AZABICYCLIC CARBOXAMIDE DERIVATIVES, PREPARATION THEREOF 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.

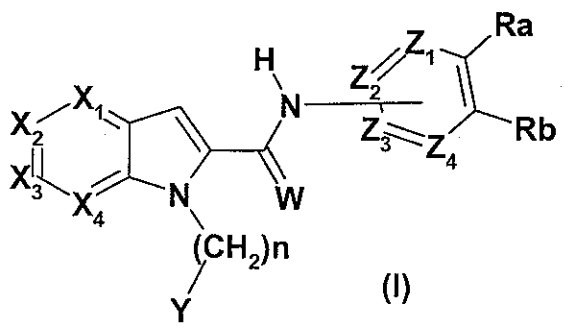
The present invention satisfies this need by providing azabicyclic carboxamide derivatives that have *in vitro* and *in vivo* antagonist or agonist activity on receptors of TRPV1 (or VR1) type.

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;

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, a 5-membered ring, this ring comprising a nitrogen atom and carbon atoms, this ring being partially saturated or unsaturated and being optionally substituted with one or more substituents R_3;

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;

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, a hydroxyl group, 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, or an 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;
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; 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, 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; 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, 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-methylethylene or propylene;

- a cycloalkyl: a saturated or partially unsaturated cyclic alkyl group. Examples that may be mentioned include the groups cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, 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 heteroaryl: a monocyclic or bicyclic aromatic group 5- to 12-membered 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, thiophenyl, 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, benzothiazolyl, 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 and pyrazolo[2,3-*a*]pyrazinyl.

- "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 one from among X_1, X_2, X_3 and X_4 represents a nitrogen atom, the others among 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 third subgroup of compounds is constituted by the compounds for which, among X_1, X_2, X_3 and X_4, one from among X_3 and X_4 represents a nitrogen atom, and the others 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 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 n is equal to 1.

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
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 and 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
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; or alternatively Y represents a pyridyl or a thiazolyl.

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 a phenyl, optionally substituted with a fluorine atom, a methyl group or CF_3; or alternatively Y represents a pyridyl or a thiazolyl.

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, optionally substituted with a fluorine atom, a methyl group or CF_3.

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 W represents an oxygen atom.

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
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 possibly being in oxidized form;
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).

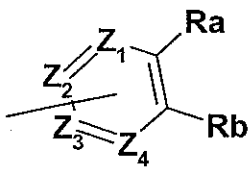
Among the compounds of general formula (I) that are subjects of the invention, a thirteenth subgroup of compounds is constituted by the compounds for which
Z_1, Z_2, Z_3 and Z_4 represent, independently of each other, a nitrogen atom, a carbon atom or a group C-R_2,
one from among Z_1, Z_2, Z_3 and Z_4 corresponding to a nitrogen atom and possibly being in oxidized form;
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.

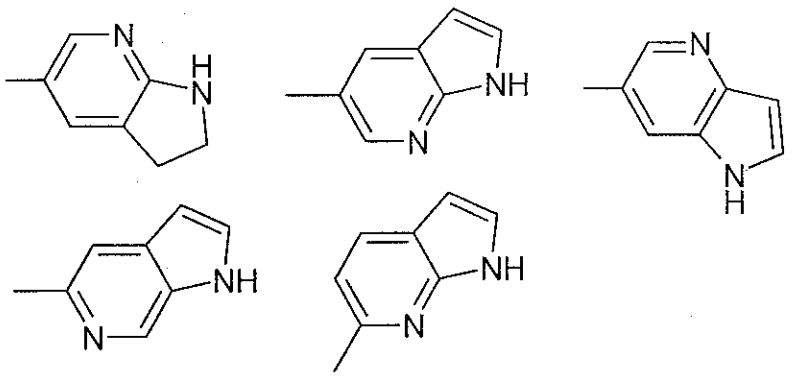
Among the compounds of general formula (I) that are subjects of the invention, a fourteenth subgroup of compounds is constituted by the compounds for which
Ra and Rb form, together with the carbon atoms that bear them, a 5-membered ring, this ring comprising a nitrogen atom and carbon atoms, this ring being partially saturated or unsaturated and being optionally substituted with one or more substituents R_3;
R_3 represents, when it is borne by a carbon atom, a hydrogen atom or an oxo group;
R_3 represents, when it is borne by a nitrogen atom, a hydrogen atom or a group C_1-C_6-alkyl or C_1-C_6-alkyl-C(O)-.

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
Ra and Rb form, together 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 and being optionally substituted with one or more substituents R_3;
R_3 represents, when it is borne by a carbon atom, a hydrogen atom or an oxo group;
R_3 represents, when it is borne by a nitrogen atom, a hydrogen atom, a methyl group or CH_3-C(O)-.

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 the group

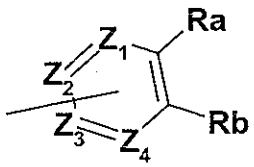


is chosen from the groups

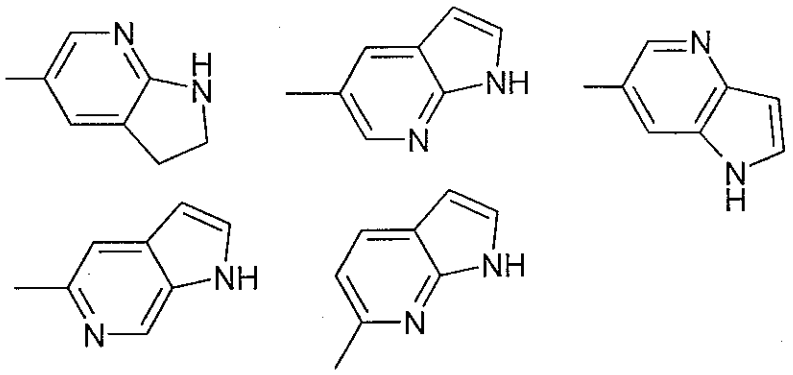


these groups being optionally substituted with R_2 and R_3 as defined in the general formula (I) hereinabove.

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



is chosen from the groups



one from among Z_1, Z_2, Z_3 and Z_4 corresponding to a nitrogen atom and possibly being in oxidized form;

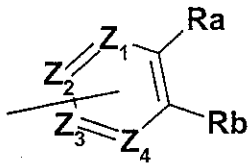
these groups being optionally substituted with R_2 and R_3 as defined in the general formula (I);

R_2 represents a hydrogen atom;

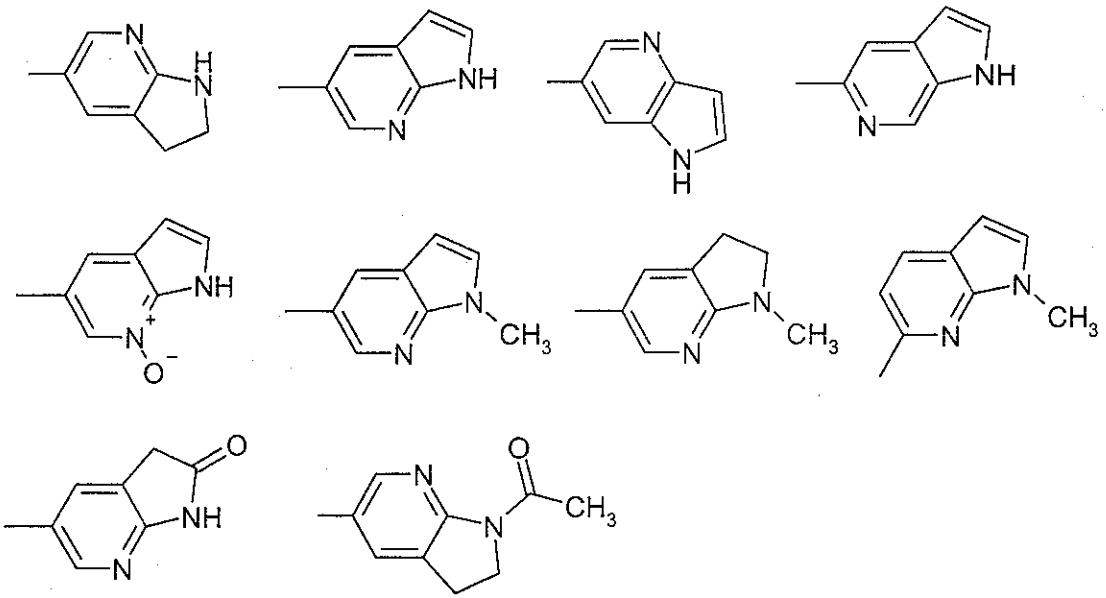
R_3 represents, when it is borne by a carbon atom, a hydrogen atom or an oxo group;

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

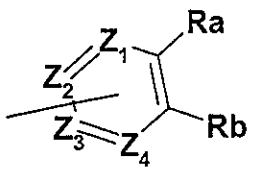
Among the compounds of general formula (I) that are subjects of the invention, an eighteenth subgroup of compounds is constituted by the compounds for which the group



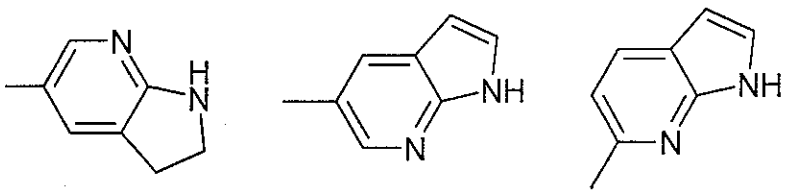
is chosen from the following groups:



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 the group



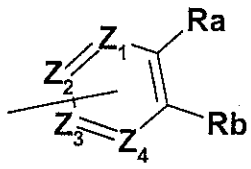
is chosen from the groups



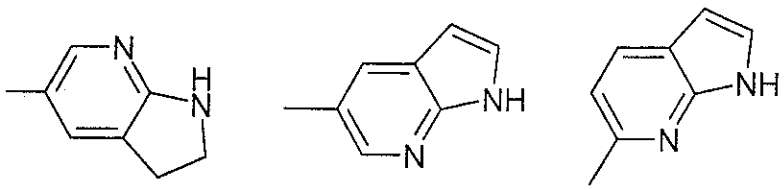
these groups being optionally substituted with R_2 and R_3 as defined in the general

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 the group



is chosen from the groups



,

one from among Z_1, Z_2, Z_3 and Z_4 corresponding to a nitrogen atom and possibly being in oxidized form;

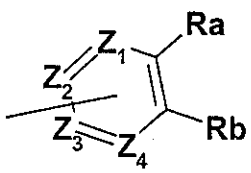
these groups being optionally substituted with R_2 and R_3 as defined in the general formula (I);

R_2 represents a hydrogen atom;

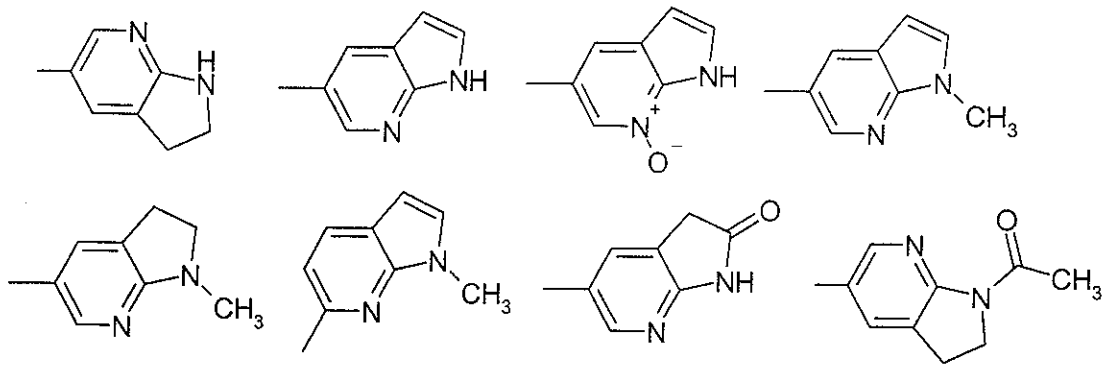
R_3 represents, when it is borne by a carbon atom, a hydrogen atom or an oxo group;

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

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 the group

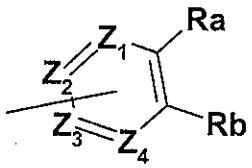


is chosen from the following groups:

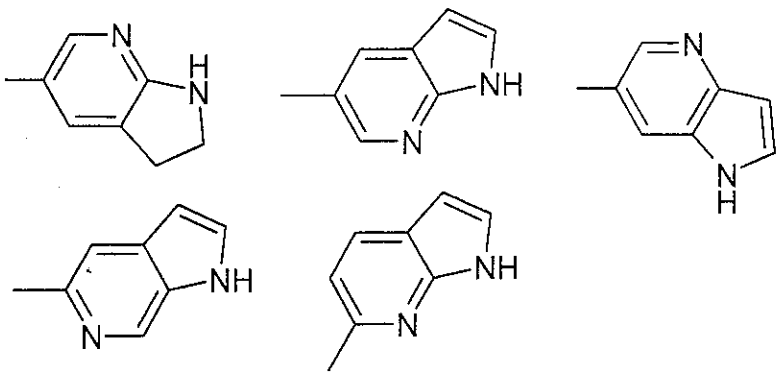


Among the compounds of general formula (I) that are subjects of the invention, a twenty-second subgroup of compounds is constituted by the compounds for which the definitions of X_1, X_2, X_3 and X_4, n, Y, W, Z_1, Z_2, Z_3, Z_4; Ra and Rb given hereinabove are combined.

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
either X_1, X_2, X_3 and X_4 represent, independently of each other, a group C-R_1; or, among X_1, X_2, X_3 and X_4, one from among X_3 and X_4 represents a nitrogen atom and the others 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)$_3$;
n is equal to 1;
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; or alternatively Y represents a pyridyl or a thiazolyl;
W represents an oxygen atom;
the group



is chosen from the groups



one from among Z_1, Z_2, Z_3 and Z_4 corresponding to a nitrogen atom and possibly being in oxidized form;

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

R_2 represents a hydrogen atom;

R_3 represents, when it is borne by a carbon atom, a hydrogen atom or an oxo group;

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

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, a group C_1-C_6-alkyl, C_1-C_6-fluoroalkyl, C_1-C_6-alkoxy, 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,

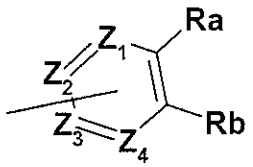
W represents an oxygen atom;

n is equal to 0;

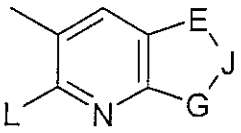
Y represents a phenyl optionally substituted with one or more substituents R_9, which may be identical to or different from each other; or Y represents an isoxazole;

R_9 represents a halogen atom or a group C_1-C_6-alkyl, C_1-C_6-alkoxy or cyano;

the group



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; when J represents N, then E and G represent, independently of each other, a group C=O or CH_2; when J represents C=O, one from among E and G represents a group C=O or CH_2, and the other from among E and G represents a group 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;

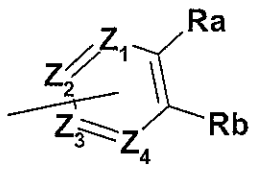
are excluded.

Among the compounds of general formula (I) that are subjects of the invention, a twenty-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.

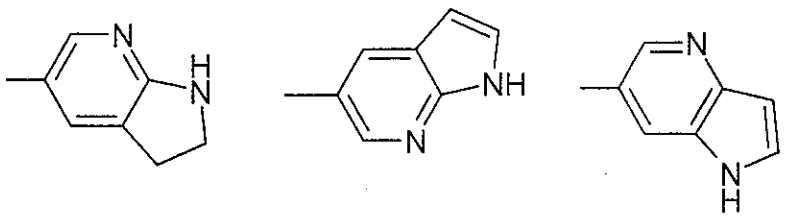
Among the compounds of general formula (I) that are subjects of the invention, a twenty-sixth subgroup of compounds is constituted by the compounds for which n is equal to 1 and Y represents an aryl, more particularly a phenyl, optionally substituted with one or more halogen atoms, more particularly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

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

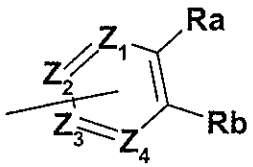


is chosen from the groups

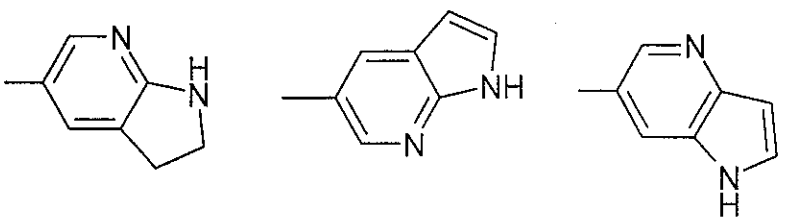


these groups being optionally substituted with R_2 and R_3 as defined in the general formula (I) hereinabove.

Among the compounds of general formula (I) that are subjects of the invention, a twenty-ninth 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;
the group



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*-(1-acetyl-2,3-dihydro-1*H*-pyrrolo[2,3-*b*]pyrid-5-yl)-5-fluoro-1-(3-fluorobenzyl)-1*H*-indole-2-carboxamide

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

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

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

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

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

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

8 *N*-(1*H*-Pyrrolo[2,3-*c*]pyrid-5-yl)-5-fluoro-1-[(3-fluorophenyl]methyl]-1*H*-indole-2-carboxamide

9 *N*-(1*H*-Pyrrolo[2,3-*b*]pyrid-5-yl)-5-trifluoromethyl-1-[(3-fluorophenyl)methyl]-1*H*-pyrrolo[2,3-b]pyridine-2-carboxamide

10 *N*-(7-Oxy-1*H*-pyrrolo[2,3-*b*]pyrid-5-yl)-5-fluoro-1-[(3-fluorophenyl)methyl]-1*H*-indole-2-carboxamide

11 *N*-(1-Methyl-1*H*-pyrrolo[2,3-*b*]pyrid-5-yl)-5-trifluoromethyl-1-[(3-fluorophenyl)-methyl]-1*H*-indole-2-carboxamide

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

13 *N*-(1-Methyl-1*H*-pyrrolo[2,3-*b*]pyrid-5-yl)-5-trifluoromethyl-1-[(3-fluorophenyl)-methyl]-1*H*-pyrrolo[2,3-b]pyridine-2-carboxamide

14 *N*-(1-Methyl-2,3-dihydro-1*H*-pyrrolo[2,3-*b*]pyrid-5-yl)-5-fluoro-1-[(3-fluorophenyl)-methyl]-1*H*-indole-2-carboxamide

15 *N*-(1-Methyl-1*H*-pyrrolo[2,3-*b*]pyrid-5-yl)-1-[[(3-trifluoromethyl)phenyl]methyl]-1*H*-indole-2-carboxamide

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

17 *N*-(1-Methyl-1*H*-pyrrolo[2,3-*b*]pyrid-5-yl)-5-fluoro-1-[[(3-trifluoromethyl)phenyl]-methyl]-1*H*-indole-2-carboxamide

18 *N*-(1-Methyl-1*H*-pyrrolo[2,3-*b*]pyrid-5-yl)-5-fluoro-1-[(3-methylphenyl)methyl]-1*H*-indole-2-carboxamide

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

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

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

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

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

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

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

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

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

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

29 *N*-(1-Methyl-1*H*-pyrrolo[2,3-*b*]pyrid-5-yl)-5-fluoro-1-[(pyrid-3-yl)methyl)]-1*H*-indole-2-carboxamide

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

31 *N*-(1*H*-Pyrrolo[2,3-*b*]pyrid-5-yl)-6-trimethylsilyl-1-[(thiazol-2-yl)methyl]-1*H*-indole-2-carboxamide

32 *N*-(1*H*-Pyrrolo[2,3-*b*]pyrid-5-yl)-5-trifluoromethyl-1-[(thiazol-2-yl)methyl]-1*H*-indole-2-carboxamide

33 *N*-(1*H*-Pyrrolo[2,3-*b*]pyrid-5-yl)-6-trifluoromethyl-1-[(thiazol-2-yl)methyl]-1*H*-indole-2-carboxamide

34 *N*-(1*H*-Pyrrolo[2,3-*b*]pyrid-5-yl)-5-trimethylsilyl-1-[(thiazol-2-yl)methyl]-1*H*-indole-2-carboxamide

35 *N*-(1*H*-Pyrrolo[2,3-*b*]pyrid-5-yl)-6-fluoro-1-[(thiazol-2-yl)methyl]-1*H*-indole-2-

carboxamide

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

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

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

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

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

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

42 *N*-(2-Oxo-2,3-dihydro-1*H*-pyrrolo[2,3-*b*]pyrid-5-yl)-5-fluoro-1-[(3-fluorophenyl)methyl]-1H-indole-2-carboxamide

43 *N*-(1*H*-Pyrrolo[2,3-*b*]pyrid-5-yl)-5-trifluoromethyl-1-[(3-fluorophenyl)methyl]-1*H*-indole-2-carboxamide

44 *N*-(1-Methyl-1*H*-pyrrolo[2,3-*b*]pyrid-5-yl)-1-[(3-fluorophenyl)methyl]-1*H*-pyrrolo[2,3-c]pyridine-2-carboxamide

45 *N*-(1*H*-pyrrolo[2,3-*b*]pyrid-5-yl)-1-[(3-fluorophenyl)methyl]-1*H*-pyrrolo[2,3-c]pyridine-2-carboxamide

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

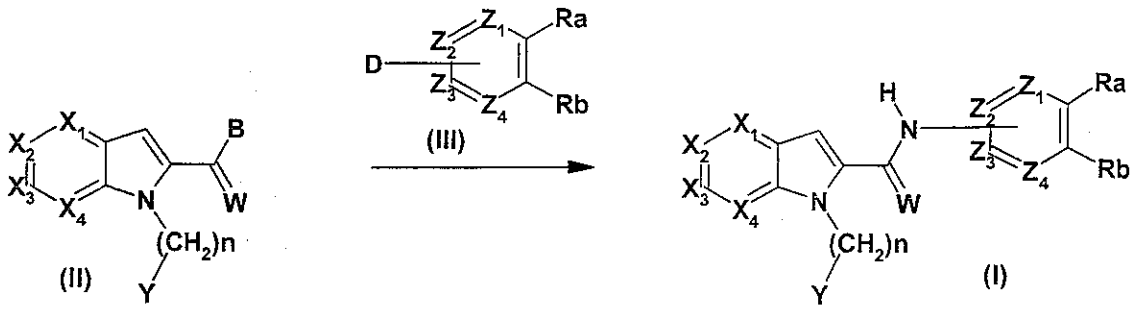
47 *N*-(1-Methyl-1*H*-Pyrrolo[2,3-*b*]pyrid-5-yl)-5-trifluoromethyl-1-[(pyrid-4-yl)methyl)]-1*H*-indole-2-carboxamide.

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 of general formula (I) may be obtained by reacting a compound of general formula (II), in which X_1, X_2, X_3, X_4, n, Y and W are as defined in the general formula (I) hereinabove and B corresponds to a hydroxyl group, 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.

The compound of general formula (II), for which B represents a group C_1-C_6-alkoxyl, may be converted into a compound of general formula (II), in which B represents a hydroxyl group, via the action of a base such as sodium hydroxide or potassium hydroxide dissolved in a solvent such as ethanol. The compound of general formula (II) in which B represents a hydroxyl group may then be converted into a compound of general formula (II), in which B represents a chlorine atom, via the action of a chlorinating agent such as thionyl chloride in a solvent such as dichloromethane.

The compounds of general formula (I) may be obtained by reacting a compound of general formula (II), in which X_1, X_2, X_3, X_4, n, Y and W are as defined in the general formula (I) hereinabove and B corresponds to a chlorine atom, 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 correspond to an amino group, via reaction in solution in a solvent such as dichloromethane or toluene.

The compounds of general formula (I) may also be obtained by reacting a compound of general formula (II) in which X_1, X_2, X_3, X_4, n, Y and W are as defined in the general formula (I) hereinabove and B corresponds to a group C_1-C_6-alkoxyl, with an amide, resulting from (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, and an organometallic reagent such as trimethylaluminium. This reaction may be performed in a solvent such as toluene.

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.

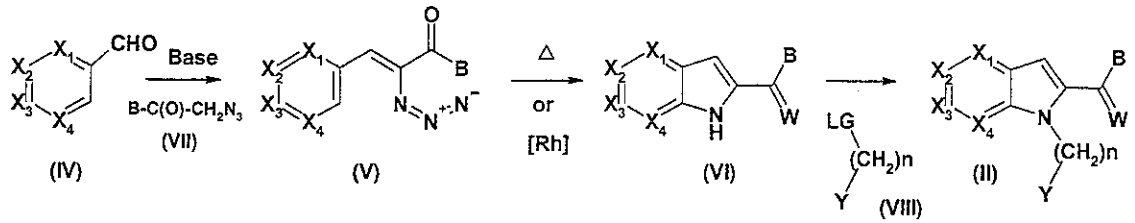
The compounds of general formula (I) for which R_3 corresponds to a protecting group borne by a nitrogen atom, such as an acetyl, ethoxycarbonyl or tert-butyloxycarbonyl group or a benzyloxycarbonyl group, may be deprotected, according to chemical methods known to those skilled in the art, to give compounds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

The compounds of general formula (I), in which at least one from among Z_1, Z_2, Z_3 and Z_4 corresponds to an N-oxide group, may be obtained, for example, by reacting the corresponding compounds of general formula (I) in which at least one from among Z_1, Z_2, Z_3 and Z_4 corresponds to a nitrogen atom, with a reagent such as meta-chloroperbenzoic acid.

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 of general formula (VI) with a reagent of general formula (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).

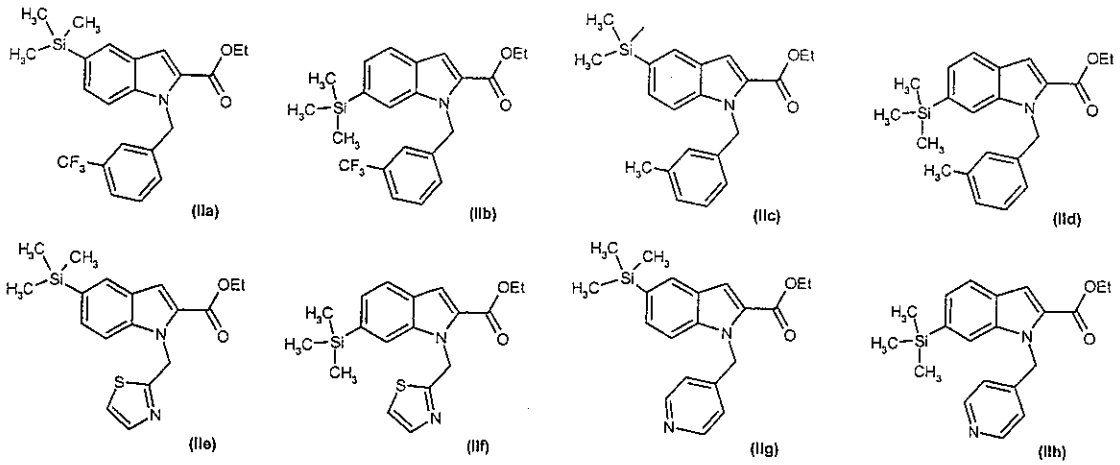
The aromatic or heteroaromatic aldehydes substituted with a silyl group of general formula (IV), when they are not commercially available, may be obtained from the corresponding aromatic or heteroaromatic aldehydes, which are preferably masked in the form of an acetal, for example, substituted with a 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 Et represents an ethyl group. These compounds are useful as intermediates for the synthesis of the compounds of formula (I).



The esters (IIa), (IIb), (IIc), (IId), (IIe), (IIf), (IIg) and (IIh) are prepared according to the processes described in Examples 9, 10, 14, 16, 21, 38, 40 and 41.

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*-[1-Acetyl-2,3-dihydro-1*H*-pyrrolo[2,3-*b*]pyrid-5-yl]-5-fluoro-1-[(3-fluorophenyl)-methyl]-1*H*-indole-2-carboxamide**

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

An 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, 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 1-Acetyl-5-amino-2,3-dihydro-1*H*-pyrrolo[2,3-*b*]pyridine

A suspension of 0.43 g (2.08 mmol) of 1-acetyl-2,3-dihydro-5-nitro-1*H*-pyrrolo[2,3-*b*]pyridine (*Tetrahedron Lett.* **1987**, 1589) and 0.044 g of 10% palladium-on-charcoal in 15 mL of ethanol is stirred vigorously for 6 hours at room temperature and under 5 atmospheres of hydrogen. After this time, the suspension is filtered through Celite and the filtrate is concentrated under reduced pressure to give 0.24 g of the expected product in the form of a solid.

m.p. = 193 – 195°C

^{1}H NMR (DMSO-D_6), δ ppm: 7.5 (s, 1H); 6.93 (s, 1H); 5 (s, 2H); 3.91 (dxd, 2H); 2.95 (dxd, 2H); 2.49 (s, 3H).

1.3 *N*-[1-Acetyl-2,3-dihydro-1*H*-pyrrolo[2,3-*b*]pyrid-5-yl]-5-fluoro-1-(3-fluorobenzyl)-1*H*-indole-2-carboxamide (Compound 1)

To a solution, stirred at 20°C, of 0.28 g (0.97 mmol) of 5-fluoro-1-(3-fluorobenzyl)-1*H*-indole-2-carboxylic acid prepared in step 1.1, 186 mg (0.97 mmol) of *N*-(3-dimethylaminopropyl)-*N'*-ethylcarbodiimide hydrochloride (EDAC) and 131 mg (0.97 mmol) of 1-hydroxybenzotriazole (HOBT) in 15 mL of DMF are added 206 mg (1.17 mmol) of 1-acetyl-5-amino-2,3-dihydro-1*H*-pyrrolo[2,3-*b*]pyridine, prepared in step 1.2. The reaction mixture is stirred for 14 hours at 20°C and then concentrated under reduced pressure. The resulting product is taken up in 100 mL of water. The suspension is then extracted with three times 30 mL of ethyl acetate. The combined organic phases are washed twice with 20 mL of water, 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 dichloromethane and methanol. 290 mg of the expected product are thus isolated.

m.p. = 186 – 188°C

^{1}H NMR (DMSO-D_6), δ ppm: 8.4 (s, 1H); 8.07 (s, 1H); 7.6 (m, 1H); 7.56 (m, 1H); 7.43 (s, 1H); 7.33 (m, 1H); 7.19 (m, 1H); 7.08 (m, 1H); 6.90 (m, 2H); 5.9 (s, 2H); 4.05 (dxd, 2H); 3.12 (dxd, 2H); 2.51 (s, 3H).

Example 2 (Compound 2)

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

The process is performed according to a method similar to that described in Example 1.3 starting with 0.4 g (1.39 mmol) of 5-fluoro-1-(3-fluorobenzyl)-1*H*-indole-2-carboxylic acid prepared in step 1.1 and 0.22 g (1.67 mmol) of 5-amino-1*H*-pyrrolo[2,3-*b*]pyridine (*Synthesis* **2005**, *15*, 2503). 0.44 g of the expected product is thus isolated in the form of a white solid.

m.p. = 266 – 267°C

^{1}H NMR (DMSO-D_6), δ ppm: 11.55 (s, 1H); 10.37 (s, 1H); 8.45 (s, 1H); 8.31 (s, 1H); 7.6 (m, 1H); 7.53 (m, 1H); 7.45 (m, 2H); 7.3 (m, 1H); 7.17 (m, 1H); 7.05 (m, 1H); 6.92 (m, 2H); 6;45 (s, 1H); 5.9 (s, 2H).

Example 3 (Compound 3)

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

0.62 mL (8.96 mmol) of acetyl chloride is added dropwise to a solution, stirred at 0°C, of 0.2 g (0.45 mmol) of compound 1, described in step 1.3, in 4 mL of methanol. The reactor is then closed and the mixture is stirred for 30 minutes at 20°C and then for 16 hours at 70°C. After this time, the mixture is concentrated under reduced pressure and then taken up in 100 mL of ethyl acetate and 50 mL of saturated sodium hydrogen carbonate solution. The organic phase is separated out, washed with saturated sodium chloride solution, 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 dichloromethane and methanol. 108 mg of the expected product are thus isolated.

m.p. = 230 – 232°C

^{1}H NMR (DMSO-D_6), δ ppm: 10.19 (s, 1H); 7.98 (s, 1H); 7.6 (s, 1H); 7.55 (m, 2H); 7.34 (m, 2H); 7.19 (m, 1H); 7.09 (m, 1H); 6.9 (m, 2H); 6.22 (s, 1H); 5.9 (s, 2H); 3.5 (dxd, 2H); 3.01 (dxd, 2H).

Example 4 (Compound 4)

***N*-[1*H*-Pyrrolo[3,2-*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 1.3 starting with 0.4 g (1.39 mmol) of 5-fluoro-1-(3-fluorobenzyl)-1*H*-indole-2-carboxylic acid prepared in step 1.1 and 0.22 g (1.67 mmol) of 6-amino-1*H*-pyrrolo[3,2-*b*]pyridine (Adesis). 0.22 g of the expected product is thus isolated in the form of a white solid.
m.p. = 277 – 278°C
^{1}H NMR (DMSO-D_6), δ ppm: 11.49 (s, 1H); 10.58 (s, 1H); 8.29 (m, 2H); 7.88 (s, 1H); 7.6 (m, 2H); 7.42 (s, 1H); 7.32 (m, 1H); 7.1 (m, 3H); 6.94 (m, 2H); 5.91 (s, 2H).

Example 5 (Compound 36)
***N*-(1*H*-Pyrrolo[2,3-*b*]pyrid-5-yl)-5-trifluoromethyl-1-[(pyrid-4-yl)methyl)]-1*H*-indole-2-carboxamide**

5.1 Ethyl 5-trifluoromethyl-1-[(pyrid-4-yl)methyl)]-1*H*-indole-2-carboxylate
To a solution of 333 mg (1.29 mmol) of ethyl 5-trifluoromethyl-1*H*-indole-2-carboxylate in 5 mL of dry toluene, maintained under an inert atmosphere, are added, at room temperature, 283 mg (2.59 mmol) of 4-pyridylmethanol and 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, eluting with a mixture of heptane and ethyl acetate to give 386 mg of the expected ethyl 5-trifluoromethyl-1-[(pyrid-4-yl)methyl)]-1*H*-indole-2-carboxylate in the form of a white solid.
^{1}H NMR (DMSO D_6), δ (ppm): 8.46 (d, 2H); 8.22 (s, 1H); 7.80 (d, 1H); 7.62 (d, 1H); 7.58 (s, 1H); 6.93 (d, 2H); 5.95 (s, 2H); 4.28 (q, 2H); 1.26 (t, 3H).
LC-MS: 349 $[M+H]^+$

5.2 *N*-(1*H*-Pyrrolo[2,3-*b*]pyrid-5-yl)-5-trifluoromethyl-1-[(pyrid-4-yl)methyl)]-1*H*-indole-2-carboxamide
To a solution of 150 mg (0.43 mmol) of ethyl 5-trifluoromethyl-1-[(pyrid-4-yl)methyl)]-1*H*-indole-2-carboxylate, obtained according to the protocol described in the preceding step, and 69 mg (0.52 mmol) of pyrrolo[2,3-*b*]pyrid-5-ylamine in 1.5 mL of dry toluene, maintained under an inert atmosphere, is added dropwise, at 0°C, 0.32 mL (0.645 mmol) of a solution of trimethylaluminium (2M/toluene). The reaction mixture is stirred at 110°C for 15 hours and then concentrated under reduced pressure. The crude reaction product is then diluted with 50 mL of normal HCl solution and 100 mL of

ethyl acetate. The organic phase is separated out, washed with 50 mL of saturated sodium chloride solution and then dried over sodium sulfate and concentrated under reduced pressure. The resulting product is purified by chromatography on a column of silica. 147 mg of the expected product are thus isolated.

^{1}H NMR (DMSO D_6), δ (ppm): 11.62 (s, 1H); 10.62 (s, 1H); 8.47 (d, 2H); 8.42 (s, 1H), 8.29-8.24 (m, 2H); 7.76 (d, 1H); 7.66 (s, 1H); 7.58 (dd, 1H); 7.46 (t, 1H); 7.03 (d, 2H); 6.45-6.43 (m, 1H); 6.00 (s, 2H).

LC-MS: 436 $[M+H]^+$

m.p. = 216 - 217°C

Example 6 (Compound 5)

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

6.1 Methyl 5-fluoro-1-[(3-methylphenyl)methyl]-1*H*-indole-2-carboxylate

This compound is prepared, according to a process similar to that described in Example 5.1, by reacting 475 mg (2.459 mmol) of methyl 6-fluoro-1*H*-indole-2-carboxylate with 0.59 mL (4.918 mmol) of 3-methylphenylmethanol in the presence of 0.92 g (3.826 mmol) of (cyanomethylene)tributylphosphorane (CMBP). The resulting crude mixture is then purified by flash chromatography on a column of silica gel in a mixture of heptane and ethyl acetate to give 539 mg of the expected product in the form of a colourless oil.

^{1}H NMR (DMSO D_6), δ (ppm): 7.76 (dd, 1H); 7.46 (dd, 1H); 7.40 (s, 1H); 7.14 (t.1 H); 7.06-6.99 (m, 2H); 6.89 (s, 1H); 6.75 (d, 1H); 5.78 (s, 2H); 3.81 (s, 3H); 2.21(s, 3H).

LC-MS: 298 $[M+H]^+$

6.2 *N*-(1*H*-Pyrrolo[2,3-*b*]pyrid-5-yl)-5-fluoro-1-[(3-methylphenyl)methyl]-1*H*-indole-2- carboxamide (Compound 5).

Compound 5 was prepared according to a process similar to that described in step 5.2 by reacting 200 mg (0.673 mmol) of methyl 5-fluoro-1-[(3-methylphenyl)methyl]-1*H*-indole-2-carboxylate prepared according to the protocol described in step 6.1 with 107 mg (0.807 mmol) of pyrrolo[2,3-*b*]pyrid-5-ylamine in the presence of 0.5 mL (1.01 mmol) of a solution of trimethylaluminium (2M/toluene). The product is collected by filtration, to give 107 mg of the expected product.

^{1}H NMR (DMSO D_6), δ (ppm): 11.61 (s, 1H); 10.45 (s, 1H); 8.44 (d, 1H); 8.32 (d, 1H);

7.76 (dd, 1H); 7.47-7.42 (m, 3H); 7.14 (t, 1H); 7.05-6.98 (m, 3H); 6.86 (d, 1H); 6.45 (m, 1H); 5.82 (s, 2H); 2.20 (s, 3H).
m.p. = 310 – 311°C

Example 7 (Compound 30)
***N*-(1*H*-Pyrrolo[2,3-*b*]pyrid-5-yl)-5-trifluoromethyl-1-[(thiazol-2-yl)methyl]-1*H*-pyrrolo[2,3-b]pyridine-2-carboxamide**

7.1 Ethyl 5-trifluoromethyl-1-[(thiazol-2-yl)methyl]-1*H*-pyrrolo[2,3-*b*]pyridine-2-carboxylate
This compound was prepared according to a process similar to that described in step 5.1. by reacting 390 mg (1.51 mmol) of ethyl 5-trifluoromethyl-1*H*-pyrrolo[2,3-b]pyridine-2-carboxylate (WO2008/107 543) with 348 mg (3.02 mmol) of thiazol-2-ylmethanol in the presence of 0.92 g (3.826 mmol) of (cyanomethylene)-tributylphosphorane (CMBP). The reaction mixture is then purified by flash chromatography on a column of silica gel in a mixture of heptane and ethyl acetate to give 446 mg of the expected product in the form of an oil.
^{1}H NMR (DMSO D_6), δ (ppm): 8.84 (s, 1H); 8.69 (s, 1H); 7.67 (d, 1H), 7.60 (d, 1H), 7.54 (s, 1H); 6.22 (s, 2H); 4.32 (q, 2H); 1.28 (t, 3H).
LC-MS: 356 $[M+H]^+$

7.2 *N*-(1*H*-Pyrrolo[2,3-*b*]pyrid-5-yl)-5-trifluoromethyl-1-[(thiazol-2-yl)methyl]-1*H*-pyrrolo[2,3-*b*]pyridine-2-carboxamide (Compound 30)
Compound 30 was prepared according to a process similar to that described in step 5.1 by reacting 186 mg (0.523 mmol) of ethyl 5-trifluoromethyl-1-[(thiazol-2-yl)methyl]-1*H*-pyrrolo[2,3-*b*]pyridine-2-carboxylate prepared according to the protocol described in step 7.1 with 84 mg (0.628 mmol) of pyrrolo[2,3-*b*]pyrid-5-ylamine in the presence of 0.39 mL (0.785 mmol) of a solution of trimethylaluminium (2M/toluene). The product is collected by filtration, to give 144 mg of expected product.
^{1}H NMR (DMSO D_6), δ (ppm): 11.70 (s, 1H); 10.76 (s, 1H); 8.81-8.76 (m, 2H); 8.47 (s, 1H); 8.35 (s, 1H); 7.67-7.58 (m, 3H); 7.50-7.49 (m, 1H); 6.49-6.47 (m, 1H); 6.29 (s, 2H).
LC-MS: 443 $[M+H]^+$
m.p. = 274 - 275°C

Example 8 (Compound 37)

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

8.1 Methyl 6-trifluoromethyl-1-[(pyrid-4-yl)methyl)]-1*H*-indole-2-carboxylate

This compound was prepared according to a process similar to that described in step 5.1 by reacting 500 mg (2.056 mmol) of methyl 6-trifluoromethyl-1*H*-indole-2-carboxylate with 449 mg (4.11 mmol) of 4-pyridylmethanol in the presence of 0.92 g (3.826 mmol) of (cyanomethylene)tributylphosphorane (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 407 mg of the expected product in the form of a beige-coloured solid.

^{1}H NMR (DMSO D_6), δ (ppm): 8.46 (d, 2H); 8.09 (s, 1H); 7.99 (d, 1H); 7.54 (s, 1H), 7.46 (d, 1 H); 6.90 (d, 2H); 6.00 (s, 2H); 3.82 (s, 3H).

LC-MS: 335 $[M+H]^+$

8.2 *N*-(1*H*-Pyrrolo[2,3-*b*]pyrid-5-yl)-6-trifluoromethyl-1-[(pyrid-4-yl)methyl)]-1*H*-indole-2-carboxamide (Compound 37).

Compound 37 was prepared according to a process similar to that described in step 5.2 by reacting 150 mg (0.449 mmol) of methyl 6-trifluoromethyl-1-[(pyrid-4-yl)methyl)]-1*H*-indole-2-carboxylate prepared in the preceding step with 72 mg (0.538 mmol) of pyrrolo[2,3-*b*]pyrid-5-ylamine in the presence of 0.34 mL (0.674 mmol) of a solution of trimethylaluminium (2M/toluene). The product is collected by filtration, to give 99 mg of expected product.

^{1}H NMR (DMSO D_6), δ (ppm): 11.71 (s, 1H); 10.72 (s, 1H); 8.77 (d, 2H); 8.45 (d, 1H), 8.30 (d, 1H); 8.12 (s, 1H); 8.06 (d, 1H); 7.76 (s, 1H); 7.52-7.47 (m, 4H); 6.45 (m, 1H); 6.23 (s, 2H).

LC-MS: 436 $[M+H]^+$

m.p. = 311 – 313°C

<u>Example 9</u> (Compound 6)

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

9.1 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).

9.2 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).

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

This compound was prepared according to a process similar to that described in step 5.1 by reacting 500 mg (1.913 mmol) of ethyl 6-trimethylsilyl-1*H*-indole-2-carboxylate with 0.52 mL (3.826 mmol) of 3-(trifluoromethyl)phenylmethanol in the presence of 0.92 g (3.826 mmol) of (cyanomethylene)tributylphosphorane (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 720 mg of the expected product.
^{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).
LC-MS: 420 [M+H]+

9.4 *N*-(1*H*-Pyrrolo[2,3-*b*]pyrid-5-yl)-6-trimethylsilyl-1-[[(3-trifluoromethyl)phenyl]-methyl]-1*H*-indole-2- carboxamide (Compound 6).
Compound 6 was prepared according to a process similar to that described in step 5.2 by reacting 200 mg (0.477 mmol) of ethyl 6-trimethylsilyl-1-[[(3-trifluoromethyl)phenyl]-methyl]-1*H*-indole-2-carboxylate prepared according to the protocol described in the preceding step with 76 mg (0.572 mmol) of pyrrolo[2,3-*b*]pyrid-5-ylamine in the presence of 0.36 mL (0.716 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. 163 mg of expected product are obtained.
^{1}H NMR (DMSO D_6), δ (ppm): 11.60 (s, 1H); 10.49 (s, 1H); 8.45 (d, 1H); 8.32 (d, 1H); 7.74-7.68 (m, 3H); 7.51-7.43 (m, 5H); 7.28 (d, 1H); 7.45-7.44 (m, 1H); 6.01 (s, 2H); 0.25 (s, 9H).
LC-MS: 507 $[M+H]^+$
m.p. = 251 – 252°C

Example 10 (Compound 7)
***N*-(1*H*-Pyrrolo[2,3-*b*]pyrid-5-yl)-5-trimethylsilyl-1-[[(3-trifluoromethyl)phenyl]-methyl]-1*H*-indole-2-carboxamide**

10.1 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).

10.2 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.
^{1}H 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)

10.3 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.

^{1}H 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

10.4 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

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

This compound was prepared according to a process similar to that described in step 5.1 by reacting 0.49 g (1.87 mmol) of ethyl 5-trimethylsilyl-1*H*-indole-2-carboxylate with 0.51 mL (3.749 mmol) of 3-(trifluoromethyl)phenylmethanol in the presence of 0.9 g (3.749 mmol) of (cyanomethylene)tributylphosphorane (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 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 $([M+H]^+$

10.6 *N*-(1*H*-Pyrrolo[2,3-*b*]pyrid-5-yl)-5-trimethylsilyl-1-[[(3-trifluoromethyl)phenyl]-methyl]-1*H*-indole-2-carboxamide (Compound 7)

Compound 7 was prepared according to a process similar to that described in step 5.2 by reacting 200 mg (0.477 mmol) of ethyl 5-trimethylsilyl-1-[[(3-trifluoromethyl)phenyl]-methyl]-1*H*-indole-2-carboxylate, prepared according to the protocol described in step 10.5, with 76 mg (0.572 mmol) of pyrrolo[2,3-*b*]pyrid-5-ylamine in the presence of 0.36 mL (0.716 mmol) of a solution of trimethylaluminium (2M/toluene). The product is collected by filtration, to give 107 mg of the expected product.

^{1}H NMR (DMSO D_6), δ (ppm): 11.51 (s, 1H); 10.38 (s, 1H); 8.34 (d, 1H); 8.21 (d, 1H); 7.80 (s, 1H); 7.51-7.41 (m, 3H); 7.38-7.30 (m, 4H); 7.26-7.23 (m, 1H); 6.36-6.34 (m, 1H); 5.87 (s, 2H); 0.19 (s, 9H).

LC-MS: 507 ($[M+H]^+$

m.p. = 199 – 200°C

Example 11 (Compound 42)

***N*-(2-Oxo-2,3-dihydro-1*H*-pyrrolo[2,3-*b*]pyrid-5-yl)-5-fluoro-1-[(3-fluorophenyl)-methyl]-1*H*-indole-2-carboxamide**

11.1 5-Fluoro-1-[(3-fluorophenyl)methyl]-1*H*-indole-2-carboxylic acid chloride

This product is prepared by refluxing for 3 hours a solution of 10 g (34.81 mmol) of 5-fluoro-1-[(3-fluorophenyl)methyl]-1*H*-indole-2-carboxylic acid, prepared in step 1.1, and 25.4 mL (0.348 mol) of sulfonyl chloride in 174 mL of toluene. After this time, the reaction mixture is concentrated under reduced pressure. The resulting mixture is taken up twice successively in 100 mL of toluene and then concentrated under reduced pressure. The product is used in the rest of the synthesis without a further purification step.

11.2 N-(2-Oxo-2,3-dihydro-1*H*-pyrrolo[2,3-*b*]pyrid-5-yl)-5-fluoro-1-[(3-fluorophenyl)-methyl]-1H-indole-2-carboxamide (Compound 42)

A solution of 1.3 g (4.25 mmol) of 5-fluoro-1-[(3-fluorophenyl)methyl]-1*H*-indole-2-carboxylic acid chloride, prepared in the preceding step, 2.1 mL (14.9 mmol) of triethylamine and 1.45 (4.68 mmol) of 5-amino-2-oxo-2,3-dihydro-1*H*-pyrrolo[2,3-*b*]pyridine dihydrobromide (US 2005/256 125) in 42.5 mL of dichloromethane is stirred for 24 hours at room temperature. After this time, the mixture is poured into 200 mL of

water. 100 mL of dichloromethane are added and the organic phase is then separated out, washed with twice 50 mL of water and concentrated under reduced pressure. The product obtained is purified by chromatography on a column of silica, eluting with a mixture of ethyl acetate and dichloromethane. The product thus purified is taken up in 100 mL of hot methanol, and the resulting suspension is filtered. The filtrate is concentrated under reduced pressure, thus allowing 0.4 g of the expected product to be isolated.

m.p. = 272 – 275°C

^{1}H NMR (DMSO-D_6), δ ppm: 10.94 (s, 1H); 10.49 (s, 1H); 8.32 (s, 1H); 7.95 (s, 1H); 7.6 (m, 1H); 7.55 (m, 1H); 7.41 (s, 1H); 7.31 (m, 1H); 7.17 (m, 1H); 7.05 (m, 1H); 6.9 (m, 2H); 5.9 (s, 2H); 3.58 (s, 2H).

Example 12 (Compound 19)

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

This compound was prepared according to a protocol similar to that described in Example 5.

m.p.: 311-312°C

^{1}H NMR (DMSO D_6), δ (ppm): 11.6 (s, 1H); 10.6 (s, 1H); 8.5 (s, 1H); 8.35 (s, 1H); 8.2 (s, 1H); 7.8 (d, 1H); 7.55 (m, 2H); 7.5 (m, 1H); 7.15 (t, 1H); 7.0 (m, 2H); 6.9 (d, 1H); 6.5 (d, 1H); 5.9 (s, 2H); 2.2 (s, 3H).

Example 13 (Compound 20)

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

This compound was prepared according to a protocol similar to that described in Example 5.

m.p.: 278-279°C

^{1}H NMR (DMSO D_6), δ (ppm): 11.7 (s, 1H); 10.6 (s, 1H); 8.5 (s, 1H); 8.4 (s, 1H); 8.05 (s, 1H); 7.95 (d, 1H); 7.50 (m, 2H); 7.45 (d, 1H); 7.15 (t, 1H); 7.05 (d, 1H); 7.0 (s, 1H); 6.9 (d, 1H); 6.5 (s, 1H); 5.95 (s, 2H); 2.2 (s, 3H).

Example 14 (Compound 21)

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

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

This compound was prepared according to a process similar to that described in step 5.1 by reacting ethyl 5-trimethylsilyl-1*H*-indole-2-carboxylate prepared according to the process described in step 10.4 with (3-methylphenyl)methanol in the presence of (cyanomethylene)tributylphosphorane (CMBP). The crude reaction product is then purified by flash chromatography on a column of silica gel to give the expected product.

^{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).

14.2 ***N*-(1*H*-Pyrrolo[2,3-*b*]pyrid-5-yl)-5-trimethylsilyl-1-[(3-methylphenyl)methyl]-1*H*-indole-2-carboxamide (Compound 21)**

This compound was prepared according to a protocol similar to that described in Example 5.

m.p.: 327-328°C

^{1}H NMR (DMSO D_6), δ (ppm): 11.6 (s, 1H); 10.4 (s, 1H); 8.5 (s, 1H); 8.3 (s, 1H); 7.9 (s, 1H); 7.55 (d, 1H); 7.45 (m, 1H); 7.4 (m, 2H); 7.15 (t, 1H); 7.0 (m, 2H); 6.9 (d, 1H); 6.45 (d, 1H); 5.85 (s, 2H); 2.2 (s, 3H); 0.3 (s, 9H).

Example 15 (Compound 22)

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

This compound was prepared according to a protocol similar to that described in Example 5.

m.p.: 305-306°C

^{1}H NMR (DMSO D_6), δ (ppm): 11.6 (s, 1H); 10.6 (s, 1H); 8.8 (s, 1H); 8.7 (s, 1H); 8.4 (s, 1H); 8.3 (s, 1H); 7.55 (s, 1H); 7.5 (m, 1H); 7.1 (t, 1H); 7.0 (m, 2H); 6.9 (d, 1H); 6.5 (d, 1H); 6.0 (s, 2H); 2.2 (s, 3H).

Example 16 (Compound 23)

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

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

This compound was prepared according to a process similar to that described in step 5.1 by reacting ethyl 6-trimethylsilyl-1*H*-indole-2-carboxylate prepared according to the process described in step 9.2 with (3-methylphenyl)methanol in the presence of (cyanomethylene)tributylphosphorane (CMBP). The crude reaction product is then purified by flash chromatography on a column of silica gel to give the expected product.

^{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).

16.2 *N*-(1*H*-Pyrrolo[2,3-*b*]pyrid-5-yl)-6-trimethylsilyl-1-[(3-methylphenyl)methyl]-1*H*-indole-2-carboxamide (Compound 23)

This compound was prepared according to a protocol similar to that described in Example 5.

m.p.: 202-203°C

^{1}H NMR (DMSO D_6), δ (ppm): 11.6 (s, 1H); 10.45 (s, 1H); 8.5 (s, 1H); 8.35 (s, 1H); 7.7 (m, 2H); 7.5 (d, 1H); 7.35 (m, 1H); 7.25 (d, 1H); 7.15 (t, 1H); 7.1 (s, 1H); 7.0 (d, 1H); 6.95 (d, 1H); 6.45 (s, 1H); 5.9 (s, 2H); 2.2 (s, 3H); 0.25 (s, 9H).

Example 17 (Compound 24)

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

This compound was prepared according to a protocol similar to that described in Example 5.

m.p.: 247-248°C

^{1}H NMR (DMSO D_6), δ (ppm): 11.65 (s, 1H); 10.7 (s, 1H); 8.5 (s, 1H); 8.35 (s, 1H); 8.25 (s, 1H); 7.9 (d, 1H); 7.7-7.5 (m, 6H); 7.4 (m, 1H); 6.5 (m, 1H); 6.1 (s, 2H).

Example 18 (Compound 25)

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

This compound was prepared according to a protocol similar to that described in Example 5.

m.p.: 334-335°C

^{1}H NMR (DMSO D_6), δ (ppm): 11.6 (s, 1H); 10.6 (s, 1H); 8.49 (s, 1H); 8.30 (s, 1H); 8.1 (s, 1H); 8.0 (d, 1H); 7.6-7.4 (m, 6H); 7.35 (m, 1H); 6.45 (m, 1H); 6.1 (s, 2H).

Example 19 (Compound 26)

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

This compound was prepared according to a protocol similar to that described in Example 5.

m.p.: 273-274°C

^{1}H NMR (DMSO D_6), δ (ppm): 11.65 (s, 1H); 10.7 (s, 1H); 8.85 (s, 1H); 8.75 (s, 1H); 8.45 (s, 1H); 8.3 (s, 1H); 7.65-7.35 (m, 6H); 6.5 (m, 1H); 6.1 (s, 2H).

Example 20 (Compound 27)

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

This compound was prepared according to a protocol similar to that described in Example 5.

m.p.: 288-289°C

^{1}H NMR (DMSO D_6), δ (ppm): 11.6 (s, 1H); 10.45 (s, 1H); 8.45 (d, 1H); 8.25 (d, 1H); 7.8 (m, 1H); 7.65-7.45 (m, 6H); 7.35 (m, 1H); 7.05 (m, 1H); 6.45 (m, 1H); 5.95 (s, 2H).

Example 21 (Compound 31)

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

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

This compound was prepared according to a process similar to that described in step 5.1 by reacting ethyl 6-trimethylsilyl-1*H*-indole-2-carboxylate prepared according to the process described in step 9.2 with (thienyl-2-yl)methanol in the presence of (cyanomethylene)tributylphosphorane (CMBP). The crude reaction product is then purified by flash chromatography on a column of silica gel to give 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 (s, 1H); 6.09 (s, 2H); 4.23 (q, 2H); 1.22 (t, 3H); 0.2 (s, 9H).

21.2 *N*-(1*H*-Pyrrolo[2,3-*b*]pyrid-5-yl)-6-trimethylsilyl-1-[(thiazol-2-yl)methyl]-1*H*-indole-2-carboxamide (Compound 31)

This compound was prepared according to a protocol similar to that described in Example 5.

m.p.: 269-270°C

^{1}H NMR (DMSO D_6), δ (ppm): 11.6 (s, 1H); 10.45 (s, 1H); 8.45 (d, 1H); 8.35 (d, 1H); 7.85 (s, 1H); 7.75 (m, 2H); 7.6 (d, 1H); 7.45 (m, 2H); 7.3 (d, 1H); 6.45 (m, 1H); 6.2 (s, 2H); 0.3 (s, 9H).

Example 22 (Compound 41)

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

This compound was prepared according to a protocol similar to that described in Example 5.

m.p.: 296-298°C

^{1}H NMR (DMSO D_6), δ (ppm): 8.8 (d, 2H); 8.6 (d, 2H); 8.4 (s, 1H); 8.30 (s, 1H); 7.75 (s, 1H); 7.5 (m, 1H); 7.35 (d, 2H); 6.45 (m, 1H); 6.1 (s, 2H).

Example 23 (Compound 8)

***N*-(1*H*-Pyrrolo[2,3-*c*]pyrid-5-yl)-5-fluoro-1-[(3-fluorophenyl]methyl]-1*H*-indole-2-carboxamide**

This compound was prepared according to a protocol similar to that described in Example 5.

m.p.: 203-204°C

^{1}H NMR (DMSO D_6), δ (ppm): 11.5 (s, 1H); 10.59 (s, 1H); 8.57 (s, 1H); 8.25 (s, 1H); 7.52 (m, 4H); 7.31 (m, 1H); 7.15 (m, 1H); 7.03 (m, 1H); 6.92 (m, 2H); 6.5 (m, 1H); 5.92 (s, 2H).

Example 24 (Compound 9)

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

This compound was prepared according to a method similar to that of Example 1.3.

m.p.: 319-320°C

^{1}H NMR (DMSO D_6), δ (ppm): 11.65 (s, 1H); 10.7 (s, 1H); 8.82 (s, 1H); 8.73 (s, 1H); 8.42 (s, 1H); 8.3 (s, 1H); 7.6 (s, 1H); 7.5 (s, 1H); 7.31 (m, 1H); 7.09 (m, 1H); 6.98 (m,

2H); 6.49 (m, 1H); 6.01 (s, 2H).

Example 25 (Compound 10)

***N*-(7-Oxy-1*H*-pyrrolo[2,3-*b*]pyrid-5-yl)-5-fluoro-1-[(3-fluorophenyl)methyl]-1*H*-indole-2-carboxamide**

This compound was prepared by stirring for 30 hours at 20°C a mixture of 0.5 g (1.24 mol) of compound 2 (Example 2) in the presence of 0.66 g (2.74 mmol) of meta-chloroperbenzoic acid in 130 mL of dichloromethane. After this time, the mixture is poured into 200 mL of water and 200 mL of dichloromethane. The organic phase is separated out, washed once with 100 mL of saturated sodium hydrogen carbonate solution, twice with 100 mL of water, dried over magnesium sulfate and then concentrated under reduced pressure. The resulting product is purified by chromatography on a column of silica, to give 0.13 g of expected product.

m.p.: 260-263°C

^{1}H NMR (DMSO D_6), δ (ppm): 12.41 (s, 1H); 10.6 (s, 1H); 8.59 (s, 1H); 8.03 (s, 1H); 7.6 (m, 2H); 7.42 (m, 2H); 7.31 (m, 1H); 7.19 (m, 1H); 7.05 (m, 1H); 6.93 (m, 2H); 6.59 (s, 1H); 5.89 (s, 2H).

Example 26 (Compound 12)

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

26.1 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 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 in water. The reaction mixture is stirred for 14 hours at 20°C. After this time, a solid is collected by filtration and triturated in 50 mL of diisopropyl ether. After filtering and drying under reduced pressure, 0.58 g of 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).

26.2 *N*-[1-Methylpyrrolo[2,3-*b*]pyrid-5-yl]-5-fluoro-1-[(3-fluorophenyl)methyl]-1*H*-indole-2-carboxamide (Compound 26)

0.4 g (1.4 mmol) of the amide prepared in the preceding step, 0.32 g (1.54 mmol) of 5-bromo-1-methylpyrrolo[2,3-*b*]pyridine (*Heterocycles* **2003**, *60*(4) 865), 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 placed in a pressure tube equipped with a magnetic stirrer. The suspension is degassed, 53 mg (0.46 mmol) of trans-cyclohexane-1,2-diamine are then added, and the tube is sealed and 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 2x30 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 dichloromethane and acetone, and then by recrystallization from isopropyl alcohol.

m.p.: 203-204°C

^{1}H NMR (DMSO D_6), δ (ppm): 10.51 (s, 1H); 8.51 (s, 1H); 8.36 (s, 1H); 7.59 (m, 2H); 7.55 (s, 1H); 7.46 (s, 1H); 7.32 (m, 1H); 7.19 (m, 1H); 7.08 (m, 1H); 6.93 (m, 2H); 6.49 (s, 1H); 5.9 (s, 2H); 3.82 (s, 3H).

Example 27 (Compound 11)

***N*-(1-Methyl-1*H*-pyrrolo[2,3-*b*]pyrid-5-yl)-5-trifluoromethyl-1-[(3-fluorophenyl)-methyl]-1*H*-indole-2-carboxamide**

This compound was prepared according to a method similar to that of Example 26.

m.p.: 249-250°C

^{1}H NMR (DMSO D_6), δ (ppm): 8.5 (s, 1H); 8.36 (s, 1H); 8.22 (s, 1H); 7.81 (m, 1H); 7.6 (m, 2H); 7.54 (s, 1H); 7.32 (m, 1H); 7.07 (m, 1H); 6.97 (m, 2H); 6.49 (s, 1H); 5.99 (s, 2H); 3.82 (s, 3H).

Example 28 (Compound 13)

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

This compound was prepared according to a method similar to that of Example 26.

m.p.: 237-238°C

^{1}H NMR (DMSO D_6), δ (ppm): 10.69 (s, 1H); 8.82 (s, 1H); 8.76 (s, 1H); 8.49 (s, 1H); 8.33 (s, 1H); 7.62 (s, 1H); 7.53 (d, 1H); 7.32 (m, 1H); 7.07 (m, 1H); 6.99 (m, 2H); 6.5 (d,

1H); 6.00 (s, 2H); 3.82 (s, 3H).

Example 29 (Compound 14)

***N*-[1-Methyl-2,3-dihydro-1*H*-pyrrolo[2,3-*b*]pyrid-5-yl]-5-fluoro-1-[(3-fluorophenyl)-methyl]-1*H*-indole-2-carboxamide.**

29.1 5-Bromo-2,3-dihydro-1-methylpyrrolo[2,3-*b*]pyridine

To a suspension stirred at 0°C, under an inert atmosphere, of 0.48 g (12.06 mmol) of 60% sodium hydride in 5 mL of dimethylformamide is added dropwise a solution of 5-bromo-2,3-dihydro-1*H*-pyrrolo[2,3-*b*]pyridine in 10 mL of dimethylformamide. The mixture is stirred at 0°C for 15 minutes and then at 20°C for 45 minutes. A solution of 0.77 mL (12.06 mmol) of methyl iodide in 5 mL of dimethylformamide is then added to this stirred suspension at 0°C. The mixture is then stirred for 48 hours. After this time, 50 mL of water and 50 mL of ethyl acetate are added to the mixture. The aqueous phase is separated out and then extracted with 3X30 mL of ethyl acetate. The organic phases are combined, washed with 2x50 mL of water and then concentrated under reduced pressure. The resulting product is purified by chromatography on a column of silica, eluting with a mixture of dichloromethane and methanol. 0.97 g of the expected product is thus isolated.

LC-MS: 213 $[M+H]^+$

^{1}H NMR (DMSO D_6), δ (ppm): 7.81 (s, 1H); 7.39 (s, 1H); 3.46 (t, 2H); 2.94 (t, 2H); 2.82 (s, 3H).

29.2 *N*-[1-Methyl-2,3-dihydro-1*H*-pyrrolo[2,3-*b*]pyrid-5-yl]-5-fluoro-1-[(3-fluorophenyl)-methyl]-1*H*-indole-2-carboxamide (Compound 14)

This compound was prepared according to a method similar to that of Example 26.

m.p.: 189-191°C

^{1}H NMR (DMSO D_6), δ (ppm): 10.21 (s, 1H); 8.06 (s, 1H); 7.65 (s, 1H); 7.57 (m, 2H); 7.35 (m, 2H); 7.18 (m, 1H); 7.05 (m, 1H); 6.91 (m, 2H); 5.9 (s, 2H); 3.42 (t, 2H); 2.95 (t, 2H); 2.85 (s, 3H).

Example 30 (Compound 15)

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

This compound was prepared according to a method similar to that of Example 26.

m.p.: 211-212°C

^{1}H NMR (DMSO D_6), δ (ppm): 10.49 (s, 1H); 8.51 (s, 1H); 8.35 (s, 1H); 7.79 (d, 1H); 7.54 (m, 6H); 7.39 (m, 1H); 7.31 (m, 1H); 7.19 (m, 1H); 6.47 (s, 1H); 6.0 (s, 2H); 3.84 (s, 3H).

Example 31 (Compound 28)

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

This compound was prepared according to a method similar to that of Example 26.

m.p.: 176-177°C

^{1}H NMR (DMSO D_6), δ (ppm): 10.51 (s, 1H); 8.7-8.4 (broad peak + s, 3H); 8.35 (s, 1H); 7.59 (m, 2H); 7.5 (m, 2H); 7.2 (m, 2H); 7.09 (broad peak, 1H); 6.48 (s, 1H); 5.91 (s, 2H); 3.85 (s, 3H).

Example 32 (Compound 29)

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

This compound was prepared according to a method similar to that of Example 26.

m.p.: 214-215°C

^{1}H NMR (DMSO D_6), δ (ppm): 10.52 (s, 1H); 8.51 (s, 1H); 8.46 (s, 2H); 8.37 (s, 1H); 7.69 (m, 1H); 7.55 (m, 4H); 7.34 (m, 1H); 7.19 (m, 1H); 6.49 (s, 1H); 5.95 (s, 2H); 3.82 (s, 3H).

Example 33 (Compound 16)

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

33.1 6-Bromo-1-methylpyrrolo[2,3-*b*]pyridine

This compound was prepared according to a method similar to that of Example 29.1 starting with commercial 6-bromo-1*H*-pyrrolo[2,3-*b*]pyridine.

LC-MS: 211 $[M+H]^+$

^{1}H NMR (DMSO D_6), δ (ppm): 7.92 (d, 1H); 7.53 (s, 1H); 7.28 (d, 1H); 6.5 (s, 1H); 3.82 (s, 3H).

33.2 *N*-[1-*M*ethylpyrrolo[2,3-*b*]pyrid-6-yl]-5-fluoro-1-[(3-fluorophenyl)methyl]-1*H*-indole-2-carboxamide (Compound 16)

This compound was prepared according to a method similar to that of Example 26 starting with 6-bromo-1-methylpyrrolo[2,3-*b*]pyridine prepared in the preceding step.
m.p.: 189-191°C
^{1}H NMR (DMSO D_6), δ (ppm): 10.8 (s, 1H); 7.99 (d, 1H); 7.81 (d, 1H); 7.59 (m, 2H); 7.53 (m, 1H); 7.45 (s, 1H); 7.32 (m, 1H); 7.18 (m, 1H); 7.05 (m, 1H); 6.91 (m, 2H); 6.49 (s, 1H); 5.93 (s, 2H); 3.84 (s, 3H).

Example 34 (Compound 17)
***N*-(1-Methyl-1*H*-pyrrolo[2,3-*b*]pyrid-5-yl)-5-fluoro-1-[[(3-trifluoromethyl)phenyl]-methyl]-1*H*-indole-2-carboxamide**

This compound was prepared according to a method similar to that of Example 26.
m.p.: 181-182°C
^{1}H NMR (DMSO D_6), δ (ppm): 10.56 (s, 1H); 8.5 (s, 1H); 8.32 (s, 1H); 7.45-7.7 (m, 7H); 7.38 (m, 1H); 7.15 (m, 1H); 6.48 (s, 1H); 6.0 (s, 2H); 3.79 (s, 3H).

Example 35 (Compound 18)
***N*-(1-Methyl-1*H*-pyrrolo[2,3-*b*]pyrid-5-yl)-5-fluoro-1-[(3-methylphenyl)methyl]-1*H*-indole-2-carboxamide**

This compound was prepared according to a method similar to that of Example 26.
m.p.: 185-186°C
^{1}H NMR (DMSO D_6), δ (ppm): 10.51 (s, 1H); 8.5 (s, 1H); 8.37 (s, 1H); 7.56 (m, 3H); 7.4 (s, 1H); 7.16 (m, 2H); 7.0 (m, 2H); 6.87 (m, 1H); 6.48 (s, 1H); 5.87 (s, 2H); 3.82 (s, 3H); 2.2 (s, 3H).

Example 36 (Compound 32)
***N*-(1*H*-Pyrrolo[2,3-*b*]pyrid-5-yl)-5-trifluoromethyl-1-[(thiazol-2-yl)methyl]-1*H*-indole-2-carboxamide**
This compound was prepared according to a protocol similar to that described in Example 5.
m.p.: 218-219°C
^{1}H NMR (DMSO D_6), δ (ppm): 11.9 (s, 1H); 10.75 (s, 1H); 8.6 (s, 1H); 8.5 (s, 1H); 8.2 (s, 1H); 7.95 (d, 1H); 7.7 (d, 1H); 7.65 (m, 3H); 7.5 (m, 1H); 6.55 (m, 1H); 6.2 (s, 2H).

Example 37 (Compound 33)

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

This compound was prepared according to a protocol similar to that described in Example 5.

m.p.: 165-166°C

^{1}H NMR (DMSO D_6), δ (ppm): 11.8 (s, 1H); 10.7 (s, 1H); 8.6 (s, 1H); 8.45 (s, 1H); 8.2 (s, 1H); 7.95 (d, 1H); 7.75 (d, 1H); 7.6 (m, 2H); 7.5 (m, 2H); 6.55 (m, 1H); 6.3 (s, 2H).

Example 38 (Compound 34)

***N*-(1*H*-Pyrrolo[2,3-*b*]pyrid-5-yl)-5-trimethylsilyl-1-[(thiazol-2-yl)methyl]-1*H*-indole-2-carboxamide**

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

This compound was prepared according to a process similar to that described in step 5.1 by reacting ethyl 5-trimethylsilyl-1*H*-indole-2-carboxylate prepared according to the process described in step 10.4 with (thienyl-2-yl)methanol in the presence of (cyanomethylene)tributylphosphorane (CMBP). The crude reaction product is then purified by flash chromatography on a column of silica gel to give the expected product.

^{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).

38.2 *N*-(1*H*-Pyrrolo[2,3-*b*]pyrid-5-yl)-5-trimethylsilyl-1-[(thiazol-2-yl)methyl]-1*H*-indole-2-carboxamide (Compound 34)

This compound was prepared according to a protocol similar to that described in Example 5.

m.p.: 213-214°C

^{1}H NMR (DMSO D_6), δ (ppm): 11.7 (s, 1H); 10.45 (s, 1H); 8.5 (d, 1H); 8.35 (d, 1H); 7.9 (s, 1H); 7.75-7.65 (m, 2H); 7.6 (d, 1H); 7.5-7.4 (m, 3H); 6.5 (m, 1H); 6.2 (s, 2H); 0.3 (s, 9H).

Example 39 (Compound 35)

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

This compound was prepared according to a protocol similar to that described in Example 5.

m.p.: 255-256°C

^{1}H NMR (DMSO D_6), δ (ppm): 11.6 (s, 1H); 10.45 (s, 1H); 8.45 (d, 1H); 8.35 (d, 1H); 7.75 (m, 2H); 7.65-7.45 (m, 4H); 7.05 (m, 1H); 6.45 (m, 1H); 6.2 (s, 2H).

Example 40 (Compound 38)

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

40.1 Ethyl (6-trimethylsilyl-1-[(pyrid-2-yl)methyl]-1*H*-indole-2-carboxylate (Compound IIh)

This compound was prepared according to a process similar to that described in step 5.1 by reacting ethyl 6-trimethylsilyl-1*H*-indole-2-carboxylate prepared according to the process described in step 9.2 with (pyrid-2-yl)methanol in the presence of (cyanomethylene)tributylphosphorane (CMBP). The crude reaction product is then purified by flash chromatography on a column of silica gel to give the expected product.

^{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).

40.2 *N*-(1*H*-Pyrrolo[2,3-*b*]pyrid-5-yl)-6-trimethylsilyl-1-[(pyrid-4-yl)methyl)]-1*H*-indole-2-carboxamide (Compound 38)

This compound was prepared according to a protocol similar to that described in Example 5.

m.p.: 235-236°C

^{1}H NMR (DMSO D_6), δ (ppm): 8.45 (m, 3H); 8.30 (d, 1H); 7.75 (d, 1H); 7.65 (s, 1H); 7.5 (m, 2H); 7.3 (d, 1H); 7.0 (d, 2H); 6.45 (d, 1H); 6.0 (s, 2H); 0.25 (s, 9H).

Example 41 (Compound 39)

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

41.1 Ethyl (5-trimethylsilyl-1-[(pyrid-4-yl)methyl]-1*H*-indole-2-carboxylate (Compound IIg)

This compound was prepared according to a process similar to that described in step

5.1 by reacting ethyl 5-trimethylsilyl-1*H*-indole-2-carboxylate prepared according to the process described in step 10.4 with (pyrid-2-yl)methanol in the presence of (cyanomethylene)tributylphosphorane (CMBP). The crude reaction product is then purified by flash chromatography on a column of silica gel to give the expected product.
^{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).

41.2 *N*-(1*H*-Pyrrolo[2,3-*b*]pyrid-5-yl)-5-trimethylsilyl-1-[(pyrid-4-yl)methyl)]-1*H*-indole-2-carboxamide (Compound 39)
This compound was prepared according to a protocol similar to that described in Example 5.
m.p.: 279-281°C
^{1}H NMR (DMSO D_6), δ (ppm): 8.45 (m, 3H); 8.30 (d, 1H); 7.9 (s, 1H); 7.6-7.35 (m, 4H); 7.0 (d, 2H); 6.45 (m, 1H); 5.9 (s, 2H); 0.3 (s, 9H).

Example 42 (Compound 40)
***N*-(1*H*-Pyrrolo[2,3-*b*]pyrid-5-yl)-6-fluoro-1-[(pyrid-4-yl)methyl)]-1*H*-indole-2-carboxamide**
This compound was prepared according to a protocol similar to that described in Example 5.
m.p.: 284-286°C
^{1}H NMR (DMSO D_6), δ (ppm): 11.6 (s, 1H); 10.4 (s, 1H); 8.45 (d, 2H); 8.4 (d, 1H); 8.3 (s, 1H); 7.8 (m, 1H); 7.55 (s, 1H); 7.45 (m, 2H); 7.0 (m, 3H); 6.45 (m, 1H); 5.9 (s, 2H).

Example 43 (Compound 43)
***N*-(1*H*-Pyrrolo[2,3-*b*]pyrid-5-yl)-5-trifluoromethyl-1-(3-fluorobenzyl)-1*H*-indole-2-carboxamide.**
This compound was prepared according to a protocol similar to that described in Example 1.3.
m.p.: 286 – 287°C
^{1}H NMR (DMSO D_6), δ (ppm): 11.61 (s, 1H); 10.62 (s, 1H); 8.47 (s, 1H); 8.35 (s, 1H); 8.21 (s, 1H); 7.82 (d, 1H); 7.6 (m, 2H); 7.5 (s, 1H); 7.33 (m, 1H); 7.08 (m, 1H); 6.98 (m, 2H); 6.48 (s, 1H); 5.98 (s, 2H).

Example 44 (Compound 44)

***N*-(1-Methyl-1*H*-pyrrolo[2,3-*b*]pyrid-5-yl)-1-[(3-fluorophenyl)methyl]-1*H*-pyrrolo[2,3-c]pyridine-2-carboxamide.**

This compound was prepared according to a protocol similar to that described in Example 26.

m.p.: 225-227°C

^{1}H NMR (DMSO D_6), δ (ppm): 10.8 (s, 1H); 9.08 (s, 1H); 8.49 (d, 1H); 8.38 (d, 1H); 8.27 (d, 1H); 7.72 (d, 1H); 7.55 (d, 1H); 7.47 (s, 1H); 7.32 (m, 1H); 7.02 (m, 3H); 6.45 (m, 1H); 5.95 (s, 2H); 3.82 (s, 3H).

Example 45 (Compound 45)

***N*-(1*H*-pyrrolo[2,3-*b*]pyrid-5-yl)-1-[(3-fluorophenyl)methyl]-1*H*-pyrrolo[2,3-c]pyridine-2-carboxamide**

This compound was prepared according to a protocol similar to that described in Example 26.

m.p.: 270-271°C

^{1}H NMR (DMSO D_6), δ (ppm): 11.62 (s, 1H); 10.68 (s, 1H); 9.04 (s, 1H); 8.49 (d, 1H); 8.38 (d, 1H); 8.28 (d, 1H); 7.73 (d, 1H); 7.4 (m, 3H); 7.05 (m, 3H); 6.49 (s, 1H); 6.01 (s, 2H).

Example 46 (Compound 46)

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

This compound was prepared according to a protocol similar to that described in Example 5.

m.p.: 259-260°C

^{1}H NMR (DMSO D_6), δ (ppm): 11.6 (s, 1H); 10.5 (s, 1H); 8.48 (m, 3H); 8.3 (s, 1H); 7.55 (m, 2H); 7.48 (m, 2H); 7.18 (m, 1H); 7.02 (m, 2H); 6.45 (s, 1H); 5.95 (s, 2H).

Example 47 (Compound 47)

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

This compound was prepared according to a protocol similar to that described in Example 5.

m.p.: 213-214°C

^{1}H NMR (DMSO D_6), δ (ppm): 10.63 (s, 1H); 8.49 (m, 3H); 8.35 (s, 1H); 8.27 (s, 1H);

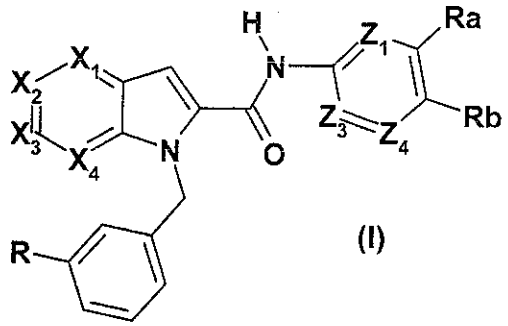
7.78 (d, 1H); 7.7(s, 1H); 7.6 (d, 1H); 7.52 (d, 1H); 7.04 (m, 2H); 6.49 (s, 1H); 6.02 (s, 2H); 3.82 (s, 3H).

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

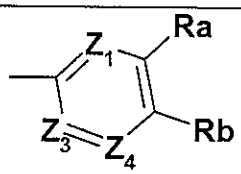
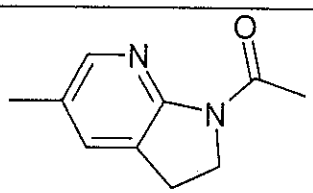
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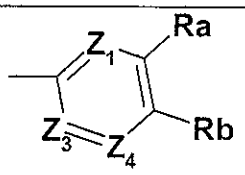
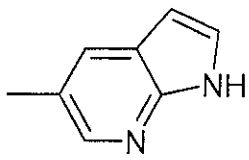
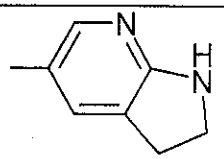
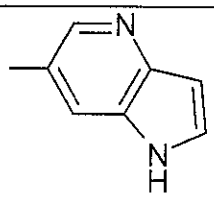
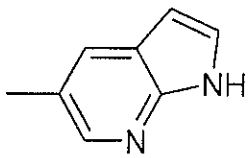
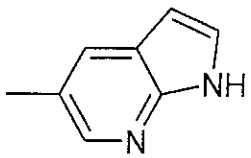
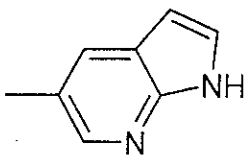
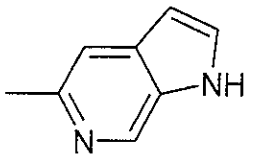
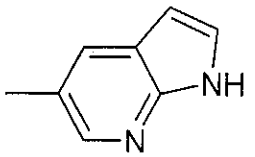
- the column "m.p. (°C)" indicates the melting points of the products in degrees Celsius (°C);
- all the compounds are in the form of the free base,
- W represents an oxygen atom;
- Z_2 represents a carbon atom bonded to the nitrogen atom of the amide of formula (I);
- n is equal to 1;
- R represents a substituent on the phenyl group;
- "Me" corresponds to a methyl group.

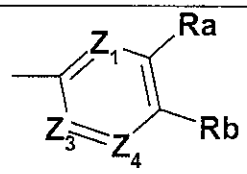
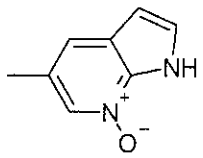
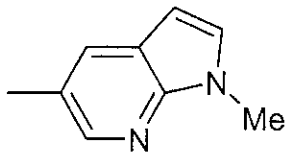
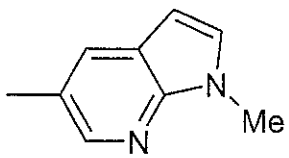
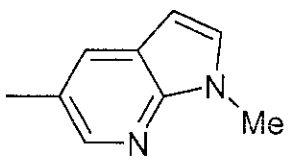
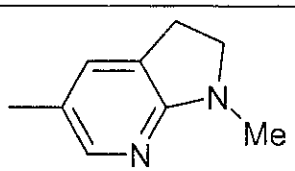
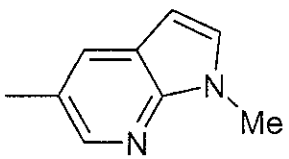
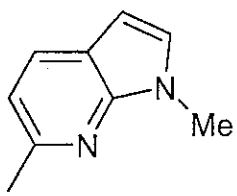
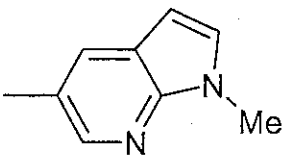
Table 1

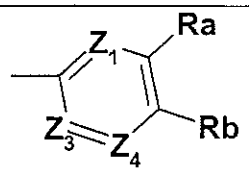
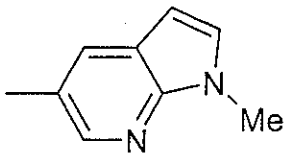
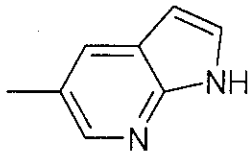
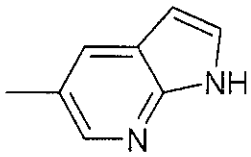
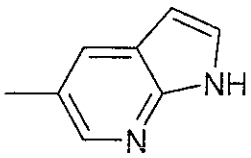
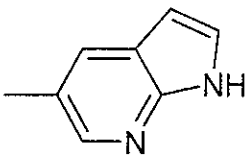
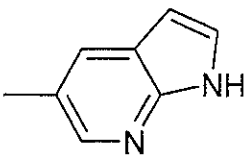
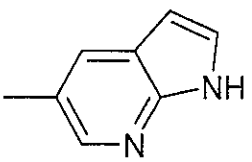
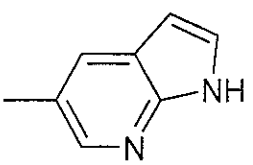


(I)

No.	X1, X2, X3, X4	R		m.p. (°C)
1	CH, C-F, CH, CH	F		186 – 188

No.	X1, X2, X3, X4	R		m.p. (°C)
2	CH, C-F, CH, CH	F		266 - 267
3	CH, C-F, CH, CH	F		230 - 232
4	CH, C-F, CH, CH	F		277 - 278
5	CH, CH, C-F, CH	Me		310 - 311
6	CH, CH, C-Si(Me)$_3$, CH	CF_3		251 – 252
7	CH, C-Si(Me)$_3$, CH, CH	CF_3		199 - 200
8	CH, C-F, CH, CH	F		203 - 204
9	CH, C-CF_3, CH, N	F		319 - 320

No.	X1, X2, X3, X4	R		m.p. (°C)
10	CH, C-F, CH, CH	F		260 - 263
11	CH, C-CF_3, CH, CH	F		249 - 250
12	CH, C-F, CH, CH	F		203 – 204°C
13	CH, C-CF_3, CH, N	F		237 - 238
14	CH, C-F, CH, CH	F		189 - 191
15	CH, CH, CH, CH	CF_3		211 - 212
16	CH, C-F, CH, CH	F		189 - 191
17	CH, C-F, CH, CH	CF_3		181 - 182

No.	X1, X2, X3, X4	R		m.p. (°C)
18	CH, C-F, CH, CH	Me		185 - 186
19	CH, C-CF_3, CH, CH	Me		311 - 312
20	CH, CH, C-CF_3, CH	Me		278 - 279
21	CH, C-$Si(Me)_3$, CH, CH	Me		327 - 328
22	CH, C-CF_3, CH, N	Me		305 - 306
23	CH, CH, C-$Si(Me)_3$, CH	Me		202 - 203
24	CH, C-CF_3, CH, CH	CF_3		247 - 248
25	CH, CH, C-CF_3, CH	CF_3		334 - 335

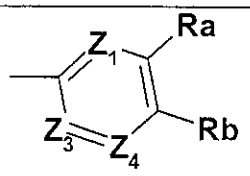
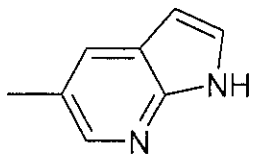
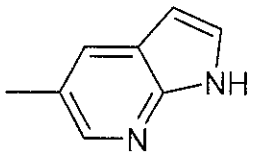
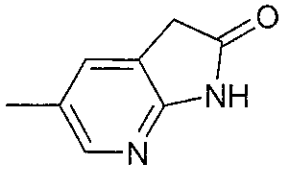
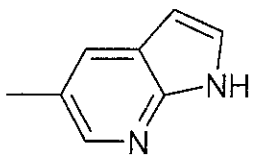
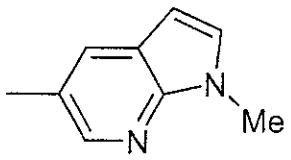
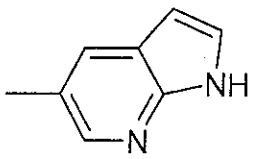
No.	X1, X2, X3, X4	R		m.p. (°C)
26	CH, C-CF_3, CH, N	CF_3		273 - 274
27	CH, CH, C-F, CH	CF_3		288 - 289
42	CH, C-F, CH, CH	F		272 - 275
43	CH, C-CF_3, CH, CH	F		286 - 287
44	CH, CH, N, CH	F		225 - 227
45	CH, CH, N, CH	F		270 - 271

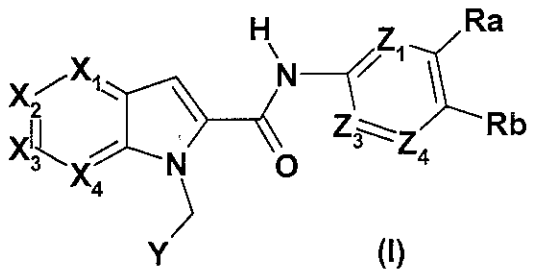
Table 2 that follows illustrates the chemical structures and the physical properties of a number of compounds according to the invention.

In this table:

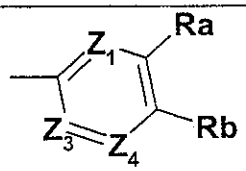
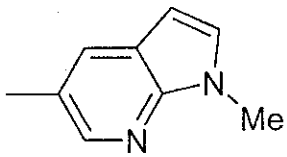
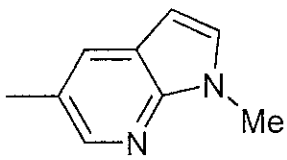
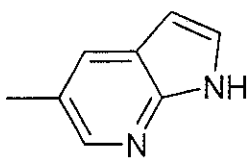
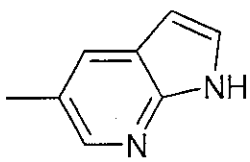
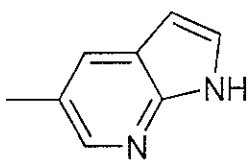
- the column "m.p. (°C)" indicates the melting points of the products in degrees Celsius (°C);
- all the compounds are in the form of the free base,
- W represents an oxygen atom;

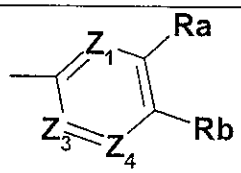
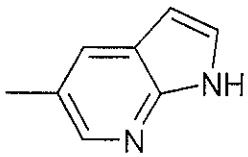
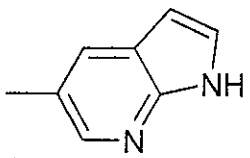
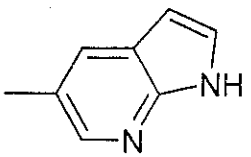
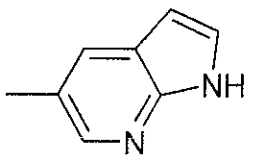
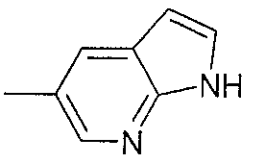
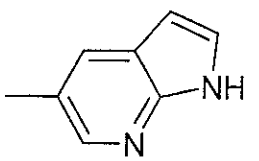
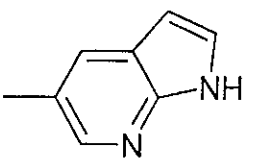
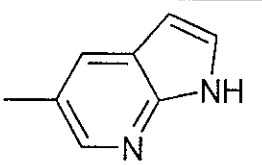
- Z_2 represents a carbon atom bonded to the nitrogen atom of the amide of formula (I);
- n is equal to 1.

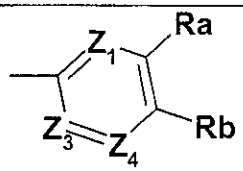
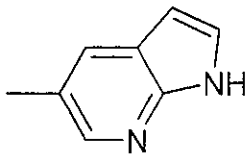
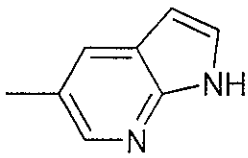
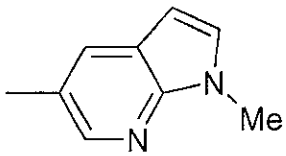
Table 2



(I)

N°	X1, X2, X3, X4	Y		m.p. (°C)
28	CH, C-F, CH, CH	Pyrid-4-yl		176 - 177
29	CH, C-F, CH, CH	Pyrid-3-yl		214 - 215
30	CH, C-CF_3, CH, N	Thiazol-2-yl		274 - 275
31	CH, CH, C-$Si(Me)_3$, CH	Thiazol-2-yl		269 - 270
32	CH, C-CF_3, CH, CH	Thiazol-2-yl		218 - 219

N°	X1, X2, X3, X4	Y		m.p. (°C)
33	CH, CH, C-CF_3, CH	Thiazol-2-yl		165 - 166
34	CH, C-$Si(Me)_3$, CH, CH	Thiazol-2-yl		213 - 214
35	CH, CH, C-F, CH	Thiazol-2-yl		255 - 256
36	CH, C-CF_3, CH, CH	Pyrid-4-yl		216 - 217
37	CH, CH, C-CF_3, CH	Pyrid-4-yl		311 - 313
38	CH, CH, C-$Si(Me)_3$, CH	Pyrid-4-yl		235 - 236
39	CH, C-$Si(Me)_3$, CH, CH	Pyrid-4-yl		279 - 281
40	CH, CH, C-F, CH	Pyrid-4-yl		284 - 286

N°	X1, X2, X3, X4	Y		m.p. (°C)
41	CH, C-CF_3, CH, N	Pyrid-4-yl		296 - 298
46	CH, C-F, CH, CH	Pyrid-4-yl		259 - 260
47	CH, C-CF_3, CH, CH	Pyrid-4-yl		213 - 214

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 (0.25×10^6 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 100 nM. They are therefore effective antagonists of receptors of TRPV1 type. Table 3 gives an example of the percentage of inhibition obtained with the compounds of the invention.

Table 3

Compound No.	% inhibition in DRG patch
2	82% (1 nM)

8	67.5% (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 4 gives an example of a percentage of inhibition obtained with the compounds of the invention.

Table 4

Compound No.	Dose	n	% inhibition of the capsaicin-induced

			nociceptive responses
2	10 mg/kg	10	61% (± 6%)

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.

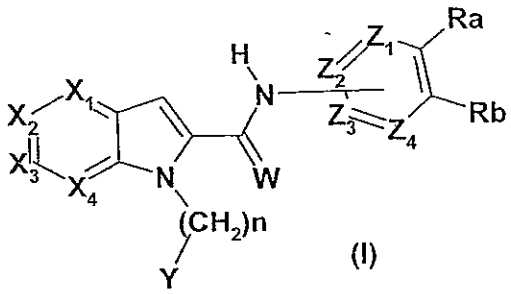
The compounds of the invention may also be used for the preparation of medicaments, especially for the preparation of a medicament for preventing or treating pathologies in which receptors of TRPV1 type are involved, as mentioned previously.

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:

either X_1, X_2, X_3 and X_4 represent, independently of each other, a group C-R_1; or, among X_1, X_2, X_3 and X_4, one from among X_3 and X_4 represents a nitrogen atom, and the others represent, independently of each other, a group C-R_1;

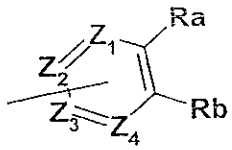
R_1 is chosen from a hydrogen atom, a halogen atom and a group C_1-C_6-fluoroalkyl or -Si(C_1-C_6-alkyl)$_3$;

n is equal to 1;

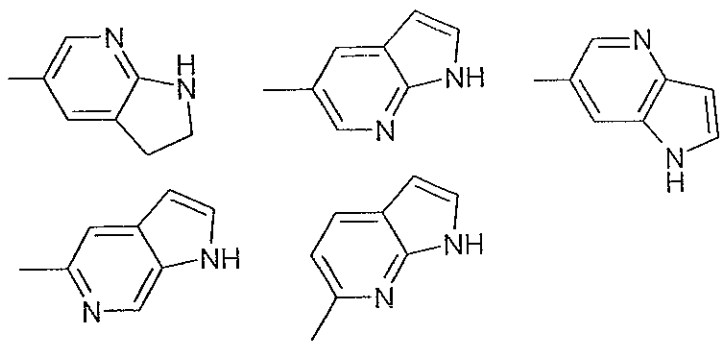
Y represents a phenyl, optionally substituted with one or more groups chosen from a halogen atom, a group C_1-C_6-alkyl or C_1-C_6-fluoroalkyl; or alternatively Y represents a pyridyl or a thiazolyl;

W represents an oxygen atom;

the group



is chosen from the groups



one from among Z_1, Z_2, Z_3 and Z_4 corresponding to a nitrogen atom and possibly being in oxidized form;

these groups being optionally substituted with R_2 and R_3,

R_2 represents a hydrogen atom;

R_3 represents, when it is borne by a carbon atom, a hydrogen atom or an oxo group;

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

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
among X_1, X_2, X_3 and X_4, one from among X_3 and X_4 represents a nitrogen atom, and the others 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.

4. Compound of formula (I) chosen from:
N-(1-acetyl-2,3-dihydro-1*H*-pyrrolo[2,3-*b*]pyrid-5-yl)-5-fluoro-1-(3-fluorobenzyl)-1*H*-indole-2-carboxamide;
N-(1*H*-pyrrolo[2,3-*b*]pyrid-5-yl)-5-fluoro-1-(3-fluorobenzyl)-1*H*-indole-2-carboxamide;
N-(2,3-dihydro-1*H*-pyrrolo[2,3-*b*]pyrid-5-yl)-5-fluoro-1-(3-fluorobenzyl)-1*H*-indole-2-carboxamide;
N-(1*H*-pyrrolo[3,2-*b*]pyrid-6-yl)-5-fluoro-1-(3-fluorobenzyl)-1*H*-indole-2-carboxamide;
N-(1*H*-Pyrrolo[2,3-*b*]pyrid-5-yl)-6-fluoro-1-[(3-methylphenyl)methyl]-1*H*-indole-2-carboxamide;
N-(1*H*-Pyrrolo[2,3-*b*]pyrid-5-yl)-6-trimethylsilyl-1-[[(3-trifluoromethyl)phenyl]methyl]-1*H*-indole-2-carboxamide;
N-(1*H*-Pyrrolo[2,3-*b*]pyrid-5-yl)-5-trimethylsilyl-1-[[(3-trifluoromethyl)phenyl]methyl]-1*H*-indole-2-carboxamide;
N-(1*H*-Pyrrolo[2,3-*c*]pyrid-5-yl)-5-fluoro-1-[(3-fluorophenyl]methyl]-1*H*-indole-2-carboxamide;
N-(1*H*-Pyrrolo[2,3-*b*]pyrid-5-yl)-5-trifluoromethyl-1-[(3-fluorophenyl)methyl]-1*H*-pyrrolo[2,3-b]pyridine-2-carboxamide;
N-(7-Oxy-1*H*-pyrrolo[2,3-*b*]pyrid-5-yl)-5-fluoro-1-[(3-fluorophenyl)methyl]-1*H*-indole-2-carboxamide;
N-(1-Methyl-1*H*-pyrrolo[2,3-*b*]pyrid-5-yl)-5-trifluoromethyl-1-[(3-fluorophenyl)methyl]-1*H*-indole-2-carboxamide;
N-(1-Methyl-1*H*-pyrrolo[2,3-*b*]pyrid-5-yl)-5-fluoro-1-[(3-fluorophenyl)methyl]-1*H*-indole-2-carboxamide;
N-(1-Methyl-1*H*-pyrrolo[2,3-*b*]pyrid-5-yl)-5-trifluoromethyl-1-[(3-fluorophenyl)methyl]-1*H*-pyrrolo[2,3-b]pyridine-2-carboxamide;
N-(1-Methyl-2,3-dihydro-1*H*-pyrrolo[2,3-*b*]pyrid-5-yl)-5-fluoro-1-[(3-fluorophenyl)methyl]-1*H*-indole-2-carboxamide;

N-(1-Methyl-1*H*-pyrrolo[2,3-*b*]pyrid-5-yl)-1-[[(3-trifluoromethyl)phenyl]methyl]-1*H*-indole-2-carboxamide;

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

N-(1-Methyl-1*H*-pyrrolo[2,3-*b*]pyrid-5-yl)-5-fluoro-1-[[(3-trifluoromethyl)phenyl]-methyl]-1*H*-indole-2-carboxamide;

N-(1-Methyl-1*H*-pyrrolo[2,3-*b*]pyrid-5-yl)-5-fluoro-1-[(3-methylphenyl)methyl]-1*H*-indole-2-carboxamide;

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

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

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

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

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

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

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

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

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

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

N-(1-Methyl-1*H*-pyrrolo[2,3-*b*]pyrid-5-yl)-5-fluoro-1-[(pyrid-3-yl)methyl)]-1*H*-indole-2-carboxamide;

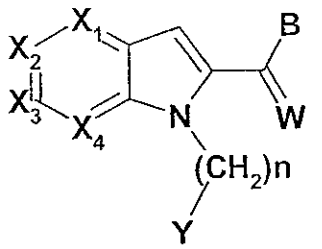
N-(1*H*-Pyrrolo[2,3-*b*]pyrid-5-yl)-5-trifluoromethyl-1-[(thiazol-2-yl)methyl]-1*H*-pyrrolo[2,3-b]pyridine-2-carboxamide;

N-(1*H*-Pyrrolo[2,3-*b*]pyrid-5-yl)-6-trimethylsilyl-1-[(thiazol-2-yl)methyl]-1*H*-indole-2-carboxamide;

N-(1*H*-Pyrrolo[2,3-*b*]pyrid-5-yl)-5-trifluoromethyl-1-[(thiazol-2-yl)methyl]-1*H*-indole-2-

carboxamide;
N-(1*H*-Pyrrolo[2,3-*b*]pyrid-5-yl)-6-trifluoromethyl-1-[(thiazol-2-yl)methyl]-1*H*-indole-2-carboxamide;
N-(1*H*-Pyrrolo[2,3-*b*]pyrid-5-yl)-5-trimethylsilyl-1-[(thiazol-2-yl)methyl]-1*H*-indole-2-carboxamide;
N-(1*H*-Pyrrolo[2,3-*b*]pyrid-5-yl)-6-fluoro-1-[(thiazol-2-yl)methyl]-1*H*-indole-2-carboxamide;
N-(1*H*-Pyrrolo[2,3-*b*]pyrid-5-yl)-5-trifluoromethyl-1-[(pyrid-4-yl)methyl)]-1*H*-indole-2-carboxamide;
N-(1*H*-Pyrrolo[2,3-*b*]pyrid-5-yl)-6-trifluoromethyl-1-[(pyrid-4-yl)methyl)]-1*H*-indole-2-carboxamide;
N-(1*H*-Pyrrolo[2,3-*b*]pyrid-5-yl)-6-trimethylsilyl-1-[(pyrid-4-yl)methyl)]-1*H*-indole-2-carboxamide;
N-(1*H*-Pyrrolo[2,3-*b*]pyrid-5-yl)-5-trimethylsilyl-1-[(pyrid-4-yl)methyl)]-1*H*-indole-2-carboxamide;
N-(1*H*-Pyrrolo[2,3-*b*]pyrid-5-yl)-6-fluoro-1-[(pyrid-4-yl)methyl)]-1*H*-indole-2-carboxamide;
N-(1*H*-Pyrrolo[2,3-*b*]pyrid-5-yl)-5-trifluoromethyl-1-[(pyrid-4-yl)methyl)]-1*H*- pyrrolo[2,3-b]pyridine -2-carboxamide;
N-(2-Oxo-2,3-dihydro-1*H*-pyrrolo[2,3-*b*]pyrid-5-yl)-5-fluoro-1-[(3-fluorophenyl)methyl]-1H-indole-2-carboxamide;
N-(1*H*-Pyrrolo[2,3-*b*]pyrid-5-yl)-5-trifluoromethyl-1-[(3-fluorophenyl)methyl]-1*H*-indole-2-carboxamide;
N-(1-Methyl-1*H*-pyrrolo[2,3-*b*]pyrid-5-yl)-1-[(3-fluorophenyl)methyl]-1*H*-pyrrolo[2,3-c]pyridine-2-carboxamide;
N-(1*H*-pyrrolo[2,3-*b*]pyrid-5-yl)-1-[(3-fluorophenyl)methyl]-1*H*-pyrrolo[2,3-c]pyridine-2-carboxamide;
N-(1*H*-Pyrrolo[2,3-*b*]pyrid-5-yl)-5-fluoro-1-[(pyrid-4-yl)methyl)]-1*H*-indole-2-carboxamide;
N-(1-Methyl-1*H*-Pyrrolo[2,3-*b*]pyrid-5-yl)-5-trifluoromethyl-1-[(pyrid-4-yl)methyl)]-1*H*-indole-2-carboxamide.

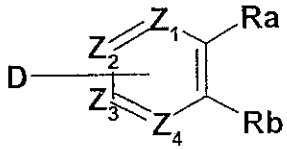
5. Process for preparing a compound of formula (I) according to any one of Claims 1 to 4 , characterized in that a compound of general formula (II)



(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),

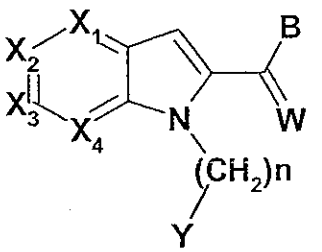


(III)

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 and D represents an amino group, by transformation of the compound of formula (III) into an amide and then by reacting the amide obtained with the compound of formula (II) in the presence of an organometallic reagent;
- 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.

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

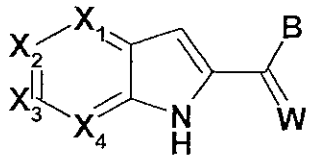


(II)

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,

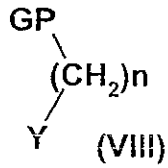
characterized in that a compound of general formula (VI)



(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)

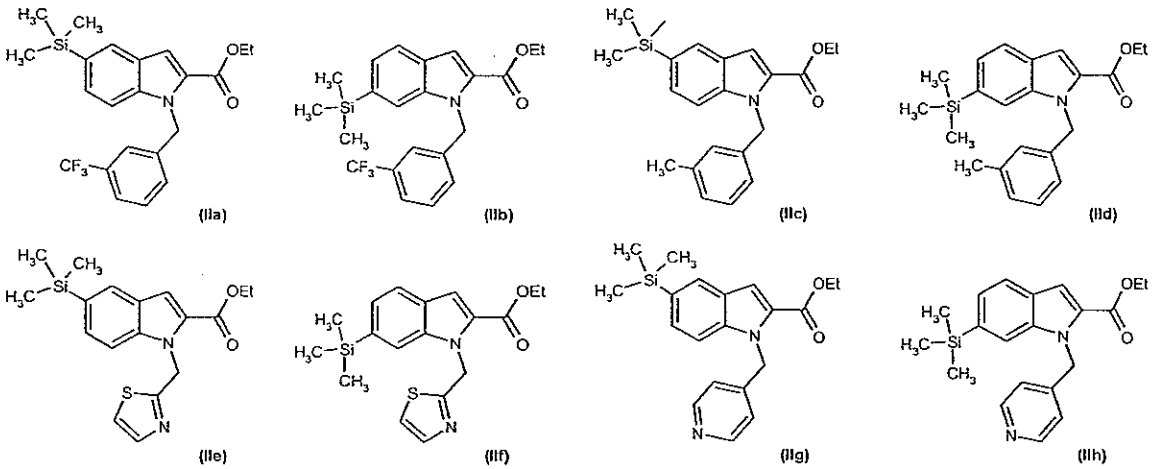


(VIII)

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.

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



8. Medicament, characterized in that it comprises a compound of formula (I) according

to any one of Claims 1 to 4 , 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).

9. Pharmaceutical composition, characterized in that it comprises a compound of formula (I) according to any one of Claims 1 to 4 , or a pharmaceutically acceptable salt, a hydrate or a solvate of this compound, and also at least one pharmaceutically acceptable excipient.

10. Use of a compound of formula (I) according to any one of Claims 1 to 4 , for the preparation of a medicament for preventing or treating pathologies in which receptors of TRPV1 type are involved.

11. Use of a compound of formula (I) according to any one of Claims 1 to 4 , 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.