Bicyclic derivatives of azabicyclic carboxamides, preparation and therapeutic use thereof.

Documents WO2006/024 776, WO2006/072 736, WO2007/010 144 and WO2007/010 138 describe bicyclic carboxamide derivatives with *in vitro* and *in vivo* antagonist or agonist activity on receptors of TRPV1 (or VR1) type.

There is still a need to find novel ligands for receptors of TRPV 1 type, which are improved in terms of functional activity, metabolic profile and/or safety profile.

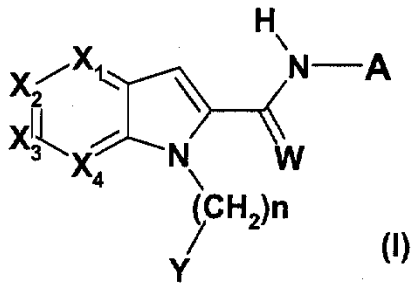
The present invention satisfies this need by providing azabicyclic carboxamide derivatives that have *in vitro* and *in vivo* antagonist or agonist activity on receptors of TRPV1 (or VR1) type.

A first subject of the invention concerns the compounds corresponding to the general formula (I) hereinbelow.

Another subject of the invention concerns processes for preparing the compounds of general formula (I).

Another subject of the invention concerns the use of the compounds of general formula (I) especially in medicaments or in pharmaceutical compositions.

The compounds of the invention correspond to the general formula (I):



(I)

in which:

X_1, X_2, X_3 and X_4 represent, independently of each other, a nitrogen atom or a group C-R_1;

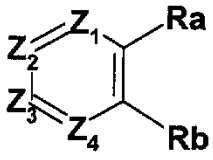
it being understood that when one from among X_1, X_2, X_3 and X_4 represents a nitrogen atom, the others correspond to a group C-R_1;

W represents an oxygen or sulfur atom;

n is equal to 0, 1, 2 or 3;

Y represents an aryl or a heteroaryl optionally substituted with one or more groups chosen from a halogen atom, a group C_1-C_6-alkyl, C_3-C_7-cycloalkyl, C_3-C_7-cycloalkyl-C_1-C_3-alkylene, C_1-C_6-fluoroalkyl, hydroxyl, C_1-C_6-alkoxy, C_3-C_7-cycloalkyloxy, C_3-C_7-cycloalkyl-C_1-C_6-alkylene-O-, C_1-C_6-fluoroalkoxy, cyano, C(O) NR_4R_5, nitro, NR_4R_5, C_1-C_6-thioalkyl, thiol, -S(O)-C_1-C_6-alkyl, -$S(O)_2$-C_1-C_6-alkyl, $SO_2NR_4R_5$, $NR_6C(O)R_7$, $NR_6SO_2R_8$, $C(O)NR_4R_5$, $OC(O)NR_4R_5$, -Si-(C_1-C_6-alkyl)$_3$, -SF_5, aryl-C_1-C_5-alkylene or aryl, heteroaryl-C_1-C_5-alkylene or heteroaryl; the groups C_1-C_6-alkyl, C_3-C_7-cycloalkyl, C_3-C_7-cycloalkyl-C_1-C_3-alkylene, C_1-C_6-fluoroalkyl, C_1-C_6-alkoxy, C_3-C_7-cycloalkyloxy and C_3-C_7-cycloalkyl-C_1-C_6-alkylene-O- being optionally substituted with a hydroxyl group, C_1-C_6-alkoxy or NR_4R_5, the aryl and heteroaryl groups being optionally substituted with one or more substituents R_9, which may be identical to or different from each other;

A represents the group of formula:



Z_1, Z_2, Z_3 and Z_4 represent, independently of each other, a nitrogen atom, a carbon atom or a group C-R_2,
at least one from among Z_1, Z_2, Z_3 and Z_4 corresponding to a nitrogen atom and
one from among Z_1, Z_2, Z_3 and Z_4, corresponding to a carbon atom, being bonded to the nitrogen atom of the amide or of the thioamide of formula (I);

Ra and Rb form, together with the carbon atoms that bear them,
either a partially unsaturated cycloalkyl, or an aryl;
or a heterocycle, or a heteroaryl, which is 5- to 7-membered, comprising from 1 to 3

heteroatoms chosen from O, S and N;
it being understood that when Ra and Rb together form, with the carbon atoms that bear them, a 5-membered ring, this ring comprising a nitrogen atom and carbon atoms, this ring being partially saturated or unsaturated, is excluded;
this partially unsaturated cycloalkyl, this aryl, this heterocycle or this heteroaryl possibly being substituted with one or more substituents R_3;

R_1 is chosen from a hydrogen atom, a halogen atom and a group C_1-C_6-alkyl, C_3-C_7-cycloalkyl, C_3-C_7-cycloalkyl-C_1-C_3-alkylene, C_1-C_6-fluoroalkyl, aryloxy-C_1-C_6-alkyl, heteroaryloxy-C_1-C_6-alkyl, aryl-C_1-C_3-alkylenoxy-C_1-C_6-alkyl, heteroaryl-C_1-C_3-alkylenoxy-C_1-C_6-alkyl, arylthio-C_1-C_6-alkyl, heteroarylthio-C_1-C_6-alkyl, aryl-C_1-C_3-alkylene-thio-C_1-C_6-alkyl, heteroaryl-C_1-C_3-alkylene-thio-C_1-C_6-alkyl, C_1-C_6-alkoxy, C_3-C_7-cycloalkyloxy, C_3-C_7-cycloalkyl-C_1-C_3-alkylenoxy, C_1-C_6-fluoroalkoxy, cyano, $C(O)NR_4R_5$, nitro, NR_4R_5, C_1-C_6-thioalkyl, C_3-C_7-cycloalkylthio, C_3-C_7-cycloalkyl-C_1-C_3-alkylene-thio, -S(O)-C_1-C_6-alkyl, -S(O)-C_3-C_7-cycloalkyl, -S(O)-C_1-C_3-alkylene-C_3-C_7-cycloalkyl, C_1-C_6-alkyl-$S(O)_2$-, C_1-C_6-fluoroalkyl-$S(O)_2$-, C_3-C_7-cycloalkyl-$S(O)_2$-, C_3-C_7-cycloalkyl-C_1-C_3-alkylene-$S(O)_2$-, $SO_2NR_4R_5$, -Si-(C_1-C_6-alkyl)$_3$, $-SF_5$, $NR_6C(O)R_7$, $NR_6SO_2R_8$, $C(O)NR_4R_5$, $OC(O)NR_4R_5$, aryl, heteroaryl, aryl-C_1-C_5-alkylene, heteroaryl-C_1-C_5-alkylene, aryloxy, arylthio, heteroaryloxy or heteroarylthio; the heteroaryl or aryl groups being optionally substituted with one or more substituents R_9, which may be identical to or different from each other;

R_2 represents a hydrogen atom, a halogen atom or a group C_1-C_6-alkyl, C_3-C_7-cycloalkyl, C_3-C_7-cycloalkyl-C_1-C_3-alkylene, C_1-C_6-fluoroalkyl, C_1-C_6-alkoxy, C_3-C_7-cycloalkyloxy, C_3-C_7-cycloalkyl-C_1-C_3-alkylene-O-, hydroxyl, thiol or C_1-C_6-fluoroalkoxy;

R_3 represents, when it is borne by a carbon atom, a hydrogen atom or a hydroxyl, thiol, C_1-C_6-alkyl, C_3-C_7-cycloalkyl, C_3-C_7-cycloalkyl-C_1-C_3-alkylene, C_1-C_6-fluoroalkyl, C_1-C_6-alkoxy, C_3-C_7-cycloalkyloxy, C_3-C_7-cycloalkyl-C_1-C_3-alkylenoxy, C_1-C_6-alkoxy-C_1-C_3-alkylene, C_3-C_7-cycloalkyloxy-C_1-C_3-alkylene, C_3-C_7-cycloalkyl-C_1-C_3-alkylenoxy-C_1-C_3-alkylene, $C(O)NR_4R_5$, C(O)O-C_1-C_6-alkyl, CO_2H, oxo or thio group; the groups C_1-C_6-alkyl, C_3-C_7-cycloalkyl, C_3-C_7-cycloalkyl-C_1-C_3-alkylene, C_1-C_6-fluoroalkyl, C_1-C_6-alkoxy, C_3-C_7-cycloalkyloxy, C_3-C_7-cycloalkyl-C_1-C_3-alkylenoxy, C_1-C_6-alkoxy-C_1-C_3-alkylene, C_3-C_7-cycloalkyloxy-C_1-C_3-alkylene and C_3-C_7-cycloalkyl-C_1-C_3-alkylenoxy-C_1-C_3-alkylene possibly being substituted with a hydroxyl group, C_1-C_6-alkoxy, -OC(O)-C_1-C_6-

alkyl or NR_4R_5;

or

R_3 represents, when it is borne by a nitrogen atom, a hydrogen atom or a group C_1-C_6-alkyl, C_3-C_7-cycloalkyl, C_3-C_7-cycloalkyl-C_1-C_3-alkylene, C_1-C_6-fluoroalkyl, aryl-C(O)-, C_1-C_6-alkyl-C(O)-, C_3-C_7-cycloalkyl-C(O)-, C_3-C_7-cycloalkyl-C_1-C_3-alkylene-C(O)-, C_1-C_6-fluoroalkyl-C(O)-, aryl-S(O), C_1-C_6-alkyl-S(O)-, C_1-C_6-fluoroalkyl-S(O)-, aryl-$S(O)_2$-, C_1-C_6-alkyl-$S(O)_2$-, C_1-C_6-fluoroalkyl-$S(O)_2$-, C_3-C_7-cycloalkyl-$S(O)_2$-, C_3-C_7-cycloalkyl-C_1-C_3-alkylene-$S(O)_2$-, C_1-C_6-alkyl-O-C(O)-, aryl-C_1-C_3-alkyl-O-C(O)-, C_3-C_7-cycloalkyl-O-C(O)-, C_3-C_7-cycloalkyl-C_1-C_3-alkylene-O-C(O)-, C_1-C_6-fluoroalkyl-O-C(O)-, aryl-O-C(O)-, heteroaryl-O-C(O)-, heteroaryl or aryl; the heteroaryl and aryl groups being optionally substituted with one or more substituents R_9, which may be identical to or different from each other; the groups C_1-C_6-alkyl, C_3-C_7-cycloalkyl, C_3-C_7-cycloalkyl-C_1-C_3-alkylene and C_1-C_6-fluoroalkyl possibly being substituted with a hydroxyl group, C_1-C_6-alkoxy or NR_4R_5;

R_4 and R_5, represent, independently of each other, a hydrogen atom or a group C_1-C_6-alkyl, C_3-C_7-cycloalkyl, C_3-C_7-cycloalkyl-C_1-C_3-alkylene, aryl-C_1-C_5-alkylene or aryl, or R_4 and R_5 together form, with the nitrogen atom that bears them, an azetidine, pyrrolidine, piperidine, azepine, morpholine, thiomorpholine, piperazine or homopiperazine group; the group NR_4R_5 being optionally substituted with a group C_1-C_6-alkyl, C_3-C_7-cycloalkyl, C_3-C_7-cycloalkyl-C_1-C_3-alkylene, aryl-C_1-C_6-alkylene, aryl, heteroaryl, aryl-$S(O)_2$-, C_1-C_6-alkyl-$S(O)_2$-, C_1-C_6-fluoroalkyl-$S(O)_2$, C_3-C_7-cycloalkyl-$S(O)_2$-, C_3-C_7-cycloalkyl-C_1-C_3-alkylene-$S(O)_2$-, aryl-C(O)-, C_1-C_6-alkyl-C(O)-, C_3-C_7-cycloalkyl-C(O)-, C_3-C_7-cycloalkyl-C_1-C_3-alkylene-C(O)-, C_1-C_6-fluoroalkyl-C(O)-, hydroxyl, C_1-C_6-alkyloxy, C_3-C_7-cycloalkyloxy, C_3-C_7-cycloalkyl-C_1-C_3-alkylenoxy, C_1-C_6-fluoroalkyl, aryloxy-C_1-C_6-alkylene, aryloxy, heteroaryloxy-C_1-C_6-alkylene or heteroaryloxy;

R_6 and R_7 represent, independently of each other, a hydrogen atom or a group C_1-C_6-alkyl, C_3-C_7-cycloalkyl, C_3-C_7-cycloalkyl-C_1-C_3-alkylene, aryl-C_1-C_6-alkylene or aryl; the aryl group being optionally substituted with one or more substituents chosen from a halogen atom and a group C_1-C_6-alkyl, C_3-C_7-cycloalkyl, C_3-C_7-cycloalkyl-C_1-C_3-alkylene, C_1-C_6-fluoroalkyl, C_1-C_6-alkoxy, C_3-C_7-cycloalkyloxy, C_3-C_7-cycloalkyl-C_1-C_3-alkylenoxy, C_1-C_6-fluoroalkoxy, nitro or cyano;

or R_6 and R_7 together form a 4- to 7-membered lactam comprising the nitrogen atom

and the C(O) group that bear them;

R_8 represents a group C_1-C_6-alkyl, C_3-C_7-cycloalkyl, C_3-C_7-cycloalkyl-C_1-C_3-alkylene, aryl-C_1-C_6-alkylene or aryl; the aryl group being optionally substituted with one or more substituents chosen from a halogen atom and a group C_1-C_6-alkyl, C_3-C_7-cycloalkyl, C_3-C_7-cycloalkyl-C_1-C_3-alkylene, C_1-C_6-fluoroalkyl, C_1-C_6-alkoxy, C_3-C_7-cycloalkyloxy, C_3-C_7-cycloalkyl-C_1-C_3-alkylenoxy, C_1-C_6-fluoroalkoxy, nitro or cyano;
or R_6 and R_8 together form a 4- to 7-membered sultam comprising the nitrogen atom and the $S(O)_2$ group that bear them;

R_9 represents a halogen atom or a group C_1-C_6-alkyl, C_3-C_7-cycloalkyl, C_3-C_7-cycloalkyl-C_1-C_3-alkylene, C_1-C_6-fluoroalkyl, C_1-C_6-alkoxy, C_3-C_7-cycloalkyloxy, C_3-C_7-cycloalkyl-C_1-C_3-alkylenoxy or C_1-C_6-fluoroalkoxy; these groups being optionally substituted with a group OH, C_1-C_6-alkoxy or NR_4R_5; or alternatively R_9 represents a nitro, cyano or NR_4R_5 group.

In the compounds of general formula (I):

- the sulfur atom(s) may be in oxidized form (S(O) or $S(O)_2$);
- the nitrogen atom(s) may optionally be in oxidized form (N-oxide).

The compounds of formula (I) may comprise one or more asymmetric carbon atoms. They may thus exist in the form of enantiomers or diastereoisomers. These enantiomers and diastereoisomers, and also mixtures thereof, including racemic mixtures, form part of the invention.

The compounds of formula (I) may exist in the form of bases or of acid-addition salts. Such addition salts form part of the invention.

These solvents may be prepared with pharmaceutically acceptable acids, but the salts of other acids that are useful, for example, for purifying or isolating the compounds of formula (I) also form part of the invention.

The compounds of formula (I) may also exist in the form of hydrates or solvates, i.e. in the form of associations or combinations with one or more water molecules or with a solvent. Such hydrates and solvates also form part of the invention.

In the context of the present invention, the following definitions apply:

- a halogen atom: a fluorine, a chlorine, a bromine or an iodine;
- C_t-C_z: a carbon-based chain possibly containing from t to z carbon atoms in which t and z may take values from 1 to 7; for example, C_1-C_3 is a carbon-based chain possibly containing from 1 to 3 carbon atoms;
- an alkyl: a linear or branched saturated aliphatic group. Examples that may be mentioned include methyl, ethyl, propyl, isopropyl, butyl, isobutyl, tert-butyl, pentyl, etc.;
- an alkylene: a linear or branched saturated divalent alkyl group, for example a group C_{1-3}-alkylene represents a linear or branched divalent carbon-based chain of 1 to 3 carbon atoms, more particularly a methylene, ethylene, 1-methylthylene or propylene;
- a cycloalkyl: a saturated or partially unsaturated cyclic alkyl group. Examples that may be mentioned include the groups cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cyclopropenyl, cyclobutenyl, cyclopentenyl, cyclohexenyl, etc.;
- a cycloalkyloxy: a radical -O-cycloalkyl in which the cycloalkyl group is as defined previously;
- a fluoroalkyl: an alkyl group, one or more hydrogen atoms of which have been replaced with a fluorine atom;
- an alkoxy: a radical -O-alkyl in which the alkyl group is as defined previously;
- a fluoroalkoxy: an alkoxy group, one or more hydrogen atoms of which have been replaced with a fluorine atom;
- a thioalkyl or alkylthio: a radical -S-alkyl in which the alkyl group is as defined previously;
- an aryl: a monocyclic or bicyclic aromatic group containing between 6 and 10 carbon atoms. Examples of aryl groups that may be mentioned include phenyl and naphthyl groups;
- a heterocycle: a saturated or partially unsaturated 5- to 7-membered monocyclic group, comprising from 1 to 3 heteroatoms chosen from O, S and N.

  Examples of heterocycles that may be mentioned include azetidinyl, piperidyl, azepinyl, morpholinyl, thiomorpholinyl, piperazinyl, homopiperazinyl, dihydrooxazolyl, dihydrothiazolyl, dihydroimidazolyl, dihydropyrrolyl or tetrahydropyridyl, [1,3]dioxolyl, [1,3]dioxinyl, dihydro[1,4]dioxinyl, dihydro[1,2]oxazinyl, dihydro[1,3]oxazinyl, dihydrooxazole, dihydroisoxazole,

dihydro[1,4]oxazinyl, tetrahydro[1,3]oxazepinyl, tetrahydro[1,4]oxazepinyl, tetrahydro[1,3]diazepinyl and tetrahydro[1,4]diazepinyl.

- a heteroaryl: a 5- to 12-membered monocyclic or bicyclic aromatic group containing from 1 to 5 heteroatoms chosen from O, S and N.

Examples of monocyclic heteroaryls that may be mentioned include imidazolyl, pyrazolyl, thiazolyl, oxazolyl, isothiazolyl, isoxazolyl, furyl, thienyl, oxadiazolyl, thiadiazolyl, triazolyl, tetrazolyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl and triazinyl.

Examples of bicyclic heteroaryls that may be mentioned include indolyl, isoindolyl, benzofuryl, benzothiophenyl, benzoxazolyl, benzimidazolyl, indazolyl, benzothienyl, isobenzofuryl, isobenzothiazolyl, pyrrolo[2,3-*c*]pyridyl, pyrrolo[2,3-*b*]pyridyl, pyrrolo[3,2-*b*]pyridyl, pyrrolo[3,2-*c*]pyridyl, pyrrolo[1,2-*a*]pyridyl, quinolyl, isoquinolyl, cinnolinyl, quinazolinyl, quinoxalinyl, pyrrolo[1,2-*a*]imidazolyl, imidazo[1,2-*a*]pyridyl, imidazo[1,2-*a*]pyridazinyl, imidazo[1,2-*c*]pyrimidinyl, imidazo[1,2-*a*]pyrimidinyl, imidazo[1,2-*a*]pyrazinyl, imidazo[4,5-*b*]pyrazinyl, imidazo[4,5-*b*]pyridyl, imidazo[4,5-*c*]pyridyl, pyrazolo[2,3-a]pyridyl, pyrazolo[2,3-*a*]pyrimidinyl, pyrazolo[2,3-*a*]pyrazinyl, thiazolo[5,4-*b*]pyridyl, thiazolo[5,4-*c*]pyridyl, thiazolo[4,5-*c*]pyridyl, thiazolo[4,5-*b*]pyridyl, oxazolo[5,4-*b*]pyridyl, oxazolo[5,4-*c*]pyridyl, oxazolo[4,5-*c*]pyridyl, oxazolo[4,5-*b*]pyridyl, isothiazolo[5,4-*b*]pyridyl, isothiazolo[5,4-*c*]pyridyl, isothiazolo[4,5-*c*]pyridyl, isothiazolo[4,5-*b*]pyridyl, isoxazolo[5,4-*b*]pyridyl, isoxazolo[5,4-*c*]pyridyl, isoxazolo[4,5-*c*]pyridyl and isoxazolo[4,5-*b*]pyridyl.

- "oxo" means "=O";
- "thio" means "=S".

Among the compounds of general formula (I) that are subjects of the invention, a first subgroup of compounds is constituted by the compounds for which X_1, X_2, X_3 and X_4 represent, independently of each other, a group C-R_1; R_1 being as defined in the general formula (I).

Among the compounds of general formula (I) that are subjects of the invention, a second subgroup of compounds is constituted by the compounds for which

X_1, X_2, X_3 and X_4 represent, independently of each other, a nitrogen atom or a group C-R_1;

it being understood that one from among X_1, X_2, X_3 and X_4 represents a nitrogen atom, the others representing a group C-R_1;

R_1 being as defined in the general formula (I).

Among the compounds of general formula (I) that are subjects of the invention, a third subgroup of compounds is constituted by the compounds for which
X_1, X_2 and X_3 represent a group C-R_1; X_4 represents a nitrogen atom;
R_1 being as defined in the general formula (I).

Among the compounds of general formula (I) that are subjects of the invention, a fourth subgroup of compounds is constituted by the compounds for which
R_1 is chosen from a hydrogen atom, a halogen atom and a group C_1-C_6-fluoroalkyl or -Si(C_1-C_6-alkyl)$_3$.

Among the compounds of general formula (I) that are subjects of the invention, a fifth subgroup of compounds is constituted by the compounds for which
R_1 is chosen from a hydrogen atom, a fluorine atom and a group CF_3 or $Si(CH_3)_3$.

Among the compounds of general formula (I) that are subjects of the invention, a sixth subgroup of compounds is constituted by the compounds for which
X_1, X_2, X_3 and X_4 represent, independently of each other, a group C-R_1; R_1 is chosen from a hydrogen atom, a halogen atom and a group C_1-C_6-fluoroalkyl or -Si-(C_1-C_6-alkyl)$_3$.

Among the compounds of general formula (I) that are subjects of the invention, a seventh subgroup of compounds is constituted by the compounds for which
X_1, X_2 and X_3 represent a group C-R_1; X_4 represents a nitrogen atom;
R_1 is chosen from a hydrogen atom and a group C_1-C_6-fluoroalkyl.

Among the compounds of general formula (I) that are subjects of the invention, an eighth subgroup of compounds is constituted by the compounds for which n is equal to 1.

Among the compounds of general formula (I) that are subjects of the invention, a ninth subgroup of compounds is constituted by the compounds for which
Y represents an aryl or a heteroaryl optionally substituted with one or more groups chosen from a halogen atom and a group C_1-C_6-alkyl or C_1-C_6-fluoroalkyl.

Among the compounds of general formula (I) that are subjects of the invention, a tenth subgroup of compounds is constituted by the compounds for which
Y represents a phenyl, a thiazolyl or a pyridyl, this group being optionally substituted with one or more groups chosen from a halogen atom and a group C_1-C_6-alkyl or C_1-C_6-fluoroalkyl.

Among the compounds of general formula (I) that are subjects of the invention, an eleventh subgroup of compounds is constituted by the compounds for which
Y represents a phenyl, a thiazolyl or a pyridyl, this group being optionally substituted with one or more groups chosen from a fluorine atom and a methyl group or CF_3.

Among the compounds of general formula (I) that are subjects of the invention, a twelfth subgroup of compounds is constituted by the compounds for which
Y represents a phenyl optionally substituted with one or more groups chosen from a fluorine atom and a methyl group or CF_3.

Among the compounds of general formula (I) that are subjects of the invention, a thirteenth subgroup of compounds is constituted by the compounds for which W represents an oxygen atom.

Among the compounds of general formula (I) that are subjects of the invention, a fourteenth subgroup of compounds is constituted by the compounds for which
Z_1, Z_2, Z_3 and Z_4 represent, independently of each other, a nitrogen atom, a carbon atom or a group C-R_2,
one from among Z_1, Z_2, Z_3 and Z_4 corresponding to a nitrogen atom and
one from among Z_1, Z_2, Z_3 and Z_4, corresponding to a carbon atom, being bonded to the nitrogen atom of the amide or of the thioamide of formula (I);
and the two others from among Z_1, Z_2, Z_3 and Z_4 corresponding to a group C-R_2;
R_2 being as defined in the general formula (I).

Among the compounds of general formula (I) that are subjects of the invention, a fifteenth subgroup of compounds is constituted by the compounds for which
Z_1, Z_2, Z_3 and Z_4 represent, independently of each other, a nitrogen atom, a carbon atom or a group C-R_2,

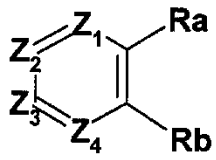
one from among Z_1, Z_2, Z_3 and Z_4 corresponding to a nitrogen atom and
one from among Z_1, Z_2, Z_3 and Z_4, corresponding to a carbon atom, being bonded to the nitrogen atom of the amide or of the thioamide of formula (I);
and the two others from among Z_1, Z_2, Z_3 and Z_4 corresponding to a CH group.

Among the compounds of general formula (I) that are subjects of the invention, a sixteenth subgroup of compounds is constituted by the compounds for which
Ra and Rb together form, with the carbon atoms that bear them,
either a partially unsaturated cycloalkyl, or an aryl;
or a heterocycle, or a heteroaryl, which is 5- or 6-membered, comprising one or two heteroatoms chosen from O, S and N;
it being understood that when Ra and Rb together form, with the carbon atoms that bear them, a 5-membered ring, this ring comprising a nitrogen atom and carbon atoms, this ring being partially saturated or unsaturated, is excluded;
this partially unsaturated cycloalkyl, this aryl, this heterocycle or this heteroaryl possibly being substituted with one or more substituents R_3;
R_3 being as defined in the general formula (I).

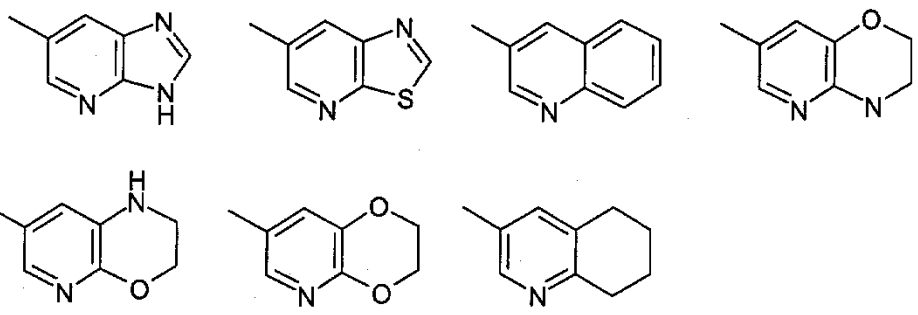
Among the compounds of general formula (I) that are subjects of the invention, a seventeenth subgroup of compounds is constituted by the compounds for which
Ra and Rb together form, with the carbon atoms that bear them,
either a partially unsaturated cycloalkyl, or an aryl;
or a heterocycle, or a heteroaryl, which is 5- or 6-membered, comprising one or two heteroatoms chosen from O, S and N;
it being understood that when Ra and Rb together form, with the carbon atoms that bear them, a 5-membered ring, this ring comprising a nitrogen atom and carbon atoms, this ring being partially saturated or unsaturated, is excluded;
this partially unsaturated cycloalkyl, this aryl, this heterocycle or this heteroaryl possibly being substituted with one or more substituents R_3;
R_3 represents, when it is borne by a carbon atom, a hydrogen atom or a hydroxyl, C_1-C_6-alkyl or oxo group; the C_1-C_6-alkyl group possibly being substituted with a hydroxyl or -OC(O)-C_1-C_6-alkyl group;
or
R_3 represents, when it is borne by a nitrogen atom, a hydrogen atom or a group C_1-C_6-alkyl.

Among the compounds of general formula (I) that are subjects of the invention, an eighteenth subgroup of compounds is constituted by the compounds for which
Ra and Rb together form, with the carbon atoms that bear them,
either a partially unsaturated cycloalkyl, or an aryl;
or a heterocycle, or a heteroaryl, which is 5- or 6-membered, comprising one or two heteroatoms chosen from O, S and N;
it being understood that when Ra and Rb together form, with the carbon atoms that bear them, a 5-membered ring, this ring comprising a nitrogen atom and carbon atoms, this ring being partially saturated or unsaturated, is excluded;
this partially unsaturated cycloalkyl, this aryl, this heterocycle or this heteroaryl possibly being substituted with one or more substituents R_3;
R_3 represents, when it is borne by a carbon atom, a hydrogen atom or a hydroxyl, methyl or oxo group; the methyl groups possibly being substituted with a hydroxyl or -OC(O)-tert-butyl group;
or
R_3 represents, when it is borne by a nitrogen atom, a hydrogen atom or a methyl group.

Among the compounds of general formula (I) that are subjects of the invention, a nineteenth subgroup of compounds is constituted by the compounds for which A represents the group of formula:



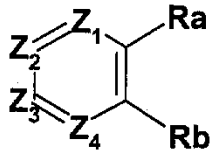
in which A is chosen from the groups



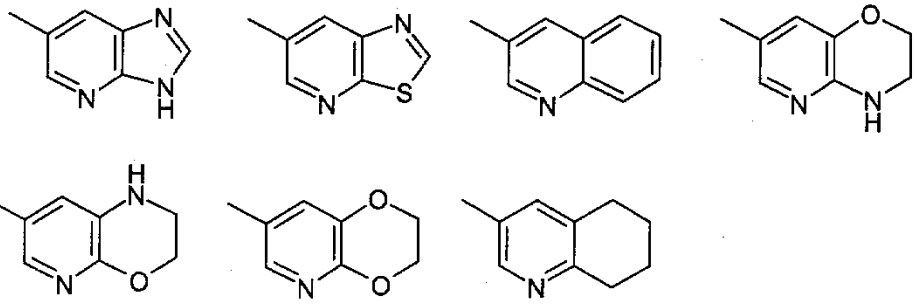
these groups being optionally substituted with R_2 and R_3 as defined in the general

formula (I) hereinabove.

Among the compounds of general formula (I) that are subjects of the invention, a twentieth subgroup of compounds is constituted by the compounds for which A represents the group of formula:



in which A is chosen from the groups



these groups being optionally substituted with R_2 and R_3 as defined in the general formula (I) hereinabove;

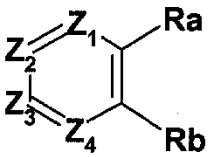
R_2 represents a hydrogen atom;

R_3 represents, when it is borne by a carbon atom, a hydrogen atom or a hydroxyl, C_1-C_6-alkyl or oxo group; the C_1-C_6-alkyl group possibly being substituted with a hydroxyl or -OC(O)-C_1-C_6-alkyl group;

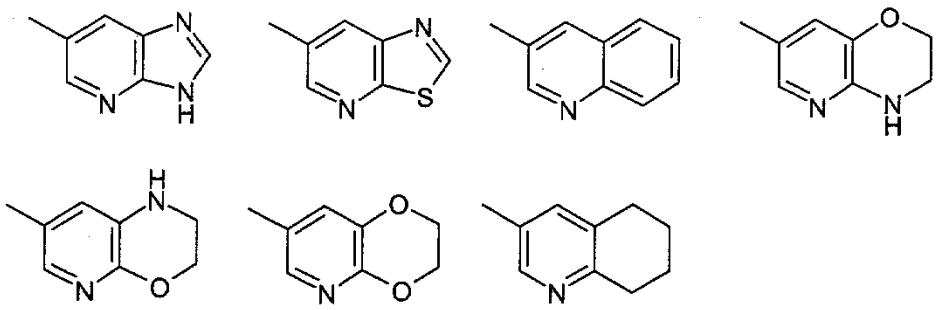
or

R_3 represents, when it is borne by a nitrogen atom, a hydrogen atom or a group C_1-C_6-alkyl.

Among the compounds of general formula (I) that are subjects of the invention, a twenty-first subgroup of compounds is constituted by the compounds for which A represents the group of formula:



in which A is chosen from the groups



these groups being optionally substituted with R_2 and R_3 as defined in the general formula (I) hereinabove;

R_3 represents, when it is borne by a carbon atom, a hydrogen atom or a hydroxyl, methyl or oxo group; the methyl groups possibly being substituted with a hydroxyl or -OC(O)-tert-butyl group;

or

R_3 represents, when it is borne by a nitrogen atom, a hydrogen atom or a methyl group.

Among the compounds of general formula (I) that are subjects of the invention, a twenty-second subgroup of compounds is constituted by the compounds for which the definitions of X_1, X_2, X_3 and X_4, n, Y, W, Z_1, Z_2, Z_3, Z_4; Ra and Rb given hereinabove are combined.

Among the compounds of general formula (I) that are subjects of the invention, a twenty-third subgroup of compounds is constituted by the compounds for which

X_1, X_2, X_3 and X_4 represent, independently of each other, a group C-R_1; or alternatively X_1, X_2 and X_3 represent a group C-R_1; X_4 represents a nitrogen atom;

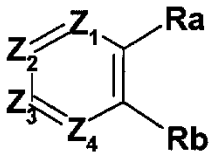
R_1 is chosen from a hydrogen atom, a halogen atom and a group C_1-C_6-fluoroalkyl or -Si-(C_1-C_6-alkyl)$_3$;

n is equal to 1;

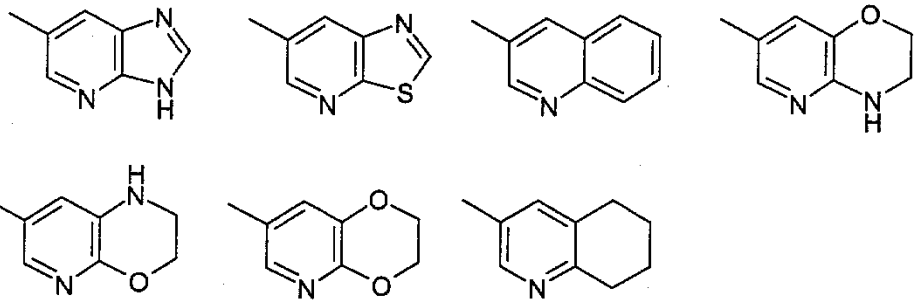
Y represents an aryl or a heteroaryl optionally substituted with one or more groups chosen from a halogen atom and a group C_1-C_6-alkyl or C_1-C_6-fluoroalkyl;

W represents an oxygen atom;

A represents the group of formula:



in which A is chosen from the groups



these groups being optionally substituted with R_2 and R_3 as defined in the general formula (I) hereinabove;

R_2 represents a hydrogen atom;

R_3 represents, when it is borne by a carbon atom, a hydrogen atom or a hydroxyl, C_1-C_6-alkyl or oxo group; the C_1-C_6-alkyl group possibly being substituted with a hydroxyl or -OC(O)-C_1-C_6-alkyl group;

or

R_3 represents, when it is borne by a nitrogen atom, a hydrogen atom or a group C_1-C_6-alkyl.

Among the compounds of general formula (I) that are subjects of the invention, a twenty-fourth subgroup of compounds is defined such that

the compounds for which

X_1, X_2, X_3 and X_4 represent, independently of each other, a group C-R_1;

R_1 is chosen from a hydrogen atom, a halogen atom and a group C_1-C_6-alkyl, C_1-C_6-fluoroalkyl, C_1-C_6-akoxy, C_1-C_6-fluoroalkoxy, NR_4R_5, C_1-C_6-thioalkyl, phenyl or isoxazolyl; the phenyl group being optionally substituted with one or more substituents R_9, which may be identical to or different from each other;

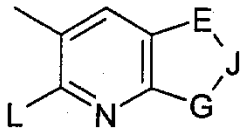
R_4 and R_5, represent, independently of each other, a hydrogen atom or a group C_1-C_6-alkyl,

W represents an oxygen atom;

n is equal to 0;

Y represents a phenyl optionally substituted with one or more substituents R_9, which may be identical to or different from each other; or Y represents an isoxazole;

R_9 represents a halogen atom or a group C_1-C_6-alkyl, C_1-C_6-alkoxy or cyano;
A represents the group D:



(D)

in which

L represents a hydrogen atom, a halogen atom or a group C_1-C_4-alkoxy;
the 5-membered ring is partially saturated or unsaturated; J represents N or C=O; E and G represent, independently of each other, an oxygen or sulfur atom, or a group C=O, CH_2 or N-R'; R' represents a hydrogen atom or a group C_1-C_4-alkyl or aryl-C(O)-, the aryl group being optionally substituted with one or more groups C_1-C_6-alkyl;
are excluded.

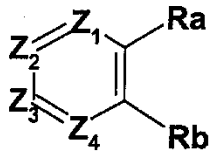
Among the compounds of general formula (I) that are subjects of the invention, one sub-family is represented by the compounds of general formula (I') for which:
R_3 represents, when it is borne by a carbon atom, a hydrogen atom or a hydroxyl, thiol, C_1-C_6-alkyl, C_3-C_7-cycloalkyl, C_3-C_7-cycloalkyl-C_1-C_3-alkylene, C_1-C_6-fluoroalkyl, C_1-C_6-alkoxy, C_3-C_7-cycloalkyloxy, C_3-C_7-cycloalkyl-C_1-C_3-alkylenoxy, C_1-C_6-alkoxy-C_1-C_3-alkylene, C_3-C_7-cycloalkyloxy-C_1-C_3-alkylene, C_3-C_7-cycloalkyl-C_1-C_3-alkylenoxy-C_1-C_3-alkylene, $C(O)NR_4R_5$, $C(O)O$-C_1-C_6-alkyl, CO_2H, oxo or thio group; the groups C_1-C_6-alkyl, C_3-C_7-cycloalkyl, C_3-C_7-cycloalkyl-C_1-C_3-alkylene, C_1-C_6-fluoroalkyl, C_1-C_6-alkoxy, C_3-C_7-cycloalkyloxy, C_3-C_7-cycloalkyl-C_1-C_3-alkylenoxy, C_1-C_6-alkoxy-C_1-C_3-alkylene, C_3-C_7-cycloalkyloxy-C_1-C_3-alkylene and C_3-C_7-cycloalkyl-C_1-C_3-alkylenoxy-C_1-C_3-alkylene possibly being substituted with a hydroxyl group, C_1-C_6-alkoxy or NR_4R_5.

Among the compounds of general formula (I') that are subjects of the invention, a first subgroup of compounds is constituted by the compounds for which X_1, X_2, X_3 and X_4 represent, independently of each other, a group C-R_1; and R_1 is chosen from a hydrogen atom and a halogen atom, more particularly a fluorine atom.

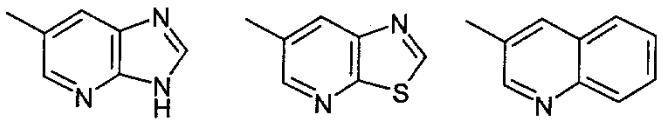
Among the compounds of general formula (I') that are subjects of the invention, a second subgroup of compounds is constituted by the compounds for which n is equal to 1 and Y represents an aryl, more particularly a phenyl, optionally substituted with one or more halogen atoms, more particularly fluorine atoms.

Among the compounds of general formula (I') that are subjects of the invention, a third subgroup of compounds is constituted by the compounds for which W represents an oxygen atom.

Among the compounds of general formula (I') that are subjects of the invention, a fourth subgroup of compounds is constituted by the compounds for which A represents the group of formula:

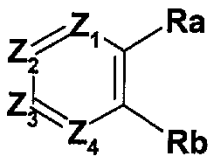


in which A is chosen from the groups

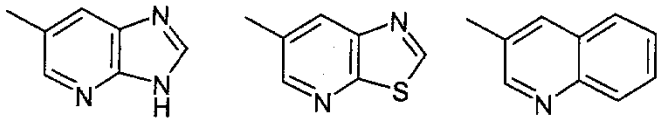


these groups being optionally substituted with R_2 and R_3 as defined in the general formula (I) hereinabove.

Among the compounds of general formula (I') that are subjects of the invention, a fifth subgroup of compounds is constituted by the compounds for which
X_1, X_2, X_3 and X_4 represent, independently of each other, a group C-R_1; and R_1 is chosen from a hydrogen atom and a halogen atom, more particularly a fluorine atom;
n is equal to 1;
Y represents an aryl, more particularly a phenyl, optionally substituted with one or more halogen atoms, more particularly fluorine atoms;
W represents an oxygen atom;
A represents the group of formula:



in which A is chosen from the groups



these groups being optionally substituted with R_2 and R_3 as defined in the general formula (I) hereinabove.

Among the compounds of general formula (I) that are subjects of the invention, mention may be made especially of the following compounds:

1 *N*-(2,3-Dimethyl-3*H*-imidazo[4,5-*b*]pyrid-6-yl)-5-fluoro-1-[(3-fluorophenyl)-methyl]-1*H*-indole-2-carboxamide;

2 *N*-(2-Methylthiazolo[5,4-*b*]pyrid-6-yl)-5-fluoro-1-[(3-fluorophenyl)methyl]-1*H*-indole-2-carboxamide;

3 *N*-(Thiazolo[5,4-*b*]pyrid-6-yl)-5-fluoro-1-[(3-fluorophenyl)methyl]-1*H*-indole-2-carboxamide;

4 *N*-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-5-fluoro-1-[(3-fluorophenyl)-methyl]-1*H*-indole-2-carboxamide;

5 *N*-(Quinol-3-yl)-5-fluoro-1-[(3-fluorophenyl)methyl]-1*H*-indole-2-carboxamide.

6 *N*-(2-Hydroxymethyl-3-methyl-3*H*-imidazo[4,5-*b*]pyrid-6-yl)-5-fluoro-1-[(3-fluorophenyl)methyl]-1*H*-indole-2-carboxamide

7 *N*-(3-Methyl-3*H*-imidazo[4,5-*b*]pyrid-6-yl)-5-fluoro-1-[(3-fluorophenyl)methyl]-1*H*-indole-2-carboxamide

8 *N*-(2,3-Dimethyl-3*H*-imidazo[4,5-*b*]pyrid-6-yl)-5-trifluoromethyl-1-[(3-fluoro-phenyl)methyl]-1*H*-pyrrolo[2,3-*b*]pyridine-2-carboxamide

9 *N*-(3,4-Dihydro-2H-pyrido[3,2-*b*][1,4]oxazin-7-yl)-5-fluoro-1-[(3-fluorophenyl)-methyl]-1*H*-indole-2-carboxamide

10 *N*-(4-Methyl-3,4-dihydro-2H-pyrido[3,2-*b*][1,4]oxazin-7-yl)-5-fluoro-1-[(3-fluoro-phenyl)methyl]-1*H*-indole-2-carboxamide

11 *N*-(2-Methyl-3*H*-imidazo[4,5-*b*]pyrid-6-yl)-5-fluoro-1-[(3-fluorophenyl)methyl]-1*H*-indole-2-carboxamide

12 *N*-(1-Methyl-2-oxo-2,3-dihydro-1H-pyrido[2,3-*b*][1,4]oxazin-7-yl)-5-fluoro-1-[(3-fluorophenyl)methyl]-1*H*-indole-2-carboxamide

13 [6-[[[5-Fluoro-1-[(3-fluorophenyl)methyl]-1*H*-indol-2-yl]carbonyl]amino]thiazolo-[5,4-*b*]pyrid-2-yl]methyl 2,2-dimethylpropanoate

14 *N*-(2,3-Dihydro-[1,4]dioxino[2,3-*b*]pyrid-7-yl))-5-fluoro-1-[(3-fluorophenyl)-methyl]-1*H*-indole-2-carboxamide

15 *N*-(6-Hydroxy-5,6,7,8-tetrahydroquinol-3-yl)-5-fluoro-1-[(3-fluorophenyl)methyl]-1*H*-indole-2-carboxamide

16 *N*-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-5-trifluoromethyl-1-[(3-methylphenyl)methyl]-1*H*-indole-2-carboxamide

17 *N*-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-6-trifluoromethyl-1-[(3-methylphenyl)methyl]-1*H*-indole-2-carboxamide

18 *N*-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-5-trimethylsilyl-1-[(3-methylphenyl)methyl]-1*H*-indole-2-carboxamide

19 *N*-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-6-fluoro-1-[(3-methylphenyl)-methyl]-1*H*-indole-2-carboxamide

20 *N*-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-5-trifluoromethyl-1-[(thiazol-2-yl)methyl]-1*H*-indole-2-carboxamide

21 *N*-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-6-trifluoromethyl-1-[(thiazol-2-yl)methyl]-1*H*-indole-2-carboxamide

22 *N*-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-5-trimethylsilyl-1-[(thiazol-2-yl)methyl]-1*H*-indole-2-carboxamide

23 *N*-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-6-fluoro-1-[(thiazol-2-yl)methyl]-1*H*-indole-2-carboxamide

24 *N*-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-5-trifluoromethyl-1-[(thiazol-2-yl)methyl]-1*H*-pyrrolo[2,3-*b*]pyridine-2-carboxamide

25 *N*-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-6-trimethylsilyl-1-[(thiazol-2-yl)methyl]-1*H*-indole-2-carboxamide

26 *N*-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-5-trifluoromethyl-1-[(pyrid-4-yl)methyl]-1*H*-indole-2-carboxamide

27 *N*-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-6-trifluoromethyl-1-[(pyrid-4-yl)methyl]-1*H*-indole-2-carboxamide

28 *N*-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-5-trimethylsilyl-1-[(pyrid-4-yl)-methyl]-1*H*-indole-2-carboxamide

29 *N*-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-6-fluoro-1-[(pyrid-4-yl)methyl]-1*H*-indole-2-carboxamide

30 *N*-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-5-trifluoromethyl-1-[(pyrid-4-yl)methyl]-1*H*-pyrrolo[2,3-*b*]pyridine-2-carboxamide

31 *N*-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-6-trimethylsilyl-1-[(pyrid-4-yl)methyl]-1*H*-indole-2-carboxamide

32 *N*-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-5-trimethylsilyl-1-[[(3-trifluoro-

methyl)phenyl]methyl]-1*H*-indole-2-carboxamide

33 *N*-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-6-fluoro-1-[[(3-trifluoromethyl)-phenyl]methyl]-1*H*-indole-2-carboxamide

34 *N*-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-5-trifluoromethyl-1-[[(3-trifluoro-methyl)phenyl]methyl]-1*H*-pyrrolo[2,3-*b*]pyridine-2-carboxamide

35 *N*-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-6-trimethylsilyl-1-[[(3-trifluoro-methyl)phenyl]methyl]-1*H*-indole-2-carboxamide

36 *N*-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-5-trifluoromethyl-1-[(3-methyl-phenyl)methyl]-1*H*-pyrrolo[2,3-*b*]pyridine-2-carboxamide

37 *N*-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-6-trimethylsilyl-1-[(3-methyl-phenyl)methyl]-1*H*-indole-2-carboxamide

38 *N*-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-5-trifluoromethyl-1-[[(3-trifluoro-methyl)phenyl]methyl]-1*H*-indole-2-carboxamide

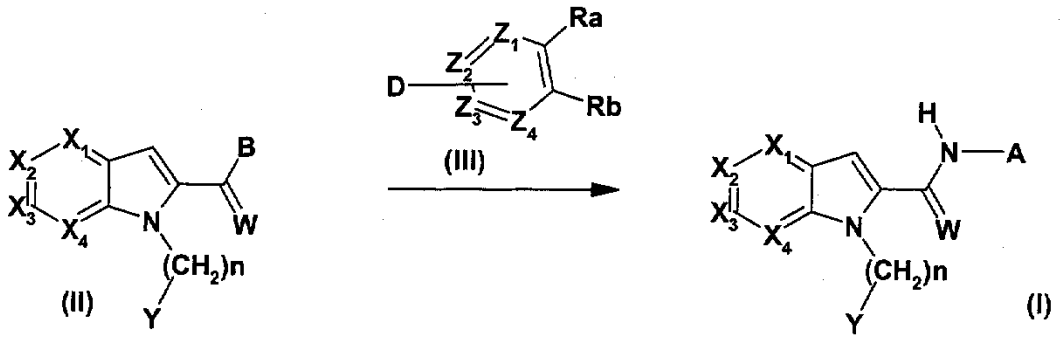
39 *N*-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-6-trifluoromethyl-1-[[(3-trifluoro-methyl)phenyl]methyl]-1*H*-indole-2-carboxamide

In the text hereinbelow, the term "leaving group" means a group that can be readily cleaved from a molecule by breaking a heterolytic bond, with loss of an electron pair. This group may thus be readily replaced by another group during a substitution reaction, for example. Such leaving groups are, for example, halogens or an activated hydroxyl group such as a methanesulfonate, benzenesulfonate, p-toluenesulfate, triflate, acetate, etc. Examples of leaving groups and references for preparing them are given in "Advances in Organic Chemistry", J. March, 5th Edition, Wiley Interscience, 2001.

In the text hereinbelow, the term "protecting group" means a group that can be momentarily incorporated into a chemical structure for the purpose of temporarily inactivating a part of the molecule during a reaction, and which may be readily removed in a subsequent synthetic step. Examples of protecting groups and references concerning their properties are given in T.W. Greene, P.G.M. Wutz, 3rd Edition, Wiley Interscience 1999.

In accordance with the invention, the compounds of general formula (I) may be prepared according to the process illustrated by the general scheme 1 below:

Scheme 1



The compounds (I) may be obtained by reacting a compound of general formula (II), in which B corresponds to a hydroxyl group and X_1, X_2, X_3, X_4, n, Y and W are as defined in the general formula (I) hereinabove, with an amine of general formula (III), in which Z_1, Z_2, Z_3, Z_4, Ra and Rb are as defined in the general formula (I) hereinabove and D corresponds to an amino group, in the presence of a coupling agent such as a dialkylcarbodiimide, [(benzotriazol-1-yl)oxy][tris(pyrrolidino)]phosphonium hexafluorophosphate, diethyl cyanophosphonate or any other coupling agent known to those skilled in the art, optionally in the presence of a base such as triethylamine, in a solvent, for instance dimethylformamide.

Moreover, the compounds (I) may be obtained by reacting a compound of general formula (II), in which B represents a group C_1-C_6-alkoxy, C_3-C_7-cycloalkyloxy, C_3-C_7-cycloalkyl-C_1-C_3-alkylenoxy- or aryl-C_1-C_3-alkylenoxy and X_1, X_2, X_3, X_4, n, Y and W are as defined in the general formula hereinabove, with an amide of the compound of general formula (III), in which Z_1, Z_2, Z_3, Z_4, Ra and Rb are as defined in the general formula (I) hereinabove and D corresponds to an amino group, in a refluxing solvent such as toluene. The aluminium amide of the compound of general formula (III) is prepared via the prior action of trimethylaluminium on the amines of general formula (III).

The compounds (I) may also be obtained by reacting a compound of general formula (II), in which B corresponds to a chlorine atom and X_1, X_2, X_3, X_4, n, Y and W are as defined in the general formula (I) hereinabove, with an amine of general formula (III), in which Z_1, Z_2, Z_3, Z_4, Ra and Rb are as defined in the general formula (I) hereinabove and D corresponds to an amino group, by reaction in solution in a solvent such as dichloromethane or toluene. The compounds of general formula (II) in which B

corresponds to a chlorine atom are prepared from compounds of general formula (II) in which B corresponds to a hydroxyl group, by reaction with a reagent such as thionyl chloride or oxalyl chloride, optionally in the presence of a base such as triethylamine, in solution in a solvent such as dichloromethane.

Starting with compounds of general formula (II), in which B represents an NH_2 group, W represents an oxygen atom and X_1, X_2, X_3, X_4, n and Y are as defined in the general formula (I) hereinabove, the compound of general formula (I) may be obtained by reaction with the compound of general formula (III), in which Z_1, Z_2, Z_3, Z_4, Ra and Rb are as defined in the general formula (I) hereinabove and D corresponds to a leaving group as defined hereinabove, such as a bromine atom or a triflate group, for example according to a method similar to that described in *J.Am.Chem.Soc.* **2001**, *123* (31), 7727, or according to methods described in the literature or known to those skilled in the art, in the presence of a copper salt in catalytic amount, in the presence of a catalytic amount of a copper ligand, such as a diamine, the whole in the presence of a base such as potassium carbonate, in a solvent such as dioxane.

In Scheme 1, the compounds of general formula (I) and the other reagents, when their mode of preparation is not described, are commercially available, are described in the literature or are prepared by analogy with processes described in the literature (D. Knittel *Synthesis* **1985**, 2, 186; T.M. Williams *J. Med. Chem.* **1993**, *36* (9), 1291; JP2001-151 771 A2, WO2006/024 776, WO2006/072 736, WO2007/010 144, WO2007/010 138 or WO2007/088 277, for example).

The compounds of general formula (III), when their mode of preparation is not described, are commercially available, are described in the literature or are prepared by analogy with processes described in the literature (*Tetrahedron Lett.* **1987**, 1589, *Synthesis* **2005**, *15*, 2503, *Synthesis* **2008**, 2, 201, WO2006/040 520).

The compounds of general formula (II) or (I), for which one from among X_1, X_2, X_3 and X_4 corresponds to a carbon atom substituted with an alkyl group, may be obtained via a coupling reaction, catalysed by a metal such as palladium or iron, performed on the corresponding compounds of general formula (II) or (I), substituted with a halogen atom, such as chlorine, in the presence, for example, of an alkylmagnesium halide or an alkylzinc halide, according to the methods described in the literature (A. Furstner et

al. *J. Am. Chem. Soc.* **2002**, *124*(46), 13856; G. Queguiner et al., *J. Org. Chem.* **1998**, *63*(9), 2892) for example, or known to those skilled in the art.

The compounds of general formula (II) or (I), for which one from among X_1, X_2, X_3 and X_4 corresponds to a carbon atom substituted with a cyano, aryl or heteroaryl group, may be obtained via a coupling reaction, catalysed with a metal such as palladium, performed on the corresponding compounds of general formula (II) or (I), substituted, for example, with a bromine atom, in the presence of trimethylsilyl cyanide, an arylboronic acid or a heteroarylboronic acid, or via any other method described in the literature or known to those skilled in the art.

The compounds of general formula (I) or (II), for which one from among X_1, X_2, X_3 and X_4 corresponds to a carbon atom substituted with a group NR_4R_5, NR_6COR_7 or $NR_6SO_2R_8$, may be obtained from the corresponding compounds of general formula (I) or (II), substituted, for example, with a bromine atom, via a coupling reaction with, respectively, an amine, an amide or a sulfonamide in the presence of a base, a phosphine and a palladium-based catalyst, according to methods described in the literature or known to those skilled in the art.

The compounds of general formula (I) or (II) substituted with a group $C(O)NR_4R_5$ may be obtained from the corresponding compounds of general formula (I) or (II) substituted with a cyano group, according to methods described in the literature or known to those skilled in the art.

The compounds of general formula (I) or (II) substituted with a group -S(O)-alkyl or $-S(O)_2$-alkyl may be obtained via oxidation of the corresponding compounds of general formula (II) or (I), substituted with a thioalkyl group, according to methods described in the literature or known to those skilled in the art.

The compounds of general formula (II) or (I) substituted with a group NR_4R_5, NR_6COR_7 or $NR_6SO_2R_8$ may be obtained from the corresponding compounds of general formula (II) or (I), substituted with a nitro group, for example via reduction, followed by acylation or sulfonylation, according to methods described in the literature or known to those skilled in the art.

The compounds of general formula (II) or (I) substituted with a group $SO_2NR_4R_5$ may be obtained via a method similar to that described in *Pharmazie* **1990**, *45*, 346, or according to methods described in the literature or known to those skilled in the art.

The compounds of general formula (I) or (II) in which W represents a sulfur atom may be obtained, for example, by reacting the corresponding compounds of general formula (I) or (II), in which W represents an oxygen atom, with a reagent such as Lawesson's reagent.

The compounds of general formula (I) for which R_3 corresponds to a protecting group borne by a nitrogen atom, such as an acetyl, ethoxycarbonyl or tert-butyloxycarbonyl group or a benzyloxycarbonyl group, may be deprotected, according to chemical methods known to those skilled in the art, to give compounds of general formula (I) in which R_3 is a hydrogen atom.

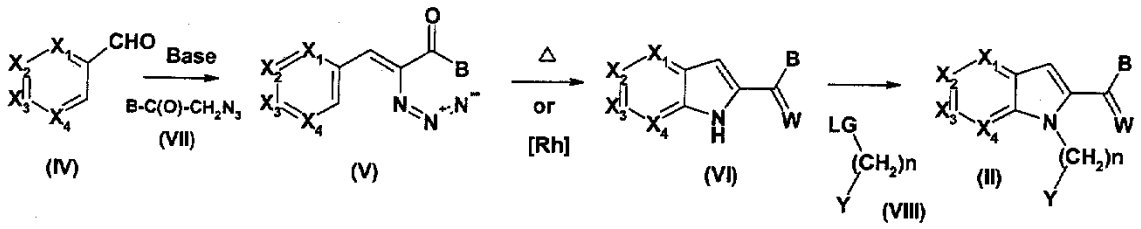
The compounds of general formula (I), for which R_3 corresponds to a hydroxyalkyl group, may be obtained from the compounds of general formula (I) for which R_3 corresponds, for example, to an acetoxyalkyl or pivaloyloxyalkyl group according to chemical methods known to those skilled in the art, such as reaction with a base, for example aqueous sodium hydroxide solution, or reaction with an alkoxide, for example a methoxide, of a salt such as lithium or sodium, in an alcoholic solvent such as methanol or ethanol, or reaction with a reducing agent such as sodium borohydride, in a solvent such as tetrahydrofuran.

Alternatively, the compounds of general formula (I) for which R_3 corresponds to a hydroxyalkyl group may be obtained from the compounds of general formula (III), in which D corresponds to an amino group and R_3 corresponds, for example, to a pivaloyloxyalkyl group, by reaction with an organometallic reagent such as trimethylaluminium, followed by coupling with a compound of general formula (II), in which B corresponds to a group C_1-C_6-alkoxy, C_3-C_7-cycloalkyloxy, C_3-C_7-cycloalkyl-C_1-C_3-alkylenoxy- or aryl-C_1-C_3-alkylenoxy and X_1, X_2, X_3, X_4, n, Y and W are as defined in the general formula (I) hereinabove, followed by a treatment in acidic aqueous medium.

The compounds of general formula (II) of Scheme 1, in which one from among X_1, X_2,

X_3 and X_4 represents a group C-R_1 in which R_1 corresponds to a group -Si-(C_1-C_6-alkyl)$_3$ and B represents a group C_1-C_6-alkoxyl, may be obtained, for example, according to the methods illustrated in Scheme 2.

Scheme 2



According to this method, the compounds of general formula (II), defined such that n is equal to 1, 2 or 3, are obtained by reaction of the corresponding compounds (VI) with a reagent (VIII), in which LG represents a leaving group such as a chlorine, bromine or iodine atom and n is equal to 1, 2 or 3. The reaction for the formation of the compounds of general formula (II) may be performed in the presence of a base such as sodium hydride or potassium carbonate, in a polar solvent such as dimethylformamide, dimethyl sulfoxide or acetone (n = 1: Kolasa T., Bioorg. Med. Chem. 1997, 5 (3) 507, n = 2: Abramovitch R., Synth. Commun., 1995, 25 (1), 1).

When the compound of general formula (VIII) is defined such that n is equal to 1, 2 or 3 and LG represents a hydroxyl group, the compounds of general formula (II) may be obtained by reacting the compound of general formula (VI) with a compound of general formula (VIII) in the presence of a phosphine, for instance triphenylphosphine, and a reagent, for instance diethyl azodicarboxylate, dissolved in a solvent such as dichloromethane or tetrahydrofuran (O. Mitsonobu, Synthesis, 1981, 1-28).

Similarly, the compounds of general formula (II) may be obtained by reacting the compound of general formula (VI) with a compound of general formula (VIII) in the presence of a phosphine supported on a resin and of a reagent such as, for example, diisopropyl azodicarboxylate, dissolved in a solvent such as dichloromethane or tetrahydrofuran.

When the compound of general formula (VIII) is defined such that n is equal to 0 and LG represents a leaving group such as a chlorine, bromine or iodine atom, the reaction

for formation of the compounds of general formula (II) may be performed by application or adaptation of the methods described by S. L. Buchwald et al. (*J. Am. Chem. Soc.*, **2001**, 123, 7727 and **2002**, 124, 11684), preferably under an inert atmosphere in basic medium, for example in the presence of potassium triphosphate, in the presence of a copper salt such as copper iodide, optionally in the presence of an additive such as N,N'-dimethylcyclohexane-1,2-diamine, the whole in an organic solvent such as toluene.

The compounds of general formula (VI) are prepared from aromatic or heteroaromatic aldehydes substituted with a silyl group of general formula (IV), in which X_1, X_2, X_3 and X_4 are as defined in the general formula (I) with one of them corresponding to a silyl group, by reaction with an alkyl azidoacetate of general formula (VII) in which B represents a group C_1-C_6-alkoxyl, for instance ethyl azidoacetate, in the presence of a base such as sodium ethoxide, in a solvent such as ethanol or methanol, to give the alkyl 2-azidocinnamates of general formula (V). These products are then converted into indole or azaindole esters in a refluxing solvent, for example in xylene or toluene, by adaptation of the protocols described in the literature (Hemetsberger et al. *Monatsh. Chem.*, **1969**, 100, 1599 and **1970**, *101*, 161; P. Roy et al., *Synthesis.*, **2005**, 16, 2751-2757; R. Guilard et al., *J. Heterocyclic. Chem.*, **1981**, 18, 1365-1377; W. Rees et al., *J. Chem. Soc., Perkin Trans. 1* **1984**, 2189-2196; P. Molina et al., *J. Org. Chem.*, **2003**, *68(2)*, 489-499; C. Moody et al., *J. Chem. Soc., Perkin Trans. 1* **1984**, 2189-2196; J. Sawyer et al., *J. Med. Chem.*, **2005**, 48, 893-896; D. Tanner *Synlett* **2006**, 18, 3140-3144).

Alternatively, the formation of the compounds of general formula (VI) may be obtained by decomposition of the alkyl 2-azidocinnamate of general formula (V), in the presence of a rhodium dimer complex, in a solvent such as toluene, at a temperature of between 25°C and 60°C, according to an adaptation of protocols described in the literature (Tom G. Drivers et al., *J. Am. Chem. Soc.*, **2007**, *129*, 7500-7501; J. Sawyer et al., *J. Med. Chem.*, **2005**, 48, 893-896).

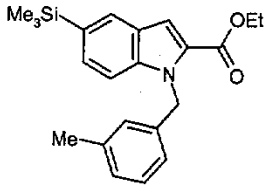
The aromatic or heteroaromatic aldehydes substituted with a silyl group of general formula (IV), when they are not commercially available, may be obtained from the corresponding aromatic or heteroaromatic aldehydes, which are preferably masked in the form of an acetal, for example, substituted with a halogen atom such as a bromine

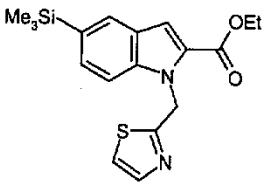
or an iodine, in the position at which the silyl group is to be introduced:
- for example by reaction with a disilane such as hexamethyldisilane, in the presence of a catalytic amount of a metal complex, preferably a palladium complex, for instance tetrakis(triphenylphosphine)palladium, without solvent or in a solvent, preferably a polar solvent, for instance hexamethylphosphoramide, in the presence of a base such as potassium carbonate, at a temperature of between 20°C and the boiling point of the solvent (adaptation of the protocols described in the literature: J. Babin et al. *J. Organometall. Chem.*, **1993**, *446 (1-2)*, 135-138; E. Shirakawa et al., *Chem. Commun.*, **2000**, 1895-1896; L. Goossen et al. *Synlett*, **2000**, 1801-1803; H. Matsumoto et al., *J. Organometall. Chem.*, **1975**, 85, C1; FR 2 677 358).
- for example by reaction with a disilane such as hexamethyldisilane, in the presence of a strong base, for instance hexamethylphosphorotriamide (HMPT), at a temperature close to 20°C (adaptation of the protocols described in the literature: A.I. Meyers et al., *J. Org. Chem.*, **1977**, *42 (15)*, 2654-2655; K. Ishimaru et al., *Heterocycles.*, **2001**, 55 (8), 1591-1597).

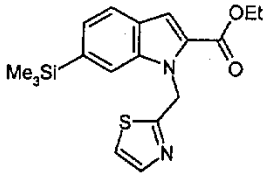
The aromatic or heteroaromatic aldehydes substituted with a silyl group of general formula (IV), when they are not commercially available, may also be obtained from the corresponding dihalo aromatic or heteroaromatic derivatives, such as a dibromo derivative, in the position at which the silyl group is to be introduced, by exchange with an organometallic reagent, for instance n-butyllithium. The metallic aromatic or heteroaromatic derivatives thus formed may then react with organohalosilanes or may be converted into formyl derivatives by adaptation of the methods described in the literature. The reaction is preferably performed at low temperatures of between -110°C and room temperature, in a solvent such as ether or THF (adaptation of the protocols described in the literature: Bao-Hui Ye et al., *Tetrahedron.*, **2003**, *59*, 3593-3601; P. Pierrat et al., *Synlett* **2004**, 13, 2319-2322; K.T. Warner et al., *Heterocycles* **2002**, 58, 383; D. Deffieux et al., *J. Organometall. Chem.*, **1994**, *13 (6)*, 2415-2422; WO2005/080 328; S.G. Davies et al., *J. Chem. Soc., Perkin Trans. 1* **1991**, 501; G. Queguiner et al., *J. Org. Chem.*, **1981**, 46, 4494-4497; G. Breton et al., *Tetrahedron* **2000**, 56 (10), 1349-1360; S. De Montis et al., *Tetrahedron* **2004**, 60 (17), 3915-3920; L. Buchwald et al., *J. Am. Chem. Soc.*, **1998**, *120*, 4960-4976).

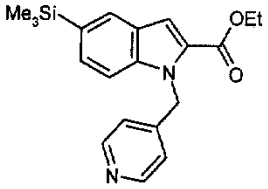
According to another of its aspects, a subject of the invention is also the compounds of general formulae (IIa), (IIb), (IIc), (IId), (IIe), (IIf), (IIg) and (IIh), in which Me represents

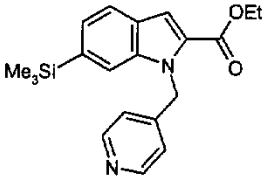
a methyl group and Et represents an ethyl group. These compounds are useful as intermediates for the synthesis of the compounds of formula (I).

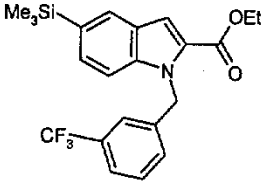

(IIa)

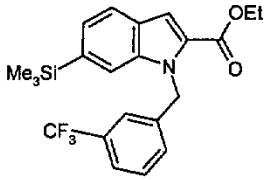

(IIb)

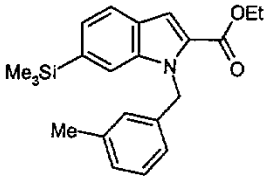

((IIc)


(IId)


(IIe)


(IIf)


(IIg)


(IIh)

The esters (IIa), (IIb), (IIc), (IId), (IIe), (IIf), (IIg) and (IIh) are prepared according to the processes described in Examples 18, 22, 25, 28, 31, 32, 35 and 37.

The examples that follow describe the preparation of certain compounds in accordance with the invention. These examples are not limiting, and serve merely to illustrate the present invention. The numbers of the illustrated compounds refer to those in Table 1. The elemental microanalyses, the LC-MS analyses (liquid chromatography coupled to mass spectrometry) and the IR or NMR spectrum confirm the structures of the compounds obtained.

Example 1 (Compound 1)

N-(2,3-Dimethyl-3*H*-imidazo[4,5-*b*]pyrid-6-yl)-5-fluoro-1-(3-fluorobenzyl)-1*H*-indole-2-carboxamide

1.1 5-Fluoro-1-(3-fluorobenzyl)-1*H*-indole-2-carboxylic acid

Aqueous sodium hydroxide solution, prepared from 1.15 g (28.92 mmol) of sodium hydroxide pellets in 50 mL of water, is added to a solution of 7.6 g (24.10 mmol) of ethyl 5-fluoro-1-(3-fluorobenzyl)-1*H*-indole-2-carboxylate (WO2006/024 776) in 241 mL of ethanol. The mixture is heated for 2 hours and then concentrated under reduced pressure. The resulting solid is taken up in 200 mL of water. The solution is washed with twice 100 mL of ethyl ether, acidified by successive addition of small amounts of concentrated hydrochloric acid and then extracted with 200 mL of ethyl acetate. The

organic phase is finally washed twice with 100 mL of water and once with 50 mL of saturated sodium chloride solution, dried over magnesium sulfate and concentrated under reduced pressure. After drying at 50°C under reduced pressure, 6.4 g of the expected product are obtained in the form of a solid, which is used without further purification in the rest of the synthesis.

1.2 *N*-(2,3-Dimethyl-3*H*-imidazo[4,5-*b*]pyrid-6-yl)-5-fluoro-1-(3-fluorobenzyl)-1*H*-indole-2-carboxamide (Compound 1)

To a solution, stirred at 20°C, of 0.25 g (0.87 mmol) of 5-fluoro-1-(3-fluorobenzyl)-1*H*-indole-2-carboxylic acid prepared in step 1.1, 183 mg (0.96 mmol) of *N*-(3-dimethylaminopropyl)-*N'*-ethylcarbodiimide hydrochloride (EDAC) and 129 mg (0.96 mmol) of 1-hydroxybenzotriazole (HOBT) in 8 mL of DMF are added 130 microlitres (0.96 mol) of triethylamine and then 224 mg (1.13 mmol) of 6-amino-2,3-dimethyl-3*H*-imidazo[4,5-*b*]pyridine hydrochloride (*Ukrainskii Khimicheskii Zhurnal* **1981**, *47*, 867). The reaction mixture is stirred for 8 hours at 20°C and then concentrated under reduced pressure. The resulting product is taken up in 100 mL of water, and a precipitate is collected by filtration and is purified by chromatography on a column of silica, eluting with a mixture of dichloromethane and methanol. The fractions containing the product are combined and evaporated to a quarter of their volume. 50 mL of n-heptane are added to the solution, and a solid is collected by filtration and dried under reduced pressure. 150 mg of the expected product are thus isolated.

m.p. = 274 – 275°C

^{1}H NMR (DMSO-D_6), δ ppm: 10.59 (s, 1H); 8.59 (s, 1H); 8.3 (s, 1H); 7.6 (m, 2H); 7.46 (s, 1H); 7.32 (m, 1H); 7.19 (m, 1H); 7.07 (m, 1H); 6.92 (m, 2H); 5.91 (s, 2H); 3.78 (s, 3H); 2.6 (s, 3H).

Example 2 (Compound 2)

N-(2-Methylthiazolo[5,4-*b*]pyrid-6-yl)-5-fluoro-1-(3-fluorobenzyl)-1*H*-indole-2-carboxamide.

The process is performed according to a method similar to that of Example 1.2, starting with 0.5 g (1.74 mmol) of 5-fluoro-1-(3-fluorobenzyl)-1*H*-indole-2-carboxylic acid prepared in step 1.1 and 0.345 g (2.09 mmol) of 6-amino-2-methylthiazolo[5,4-*b*]pyridine (*Yakugaku Zasshi* **1950**, *70*, 187). At the end of the reaction, the product is concentrated under reduced pressure and then taken up in 100 mL of water. A

precipitate is collected by filtration, and is purified by chromatography on a column of alumina, eluting with a mixture of dichloromethane and methanol. The resulting product is recrystallized from methanol, and a solid is collected by filtration, and dried under reduced pressure. 340 mg of the expected product are thus isolated.

m.p. = 264 – 265°C

^{1}H NMR (DMSO-D_6), δ ppm: 10.85 (s, 1H); 8.9 (s, 1H); 8.67 (s, 1H); 7.61 (m, 2H); 7.51 (s, 1H); 7.31 (m, 1H); 7.2 (m, 1H); 7.05 (m, 1H); 6.9 (m, 2H); 5.9 (s, 2H); 2.87 (s, 3H).

Example 3 (Compound 3)

N-(Thiazolo[5,4-*b*]pyrid-6-yl)-5-fluoro-1-(3-fluorobenzyl)-1*H*-indole-2-carboxamide

The process is performed according to a method similar to that of Example 1.2, starting with 0.32 g (1.11 mmol) of 5-fluoro-1-(3-fluorobenzyl)-1*H*-indole-2-carboxylic acid prepared in step 1.1 and 0.2021 g (1.34 mmol) of 6-amino-thiazolo[5,4-*b*]pyridine (WO2007/100 758). At the end of the reaction, the product is concentrated under reduced pressure and then taken up in 100 mL of water. A precipitate is collected by filtration, and is purified by chromatography on a column of alumina, eluting with a mixture of dichloromethane and methanol. The resulting product is recrystallized from methanol, and a solid is collected by filtration and dried under reduced pressure. 340 mg of the expected product are thus isolated.

m.p. = 250 – 251°C

^{1}H NMR (DMSO-D_6), δ ppm: 10.9 (s, 1H); 9.57 (s, 1H); 9 (s, 1H); 8.98 (s, 1H); 7.61 (m, 2H); 7.51 (s, 1H); 7.31 (m, 1H); 7.2 (m, 1H); 7.08 (m, 1H); 6.92 (m, 2H); 5.91 (s, 2H).

Example 4 (Compound 13)

[6-[[[5-Fluoro-1-[(3-fluorophenyl)methyl]-1*H*-indol-2-yl]carbonyl]amino]thiazolo[5,4-*b*]pyrid-2-yl]methyl 2,2-dimethylpropanoate

4.1 (6-Nitrothiazolo[5,4-*b*]pyrid-2-yl)methyl 2,2-dimethylpropanoate

A mixture of 6 g (29.48 mmol) of 2-chloro-3,5-dinitropyridine and 7.74 g (44.22 mmol) of 2-amino-2-thioxoethyl pivalate in 50 mL of sulfolane is heated for 2 hours at 105°C. After this time, 150 mL of ethyl acetate are added to the mixture, and the organic phase is washed three times with 200 mL of water and then once with 100 mL of saturated sodium chloride solution. The organic phase is then separated out, dried over sodium sulfate and then concentrated under reduced pressure. The product

obtained is purified by chromatography on a column of silica, eluting with a mixture of heptane and ethyl acetate. 1.45 g of a yellow solid are obtained.
^{1}H NMR ($CDCl_3$), δ ppm: 9.55 (d, 1H); 9.09 (d, 1H); 5.59 (s, 2H); 1.38 (s, 9H).

4.2 (6-Aminothiazolo[5,4-*b*]pyrid-2-yl)methyl 2,2-dimethylpropanoate
A mixture of 0.75 g (2.54 mmol) of (6-amino-thiazolo[5,4-*b*]pyrid-2-yl)methyl 2,2-dimethylpropanoate, prepared in step 4.1, and 1.68 g (8.89 mmol) of tin chloride in 50 mL of ethyl acetate is stirred for 30 minutes at 50°C. After this time, the reaction mixture is poured into 100 mL of ice-cold water. The pH of the aqueous solution is neutralized by successive addition of sodium hydroxide solution. The aqueous phase is then extracted with 3 times 50 mL of ethyl acetate. The organic phases are combined, dried and then concentrated under reduced pressure. 0.7 g of a solid is thus obtained, which product is used without further purification in the rest of the synthesis.
^{1}H NMR ($CDCl_3$), δ ppm: 8.05 (d, 1H); 7.42 (d, 1H); 5.37 (s, 2H); 1.21 (s, 9H).

4.3 [6-[[[5-Fluoro-1-[(3-fluorophenyl)methyl]-1*H*-indol-2-yl]carbonyl]amino]thiazolo-[5,4-*b*]pyrid-2-yl]methyl 2,2-dimethylpropanoate (Compound 13)
240 microlitres (2.78 mmol) of oxalyl chloride are added, dropwise at 0°C, to a solution of 0.4 g (1.39 mmol) of 5-fluoro-1-[(3-fluorophenyl)methyl]-1*H*-indole-2-carboxylic acid, prepared in step 1.1, in 10 mL of dichloromethane and 0.5 mL of dimethylformamide. The mixture is stirred for 15 minutes at 0°C and then for 1 hour at 20°C. After this time, a further 120 microlitres (1.39 mmol) of oxalyl chloride are added and stirring is continued for 30 minutes at 20°C. The reaction mixture is then concentrated under reduced pressure and taken up in 5 mL of tetrahydrofuran. 219 microlitres of triethylamine and then a solution of 0.44 g (1.67 mmol) of (6-amino-thiazolo[5,4-*b*]pyrid-2-yl)methyl 2,2-dimethylpropanoate, prepared in step 4.2, in 10 mL of tetrahydrofuran are added, under an inert atmosphere. The reaction mixture is stirred for 15 hours at 20°C and for 1 hour at 40°C, and then concentrated under reduced pressure and taken up in 100 mL of water. The aqueous phase is extracted three times with 50 mL of ethyl acetate. The organic phases are combined, washed successively with 50 mL of saturated sodium hydrogen carbonate solution and with 50 mL of saturated sodium chloride solution, and then dried over sodium sulfate and concentrated under reduced pressure. The product thus obtained is purified on a column of alumina, eluting with dichloromethane. 0.15 g of the expected product is thus isolated.

m.p. = 224 – 225°C

^{1}H NMR (DMSO-D_6), δ ppm: 8.89 (s, 1H); 8.71 (s, 1H); 7.52 (m, 2H); 7.45 (s, 1H); 7.29 (m, 1H); 7.15 (m, 1H); 7.00 (m, 1H); 6.9 (m, 1H); 6.81 (m, 1H); 5.86 (s, 2H); 5.49 (s, 2H); 1.12 (s, 9H).

Example 5 (Compound 5)

N-(Quinol-3-yl)-5-fluoro-1-(3-fluorobenzyl)-1*H*-indole-2-carboxamide

1.19 mL (2.38 mmol) of a 2M solution of trimethylaluminium in toluene are added dropwise to a solution, stirred at 0°C under an inert atmosphere, of 0.274 g (1.9 mmol) of 3-aminoquinoline in 40 mL of dry toluene. The mixture is then stirred at 50°C. After 15 minutes, a solution of 0.5 g (1.59 mmol) of ethyl 5-fluoro-1-(3-fluorobenzyl)-1*H*-indole-2-carboxylate (WO2006/024 776) in 10 mL of toluene is added dropwise. 15 mL of 1N hydrochloric acid solution and 100 mL of ethyl acetate are added to the mixture. The organic phase is separated out and then washed successively with 20 mL of 1N hydrochloric acid solution, 20 mL of water and 20 mL of saturated sodium chloride solution, and then concentrated under reduced pressure. The product thus obtained is triturated in 10 mL of hot toluene. A precipitate is collected by filtration. After drying, 295 mg of the expected product are thus isolated.

m.p. = 244 – 246°C

^{1}H NMR ($CDCl_3$), δ ppm: 10.91 (s, 1H); 9.15 (d, 1H); 8.88 (d, 1H); 8 (m, 2H); 7.62 (m, 5H); 7.32 (m, 1H); 7.21 (m, 1H); 7.08 (m, 1H); 6.92 (m, 2H); 5.95 (s, 2H).

Example 6 (Compound 4)

N-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-5-fluoro-1-[(3-fluorophenyl)methyl]-1*H*-indole-2-carboxamide

50 mg (2.03 mmol) of sodium are added to 8 mL of methanol with stirring at 20°C. After 15 minutes, a solution of 0.15 g (0.28 mmol) of [6-[[[5-fluoro-1-[(3-fluorophenyl)methyl]-1*H*-indol-2-yl]carbonyl]amino]thiazolo[5,4-*b*]pyrid-2-yl]methyl 2,2-dimethylpropanoate (Compound 13), prepared in step 4.3, in 16 mL of methanol is added. Stirring is continued for 15 minutes at 20°C, and the reaction mixture is then concentrated under reduced pressure and taken up in 200 mL of molar ammonium chloride solution. The aqueous phase is extracted three times with 50 mL of ethyl acetate. The organic phases are combined, washed with 50 mL of saturated sodium chloride solution and

then dried over sodium sulfate and concentrated under reduced pressure. The product thus obtained is purified on a column of silica, eluting with a mixture of dichloromethane and methanol. 70 mg of the expected product are thus isolated.
m.p. = 225 – 226°C
^{1}H NMR ($CDCl_3$), δ ppm: 10.84 (s, 1H); 8.92 (d, 1H); 8.72 (d, 1H); 7.61 (m, 2H); 7.5 (s, 1H); 7.35 (m, 1H); 7.2 (m, 1H); 7.08 (m, 1H); 6.92 (m, 2H); 6.37 (m, 1H); 5.91 (s, 2H); 4.9 (s, 2H).

Example 7 (Compound 6)

N-(2-Hydroxymethyl-3-methyl-3*H*-imidazo[4,5-*b*]pyrid-6-yl)-5-fluoro-1-[(3-fluorophenyl)-methyl]-1*H*-indole-2-carboxamide

7.1 2-Hydroxymethyl-6-nitro-3-methyl-3*H*-imidazo[4,5-*b*]pyridine and 3-methyl-6-nitro-3*H*-imidazo[4,5-*b*]pyridine.

A mixture of 3.1 g (18.44 mmol) of 3-amino-5-nitro-2-methylaminopyridine and 3.5 g (46.09 mmol) of glycolic acid is heated at 150°C. After 75 minutes, the mixture is cooled and then dissolved in 50 mL of 1N hydrochloric acid. The pH of the aqueous phase is adjusted to 9 by successive additions of concentrated sodium hydroxide, and the mixture is then concentrated under reduced pressure. The resulting solid is purified by chromatography on a column of silica, eluting with a mixture of dichloromethane and methanol. 1.5 g of the expected product are thus isolated. This purification also allows 0.2 g of 3-methyl-6-nitro-3*H*-imidazo[4,5-*b*]pyridine to be isolated.
2-Hydroxymethyl-6-nitro-3-methyl-3*H*-imidazo[4,5-*b*]pyridine:
LCMS: $[MH]^+$ = 209
^{1}H NMR (DMSO-D_6), δ ppm: 9.3 (d, 1H); 8.89 (d, 1H); 5.88 (m, 1H); 4.83 (m, 2H); 3.95 (t, 3H).
3-Methyl-6-nitro-3*H*-imidazo[4,5-*b*]pyridine:
LCMS: $[MH]^+$ = 179
^{1}H NMR (DMSO-D_6), δ ppm: 9.31 (d, 1H); 8.95 (d, 1H); 8.79 (s, 1H); 3.95 (t, 3H).

7.2 6-Amino-2-hydroxymethyl-3-methyl-3*H*-imidazo[4,5-*b*]pyridine

A suspension of 0.5 g (2.4 mol) of 2-hydroxymethyl-6-nitro-3-methyl-3*H*-imidazo[4,5-*b*]pyridine, prepared in the preceding step, and 0.3 g of 10% palladium-on-charcoal is stirred for 3 hours under 2.5 atm. of hydrogen. After this time, the suspension is filtered through a pad of Celite and the filtrate is concentrated under reduced pressure. 0.4 g

of the expected product is thus isolated, and is used without further purification in the rest of the synthesis.
LCMS: $[MH]^+$ = 179

7.3 *N*-(2-Hydroxymethyl-3-methyl-3*H*-imidazo[4,5-*b*]pyrid-6-yl)-5-fluoro-1-[(3-fluorophenyl)methyl]-1*H*-indole-2-carboxamide (Compound 6)
Compound 6 is synthesized according to a process similar to that described in Example 1.2, starting with 6-amino-2-hydroxymethyl-3-methyl-3*H*-imidazo[4,5-*b*]-pyridine described in the preceding step and 5-fluoro-1-[(3-fluorophenyl)methyl]-1*H*-indole-2-carboxylic acid described in step 1.1.
m.p.: 231 – 232°C
^{1}H NMR (DMSO-D_6), δ ppm: 10.67 (s, 1H); 8.68 (s, 1H); 8.4 (s, 1H); 7.6 (m, 2H); 7.48 (s, 1H); 7.33 (m, 1H); 7.18 (txd, 1H); 7.055 (txd, 1H); 6.94 (m, 2H); 5.92 (s, 2H); 5.69 (t, 1H); 4.8 (d, 2H); 3.88 (s, 3H)
.

Example 8 (Compound 7)
N-(3-Methyl-3*H*-imidazo[4,5-*b*]pyrid-6-yl)-5-fluoro-1-[(3-fluorophenyl)methyl]-1*H*-indole-2-carboxamide

8.1 6-Amino-3-methyl-3*H*-imidazo[4,5-*b*]pyridine
This compound is prepared according to a process similar to that described in step 7.2, starting with 3-methyl-6-nitro-3*H*-imidazo[4,5-*b*]pyridine prepared in step 7.1.
LCMS: $[MH]^+$ = 149

8.3 *N*-(3-Methyl-3*H*-imidazo[4,5-*b*]pyrid-6-yl)-5-fluoro-1-[(3-fluorophenyl)methyl]-1*H*-indole-2-carboxamide (Compound 7)
Compound 7 is synthesized according to a process similar to that described in Example 1.2, starting with 6-amino-3-methyl-3*H*-imidazo[4,5-*b*]pyridine, described in the preceding step, and 5-fluoro-1-[(3-fluorophenyl)methyl]-1*H*-indole-2-carboxylic acid, described in step 1.1.
m.p.: 235 – 236°C
^{1}H NMR (DMSO-D_6), δ ppm: 10.68 (s, 1H); 8.69 (s, 1H); 8.42 (m, 2H); 7.6 (m, 2H); 7.49 (s, 1H); 7.32 (m, 1H); 7.19 (m, 1H); 7.06 (m, 1H); 6.92 (m, 2H); 5.91 (s, 2H); 3.87 (s, 3H).

Example 9 (Compound 8)

N-(2,3-Dimethyl-3*H*-imidazo[4,5-*b*]pyrid-6-yl)-5-trifluoromethyl-1-[(3-fluorophenyl)-methyl]-1*H*-pyrrolo[2,3-*b*]pyridine-2-carboxamide

This compound was prepared according to a process similar to that described in Example 1.2, starting with 5-trifluoromethyl-1-[(3-fluorophenyl)methyl]-1H-pyrrolo[2,3-b]pyridine-2-carboxylic acid (WO2008/093 024).

m.p.: 274 – 275°C

^{1}H NMR (DMSO-D_6), δ ppm: 10.75 (s, 1H); 8.83 (s, 1H); 8.76 (s, 1H); 8.55 (s, 1H); 8.28 (s, 1H); 7.63 (s, 1H); 7.32 (m, 1H); 7.07 (m, 1H); 6.98 (m, 2H); 6.01 (s, 2H); 3.76 (s, 3H); 2.6 (s, 3H).

Example 10 (Compound 9)

N-(3,4-Dihydro-2*H*-pyrido[3,2-*b*][1,4]oxazin-7-yl)-5-fluoro-1-[(3-fluorophenyl)methyl]-1*H*-indole-2-carboxamide

10.1 5-Fluoro-1-[(3-fluorophenyl)methyl]- 1*H*-indole-2-carboxamide

To a suspension, stirred at 20°C, of 2 g (6.96 mmol) of 5-fluoro-1-[(3-fluorophenyl)-methyl]-1*H*-indole-2-carboxylic acid, prepared in step 1.1, in 80 mL of dry toluene are added 5.08 mL (69.62 mmol) of thionyl chloride. The reaction mixture is stirred for 2 hours at reflux and is then concentrated under reduced pressure. The resulting product is taken up in 10 mL of dichloromethane, and this solution is poured dropwise into a solution of 9.12 mL (69.62 mmol) of 30% aqueous ammonia. The reaction mixture is stirred for 14 hours at 20°C. After this time, a solid is collected by filtration, and is triturated in 50 mL of diisopropyl ether. After filtering off and drying under reduced pressure, 0.58 g of the expected product is collected.

^{1}H NMR (DMSO-D_6), δ ppm: 8.11 (broad peak, 1H); 7.5 (m, 3H); 7.32 (m, 1H); 7.25 (s, 1H); 7.09 (m, 2H); 6.89 (m, 2H); 5.91 (s, 2H).

10.2 *N*-(3,4-Dihydro-2*H*-pyrido[3,2-*b*][1,4]oxazin-7-yl)-5-fluoro-1-[(3-fluorophenyl)-methyl]-1*H*-indole-2-carboxamide (Compound 9)

0.4 g (1.4 mmol) of the amide prepared in the preceding step, 0.31 g (1.47 mmol) of 7-bromo-3,4-dihydro-2*H*-pyrido[3,2-*b*][1,4]oxazine, 0.08 g (0.42 mmol) of copper iodide, 0.39 g (2.79 mmol) of potassium carbonate and 10 mL of dry dioxane are introduced into a pressure tube equipped with a magnetic stirrer. The suspension is degassed,

53 mg (0.46 mmol) of *trans*-1,2-cyclohexanediamine are added, and the tube is heated at 120°C with stirring for 16 hours. After this time, 50 mL of ethyl acetate and 50 mL of water are added to the medium. The aqueous phase is separated out and then extracted with 2×30 mL of ethyl acetate. The organic phases are combined, washed with 50 mL of water, dried over sodium sulfate and then concentrated under reduced pressure. The resulting product is purified by chromatography on a column of silica, eluting with a mixture of heptane and ethyl acetate, followed by crystallization from a mixture of heptane and dichloromethane. 0.4 g of the expected product is thus isolated.

m.p.: 265-266°C

^{1}H NMR (DMSO D_6), δ (ppm): 10.22 (s, 1H); 7.98 (s, 1H); 7.58 (m, 2H); 7.34 (m, 3H); 7.18 (m, 1H); 7.06 (m, 1H); 6.91 (m, 2H); 6.58 (s, 1H); 5.9 (s, 2H); 4.14 (m, 2H); 3.4 (m, 2H).

Example 11 (Compound 10)

N-(4-Methyl-3,4-dihydro-2*H*-pyrido[3,2-*b*][1,4]oxazin-7-yl)-5-fluoro-1-[(3-fluorophenyl)-methyl]-1*H*-indole-2-carboxamide

This compound was prepared according to a process similar to that described in Example 10.2, starting with 7-amino-4-methyl-3,4-dihydro-2*H*-pyrido[3,2-*b*][1,4]oxazine.

m.p.: 214 – 215°C

^{1}H NMR (DMSO D_6), δ (ppm): 10.29 (s, 1H); 8.03 (s, 1H); 7.58 (m, 2H); 7.34 (m, 3H); 7.18 (m, 1H); 7.05 (m, 1H); 6.91 (m, 2H); 5.9 (s, 2H); 4.26 (m, 2H); 3.41 (m, 2H); 3.02 (s, 3H).

Example 12 (Compound 11)

N-(2-Methyl-3*H*-imidazo[4,5-*b*]pyrid-6-yl)-5-fluoro-1-[(3-fluorophenyl)methyl]-1*H*-indole-2-carboxamide

12.1 2-Methyl-6-nitro-3*H*-imidazo[4,5-*b*]pyridine

2.3 mL (24.33 mol) of acetic anhydride are added to a solution, stirred at 15°C, of 1.5 g (9.73 mmol) of 2,3-diamino-5-nitropyridine in 15 mL of acetic acid. After stirring for 15 minutes at room temperature, the mixture is heated at 110°C for 2 hours and then at 140°C for 7 hours. The resulting mixture is concentrated under reduced pressure

and taken up in 100 mL of water. A precipitate is collected by filtration. After purification by chromatography on a column of silica, 0.4 g of the expected product is obtained.
LCMS: $[MH]^+$ = 179
^{1}H NMR (DMSO D_6), δ (ppm): 9.2 (d, 1H); 8.7 (d, 1H); 2.62 (s, 3H).

12.2 6-Amino-2-methyl-3*H*-imidazo[4,5-*b*]pyridine
This compound is prepared according to a process similar to that described in step 7.2, starting with 2-methyl-6-nitro-3*H*-imidazo[4,5-*b*]pyridine prepared in step 12.1.
LCMS: $[MH]^+$ = 149
^{1}H NMR (DMSO D_6), δ (ppm): 7.7 (d, 1H); 6.99 (d, 1H); 2.4 (s, 3H).

12.3 *N*-(2-Methyl-3*H*-imidazo[4,5-*b*]pyrid-6-yl)-5-fluoro-1-[(3-fluorophenyl)methyl]-1*H*-indole-2-carboxamide (Compound 11).
This compound was prepared according to a process similar to that described in Example 1.2, starting with 5-fluoro-1-[(3-fluorophenyl)methyl]-1*H*-indole-2-carboxylic acid, prepared in Example 1.1 and 6-amino-2-methyl-3*H*-imidazo[4,5-*b*]pyridine, prepared in the preceding step.
m.p.: 299 – 300°C
^{1}H NMR (DMSO D_6), δ (ppm): 12.37 (s, 1H); 10.6 (s, 1H); 8.53 (s, 1H); 8.29 (m, 1H); 7.61 (dxd, 1H); 7.58 (dxd, 1H); 7.46 (s, 1H); 7.33 (m, 1H); 7.18 (txd, 1H); 7.05 (txd, 1H); 6.94 (m, 2H); 5.9 (s, 2H); 2.48 (s, 3H).

Example 13 (Compound 12)
N-(1-Methyl-2-oxo-2,3-dihydro-1*H*-pyrido[2,3-*b*][1,4]oxazin-7-yl)-5-fluoro-1-[(3-fluorophenyl)methyl]-1*H*-indole-2-carboxamide

13.1 7-Bromo-1-methyl-2-oxo-2,3-dihydro-1*H*-pyrido[2,3-*b*][1,4]oxazine
0.16 mL (2.62 mmol) of methyl iodide is added to a suspension of 0.5 g (2.18 mol) of 7-bromo-2-oxo-2,3-dihydro-1*H*-pyrido[2,3-*b*][1,4]oxazine, 0.24 g (1.09 mmol) of benzyltriethylammonium chloride and 0.75 g (5.46 mmol) of potassium carbonate in 25 mL of acetonitrile. The mixture is stirred for 6 hours at 60°C. After this time, a precipitate is removed by filtration. The filtrate is concentrated under reduced pressure and the resulting solid is taken up in 15 mL of dichloromethane and then washed successively with 20 ml of water, 10 mL of 0.1N hydrochloric acid solution, 10 mL of saturated sodium hydrogen carbonate solution and then 10 mL of water. After drying

over sodium sulfate, the solution is finally concentrated under reduced pressure to give the expected product, which is used without further purification in the following step.
^{1}H NMR (DMSO D_6), δ (ppm): 7.98 (d, 1H); 7.79 (d, 1H); 4.9 (s, 2H); 3.29 (s, 3H).

13.2 *N*-(1-Methyl-2-oxo-2,3-dihydro-1*H*-pyrido[2,3-*b*][1,4]oxazin-7-yl)-5-fluoro-1-[(3-fluorophenyl)methyl]-1*H*-indole-2-carboxamide (Compound 12)
This compound was prepared according to a process similar to that described in Example 10.2, starting with 7-bromo-1-methyl-2-oxo-2,3-dihydro-1*H*-pyrido[2,3-*b*][1,4]oxazine prepared in the preceding step.
m.p.: 248 – 250°C
^{1}H NMR (DMSO D_6), δ (ppm): 10.61 (s, 1H); 8.23 (d, 1H); 7.91 (d, 1H); 7.59 (txd, 2H); 7.46 (s, 1H); 7.33 (m, 1H); 7.19 (txd, 1H); 7.06 (txd, 1H); 6.9 (m, 2H); 5.91 (s, 2H); 4.87 (s, 2H); 3.25 (s, 3H).

Example 14 (Compound 14)
N-(2,3-Dihydro-[1,4]dioxino[2,3-*b*]pyrid-7-yl))-5-fluoro-1-[(3-fluorophenyl)methyl]-1*H*-indole-2-carboxamide

This compound was prepared according to a process similar to that described in Example 10.2, starting with 7-bromo-2,3-dihydro-[1,4]dioxino[2,3-*b*]pyridine (WO2003/087 098).
m.p.: 224 – 225°C
^{1}H NMR (DMSO D_6), δ (ppm): 10.49 (s, 1H); 8.1 (s, 1H); 7.71 (s, 1H); 7.59 (m, 2H); 7.41 (s, 1H); 7.31 (m, 1H); 7.18 (m, 1H); 7.04 (m, 1H); 6.91 (m, 2H); 5.89 (s, 2H); 4.4 (m, 2H); 3.88 (m, 2H).

Example 15 (Compound 15)
N-(6-Hydroxy-5,6,7,8-tetrahydroquinol-3-yl)-5-fluoro-1-[(3-fluorophenyl)methyl]-1*H*-indole-2-carboxamide

This compound was prepared according to a process similar to that described in Example 1.2, starting with 3-amino-6-hydroxy-5,6,7,8-tetrahydroquinoline (WO2007/100 758).
m.p.: 204 – 206°C
^{1}H NMR (DMSO D_6), δ (ppm): 10.51 (s, 1H); 8.61 (s, 1H); 7.89 (s, 1H); 7.59 (m, 2H);

7.43 (s, 1H); 7.32 (m, 1H); 7.19 (m, 1H); 7.04 (m, 1H); 6.90 (m, 2H); 5.90 (s, 2H); 4.82 (d, 1H); 4.01 (m, 1H); 2.92 (m, 2H); 2.78 (m, 1H); 2.62 (m, 1H); 1.93 (m, 1H); 1.79 (m, 1H).

Example 16 (Compound 16)

N-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-5-trifluoromethyl-1-[(3-methylphenyl)-methyl]-1*H*-indole-2-carboxamide

16.1 Ethyl 5-trifluoromethyl-1-[(3-methylphenyl)methyl]-1*H*-indole-2-carboxylate

This compound was prepared by reacting 333 mg (1.295 mmol) of ethyl 5-trifluoromethyl-1*H*-indole-2-carboxylate with 0.31 mL (2.59 mmol) of 3-methylphenylmethanol in the presence of 0.92 g (3.826 mmol) of (cyanomethylene)tributylphosphorane (CMBP). The reaction mixture is stirred at 110°C for 15 hours and then concentrated to dryness. The crude reaction product is then purified by flash chromatography on a column of silica gel in a mixture of heptane and ethyl acetate, to give 376 mg of the expected product in the form of an oil.

^{1}H NMR (DMSO D_6), δ (ppm): 8.18 (s, 1H); 7.81-7.78 (m, 1H); 7.61-7.57 (m, 1H), 7.53 (s, 1H); 7.14-7.12 (m, 2H); 7.01-6.91 (m, 1H); 6.75-6.73 (m, 1H); 5.88 (s, 2H); 4.31 (q, 2H); 2.21 (s, 3 H); 1.30 (t, 3H).

LC-MS: 362($[M+H]^+$)

16.2 *N*-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-5-trifluoromethyl-1-[(3-methyl-phenyl)methyl]-1*H*-indole-2-carboxamide (Compound 16)

To a solution of 150 mg (0.415 mmol) of ethyl 5-trifluoromethyl-1-[(3-methylphenyl)methyl]-1*H*-indole-2-carboxylate prepared according to the protocol described in the preceding step and 132 mg (0.498 mmol) of (6-amino-thiazolo[5,4-*b*]pyrid-2-yl)methyl 2,2-dimethylpropanoate, obtained in step 4.2, in 1.5 mL of dry toluene, maintained under an inert atmosphere, is added dropwise, at 0°C, 0.31 mL (0.623 mmol) of a trimethylaluminium solution (2M/toluene). The reaction mixture is stirred at 110°C for 15 hours and then concentrated to dryness. The crude reaction product is then diluted with normal hydrochloric acid solution. The product is extracted with ethyl acetate and then purified by chromatography on a column of silica, eluting with a mixture of heptane and ethyl acetate, to give 82 mg of the expected product.

m.p.: 315 – 316°C

^{1}H NMR (DMSO D_6), δ (ppm): 10.97 (s, 1H); 8.92 (d, 1H); 8.70 (d, 1H); 8.22 (s, 1H);

7.81 (d, 1H); 7.62 (s, 1H); 7.60 (d, 1H); 7.14 (t, 1H); 7.03-6.97 (m, 2H); 6.87-6.84 (m, 1H), 6.38 (t, 1H); 5.91 (s, 2H); 4.87 (d, 2H); 2.19 (s, 3H).

Example 17 (Compound 17)

N-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-6-trifluoromethyl-1-[(3-methylphenyl)-methyl]-1*H*-indole-2-carboxamide

The product is prepared according to a process similar to that described in Example 16.

m.p.: 221-222°C

^{1}H NMR (DMSO D_6), δ (ppm): 11.0 (s, 1H); 8.95 (s, 1H); 8.7 (s, 1H); 8.1 (s, 1H); 8.0 (d, 1H); 7.6 (s, 1H); 7.5 (d, 1H); 7.15 (t, 1H); 7.05 (m, 1H); 6.95 (s, 1H); 6.85 (m, 1H); 6.35 (t, 1H); 5.95 (s, 2H); 4.9 (d, 2H); 2.2 (s, 3H).

Example 18 (Compound 18)

N-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-5-trimethylsilyl-1-[(3-methylphenyl)-methyl]-1*H*-indole-2-carboxamide

18.1 1-Bromo-3-trimethylsilylbenzene

To a solution of 10 g (42.39 mmol) of 1,3-dibromobenzene in 80 mL of anhydrous Et_2O, cooled to -78°C and maintained under a nitrogen atmosphere, are added dropwise with stirring, over 30 minutes, 26.49 mL (42.39 mmol) of a solution of BuLi (1.5M/hexane). After stirring for a further 30 minutes at -78°C, 5.96 mL (46.63 mmol) of TMSCl are added dropwise to the reaction mixture. Stirring is maintained at this temperature for 90 minutes and the reaction mixture is then hydrolysed by adding 15 mL of water. The product is extracted with ethyl acetate (3 x 50 mL). The combined organic phases are washed with saturated aqueous NaCl solution (2 x 25 mL), dried over Na_2SO_4, filtered and evaporated under reduced pressure. The crude reaction product is purified by chromatography on a column of silica gel, eluting with heptane, to give 9.3 g of the expected 1-bromo-3-trimethylsilylbenzene, in the form of a colourless oil.

^{1}H NMR (DMSO D_6), δ (ppm): 5.75 (s, 1H), 7.46 (m, 1H), 7.4 (m, 1H), 7.22 (t, 1H), 0.2 (s, 9H).

18.2 3-Trimethylsilylbenzaldehyde

To a solution of 5 g (21.89 mmol) of 1-bromo-3-trimethylsilylbenzene prepared

according to the protocol described in the preceding step, in 40 mL of anhydrous Et_2O, cooled to 0°C and maintained under a nitrogen atmosphere, are added dropwise, with stirring and over 30 minutes, 16.36 mL (26.18 mmol) of BuLi (1.6M/hexane). Stirring is continued at 0°C for a further 30 minutes, and the mixture is then maintained at room temperature for 90 minutes. 2.69 mL (34.91 mmol) of DMF, diluted with 17 mL of anhydrous Et_2O, are then introduced into the reaction mixture. After stirring for 3 hours at room temperature, the reaction mixture is hydrolysed at 0°C by successive addition of 10 mL of concentrated HCl solution and 100 mL of water. The product is extracted with 3 x 50 mL of CH_2Cl_2. The combined organic phases are washed with 100 mL of water, dried over Na_2SO_4, filtered and evaporated under reduced pressure. The crude reaction product is purified by flash chromatography on a column of silica gel, eluting with a gradient of from 10 to 20% of CH_2Cl_2 in heptane to give 1.82 g of the expected 3-trimethylsilylbenzaldehyde in the form of a yellow oil.

^1H NMR (DMSO D_6), δ (ppm): 10.01 (s, 1H); 8.0 (s, 1H); 7.85 (d, 1H); 7.8 (d, 1H); 7.5 (dd, 1H) 0.3 (s, 9H)

18.3 Ethyl 2-azido-3-(3-trimethylsilylphenyl)propenoate

To a solution of 2 g (87.5 mmol) of sodium in 30 mL of anhydrous EtOH, maintained under a nitrogen atmosphere and cooled to -10°C, is added, dropwise, a mixture of 31.4 mL (87.5 mmol) of ethyl azidoacetate (at 34% in CH_2Cl_2) and 3.9 g (21.87 mmol) of 3-trimethylsilylbenzaldehyde prepared according to the procedure described in the preceding step, diluted with 3 mL of EtOH. The reaction mixture is stirred at 0°C for 4 hours. It is then hydrolysed by adding, with vigorous stirring, 100 mL of aqueous NH_4Cl solution (30%). The aqueous phase is extracted with 3 x 50 mL of EtOAc. The combined organic phases are washed with water, dried over Na_2SO_4 and concentrated under reduced pressure. The crude reaction product is purified by chromatography on a column of silica gel, eluting with an isocratic mixture of heptane and CH_2Cl_2 (80/20). 1.7 g of the expected ethyl 2-azido-3-(3-trimethylsilylphenyl)propenoate are thus isolated in the form of a yellow oil.

^1H NMR (DMSO D_6), δ (ppm): 7.9 (d, 1H); 7.8 (s, 1H); 7.4 (d, 1H); 7.3 (dd, 1H); 6.9 (s, 1H); 4.2 (q, 2H); 1.2 (t, 3H); 0.15 (s, 9H)

MS: $[MH]^+ = 289$

18.4 Ethyl 5-trimethylsilyl-1*H*-indole-2-carboxylate

To a solution of 1.7 g (5.90 mmol) of ethyl 2-azido-3-(3-trimethylsilylphenyl)propenoate

prepared according to the procedure described in the preceding step, in 25 mL of dry toluene, maintained under an inert atmosphere, is added 0.62 g (0.59 mmol) of dirhodium (II) heptafluorobutyrate dimer complex. The reaction mixture is stirred for 7 hours at 40°C. A second portion of 0.62 g (0.59 mmol) of dirhodium (II) heptafluorobutyrate dimer complex is added to the reaction mixture while maintaining the stirring and heating at 40°C for a further 1 hour. After cooling to room temperature, the reaction mixture is filtered through silica gel, eluting with toluene. The filtrate is then concentrated under reduced pressure. The greenish solid obtained is triturated several times in a minimum amount of heptane, until a white powder is obtained. This powder is dried under reduced pressure to give 0.87 g of the expected ethyl 5-trimethylsilyl-1*H*-indole-2-carboxylate in the form of a white powder.

m.p. = 114-115°C

^{1}H NMR (DMSO D_6), δ (ppm): 7.7 (s, 1H); 7.35 (d, 1H); 7.25 (d, 1H); 7.0 (s, 1H); 4.2 (q, 2H); 1.2 (t, 3H); 0.15 (s, 9H)

LC-MS: $[MH]^-$ = 260

18.5 Ethyl 5-trimethylsilyl-1-[(3-methylphenyl)methyl]-1*H*-indole-2-carboxylate (Compound IIa)

The product is prepared according to a process similar to that described in Example 16.1

^{1}H NMR (DMSO D_6), δ (ppm): 7.87 (s, 1H); 7.55 (d, 1H); 7.43 (d, 1H); 7.36 (s, 1H); 7.13 (t, 1H); 7.01 (d, 1H); 6.91 (s, 1H); 6.73 (d, 1H); 5.80 (s, 2H); 4.29 (q, 2H); 2.21 (s, 3H); 1.29 (t, 3H); 0.26 (s, 9H).

18.6 *N*-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-5-trimethylsilyl-1-[(3-methylphenyl)methyl]-1*H*-indole-2-carboxamide (Compound 18)

The product is prepared according to a process similar to that described in Example 16.2, starting with ethyl 5-trimethylsilyl-1-[(3-methylphenyl)methyl]-1*H*-indole-2-carboxylate (Compound IIa).

m.p.: 154-155°C

^{1}H NMR (DMSO D_6), δ (ppm): 10.8 (s, 1H); 8.95 (s, 1H); 8.7 (s, 1H); 7.9 (s, 1H); 7.6 (d, 1H); 7.45 (s, 1H); 7.4 (d, 1H); 7.15 (t, 1H); 7.0 (m, 2H); 6.85 (d, 1H); 6.35 (t, 1H); 5.9 (s, 2H); 4.9 (d, 2H); 2.2 (s, 3H); 0.3 (s, 9H).

Example 19 (Compound 19)

N-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-6-fluoro-1-[(3-methylphenyl)methyl]-1*H*-indole-2-carboxamide

The product is prepared according to a process similar to that described in Example 16.

m.p.: 257-258°C

^{1}H NMR (DMSO D_6), δ (ppm): 10.8 (s, 1H); 8.95 (s, 1H); 8.7 (s, 1H); 7.8 (m, 1H); 7.55 (s, 1H); 7.45 (d, 1H); 7.15 (t, 1H); 7.05 (m, 2H); 6.95 (s, 1H); 6.85 (m, 1H); 6.35 (t, 1H); 5.9 (s, 2H); 4.9 (d, 2H); 2.2 (s, 3H).

Example 20 (Compound 20)

N-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-5-trifluoromethyl-1-[(thiazol-2-yl)methyl]-1*H*-indole-2-carboxamide

20.1 2-(Chloromethyl)thiazole

To a solution of 0.5 g (4.34 mmol) of thiazol-2-ylmethanol in 5 mL of carbon tetrachloride and 6 mL of benzene are added 1.71 g (6.51 mmol) of triphenylphosphine. The reaction mixture is stirred at 95°C for 2 hours. After cooling to room temperature, the reaction mixture is diluted with dichloromethane and then filtered through Celite. The filtrate is concentrated under reduced pressure and the residue obtained is purified by flash chromatography on a column of silica gel, eluting with a mixture of hexane and ethyl acetate, to give 0.4 g of the expected 2-(chloromethyl)thiazole in the form of a pale yellow oil.

^{1}H NMR (DMSO D_6), δ (ppm): 7.83-7.80 (m, 2H); 5.11 (s, 2H).

20.2 Ethyl 5-trifluoromethyl-1-[(thiazol-2-yl)]methyl-1*H*-indole-2-carboxylate

To a suspension of 87 mg (1.983 mmol) of sodium hydride (55%) in 10 mL of dry DMF, maintained under an inert atmosphere, are added dropwise, at room temperature, 340 mg (1.322 mmol) of ethyl 5-trifluoromethyl-1*H*-indole-2-carboxylate in 5 mL of dry DMF. The reaction mixture is stirred at 50°C for 1 hour. A solution of 265 mg (1.983 mmol) of 2-(chloromethyl)thiazole, prepared according to the protocol described in the preceding step, in 10 mL of THF is then added dropwise, at 0°C. The reaction mixture is then stirred for 20 hours at room temperature, and then diluted with 100 mL of ethyl acetate. The aqueous phase is extracted with 30 mL of ethyl acetate. The combined organic phases are washed successively with saturated aqueous sodium

hydrogen carbonate solution, with water, with saturated aqueous sodium chloride solution and then dried over sodium sulfate, filtered and concentrated under reduced pressure. The resulting oil is purified by chromatography on a column of silica, eluting with a mixture of heptane and ethyl acetate. 265 mg of the expected product are isolated in the form of a colourless oil.

^{1}H NMR (DMSO D_6), δ (ppm): 8.18 (s, 1H); 7.95 (d, 1H); 7.72 (d, 1H); 7.65 (d, 1H); 7.62 (d, 1H); 7.54 (s, 1H); 6.20 (s, 2H); 4.34 (q, 2H); 1.31 (t, 3H).

LC-MS: 355 ($[M+H]^+$

20.3 *N*-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-5-trifluoromethyl-1-[(thiazol-2-yl)-methyl]-1*H*-indole-2-carboxamide (Compound 20)

This compound was prepared according to a process similar to that described in step 16.2, by reacting 125 mg (0.353 mmol) of ethyl 5-trifluoromethyl-1-[(thiazol-2-yl)]methyl]-1*H*-indole-2-carboxylate, prepared according to the protocol described in the preceding step, with 94 mg (0.353 mmol) of (6-amino-thiazolo[5,4-*b*]pyrid-2-yl)methyl 2,2-dimethylpropanoate, obtained in step 4.2, in the presence of 0.26 mL (0.529 mmol) of a solution of trimethylaluminium (2M/toluene). The crude reaction product is then purified by flash chromatography on a column of silica gel, in a mixture of dichloromethane and methanol, and then washed with a mixture (1/1) of ether and dichloromethane, to give 64 mg of the expected product.

m.p.: 282 – 283°C

^{1}H NMR (DMSO D_6), δ (ppm): 10.99 (s, 1H); 8.94 (d, 1H); 8.72 (d, 1H); 8.23 (s, 1H), 7.95 (d, 1H); 7.72-7.61 (m, 4H); 6.38 (t, 1H); 6.24 (s, 2H); 4.88 (d, 2H).

LC-MS: 490 ($[M+H]^+$

Example 21 (Compound 21)

N-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-6-trifluoromethyl-1-[(thiazol-2-yl)methyl]-1*H*-indole-2-carboxamide

The product is prepared according to a process similar to that described in Example 20.

m.p.: 243-244°C

^{1}H NMR (DMSO D_6), δ (ppm): 11.0 (s, 1H); 8.95 (d, 1H); 8.7 (d, 1H); 8.2 (s, 1H); 8.0 (d, 1H); 7.75 (d, 1H); 7.6 (m, 2H); 7.5 (d, 1H); 6.35 (t, 1H); 6.25 (s, 2H); 4.9 (d, 2H).

Example 22 (Compound 22)

N-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-5-trimethylsilyl-1-[(thiazol-2-yl)methyl]-1*H*-indole-2-carboxamide

22.1 Ethyl 5-trimethylsilyl-1-[(thiazol-2-yl)methyl]-1*H*-indole-2-carboxylate (Compound IIb)

This compound is prepared according to a process similar to that described in step 20.2, starting with ethyl 5-trimethylsilyl-1*H*-indole-2-carboxylate described in step 18.4.

^{1}H NMR (DMSO D_6), δ (ppm): 7.80 (s, 1H); 7.64 (d, 1H); 7.61 (d, 1H); 7.51 (d, 1H); 7.40 (d, 1 H); 7.30 (s, 1H); 6.04 (s, 2H) 4.24 (q, 2H); 1.23 (t, 3H); 0.19 (s, 9H).

22.6 *N*-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-5-trimethylsilyl-1-[(thiazol-2-yl)-methyl]-1*H*-indole-2-carboxamide (Compound 22)

This compound is prepared according to a process similar to that described in step 16.2, starting with ethyl 5-trimethylsilyl-1-[(thiazol-2-yl)methyl]-1*H*-indole-2-carboxylate described in the preceding step.

m.p.: 270-271°C

^{1}H NMR (DMSO D_6), δ (ppm): 10.8 (s, 1H); 8.95 (d, 1H); 8.7 (d, 1H); 7.9 (s, 1H); 7.7 (m, 2H); 7.55 (d, 1H); 7.5 (s, 1H); 7.45 (d, 1H); 6.35 (t, 1H); 6.2 (s, 2H); 4.9 (d, 2H); 0.3 (s, 9H).

Example 23 (Compound 23)

N-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-6-fluoro-1-[(thiazol-2-yl)methyl]-1*H*-indole-2-carboxamide

The product is prepared according to a process similar to that described in Example 20.

m.p.: 151-153°C

^{1}H NMR (DMSO D_6), δ (ppm): 10.8 (s, 1H); 8.95 (d, 1H); 8.7 (d, 1H); 7.8 (m, 1H); 7.7 (d, 1H); 7.6 (m, 3H); 7.1 (m, 1H); 6.35 (t, 1H); 6.2 (s, 2H); 4.9 (d, 2H).

Example 24 (Compound 24)

N-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-5-trifluoromethyl-1-[(thiazol-2-yl)methyl]-1*H*-pyrrolo[2,3-*b*]pyridine-2-carboxamide

The product is prepared according to a process similar to that described in Example 20.

m.p.: 207-208°C

^{1}H NMR (DMSO D_6), δ (ppm): 11.1 (s, 1H); 8.95 (d, 1H); 8.85 (s, 1H); 8.8 (s, 1H); 8.7 (s, 1H); 7.7 (s, 1H); 7.65 (d, 1H); 7.58 (d, 1H); 6.35 (t, 1H); 6.3 (s, 2H); 4.9 (d, 2H).

Example 25 (Compound 25)

N-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-6-trimethylsilyl-1-[(thiazol-2-yl)methyl]-1*H*-indole-2-carboxamide

25.1 Ethyl 2-azido-3-(4-trimethylsilylphenyl)propenoate

1.26 g (54.96 mmol) of sodium and 30 mL of anhydrous ethanol are introduced into a 100 mL round-bottomed flask, equipped with a magnetic stirrer and maintained under a nitrogen atmosphere. The reaction mixture is stirred at room temperature until a homogeneous solution is obtained. To this solution, cooled to -10°C, is added dropwise a solution containing 16.83 mL (54.96 mmol) of ethyl azidoacetate (34% in CH_2Cl_2) and 5 g (27.48 mmol) of 4-trimethylsilylbenzaldehyde in 5 mL of ethanol. The reaction mixture is then stirred at 0°C for 4 hours. The reaction medium is hydrolysed by adding, with vigorous stirring, 100 mL of ammonium chloride solution (30% aqueous). The product is extracted with three times 50 mL of ethyl acetate. The combined organic phases are washed with twice 20 mL of water, dried over sodium sulfate and concentrated under reduced pressure. The resulting oil is purified by chromatography on a column of silica gel, eluting with a mixture of heptane and dichloromethane. 4.96 g of the expected product are isolated in the form of a yellow oil.

^{1}H NMR (DMSO D_6), δ (ppm): 7.6 (d, 2H); 7.35 (d, 2H); 6.7 (s, 1H); 4.1 (q, 2H); 1.1 (t, 3H); 0 (s, 9H).

25.2 Ethyl 6-trimethylsilyl-1*H*-indole-2-carboxylate

To a solution of 1.0 g (3.14 mmol) of ethyl 2-azido-3-(4-trimethylsilylphenyl)propenoate obtained in the preceding step, in 20 mL of dry toluene, maintained under an inert atmosphere, is added 0.17 g (0.16 mmol) of dirhodium (II) heptafluorobutyrate dimer complex. The reaction mixture is then stirred for 12 hours at 70°C. After cooling to room temperature, the reaction mixture is filtered through silica gel, eluting with ethyl acetate. The filtrate is then concentrated under reduced pressure. The residue is purified by chromatography on a column of silica gel, eluting with a mixture of heptane and dichloromethane. 0.61 g of the expected product is isolated in the form of a beige-coloured powder.

m.p. = 127-129°C

^{1}H NMR (DMSO D_6), δ (ppm): 11.7 (s, 1H); 7.41 (dd, 1H); 7.39 (d, 1H); 6.97 (dd, 1H); 6.88 (d, 1H); 4.1 (q, 2H); 1.1 (t, 3H); 0.0 (s, 9H).

25.3 Ethyl 6-trimethylsilyl-1-[(thiazol-2-yl)methyl]-1*H*-indole-2-carboxylate (Compound IIc)

This compound was prepared according to a process similar to that described in step 20.2, by reacting 570 mg (2.18 mmol) of ethyl 6-trimethylsilyl-1*H*-indole-2-carboxylate with 440 mg (3.27 mmol) of 2-(chloromethyl)thiazole in the presence of 0.14 g (3.27 mmol) of sodium hydride (55%). The crude reaction product is then purified by flash chromatography on a column of silica gel in a mixture of heptane and ethyl acetate, to give 520 mg of the expected product.

^{1}H NMR (DMSO D_6), δ (ppm): 7.76 (s, 1H); 7.65-7.61 (m, 2H); 7.52 (d, 1H); 7.28 (s, 1H); 7.22 (d, 1H); 6.09 (s, 2H); 4.23 (q, 2H); 1.22 (t, 3H); 0.2 (s, 9H).

LC-MS: 359 ($[M+H]^+$

25.4 *N*-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-6-trimethylsilyl-1-[(thiazol-2-yl)-methyl]-1*H*-indole-2-carboxamide (Compound 25)

This compound was prepared according to a process similar to that described in step 16.2, by reacting 200 mg (0.523 mmol) of ethyl 6-trimethylsilyl-1-[(thiazol-2-yl)]methyl-1*H*-indole-2-carboxylate, prepared in the preceding step, with 178 mg (0.670 mmol) of (6-amino-thiazolo[5,4-*b*]pyrid-2-yl)methyl 2,2-dimethylpropanoate, obtained in step 4.2, in the presence of 0.39 mL (0.784 mmol) of a solution of trimethylaluminium (2M/toluene). The product was isolated by purification by chromatography on a column of silica, eluting with a mixture of dichloromethane and ethanol. 120 mg of the expected product are obtained.

m.p.: 219 – 220°C

^{1}H NMR (DMSO D_6), δ (ppm): 10.76 (s, 1H); 8.86 (d, 1H); 8.64 (d, 1H); 7.76 (s, 1H); 7.67 (d, 1H); 7.63 (d, 1H); 7.50 (d, 1H); 7.42 (s, 1H); 7.22 (d, 1H); 6.29 (t, 1H); 6.14 (s, 2H); 4.79 (d, 2H); 0.19 (s, 9H).

LC-MS: 494 ($[M+H]^+$

Example 26 (Compound 26)

N-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-5-trifluoromethyl-1-[(pyrid-4-yl)methyl]-1*H*-indole-2-carboxamide

The product is prepared according to a process similar to that described in Example

16.

m.p.: 237-238°C

^{1}H NMR (DMSO D_6), δ (ppm): 8.9 (s, 1H); 8.7 (s, 1H); 8.5 (d, 2H); 8.3 (s, 1H); 7.8 (d, 1H); 7.75 (s, 1H); 7.6 (d, 1H); 7.0 (m, 2H); 6.35 (t, 1H); 6.0 (s, 2H); 4.9 (d, 2H).

Example 27 (Compound 27)

N-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-6-trifluoromethyl-1-[(pyrid-4-yl)methyl]-1*H*-indole-2-carboxamide

The product is prepared according to a process similar to that described in Example 16.

MP: 261-263°C

^{1}H NMR (DMSO D_6), δ (ppm): 8.9 (s, 1H); 8.7 (s, 1H); 8.5 (d, 2H); 8.1 (m, 2H); 7.7 (s, 1H); 7.5 (d, 1H); 6.95 (d, 2H); 6.35 (t, 1H); 6.0 (s, 2H); 4.9 (d, 2H).

Example 28 (Compound 28)

N-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-5-trimethylsilyl-1-[(pyrid-4-yl)methyl]-1*H*-indole-2-carboxamide

28.1 Ethyl 5-trimethylsilyl-1-[(pyrid-4-yl)methyl]-1*H*-indole-2-carboxylate (Compound IId).

The product is prepared according to a process similar to that described in Example 16.1, starting with ethyl 5-trimethylsilyl-1*H*-indole-2-carboxylate prepared in step 18.4.

^{1}H NMR (DMSO D_6), δ (ppm): 8.37 (d, 2H), 7.83 (s, 1H), 7.47 (d, 1H), 7.37 (d, 1H), 7.34 (s, 1H), 6.84 (d, 2H), 5.80 (s, 2H), 4.18 (q, 2H), 1.18 (t, 3H), 0.19 (s, 9H).

28.2 *N*-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-5-trimethylsilyl-1-[(pyrid-4-yl)-methyl]-1*H*-indole-2-carboxamide (Compound 28)

The product is prepared according to a process similar to that described in Example 16.2, starting with ethyl 5-trimethylsilyl-1-[(pyrid-4-yl)methyl]-1*H*-indole-2-carboxylate prepared in the preceding step.

m.p.: 208-210°C

^{1}H NMR (DMSO D_6), δ (ppm): 8.9 (s, 1H); 8.7 (s, 1H); 8.45 (d, 2H); 7.95 (s, 1H); 7.58 (s, 1H); 7.5 (d, 1H); 7.4 (d, 1H); 7.0 (d, 2H); 6.35 (t, 1H); 5.9 (s, 2H); 4.9 (d, 2H); 0.3 (s, 9H).

Example 29 (Compound 29)

N-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-6-fluoro-1-[(pyrid-4-yl)methyl]-1*H*-indole-2-carboxamide

The product is prepared according to a process similar to that described in Example 16.

m.p.: 290-291°C

^{1}H NMR (DMSO D_6), δ (ppm): 8.9 (s, 1H); 8.7 (s, 1H); 8.45 (d, 2H); 7.8 (m, 1H); 7.6 (s, 1H); 7.5 (dd, 1H); 7.1 (m, 1H); 7.0 (d, 2H); 6.35 (t, 1H); 5.9 (s, 2H); 4.9 (d, 2H).

Example 30 (Compound 30)

N-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-5-trifluoromethyl-1-[(pyrid-4-yl)methyl]-1*H*-pyrrolo[2,3-*b*]pyridine-2-carboxamide

30.1 Ethyl 5-trifluoromethyl-1-[(4-pyridyl)methyl)]-1*H*-pyrrolo[2,3-*b*]pyrid-2-carboxylate

This compound was prepared according to a process similar to that described in step 16.1, by reacting 480 mg (1.859 mmol) of ethyl 5-trifluoromethyl-1*H*-pyrrolo[2,3-*b*]pyrid-2-carboxylate with 406 mg (3.718 mmol) of 4-pyridylmethanol in the presence of 0.89 g (3.718 mmol) of cyanomethylenetributylphosphorane (CMBP). The crude reaction product is then purified by flash chromatography on a column of silica gel in a mixture of heptane and ethyl acetate, to give 582 mg of the expected product in the form of a white solid.

^{1}H NMR (DMSO D_6), δ (ppm): 8.84 (s, 1H); 8.72 (s, 1H); 8.45 (d, 2H); 7.56 (s, 1H); 6.98 (d, 2H); 5.94 (s, 2H); 4.29 (q, 2H); 1.25 (t, 3H).

LC-MS: 350 ($[M+H]^+$

30.2 *N*-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-5-trifluoromethyl-1-[(pyrid-4-yl)-methyl]-1*H*-pyrrolo[2,3-*b*]pyridine-2-carboxamide (Compound 30)

This compound was prepared according to a process similar to that described in step 16.2, by reacting 200 mg (0.573 mmol) of ethyl 5-trifluoromethyl-1-[(4-pyridyl)methyl)]-1*H*-pyrrolo[2,3-*b*]pyrid-2-carboxylate, prepared according to the protocol described in the preceding step, with 182 mg (0.687 mmol) of (6-amino-thiazolo[5,4-*b*]pyrid-2-yl)-methyl 2,2-dimethylpropanoate, obtained in step 4.2, in the presence of 0.43 mL 0.859 mmol) of a solution of trimethylaluminium (2M/toluene). The crude reaction product is then purified by chromatography on a column of silica, eluting with a mixture of

dichloromethane and methanol, to give 71 mg of the expected product.

m.p.: 275 – 276°C

^{1}H NMR (DMSO D_6), δ (ppm): 11.03 (s, 1H); 8.89 (d, 1H); 8.82 (s, 2H); 8.65 (d, 1H); 8.45 (d, 2H); 7.74 (s, 1H); 7.04 (d, 2H); 6.38 (t, 1H); 5.99 (s, 2H); 4.87 (d, 2H).

LC-MS: 485 ($[M+H]^+$

Example 31 (Compound 31)

N-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-6-trimethylsilyl-1-[(pyrid-4-yl)methyl]-1*H*-indole-2-carboxamide

31.1 Ethyl 6-trimethylsilyl-1-[(pyrid-4-yl)methyl]-1*H*-indole-2-carboxylate (Compound IIe)

The product is prepared according to a process similar to that described in Example 16.1, starting with ethyl 6-trimethylsilyl-1*H*-indole-2-carboxylate prepared in step 25.2.

^{1}H NMR (DMSO D_6), δ (ppm): 8.2 (d, 2H); 7.49 (d, 1H); 7.42 (s, 1H); 7.15 (s, 1H); 7.05 (d, 1H); 6.70 (d, 2H); 5.68 (s, 2H); 4.01 (q, 2H); 1.01 (t, 3H); 0.0 (s, 9H).

31.2 *N*-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-6-trimethylsilyl-1-[(pyrid-4-yl)-methyl]-1*H*-indole-2-carboxamide (Compound 31)

The product is prepared according to a process similar to that described in Example 16.2, starting with ethyl 6-trimethylsilyl-1-[(pyrid-4-yl)methyl]-1*H*-indole-2-carboxylate prepared in the preceding step.

m.p.: 213-214°C

^{1}H NMR (DMSO D_6), δ (ppm): 8.9 (s, 1H); 8.7 (s, 1H); 8.45 (d, 2H); 7.8 (d, 1H); 7.65 (s, 1H); 7.55 (s, 1H); 7.35 (d, 1H); 7.05 (d, 2H); 6.35 (t, 1H); 6.0 (s, 2H); 4.9 (d, 2H); 0.25 (s, 9H).

Example 32 (Compound 32)

N-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-5-trimethylsilyl-1-[[(3-trifluoromethyl)-phenyl]methyl]-1*H*-indole-2-carboxamide

32.1 Ethyl 5-trimethylsilyl-1-[[(3-trifluoromethyl)phenyl]methyl]-1*H*-indole-2-carboxylate (Compound IIf)

The compound was prepared according to a process similar to that described in step 16.1, by reacting 0.49 g (1.87 mmol) of ethyl 5-trimethylsilyl-1*H*-indole-2-carboxylate,

prepared in step 18.4, with 0.51 mL (3.749 mmol) of 3-(trifluoromethyl)phenylmethanol in the presence of 0.9 g (3.749 mmol) of cyanomethylenetributylphosphorane (CMBP). The crude reaction product is then purified by chromatography on a column of silica in a mixture of heptane and ethyl acetate, to give 730 mg of the expected product.

^{1}H NMR (DMSO D_6), δ (ppm): 7.90 (s, 1H); 7.62-7.57 (m, 2H); 7.51-7.43 (m, 3H); 7.40 (s, 1H); 7.17 (d, 1H); 5.92 (s, 2H); 4.28 (q, 2H); 1.26 (t, 3H); 0.27 (s, 9H).

LC-MS: 420 ($[M+H]^+$)

32.2 *N*-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-5-trimethylsilyl-1-[[(3-trifluoromethyl)phenyl]methyl]-1*H*-indole-2-carboxamide

This compound was prepared according to a process similar to that described in step 16.2, by reacting 200 mg (0.477 mmol) of ethyl 5-trimethylsilyl-1-[[(3-trifluoromethyl)phenyl]methyl]-1*H*-indole-2-carboxylate, prepared in the preceding step, with 152 mg (0.572 mmol) of (6-amino-thiazolo[5,4-*b*]pyrid-2-yl)methyl 2,2-dimethylpropanoate, obtained in step 4.2, in the presence of 0.36 mL (0.715 mmol) of a solution of trimethylaluminium (2M/toluene). The product is isolated by purification by flash chromatography on a column of silica gel in a mixture of heptane and ethyl acetate. 128 mg of the expected product are obtained.

m.p.: 152 – 153°C

^{1}H NMR (DMSO D_6), δ (ppm): 10.82 (s, 1H); 8.91 (d, 1H); 8.68 (d, 1H); 7.92 (s, 1H); 7.61-7.42 (m, 6H); 7.31 (d, 1H); 6.37 (t, 1H); 5.97 (s, 2H); 4.87 (d, 2H); 0.28 (s, 9H).

LC-MS: 555 ($[M+H]^+$)

Example 33 (Compound 33)

N-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-6-fluoro-1-[[(3-trifluoromethyl)phenyl]-methyl]-1*H*-indole-2-carboxamide

33.1 Methyl 6-fluoro-1-[(3-trifluoromethylphenyl)methyl]-1*H*-indole-2-carboxylate

This compound was prepared according to a process similar to that described in step 16.1, by reacting 475 mg (2.459 mmol) of methyl 6-fluoro-1*H*-indole-2-carboxylate with 0.67 mL (4.918 mmol) of 3-trifluoromethylphenylmethanol in the presence of 1.18 g (4.918 mmol) of cyanomethylenetributylphosphorane (CMBP). The crude reaction product is then purified by chromatography on a column of silica in a mixture of heptane and ethyl acetate, to give 706 mg of the expected product in the form of a white solid.

^{1}H NMR (DMSO D_6), δ (ppm): 7.78 (dd, 1H); 7.61-7.49 (m, 4H); 7.43 (s, 1H); 7.19 (d, 1H); 7.05 (dt, 1H); 5.91 (s, 2H); 3.80 (s, 3H).
LC-MS: 351 ([M+H]$^+$

33.2 *N*-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-6-fluoro-1-[[(3-trifluoromethyl)-phenyl]methyl]-1*H*-indole-2-carboxamide (Compound 33)
This compound was prepared according to a process similar to that described in step 16.2, by reacting 200 mg (0.569 mmol) of methyl 6-fluoro-1-[(3-trifluoromethylphenyl)methyl]-1*H*-indole-2-carboxylate, prepared according to the protocol described in the preceding step, with 181 mg (0.683 mmol) of (6-amino-thiazolo[5,4-*b*]pyrid-2-yl)methyl 2,2-dimethylpropanoate, obtained in step 4.2, in the presence of 0.43 mL (0.853 mmol) of a solution of trimethylaluminium (2M/toluene). The crude reaction product is then purified by chromatography on a column of silica gel in a mixture of dichloromethane and methanol, to give 89 mg of the expected product.
m.p.: 217 – 218°C
^{1}H NMR (DMSO D_6), δ (ppm): 10.81 (s, 1H); 8.89 (d, 1H); 8.67 (d, 1H); 7.82 (dd, 1H); 7.60-7.49 (m, 5H); 7.33 (d, 1H); 7.06 (dt, 1H); 6.37 (t, 1H); 5.95 (s, 2H); 4.87 (d, 2H).
LC-MS: 501 ([M+H]$^+$

Example 34 (Compound 34)
N-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-5-trifluoromethyl-1-[[(3-trifluoromethyl)-phenyl]methyl]-1*H*-pyrrolo[2,3-*b*]pyridine-2-carboxamide
The product is prepared according to a process similar to that described in Example 16.
m.p.: 312-314°C
^{1}H NMR (DMSO D_6), δ (ppm): 11.0 (s, 1H); 8.90 (s, 1H); 8.85 (s, 1H); 8.8 (s, 1H); 8.65 (s, 1H); 7.7 (s, 1H); 7.6 (m, 2H); 7.5 (m, 1H); 7.35 (m, 1H); 6.35 (t, 1H); 6.05 (s, 2H); 4.9 (d, 2H).

Example 35 (Compound 35)
N-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-6-trimethylsilyl-1-[[(3-trifluoromethyl)-phenyl]methyl]-1*H*-indole-2-carboxamide

35.1 Ethyl 6-trimethylsilyl-1-[[(3-trifluoromethyl)phenyl]methyl]-1*H*-indole-2-carboxylate (Compound IIg)

The product is prepared according to a protocol similar to that described in Example 32.1, starting with ethyl 6-trimethylsilyl-1*H*-indole-2-carboxylate described in Example 25.

^{1}H NMR (DMSO D_6), δ (ppm): 7.49-7.45 (m, 2H); 7.36-7.33 (m, 2H); 7.25 (t, 1H); 7.12 (s, 1H); 7.04-7.00 (m, 2H); 5.73 (s, 2H); 4.04 (q, 2H); 1.03 (t, 3H); 0.00 (s, 9H).

35.2 *N*-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-6-trimethylsilyl-1-[[(3-trifluoromethyl)phenyl]methyl]-1*H*-indole-2-carboxamide (Compound 35)

The product is prepared according to a process similar to that described in Example 32.2, starting with ethyl 6-trimethylsilyl-1-[[(3-trifluoromethyl)phenyl]methyl]-1*H*-indole-2-carboxylate prepared in the preceding step.

m.p.: 180-181°C

^{1}H NMR (DMSO D_6), δ (ppm): 10.85 (s, 1H); 8.95 (s, 1H); 8.75 (s, 1H); 7.75 (m, 2H); 7.65 (s, 1H); 7.6-7.4 (m, 4H); 7.3 (d, 1H); 6.35 (t, 1H); 6.0 (s, 2H); 4.9 (d, 2H); 0.25 (s, 9H).

Example 36 (Compound 36)

N-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-5-trifluoromethyl-1-[(3-methylphenyl)-methyl]-1*H*-pyrrolo[2,3-*b*]pyridine-2-carboxamide

The product is prepared according to a process similar to that described in Example 16.

m.p.: 335-336°C

^{1}H NMR (DMSO D_6), δ (ppm): 11.0 (s, 1H); 8.9 (s, 1H); 8.85 (s, 1H); 8.75 (s, 1H); 8.65 (s, 1H); 7.6 (s, 1H); 7.1 (m, 1H); 7.0 (m, 2H); 6.9 (m, 1H); 6.3 (t, 1H); 5.95 (s, 2H); 4.9 (d, 2H); 2.15 (s, 3H).

Example 37 (Compound 37)

N-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-6-trimethylsilyl-1-[(3-methylphenyl)-methyl]-1*H*-indole-2-carboxamide

37.1 Ethyl 6-trimethylsilyl-1-[(3-methylphenyl)methyl]-1*H*-indole-2-carboxylate (Compound IIh)

The product is prepared according to a protocol similar to that described in Example 32.1, starting with ethyl 6-trimethylsilyl-1*H*-indole-2-carboxylate described in Example 25.

^{1}H NMR (DMSO D_6), δ (ppm): 7.71-7.68 (m, 2H); 7.33 (s, 1H); 7.24-7.21 (m, 1 H); 7.14-7.11 (m, 2H); 7.09-7.0 (m, 1H); 6.81-6.79 (m, 1H); 5.85 (s, 2H); 4.30 (q, 2 H); 2.21 (s, 3H); 1.17 (t, 3H), 0.25 (s, 9H).

37.2 *N*-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-6-trimethylsilyl-1-[(3-methylphenyl)methyl]-1*H*-indole-2-carboxamide (Compound 37)

The product is prepared according to a process similar to that described in Example 32.2, starting with ethyl 6-trimethylsilyl-1-[(3-methylphenyl)methyl]-1*H*-indole-2-carboxylate prepared in the preceding step.

m.p.: 168-169°C

^{1}H NMR (DMSO D_6), δ (ppm): 10.8 (s, 1H); 8.9 (s, 1H); 8.7 (s, 1H); 7.7 (m, 2H); 7.48 (s, 1H); 7.25 (d, 1H); 7.15 (m, 1H); 7.0 (m, 2H); 6.9 (m, 1H); 6.35 (t, 1H); 5.9 (s, 2H); 4.9 (d, 2H); 2.2 (s, 3H); 0.3 (s, 9H).

Example 38 (Compound 38)

N-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-5-trifluoromethyl-1-[[(3-trifluoromethyl)-phenyl]methyl]-1*H*-indole-2-carboxamide

The product is prepared according to a process similar to that described in Example 16.

m.p.: 237-239°C

^{1}H NMR (DMSO D_6), δ (ppm): 11.0 (s, 1H); 8.95 (s, 1H); 8.7 (s, 1H); 8.25 (s, 1H); 7.85 (d, 1H); 7.7 (s, 1H); 7.65-7.5 (m, 4H); 7.35 (m, 1H); 6.35 (t, 1H); 6.0 (s, 2H); 4.9 (d, 2H).

Example 39 (Compound 39)

N-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-6-trifluoromethyl-1-[[(3-trifluoromethyl)-phenyl]methyl]-1*H*-indole-2-carboxamide

The product is prepared according to a process similar to that described in Example 16.

m.p.: 197-198°C

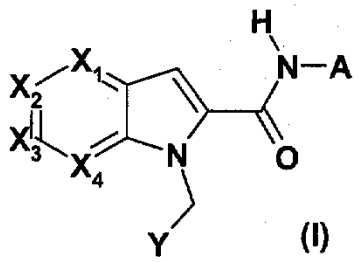
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Table I that follows illustrates the chemical structures and the physical properties of a number of examples of compounds according to the invention.

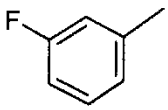
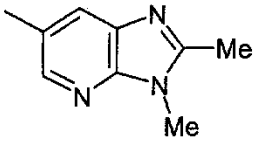
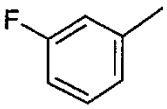
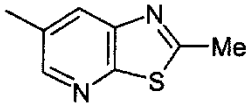
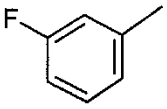
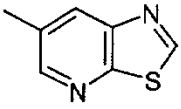
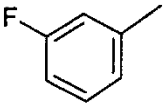
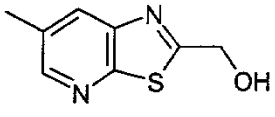
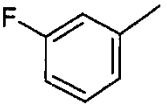
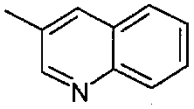
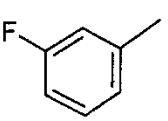
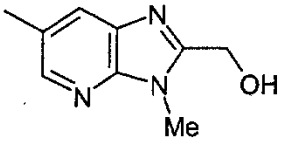
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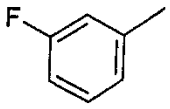
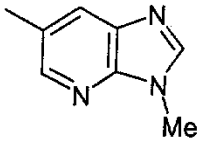
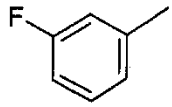
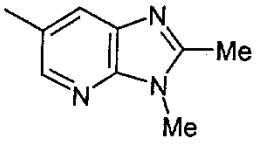
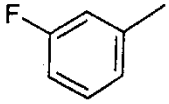
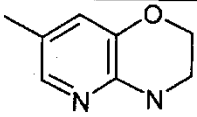
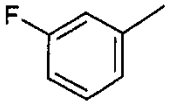
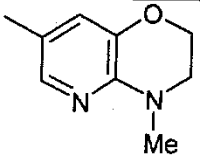
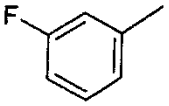
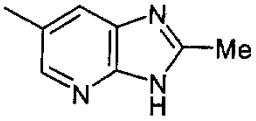
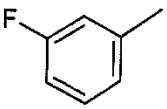
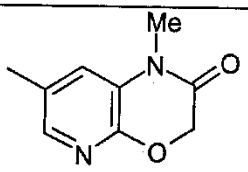
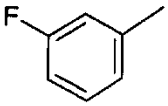
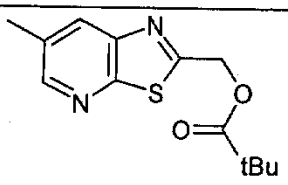
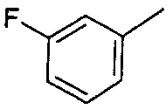
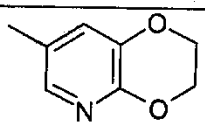
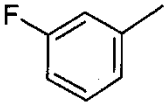
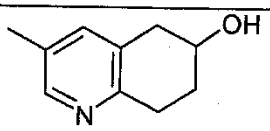
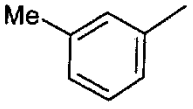
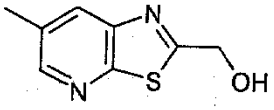
- the column "m.p. (°C)" indicates the melting points of the products in degrees Celsius (°C);
- W represents an oxygen atom;
- n is equal to 1;
- all the compounds are in the form of the free base;
- Me corresponds to a methyl group;
- tBu corresponds to a tert-butyl group.

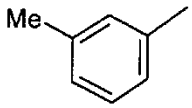
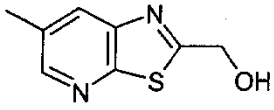
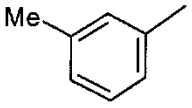
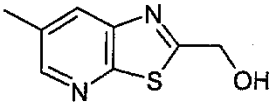
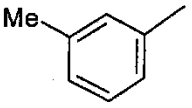
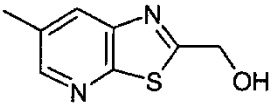
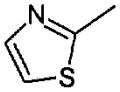
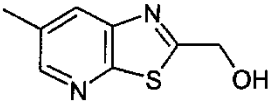
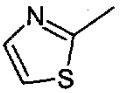
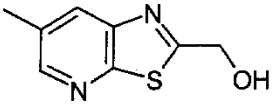
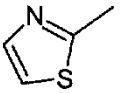
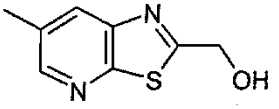
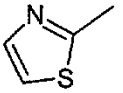
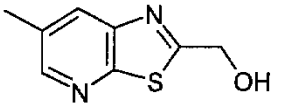
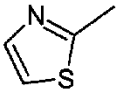
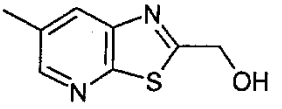
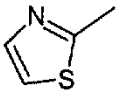
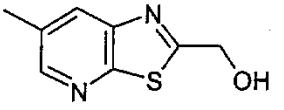
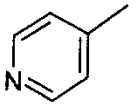
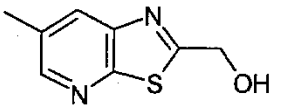
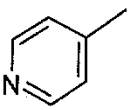
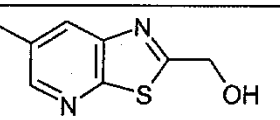
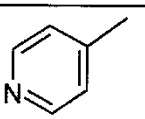
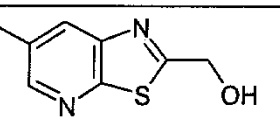
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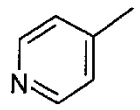
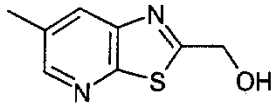
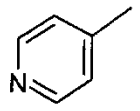
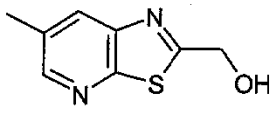
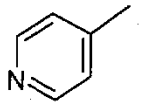
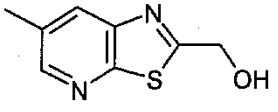
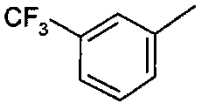
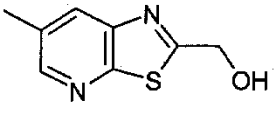
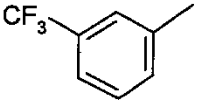
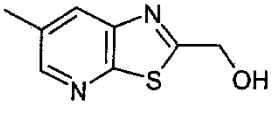
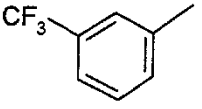
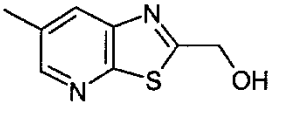
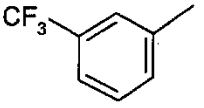
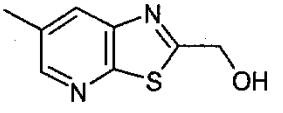
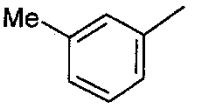
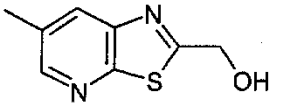
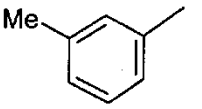
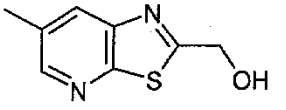
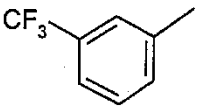
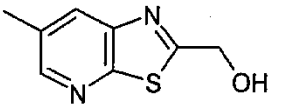
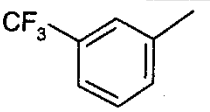
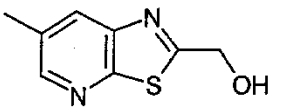


(I)

No.	X_1, X_2, X_3, X_4	Y	A	m.p. (°C)
1	CH, C-F, CH, CH			274 – 275
2	CH, C-F, CH, CH			264 - 265
3	CH, C-F, CH, CH			250 - 251
4	CH, C-F, CH, CH			225 - 226
5	CH, C-F, CH, CH			244 - 246
6	CH, C-F, CH, CH			231 - 232

No.	X_1, X_2, X_3, X_4	Y	A	m.p. (°C)
7	CH, C-F, CH, CH			235 - 236
8	CH, C-CF_3, CH, N			274 - 275
9	CH, C-F, CH, CH			265 - 266
10	CH, C-F, CH, CH			214 - 215
11	CH, C-F, CH, CH			299 - 300
12	CH, C-F, CH, CH			248 - 250
13	CH, C-F, CH, CH			224 - 225
14	CH, C-F, CH, CH			224 - 225
15	CH, C-F, CH, CH			204 - 206
16	CH, C-CF_3, CH, CH			315 - 316

No.	X_1, X_2, X_3, X_4	Y	A	m.p. (°C)
17	CH, CH, C-CF_3, CH			221 - 222
18	CH, C-$SiMe_3$, CH, CH			154 - 155
19	CH, CH, C-F, CH			257 - 258
20	CH, C-CF_3, CH, CH			282 - 283
21	CH, CH, C-CF_3, CH			243 - 244
22	CH, C-$SiMe_3$, CH, CH			270 - 271
23	CH, CH, C-F, CH			151 - 153
24	CH, C-CF_3, CH, N			207 - 208
25	CH, CH, C-$SiMe_3$, CH			219 - 220
26	CH, C-CF_3, CH, CH			237 - 238
27	CH, CH, C-CF_3, CH			261 - 263
28	CH, C-$SiMe_3$, CH, CH			208 - 210

No.	X_1, X_2, X_3, X_4	Y	A	m.p. (°C)
29	CH, CH, C-F, CH			290 - 291
30	CH, C-CF_3, CH, N			275 - 276
31	CH, CH, C-$SiMe_3$, CH			213 - 214
32	CH, C-$SiMe_3$, CH, CH			152 - 153
33	CH, CH, C-F, CH			217 - 218
34	CH, C-CF_3, CH, N			312 - 314
35	CH, CH, C-$SiMe_3$, CH			180 - 181
36	CH, C-CF_3, CH, N			335 - 336
37	CH, CH, C-$SiMe_3$, CH			168 - 169
38	CH, C-CF_3, CH, CH			237 - 239
39	CH, CH, C-CF_3, CH			197 - 198

The compounds according to the invention underwent *in vitro* and *in vivo* pharmacological tests that demonstrated their value as therapeutically active

substances. These compounds have antagonist or agonist activity towards the TRPV1 (or VR1) receptors.

Test of inhibition of the current induced with capsaicin on rat DRGs

- Primary culture of rat dorsal root ganglion (DRG) cells:

DRG neurones naturally express the TRPV1 receptor.

The primary cultures of newborn rat DRGs are prepared using 1-day-old rats. Briefly, after dissection, the ganglions are trypsinized and the cells dissociated by mechanical trituration. The cells are resuspended in an Eagle basal culture medium containing 10% foetal calf serum, 25 mM KCl, 2 mM glutamine, 100 μg/ml gentamicin and 50 ng/ml of NGF, and then deposited on glass slides coated with laminin ($0.25x10^6$ cells per slide), which are then placed in Corning 12-well dishes. The cells are incubated at 37°C in a humidified atmosphere containing 5% CO_2 and 95% air. Cytosine β-D-arabinoside (1 μM) is added 48 hours after culturing, to prevent the growth of non-neuronal cells. The slides are transferred into experimental chambers for the patch-clamp studies after 7-10 days of culturing.

- Electrophysiology:

The measuring chambers (volume 800 μl) containing the cell preparation are placed on the platform of an inverted microscope (Olympus IMT2) equipped with Hoffman optics (Modulation Contrast, New York) and observed at a magnification of 400X. The chambers are continuously gravity-influxed (2.5 ml/min) using a solution distributor accepting 8 inlets and whose sole outlet, consisting of a polyethylene tube (aperture 500 μm), is placed less than 3 mm from the cell under study. The "whole cell" configuration of the patch-clamp technique was used. The borosilicate-glass pipettes (resistance 5-10 MOhms) are brought to the cell by means of a 3D piezoelectric micromanipulator (Burleigh, PC1000). The overall currents (membrane potential set at -60 mV) are recorded with an Axopatch 1D amplifier (Axon Instruments, Foster City, California), connected to a PC running the Pclamp8 software (Axon Instrument). The current plots are recorded on paper and simultaneously digitized (sampling frequency 15 to 25 Hz) and acquired on the hard drive of the PC.

The application of a 300 nM capsaicin solution induces on the DRG cells (voltage set at -70 mV) an entering cationic current. In order to minimize the desensitization of the

receptors, a minimum interval of 1 minute between two applications of capsaicin is observed. After a control period (stabilization of the capsaicin response alone), the test compounds are applied alone at a given concentration (concentration of 10 nM or 1 nM) for a time of 4 to 5 minutes, during which several capsaicin + compound tests are performed (to obtain the maximum inhibition). The results are expressed as a percentage of inhibition of the control capsaicin response.

In the case of the VR1 antagonist compounds, the percentages of inhibition of the capsaicin response (1 μM) are between 20% and 100% for the most active compounds of the invention tested at concentrations of from 0.1 to 10 nM. They are therefore effective antagonists of receptors of TRPV1 type. Table 2 gives an example of the percentage of inhibition obtained with the compounds of the invention.

Table 2

Compound No.	% inhibition in DRG patch
4	65.5% (0.1 nM)
11	62% (100 nM)

Pain induced by intraplantar administration of capsaicin to mice.

The intraplantar injection of capsaicin to mice rapidly produces short-lived nociceptive behaviour, which is reflected by licking, biting and flexing of the administered leg. These nociceptive responses are probably associated with the activation of the local TRPV1 receptors by the capsaicin.

Methodology:

(E)-Capsaicin is initially diluted to 3 mg/ml in DMSO, and then diluted again for its final use to 1.5 μg/20 μl in physiological saline. The administration of solvent has no effect on the behaviour of the mouse. The capsaicin is injected into the hind legs of the animal, on the upper face.

The test compounds are administered orally 120 minutes before the injection of capsaicin. Two hours after administration of the compounds, the mice are placed in a

glass beaker. The nociceptive behaviour of the animals is then assessed immediately by the experimenter, and the duration of the capsaicin-induced behavioural manifestations is timed over a period of 2 minutes (licking and biting, total or partial flexure of the injected leg).

For each compound, an inhibition corresponding to the mean of the capsaicin-induced nociceptive responses, in response to a dose of test product (expressed in mg/kg) administered orally to a sample of a given number (n) of mice, is determined.

Table 3 gives an example of a percentage of inhibition obtained with the compounds of the invention.

Table 3

Compound No.	Dose	n	% inhibition of the capsaicin-induced nociceptive responses
4	10 mg/kg	10	37% (± 8%)

The compounds of the invention may thus be used for the preparation of medicaments, especially for the preparation of a medicament for preventing or treating pathologies in which receptors of TRPV1 type are involved.

The compounds of the invention may be useful for preventing or treating pathologies in which receptors of TRPV1 type are involved.

Thus, a subject of the invention is medicaments comprising at least one compound of formula (I), or a pharmaceutically acceptable salt, or alternatively a hydrate or a solvate of the said compound.

These medicaments find their therapeutic use especially in the prevention and/or treatment of pain and inflammation, chronic pain, neuropathic pain (trauma-related, diabetic, metabolic, infection-related or toxic pain, or pain induced by an anticancer or iatrogenic treatment), (osteo)arthritic pain, rheumatic pain, fibromyalgia, back pain, cancer-related pain, facial neuralgia, headaches, migraine, dental pain, burns,

sunburn, animal bites or insect bites, post-herpetic neuralgia, muscular pain, trapped nerves (central and/or peripheral), spinal column and/or brain trauma, ischaemia (of the spinal column and/or the brain), neurodegeneration, haemorrhagic strokes (of the spinal column and/or of the brain) and post-stroke pain.

The compounds of the invention may also be used for preventing and/or treating metabolic disorders such as diabetes.

The compounds of the invention may be used for preventing and/or treating urological disorders such as hyperactivity of the bladder, vesical hyperreflexia, vesical instability, incontinence, urgent micturition, urinary incontinence, cystitis, nephritic colic, pelvic hypersensitivity and pelvic pain.

The compounds of the invention may be useful for preventing and/or treating gynaecological disorders, for instance vulvodynia and pain associated with salpingitis or with dysmenorrhoea.

These products may also be used for preventing and/or treating gastrointestinal disorders such as gastro-oesophageal reflux disorder, stomach ulcers, duodenal ulcers, functional dyspepsia, colitis, IBS, Crohn's disease, pancreatitis, oesophagitis and biliary colic.

Similarly, the products of the present invention may be useful in the prevention and/or treatment of respiratory disorders such as asthma, coughing, chronic obstructive pulmonary disease (COPD), bronchoconstriction and inflammatory disorders of the respiratory system.

These products may also be used for preventing and/or treating psoriasis, pruritus, dermal, ocular or mucous irritation, herpes and zona.

The compounds of the invention may also be used for treating depression.

The compounds of the invention may also be used for treating central nervous system diseases such as multiple sclerosis.

The compounds of the invention may also be used for treating cancers.

According to another of its aspects, the present invention relates to pharmaceutical compositions comprising, as active principle, at least one compound according to the invention. These pharmaceutical compositions contain an effective dose of at least one compound according to the invention or a pharmaceutically acceptable salt, a hydrate or a solvate of the said compound and also at least one pharmaceutically acceptable excipient.

The said excipients are chosen, according to the pharmaceutical form and the desired mode of administration, from the usual excipients known to those skilled in the art.

The pharmaceutical compositions of the present invention may be administered via the oral, sublingual, subcutaneous, intramuscular, intravenous, topical, local, intratracheal, intranasal, transdermal or rectal route. These compositions may be administered in a unit administration form, as a mixture with standard pharmaceutical excipients. They are intended to be administered to animals and human beings for the prophylaxis or treatment of the disorders or diseases mentioned above.

The appropriate unit forms of administration include oral forms such as tablets, soft or hard gel capsules, powders, granules and oral solutions or suspensions, sublingual, buccal, intratracheal, intraocular and intranasal administration forms, forms for administration by inhalation, topical, transdermal, subcutaneous, intramuscular or intravenous administration forms, rectal administration forms and implants. For topical application, the compounds according to the invention may be used in creams, gels, pomades or lotions.

By way of example, a unit form of administration of a compound according to the invention in tablet form may comprise the following components:

Compound according to the invention	50.0 mg
Mannitol	223.75 mg
Croscarmellose sodium	6.0 mg
Corn starch	15.0 mg
Hydroxypropylmethylcellulose	2.25 mg
Magnesium stearate	3.0 mg

The said unit forms are dosed to allow a daily administration of from 0.001 to 30 mg of active principle per kg of body weight, according to the galenical form.

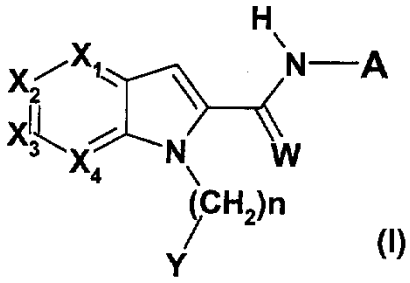
There may be particular cases in which higher or lower dosages are appropriate: such dosages do not depart from the scope of the invention. According to the usual practice, the dosage that is appropriate for each patient is determined by the doctor according to the mode of administration, the weight and the response of the said patient.

The compounds of the invention may also be used for the preparation of medicaments, especially for the preparation of a medicament for preventing or treating pathologies in which receptors of TRPV1 type are involved, as mentioned previously.

According to another of its aspects, the present invention also relates to a method for treating the pathologies indicated above, which comprises the administration to a patient of an effective dose of a compound according to the invention, or a pharmaceutically acceptable salt, or hydrate or solvate thereof.

CLAIMS

1. Compound corresponding to formula (I)



(I)

in which:

X_1, X_2, X_3 and X_4 represent, independently of each other, a nitrogen atom or a group C-R_1;

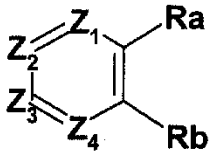
it being understood that when one from among X_1, X_2, X_3 and X_4 represents a nitrogen atom, the others correspond to a group C-R_1;

W represents an oxygen or sulfur atom;

n is equal to 0, 1, 2 or 3;

Y represents an aryl or a heteroaryl optionally substituted with one or more groups chosen from a halogen atom, a group C_1-C_6-alkyl, C_3-C_7-cycloalkyl, C_3-C_7-cycloalkyl-C_1-C_3-alkylene, C_1-C_6-fluoroalkyl, hydroxyl, C_1-C_6-alkoxy, C_3-C_7-cycloalkyloxy, C_3-C_7-cycloalkyl-C_1-C_6-alkylene-O-, C_1-C_6-fluoroalkoxy, cyano, C(O) NR_4R_5, nitro, NR_4R_5, C_1-C_6-thioalkyl, thiol, -S(O)-C_1-C_6-alkyl, -$S(O)_2$-C_1-C_6-alkyl, $SO_2NR_4R_5$, $NR_6C(O)R_7$, $NR_6SO_2R_8$, $C(O)NR_4R_5$, $OC(O)NR_4R_5$, -Si-(C_1-C_6-alkyl)$_3$, -SF_5, aryl-C_1-C_5-alkylene or aryl, heteroaryl-C_1-C_5-alkylene or heteroaryl; the groups C_1-C_6-alkyl, C_3-C_7-cycloalkyl, C_3-C_7-cycloalkyl-C_1-C_3-alkylene, C_1-C_6-fluoroalkyl, C_1-C_6-alkoxy, C_3-C_7-cycloalkyloxy, C_3-C_7-cycloalkyl-C_1-C_6-alkylene-O- being optionally substituted with a hydroxyl group, C_1-C_6-alkoxy or NR_4R_5, the aryl and heteroaryl groups being optionally substituted with one or more substituents R_9, which may be identical to or different from each other;

A represents the group of formula:



Z_1, Z_2, Z_3 and Z_4 represent, independently of each other, a nitrogen atom, a carbon atom or a group C-R_2,

at least one from among Z_1, Z_2, Z_3 and Z_4 corresponding to a nitrogen atom and one from among Z_1, Z_2, Z_3 and Z_4, corresponding to a carbon atom, being bonded to the nitrogen atom of the amide or of the thioamide of formula (I);

Ra and Rb form, together with the carbon atoms that bear them,

either a partially unsaturated cycloalkyl, or an aryl;

or a heterocycle, or a heteroaryl, which is 5- to 7-membered, comprising from 1 to 3 heteroatoms chosen from O, S and N;

it being understood that when Ra and Rb together form, with the carbon atoms that bear them, a 5-membered ring, this ring comprising a nitrogen atom and carbon atoms, this ring being partially saturated or unsaturated, is excluded;

this partially unsaturated cycloalkyl, this aryl, this heterocycle or this heteroaryl possibly being substituted with one or more substituents R_3;

R_1 is chosen from a hydrogen atom, a halogen atom, C_1-C_6-alkyl, C_3-C_7-cycloalkyl, C_3-C_7-cycloalkyl-C_1-C_3-alkylene, C_1-C_6-fluoroalkyl, aryloxy-C_1-C_6-alkyl, heteroaryloxy-C_1-C_6-alkyl, aryl-C_1-C_3-alkylenoxy-C_1-C_6-alkyl, heteroaryl-C_1-C_3-alkylenoxy-C_1-C_6-alkyl, arylthio-C_1-C_6-alkyl, heteroarylthio-C_1-C_6-alkyl, aryl-C_1-C_3-alkylene-thio-C_1-C_6-alkyl, heteroaryl-C_1-C_3-alkylene-thio-C_1-C_6-alkyl, C_1-C_6-alkoxy, C_3-C_7-cycloalkyloxy, C_3-C_7-cycloalkyl-C_1-C_3-alkylenoxy, C_1-C_6-fluoroalkoxy, cyano, C(O)NR_4R_5, nitro, NR_4R_5, C_1-C_6-thioalkyl, C_3-C_7-cycloalkylthio, C_3-C_7-cycloalkyl-C_1-C_3-alkylene-thio, -S(O)-C_1-C_6-alkyl, -S(O)-C_3-C_7-cycloalkyl, -S(O)-C_1-C_3-alkylene-C_3-C_7-cycloalkyl, C_1-C_6-alkyl-$S(O)_2$-, C_1-C_6-fluoroalkyl-$S(O)_2$-, C_3-C_7-cycloalkyl-$S(O)_2$-, C_3-C_7-cycloalkyl-C_1-C_3-alkylene-$S(O)_2$-, $SO_2NR_4R_5$, -Si-(C_1-C_6-alkyl)$_3$, -SF_5, $NR_6C(O)R_7$, $NR_6SO_2R_8$, C(O)NR_4R_5, OC(O)NR_4R_5, aryl, heteroaryl, aryl-C_1-C_5-alkylene, heteroaryl-C_1-C_5-alkylene, aryloxy, arylthio, heteroaryloxy or heteroarylthio; the heteroaryl or aryl groups being optionally substituted with one or more substituents R_9, which may be identical to or different from each other;

R_2 represents a hydrogen atom, a halogen atom or a group C_1-C_6-alkyl, C_3-C_7-cycloalkyl, C_3-C_7-cycloalkyl-C_1-C_3-alkylene, C_1-C_6-fluoroalkyl, C_1-C_6-alkoxy, C_3-C_7-cycloalkyloxy, C_3-C_7-cycloalkyl-C_1-C_3-alkylene-O-, hydroxyl, thiol or C_1-C_6-fluoroalkoxy;

R_3 represents, when it is borne by a carbon atom, a hydrogen atom or a hydroxyl, thiol, C_1-C_6-alkyl, C_3-C_7-cycloalkyl, C_3-C_7-cycloalkyl-C_1-C_3-alkylene, C_1-C_6-fluoroalkyl, C_1-C_6-alkoxy, C_3-C_7-cycloalkyloxy, C_3-C_7-cycloalkyl-C_1-C_3-alkylenoxy, C_1-C_6-alkoxy-C_1-C_3-alkylene, C_3-C_7-cycloalkyloxy-C_1-C_3-alkylene, C_3-C_7-cycloalkyl-C_1-C_3-alkylenoxy-C_1-C_3-alkylene, $C(O)NR_4R_5$, $C(O)O$-C_1-C_6-alkyl, CO_2H, oxo or thio group; the groups C_1-C_6-alkyl, C_3-C_7-cycloalkyl, C_3-C_7-cycloalkyl-C_1-C_3-alkylene, C_1-C_6-fluoroalkyl, C_1-C_6-alkoxy, C_3-C_7-cycloalkyloxy, C_3-C_7-cycloalkyl-C_1-C_3-alkylenoxy, C_1-C_6-alkoxy-C_1-C_3-alkylene, C_3-C_7-cycloalkyloxy-C_1-C_3-alkylene, C_3-C_7-cycloalkyl-C_1-C_3-alkylenoxy-C_1-C_3-alkylene possibly being substituted with a hydroxyl group, C_1-C_6-alkoxy, -$OC(O)$-C_1-C_6-alkyl or NR_4R_5;

or

R_3 represents, when it is borne by a nitrogen atom, a hydrogen atom or a group C_1-C_6-alkyl, C_3-C_7-cycloalkyl, C_3-C_7-cycloalkyl-C_1-C_3-alkylene, C_1-C_6-fluoroalkyl, aryl-C(O)-, C_1-C_6-alkyl-C(O)-, C_3-C_7-cycloalkyl-C(O)-, C_3-C_7-cycloalkyl-C_1-C_3-alkylene-C(O)-, C_1-C_6-fluoroalkyl-C(O)-, aryl-S(O), C_1-C_6-alkyl-S(O)-, C_1-C_6-fluoroalkyl-S(O)-, aryl-$S(O)_2$-, C_1-C_6-alkyl-$S(O)_2$-, C_1-C_6-fluoroalkyl-$S(O)_2$-, C_3-C_7-cycloalkyl-$S(O)_2$-, C_3-C_7-cycloalkyl-C_1-C_3-alkylene-$S(O)_2$-, C_1-C_6-alkyl-O-C(O)-, aryl-C_1-C_3-alkyl-O-C(O)-, C_3-C_7-cycloalkyl-O-C(O)-, C_3-C_7-cycloalkyl-C_1-C_3-alkylene-O-C(O)-, C_1-C_6-fluoroalkyl-O-C(O), aryl-O-C(O)-, heteroaryl-O-C(O)-, heteroaryl or aryl; the heteroaryl and aryl groups being optionally substituted with one or more substituents R_9, which may be identical to or different from each other; the groups C_1-C_6-alkyl, C_3-C_7-cycloalkyl, C_3-C_7-cycloalkyl-C_1-C_3-alkylene and C_1-C_6-fluoroalkyl possibly being substituted with a hydroxyl group, C_1-C_6-alkoxy or NR_4R_5;

R_4 and R_5, represent, independently of each other, a hydrogen atom or a group C_1-C_6-alkyl, C_3-C_7-cycloalkyl, C_3-C_7-cycloalkyl-C_1-C_3-alkylene, aryl-C_1-C_5-alkylene or aryl, or R_4 and R_5 together form, with the nitrogen atom that bears them, an azetidine, pyrrolidine, piperidine, azepine, morpholine, thiomorpholine, piperazine or homopiperazine group; the group NR_4R_5 being optionally substituted with a group C_1-C_6-alkyl, C_3-C_7-cycloalkyl, C_3-C_7-cycloalkyl-C_1-C_3-alkylene, aryl-C_1-C_6-alkylene, aryl, heteroaryl, aryl-$S(O)_2$-, C_1-C_6-alkyl-$S(O)_2$-, C_1-C_6-fluoroalkyl-$S(O)_2$, C_3-C_7-cycloalkyl-

$S(O)_2$-, C_3-C_7-cycloalkyl-C_1-C_3-alkylene-$S(O)_2$-, aryl-C(O)-, C_1-C_6-alkyl-C(O)-, C_3-C_7-cycloalkyl-C(O)-, C_3-C_7-cycloalkyl-C_1-C_3-alkylene-C(O)-, C_1-C_6-fluoroalkyl-C(O)-, hydroxyl, C_1-C_6-alkyloxy, C_3-C_7-cycloalkyloxy, C_3-C_7-cycloalkyl-C_1-C_3-alkylenoxy, C_1-C_6-fluoroalkyl, aryloxy-C_1-C_6-alkylene, aryloxy, heteroaryloxy-C_1-C_6-alkylene or heteroaryloxy;

R_6 and R_7 represent, independently of each other, a hydrogen atom or a group C_1-C_6-alkyl, C_3-C_7-cycloalkyl, C_3-C_7-cycloalkyl-C_1-C_3-alkylene, aryl-C_1-C_6-alkylene or aryl; the aryl group being optionally substituted with one or more substituents chosen from a halogen atom and a group C_1-C_6-alkyl, C_3-C_7-cycloalkyl, C_3-C_7-cycloalkyl-C_1-C_3-alkylene, C_1-C_6-fluoroalkyl, C_1-C_6-alkoxy, C_3-C_7-cycloalkyloxy, C_3-C_7-cycloalkyl-C_1-C_3-alkylenoxy, C_1-C_6-fluoroalkoxy, nitro or cyano;
or R_6 and R_7 together form a 4- to 7-membered lactam comprising the nitrogen atom and the C(O) group that bear them;

R_8 represents a group C_1-C_6-alkyl, C_3-C_7-cycloalkyl, C_3-C_7-cycloalkyl-C_1-C_3-alkylene, aryl-C_1-C_6-alkylene or aryl; the aryl group being optionally substituted with one or more substituents chosen from a halogen atom, a group C_1-C_6-alkyl, C_3-C_7-cycloalkyl, C_3-C_7-cycloalkyl-C_1-C_3-alkylene, C_1-C_6-fluoroalkyl, C_1-C_6-alkoxy, C_3-C_7-cycloalkyloxy, C_3-C_7-cycloalkyl-C_1-C_3-alkylenoxy, C_1-C_6-fluoroalkoxy, nitro or cyano;
or R_6 and R_8 together form a 4- to 7-membered sultam comprising the nitrogen atom and the $S(O)_2$ group that bear them;

R_9 represents a halogen atom, a group C_1-C_6-alkyl, C_3-C_7-cycloalkyl, C_3-C_7-cycloalkyl-C_1-C_3-alkylene, C_1-C_6-fluoroalkyl, C_1-C_6-alkoxy, C_3-C_7-cycloalkyloxy, C_3-C_7-cycloalkyl-C_1-C_3-alkylenoxy, C_1-C_6-fluoroalkoxy; these groups being optionally substituted with a group OH, C_1-C_6-alkoxy or NR_4R_5; or alternatively R_9 represents a nitro group, cyano or NR_4R_5;

the sulfur atom(s) of the compound of general formula (I) possibly being in oxidized form;
the nitrogen atom(s) of the compound of general formula (I) possibly being in oxidized form;
in the form of the base or of an acid-addition salt, and also in the form of hydrate or solvate.

2. Compound of formula (I) according to Claim 1, characterized in that X_1, X_2, X_3 and X_4 represent, independently of each other, a group C-R_1; R_1 being as defined in the general formula (I) according to Claim 1;
in the form of the base or of an acid-addition salt, and also in the form of hydrate or solvate.

3. Compound of formula (I) according to Claim 1, characterized in that X_1, X_2, X_3 represent a group C-R_1; X_4 represents a nitrogen atom;
R_1 being as defined in the general formula (I) according to Claim 1;
in the form of the base or of an acid-addition salt, and also in the form of hydrate or solvate.

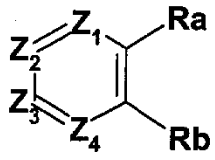
4. Compound of formula (I) according to any one of Claims 1 to 3, characterized in that R_1 is chosen from a hydrogen atom, a halogen atom and a group C_1-C_6-fluoroalkyl or -Si(C_1-C_6-alkyl)$_3$;
in the form of the base or of an acid-addition salt, and also in the form of hydrate or solvate.

5. Compound of formula (I) according to any one of Claims 1 to 4, characterized in that n is equal to 1;
in the form of the base or of an acid-addition salt, and also in the form of hydrate or solvate.

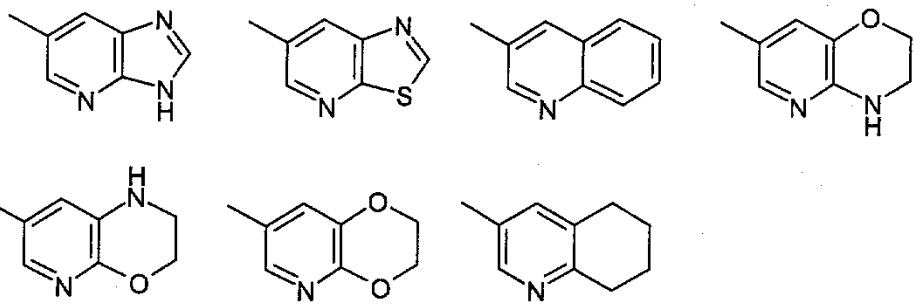
6. Compound of formula (I) according to any one of Claims 1 to 5, characterized in that Y represents a phenyl, optionally substituted with one or more groups chosen from a halogen atom and a group C_1-C_6-alkyl or C_1-C_6-fluoroalkyl;
in the form of the base or of an acid-addition salt, and also in the form of hydrate or solvate.

7. Compound of formula (I) according to any one of Claims 1 to 6, characterized in that W represents an oxygen atom;
in the form of the base or of an acid-addition salt, and also in the form of hydrate or solvate.

8. Compound of formula (I) according to any one of Claims 1 to 7, characterized in that A represents the group of formula:



in which A is chosen from the groups



these groups being optionally substituted with R_2 and R_3 as defined in the general formula (I) hereinabove;

R_2 represents a hydrogen atom;

R_3 represents, when it is borne by a carbon atom, a hydrogen atom or a hydroxyl, C_1-C_6-alkyl or oxo group; the C_1-C_6-alkyl group possibly being substituted with a hydroxyl or -OC(O)-C_1-C_6-alkyl group;

or

R_3 represents, when it is borne by a nitrogen atom, a hydrogen atom or a group C_1-C_6-alkyl;

in the form of the base or of an acid-addition salt, and also in the form of hydrate or solvate.

9. Compound of formula (I) according to any one of Claims 1 to 8, characterized in that X_1, X_2, X_3 and X_4 represent, independently of each other, a group C-R_1; or alternatively X_1, X_2 and X_3 represent a group C-R_1; X_4 represents a nitrogen atom;

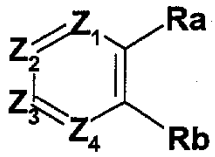
R_1 is chosen from a hydrogen atom, a halogen atom and a group C_1-C_6-fluoroalkyl or -Si-(C_1-C_6-alkyl)$_3$;

n is equal to 1;

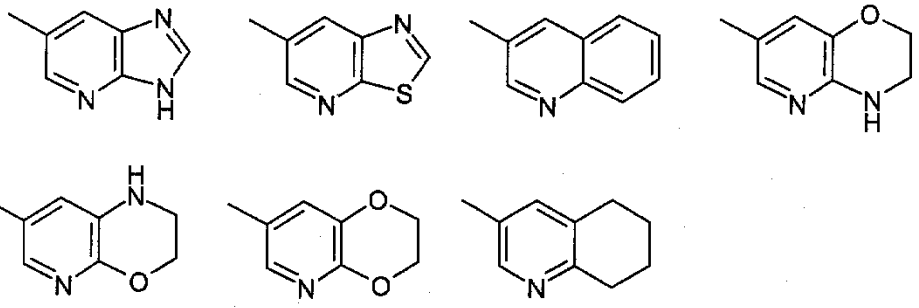
Y represents an aryl or a heteroaryl optionally substituted with one or more groups chosen from a halogen atom and a group C_1-C_6-alkyl or C_1-C_6-fluoroalkyl;

W represents an oxygen atom;

A represents the group of formula:



in which A is chosen from the groups



these groups being optionally substituted with R_2 and R_3 as defined in the general formula (I) hereinabove;

R_2 represents a hydrogen atom;

R_3 represents, when it is borne by a carbon atom, a hydrogen atom or a hydroxyl, C_1-C_6-alkyl or oxo group; the C_1-C_6-alkyl group possibly being substituted with a hydroxyl or -OC(O)-C_1-C_6-alkyl group;

or

R_3 represents, when it is borne by a nitrogen atom, a hydrogen atom or a group C_1-C_6-alkyl;

in the form of the base or of an acid-addition salt, and also in the form of hydrate or solvate.

10. Compound of formula (I) according to Claim 1, chosen from:

N-(2,3-Dimethyl-3*H*-imidazo[4,5-*b*]pyrid-6-yl)-5-fluoro-1-[(3-fluorophenyl)methyl]-1*H*-indole-2-carboxamide;

N-(2-Methylthiazolo[5,4-*b*]pyrid-6-yl)-5-fluoro-1-[(3-fluorophenyl)methyl]-1*H*-indole-2-carboxamide;

N-(Thiazolo[5,4-*b*]pyrid-6-yl)-5-fluoro-1-[(3-fluorophenyl)methyl]-1*H*-indole-2-carboxamide;

N-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-5-fluoro-1-[(3-fluorophenyl)methyl]-1*H*-indole-2-carboxamide;

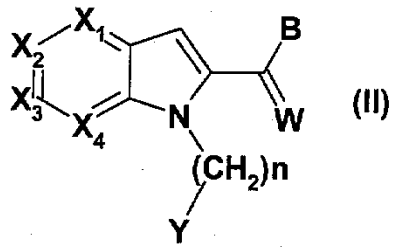
N-(Quinol-3-yl)-5-fluoro-1-[(3-fluorophenyl)methyl]-1*H*-indole-2-carboxamide;

N-(2-Hydroxymethyl-3-methyl-3*H*-imidazo[4,5-*b*]pyrid-6-yl)-5-fluoro-1-[(3-fluorophenyl)-methyl]-1*H*-indole-2-carboxamide;
N-(3-Methyl-3*H*-imidazo[4,5-*b*]pyrid-6-yl)-5-fluoro-1-[(3-fluorophenyl)methyl]-1*H*-indole-2-carboxamide;
N-(2,3-Dimethyl-3*H*-imidazo[4,5-*b*]pyrid-6-yl)-5-trifluoromethyl-1-[(3-fluorophenyl)-methyl]-1*H*-pyrrolo[2,3-*b*]pyridine-2-carboxamide;
N-(3,4-Dihydro-2H-pyrido[3,2-*b*][1,4]oxazin-7-yl)-5-fluoro-1-[(3-fluorophenyl)methyl]-1*H*-indole-2-carboxamide;
N-(4-Methyl-3,4-dihydro-2H-pyrido[3,2-*b*][1,4]oxazin-7-yl)-5-fluoro-1-[(3-fluorophenyl)-methyl]-1*H*-indole-2-carboxamide;
N-(2-Methyl-3*H*-imidazo[4,5-*b*]pyrid-6-yl)-5-fluoro-1-[(3-fluorophenyl)methyl]-1*H*-indole-2-carboxamide;
N-(1-Methyl-2-oxo-2,3-dihydro-1H-pyrido[2,3-*b*][1,4]oxazin-7-yl)-5-fluoro-1-[(3-fluoro-phenyl)methyl]-1*H*-indole-2-carboxamide;
[6-[[[5-Fluoro-1-[(3-fluorophenyl)methyl]-1*H*-indol-2-yl]carbonyl]amino]thiazolo[5,4-*b*]pyrid-2-yl]methyl 2,2-dimethylpropanoate;
N-(2,3-Dihydro-[1,4]dioxino[2,3-*b*]pyrid-7-yl))-5-fluoro-1-[(3-fluorophenyl)methyl]-1*H*-indole-2-carboxamide;
N-(6-Hydroxy-5,6,7,8-tetrahydroquinol-3-yl)-5-fluoro-1-[(3-fluorophenyl)methyl]-1*H*-indole-2-carboxamide;
N-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-5-trifluoromethyl-1-[(3-methylphenyl)-methyl]-1*H*-indole-2-carboxamide;
N-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-6-trifluoromethyl-1-[(3-methylphenyl)-methyl]-1*H*-indole-2-carboxamide;
N-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-5-trimethylsilyl-1-[(3-methylphenyl)-methyl]-1*H*-indole-2-carboxamide;
N-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-6-fluoro-1-[(3-methylphenyl)methyl]-1*H*-indole-2-carboxamide;
N-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-5-trifluoromethyl-1-[(thiazol-2-yl)methyl]-1*H*-indole-2-carboxamide;
N-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-6-trifluoromethyl-1-[(thiazol-2-yl)methyl]-1*H*-indole-2-carboxamide;
N-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-5-trimethylsilyl-1-[(thiazol-2-yl)methyl]-1*H*-indole-2-carboxamide;
N-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-6-fluoro-1-[(thiazol-2-yl)methyl]-1*H*-indole-

2-carboxamide;
N-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-5-trifluoromethyl-1-[(thiazol-2-yl)methyl]-1*H*-pyrrolo[2,3-*b*]pyridine-2-carboxamide;
N-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-6-trimethylsilyl-1-[(thiazol-2-yl)methyl]-1*H*-indole-2-carboxamide;
N-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-5-trifluoromethyl-1-[(pyrid-4-yl)methyl]-1*H*-indole-2-carboxamide;
N-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-6-trifluoromethyl-1-[(pyrid-4-yl)methyl]-1*H*-indole-2-carboxamide;
N-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-5-trimethylsilyl-1-[(pyrid-4-yl)methyl]-1*H*-indole-2-carboxamide;
N-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-6-fluoro-1-[(pyrid-4-yl)methyl]-1*H*-indole-2-carboxamide;
N-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-5-trifluoromethyl-1-[(pyrid-4-yl)methyl]-1*H*-pyrrolo[2,3-*b*]pyridine-2-carboxamide;
N-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-6-trimethylsilyl-1-[(pyrid-4-yl)methyl]-1*H*-indole-2-carboxamide;
N-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-5-trimethylsilyl-1-[[(3-trifluoromethyl)-phenyl]methyl]-1*H*-indole-2-carboxamide;
N-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-6-fluoro-1-[[(3-trifluoromethyl)phenyl]-methyl]-1*H*-indole-2-carboxamide;
N-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-5-trifluoromethyl-1-[[(3-trifluoromethyl)-phenyl]methyl]-1*H*-pyrrolo[2,3-*b*]pyridine-2-carboxamide;
N-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-6-trimethylsilyl-1-[[(3-trifluoromethyl)-phenyl]methyl]-1*H*-indole-2-carboxamide;
N-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-5-trifluoromethyl-1-[(3-methylphenyl)-methyl]-1*H*-pyrrolo[2,3-*b*]pyridine-2-carboxamide;
N-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-6-trimethylsilyl-1-[(3-methylphenyl)-methyl]-1*H*-indole-2-carboxamide;
N-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-5-trifluoromethyl-1-[[(3-trifluoromethyl)-phenyl]methyl]-1*H*-indole-2-carboxamide;
N-(2-Hydroxymethylthiazolo[5,4-*b*]pyrid-6-yl)-6-trifluoromethyl-1-[[(3-trifluoromethyl)-phenyl]methyl]-1*H*-indole-2-carboxamide.

11. Process for preparing a compound of formula (I) according to any one of Claims 1

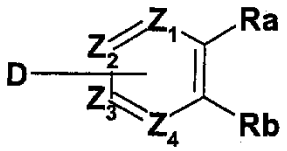
to 10, characterized in that a compound of general formula (II)



(II)

in which X_1, X_2, X_3, X_4, n, Y and W are as defined in the general formula (I) according to Claim 1,

is reacted with a compound of general formula (III),

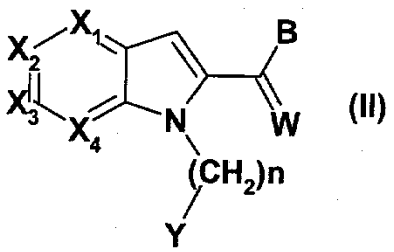


(III)

in which Z_1, Z_2, Z_3, Z_4, Ra and Rb are as defined in the general formula (I) according to Claim 1,

- when B represents a hydroxyl group and D represents an amino group, in the presence of a coupling agent in a solvent;
- when B represents a chlorine atom and D represents an amino group, by reaction in solution in a solvent;
- when B represents a group C_1-C_6-alkoxyl, C_3-C_7-cycloalkyloxy, C_3-C_7-cycloalkyl-C_1-C_3-alkylenoxy- or aryl-C_1-C_3-alkylenoxy and D represents an amino group, by transformation of the compound of formula (III) into an amide via the prior action of trimethylaluminium on the amines of general formula (III), and then by reacting the amide obtained with the compound of formula (II) in a refluxing solvent;
- when B represents an NH_2 group, W represents an oxygen atom and D corresponds to a leaving group, in the presence of a copper salt in catalytic amount, a catalytic amount of a copper ligand, and a base, in a solvent.

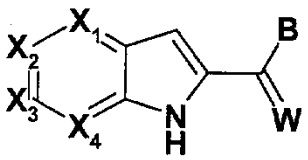
12. Process for preparing a compound of general formula (II)



(II)

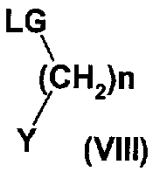
in which X_1, X_2, X_3, X_4, n, Y and W are as defined in the general formula (I) according

to Claim 1, one from among X_1, X_2, X_3 and X_4 corresponding to a group C-R_1 in which R_1 represents a group -Si-(C_1-C_6-alkyl)$_3$ as defined in the general formula (I) according to Claim 1 and B represents a group C_1-C_6-alkoxyl,
characterized in that a compound of general formula (VI)



(VI)

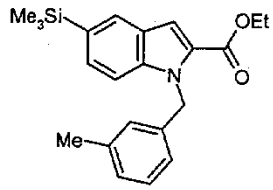
in which X_1, X_2, X_3, X_4 and W are as defined in the general formula (I) according to Claim 1 and B represents a group C_1-C_6-alkoxyl
is reacted with a compound of general formula (VIII)



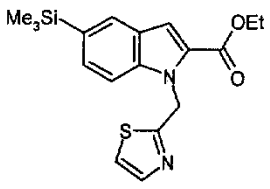
(VIII)

in which Y and n are as defined in the general formula (I) according to Claim 1,
- when n is equal to 1, 2 or 3, with a reagent of general formula (VIII) in which LG represents a leaving group, in the presence of a base in a polar solvent;
- when n is equal to 1, 2 or 3, with a reagent of general formula (VIII) in which LG represents a hydroxyl group, in the presence of a phosphine and diethyl azodicarboxylate in a solvent; or alternatively in the presence of a phosphine supported on a resin and diisopropyl azodicarboxylate in solution in a solvent;
- when n is equal to 0, with a reagent of general formula (VIII) in which LG represents a leaving group, under an inert atmosphere in basic medium, in the presence of a copper salt in an organic solvent.

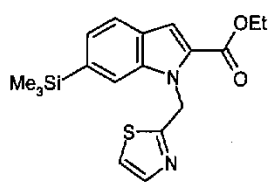
13. Compound of general formula (IIa), (IIb), (IIc), (IId), (IIe), (IIf), (IIg) or (IIh):



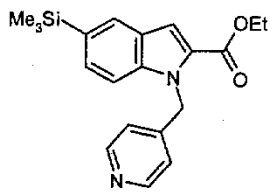
(IIa)



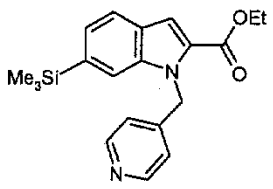
(IIb)



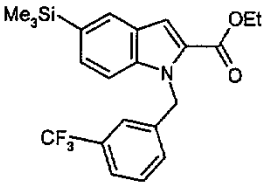
((IIc)



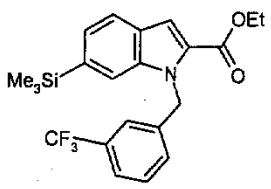
(IId)



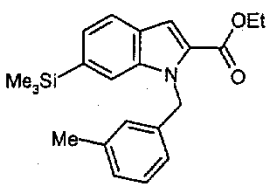
(IIe)



(IIf)



(IIg)



(IIh)

14. Medicament, characterized in that it comprises a compound of formula (I) according to any one of Claims 1 to 10, or an addition salt of this compound with a pharmaceutically acceptable acid, or alternatively a hydrate or a solvate of the compound of formula (I).

15. Pharmaceutical composition, characterized in that it comprises a compound of formula (I) according to any one of Claims 1 to 10, or a pharmaceutically acceptable salt, a hydrate or a solvate of this compound, and also at least one pharmaceutically acceptable excipient.

16. Use of a compound of formula (I) according to any one of Claims 1 to 10, for the preparation of a medicament for preventing or treating pathologies in which receptors of TRPV1 type are involved.

17. Use of a compound of formula (I) according to any one of Claims 1 to 10, for the preparation of a medicament for preventing or treating pain, inflammation, metabolic disorders, urological disorders, gynaecological disorders, gastrointestinal disorders, respiratory disorders, psoriasis, pruritus, dermal, ocular or mucous irritations, herpes, zona, multiple sclerosis, depression and cancers.