C_1-C_3 alkyl, a C_1-C_3 alkyl ester, a heteroaryl, a substituted or unsubstituted C_1-C_6 alkoxyl or a sulfonic acid, a

sulfonamide that may be singly substituted with a C₁-C₃ alkyl group or with a C₃-C₆ cyclic alkyl. In some embodiments, R₆ is H-COOH or salt thereof, tetrazole, particularly a tetrazole bonded to the parent compound at the N1 position, C₁-C₃ alkyl ester, in particular methylester.

5 In some embodiments, n is 0, 1 or 2. In some embodiments, n is 0.

In some embodiments, R₇ and R₁₀ being independently from each other selected from H, Br, Cl, F, NO₂ or a substituted or unsubstituted C₁-C₃ alkanol, C₁-C₃ alkyl, C₁-C₃ haloalkyl, substituted or unsubstituted C₁-C₃ alkoxy, C₃-C₆ cycloalkyl, C₂-C₄ alkyl ether, 3- to 6-membered saturated heterocycle, a 3- to 6-membered heteroaryl moiety, wherein said
10 moieties may be substituted or unsubstituted, wherein the substituents of said substituted moieties with respect to R₄ and R₇ are selected from 3- to 6-membered heteroaryls and aryls, or 3- to 6-membered saturated heterocycles, which may also be substituted with one or more hydroxyl, amine or C₁-C₃ alkoxy groups.

In some embodiments, R₇ and R₁₀ being independently from each other selected from H, Cl, F or C₁-C₃ alkanol, C₁-C₃ alkyl, C₁-C₃ haloalkyl, C₁-C₃ alkoxy, C₃-C₆ cycloalkyl, C₂-C₄ alkyl
15 ether, 3- to 6-membered saturated heterocycle, a 3- to 6-membered heteroaryl moiety, wherein said moieties may be substituted or unsubstituted, wherein the substituents of said substituted moieties with respect to R₄ and R₇ are selected from 3- to 6-membered heteroaryls and aryls, or 3- to 6-membered saturated heterocycles, which may also be
20 substituted with one or more hydroxyl, amine or C₁-C₃ alkoxy groups.

In some embodiments, R₇ is pyridine, furan, CH₂OH, CH₂OCH₃ or CH₂-O-tetrahydropyran, in particular pyridine and furan, more particularly furan.

In some embodiments, R₇ is pyridine, furan, CH₂OH, CH₂OCH₃ or CH₂-O-tetrahydropyran, more particularly furan.

25 In some embodiments, R₁₀ is H or methyl, in particular H.

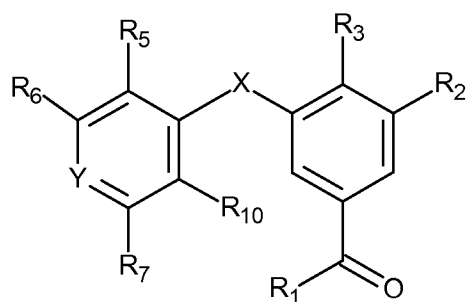
In some embodiments, Y is N, CH or C-R₁₁, with R₁₁ being a hydroxyl, a C₁-C₅ heteroalkyl, particularly a -(CH₂)_p-OT₃ or a -(CH₂)_p-N(T₃)(T₄), with T₃ and T₄ being independently from each other H or C₁-C₃ alkyl, and p is 0, 1, 2, 3, 4 or 5, a substituted or unsubstituted C₁-C₆ alkoxy, a heteroaryl, a saturated heterocycle, -O-(CH₂)_q-phenyl or -O-(CH₂)_q-heterocycle,
30 with q being 0, 1 or 2, wherein the saturated heterocycle or the -O-(CH₂)_q-heterocycle are preferably C₃-C₆ heterocycles, more preferably C₅-C₆ heterocycles, and in case of formula (5) T₁ and T₂ being independently from each other H, CH₃ or CH₂CH₃, particularly H.

In some embodiments, Y is N, CH or C-R₁₁, with R₁₁ being a substituted or unsubstituted C₁-C₆ alkoxy, a heteroaryl, -O-(CH₂)_q-phenyl or -O-(CH₂)_q-heterocycle, with q being 0, 1 or 2.

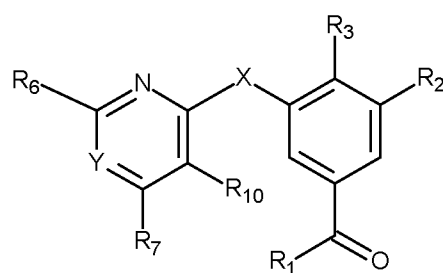
In some embodiments, Y is N, CH or C-R₁₁ with R₁₁ being a substituted or unsubstituted C₁-C₆ alkoxy, a heteroaryl, in particular morpholino or piperazine bonded via a N atom, -O-(CH₂)_q-phenyl or -O-(CH₂)_q-heterocycle, morpholino, piperazine or pyridine and q is 0, 1 or 2, wherein said phenyl and said heterocycle of R₁₁ may optionally be substituted with one or more methoxy or hydroxy groups, wherein preferably Y is CH.

In some embodiments, Y is N, CH or C-R₁₁ with R₁₁ being a substituted or unsubstituted C₁-C₆ alkoxy, a heteroaryl, in particular morpholino or piperazine bonded via a N atom, -O-(CH₂)_q-phenyl or -O-(CH₂)_q-heterocycle, morpholino, piperazine or pyridine and q is 0, 1 or 2, wherein said phenyl and said heterocycle of R₁₁ is substituted with one or more methoxy or hydroxy groups, wherein preferably Y is CH.

In some embodiments, the compound according to second aspect of the invention is characterized by a general formula (3a) or (4a),



(3a), or



(4a),

particularly of formula (3a), wherein

- R₁ is a methyl or -NHR₈ where R₈ is a C₁-C₃; and/or
- R₂ is a hydrogen, a methyl or a C₁-C₄ alkanol; and/or
- R₃ is H, F, a C₁-C₆ alkyl or a C₁-C₄ alkoxy, a benzyloxy or a morpholino, in particular R₃ is an ethoxy, a propoxy, a butoxy, cyclopropane, cyclopropylethoxy, benzyloxy or a morpholino, more particularly ethoxy; and/or
- R₅ is H, -COOH or salt thereof, a C₁-C₃ alkoxy, a C₁-C₃ alkyl, a C₁-C₃ alkyl ester, a heteroaryl, a substituted or unsubstituted C₁-C₆ alkoxy or a sulfonic acid, an S-linked sulfonamide that may be singly substituted with a C₁-C₃ alkyl group or with a C₃-C₆ cyclic alkyl; and/or
- R₆ is H, -COOH or salt thereof, a C₁-C₃ alkoxy, a C₁-C₃ alkyl, a C₁-C₃ alkyl ester, a substituted or unsubstituted heteroaryl, a substituted or unsubstituted C₁-C₆ alkoxy or a sulfonic acid, an S-linked sulfonamide that may be singly substituted with a C₁-C₃ alkyl group or with a C₃-C₆ cyclic alkyl; and/or
- R₁₀ is H or methyl, in particular H; and/or
- R₇ is pyridine, furan, CH₂OH, CH₂OCH₃ or CH₂-O-tetrahydropyran, more particularly furan; and/or

- Y is N, CH or C-R₁₁ with R₁₁ being a hydroxyl, a substituted or unsubstituted C₁-C₆ alkoxy, a saturated heterocycle, -O-(CH₂)_q-phenyl or -O-(CH₂)_q-heterocycle, wherein the saturated heterocycle or the -O-(CH₂)_q-heterocycle are preferably C₃-C₆ heterocycles, more preferably C₅-C₆ heterocycles, and q is 0, 1 or 2, wherein said phenyl and said heterocycle of R₁₁ may optionally be substituted with one or more methoxy or hydroxy groups, wherein preferably Y is CH; and/or
- X is -C(=O)NH-, -NHC(=O)-, -NHC(=O)NH-, -N(R₉)C(=O)NH-, -NHC(=O)NR₉-, -C(=S)NH-, -NHC(=S)-, -NHC(=S)NH-, -N(R₉)C(=S)NH-, -NHC(=S)N(R₉)-, -N-S(=O)₂-, -S(=O)₂-N-, in particular -C(=O)NH-, -NHC(=O)-, -NHC(=O)NH-, -N(R₉)C(=O)NH-, -NHC(=O)NR₉-, more particularly -C(=O)NH- or -NHC(=O)-, wherein R₉ is a C₁-C₃ alkyl, C₁-C₃ alkoxy, C₁-C₃ haloalkyl, C₁-C₃ alkanol, C₂-C₄ ether, 3- to 6-membered heterocycle, or substituted or unsubstituted aryl.

In some embodiments, the compound according to second aspect of the invention is characterized by a general formula (3a) or (4a), particularly of formula (3a), wherein R₁ is a methyl or -NHR₈ where R₈ is a methyl, in particular R₁ is a methyl; and/or R₂ is a hydrogen; and/or R₃ is ethoxy, a propoxy, a butoxy, cyclopropane, cyclopropylethoxy, benzyloxy or a morpholino, more particularly ethoxy; and/or R₅ is H, -COOH or salt thereof, a C₁-C₃ alkoxy, a C₁-C₃ alkyl, a C₁-C₃ alkyl ester, a heteroaryl, a substituted or unsubstituted C₁-C₆ alkoxy or a sulfonic acid, an S-linked sulfonamide that may be singly substituted with a C₁-C₃ alkyl group or with a C₃-C₆ cyclic alkyl; and/or R₆ is H, -COOH or salt thereof, a C₁-C₃ alkoxy, a C₁-C₃ alkyl, a C₁-C₃ alkyl ester, a substituted or unsubstituted heteroaryl, a substituted or unsubstituted C₁-C₆ alkoxy or a sulfonic acid, an S-linked sulfonamide that may be singly substituted with a C₁-C₃ alkyl group or with a C₃-C₆ cyclic alkyl; and/or R₁₀ is H or methyl, in particular H; and/or R₇ is pyridine, furan, CH₂OH, CH₂OCH₃ or CH₂-O-tetrahydropyran, in particular furan; and/or Y is N, CH or C-R₁₁ with R₁₁ being a hydroxyl, a substituted or unsubstituted C₁-C₆ alkoxy, a saturated heterocycle, -O-(CH₂)_q-phenyl or -O-(CH₂)_q-heterocycle, wherein the saturated heterocycle or the -O-(CH₂)_q-heterocycle are preferably C₃-C₆ heterocycles, more preferably C₅-C₆ heterocycles, and q is 0, 1 or 2, wherein said phenyl and said heterocycle of R₁₁ is substituted with one or more methoxy or hydroxy groups, wherein preferably Y is CH; and/or X is C(=O)NH-, -NHC(=O)-, -NHC(=O)NH-, -N(R₉)C(=O)NH-, -NHC(=O)NR₉-, in particular X is -C(=O)NH- or -NHC(=O)-, wherein R₉ is a C₁-C₃ alkyl, C₁-C₃ alkoxy, C₁-C₃ haloalkyl, C₁-C₃ alkanol, C₂-C₄ ether, 3- to 6-membered heterocycle, or substituted or unsubstituted aryl, wherein in particular R₉ is a C₁-C₃ alkoxy, C₁-C₃ haloalkyl, C₁-C₃ alkanol, C₂-C₄ ether, 3- to 6-membered heterocycle, or substituted or unsubstituted aryl.

In some embodiments, the compound according to second aspect of the invention is characterized by a general formula (3a), wherein R₁ is a methyl or -NHR₈ where R₈ is a C₁-

C₃; R₂ is a hydrogen, a methyl or a C₁-C₄ alkanol; R₃ is H, F, a C₁-C₆ alkyl or a C₁-C₄ alkoxy, a benzyloxy or a morpholino, in particular R₃ is an ethoxy, a propoxy, a butoxy, cyclopropane, cyclopropylethoxy, benzyloxy or a morpholino, more particularly ethoxy; R₅ is H, -COOH or salt thereof, a C₁-C₃ alkoxy, a C₁-C₃ alkyl, a C₁-C₃ alkyl ester, a heteroaryl, a substituted or unsubstituted C₁-C₆ alkoxy or a sulfonic acid, a sulfonamide that may be singly substituted with a C₁-C₃ alkyl group or with a C₃-C₆ cyclic alkyl; R₆ is H, -COOH or salt thereof, a C₁-C₃ alkoxy, a C₁-C₃ alkyl, a C₁-C₃ alkyl ester, a heteroaryl, a substituted or unsubstituted C₁-C₆ alkoxy or a sulfonic acid, a sulfonamide that may be singly substituted with a C₁-C₃ alkyl group or with a C₃-C₆ cyclic alkyl; R₁₀ is H or methyl, in particular H; R₇ is pyridine, furan, CH₂OH, CH₂OCH₃ or CH₂-O-tetrahydropyran, more particularly furan; Y is N, CH or C-R₁₁ with R₁₁ being a substituted or unsubstituted C₁-C₆ alkoxy, a heteroaryl, in particular morpholino or piperazine bonded via a N atom, -O-(CH₂)_q-phenyl or -O-(CH₂)_q-heterocycle, morpholino, piperazine or pyridine and q is 0, 1 or 2, wherein said phenyl and said heterocycle of R₁₁ may optionally be substituted with one or more methoxy or hydroxy groups, wherein preferably Y is CH; X is -C(=O)NH-, -NHC(=O)-, -NHC(=O)NH-, -N(R₉)C(=O)NH-, -NHC(=O)NR₉-, -C(=S)NH-, -NHC(=S)-, -NHC(=S)NH-, -N(R₉)C(=S)NH-, -NHC(=S)N(R₉)-, in particular -C(=O)NH-, -NHC(=O)-, -NHC(=O)NH-, -N(R₉)C(=O)NH-, -NHC(=O)NR₉-, more particularly -C(=O)NH- or -NHC(=O)-, wherein R₉ is a C₁-C₃ alkyl, C₁-C₃ alkoxy, C₁-C₃ haloalkyl, C₁-C₃ alkanol, C₂-C₄ ether, 3- to 6-membered heterocycle, or substituted or unsubstituted aryl.

In some embodiments, the compound according to first aspect of the invention is characterized by a general formula (3a), wherein R₁ is a methyl or -NHR₈ where R₈ is a methyl, in particular R₁ is a methyl; R₂ is a hydrogen; R₃ is ethoxy, a propoxy, a butoxy, cyclopropane, cyclopropylethoxy, benzyloxy or a morpholino, more particularly ethoxy; R₅ is -COOH or salt thereof, a C₁-C₃ alkyl ester, a sulfonic acid, a sulfonamide that may be singly substituted with a C₁-C₃ alkyl group or with a C₃-C₆ cyclic alkyl, or a 5-membered heteroaryl, in particular H, -COOH or salt thereof, tetrazole, particularly a tetrazole bonded to the parent compound at the N1 position, C₁-C₃ alkyl ester, in particular methylester; R₆ is H, -COOH or salt thereof, a C₁-C₃ alkoxy, a C₁-C₃ alkyl, a C₁-C₃ alkyl ester, a heteroaryl, a substituted or unsubstituted C₁-C₆ alkoxy or a sulfonic acid, a sulfonamide that may be singly substituted with a C₁-C₃ alkyl group or with a C₃-C₆ cyclic alkyl, in particular H, -COOH or salt thereof, tetrazole, particularly a tetrazole bonded to the parent compound at the N1 position, C₁-C₃ alkyl ester, in particular methylester; R₁₀ is H or methyl, in particular H; and/or R₇ is pyridine, furan, CH₂OH, CH₂OCH₃ or CH₂-O-tetrahydropyran, in particular furan; and/or Y is N, CH or C-R₁₁ with R₁₁ being a substituted or unsubstituted C₁-C₆ alkoxy, a heteroaryl, in particular morpholino or piperazine bonded via a N atom, -O-(CH₂)_q-phenyl or -O-(CH₂)_q-heterocycle, morpholino, piperazine or pyridine and q is 0, 1 or 2, wherein said phenyl and said

heterocycle of R₁₁ is substituted with one or more methoxy or hydroxy groups, wherein preferably Y is CH; and/or X is C(=O)NH-, -NHC(=O)-, -NHC(=O)NH-, -N(R₉)C(=O)NH-, -NHC(=O)NR₉, in particular X is -C(=O)NH- or -NHC(=O)-, wherein R₉ is a C₁-C₃ alkyl, C₁-C₃ alkoxy, C₁-C₃ haloalkyl, C₁-C₃ alkanol, C₂-C₄ ether, 3- to 6-membered heterocycle, or substituted or unsubstituted aryl, wherein in particular R₉ is a C₁-C₃ alkoxy, C₁-C₃ haloalkyl, C₁-C₃ alkanol, C₂-C₄ ether, 3- to 6-membered heterocycle, or substituted or unsubstituted aryl.

A preferred embodiment for R₁ is a methyl. A preferred embodiment for R₂ is a H. Preferred embodiments for R₃ are an ethoxy, a propoxy, a butoxy, cyclopropane, cyclopropylethoxy, benzyloxy or a morpholino, more particularly ethoxy. Preferred embodiments for R₄ are H or a methyl group. A preferred embodiment for R₅ is H

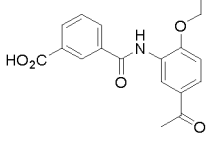
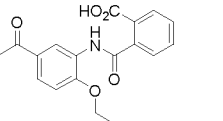
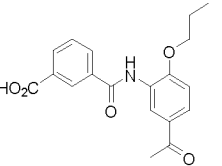
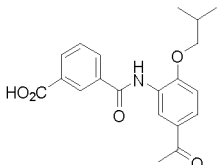
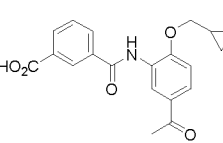
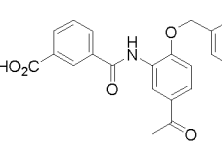
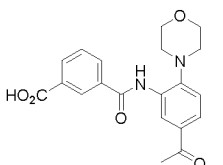
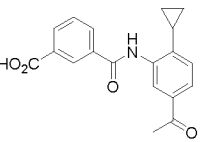
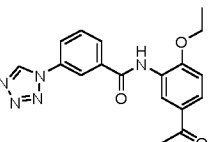
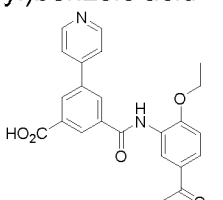
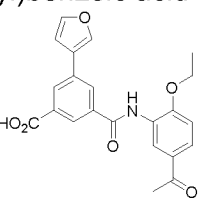
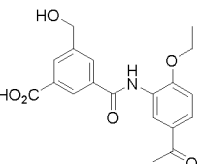
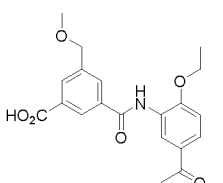
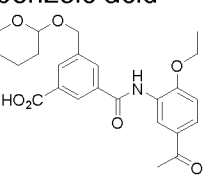
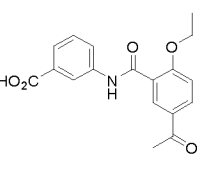
Preferred embodiments for R₆ are -COOH or salt thereof, a C₁-C₃ alkyl ester, an S-linked sulfonamide that may be singly substituted with a C₁-C₃ alkyl group or with a C₃-C₆ cyclic alkyl or a substituted or unsubstituted heteroaryl, more preferred a C₁-C₃ alkyl ester, particularly -COOH or salt thereof, a methylester, a tetrazole, particularly linked by its carbon moiety (C- tetrazole).

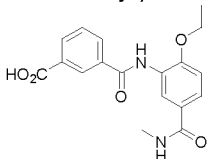
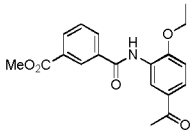
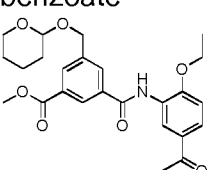
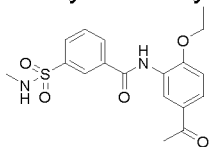
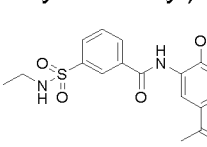
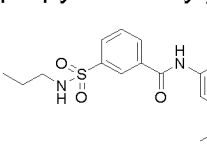
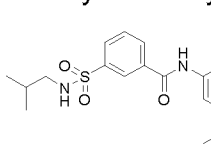
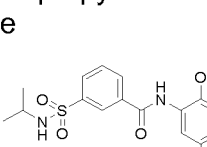
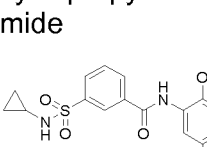
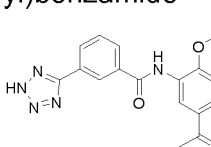
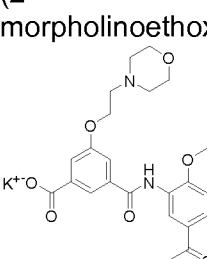
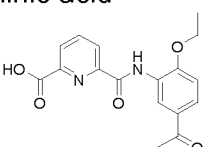
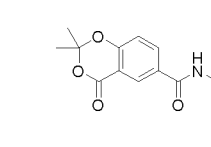
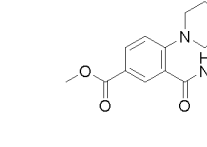
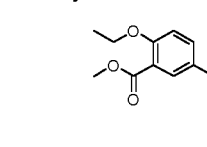
Preferred embodiments for the substituted or unsubstituted heteroaryl of R₆ are 3-hydroxy-isoxazole bound via C4 (a') or C5 (a''), 4-alkyl-3-hydroxy-isoxazole bound via C5, where said alkyl (depicted with R) is a C₁-C₃ alkyl, 5-alkyl-3-hydroxy-isoxazole bound via C4, where said alkyl (depicted with R) is a C₁-C₃ alkyl, 1,2,5-oxadiazol-3(2H)-one bound via C4 (d') or 1,2,5-oxadiazol-3-ol bound via C4 (d''), 1,2,5-thiadiazol-3(2H)-one bound via C4 (e') or 1,2,5-thiadiazol-3-ol bound via C4 (e''), 1,2,5-oxadiazole-3(2H)-thione bound via C4 (f') or 1,2,5-oxadiazole-3-thiol bound via C4 (f''), 1,2,5-thiadiazole-3(2H)-thione bound via C4 (g') or 1,2,5-thiadiazole-3-thiol bound via C4 (g''), 1H-tetrazol-5-one bound via N4 (h') or 1H-tetrazol-5-thione bound via N4 (h''), 1,2,4-oxadiazolidine-3,5-dione bound via N2 (i') or 1,2,4-oxadiazolidine-5-dione bound via N2 (i''), 1,2,4-oxadiazolidine-3,5-dithione bound via N2 (i''') or 5-thioxo 1,2,4-oxadiazolidine-3-dione bound via N2 (i'''), 1,2,4-oxadiazol-5(4H)-one bound via C3 (j'), 1,2,4-oxadiazole-5(4H)-thione bound via C3 (j'') 1,2,4-thiadiazol-5(4H)-one bound via C3 (j''') or 1,2,4-thiadiazole-5(4H)-thione bound via C3 (j'''), 2,4-oxazolidinedione bound via C5 (k) more preferred are a'', b, c h', h'', j', j'' and j'''.

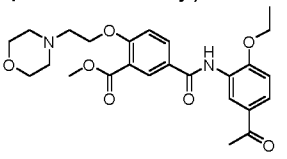
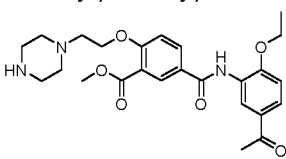
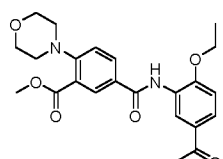
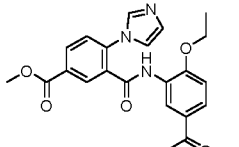
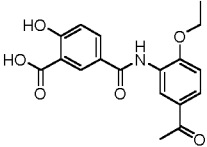
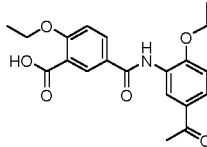
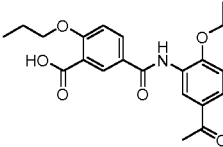
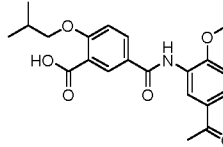
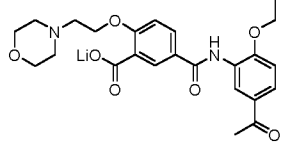
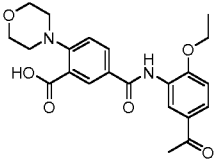
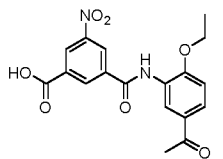
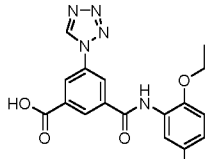
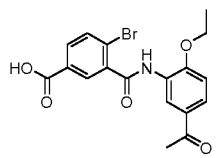
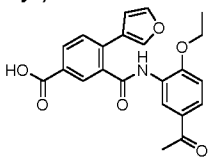
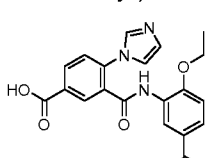
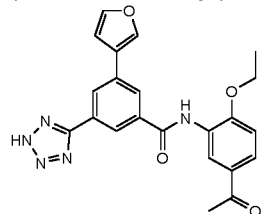
The selection of R₅ and R₆, in the previously discussed embodiments, may be dependent on the selection of X. References is made to the respective section under the first aspect of the invention.

Concerning the preferred embodiments for R₁, R₂, R₃, R₄, R₅, R₆, R₇, R₈, R₉, R₁₀, R₁₁, R₁₂, X and Y reference is made to the respective section under the first aspect of the invention.

Particular embodiments of the invention according to the first and second aspect (if applicable) are:

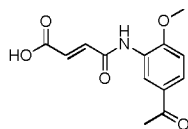
Compound 1: 3-((5-Acetyl-2-ethoxyphenyl)carbamoyl)benzoic acid 	Compound 2: 2-((5-Acetyl-2-ethoxyphenyl)carbamoyl)benzoic acid 	Compound 3: 3-((5-Acetyl-2-propoxyphenyl)carbamoyl)benzoic acid 
Compound 4: 3-((5-Acetyl-2-isobutoxyphenyl)carbamoyl)benzoic acid 	Compound 5: 3-((5-Acetyl-2-(cyclopropylmethoxy)phenyl)carbamoyl)benzoic acid 	Compound 6: 3-((5-Acetyl-2-(benzyloxy)phenyl)carbamoyl)benzoic acid 
Compound 7: 3-((5-Acetyl-2-morpholino)phenyl)carbamoyl)benzoic acid 	Compound 8: 3-((5-Acetyl-2-cyclopropylphenyl)carbamoyl)benzoic acid 	Compound 9: N-(5-Acetyl-2-ethoxyphenyl)-3-(1H-tetrazol-1-yl)benzamide 
Compound 10: 3-((5-Acetyl-2-ethoxyphenyl)carbamoyl)-5-(pyridin-4-yl)benzoic acid 	Compound 11: 3-((5-Acetyl-2-ethoxyphenyl)carbamoyl)-5-(furan-3-yl)benzoic acid 	Compound 12: 3-((5-Acetyl-2-ethoxyphenyl)carbamoyl)-5-(hydroxymethyl)benzoic acid 
Compound 13: 3-((5-Acetyl-2-ethoxyphenyl)carbamoyl)-5-(methoxymethyl)benzoic acid 	Compound 14: 3-((5-Acetyl-2-ethoxyphenyl)carbamoyl)-5-(((tetrahydro-2H-pyran-2-yl)oxy)methyl)benzoic acid 	Compound 15: 3-(5-Acetyl-2-ethoxybenzamido)benzoic acid 

Compound 16: 3-((2-Ethoxy-5-(methyl carbamoyl)phenyl) carbamoyl)benzoic acid 	Compound 19: Methyl 3-((5-acetyl-2-ethoxy phenyl)carbamoyl)benzoate 	Compound 20: 3-((5-Acetyl-2-ethoxyphenyl) carbamoyl)-5-(((tetrahydro-2H-pyran-2-yl)oxy)methyl) benzoate 
Compound 21: N-(5-acetyl-2-ethoxyphenyl)-3-(N-methylsulfamoyl)benzamide 	Compound 22: N-(5-acetyl-2-ethoxyphenyl)-3-(N-ethylsulfamoyl)benzamide 	Compound 23: N-(5-acetyl-2-ethoxyphenyl)-3-(N-propylsulfamoyl)benzamide 
Compound 24: N-(5-acetyl-2-ethoxyphenyl)-3-(N-isobutylsulfamoyl)benzamide 	Compound 25: N-(5-acetyl-2-ethoxyphenyl)-3-(N-isopropylsulfamoyl)benzamide 	Compound 26: N-(5-acetyl-2-ethoxyphenyl)-3-(N-cyclopropylsulfamoyl)benzamide 
Compound 27: N-(5-acetyl-2-ethoxyphenyl)-3-(2H-tetrazol-5-yl)benzamide 	Compound 28: potassium 3-((5-acetyl-2-ethoxyphenyl)carbamoyl)-5-(2-morpholinoethoxy)benzoate 	Compound 29: 6-((5-acetyl-2-ethoxyphenyl)carbamoyl)picolinic acid 
Compound 30: N-(5-Acetyl-2-ethoxyphenyl)-2,2-dimethyl-4-oxo-4H-benzo[d][1,3]dioxine-6-carboxamide 	Compound 31: Methyl 3-((5-acetyl-2-ethoxyphenyl)carbamoyl)-4-morpholinobenzoate 	Compound 32: Methyl 5-((5-acetyl-2-ethoxyphenyl)carbamoyl)-2-ethoxybenzoate 

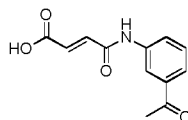
Compound 33: Methyl 5-((5-acetyl-2-ethoxyphenyl)carbamoyl)-2-(2-morpholinoethoxy) benzoate 	Compound 34: Methyl 5-((5-acetyl-2-ethoxyphenyl)carbamoyl)-2-(2-(piperazin-1-yl)ethoxy) benzoate 	Compound 35: Methyl 5-((5-acetyl-2-ethoxyphenyl)carbamoyl)-2-morpholinobenzoate 
Compound 36: Methyl 3-((5-acetyl-2-ethoxyphenyl)carbamoyl)-4-(1H-imidazol-1-yl)benzoate 	Compound 37: 5-((5-Acetyl-2-ethoxyphenyl)carbamoyl)-2-hydroxybenzoic acid 	Compound 38: 5-((5-acetyl-2-ethoxyphenyl)carbamoyl)-2-ethoxybenzoic acid 
Compound 39: 5-((5-Acetyl-2-ethoxyphenyl) carbamoyl)-2-propoxy benzoic acid 	Compound 40: 5-((5-Acetyl-2-ethoxyphenyl) carbamoyl)-2-isobutoxy benzoic acid 	Compound 41: Lithium 5-((5-acetyl-2-ethoxyphenyl)carbamoyl)-2-(2-morpholinoethoxy)benzoate 
Compound 42: 5-((5-Acetyl-2-ethoxyphenyl)carbamoyl)-2-morpholinobenzoic acid 	Compound 43: 3-((5-Acetyl-2-ethoxyphenyl)carbamoyl)-5-nitrobenzoic acid 	Compound 44: 3-((5-Acetyl-2-ethoxyphenyl)carbamoyl)-5-(1H-tetrazol-1-yl)benzoic acid 
Compound 45: 3-((5-Acetyl-2-ethoxyphenyl) carbamoyl)-4-bromobenzoic acid 	Compound 46: 3-((5-Acetyl-2-ethoxyphenyl) carbamoyl)-4-(furan-3-yl)benzoic acid 	Compound 47: 3-((5-Acetyl-2-ethoxyphenyl) carbamoyl)-4-(1H-imidazol-1-yl)benzoic acid 
Compound 48: N-(5-acetyl-2-ethoxy-phenyl)-3-(3-furyl)-5-(2H-tetrazol-5-yl)benzamide 		

Further compounds in addition to the above falling within the method according to the present invention include the following:

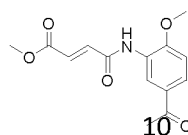
Compound 17: (E)-4-((5-Acetyl-2-methoxyphenyl)amino)-4-oxobut-2-enoic acid



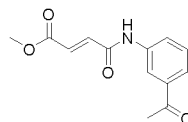
5 Compound 18: (E)-4-((3-Acetylphenyl)amino)-4-oxobut-2-enoic acid



Compound 49: Methyl (E)-4-((5-acetyl-2-methoxyphenyl)amino)-4-oxobut-2-enoate



Compound 50: Methyl (E)-4-((3-acetylphenyl)amino)-4-oxobut-2-enoate



- 15 The compound according to the first or second aspect of the invention is for use in the treatment of a disease or condition for which a bromodomain inhibitor is indicated, wherein said disease or condition is cancer, an autoimmune disease or alzheimer's disease, in particular leukemia and more particularly an acute myeloid leukemia.

In some embodiments, said bromodomain is CBP or EP300.

- 20 A third aspect of the present invention relates to a method of treating a disease or condition for which a bromodomain inhibitor is indicated in a subject in need thereof which comprises administering a therapeutically effective amount of a compound, or salt or prodrug thereof, where said compound is characterized by the general formula (1), (2), (3), (4) or (5), particularly by the general formula (1), (2) or (3).
- 25 Concerning particular embodiments, reference is made to the detailed description of the first or second aspect of the invention.

A fourth aspect of the present invention relates to a pharmaceutical composition comprising a therapeutically effective amount of a compound of general formula (3), (4) or (5), particularly (3), and one or more pharmaceutically acceptable carriers, diluents or excipients.

- 30 In some embodiments, the pharmaceutical preparation further comprises at least one pharmaceutically acceptable carrier. Furthermore, the invention relates to pharmaceutical

preparations comprising at least one compound mentioned hereinbefore as active ingredient, which can be used especially in the treatment of the diseases mentioned. The pharmaceutical preparations may be used in particular for a method for treatment of cancer.

In some embodiments, the pharmaceutical preparations are for enteral administration, such as nasal, buccal, rectal or, especially, oral administration, and for parenteral administration, such as intravenous, intramuscular or subcutaneous administration, to mammals, in particular humans, are especially preferred. The dosage of the active ingredient depends upon the disease to be treated and upon the species, its age, weight, and individual condition, the individual pharmacokinetic data, and the mode of administration. In some
5 embodiments, the pharmaceutical preparations comprise from approximately 1% to approximately 95% active ingredient. Unit dose forms are, for example, coated and uncoated tablets, ampoules, vials, suppositories, or capsules. Further dosage forms are, for example, ointments, creams, pastes, foams, tinctures, lipsticks, drops, sprays, dispersions, etc.

In some embodiments, the pharmaceutical preparations of the present invention are
15 prepared in a manner known *per se*, for example by means of conventional mixing, granulating, coating, dissolving or lyophilizing processes.

In some embodiments, the pharmaceutical preparations are in form of solutions of the active ingredient, and also suspensions or dispersions, especially isotonic aqueous solutions, dispersions or suspensions which, for example in the case of lyophilized preparations
20 comprising the active ingredient alone or together with a carrier, for example mannitol, can be made up before use.

In some embodiments, the pharmaceutical preparations may be sterilized and/or may comprise excipients, for example preservatives, stabilizers, wetting agents and/or emulsifiers, solubilizers, salts for regulating osmotic pressure and/or buffers and are
25 prepared in a manner known *per se*, for example by means of conventional dissolving and lyophilizing processes. The said solutions or suspensions may comprise viscosity-increasing agents, typically sodium carboxymethylcellulose, carboxymethylcellulose, dextran, polyvinylpyrrolidone, or gelatins, or also solubilizers, e.g. Tween 80® (polyoxyethylene(20)sorbitan mono-oleate).

In some embodiments, the pharmaceutical preparation comprises suspensions in oil, which
30 comprise as the oil component a vegetable, synthetic- or semi-synthetic oils customary for injection purposes.

In some embodiments, the pharmaceutical preparation comprises liquid fatty acid esters that contain as the acid component a long-chained fatty acid having from 8 to 22, especially from
35 12 to 22, carbon atoms. The alcohol component of these fatty acid esters has a maximum of

6 carbon atoms and is monovalent or polyvalent, for example a mono-, di- or trivalent, alcohol, especially glycol and glycerol.

In some embodiments, the pharmaceutical preparation comprises a mixture of fatty acid esters, vegetable oils such as, without being limited to, cottonseed oil, almond oil, olive oil, castor oil, sesame oil, soybean oil and groundnut oil.

Suitable carriers are especially fillers, such as sugars, for example lactose, saccharose, mannitol or sorbitol, cellulose preparations, and/or calcium phosphates, for example tricalcium phosphate or calcium hydrogen phosphate, and also binders, such as starches, for example corn, wheat, rice or potato starch, methylcellulose, hydroxypropyl methylcellulose, sodium carboxymethylcellulose, and/or polyvinylpyrrolidone, and/or, if desired, disintegrators, such as the above-mentioned starches, also carboxymethyl starch, crosslinked polyvinyl pyrrolidone, alginic acid or a salt thereof, such as sodium alginate. Additional excipients are especially flow conditioners and lubricants, for example silicic acid, talc, stearic acid or salts thereof, such as magnesium or calcium stearate, and/or polyethylene glycol, or derivatives thereof.

Tablet cores can be provided with suitable, optionally enteric, coatings through the use of, inter alia, concentrated sugar solutions which may comprise gum arabic, talc, polyvinylpyrrolidone, polyethylene glycol and/or titanium dioxide, or coating solutions in suitable organic solvents or solvent mixtures, or, for the preparation of enteric coatings, solutions of suitable cellulose preparations, such as acetylcellulose phthalate or hydroxypropylmethylcellulose phthalate. Dyes or pigments may be added to the tablets or tablet coatings, for example for identification purposes or to indicate different doses of active ingredient.

In some embodiments, the pharmaceutical preparation is suitable for oral administration also include hard capsules consisting of gelatin, and soft, sealed capsules consisting of gelatin and a plasticizer, such as glycerol or sorbitol. The hard capsules may contain the active ingredient in the form of granules, for example in admixture with fillers, such as corn starch, binders, and/or glidants, such as talc or magnesium stearate, and optionally stabilizers. In soft capsules, the active ingredient is preferably dissolved or suspended in suitable liquid excipients, such as fatty oils, paraffin oil or liquid polyethylene glycols or fatty acid esters of ethylene or propylene glycol, to which stabilizers and detergents, for example of the polyoxyethylene sorbitan fatty acid ester type, may also be added.

In some embodiments, the pharmaceutical preparation is suitable for rectal administration and is, for example, a suppository that consist of a combination of the active ingredient and a suppository base. Suitable suppository bases are, for example, natural or synthetic triglycerides, paraffin hydrocarbons, polyethylene glycols or higher alkanols.

In some embodiments, the pharmaceutical preparation is suitable for parenteral administration. Aqueous solutions of an active ingredient in water-soluble form or aqueous injection suspensions that contain viscosity-increasing substances, for example sodium carboxymethylcellulose, sorbitol and/or dextran, and, if desired, stabilizers, are especially suitable. The active ingredient, optionally together with excipients, can also be in the form of a lyophilizate and can be made into a solution before parenteral administration by the addition of suitable solvents. Solutions such as are used, for example, for parenteral administration can also be employed as infusion solutions.

A further aspect of the invention relates to a compound according to any of the claims or a pharmaceutical preparation according to the claims for use in a method of treatment of disease. The compounds of the general formula (1) have valuable pharmacological properties.

A further aspect relates to a bromodomain inhibitor comprising a compound according to the first or second aspect of the invention, in particular for use in the treatment of a disease or condition for which a bromodomain inhibitor is indicated, wherein said disease or condition is cancer, an autoimmune disease or alzheimer's disease, in particular leukemia and more particularly an acute myeloid leukemia.

In some embodiments, the said bromodomain is CBP or EP300.

Examples

All reactions, unless otherwise stated, were carried out under inert gas atmosphere using standard Schlenk-techniques. Reagents were used as received unless otherwise noted. Solvents were purchased in the best quality available, degassed by purging thoroughly with nitrogen and dried over activated molecular sieves of appropriate size. Alternatively, they were purged with argon and passed through alumina columns in a solvent purification system (Innovative Technology). Reactions were monitored by thin layer chromatography (TLC) using Merck TLC silica gel 60 F₂₅₄. Flash column chromatography was performed over silica gel (230-400 mesh). High-resolution electrospray ionization mass spectrometry was performed on a Finnigan MAT 900 (Thermo Finnigan, San Jose, CA, USA) double-focusing magnetic sector mass spectrometer. Ten spectra were acquired. A mass accuracy ≤ 2 ppm was obtained in the peak matching acquisition mode by using a solution containing 2 μ L PEG200, 2 μ L PPG450, and 1.5 mg NaOAc (all obtained from Sigma-Aldrich, Buchs, Switzerland) dissolved in 100 mL MeOH (HPLC Supra grade, Scharlau, E-Barcelona) as internal standard.

The following compounds were prepared according to previously reported procedures: 3-(1*H*-tetrazol-1-yl)benzoic acid (Khim. Geterotsikl, 1174-1179, 2011), 3-bromo-5-

(methoxycarbonyl)benzoic acid (WO2013037705 (A2), 2012), dimethyl 5-(hydroxymethyl)isophthalate (Angew. Chem. Int. Edit. 51: 10082-10085, 2012), dimethyl 5-(((tetrahydro-2H-pyran-2-yl)methyl)isophthalate (Chem-Eur. J. 19:12923-12923, 2013), 3-(methoxycarbonyl)-5-(methoxymethyl)benzoic acid (WO2005066155 (A1)), methyl 5-acetyl-2ethoxybenzoate (US2002164649 (A1), 2002), 5-acetyl-2-ethoxybenzoic acid (US6562830 (B1), 2003), 2,2-dimethyl-4-oxo-4H-benzo[d][1,3]dioxine-6-carboxylic acid (WO2005/97773 A1 2005), methyl 4-bromo-3-(dibromomethyl)benzoate (J. Org. Chem. 73, 4464, 2008) and methyl 4-bromo-3-formylbenzoate (J. Org. Chem. 73, 4464, 2008).

1. Synthesis of non-commercially available carboxylic acids

10 **3-(1H-Tetrazol-1-yl)benzoic acid:** White solid; Yield: 95 %; mp 174-176 °C; MS (ESI), *m/z*: calcd for $C_8H_5N_4O_2^-$, 189.0; found, 188.8.

3-Bromo-5-(methoxycarbonyl)benzoic acid was prepared using the reported procedure and used without further purification. The presence of the acid was confirmed by IR and MS. MS (ESI), *m/z*: calcd for $C_9H_6BrO_4^-$, 256.9; found, 256.8.

15 **Dimethyl 5-(hydroxymethyl)isophthalate:** White solid; Yield: 47 %; mp 106-108 °C; MS (ESI), *m/z*: calcd for $C_{11}H_{12}NaO_5^+$, 247.1; found, 246.9.

Dimethyl 5-(methoxymethyl)isophthalate: To a solution of dimethyl 5-(hydroxymethyl)isophthalate (150 mg, 0.669 mmol) in DMF (1.50 mL) NaH (53.5 mg, 1.34 mmol) was added and stirred at 25 °C for 30 minutes. Methyl iodide (83.3 μ L, 1.34 mmol) was added and the reaction mixture stirred for 3 hours at 25 °C. The reaction was quenched by addition of 1 M HCl solution and extracted with EtOAc three times. The combined organic phases were dried over $MgSO_4$ and concentrated under reduced pressure. The residue was then purified by flash column chromatography (hexane: EtOAc, 3:1) affording the desired product in pure form as a white solid (133 mg, 0.558 mmol, 83 % yield). mp 83-85 °C; MS (ESI), *m/z*: calcd for $C_{12}H_{14}NaO_5^+$, 261.1; found, 261.0.

Dimethyl 5-((tetrahydro-2H-pyran-2-yl)methyl)isophthalate: White solid; Yield: 87 %; mp 45-48 °C; MS (ESI), *m/z*: calcd for $C_{16}H_{20}NaO_6^+$, 331.1; found, 331.1.

3-(Methoxycarbonyl)-5-(methoxymethyl)benzoic acid was prepared using the reported procedure and used without further purification. The presence of the acid was confirmed by IR and MS. MS (ESI), *m/z*: calcd for $C_{11}H_{11}O_5^-$, 223.1; found, 222.9.

3-(Methoxycarbonyl)-5-(((tetrahydro-2H-pyran-2-yl)oxy)methyl)benzoic acid: To a solution of dimethyl 5-((tetrahydro-2H-pyran-2-yl)methyl)isophthalate (150 mg, 0.486 mmol), 1M NaOH solution (0.486 mL, 0.486 mmol) was added and stirred at 25 °C for 12 hours. The pH of the reaction mixture was then adjusted to 3-4 by adding 10 % citric acid solution and

extracted with EtOAc three times and brine. The combined organic phases were dried over MgSO_4 and concentrated under reduced pressure. The residue was then purified by flash column chromatography (5% MeOH in DCM) affording the desired product in pure form as a white solid (102 mg, 0.347 mmol, 72 %). mp 87-93 °C; MS (ESI), m/z : calcd for $\text{C}_{15}\text{H}_{18}\text{NaO}_6^+$, 317.0996; found, 317.0994.

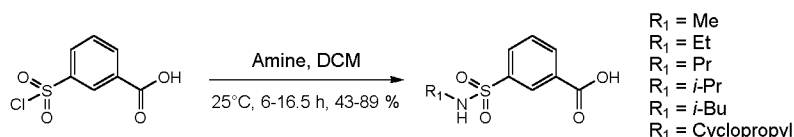
Methyl 5-acetyl-2-ethoxybenzoate: White solid; Yield: 88 %; mp 50-53 °C; MS (ESI), m/z : calcd for $\text{C}_{12}\text{H}_{14}\text{NaO}_4^+$, 245.1; found, 244.9.

5-Acetyl-2-ethoxybenzoic acid: Pale yellow solid; Yield: 77 %; mp 118-121 °C; MS (ESI), m/z : calcd for $\text{C}_{11}\text{H}_{11}\text{NaO}_4^+$, 230.1; found, 230.9.

Dimethyl 5-(benzyloxy)isophthalate: To a stirred solution of dimethyl 5-hydroxyisophthalate (8 g, 38 mmol) in dry DMF (190 mL) K_2CO_3 (7.9 g, 57 mmol) and BnBr (4.5 mL, 38 mmol) were added. The mixture was stirred for 2 hours at 25 °C and heated at 80 °C for 2 hours. The reaction was cooled to room temperature and water was added. The resulting precipitate was filtered, washed with water and dried to afford the product in pure form as a white solid (10.35 g, 34.5 mmol, 91 % yield). Mp 89-92 °C.

3-(Benzyloxy)-5-(methoxycarbonyl)benzoic acid: To a stirred solution of dimethyl 5-(benzyloxy)isophthalate (5.37 g, 18 mmol) in a mixture of acetone and methanol (182 mL, 1:1 v/v) NaOH (750 mg, 18 mmol, 1 M in water) was added. The reaction mixture was stirred at 25 °C for 15 h and concentrated under reduced pressure. The residue was diluted with water and quenched with HCl (1 M). The resulting precipitate was filtered, washed with water and dried to afford the product in pure form as a white solid (5.15 g, 0.179 mmol, 99 % yield). Mp 235-237 °C.

General procedure for the synthesis of sulfonamide benzoic acids

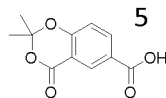


To a stirred solution of 3-(chlorosulfonyl)benzoic acid (1.0 eq.) in DCM (0.30 M), the amine (2.5 eq.) was added dropwise. The reaction was stirred at 25 °C for 6-16.5 h and it was then concentrated under reduced pressure. The residue was diluted with water and HCl (1 M) was added. The resulting precipitate was filtered, washed with water and dried to afford the pure sulfonamide benzoic acids.

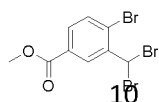
3-(N-Methylsulfamoyl)benzoic acid: White solid; Yield: 43 %; mp 211-213 °C. **3-(N-Ethylsulfamoyl)benzoic acid:** White solid; Yield: 44 %; mp 198-199 °C. **3-(N-Propylsulfamoyl)benzoic acid:** White solid; Yield: 85 %; mp 196-197 °C. **3-(N-**

Isopropylsulfamoyl)benzoic acid: White solid; Yield: 73 %; mp 165-168 °C. **3-(*N*-Isobutylsulfamoyl)benzoic acid:** White solid; Yield: 88 %; mp 212-214 °C. **3-(*N*-Cyclopropylsulfamoyl)benzoic acid:** White solid; Yield: 89 %; mp 226-227 °C.

2,2-Dimethyl-4-oxo-4*H*-benzo[d][1,3]dioxine-6-carboxylic acid was prepared using the reported procedure. White solid; Yield: 79%; mp: 236-238 °C.

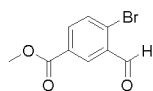


Methyl 4-bromo-3-(dibromomethyl)benzoate was prepared using the reported procedure.

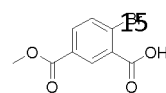


Off-white solid; Yield: 65%; mp 85-89 °C.

Methyl 4-bromo-3-formylbenzoate was prepared using the reported procedure. White solid; Yield: 90%; mp 66-70 °C.

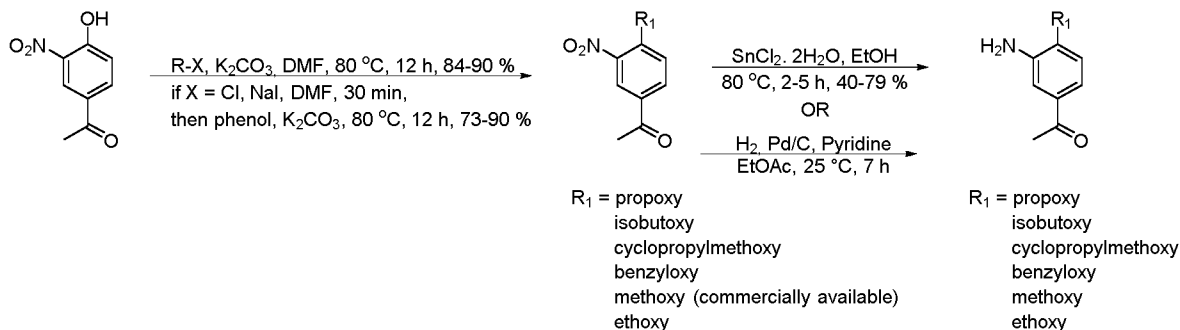


2-Bromo-5-(methoxycarbonyl)benzoic acid



To a solution of methyl 4-bromo-3-formylbenzoate (1.00 g, 4.11 mmol) and sulfamic acid (0.60 g, 6.17 mmol) in dioxane (34.0 mL) and water (13.6 mL) a solution of sodium chlorite (0.48 g, 5.35 mmol) in water (3.4 mL) was added at 0 °C. The reaction mixture was stirred at 0 °C for 1 hour and concentrated HCl was added to afford pH1. The reaction mixture was concentrated, diluted with water and extracted it with EtOAc three times. The combined organic phases were dried over MgSO₄ and concentrated under reduced pressure affording the desired acid as a white solid in pure form. Yield: 66%; mp 162-166 °C.

2. Synthesis of non-commercially available anilines



General procedure for ether synthesis

To a solution of 1-(4-hydroxy-3-nitrophenyl)ethan-1-one (1.0 eq) in DMF (0.30 M), the alkyl iodide (1.2 eq) and K₂CO₃ (4.0 eq) were added. The reaction mixture was stirred at 80 °C for 12 h. A saturated solution of NH₄Cl was added and it was extracted with Et₂O three times. The combined organic phases were dried over MgSO₄ and concentrated under reduced

pressure. The obtained residue was purified by flash column chromatography (2:1, hexane:EtOAc) affording the desired products in pure form. In the case of alkyl chlorides (products 1-(4-isobutoxy-3-nitrophenyl)ethan-1-one and 1-(4-(cyclopropylmethoxy)-3-nitrophenyl)ethan-1-one), the alkyl chloride (2.0 eq) was first stirred in DMF (0.30 M) in the presence of NaI (2.0 eq) for 30 min. The phenol (1.0 eq) and K₂CO₃ (4.0 eq) were then added and the same procedure as the one described above was followed.

1-(3-Nitro-4-propoxyphenyl)ethan-1-one: White solid; Yield: 84 %; mp 57-60 °C; MS (ESI), *m/z*: calcd for C₁₁H₁₄NO₄⁺, 224.0917; found, 224.0918. **1-(4-Isobutoxy-3-nitrophenyl)ethan-1-one:** Pale yellow solid; Yield: 90 %; mp 61-63 °C; MS (ESI), *m/z*: calcd

for C₁₂H₁₆NO₄⁺, 238.1074; found, 238.1077. **1-(4-(Cyclopropylmethoxy)-3-nitrophenyl)ethan-1-one:** Yellow solid; Yield: 73 %; mp 74-77 °C; MS (ESI), *m/z*: calcd for

C₁₂H₁₄NO₄⁺, 236.0917; found, 236.0918. **1-(4-(Benzyloxy)-3-nitrophenyl)ethan-1-one:** Pale yellow solid; Yield: 90 %; mp 132-135 °C; MS (ESI), *m/z*: calcd for C₁₅H₁₄NO₄⁺, 272.0917; found, 272.0917. **1-(4-ethoxy-3-nitrophenyl)ethan-1-one:** Beige solid; Yield: 81

% yield; mp: 58-62 °C.

Reduction of Nitro phenyls

1-(3-amino-4-ethoxyphenyl)ethan-1-one: To a stirred solution of 1-(4-ethoxy-3-nitrophenyl)ethan-1-one (10 g, 48 mmol) in EtOAc (230 mL), was added Pd/C (2.6 g, 2.4 mmol, 10 % w. Pd) portionwise and pyridine (390 µL, 0.48 mmol). Nitrogen gas was bubbled in the flask and through the mixture and two balloons of H₂ were added. The reaction was stirred for 7 hours at 25 °C, it was filtered over a short pad of Celite® and washed with MeOH. The filtrate was evaporated to afford the desired aniline as a brown solid in pure form (8.44 g, 47 mmol, 98 % yield. Mp 83-85 °C.

General procedure for the reduction of nitro phenyls

To a mixture of nitrophenyl (1 eq) in EtOH (0.3 M) was added SnCl₂ · 2H₂O (4 eq). The reaction mixture was heated to 80 °C for 2-5 h, cooled, and concentrated under reduced pressure. The pH was basified to pH 5 by the addition of a 5 M NaOH solution. The resulting precipitate was filtered off and washed with EtOAc. The organic layer was washed with brine, dried over MgSO₄, filtered, and concentrated under reduced pressure. The obtained residue was purified by flash column chromatography (hex: EtOAc, 3:1-1:1) affording the desired anilines in pure form.

1-(3-Amino-4-propoxyphenyl)ethan-1-one: Brown solid; Yield: 40%; mp 53-55 °C; MS (ESI), *m/z*: calcd for C₁₁H₁₆NO₂⁺, 194.1176; found, 194.1179. **1-(3-Amino-4-isobutoxyphenyl)ethan-1-one:** Brown-red oil; Yield: 53 %; MS (ESI), *m/z*: calcd for

C₁₂H₁₈NO₂⁺, 208.1332; found, 208.1334. **1-(3-Amino-4-**

(cyclopropylmethoxy)phenyl)ethan-1-one: Brown solid; Yield: 61 %; mp 44-46 °C; MS (ESI), m/z : calcd for $C_{12}H_{16}NO_2^+$, 206.1176; found, 206.1175. **1-(3-Amino-4-(benzyloxy)phenyl)ethan-1-one:** Yellow solid; Yield: 53 %; mp 119-122 °C; MS (ESI), m/z : calcd for $C_{15}H_{16}NO_2^+$, 242.1176; found, 242.1176.

5 **1-(3-Amino-4-morpholinophenyl)ethan-1-one:** A solution of 1-(4-Bromo-3-nitrophenyl)ethanone (500 mg, 2.05 mmol) in isopropanol (5.00 mL) was heated at 110 °C for 3 h. $SnCl_2 \cdot 2H_2O$ (1.80 g, 7.98 mmol) was then added and heated at 110 °C for 5 h. The reaction mixture was concentrated under reduced pressure and the pH was basified to pH 5 by the addition of a 5 M NaOH solution. The resulting precipitate was filtered off and washed
10 with EtOAc. The organic layer was washed with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The obtained residue was purified by flash column chromatography (hex: EtOAc, 1:1) affording the desired aniline in pure form as a brown solid (145 mg, 0.579 mmol, 32 % yield over two steps). Mp 141-144 °C; MS (ESI), m/z : calcd for $C_{12}H_{17}N_2O_2^+$, 221.1285; found, 221.1283.

15 **3-Amino-4-ethoxy-N-methylbenzamide:** To a solution of 3-amino-4-ethoxybenzoic acid (**66**, 100 mg, 0.552 mmol) in DMF (1.80 mL), methylamine hydrochloride (150 mg, 2.22 mmol), HOBt (89.4 mg, 0.662 mmol), EDC.HCl (1.104 mmol, 212 mg) and DIPEA (385 μ L, 2.21 mmol) were added. The solution was stirred at 55 °C for 12 h, it was concentrated and purified by flash column chromatography (5 % MeOH in DCM) affording the desired amide as
20 a white solid in pure form (75.0 mg, 0.384 mmol, 70 % yield). Mp 142-145 °C; MS (ESI), m/z : calcd for $C_{10}H_{15}N_2O_2^+$, 195.1128; found, 195.1129.

1-(3-Amino-4-methoxyphenyl)ethan-1-one: Light yellow solid; Yield: 48 %; mp 96-99 °C; MS (ESI), m/z : calcd for $C_9H_{11}NNaO_2^+$, 188.1; found, 187.9.

3. Amide coupling reactions

25 **General procedure A for amide formation**

The desired aniline (1.0 eq) and carboxylic acid (1.2 or 1.3 eq) were dissolved in DMF (0.10 M) and EDC.HCl (1.5-2.0 eq), DIPEA (1.5 eq) and HOBt (1.5-2 eq) were added at 25 °C. In the case of methyl 3-((5-acetyl-2-ethoxyphenyl)carbamoyl)benzoate, methyl 3-((5-acetyl-2-ethoxyphenyl)carbamoyl)-5-(methoxymethyl)benzoate, methyl 3-((5-acetyl-2-ethoxyphenyl)
30 carbamoyl)-5-bromobenzoate and methyl (*E*)-4-((5-acetyl-2-methoxyphenyl)amino)-4-oxobut-2-enoate, EDC (1.5-2.0 eq) and no DIPEA was used. The reaction mixture was stirred for 12-48 h at 25 °C, it was concentrated and redissolved in EtOAc. The organic phase was extracted with saturated $NaHCO_3$ solution, 1M HCl and brine. The combined organic phases were dried over $MgSO_4$ and concentrated under reduced pressure. The obtained residue
35 was purified by flash column chromatography (using 1:1 hex: EtOAc, EtOAc or 2:1

EtOAc:hex as eluent), affording the desired amides in pure form. This method was used to obtain methyl 3-((5-acetyl-2-ethoxyphenyl)carbamoyl)benzoate (**19**), methyl 3-((2-ethoxy-5-(methylcarbamoyl)phenyl)carbamoyl)benzoate, methyl 2-((5-acetyl-2-ethoxyphenyl)carbamoyl)benzoate, methyl 3-((5-acetyl-2-ethoxyphenyl)carbamoyl)-5-bromobenzoate, methyl 3-((5-acetyl-2-ethoxyphenyl)carbamoyl)-5-(methoxymethyl)benzoate, methyl 3-((5-acetyl-2-ethoxyphenyl)carbamoyl)-5-(((tetrahydro-2H-pyran-2-yl)oxy)methyl)benzoate (**20**), methyl (*E*)-4-((5-acetyl-2-methoxyphenyl)amino)-4-oxobut-2-enoate, methyl (*E*)-4-((3-acetylphenyl)amino)-4-oxobut-2-enoate, N-(5-acetyl-2-ethoxyphenyl)-3-(N-methylsulfamoyl)benzamide (**21**), N-(5-acetyl-2-ethoxyphenyl)-3-(Nethylsulfamoyl)benzamide (**22**), N-(5-acetyl-2-ethoxyphenyl)-3-(N-propylsulfamoyl)benzamide (**23**), N-(5-acetyl-2-ethoxyphenyl)-3-N-isopropylsulfamoyl)benzamide (**25**), N-(5-acetyl-2-ethoxyphenyl)-3-(N-isobutylsulfamoyl)benzamide (**24**), N-(5-acetyl-2-ethoxyphenyl)-3-(N-cyclopropylsulfamoyl)benzamide (**26**), methyl 3-((5-acetyl-2-ethoxyphenyl)carbamoyl)-5-(benzyloxy)benzoate and N-(5-acetyl-2-ethoxyphenyl)-2,2-dimethyl-4-oxo-4*H*-benzo[d][1,3]dioxine-6-carboxamide (**30**).

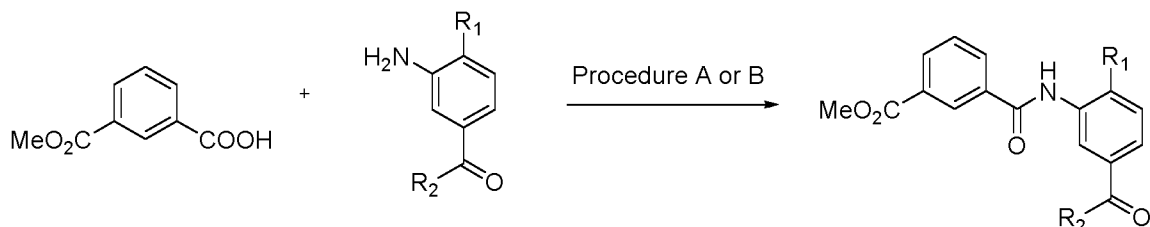
For the synthesis of N-(5-acetyl-2-ethoxyphenyl)-3-cyanobenzamide, methyl 6-((5-acetyl-2-ethoxyphenyl)carbamoyl)picolinate and N-(5-acetyl-2-ethoxyphenyl)-3-bromo-5-iodobenzamide, when the reaction was completed according to TLC, water was added and the resulting precipitate was filtered, washed with water and dried to afford the desired amide in pure form. In the case of N-(5-acetyl-2-ethoxyphenyl)-2,2-dimethyl-4-oxo-4*H*-benzo[d][1,3]dioxine-6-carboxamide, upon the addition of Et₂O after work-up, the desired amide precipitated. It was filtered off and washed with Et₂O affording the coupling product in pure form.

General procedure B for amide formation

To a solution of the carboxylic acid (1.0 eq) in toluene (1.0 M) thionyl chloride (2.0 eq) and one drop of DMF were added. The solution was refluxed for 3 h, concentrated and dissolved in DCM (0.50 M). The corresponding aniline (1.2 eq) was added and the reaction mixture was stirred at 25 °C for 12h. The reaction mixture was concentrated and purified by flash column chromatography (hex:EtOAc, 2:1) obtaining the desired amides in pure form. This method was used to obtain intermediates methyl 3-((5-acetyl-2-bromophenyl)carbamoyl)benzoate, methyl 3-((5-acetyl-2-propoxyphenyl)carbamoyl)benzoate, methyl 3-((5-acetyl-2-isobutoxyphenyl)carbamoyl)benzoate, methyl 3-((5-acetyl-2-(cyclopropylmethoxy)phenyl)carbamoyl)benzoate, methyl 3-((5-acetyl-2-(benzyloxy)phenyl)carbamoyl)benzoate, methyl 3-((5-acetyl-2-morpholinophenyl)carbamoyl)benzoate, methyl 3-(5-acetyl-2-ethoxybenzamido)benzoate, methyl 3-((5-acetyl-2-ethoxyphenyl)carbamoyl)-5-nitrobenzoate and methyl 3-((5-acetyl-2-ethoxyphenyl)carbamoyl)-4-bromobenzoate.

In the case of methyl 3-((5-acetyl-2-ethoxyphenyl)carbamoyl)-5-nitrobenzoate and methyl 3-((5-acetyl-2-ethoxyphenyl)carbamoyl)-4-bromobenzoate, after work up, Et₂O was added to the obtained residue and the desired amides precipitated. It was filtered off and washed with Et₂O affording the desired products in pure form.

5 3.1 Synthesis of benzoic acid derivatives. Scope on the acyl benzene



R₁ = OEt, R₂ = Me (commercially available)

R₁ = Br, R₂ = Me (commercially available)

R₁ = OPr, R₂ = Me

R₁ = OⁱBu, R₂ = Me

R₁ = , R₂ = Me

R₁ = OBenzyl, R₂ = Me

R₁ = morpholine, R₂ = Me

R₁ = OEt, R₂ = NHMe

R₁ = OEt, R₂ = Me

R₁ = Br, R₂ = Me

R₁ = OPr, R₂ = Me

R₁ = OⁱBu, R₂ = Me

R₁ = , R₂ = Me

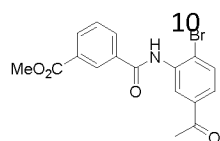
R₁ = OBenzyl, R₂ = Me

R₁ = morpholine, R₂ = Me

R₁ = OEt, R₂ = NHMe

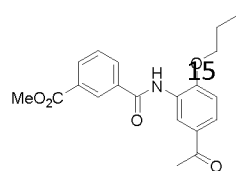
Methyl 3-((5-acetyl-2-ethoxyphenyl)carbamoyl)benzoate (**19**): White solid; Yield: 80%; mp 137-140 °C; MS (ESI), *m/z*: calcd for C₁₉H₂₀NO₅⁺, 342.1336; found, 342.1331.

Methyl 3-((5-acetyl-2-bromophenyl)carbamoyl)benzoate



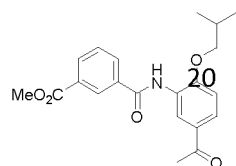
White solid; Yield: 60 %; mp 133-135 °C; MS (ESI), *m/z*: calcd for C₁₇H₁₄BrNNaO₄⁺, 397.9998; found, 397.9996.

Methyl 3-((5-acetyl-2-propoxyphenyl)carbamoyl)benzoate

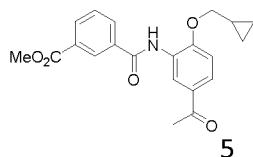


White solid; Yield: 40 %; mp 132-135 °C; MS (ESI), *m/z*: calcd for C₂₀H₂₂NO₅⁺, 356.1493; found, 356.1493.

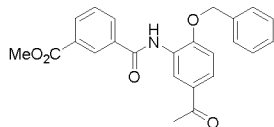
Methyl 3-((5-acetyl-2-isobutoxyphenyl)carbamoyl)benzoate



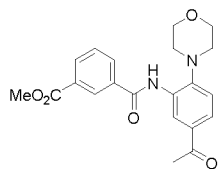
Beige solid; Yield: 89 %; mp 116-119 °C; MS (ESI), *m/z*: calcd for C₂₁H₂₄NO₅⁺, 370.1649; found, 370.1649.

Methyl 3-((5-acetyl-2-(cyclopropylmethoxy)phenyl)carbamoyl)benzoate

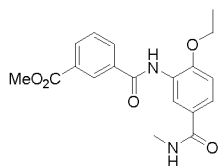
Pale yellow solid; Yield: 91 %; mp 141-142 °C; MS (ESI), m/z : calcd for $C_{21}H_{22}NO_5^+$, 368.1493; found, 368.1495.

Methyl 3-((5-acetyl-2-(benzyloxy)phenyl)carbamoyl)benzoate

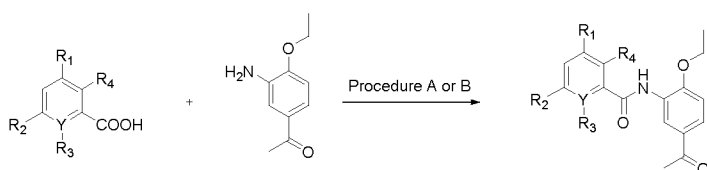
White solid; Yield: 74 %; mp 149-152 °C; MS (ESI), m/z : calcd for $C_{24}H_{21}NNaO_5^+$, 426.1312; found, 426.1307.

10 Methyl 3-((5-acetyl-2-morpholinophenyl)carbamoyl)benzoate

Pale yellow solid; Yield: 95 %; mp 152-155 °C; MS (ESI), m/z : calcd for $C_{21}H_{23}N_2O_5^+$, 383.1602; found, 383.1602.

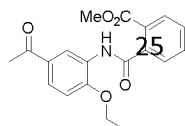
15 Methyl 3-((2-ethoxy-5-(methylcarbamoyl)phenyl)carbamoyl)benzoate

White solid; Yield: 66 %; mp 161-163 °C; MS (ESI), m/z : calcd for $C_{19}H_{20}N_2NaO_5^+$, 379.1264; found, 379.1262.

20 3.3 Synthesis of benzoic acid derivatives. Scope on the side chain

$R_1 = H, R_2 = H, R_3 = CO_2Me$ (commercially available), $Y = C, R_4 = H$
 $R_1 = H, R_2 = \text{tetrazole}, R_3 = H, Y = C, R_4 = H$
 $R_1 = Br, R_2 = CO_2Me, R_3 = H, Y = C, R_4 = H$
 $R_1 = CH_2OMe, R_2 = CO_2Me, R_3 = H, Y = C, R_4 = H$
 $R_1 = CH_2OTHP, R_2 = CO_2Me, R_3 = H, Y = C, R_4 = H$
 $R_1 = OBenzyl, R_2 = CO_2Me, R_3 = H, Y = C, R_4 = H$
 $R_1 = H, R_2 = CO_2Me, Y = N, R_4 = H$
 $R_1 = NO_2, R_2 = CO_2Me, R_3 = H, Y = C, R_4 = H$
 $R_1 = H, R_2 = CO_2Me, R_3 = H, Y = C, R_4 = Br$
 $R_1 = H, R_2 = SO_2NHMe, R_3 = H, Y = C, R_4 = H$
 $R_1 = H, R_2 = SO_2NHMe, R_3 = H, Y = C, R_4 = H$
 $R_1 = H, R_2 = SO_2NHPr, R_3 = H, Y = C, R_4 = H$
 $R_1 = H, R_2 = SO_2NH*i*-Pr, R_3 = H, Y = C, R_4 = H$
 $R_1 = H, R_2 = SO_2NH*i*-Bu, R_3 = H, Y = C, R_4 = H$
 $R_1 = H, R_2 = SO_2NHCyclopropyl, R_3 = H, Y = C, R_4 = H$

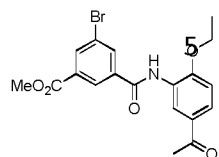
$R_1 = H, R_2 = H, R_3 = CO_2Me, Y = C, R_4 = H$
 $R_1 = H, R_2 = \text{tetrazole}, R_3 = H, Y = C, R_4 = H$
 $R_1 = Br, R_2 = CO_2Me, R_3 = H, Y = C, R_4 = H$
 $R_1 = CH_2OMe, R_2 = CO_2Me, R_3 = H, Y = C, R_4 = H$
 $R_1 = CH_2OTHP, R_2 = CO_2Me, R_3 = H, Y = C, R_4 = H$
 $R_1 = OBenzyl, R_2 = CO_2Me, R_3 = H, Y = C, R_4 = H$
 $R_1 = H, R_2 = CO_2Me, Y = N, R_4 = H$
 $R_1 = NO_2, R_2 = CO_2Me, R_3 = H, Y = C, R_4 = H$
 $R_1 = H, R_2 = CO_2Me, R_3 = H, Y = C, R_4 = Br$
 $R_1 = H, R_2 = SO_2NHMe, R_3 = H, Y = C, R_4 = H$
 $R_1 = H, R_2 = SO_2NHMe, R_3 = H, Y = C, R_4 = H$
 $R_1 = H, R_2 = SO_2NHPr, R_3 = H, Y = C, R_4 = H$
 $R_1 = H, R_2 = SO_2NH*i*-Pr, R_3 = H, Y = C, R_4 = H$
 $R_1 = H, R_2 = SO_2NH*i*-Bu, R_3 = H, Y = C, R_4 = H$
 $R_1 = H, R_2 = SO_2NHCyclopropyl, R_3 = H, Y = C, R_4 = H$

Methyl 2-((5-acetyl-2-ethoxyphenyl)carbamoyl)benzoate

Yield: 40 %; mp 130-134 °C; MS (ESI), m/z : calcd for $C_{19}H_{19}NNaO_5^+$, 364.1155; found, 364.1155.

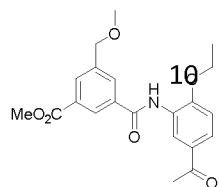
N-(5-Acetyl-2-ethoxyphenyl)-3-(1H-tetrazol-1-yl)benzamide (9) Brown solid; Yield: 98 %; mp 168-169 °C; MS (ESI), m/z : calcd for $C_{18}H_{18}N_5O_3^+$, 352.1404; found, 352.1404.

Methyl 3-((5-acetyl-2-ethoxyphenyl)carbamoyl)-5-bromobenzoate



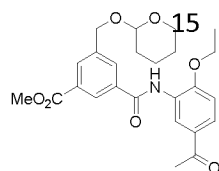
Pale yellow solid; Yield: 44 % over two steps; mp 159-161 °C; MS (ESI), m/z : calcd for $C_{19}H_{18}BrNNaO_5^+$, 442.0261; found, 442.0264.

Methyl 3-((5-acetyl-2-ethoxyphenyl)carbamoyl)-5-(methoxymethyl)benzoate



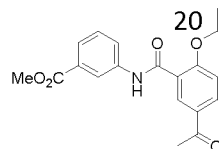
White solid; Yield: 17 % over two steps; mp 123-125 °C; MS (ESI), m/z : calcd for $C_{21}H_{24}NO_6^+$, 386.1598; found, 386.1596.

Methyl 3-((5-acetyl-2-ethoxyphenyl)carbamoyl)-5-(((tetrahydro-2H-pyran-2-yl)oxy)methyl)benzoate



White solid; Yield: 44 %; mp 133-135 °C; MS (ESI), m/z : calcd for $C_{25}H_{29}NnaO_7^+$, 478.1836; found, 478.1835.

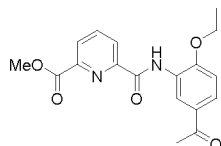
Methyl 3-(5-acetyl-2-ethoxybenzamido)benzoate



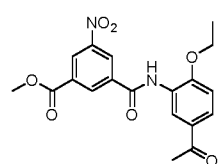
Pale yellow solid; Yield: 34 %; mp 128-130 °C; MS (ESI), m/z : calcd for $C_{19}H_{20}NO_5^+$, 342.1336; found, 342.1336.

Methyl 3-((5-acetyl-2-ethoxyphenyl)carbamoyl)-5-(benzyloxy)benzoate: White solid; Yield: 51 %; mp 141-142 °C.

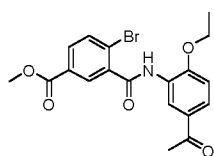
Methyl 6-((5-acetyl-2-ethoxyphenyl)carbamoyl)picolinate: White solid; Yield: 92 %; mp 176-177 °C.



Methyl 3-((5-acetyl-2-ethoxyphenyl)carbamoyl)-5-nitrobenzoate

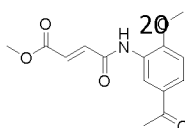
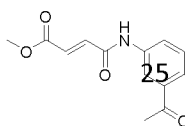
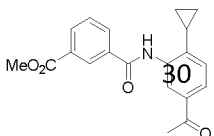


Light yellow solid; Yield: 75%; mp 165-171 °C.

Methyl 3-((5-acetyl-2-ethoxyphenyl)carbamoyl)-4-bromobenzoate

White solid; Yield: 72%; mp 160-164 °C.

5

N-(5-Acetyl-2-ethoxyphenyl)-2,2-dimethyl-4-oxo-4H-benzo[d][1,3]dioxine-6-**carboxamide (30).** White solid; Yield: 72 %; mp 154-159 °C. **N-(5-acetyl-2-ethoxyphenyl)-****3-(N-methylsulfamoyl)benzamide (21):** White solid; Yield: 75%; mp 128-131 °C. **N-(5-****acetyl-2-ethoxyphenyl)-3-(N-ethylsulfamoyl)benzamide (22):** White solid; Yield: 87 %; mp10 131-132 °C. **N-(5-acetyl-2-ethoxyphenyl)-3-(N-propylsulfamoyl)benzamide (23):** Whitesolid; Yield: 51 %; mp 132-134 °C. **N-(5-acetyl-2-ethoxyphenyl)-3-(N-****isopropylsulfamoyl)benzamide (25):** White solid; Yield: 71 %; mp 170-171 °C. **N-(5-acetyl-****2-ethoxyphenyl)-3-(N-isobutylsulfamoyl)benzamide (24):** White solid; Yield: 87 %; mp103-105 °C. **N-(5-acetyl-2-ethoxyphenyl)-3-(N-cyclopropylsulfamoyl)benzamide (26):**15 White solid; Yield: 72 %; mp 178-180 °C. **N-(5-acetyl-2-ethoxyphenyl)-3-cyanobenzamide:**White solid; Yield: 83 %; mp 161-164 °C. **N-(5-acetyl-2-ethoxyphenyl)-3-bromo-5-****iodobenzamide:** White solid; Yield: 92 %; mp: 179-181 °C.**3.2 Synthesis of fumaric acid derivatives****Methyl (E)-4-((5-acetyl-2-methoxyphenyl)amino)-4-oxobut-2-enoate**White solid; Yield: 35 %; mp 191-194 °C; MS (ESI), m/z : calcd for $C_{14}H_{16}NO_5^+$, 278.1023; found, 278.1022.**Methyl (E)-4-((3-acetylphenyl)amino)-4-oxobut-2-enoate**White solid; Yield: 50 %; mp 177-178 °C; MS (ESI), m/z : calcd for $C_{13}H_{14}NO_4^+$, 248.0917; found, 248.09144.**4. Suzuki cross-coupling reactions****Methyl 3-((5-acetyl-2-cyclopropylphenyl)carbamoyl)benzoate**To a solution of methyl 3-((5-acetyl-2-bromophenyl)carbamoyl)benzoate (33 mg, 0.088 mmol) in THF:H₂O (3:1, 0.22 M) was added Pd(OAc)₂ (2.0 mg, 0.0089 mmol), S-Phos (4.0 mg, 0.0097 mmol) and K₃PO₄ (68 mg,0.312 mmol). The solution was purged with N₂ and heated to 90 °C for 12 hours. The reaction mixture was diluted with water and extracted with EtOAc three times. The combined organic phases were dried over MgSO₄ and concentrated under reduced pressure. The residue was purified by flash column chromatography (1:1 hex:EtOAc) affording the final

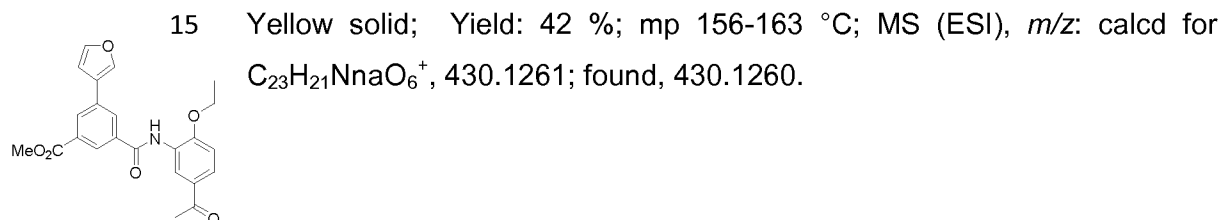
35

product in pure form as a pale brown solid (15 mg, 0.044 mmol, 51 % yield). Mp 125-130 °C; MS (ESI), m/z : calcd for $C_{20}H_{19}NNaO_4^+$, 360.1206; found, 360.1203.

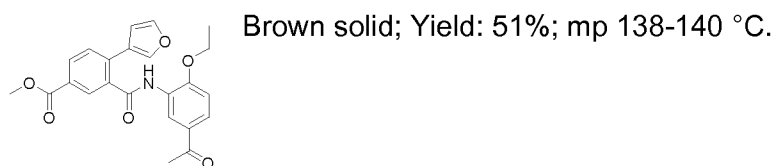
General procedure for Suzuki cross-couplings

To a solution of methyl 3-((5-acetyl-2-ethoxyphenyl)carbamoyl)-5-bromobenzoate in dioxane (0.24 M) and water (1 drop), the corresponding boronic acid (1.1 eq), K_2CO_3 (3.0 eq) and $Pd(PPh_3)_4$ (0.25 eq) were added. The reaction was stirred for 12 h at 90 °C. It was diluted with water and extracted with EtOAc three times. The combined organic phases were dried over $MgSO_4$ and concentrated under reduced pressure. The obtained residue was purified by flash column chromatography (hex: EtOAc, 2:1 to pure EtOAc) affording the coupled products. This procedure was used to obtain intermediates methyl 3-((5-acetyl-2-ethoxyphenyl)carbamoyl)-5-(furan-3-yl)benzoate and methyl 3-((5-acetyl-2-ethoxyphenyl)carbamoyl)-5-(pyridine-4-yl)benzoate. The last one was extracted and used in the next step without further purification.

Methyl 3-((5-acetyl-2-ethoxyphenyl)carbamoyl)-5-(furan-3-yl)benzoate



Methyl 3-((5-acetyl-2-ethoxyphenyl)carbamoyl)-4-(furan-3-yl)benzoate



25 **N-(5-acetyl-2-ethoxyphenyl)-3-cyano-5-(furan-3-yl)benzamide**: White solid; Yield: 46 %; mp: 208-209 °C.

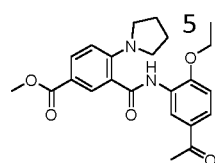
5. Buchwald-Hartwig Cross Coupling reactions

General procedure for the Buchwald-Hartwig Cross Coupling reaction

To a mixture of methyl 3-((5-acetyl-2-ethoxyphenyl)carbamoyl)-4-bromobenzoate in toluene (0.2 M), the desired amine (1.2 eq), (±)-BINAP (0.08 eq), Na^tOBu (1.0 eq) and $Pd_2(dba)_3$ (0.04 eq) were added. The reaction was purged with nitrogen and it was heated to reflux for 4-12 hours. The reaction mixture was cooled to room temperature and filtered through celite. The residue was diluted with water and extracted with EtOAc three times. The combined organic phases were dried over $MgSO_4$ and concentrated under reduced pressure. The obtained residue was purified by flash column chromatography (1:1, hexane:EtOAc)

affording the desired product in pure form. This procedure was used to obtain intermediates methyl 3-((5-acetyl-2-ethoxyphenyl)carbamoyl)-4-(pyrrolidin-1-yl)benzoate and Methyl 3-((5-acetyl-2-ethoxyphenyl)carbamoyl)-4-morpholinobenzoate.

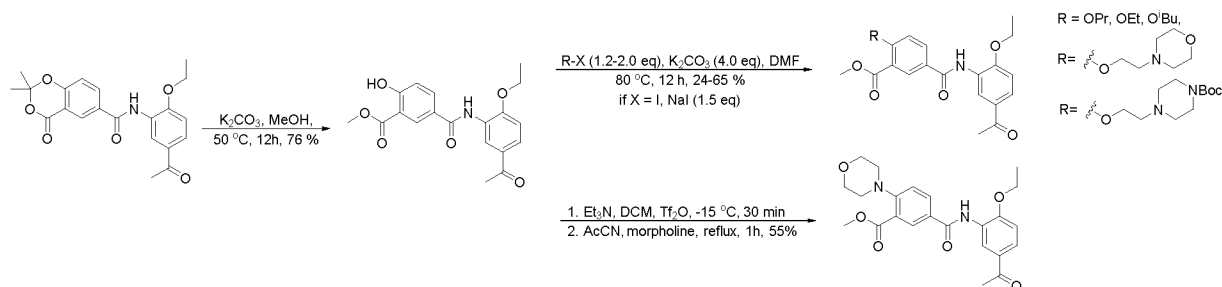
Methyl 3-((5-acetyl-2-ethoxyphenyl)carbamoyl)-4-(pyrrolidin-1-yl)benzoate



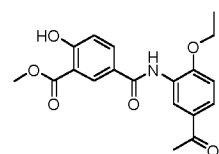
Light yellow solid; Yield: 37%; mp 159-168 °C.

Methyl 3-((5-acetyl-2-ethoxyphenyl)carbamoyl)-4-morpholinobenzoate (31) Light brown solid; Yield: 22%; mp 135-139 °C.

6. Etherification and substitution reactions on methyl 5-((5-acetyl-2-ethoxyphenyl)carbamoyl)-2-hydroxybenzoate



Methyl 5-((5-acetyl-2-ethoxyphenyl)carbamoyl)-2-hydroxybenzoate



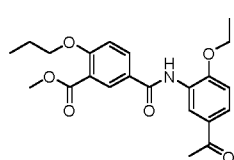
To a solution of *N*-(5-acetyl-2-ethoxyphenyl)-2,2-dimethyl-4-oxo-4*H*-benzo[d][1,3]dioxine-6-carboxamide (300 mg, 0.782 mmol) in MeOH (7.8 mL), K₂CO₃ (119 mg, 0.861 mmol) was added. The solution was heated to 50 °C for 12 hours and it was concentrated under reduced pressure. The obtained residue was dissolved in DCM and extracted with a saturated solution of NH₄Cl, 1M HCl and brine. The organic phase was dried over MgSO₄ and concentrated under reduced pressure. The desired phenol precipitated upon the addition of Et₂O. It was filtered and washed with Et₂O affording the product in pure form (76% yield, 212 mg, 0.593 mmol). Off-white solid; mp 209-213 °C.

General procedure for ether synthesis

To a solution of methyl 5-((5-acetyl-2-ethoxyphenyl)carbamoyl)-2-hydroxybenzoate (1.0 eq) in DMF (0.30 M), the alkyl iodide (1.2 eq) and K₂CO₃ (4.0 eq) were added. The reaction mixture was stirred at 80 °C for 12 h. In the case of the alkyl chlorides, 1.5-2 eq of the alkyl chloride, 1.5 eq of NaI and 4.0 eq of K₂CO₃ were added. Upon completion of the reaction, a saturated solution of NH₄Cl was added and it was extracted with DCM three times. The

combined organic phases were dried over MgSO_4 and concentrated under reduced pressure. The product precipitated upon the addition of Et_2O and it was filtered off affording the desired compound in pure form. For *tert*-butyl 4-(2-(4-((5-acetyl-2-ethoxyphenyl)carbamoyl)-2-(methoxycarbonyl)phenoxy)ethyl)piperazine-1-carboxylate, the product was purified by flash column chromatography (4% MeOH in DCM) and the alkyl chloride was previously prepared as follow: To a stirred solution of *tert*-butyl 4-(2-hydroxyethyl)piperazine-1-carboxylate (890 mg, 3.9 mmol) in DCM (10 mL) at 0 °C, was added Et_3N (800 μL , 5.8 mmol) and MeSO_2Cl (452 μL , 4.6 mmol). After 16 hours, the mixture was washed with brine and evaporated. The resulting solid was used as such without further purification.

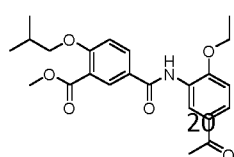
10 **Methyl 5-((5-acetyl-2-ethoxyphenyl)carbamoyl)-2-propoxybenzoate**



Pale yellow solid; Yield: 65%; mp 143-145 °C.

15 **Methyl 5-((5-acetyl-2-ethoxyphenyl)carbamoyl)-2-ethoxybenzoate (32)** Pale yellow solid; Yield: 49%; mp 142-145 °C.

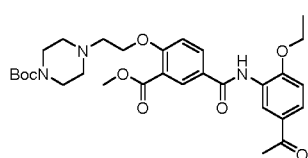
Methyl 5-((5-acetyl-2-ethoxyphenyl)carbamoyl)-2-isobutoxybenzoate



White solid; Yield: 24%; mp 140-145 °C.

Methyl 5-((5-acetyl-2-ethoxyphenyl)carbamoyl)-2-(2-morpholinoethoxy)benzoate (33) White solid; Yield: 52%; mp 130-136 °C.

25 ***Tert*-butyl 4-(2-(4-((5-acetyl-2-ethoxyphenyl)carbamoyl)-2-(methoxycarbonyl)phenoxy)ethyl)piperazine-1-carboxylate**



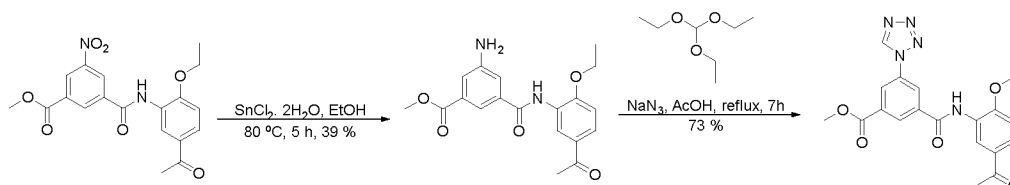
Pale yellow solid; Yield: 59%; mp 115-120 °C.

30 **Methyl 5-((5-acetyl-2-ethoxyphenyl)carbamoyl)-2-(2-(piperazin-1-yl)ethoxy)benzoate (34)** To a solution of *tert*-butyl 4-(2-(4-((5-acetyl-2-ethoxyphenyl)carbamoyl)-2-(methoxycarbonyl)phenoxy)ethyl)piperazine-1-carboxylate (140 mg, 0.246 mmol) in DCM (4.4 mL) TFA (1.3 mL) was added at 0 °C. The reaction mixture was stirred at 25 °C for 3 hours, it was concentrated, redissolved in EtOAc and extracted with 1M NaHCO_3 solution.
35 The EtOAc phase was dried over MgSO_4 and concentrated under reduced pressure. The

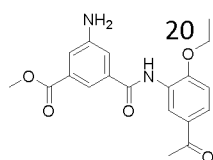
obtained residue was purified by flash column chromatography (9 % MeOH, 1% Et₃N and 90 % DCM) obtaining the desired product together with Et₃N.HCl, which was removed by dissolving the product in EtOAc and extracting it with 1M NaHCO₃. The EtOAc phase was once again dried over MgSO₄ and concentrated under reduced pressure to afford the desired

Methyl 5-((5-acetyl-2-ethoxyphenyl)carbamoyl)-2-morpholinobenzoate (35) To a solution of methyl 5-((5-acetyl-2-ethoxyphenyl)carbamoyl)-2-hydroxybenzoate (150 mg, 0.420 mmol) and Et₃N (176 μ L, 1.259 mmol) in DCM (1.7 mL), triflic anhydride (106 μ L, 0.630 mmol) was added at -15 °C. The reaction was stirred at -15 °C for 30 min. It was then diluted with DCM (10.0 mL) and extracted with saturated NaHCO₃ and brine. The DCM phase was dried over MgSO₄ and concentrated under reduced pressure. The residue was then dissolved in acetonitrile (2.0 mL) and morpholine was added (111 μ L, 1.259 mmol). The reaction mixture was refluxed for one hour, concentrated and the residue was purified by flash column chromatography (2:1, EtOAc/hexane) affording the desired product in pure form (99 mg, 0.233 mmol, 55%). Light yellow solid; mp 160-166 °C.

7. Synthesis of methyl 3-((5-acetyl-2-ethoxyphenyl)carbamoyl)-5-(1H-tetrazol-1-yl)benzoate

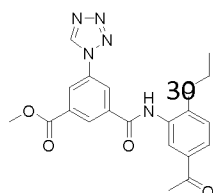


Methyl 3-((5-acetyl-2-ethoxyphenyl)carbamoyl)-5-aminobenzoate



To a mixture of nitrophenyl (1.0 eq) in EtOH (0.3 M) SnCl₂ · 2H₂O (4.0 eq) was added. The reaction mixture was heated to 80 °C for 5 h, cooled, and concentrated under reduced pressure. The pH was basified to pH 5 by the addition of a 5 M NaOH solution. The resulting precipitate was filtered off and washed with EtOAc. The organic layer was washed with brine, dried over MgSO₄, filtered, and concentrated under reduced pressure. The residue obtained after the work-up was concentrated and upon the addition of Et₂O, the desired compound precipitated, it was filtered off and washed with Et₂O. Light yellow solid; Yield: 39%; mp 270-274 °C.

Methyl 3-((5-acetyl-2-ethoxyphenyl)carbamoyl)-5-(1H-tetrazol-1-yl)benzoate



To a solution of methyl 3-((5-acetyl-2-ethoxyphenyl)carbamoyl)-5-aminobenzoate (100 mg, 0.281 mmol) in acetic acid (0.54 mL), NaN₃ (34 mg, 0.519 mmol) and triethyl orthoformate (224 μ L, 1.347 mmol) were

added. The reaction mixture was refluxed for 7 hours. Upon the addition of one drop of concentrated HCl the product precipitated. It was filtered off and washed with water affording the tetrazole in pure form as a white solid (84 mg, 73 % yield). mp 242-246 °C.

8. Synthesis of other benzoic acid isosteres and intermediates

5 **N-(5-acetyl-2-ethoxyphenyl)-3-bromo-5-cyanobenzamide**

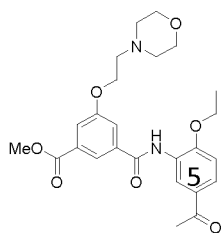
To a stirred solution of N-(5-acetyl-2-ethoxyphenyl)-3-bromo-5-iodobenzamide (100 mg, 0.20 mmol) in DMF (800 µL) was added ZnCN₂ (23 mg, 0.20 mmol) and Pd(PPh₃)₄ (11 mg, 0.01 mmol). The reaction was heated at 80 °C for 6 hours then diluted with water and extracted with EtOAc three times. The combined organic phases were washed with a saturated solution of NaCl, dried over MgSO₄ and concentrated under reduced pressure. The obtained residue was purified by flash column chromatography (EtOAc/hex: 4:6, dry load) to afford the desired product in pure form as a white solid (72 mg, 0.186 mmol, 92 % yield). Mp: 172-173 °C.

General procedure for tetrazoles synthesis:

15 To a stirred solution of the cyanide (0.37-8.1 mmol) in dry DMF (0.5 M) was added ZnBr₂ (1 eq.) and NaN₃ (1.1 eq.). The mixture was heated at 130 °C for 16-20 h and then concentrated under reduced pressure. The residue was and dried to afford the product in pure form. For N-(5-acetyl-2-ethoxyphenyl)-3-(furan-3-yl)-5-(2H-tetrazol-5-yl)benzamide, the solid was also washed with acetone.

20 **N-(5-acetyl-2-ethoxyphenyl)-3-(2H-tetrazol-5-yl)benzamide (27):** Yellow solid; Yield: 97 %; mp 238-239 °C **N-(5-acetyl-2-ethoxyphenyl)-3-(furan-3-yl)-5-(2H-tetrazol-5-yl)benzamide (48)** Brown solid; Yield: 66 %; 265-267 °C. **Methyl 3-((5-acetyl-2-ethoxyphenyl)carbamoyl)-5-hydroxybenzoate:**

To a stirred and previously sonicated solution of 3-((5-acetyl-2-ethoxyphenyl)carbamoyl)-5-(benzyloxy)benzoate (3.7 g, 8.3 mmol) in EtOAc (42 mL) was added Pd/C (441 mg, 0.42 mmol, 10 % w. Pd) and pyridine (67 µL, 0.83 mmol). N₂ was bubbled in the flask and through the suspension before addition of two balloons of H₂. The reaction was stirred for 4 hours at 25°C then filtered over a short pad of Celite[®] and washed with Methanol. The filter cake was poured in MeOH, stirred and sonicate for 30 min. The resulting suspension was filtered over a short pad of Celite[®] and washed with Methanol. All the filtrates were combine and concentrated under reduced pressure to afford the product in pure form as a white solid (2.6 g, 7.3 mmol, 88 % yield). Mp 195-197 °C.

Methyl 3-((5-acetyl-2-ethoxyphenyl)carbamoyl)-5-(2-morpholinoethoxy)benzoate:

To a stirred solution of methyl 3-((5-acetyl-2-ethoxyphenyl)carbamoyl)-5-hydroxybenzoate (200 mg, 0.56 mmol) in dry DMF (2.8 mL) was added K_2CO_3 (340 mg, 2.46 mmol), 4-(2-chloroethyl)morpholine hydrochloride (156 mg, 0.84 mol) and NaI (40 mg, 0.28 mmol). The mixture was stirred for 15 h at 80 °C. The reaction was cooled to room temperature and water was added. The resulting precipitate was filtered, washed with water and dried to afford the product in pure form as a white solid (220 g, 0.47 mmol, 84 % yield). Mp 68-71 °C.

Methyl 3-((5-acetyl-2-ethoxyphenyl)carbamoyl)-4-(1H-imidazol-1-yl)benzoate (36)

- 10 To a solution of methyl 3-((5-acetyl-2-ethoxyphenyl)carbamoyl)-4-bromobenzoate (150.0 mg, 0.357 mmol) in DMF (2.0 mL), CuI (13.6 mg, 0.071 mmol), K_2CO_3 (98.7 mg, 0.714 mmol) and imidazole (29.2 mg, 0.428 mmol) were added. The reaction mixture was stirred at 100 °C for 12 hours, it was filtered through a pad of celite, diluted with water and extracted with EtOAc three times. The combined organic phases were dried over $MgSO_4$ and concentrated under
- 15 reduced pressure. The obtained residue was purified by flash column chromatography (2% MeOH in DCM) affording the desired product in pure form (106.2 mg, 0.261 mmol, 73 % yield). Light yellow solid; mp 153-155 °C.

9. Methyl ester hydrolysis of the amide coupling products**General procedure for ester hydrolysis**

- 20 To a solution of the methyl ester (1 eq) in THF (0.1 M) a 1M LiOH solution (5 eq) was added. The reaction mixture was stirred at 25 °C for 2-6 h. It was then concentrated under reduced pressure and 1M HCl was added. The obtained precipitate was washed with hexanes, ether and cold DCM, affording the desired carboxylic acids in pure form. For the synthesis of **12**, the reaction mixture was diluted with water and extracted with DCM and Et_2O three times.
- 25 The pH of the water phase was then brought to pH 3-4 by addition of 1M HCl and the resulting precipitate was filtered off and washed with DCM.

- For the synthesis of **14**, the pH of the reaction mixture was brought to 1 by the addition of a 1M HCl solution. It was then concentrated, redissolved in EtOH (0.1 M) and PTSA (0.1 eq) was added. The solution was stirred at 25 °C for 5 h and concentrated. Upon the addition of
- 30 1M HCl solution, the final product precipitated. It was filtered out and washed with 1M HCl solution and Et_2O affording the desired alcohol in pure form.

In the case of **16**, the reaction mixture was diluted with water and extracted with hexane. The aqueous phase was then brought to pH 3-4 by addition of a 10% citric acid solution. It was

then extracted with EtOAc three times, the combined organic phases were dried over MgSO_4 and evaporated under reduced pressure obtaining the final product **16** in pure form.

In the case of **41** 1.0 eq of LiOH were added and the reaction mixture was concentrated affording the lithium salt in pure form.

- 5 **3-((5-Acetyl-2-ethoxyphenyl)carbamoyl)benzoic acid (1)**: White solid; Yield: 60 %; mp 224-226 °C; MS (ESI), m/z : calcd for $\text{C}_{18}\text{H}_{18}\text{NO}_5^+$, 328.1180; found, 328.1176. **2-((5-Acetyl-2-ethoxyphenyl)carbamoyl)benzoic acid (2)**: White solid; Yield: 57 %; mp 143-146 °C; MS (ESI), m/z : calcd for $\text{C}_{18}\text{H}_{18}\text{NO}_5^+$, 328.1180; found, 328.1181. **3-((5-Acetyl-2-propoxyphenyl)carbamoyl)benzoic acid (3)**: Beige solid; Yield: 77 %; mp 208-211 °C; MS
- 10 (ESI), m/z : calcd for $\text{C}_{19}\text{H}_{20}\text{NO}_5^+$, 342.1336; found, 342.1341. **3-((5-Acetyl-2-isobutoxyphenyl)carbamoyl)benzoic acid (4)**: White solid; Yield: 94 %; mp 221-223 °C; MS (ESI), m/z : calcd for $\text{C}_{20}\text{H}_{21}\text{NnaO}_4^+$, 378.1312; found, 378.1309. **3-((5-Acetyl-2-(cyclopropylmethoxy)phenyl)carbamoyl)benzoic acid (5)**: Beige solid; Yield: 54 %; mp 221-223 °C; MS (ESI), m/z : calcd for $\text{C}_{20}\text{H}_{19}\text{NnaO}_5^+$, 376.1155; found, 376.1151. **3-((5-**
- 15 **Acetyl-2-(benzyloxy)phenyl)carbamoyl)benzoic acid (6)**: White solid; Yield: 79 %; mp 210-215 °C; MS (ESI), m/z : calcd for $\text{C}_{23}\text{H}_{20}\text{NO}_5^+$, 390.1336; found, 390.1335. **3-((5-Acetyl-2-morpholinophenyl)carbamoyl)benzoic acid (7)**: White solid; Yield: 76 %; mp 249-252 °C; MS (ESI), m/z : calcd for $\text{C}_{20}\text{H}_{21}\text{N}_2\text{O}_5^+$, 369.1445; found, 369.1444. **3-((5-Acetyl-2-cyclopropylphenyl)carbamoyl)benzoic acid (8)**: Pale yellow solid; Yield: 57 %; mp 95-
- 20 100 °C; MS (ESI), m/z : calcd for $\text{C}_{19}\text{H}_{17}\text{NnaO}_4^+$, 346.1050; found, 346.1047. **3-((5-Acetyl-2-ethoxyphenyl)carbamoyl)-5-(pyridin-4-yl)benzoic acid (10)**: White solid; Yield: 40 % over two steps; mp 270-276 °C; MS (ESI), m/z : calcd for $\text{C}_{23}\text{H}_{21}\text{N}_2\text{O}_5^+$, 405.1445; found, 405.1440. **3-((5-Acetyl-2-ethoxyphenyl)carbamoyl)-5-(furan-3-yl)benzoic acid (11)**: Beige solid; Yield: 55 %; mp 210-214 °C; MS (ESI), m/z : calcd for $\text{C}_{22}\text{H}_{19}\text{NO}_6^+$, 394.1285; found,
- 25 394.1279. **3-((5-Acetyl-2-ethoxyphenyl)carbamoyl)-5-(methoxymethyl)benzoic acid (13)**: White solid; Yield: 50 %; mp 185-187 °C; MS (ESI), m/z : calcd for $\text{C}_{20}\text{H}_{21}\text{NnaO}_6^+$, 394.1261; found, 394.1263. **3-((5-Acetyl-2-ethoxyphenyl)carbamoyl)-5-(((tetrahydro-2H-pyran-2-yl)oxy)methyl) benzoic acid (14)**: White solid; Yield: 78 %; mp 165-170 °C; MS (ESI), m/z : calcd for $\text{C}_{24}\text{H}_{27}\text{NnaO}_7^+$, 464.1680; found, 464.1678. **3-((5-Acetyl-2-**
- 30 **ethoxyphenyl)carbamoyl)-5-(hydroxymethyl)benzoic acid (12)**: White solid; Yield: 27 % over two steps; mp 225-228 °C; MS (ESI), m/z : calcd for $\text{C}_{19}\text{H}_{20}\text{NO}_6^+$, 358.1285; found, 358.1285. **3-(5-Acetyl-2-ethoxybenzamido)benzoic acid (15)**: Pale yellow solid; Yield: 69 %; mp 209-212 °C; MS (ESI), m/z : calcd for $\text{C}_{18}\text{H}_{17}\text{NnaO}_5^+$, 350.0999; found, 350.0995. **3-((2-Ethoxy-5-(methylcarbamoyl)phenyl)carbamoyl)benzoic acid (16)**: Pale brown solid;
- 35 Yield: 62 %; mp 226-229 °C; MS (ESI), m/z : calcd for $\text{C}_{18}\text{H}_{18}\text{N}_2\text{O}_5^+$, 343.1289; found, 343.1283. **(E)-4-((5-Acetyl-2-methoxyphenyl)amino)-4-oxobut-2-enoic acid (17)**: Yellow

solid; Yield: 53 %; mp 172-174 °C; MS (ESI), m/z : calcd for $C_{13}H_{14}NO_5^+$, 264.0867; found, 264.0869. **(E)-4-((3-Acetylphenyl)amino)-4-oxobut-2-enoic acid (18)**: Off white solid; Yield: 90 %; mp 237-239 °C; MS (ESI), m/z : calcd for $C_{12}H_{12}NO_4^+$, 234.0761; found, 234.0760. **5-((5-Acetyl-2-ethoxyphenyl)carbamoyl)-2-hydroxybenzoic acid (37)** White solid; Yield: quantitative; mp 243-248 °C. **5-((5-acetyl-2-ethoxyphenyl)carbamoyl)-2-ethoxybenzoic acid (38)** White solid; Yield: 88%; mp 209-212 °C. **5-((5-Acetyl-2-ethoxyphenyl)carbamoyl)-2-propoxybenzoic acid (39)** White solid; Yield: 92%; mp 220-224 °C. **5-((5-Acetyl-2-ethoxyphenyl)carbamoyl)-2-isobutoxybenzoic acid (40)** White solid; Yield: 80%; mp 194-198 °C. **Lithium 5-((5-acetyl-2-ethoxyphenyl)carbamoyl)-2-(2-morpholinoethoxy)benzoate (41)** White solid; Yield: 99%; mp 192-195 °C. **5-((5-Acetyl-2-ethoxyphenyl)carbamoyl)-2-morpholinobenzoic acid (42)** White solid; Yield: 99%; mp 247-253 °C. **3-((5-Acetyl-2-ethoxyphenyl)carbamoyl)-5-nitrobenzoic acid (43)** Pale yellow solid; Yield: 31%; mp 220-223 °C... **3-((5-Acetyl-2-ethoxyphenyl)carbamoyl)-5-(1H-tetrazol-1-yl)benzoic acid (44)** Off-white solid; Yield: 55%. **3-((5-Acetyl-2-ethoxyphenyl)carbamoyl)-4-bromobenzoic acid (45)** White solid; Yield: 59%; mp 248-251 °C. **3-((5-Acetyl-2-ethoxyphenyl)carbamoyl)-4-(furan-3-yl)benzoic acid (46)** Yellow solid; Yield: 70%; mp 172-177 °C. **3-((5-Acetyl-2-ethoxyphenyl)carbamoyl)-4-(1H-imidazol-1-yl)benzoic acid (47)** White solid; Yield: 69%; mp 237-240 °C.

General procedure B for ester hydrolysis

To a stirred solution of the methyl ester (1 eq.) in acetone (0.20 M), was added KOH (1 eq., 1 M in water). The reaction mixture was stirred at 25 °C for 0.5-17 h. It was then quenched with HCl (1 M) and the resulting precipitate was filtered off, washed with water and dried to afford the desired product in pure form as a white solid. In the case of potassium 3-((5-acetyl-2-ethoxyphenyl)carbamoyl)-5-(2-morpholinoethoxy)benzoate, the reaction mixture was concentrated under reduced pressure. The residue was triturated in Et_2O , filtered, washed with Et_2O and dried to afford the desired carboxylate salt.

6-((5-acetyl-2-ethoxyphenyl)carbamoyl)picolinic acid (29): White solid; Yield: 88 %; mp 272-274 °C. **Potassium 3-((5-acetyl-2-ethoxyphenyl)carbamoyl)-5-(2-morpholinoethoxy)benzoate (28)**: White solid; Yield: 43 %; mp 185-188 °C.

Thermal shift assays:

Protein purification

Proteins for thermal shift assays were purified as described previously (Filippakopoulos et al., 2012. Cell. 149(1): 214–231). Plasmids bearing the His-tagged bromodomain constructs in the following table were kindly provided by the Structural Genomics Consortium. His-tagged bromodomains were expressed in *Escherichia coli* BL21(DE3) cells upon induction

with 0.1 mM isopropyl thio-beta-D-galactoside (IPTG) for 16 h at 18°C. Cells were lysed and the resulting extract treated to remove DNA, either by passing it through diethylaminoethyl cellulose resin or by incubation on ice with 0.15% polyethyleneimine for 30 minutes. The His-tagged proteins were loaded on HisTrap columns (GE Healthcare) and eluted using a step gradient of imidazole. The poly-Histidine tags were removed by overnight incubation with homemade His-tagged Tobacco Etch Virus protease. A size-exclusion chromatography step (HiLoad 16/600 Superdex75 column) and a second Ni-affinity chromatography step were performed to purify the cleaved bromodomain. Samples were then concentrated, flash frozen and stored at -80°C.

10 Thermal Shift Assays

Thermal shift measurements were carried out as described in Filippakopoulos et al., 2010. Nature. 468(7327):1067-1073 with a final volume of 20 µl. Protein and ligand concentrations were 2 and 100 µM, respectively, while DMSO concentration was maintained at 0.4% (v/v). Individual values of ΔT_m are calculated as the difference between the transition midpoint of each well and the average of the reference wells (containing the protein and DMSO only) in the same plate. At least 6 measurements were performed for each protein/ligand combination; their averaged values are reported below (S.E. is the Standard Error).

Cmp d	Thermal Shift (ΔT_m , °C, S.E. $\leq 1.0^\circ\text{C}$)									
	CB P	EP 300	BRD 4(1)	BRD 4(2)	BAZ 2B	TAF 1(2)	BRD 1	SMARCA 4	BRD 9	BRDT
1	3.6		0.5		0.1	0.6	-0.2	-0.4		
2	1.9		-		-	-	-	-		
3	4.0		1.1		0.1	0.8	0.1	0.1		
4	3.5		-		-	-	-	-		
5	3.5		-		-	-	-	-		
6	3.3		-		-	-	-	-		
7	1.5		-		-	-	-	-		
8	3.1		0.2		-0.2	0.3	0.1	0.0		
9	3.1		-0.2		0.0	0.6	0.2	0.3		
10	4.0		-		-	-	-	-		
11	4.9		1.7		-0.6	1.8	-0.1	-0.2		
12	3.9		1.2		0.1	0.6	0.0	-0.1		
13	5.0		1.3		0.2	1.2	0.2	0.2		
14	6.0		1.6		0.1	1.4	0.1	-0.1		
15	3.2		1.1		0.0	1.4	0.1	0.2		
16	1.0		-		-	-	-	-		
17	1.1		0.2		-0.3	0.2	0.2	0.3		
21	2.1	2.6	0.3	0.1	0.3	0.2	-0.2	0.0	-0.4	-0.4
22	2.8	2.7	0.3	0.1	0.1	0.3	0.1	0.5	0.1	0.5
23	1.8	2.2	0.0	0.1	0.1	0.1	-0.3	0.3	-0.3	-0.3
24	1.3	0.4	0.2	0.1	0.1	0.0	0.0	0.1	-0.4	-0.3
25	1.9	1.7	0.3	0.8	0.1	0.1	0.3	0.0	0.4	-0.2
26	1.8	2.5	0.0	0.1	0.3	0.2	0.2	-0.3	-0.4	0.5

27	8.0	8.6	-1.1	-	-4.1	-1.2	-3.2	-0.3	-2.5	-0.6
28	4.8	4.2	0.9	0.0	-0.8	0.4	-0.3	-0.3	-0.1	-0.3
29	3.0	2.9	1.5	0.1	0.5	0.2	0.1	0.2	0.9	0.3
30	1.2	0.9	-0.9	-0.7	-0.1	-0.2	-0.5	-0.2	-0.9	-0.3
31	-2.6	2.0	-5.8	-8.7	-4.6	0.4	-0.6	-10.3	-0.4	-8.0
32	1.7	1.7	-1.1	-0.4	0.1	0.3	-0.5	-0.1	-0.7	-0.6
33	5.4	5.5	2.0	0.3	0.5	2.4	0.1	0.4	0.4	-0.6
34	4.6	3.9	1.5	-	-0.4	0.6	0.0	0.0	0.1	-0.5
35	1.0	0.8	0.4	-0.1	0.2	0.1	-0.2	0.5	0.0	-0.5
36	3.6	1.5	0.0	1.3	0.2	0.3	0.0	0.0	-0.6	-0.1
37	7.0	6.0	1.6	-	0.2	1.1	0.2	-0.3	0.1	0.1
38	3.1	2.6	-0.1	-0.2	0.5	0.7	-0.2	-0.1	-0.1	-0.1
39	3.1	2.7	-0.1	-0.1	-0.3	0.4	-0.5	-0.1	-0.1	-0.2
40	2.9	2.9	-0.4	-0.7	0.2	0.6	0.0	-0.5	0.7	-0.9
41	2.7	2.1	0.9	-0.1	0.2	0.2	0.0	0.0	-0.1	0.2
43	5.6	-	0.2	-	-0.4	-	-	-0.1	-	-0.8
42	3.3	3.0	0.7	-	0.0	0.7	0.2	-	-	-0.2
44	4.6	3.9	1.0	0.1	0.4	0.1	0.0	-0.2	-0.1	0.7
45	3.3	1.3	0.6	0.2	0.2	-0.1	0.3	-0.3	0.3	-0.1
46	2.2	1.4	1.1	-	-0.6	0.0	0.0	-	-	-1.0
47	1.6	0.5	1.0	-	0.0	0.1	0.5	-	-	0.0
48	10.7	-	-	-	-	-	-	-	-	-

TR-FRET assays to determine IC₅₀ values:

TR-FRET assays were carried out in duplicate at BPS Bioscience using a recombinant CBP bromodomain (BPS catalogue #31128) and the BET Ligand (BPS catalogue #33000) as provided in the CREBBP TR-FRET Assay Kit (BPS catalogue #32619). A 10 mM solution of the compound under investigation in DMSO was prepared and shipped to BPS Bioscience, where it was tested at 10 concentrations over the range listed in the table below. Each compound solution was then diluted in water to obtain a 10% DMSO solution. 2 µL of this dilution were added to a 20 µL reaction mixture (12.5 nM CBP, 125 nM BET Ligand, including FRET dyes and the amount of compound needed to reach the indicated concentration in the Table below). The resulting mixture was incubated for 2 hours at room temperature prior to reading the TR (time resolved)-FRET signal using a Tecan Infinite M1000 plate reader. The negative control consisted of the aforementioned mixture in which the buffer was added in place of compound. TR-FRET was recorded as the ratio of the fluorescence of the acceptor and the donor dyes (acceptor/donor).

The TR-FRET data was analyzed using Graphpad Prism software. The percent activity in the presence of each compound was calculated according to the following equation: % activity = $[(F - F_b)/(F_t - F_b)] \times 100$, where F_t is the TR-FRET signal in the absence of any compound (100 % activity), F_b the TR-FRET signal in the absence of the bromodomain (0 % activity) and F the TR-FRET signal in the presence of the compound. The percent inhibition was calculated according to the following equation: % inhibition = 100 - % activity. The values of

% activity versus a series of compound concentrations were then plotted using non-linear regression analysis of Sigmoidal dose-response curve generated with the equation $Y=B+(T-B)/(1+10^{((\text{LogIC}_{50}-X)\times\text{Hill Slope})})$, where Y=percent activity, B=minimum percent activity, T=maximum percent activity, X= logarithm of compound and Hill Slope=slope factor or Hill coefficient. The

5 IC_{50} value corresponds to the concentration causing a half-maximal percent activity.

Compound	IC_{50} (μM)	Concentration range
1	8.7	0.001 - 10 μM
2	64	0.01 - 100 μM
3	7.4	0.001 - 10 μM
8	15	0.01 - 100 μM
9	7.5	0.001 - 10 μM
10	3	0.001 - 10 μM
11	1	0.001 - 10 μM
12	3	0.01 - 100 μM
13	2	0.001 - 10 μM
14	1	0.001 - 10 μM
15	1	0.001 - 10 μM
16	37	0.01 - 100 μM
17	60	0.01 - 100 μM
18	30	0.01 - 100 μM

BROMOscan:

K_D determinations by means of BROMOscan technology was carried out at DiscoverX.

10 *Escherichia coli* derived from BL21 strain was used as host to grow T7 phage strains displaying the corresponding bromodomain. *Escherichia coli*, grown to log-phase, were infected with T7 phage (from a frozen stock, being the multiplicity of infection 0.4) and incubated while shaking at 32 °C for 90-150 minutes, until lysis. To remove cell debris, lysates were centrifuged at 5,000 x g and filtered (0.2 μm). Affinity resins were obtained by
 15 treating streptavidin-coated magnetic beads with biotinylated acetylated peptide ligands for 30 minutes at 25 °C. These beads were then blocked with excess of biotin and washed with blocking buffer (SeaBlock (Pierce), 1 % BSA, 0.05 % Tween 20, 1 mM DTT) removing the unbound ligand and reducing non-specific phage binding.

During the experiment, the bromodomain, ligand-bound affinity beads and test compounds
 20 were combined in a buffer composed of 17% SeaBlock, 0.33x PBS, 0.04% Tween 20, 0.02% BSA, 0.004% Sodium azide and 7.4 mM DTT. Test compounds were prepared as 50 mM in pure DMSO and diluted to 5 mM with monoethyl glycol (100X concentrated in respect to the top screening concentration, 50 μM). During the assay, a DMSO and MEG final concentration of 0.1 % and 0.9 %, respectively, were used. The assays were carried out in
 25 polystyrene 96-well plates in a final volume of 0.135 mL. Assay plates were incubated at 25

°C with shaking for 1 hour and the affinity beads were washed with a buffer composed of 0.05% Tween 20 in PBS. The beads were then re-suspended in the elution buffer (1x PBS, 0.05% Tween 20, 2 μ M non-biotinylated affinity ligand) and incubated at 25 °C with shaking for 30 minutes. The bromodomain concentration in the eluates was measured by qPCR.

- 5 Binding constants (K_D) were calculated with a standard dose-response curve using the Hill equation and curves were fitted using a non-linear least square fit with the Levenberg-Marquardt algorithm.

Compound	CBP K_D (nM)	BRD4(1) K_D (nM)
1	770	>50000
11	170	10000
13	540	26000
14	400	-
15	2500	-
19	590	-
22	2300	-
27	87	-
28	540	-
29	1800	-
33	750	-
34	1400	-
37	350	-
38	2100	-
39	170	-

10 Cell culture and cytotoxicity measurements

HL-60, ML2 and OCI-AML2 cells (obtained from Dr. Nathan Luedtke, Chemistry Department, University of Zurich) and Kasumi-1 cells (obtained from Dr. Juerg Schwaller, Department of Biomedicine, University Hospital Basel) were cultured using RPMI medium supplemented with 10 % (v/v) fetal bovine serum, whereas MOLM-13 cells (obtained from Dr. Nathan Luedtke, Chemistry Department, University of Zurich) were cultured using RPMI medium supplemented with 20 % (v/v) fetal bovine serum. All the media were additionally supplemented with 100 units/mL of penicillin, 100 μ g/mL of streptomycin, 4.5 g/L glucose, 0.11g/L sodium pyruvate and 2mM glutamine and the cells were grown at 37 °C in 5 % CO₂ atmosphere with 80 % relative humidity.

20

The cells they were seeded at a density of 20,000 cells per well in 100 μ L of RMPI media in a 96 well microtiter plates. After 24 hours, 12.5 μ L of a 10 fold concentrated drug or DMSO solution in RMPI media was added in every well. Control cells were treated with the same DMSO concentrations. After 72 hour incubation, cell viability was studied by measuring the ability of the cells to process resazurin. Resazurin was added to every well to obtain a final concentration of 86 nM, and after 3 hours, the fluorescence was quantified using a

25

fluorescence microplate reader (Biotek, FLx800™) at the respective excitation and emission wavelength of 560 and 590 nm. Resazurin becomes fluorescent under mitochondrial reduction and its emission directly correlates with the metabolic viability of the cells. The measured fluorescence values were corrected from the control samples containing DMSO.

Table 1. Percentage of metabolic activity in reducing resazurin observed after incubation of compounds **1, 3, 4, 9, 11-15** for 72 h at a concentration of 50 μ M (compounds **1, 3, 4, 9, 11-15, 20** (except on OCI-AML2 and Kasumi-1 cells) or 25 μ M (compound 20 on OCI-AML2 and Kasumi-1) in comparison to the DMSO treated cells (100 % metabolic activity). This preliminary screening of toxicity was done as a single experiment (compounds **1, 3, 4, 9, 11-15, 20** (except on OCI-AML2 and Kasumi-1 cells)) or in triplicates (compound 20 on OCI-AML2 and Kasumi-1). NM stands for no metabolic activity change in comparison to the DMSO treated cells. A dash indicates that no experiment was performed.

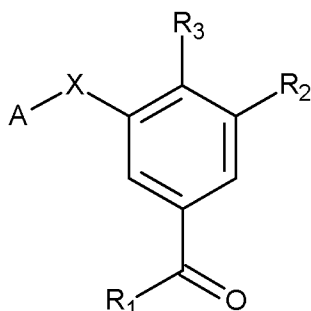
	HL-60	ML2	MOLM-13	OCI-AML2	Kasumi-1
1	77.1	98.3	65.2	-	-
3	62.8	NM	15.1	-	-
4	87.8	97.3	NM	-	-
9	43.2	64.1	50.2	-	-
11	42.1	53.2	49.4	-	-
12	90.3	NM	76.3	-	-
13	84.7	NM	73.2	-	-
14	45.7	26.5	43.0	-	-
15	68.6	NM	74.8	-	-
20	73	36	11	87	67

Table 2. GI_{50} (μ M) values calculated as the intercept at 50 % growth inhibition between two drug concentrations (50 and 25 μ M). NA indicates that no GI_{50} value could be obtained. A dash indicates that no experiment was performed.

	HL-60	ML2	MOLM-13	OCI-AML2
3	NA	NA	28	-
9	47	NA	NA	-
11	45	NA	50	-
14	42	42	46	-
20	-	14.4	5.3	-
33	-	-	40	46
34	-	-	36	42

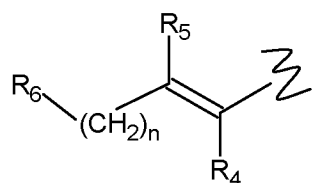
CLAIMS

1. A compound for use in the treatment of a disease or condition for which a bromodomain inhibitor is indicated characterized by a general formula (1),



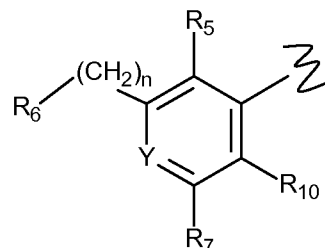
(1), wherein

- 5 - R_1 is a C_1 - C_3 alkyl, cyclopropane, a C_1 - C_3 haloalkyl, halocyclopropane or $-NHR_8$, wherein R_8 is a C_1 - C_3 alkyl, cyclopropane, a C_1 - C_3 haloalkyl or halocyclopropane;
- R_2 is H, F, a C_1 - C_4 alkyl or a C_1 - C_4 alkanol;
- R_3 is H, F, Cl, a C_1 - C_6 alkyl, a C_1 - C_3 haloalkyl, a C_1 - C_4 alkoxy, a C_1 - C_4 alkanol, a C_2 - C_4 ether, a 3- to 6-membered saturated heterocycle, a 3- to 6-membered heteroaryl, a benzyloxy or a substituted amine of the form $-NHR_8$, wherein R_8 is a C_1 - C_3 alkyl, cyclopropane, a C_1 - C_3 haloalkyl or halocyclopropane;
- 10 - X is $-C(=O)NH-$, $-NHC(=O)-$, $-C(=O)NR_{12}-$, $-NR_{12}C(=O)-$, $-NHC(=O)NH-$, $-N(R_9)C(=O)NH-$, $-NHC(=O)NR_9-$, $-C(=S)NH-$, $-NHC(=S)-$, $-NHC(=S)NH-$, $-N(R_9)C(=S)NH-$, $-NHC(=S)N(R_9)-$, $-N-S(=O)_2-$, $-S(=O)_2-N-$, particularly X is $-C(=O)NH-$, $-NHC(=O)-$, $-C(=O)NR_{12}-$, $-NR_{12}C(=O)-$, $-NHC(=O)NH-$, $-N(R_9)C(=O)NH-$, $-NHC(=O)NR_9-$, $-C(=S)NH-$, $-NHC(=S)-$, $-NHC(=S)NH-$, $-N(R_9)C(=S)NH-$, $-NHC(=S)N(R_9)-$, wherein
- 15 - R_9 is C_1 - C_3 alkyl, C_1 - C_3 alkoxy, C_1 - C_3 haloalkyl, C_1 - C_3 alkanol, C_2 - C_4 ether, 3- to 6-membered heterocycle, or substituted or unsubstituted aryl, and wherein
- 20 - R_{12} is $-(CH_2)_r$ -phenyl with r being 0, 1 or 2 and said phenyl may be substituted with one or more electron donating groups, in particular one or more electron donating groups selected from $-OR_{13}$, with R_{13} being H, a methyl group or an ethyl group;
- A is selected from

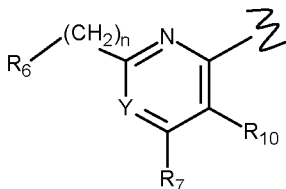


(2'),

or



(3'),

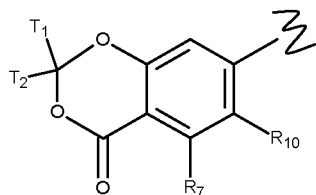


or (4'), particularly from (2') or (3'), wherein

- R_4 is H or a methyl group;
- R_5 is H, -COOH or salt thereof, a C_1 - C_3 alkoxy, a C_1 - C_3 alkyl, a C_1 - C_3 alkyl ester, a heteroaryl, a substituted or unsubstituted C_1 - C_6 alkoxy or a sulfonic acid, a sulfonamide, particularly an S-linked sulfonamide, that may be singly substituted with a C_1 - C_3 alkyl group or with a C_3 - C_6 cyclic alkyl; and
- R_6 is H, -COOH or salt thereof, a C_1 - C_3 alkoxy, a C_1 - C_3 alkyl, a C_1 - C_3 alkyl ester, a substituted or unsubstituted heteroaryl, a substituted or unsubstituted C_1 - C_6 alkoxy or a sulfonic acid, a sulfonamide, particularly an S-linked sulfonamide, that may be singly substituted with a C_1 - C_3 alkyl group or with a C_3 - C_6 cyclic alkyl; and wherein
- R_7 and R_{10} being independently from each other selected from
 - H, Br, Cl, F, NO_2 or
 - substituted or unsubstituted C_1 - C_3 alkanol, C_1 - C_3 alkyl, C_1 - C_3 haloalkyl, substituted or unsubstituted C_1 - C_3 alkoxy, C_3 - C_6 cycloalkyl, C_2 - C_4 alkyl ether, 3- to 6-membered saturated heterocycle, a 3- to 6-membered heteroaryl moiety, wherein said moieties may be substituted or unsubstituted, wherein the substituents of said substituted moieties with respect to R_4 and R_7 are selected from 3- to 6-membered heteroaryls and aryls, or 3- to 6-membered saturated heterocycles, which may also be substituted with one or more hydroxyl, amine or C_1 - C_3 alkoxy groups;
- n is 0, 1 or 2;
- Y is N, CH or $C-R_{11}$, with
 - R_{11} being a hydroxyl, a C_1 - C_5 heteroalkyl, particularly a $-(CH_2)_p-OT_3$ or a $-(CH_2)_p-N(T_3)(T_4)$, with T_3 and T_4 being independently from each other H, or C_1 - C_3 alkyl, and p is 0, 1, 2, 3, 4 or 5, a substituted or unsubstituted C_1 - C_6 alkoxy, a heteroaryl, a saturated heterocycle, $-O-(CH_2)_q$ -phenyl or $-O-(CH_2)_q$ -heterocycle, with q being 0, 1 or 2, wherein the saturated heterocycle or the $-O-(CH_2)_q$ -

heterocycle are preferably C₃-C₆ heterocycles, more preferably C₅-C₆ heterocycles,

or wherein R⁶ and Y are connected forming a cyclic moiety of the formula 5'



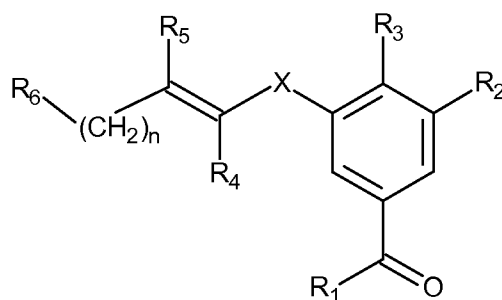
(5'), with T₁ and T₂ being independently from each other H, CH₃ or

5 CH₂CH₃, particularly H, and R₇ and R₁₀ having the same meaning as above.

2. The compound according to claim 1, wherein:

- R₁ is a methyl or -NHR₈ where R₈ is a methyl, in particular R₁ is a methyl; and/or
- R₂ is a hydrogen; and/or
- R₃ is H, F, a C₁-C₆ alkyl or a C₁-C₄ alkoxy, a benzyloxy or a morpholino, in particular
10 R₃ is an ethoxy, a propoxy, a butoxy, cyclopropane, cyclopropylethoxy, benzyloxy or a morpholino, more particularly ethoxy; and/or
- R₄ is H or a methyl group; and/or
- R₅ is H, -COOH or salt thereof, a C₁-C₃ alkoxyl, a C₁-C₃ alkyl, a C₁-C₃ alkyl ester, a
15 heteroaryl, a substituted or unsubstituted C₁-C₆ alkoxy or a sulfonic acid, an S-linked sulfonamide that may be singly substituted with a C₁-C₃ alkyl group or with a C₃-C₆ cyclic alkyl, and preferably R₅ is H-COOH or salt thereof, C₁-C₃ alkyl ester, in particular methylester, a tetrazole, which is preferably linked by its carbon moiety, and/or
- R₆ is H, -COOH or salt thereof, a C₁-C₃ alkoxyl, a C₁-C₃ alkyl, a C₁-C₃ alkyl ester, a
20 substituted or unsubstituted heteroaryl, a substituted or unsubstituted C₁-C₆ alkoxy or a sulfonic acid, an S-linked sulfonamide that may be singly substituted with a C₁-C₃ alkyl group or with a C₃-C₆ cyclic alkyl, and preferably R₆ is H-COOH or salt thereof, C₁-C₃ alkyl ester, in particular methylester, a tetrazole,; and/or
- n is 0 or 1, in particular n is 0; and/or
- Y is N, CH or C-R₁₁ with R₁₁ being a hydroxyl, a substituted or unsubstituted C₁-C₆
25 alkoxy, a saturated heterocycle,, -O-(CH₂)_q-phenyl or -O-(CH₂)_q-heterocycle, and q is 0, 1 or 2, wherein the saturated heterocycle or the -O-(CH₂)_q-heterocycle are preferably C₃-C₆ heterocycles, more preferably C₅-C₆ heterocycles, wherein said phenyl and said heterocycle of R₁₁ may optionally be substituted with one or more
30 methoxy or hydroxy groups, wherein preferably Y is CH, -O-(CH₂)_q-heterocycle or hydroxyl, and/or

- X is -C(=O)NH-, -NHC(=O)-, -C(=O)NR₁₂-, -NR₁₂C(=O)-, -NR₁₂C(=O)-, -NHC(=O)NH-, -N(R₉)C(=O)NH-, -NHC(=O)NR₉-, -C(=S)NH-, -NHC(=S)-, -NHC(=S)NH-, -N(R₉)C(=S)NH-, -NHC(=S)N(R₉)-, -N-S(=O)₂-, -S(=O)₂N-, in particular -C(=O)NH-, -NHC(=O)-, -NHC(=O)NH-, -N(R₉)C(=O)NH-, -NHC(=O)NR₉-, more particularly -C(=O)NH- or -NHC(=O)-, wherein
 - R₉ is a C₁-C₃ alkyl, C₁-C₃ alkoxy, C₁-C₃ haloalkyl, C₁-C₃ alkanol, C₂-C₄ ether, 3- to 6-membered heterocycle, or substituted or unsubstituted aryl, and wherein
 - R₁₂ is -(CH₂)_r-phenyl with r being 0, 1 or 2 and said phenyl is substituted with one or more electron donating groups, in particular one or more electron donating groups selected from -OR₁₂, with R₁₂ being H, a methyl group or an ethyl group, and/or
 - R₇ and R₁₀ being independently from each other selected from
 - H, Br, Cl, F, NO₂ or
 - substituted or unsubstituted C₁-C₃ alkanol, C₁-C₃ alkyl, C₁-C₃ haloalkyl, substituted or unsubstituted C₁-C₃ alkoxy, C₃-C₆ cycloalkyl, C₂-C₄ alkyl ether, 3- to 6-membered saturated heterocycle, a 3- to 6-membered heteroaryl moiety, wherein said moieties may be substituted or unsubstituted, wherein the substituents of said substituted moieties with respect to R₄ and R₇ are selected from 3- to 6-membered heteroaryls and aryls, or 3- to 6-membered saturated heterocycles, which may also be substituted with one or more hydroxyl, amine or C₁-C₃ alkoxy groups, wherein in particular R₇ is pyridine, furan, CH₂OH, CH₂OCH₃ or CH₂-O-tetrahydropyran, more particularly furan, and R₁₀ is H or methyl, more particularly H, and
 - wherein A has the same meaning as defined previously.
3. The compound according to claim 1, wherein said compound is characterized by a general formula (2),



(2), wherein

- R₁ is a C₁-C₃ alkyl, cyclopropane, a C₁-C₃ haloalkyl, halocyclopropane or -NHR₈, wherein R₈ is a C₁-C₃ alkyl, cyclopropane, a C₁-C₃ haloalkyl or halocyclopropane;
- R₂ is H, F, a C₁-C₄ alkyl or a C₁-C₄ alkanol;

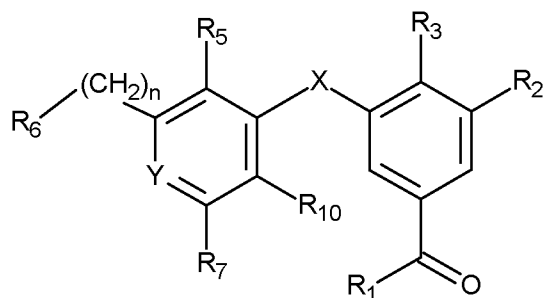
- R₃ is H, F, Cl, a C₁-C₆ alkyl, a C₁-C₃ haloalkyl, a C₁-C₄ alkoxy, a C₁-C₄ alkanol, a C₂-C₄ ether, a 3- to 6-membered saturated heterocycle, a 3- to 6-membered heteroaryl, a benzyloxy or a substituted amine of the form -NHR₈, wherein R₈ is a C₁-C₃ alkyl, cyclopropane, a C₁-C₃ haloalkyl or halocyclopropane;
- 5 - X is -C(=O)NH-, -NHC(=O)-, -C(=O)NR₁₂-, -NR₁₂C(=O)-, -NR₁₂C(=O)-, -NHC(=O)NH-, -N(R₉)C(=O)NH-, -NHC(=O)NR₉-, -C(=S)NH-, -NHC(=S)-, -NHC(=S)NH-, -N(R₉)C(=S)NH-, -NHC(=S)N(R₉)-, -N-S(=O)₂-, -S(=O)₂-N-, particularly X is -C(=O)NH-, -NHC(=O)-, -C(=O)NR₁₂-, -NR₁₂C(=O)-, -NHC(=O)NH-, -N(R₉)C(=O)NH-, -NHC(=O)NR₉-, -C(=S)NH-, -NHC(=S)-, -NHC(=S)NH-, -N(R₉)C(=S)NH-, -NHC(=S)N(R₉)-, wherein
- 10 - R₉ is C₁-C₃ alkyl, C₁-C₃ alkoxy, C₁-C₃ haloalkyl, C₁-C₃ alkanol, C₂-C₄ ether, 3- to 6-membered heterocycle, or substituted or unsubstituted aryl, and wherein
- 15 - R₁₂ is -(CH₂)_r-phenyl with r being 0, 1 or 2 and said phenyl may be substituted with one or more electron donating groups, in particular one or more electron donating groups selected from -OR₁₃, with R₁₃ being H, a methyl group or an ethyl group;
- R₄ is H or a methyl group;
- R₅ being H, -COOH or salt thereof, a C₁-C₃ alkoxy, a C₁-C₃ alkyl, a C₁-C₃ alkyl ester, a heteroaryl, a substituted or unsubstituted C₁-C₆ alkoxy or a sulfonic acid, a sulfonamide, particularly an S-linked sulfonamide, that may be singly substituted with a C₁-C₃ alkyl group or with a C₃-C₆ cyclic alkyl; and
- 20 - R₆ being H, -COOH or salt thereof, a C₁-C₃ alkoxy, a C₁-C₃ alkyl, a C₁-C₃ alkyl ester, a substituted or unsubstituted heteroaryl, a substituted or unsubstituted C₁-C₆ alkoxy or a sulfonic acid, a sulfonamide, particularly an S-linked sulfonamide, that may be singly substituted with a C₁-C₃ alkyl group or with a C₃-C₆ cyclic alkyl; and wherein
- 25 - n is 0, 1 or 2.
- 4. The compound according to claim 3, wherein
- R₁ is a methyl or -NHR₈ where R₈ is a C₁-C₃ alkyl; and/or
- R₂ is a hydrogen, a methyl or a C₁-C₄ alkanol; and/or
- 30 - R₃ is H, F, a C₁-C₆ alkyl or a C₁-C₄ alkoxy, a benzyloxy or a morpholino, in particular R₃ is an ethoxy, a propoxy, a butoxy, cyclopropane, cyclopropylethoxy, benzyloxy or a morpholino, more particularly ethoxy; and/or
- R₄ is H or a methyl group; and/or
- R₅ is H, -COOH or salt thereof, C₁-C₃ alkyl ester, in particular methylester, or
- 35 tetrazole, which is preferably linked by its carbon moiety; more particularly R₅ is H and/or

- R₆ is H, -COOH or salt thereof, C₁-C₃ alkyl ester, in particular methylester, a substituted or unsubstituted heteroaryl, a tetrazole, which is preferably linked by its carbon moiety,; and/or
- n is 0, 1 or 2; and/or
- 5 - X is -C(=O)NH-, -NHC(=O)-, -NHC(=O)NH-, -N(R₉)C(=O)NH-, -NHC(=O)NR₉-, -C(=S)NH-, -NHC(=S)-, -NHC(=S)NH-, -N(R₉)C(=S)NH-, -NHC(=S)N(R₉)-, in particular -C(=O)NH-, -NHC(=O)-, -NHC(=O)NH-, -N(R₉)C(=O)NH-, -NHC(=O)NR₉-, more particularly -C(=O)NH- or -NHC(=O)-, wherein R₉ is a C₁-C₃ alkyl, C₁-C₃ alkoxy, C₁-C₃ haloalkyl, C₁-C₃ alkanol, C₂-C₄ ether, 3- to 6-membered heterocycle, or
10 substituted or unsubstituted aryl.

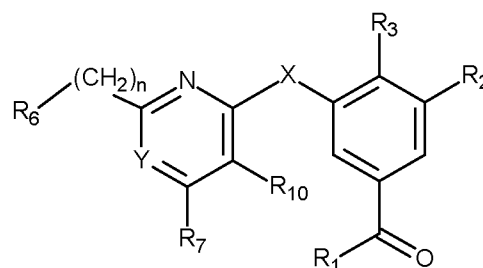
5. The compound according to claim 4,

wherein:

- R₁ is a methyl or -NHR₈ where R₈ is a methyl, in particular R₁ is a methyl; and/or
 - R₂ is a hydrogen; and/or
 - 15 - R₃ is H, F, a C₁-C₆ alkyl or a C₁-C₄ alkoxy, in particular R₃ is an ethoxy; and/or
 - R₄ is H or a methyl group; and/or
 - R₅ is H, -COOH or salt thereof, C₁-C₃ alkyl ester, in particular methylester, tetrazole, which is preferably linked by its carbon moiety, more particularly R₅ is H; and/or
 - R₆ is H, -COOH or salt thereof, C₁-C₃ alkyl ester, in particular methylester, a
20 substituted or unsubstituted heteroaryl, a tetrazole, which is preferably linked by its carbon moiety,; and/or
 - n is 0; and/or
 - X is -C(=O)NH-, -NHC(=O)-, -NHC(=O)NH-, -N(R₉)C(=O)NH-, -NHC(=O)NR₉, in particular X is -C(=O)NH- or -NHC(=O)-wherein R₉ is a C₁-C₃ alkyl, C₁-C₃ alkoxy, C₁-
25 C₃ haloalkyl, C₁-C₃ alkanol, C₂-C₄ ether, 3- to 6-membered heterocycle, or substituted or unsubstituted aryl, wherein in particular R₉ is a C₁-C₃ alkoxy, C₁-C₃ haloalkyl, C₁-C₃ alkanol, C₂-C₄ ether, 3- to 6-membered heterocycle, or substituted or unsubstituted aryl.
6. The compound according to claim 1, wherein said compound is characterized by a
30 general formula (3) or (4),



(3), or



(4), particularly of formula (3), wherein

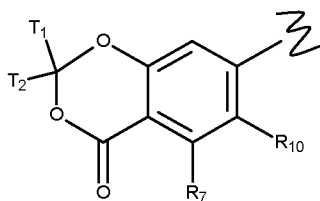
- R₁ is a C₁-C₃ alkyl, cyclopropane, a C₁-C₃ haloalkyl, halocyclopropane or -NHR₈, wherein R₈ is a C₁-C₃ alkyl, cyclopropane, a C₁-C₃ haloalkyl or halocyclopropane;
- R₂ is H, F, a C₁-C₄ alkyl or a C₁-C₄ alkanol;
- R₃ is H, F, Cl, a C₁-C₆ alkyl, a C₁-C₃ haloalkyl, a C₁-C₄ alkoxy, a C₁-C₄ alkanol, a C₂-C₄ ether, a 3- to 6-membered saturated heterocycle, a 3- to 6-membered heteroaryl, a benzyloxy or a substituted amine of the form -NHR₈, wherein R₈ is a C₁-C₃ alkyl, cyclopropane, a C₁-C₃ haloalkyl or halocyclopropane;
- X is -C(=O)NH-, -NHC(=O)-, -C(=O)NR₁₂-, -NR₁₂C(=O)-, -NR₁₂C(=O)-, -NHC(=O)NH-, -N(R₉)C(=O)NH-, -NHC(=O)NR₉-, -C(=S)NH-, -NHC(=S)-, -NHC(=S)NH-, -N(R₉)C(=S)NH-, -NHC(=S)N(R₉)-, -N-S(=O)₂-, -S(=O)₂-N-, wherein
 - R₉ is C₁-C₃ alkyl, C₁-C₃ alkoxy, C₁-C₃ haloalkyl, C₁-C₃ alkanol, C₂-C₄ ether, 3- to 6-membered heterocycle, or substituted or unsubstituted aryl, and wherein
 - R₁₂ is -(CH₂)_r-phenyl with r being 0, 1 or 2 and said phenyl may be substituted with one or more electron donating groups, in particular one or more electron donating groups selected from -OR₁₃, with R₁₃ being H, a methyl group or an ethyl group;
- R₅ being H, -COOH or salt thereof, a C₁-C₃ alkoxy, a C₁-C₃ alkyl, a C₁-C₃ alkyl ester, a heteroaryl, a substituted or unsubstituted C₁-C₆ alkoxy or a sulfonic acid, a sulfonamide, particularly an S-linked sulfonamide, that may be singly substituted with a C₁-C₃ alkyl group or with a C₃-C₆ cyclic alkyl; and
- R₆ being H, -COOH or salt thereof, a C₁-C₃ alkoxy, a C₁-C₃ alkyl, a C₁-C₃ alkyl ester, a substituted or unsubstituted heteroaryl, a substituted or unsubstituted C₁-C₆ alkoxy or a sulfonic acid, a sulfonamide, particularly an S-linked sulfonamide, that may be singly substituted with a C₁-C₃ alkyl group or with a C₃-C₆ cyclic alkyl; and wherein
- R₇ and R₁₀ being independently from each other selected from
 - H, Br, Cl, F, NO₂ or
 - substituted or unsubstituted C₁-C₃ alkanol, C₁-C₃ alkyl, C₁-C₃ haloalkyl, substituted or unsubstituted C₁-C₃ alkoxy, C₃-C₆ cycloalkyl, C₂-C₄ alkyl ether, 3- to 6-membered saturated heterocycle, a 3- to 6-membered heteroaryl moiety,

wherein said moieties may be substituted or unsubstituted, wherein the substituents of said substituted moieties with respect to R_4 and R_7 are selected from 3- to 6-membered heteroaryls and aryls, or 3- to 6-membered saturated heterocycles, which may also be substituted with one or more hydroxyl, amine or C_1 - C_3 alkoxy groups;

- n is 0, 1 or 2;
- Y is N, CH or $C-R_{11}$, with

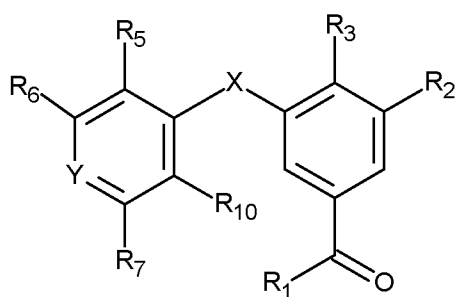
R_{11} being a hydroxyl, a C_1 - C_5 heteroalkyl, particularly a $-(CH_2)_p-OT_3$ or a $-(CH_2)_p-N(T_3)(T_4)$, with T_3 and T_4 being independently from each other H or C_1 - C_3 alkyl, and p is 0, 1, 2, 3, 4 or 5, a substituted or unsubstituted C_1 - C_6 alkoxy, a heteroaryl, a saturated heterocycle, $-O-(CH_2)_q$ -phenyl or $-O-(CH_2)_q$ -heterocycle, with q being 0, 1 or 2, wherein the saturated heterocycle or the $-O-(CH_2)_q$ -heterocycle are preferably C_3 - C_6 heterocycles, more preferably C_5 - C_6 heterocycles, or

wherein R^6 and Y are connected forming a cyclic moiety of the formula 5'

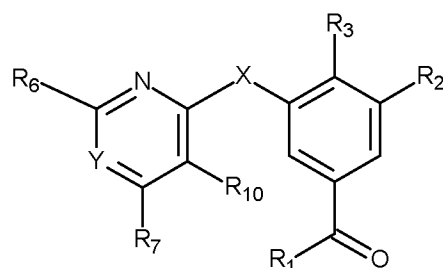


(5'), with T_1 and T_2 being independently from each other H, CH_3 or CH_2CH_3 , particularly H, and R_7 and R_{10} having the same meaning as above.

7. The compound according to claim 6, wherein said compound is characterized by a general formula (3a) or (4a)



(3a), or



(4a),

particularly of formula (3a), wherein

- R_1 is a methyl or $-NHR_8$ where R_8 is a C_1 - C_3 ; and/or
- R_2 is a hydrogen, a methyl or a C_1 - C_4 alkanol; and/or
- R_3 is H, F, a C_1 - C_6 alkyl or a C_1 - C_4 alkoxy, a benzyloxy or a morpholino, in particular R_3 is an ethoxy, a propoxy, a butoxy, cyclopropane, cyclopropylethoxy, benzyloxy or a morpholino, more particularly ethoxy; and/or

- R₅ is H, -COOH or salt thereof, a C₁-C₃ alkoxy, a C₁-C₃ alkyl, a C₁-C₃ alkyl ester, a heteroaryl, a substituted or unsubstituted C₁-C₆ alkoxy or a sulfonic acid, an S-linked sulfonamide that may be singly substituted with a C₁-C₃ alkyl group or with a C₃-C₆ cyclic alkyl, and/or
- 5 - R₆ is H, -COOH or salt thereof, a C₁-C₃ alkoxy, a C₁-C₃ alkyl, a C₁-C₃ alkyl ester, a substituted or unsubstituted heteroaryl, a substituted or unsubstituted C₁-C₆ alkoxy or a sulfonic acid, an S-linked sulfonamide that may be singly substituted with a C₁-C₃ alkyl group or with a C₃-C₆ cyclic alkyl; and/or
- R₁₀ is H or methyl, in particular H; and/or
- 10 - R₇ is pyridine, furan, CH₂OH, CH₂OCH₃ or CH₂-O-tetrahydropyran, more particularly furan; and/or
- Y is N, CH or C-R₁₁ with R₁₁ being a hydroxyl, a C₁-C₅ heteroalkyl, particularly a - (CH₂)_p-OT₃ or a -(CH₂)_p-N(T₃)(T₄), with T₃ and T₄ being independently from each other H or C₁-C₃ alkyl, and p is 0, 1, 2, 3, 4 or 5, a substituted or unsubstituted C₁-C₆ alkoxy, a saturated heterocycle, -O-(CH₂)_q-phenyl or -O-(CH₂)_q-heterocycle, wherein the saturated heterocycle or the -O-(CH₂)_q-heterocycle are preferably C₃-C₆ heterocycles, more preferably C₅-C₆ heterocycles, and q is 0, 1 or 2, wherein said phenyl and said heterocycle of R₁₁ may optionally be substituted with one or more methoxy or hydroxy groups, wherein preferably Y is CH, -O-(CH₂)_q-heterocycle or hydroxyl; and/or
- 20 - X is -C(=O)NH-, -NHC(=O)-, -NHC(=O)NH-, -N(R₉)C(=O)NH-, -NHC(=O)NR₉-, -C(=S)NH-, -NHC(=S)-, -NHC(=S)NH-, -N(R₉)C(=S)NH-, -NHC(=S)N(R₉)-, -N-S(=O)₂-, -S(=O)₂-N-, in particular -C(=O)NH-, -NHC(=O)-, -NHC(=O)NH-, -N(R₉)C(=O)NH-, -NHC(=O)NR₉-, more particularly -C(=O)NH- or -NHC(=O)-, wherein R₉ is a C₁-C₃ alkyl, C₁-C₃ alkoxy, C₁-C₃ haloalkyl, C₁-C₃ alkanol, C₂-C₄ ether, 3- to 6-membered heterocycle, or substituted or unsubstituted aryl.
- 25
- 8. The compound according to claim 7, wherein
- R₁ is a methyl or -NHR₈ where R₈ is a methyl, in particular R₁ is a methyl; and/or
- R₂ is a hydrogen; and/or
- 30 - R₃ is ethoxy, a propoxy, a butoxy, cyclopropane, cyclopropylethoxy, benzyloxy or a morpholino, more particularly ethoxy; and/or
- R₅ is H, -COOH or salt thereof, a C₁-C₃ alkoxy, a C₁-C₃ alkyl, a C₁-C₃ alkyl ester, a heteroaryl, a substituted or unsubstituted C₁-C₆ alkoxy or a sulfonic acid, an S-linked sulfonamide that may be singly substituted with a C₁-C₃ alkyl group or with a C₃-C₆ cyclic alkyl; and/or
- 35 - R₆ is H, -COOH or salt thereof, a C₁-C₃ alkoxy, a C₁-C₃ alkyl, a C₁-C₃ alkyl ester, a substituted or unsubstituted heteroaryl, a substituted or unsubstituted C₁-C₆ alkoxy or

a sulfonic acid, an S-linked sulfonamide that may be singly substituted with a C₁-C₃ alkyl group or with a C₃-C₆ cyclic alkyl; and/or

- R₁₀ is H or methyl, in particular H; and/or
- R₇ is pyridine, furan, CH₂OH, CH₂OCH₃ or CH₂-O-tetrahydropyran, in particular furan; and/or
- Y is N, CH or C-R₁₁ with R₁₁ being a hydroxyl, a substituted or unsubstituted C₁-C₆ alkoxy, a saturated heterocycle, -O-(CH₂)_q-phenyl or -O-(CH₂)_q-heterocycle, and q is 0, 1 or 2, wherein the saturated heterocycle or the -O-(CH₂)_q-heterocycle are preferably C₃-C₆ heterocycles, more preferably C₅-C₆ heterocycles, wherein said phenyl and said heterocycle of R₁₁ is substituted with one or more methoxy or hydroxy groups, wherein preferably Y is CH, -O-(CH₂)_q-heterocycle or hydroxyl; and/or
- X is C(=O)NH-, -NHC(=O)-, -NHC(=O)NH-, -N(R₉)C(=O)NH-, -NHC(=O)NR₉, in particular X is -C(=O)NH- or -NHC(=O)-, wherein R₉ is a C₁-C₃ alkyl, C₁-C₃ alkoxy, C₁-C₃ haloalkyl, C₁-C₃ alkanol, C₂-C₄ ether, 3- to 6-membered heterocycle, or substituted or unsubstituted aryl, wherein in particular R₉ is a C₁-C₃ alkoxy, C₁-C₃ haloalkyl, C₁-C₃ alkanol, C₂-C₄ ether, 3- to 6-membered heterocycle, or substituted or unsubstituted aryl.

9. The compound according to any one of the previous claims, wherein,

- X is -N(R₉)C(=O)NH-, -NHC(=O)NR₉-, -NHC(=O)NH-, -N(R₉)C(=S)NH- or -NHC(=S)N(R₉)-, -NHC(=S)NH- or -NHC(=S)N(R₉)-, then
- R₅ is -COOH or salt thereof, a C₁-C₃ alkyl ester, a sulfonic acid, an S-linked sulfonamide that may be singly substituted with a C₁-C₃ alkyl group or with a C₃-C₆ cyclic alkyl, or a 5-membered heteroaryl, in particular H, -COOH or salt thereof, C₁-C₃ alkyl ester, in particular methylester, a substituted or unsubstituted heteroaryl, a tetrazole,; and
- R₆ is H, a C₁-C₃ alkoxy or a C₁-C₃ alkyl, in particular H;

or

- X is -C(=O)NH-, -NHC(=O)-, -C(=O)NR₁₂-, -NR₁₂C(=O)-, -C(=S)NH-, -NHC(=S)-, then
- R₅ is H, a C₁-C₃ alkoxy or a C₁-C₃ alkyl; in particular H,
- R₆ is -COOH or salt thereof, a C₁-C₃ alkyl ester, a sulfonic acid, a substituted or unsubstituted heteroaryl, an S-linked sulfonamide that may be singly substituted with a C₁-C₃ alkyl group or with a C₃-C₆ cyclic alkyl, or a 5-membered heteroaryl, in particular H, -COOH or salt thereof, C₁-C₃ alkyl ester, in particular methylester, a substituted or unsubstituted heteroaryl, tetrazole,; and

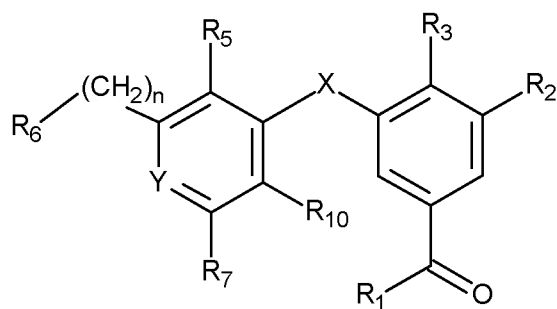
wherein n , R_1 , R_2 , R_3 , A , R_4 , R_7 , R_8 , R_9 , R_{10} , Y , R_{11} have the same meaning as defined previously.

10. The compound according to any one of the previous claims, wherein the substituted or unsubstituted heteroaryl of R_6 are 3-hydroxy-isoxazole bound via C4 (a') or C5 (a''), 4-alkyl-3-hydroxy-isoxazole bound via C5, where said alkyl (depicted with R) is a C1-C3 alkyl, 5-alkyl-3-hydroxy-isoxazole bound via C4, where said alkyl (depicted with R) is a C1-C3 alkyl, 1,2,5-oxadiazol-3(2H)-one bound via C4 (d') or 1,2,5-oxadiazol-3-ol bound via C4 (d''), 1,2,5-thiadiazol-3(2H)-one bound via C4 (e') or 1,2,5-thiadiazol-3-ol bound via C4 (e''), 1,2,5-oxadiazole-3(2H)-thione bound via C4 (f') or 1,2,5-oxadiazole-3-thiol bound via C4 (f''), 1,2,5-thiadiazole-3(2H)-thione bound via C4 (g') or 1,2,5-thiadiazole-3-thiol bound via C4 (g''), 1H-tetrazol-5-one bound via N4 (h') or 1H-tetrazol-5-thione bound via N4 (h''), 1,2,4-oxadiazolidine-3,5-dione bound via N2 (i'), 3-thioxo 1,2,4-oxadiazolidine-5-dione bound via N2 (i''), 1,2,4-oxadiazolidine-3,5-dithione bound via N2 (i''') or 5-thioxo 1,2,4-oxadiazolidine-3-dione bound via N2 (i'''), 1,2,4-oxadiazol-5(4H)-one bound via C3 (j'), 1,2,4-oxadiazole-5(4H)-thione bound via C3 (j''), 1,2,4-thiadiazol-5(4H)-one bound via C3 (j''') or 1,2,4-thiadiazole-5(4H)-thione bound via C3 (j'''), 2,4-oxazolidinedione bound via C5 (k) more preferred are a'', b, c h', h'', j', j'' and j'''.

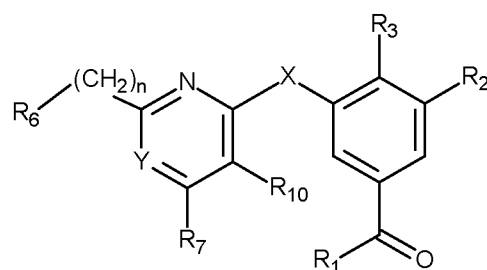
11. The compound according to any one of the previous claims, wherein

- each of R_6 and R_7 is a tetrazole, particularly one of R_6 or R_7 is a tetrazole connected by its carbon moiety,
- R_6 is a tetrazole connected by its carbon moiety and R_7 is a tetrazole connected by its nitrogen moiety,
- Each of R_6 and R_7 is a tetrazole, which are both connected by their carbon moiety;
- R_6 is a tetrazole, particularly a tetrazole connected by its carbon moiety, and R_7 is furan,
- R_6 is -COOH or salt thereof, a C₁-C₃ alkyl ester and R_7 is a tetrazole, particularly a tetrazole connected by its carbon moiety,
- R_6 is a tetrazole, particularly a tetrazole connected by its carbon moiety, and R_7 is -O-(CH₂)_q-heterocycle, with q being 0, 1 or 2,
- R_6 is a tetrazole, particularly a tetrazole connected by its carbon moiety, and Y is C-R₁₁, with R₁₁ being H, a hydroxyl or -O-(CH₂)_q-heterocycle, with q being 0, 1 or 2.

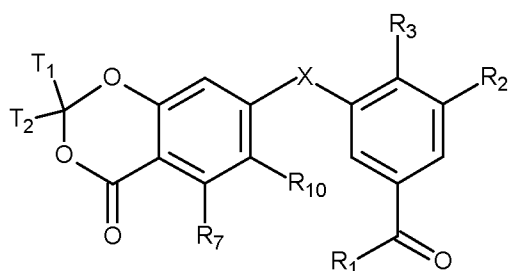
12. A compound, or prodrug or salt thereof, of formula (3), (4) or (5),



(3), or



(4), or



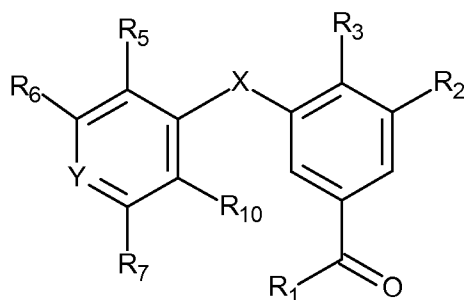
(5), particularly of formula (3), wherein

- R₁ is a C₁-C₃ alkyl, cyclopropane, a C₁-C₃ haloalkyl, halocyclopropane or -NHR₈,
wherein R₈ is a C₁-C₃ alkyl, cyclopropane, a C₁-C₃ haloalkyl or halocyclopropane;
- R₂ is H, F, a C₁-C₄ alkyl or a C₁-C₄ alkanol;
- R₃ is H, F, Cl, a C₁-C₆ alkyl, a C₁-C₃ haloalkyl, a C₁-C₄ alkoxy, a C₁-C₄ alkanol, a C₂-C₄ ether, a 3- to 6-membered saturated heterocycle, a 3- to 6-membered heteroaryl, a benzyloxy or a substituted amine of the form -NHR₈, wherein R₈ is a C₁-C₃ alkyl, cyclopropane, a C₁-C₃ haloalkyl or halocyclopropane;
- X is -C(=O)NH-, -NHC(=O)-, -C(=O)NR₁₂-, -NR₁₂C(=O)-, -NR₁₂C(=O)-, -NHC(=O)NH-, -N(R₉)C(=O)NH-, -NHC(=O)NR₉-, -C(=S)NH-, -NHC(=S)-, -NHC(=S)NH-, -N(R₉)C(=S)NH-, -NHC(=S)N(R₉)-, -N-S(=O)₂-, -S(=O)₂-N-, particularly X is -C(=O)NH-, -NHC(=O)-, -C(=O)NR₁₂-, -NR₁₂C(=O)-, -NHC(=O)NH-, -N(R₉)C(=O)NH-, -NHC(=O)NR₉-, -C(=S)NH-, -NHC(=S)-, -NHC(=S)NH-, -N(R₉)C(=S)NH-, -NHC(=S)N(R₉)-, wherein
 - R₉ is C₁-C₃ alkyl, C₁-C₃ alkoxy, C₁-C₃ haloalkyl, C₁-C₃ alkanol, C₂-C₄ ether, 3- to 6-membered heterocycle, or substituted or unsubstituted aryl, and wherein
 - R₁₂ is -(CH₂)_r-phenyl with r being 0, 1 or 2 and said phenyl may be substituted with one or more electron donating groups, in particular one or more electron donating groups selected from -OR₁₃, with R₁₃ being H, a methyl group or an ethyl group;
- R₅ being H, -COOH or salt thereof, a C₁-C₃ alkoxy, a C₁-C₃ alkyl, a C₁-C₃ alkyl ester, a heteroaryl, a substituted or unsubstituted C₁-C₆ alkoxy or a sulfonic acid, a

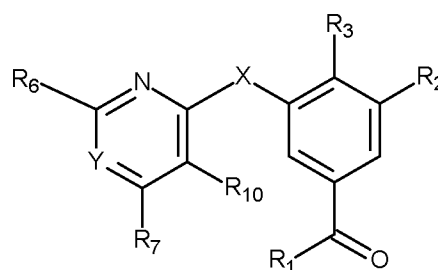
sulfonamide, particularly an S-linked sulfonamide, that may be singly substituted with a C₁-C₃ alkyl group or with a C₃-C₆ cyclic alkyl; and

- R₆ being H, -COOH or salt thereof, a C₁-C₃ alkoxy, a C₁-C₃ alkyl, a C₁-C₃ alkyl ester, a substituted or unsubstituted heteroaryl, a substituted or unsubstituted C₁-C₆ alkoxy or a sulfonic acid, a sulfonamide, particularly an S-linked sulfonamide, that may be singly substituted with a C₁-C₃ alkyl group or with a C₃-C₆ cyclic alkyl; and wherein
- R₇ and R₁₀ being independently from each other selected from
 - H, Br, Cl, F, NO₂ or
 - substituted or unsubstituted C₁-C₃ alkanol, C₁-C₃ alkyl, C₁-C₃ haloalkyl, substituted or unsubstituted C₁-C₃ alkoxy, C₃-C₆ cycloalkyl, C₂-C₄ alkyl ether, 3- to 6-membered saturated heterocycle, a 3- to 6-membered heteroaryl moiety, wherein said moieties may be substituted or unsubstituted, wherein the substituents of said substituted moieties with respect to R₄ and R₇ are selected from 3- to 6-membered heteroaryls and aryls, or 3- to 6-membered saturated heterocycles, which may also be substituted with one or more hydroxyl, amine or C₁-C₃ alkoxy groups;
- n is 0, 1 or 2;
 - Y being N, CH or C-R₁₁, with R₁₁ being a hydroxyl, a C₁-C₅ heteroalkyl, particularly a -(CH₂)_p-OT₃ or a -(CH₂)_p-N(T₃)(T₄), with T₃ and T₄ being independently from each other H or C₁-C₃ alkyl, and p is 0, 1, 2, 3, 4 or 5, a substituted or unsubstituted C₁-C₆ alkoxy, a heteroaryl, a saturated heterocycle, -O-(CH₂)_q-phenyl or -O-(CH₂)_q-heterocycle, with q being 0, 1 or 2, wherein the saturated heterocycle or the -O-(CH₂)_q-heterocycle are preferably C₃-C₆ heterocycles, more preferably C₅-C₆ heterocycles, and
 - in case of formula (5) T₁ and T₂ being independently from each other H, CH₃ or CH₂CH₃, particularly H.

13. The compound or prodrug or salt thereof according to claim 12, wherein said compound is characterized by a general formula (3a) or (4a)



(3a), or



(4a), particularly of formula (3a), wherein

- R₁ is a methyl or -NHR₈ where R₈ is a C₁-C₃; and/or
- R₂ is a hydrogen, a methyl or a C₁-C₄ alkanol; and/or
- R₃ is H, F, a C₁-C₆ alkyl or a C₁-C₄ alkoxy, a benzyloxy or a morpholino, in particular R₃ is an ethoxy, a propoxy, a butoxy, cyclopropane, cyclopropylethoxy, benzyloxy or a morpholino, more particularly ethoxy; and/or
- R₅ is H, -COOH or salt thereof, a C₁-C₃ alkoxy, a C₁-C₃ alkyl, a C₁-C₃ alkyl ester, a heteroaryl, a substituted or unsubstituted C₁-C₆ alkoxy or a sulfonic acid, an S-linked sulfonamide that may be singly substituted with a C₁-C₃ alkyl group or with a C₃-C₆ cyclic alkyl; and/or
- R₆ is H, -COOH or salt thereof, a C₁-C₃ alkoxy, a C₁-C₃ alkyl, a C₁-C₃ alkyl ester, a substituted or unsubstituted heteroaryl, a substituted or unsubstituted C₁-C₆ alkoxy or a sulfonic acid, an S-linked sulfonamide that may be singly substituted with a C₁-C₃ alkyl group or with a C₃-C₆ cyclic alkyl; and/or
- R₁₀ is H or methyl, in particular H; and/or
- R₇ is pyridine, furan, CH₂OH, CH₂OCH₃ or CH₂-O-tetrahydropyran, more particularly furan; and/or
- Y is N, CH or C-R₁₁ with R₁₁ being a hydroxyl, a substituted or unsubstituted C₁-C₆ alkoxy, a saturated heterocycle, -O-(CH₂)_q-phenyl or -O-(CH₂)_q-heterocycle, wherein the saturated heterocycle or the -O-(CH₂)_q-heterocycle are preferably C₃-C₆ heterocycles, more preferably C₅-C₆ heterocycles, and q is 0, 1 or 2, wherein said phenyl and said heterocycle of R₁₁ may optionally be substituted with one or more methoxy or hydroxy groups, wherein preferably Y is CH; and/or
- X is -C(=O)NH-, -NHC(=O)-, -NHC(=O)NH-, -N(R₉)C(=O)NH-, -NHC(=O)NR₉-, -C(=S)NH-, -NHC(=S)-, -NHC(=S)NH-, -N(R₉)C(=S)NH-, -NHC(=S)N(R₉)-, -N-S(=O)₂-, -S(=O)₂-N-, in particular -C(=O)NH-, -NHC(=O)-, -NHC(=O)NH-, -N(R₉)C(=O)NH-, -NHC(=O)NR₉-, more particularly -C(=O)NH- or -NHC(=O)-, wherein R₉ is a C₁-C₃ alkyl, C₁-C₃ alkoxy, C₁-C₃ haloalkyl, C₁-C₃ alkanol, C₂-C₄ ether, 3- to 6-membered heterocycle, or substituted or unsubstituted aryl.

14. The compound or prodrug or salt thereof according to claim 13, wherein

- R₁ is a methyl or -NHR₈ where R₈ is a methyl, in particular R₁ is a methyl; and/or
- R₂ is a hydrogen; and/or
- R₃ is ethoxy, a propoxy, a butoxy, cyclopropane, cyclopropylethoxy, benzyloxy or a morpholino, more particularly ethoxy; and/or
- R₅ is H, -COOH or salt thereof, a C₁-C₃ alkoxy, a C₁-C₃ alkyl, a C₁-C₃ alkyl ester, a heteroaryl, a substituted or unsubstituted C₁-C₆ alkoxy or a sulfonic acid, an S-linked sulfonamide that may be singly substituted with a C₁-C₃ alkyl group or with a C₃-C₆ cyclic alkyl; and/or

- R₆ is H, -COOH or salt thereof, a C₁-C₃ alkoxyl, a C₁-C₃ alkyl, a C₁-C₃ alkyl ester, a substituted or unsubstituted heteroaryl, a substituted or unsubstituted C₁-C₆ alkoxyl or a sulfonic acid, an S-linked sulfonamide that may be singly substituted with a C₁-C₃ alkyl group or with a C₃-C₆ cyclic alkyl; and/or
- R₁₀ is H or methyl, in particular H; and/or
- R₇ is pyridine, furan, CH₂OH, CH₂OCH₃ or CH₂-O-tetrahydropyran, in particular furan; and/or
- Y is N, CH or C-R₁₁ with R₁₁ being a hydroxyl, a substituted or unsubstituted C₁-C₆ alkoxyl, a saturated heterocycle, -O-(CH₂)_q-phenyl or -O-(CH₂)_q-heterocycle, wherein the saturated heterocycle or the -O-(CH₂)_q-heterocycle are preferably C₃-C₆ heterocycles, more preferably C₅-C₆ heterocycles, and q is 0, 1 or 2, wherein said phenyl and said heterocycle of R₁₁ is substituted with one or more methoxy or hydroxy groups, wherein preferably Y is CH; and/or
- X is C(=O)NH-, -NHC(=O)-, -NHC(=O)NH-, -N(R₉)C(=O)NH-, -NHC(=O)NR₉, in particular X is -C(=O)NH- or -NHC(=O)-, wherein R₉ is a C₁-C₃ alkyl, C₁-C₃ alkoxy, C₁-C₃ haloalkyl, C₁-C₃ alkanol, C₂-C₄ ether, 3- to 6-membered heterocycle, or substituted or unsubstituted aryl, wherein in particular R₉ is a C₁-C₃ alkoxy, C₁-C₃ haloalkyl, C₁-C₃ alkanol, C₂-C₄ ether, 3- to 6-membered heterocycle, or substituted or unsubstituted aryl.

15. The compound according to any of the claims 12 to 14, wherein the substituted or unsubstituted heteroaryl of R₆ are 3-hydroxy-isoxazole bound via C4 (a') or C5 (a''), 4-alkyl-3-hydroxy-isoxazole bound via C5, where said alkyl (depicted with R) is a C₁-C₃ alkyl, 5-alkyl-3-hydroxy-isoxazole bound via C4, where said alkyl (depicted with R) is a C₁-C₃ alkyl, 1,2,5-oxadiazol-3(2H)-one bound via C4 (d') or 1,2,5-oxadiazol-3-ol bound via C4 (d''), 1,2,5-thiadiazol-3(2H)-one bound via C4 (e') or 1,2,5-thiadiazol-3-ol bound via C4 (e''), 1,2,5-oxadiazole-3(2H)-thione bound via C4 (f') or 1,2,5-oxadiazole-3-thiol bound via C4 (f''), 1,2,5-thiadiazole-3(2H)-thione bound via C4 (g') or 1,2,5-thiadiazole-3-thiol bound via C4 (g''), 1H-tetrazol-5-one bound via N4 (h') or 1H-tetrazol-5-thione bound via N4 (h''), 1,2,4-oxadiazolidine-3,5-dione bound via N2 (i'), 3-thioxo 1,2,4-oxadiazolidine-5-dione bound via N2 (i''), 1,2,4-oxadiazolidine-3,5-dithione bound via N2 (i''') or 5-thioxo 1,2,4-oxadiazolidine-3-dione bound via N2 (i'''), 1,2,4-oxadiazol-5(4H)-one bound via C3 (j'), 1,2,4-oxadiazole-5(4H)-thione bound via C3 (j''), 1,2,4-thiadiazol-5(4H)-one bound via C3 (j''') or 1,2,4-thiadiazole-5(4H)-thione bound via C3 (j'''), 2,4-oxazolidinedione bound via C5 (k) more preferred are a'', b, c h', h'', j', j'' and j'''.

16. The compound according to any one of the claims 12 to 15, wherein

- each of R₆ and R₇ is a tetrazole, particularly one of R₆ or R₇ is a tetrazole connected by its carbon moiety,
 - R₆ is a tetrazole connected by its carbon moiety and R₇ is a tetrazole connected by its nitrogen moiety,
 - 5 - Each of R₆ and R₇ is a tetrazole, which are both connected by their carbon moiety;
 - R₆ is a tetrazole, particularly a tetrazole connected by its carbon moiety, and R₇ is furan,
 - R₆ is -COOH or salt thereof, a C₁-C₃ alkyl ester and R₇ is a tetrazole, particularly a tetrazole connected by its carbon moiety,
 - 10 - R₆ is a tetrazole, particularly a tetrazole connected by its carbon moiety, and R₇ is -O-(CH₂)_q-heterocycle, with q being 0, 1 or 2,
 - R₆ is a tetrazole, particularly a tetrazole connected by its carbon moiety, and Y is C-R₁₁, with R₁₁ being H, a hydroxyl or -O-(CH₂)_q-heterocycle, with q being 0, 1 or 2.
17. The compound according to any one of the preceding claims for use in the treatment
15 of a disease or condition for which a bromodomain inhibitor is indicated, wherein said disease or condition is cancer, an autoimmune disease or alzheimer's disease, in particular leukemia and more particularly an acute myeloid leukemia, wherein in particular said bromodomain is CBP or EP300.
18. A bromodomain inhibitor comprising a compound according to any one of the
20 preceding claims, in particular for use in the treatment of a disease or condition for which a bromodomain inhibitor is indicated, wherein said disease or condition is cancer, an autoimmune disease or alzheimer's disease, in particular leukemia and more particularly an acute myeloid leukemia, wherein in particular said bromodomain is CBP or EP300.
19. A pharmaceutical composition comprising a therapeutically effective amount of a
25 compound according to any one of claim 12 to 16 and one or more pharmaceutically acceptable carriers, diluents or excipients.

INTERNATIONAL SEARCH REPORT

International application No

PCT/EP2015/065404

A. CLASSIFICATION OF SUBJECT MATTER

INV. A61K31/18 A61K31/192 A61K31/235 A61K31/341 A61K31/351
 A61K31/366 A61K31/41 A61K31/4164 A61K31/44 A61K31/4409
 A61K31/4965 A61K31/5375 A61P35/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

EPO-Internal, BIOSIS, CHEM ABS Data, EMBASE, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2013/063321 A1 (GEN HOSPITAL CORP [US]) 2 May 2013 (2013-05-02) claim 1 -----	1,2,6-8, 12-14, 17-19
X	US 2010/197688 A1 (NANTERMET PHILIPPE G [US] ET AL) 5 August 2010 (2010-08-05) page 12; claims -----	1,2,6-8, 12-14, 17-19
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Further documents are listed in the continuation of Box C.



See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

23 September 2015

Date of mailing of the international search report

14/10/2015

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INTERNATIONAL SEARCH REPORT

International application No

PCT/EP2015/065404

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
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A	WO 2007/084625 A2 (SINAI SCHOOL MEDICINE [US]; ZHOU MING-MING [US]; SACHCHIDANAND D PHIL) 26 July 2007 (2007-07-26) claims -----	1-19
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INTERNATIONAL SEARCH REPORT

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Information on patent family members

International application No

PCT/EP2015/065404

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